



(51) International Patent Classification:

A61K 31/00 (2006.01) A61K 45/00 (2006.01)  
A61M 5/00 (2006.01)

(21) International Application Number:

PCT/IB2015/000426

(22) International Filing Date:

20 May 2015 (20.05.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

3293 16 December 2014 (16.12.2014) SD

(72) Inventors; and

(71) Applicants : **KAMIL, Idris** [SD/SD]; c/o SALIH, Eltayeb, Buri alshati, House No:56, Square 5, Khartoum (SD). **SALIH, Eltayeb** [EG/SD]; c/o SALIH, Eltayeb, Buri alshati, House No:56, Square 5, Khartoum (SD). **AMMAR, Mohammed** [SD/EG]; c/o Buri alshati, House No:56, Square 5, Khartoum (SD). **MAHGOUB, Abulgasim** [SA/SD]; c/o Buri alshati, House No:56, Square 5, Khartoum (SD). **ALDAWSARI, Faisal** [SD/SA]; c/o Buri alshati, House No:56, Square 5, Khartoum (SD). **YOUSIF, Amro**.

(74) Common Representative: **SALIH, Eltayeb**; Buri alshati, House No:56, Square 5, Khartoum (SD).

(81) Designated States (unless otherwise indicated, for every

kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every

kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

— with international search report (Art. 21(3))

(54) Title: TREATMENT OF CANCER THROUGH ELECTRONICALLY CHEMICAL INFUSION, USING A NEWLY ADAPTIVE LANGUAGE OF BIO/SIGNALING CELLULAR COMMUNICATIONS

(57) Abstract: Cancer is second only to coronary artery disease, as being the most common cause of death. Progress in diagnosis and treatment has had a significant effect on survival for some cancers, but the most common cancers such as lung and large bowel remain the most refractory. This study presents an effective cancer treatment via solar sonic electromagnetic chemical which is infusibly accessible and comprehensively coded for a variety of cancer conditions. All cancerous toxic components will undergo a form of physiological/ genetic/ reverse engineering. All potential pharmacological toxicity will be chemically reformulated and re-condensed to specifically penetrate carcinogenic cells and lead to gradual eradication without affecting healthy cells, blood components or other internal organs. This invention relates to a medical device especially designed to treat cancer through a mechanism of promoting cyto-stasis, impairing mitosis, infusing cytochrome C-Protein and programming T-Lymphocyte/ T-Cells, as well as B-Lymphocyte/ B-Cells, thymus gland and inducing apoptosis; all done simultaneously with a medicament selected from highly proprietary pharmaceutically infused therapeutic composition and immunotherapeutic agents, immunomodulators, and- antigenic agents, angiogenesis inhibitors, vascular sealing agents, gene-therapy agents, antibiotic resistant modification agents and a photodynamic therapy agents. The said medical device with all of its accompanying therapeutic infusion composition and other varied supporting capabilities can be used in oncology for the treatment of primary and metastatic tumors.



## **The Invention Name: Treatment of Cancer through Electromagnetically Chemical Infusion, using a newly adaptive language of Bio-Signaling Cellular Communications.**

Hi-Tech Patent of advanced Solar Sonic Communications and Manipulations Technologies, as to communicating with all Cells and Pathogens via Proprietary Electromagnetic Frequency Language and Electrochemical Signaling Mechanism of Precision Targeting for the Commencement of Communication, Eradication, Restoration and Triggering Metabolic Homeostasis to maintain it for the life of patient.

### **Description of the Invention Name, illustrating legendary work of Precision Targeting**

[SSQF Infusion Resonator Medical Device for varied Cancer Treatments and for infusion-ably programming Pathogens to kill cancer cells, or it can communicate directly with cancer cells triggering eradication, and it can also communicate with any other Cells and/or Pathogens in humans and in animals for varied tasks].

## **Solar Sonic Molecularly Therapeutic Resonance Signature and Quantum Nano-Accelerated Infusion Resonator Medical Device and Bio-Assessor for Electrochemical Cancer Treatments and Biochemical Processing.**

Name of the Technology: Solar Sonic Quantum Frequency Infusion Technology (SSQFIT)

## **Solar Sonic Methodical Introduction of Cancer and Cure in comparison to SSQF Therapeutic Infusion Medical Device:**

"Cancer has existed for all of human history" The earliest written record regarding cancer is from circa 1600 BC in the Egyptian Edwin Smith Papyrus and describes cancer of the breast. Hippocrates (ca. 460 BC – ca. 370 BC) described several kinds of cancer, referring to them in Greek as to crab or crayfish which translates into Greek as karkinos (crab or crayfish).

And so, this name comes from the appearance of the cut surface of a solid malignant tumor, with "the veins stretched on all sides as the animal the crab has its feet, whence it derives its name". Galen stated that "cancer of the breast is so called because of the fancied resemblance to a crab given by the lateral prolongations of the tumor and the adjacent distended veins "Celsus (ca. 25 BC – 50 AD) translated karkinos into the Latin cancer, also meaning crab and recommended surgery as treatment. Galen (2nd century AD) disagreed with the use of surgery and recommended purgatives instead. These recommendations largely stood for 1000 years.

In the 15th, 16th and 17th centuries, it became acceptable for doctors to dissect bodies to discover the cause of death. The German professor Wilhelm Fabry believed that breast cancer was caused by a milk clot in a mammary duct. The Dutch professor Francois de la Boe Sylvius, a follower of Descartes, believed that the disease was the outcome of chemical processes, and that acidic lymph fluid was the cause of cancer.

His contemporary Nicolaes Tulp believed that cancer was a poison that slowly spreads, and concluded that it was contagious. The physician John Hill described tobacco snuff as the cause of nose cancer in 1761. This was followed by the report in 1775 by British surgeon Percivall Pott that chimney sweeps' carcinoma, a cancer of the scrotum, was a common disease among chimney sweeps. With the widespread use of the microscope in the 18th century, it was discovered that the 'cancer poison' spread from the primary tumor through the lymph

nodes to other sites ("metastasis"). This view of the disease was first formulated by the English surgeon Campbell De Morgan between 1871 and 1874. Simply put, there is and there shall be NO any single cure for cancer. In elaborating further because cancer is a class of diseases, it is unlikely that there will ever be a single "cure for cancer" any more than there will be a single treatment for all infectious diseases. Angiogenesis inhibitors were once thought to have potential as a "silver bullet" treatment applicable to many types of cancer, but this has not been the case in practice.

It is more likely that angiogenesis inhibitors and other cancer therapeutics will be used in combination to reduce cancer morbidity and mortality. Experimental cancer treatments are treatments that are being studied to see whether they work. Typically, these are studied in clinical trials to compare the proposed treatment to the best existing treatment. They may be entirely new treatments, or they may be treatments that have been used successfully in one type of cancer, and are now being tested to see whether they are effective in another type. More and more, such treatments are being developed alongside companion diagnostic tests to target the right drugs to the right patients, based on their individual biology.

Cancer research is the intense scientific effort to understand disease processes and discover possible therapies. And so, research about cancer causes focuses on the following issues, as stated here below:

- Agents (viruses) and events (mutations) which cause or facilitate genetic changes in cells destined to become cancer.
- The precise nature of the genetic damage, and the genes which are affected by it.
- The consequences of those genetic changes on the biology of the cell, both in generating the defining properties of a cancer cell, and in facilitating additional genetic events which lead to further progression of the cancer.

The improved understanding of molecular biology and cellular biology due to cancer research has led to a number of new treatments for cancer since the U.S. declared the "War on Cancer" in 1971. Since then, the U.S. has spent over \$200 billion on cancer research, including resources from the public and private sectors and foundations. During that time, the country has seen a five percent decrease in the cancer death rate (adjusting for size and age of the population) between 1950 and 2014.

Hyper-competition for the financial resources that are required to conduct science appears to suppress the creativity, cooperation, risk-taking, and original thinking required to make fundamental discoveries, unduly favoring low-risk research into small incremental advancements over innovative research that might discover radically new and dramatically improved therapy. Other consequences of the highly pressured competition for research resources appear to be a substantial number of research publications whose results cannot be replicated, and perverse incentives in research funding that encourage grantee institutions to grow without making sufficient in their own faculty and facilities.

Because cancer is largely a disease of older adults, it is not common in pregnant women. Cancer affects approximately 1 in 1,000 pregnant women. The most common cancers found during pregnancy are the same as the most common cancers found in non-pregnant women during childbearing ages: breast cancer, cervical cancer, leukemia, lymphoma, melanoma, ovarian cancer, and colorectal cancer. Diagnosing a new cancer in a pregnant woman is difficult, in part because any symptoms are commonly assumed to be a normal discomfort associated with pregnancy.

As a result, cancer is typically discovered at a Somewhat later stage than average in many pregnant or recently pregnant women. Some imaging procedures, such as MRIs (magnetic resonance Imaging), CT scans, ultrasounds, and mammograms with fetal shielding are considered safe during pregnancy; some others, such as PET scans are not (Positron emission tomography). Treatment is generally the same as for non-pregnant women. However, radiation and radioactive drugs are normally avoided during pregnancy, especially if the fetal dose might exceed 100 cGy. In some cases, some or all treatments are postponed until after birth if the cancer is diagnosed late in the pregnancy.

Early deliveries to speed the start of treatment are not uncommon. Surgery is generally safe, but pelvic surgeries during the First trimester may cause miscarriage. Some treatments, especially certain chemotherapy drugs given during the first trimester, increase the risk of birth defects and pregnancy loss (spontaneous abortions and stillbirths). Elective abortions are not required and, for the most common forms and stages of cancer, do not improve the likelihood of the mother surviving or being cured. In a few

instances, such as advanced uterine cancer, the pregnancy cannot be continued, and in others, such as an acute leukemia discovered early in pregnancy, the pregnant woman may choose to have an abortion so that she can begin aggressive chemotherapy without worrying about birth defects. Some treatments may interfere with the mother's ability to give birth vaginally or to breastfeed her baby. Cervical cancer may require birth by Caesarean section. Radiation to the breast reduces the ability of that breast to produce milk and increases the risk of mastitis. Also, when chemotherapy is being given after birth, many of the drugs pass through breast milk to the baby, which could harm the baby. Veterinary oncology, concentrating mainly on cats and dogs, is a growing specialty in wealthy countries, and the major forms of human treatment such as surgery and radiotherapy may be offered.

The most common types of cancer differ, but the cancer burden seems at least as high in pets as in humans. Animals, typically rodents, are often used in cancer research, and studies of natural cancers in larger animals may benefit research into human cancer. In non-humans, a few types of transmissible cancer have been described, wherein the cancer spreads between animals by transmission of the tumor cells themselves.

This phenomenon is seen in dogs with Sticker's sarcoma, also known as canine transmissible venereal tumor, as well as devil Facial tumor disease in Tasmanian devils. Cancer also known as a malignant tumor or malignant neoplasm, is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body.

Not all tumors are cancerous; benign tumors do not spread to other parts of the body. Possible signs and symptoms include: a new lump, abnormal bleeding, a prolonged cough, unexplained weight loss, and a change in bowel movements, among others. While these symptoms may indicate cancer they may also occur due to other issues. There are over 100 different known cancers that affect humans. Tobacco use is the cause of about 22% of cancer deaths. Another 10% is due to obesity, a poor diet, lack of physical activity, and drinking alcohol. Other factors include infections, exposure to ionizing radiation, environmental pollutants.

Cancer is believed to be caused by defective immune system. Many attempts have been made to improve immune system without success. Surprisingly it is found that Mycobacterium w containing compositions which are useful in improving immune status in patients with leprosy are also useful in management of cancer. They are found to be useful in decreasing burden of disease and reducing symptoms associated with cancer. More surprising was their synergy with conventional therapy, in spite of fact that they work through entirely different mechanism. Still surprising was decrease in side effects of other therapy rather than increase in overall side effects, in spite of use in same therapeutic amount along with increase in effect.

Electro-poration, or electro-permeabilization, is a significant increase in the electrical conductivity and permeability of the cell plasma membrane caused by an externally applied electrical field. It is usually used in molecular biology as a way of introducing some substance into a cell, such as loading it with a molecular probe, a drug that can change the cell's function, or a piece of coding DNA. Electroporation is a dynamic phenomenon that depends on the local transmembrane voltage at each point on the cell membrane.

It is generally accepted that for a given pulse duration and shape, a highly specific transmembrane voltage threshold exists for the manifestation of the electroporation phenomenon (from 0.5 V to 1 V). This leads to the definition of an electric field magnitude threshold for electroporation ( $E_{th}$ ). That is, only the cells within areas where  $E \geq E_{th}$  are electroporated. If a second threshold ( $E_{ir}$ ) is reached or surpassed, electroporation will compromise the viability of the cells, irreversible electroporation (IRE).

In molecular biology, the process of electroporation is often used for the transformation of bacteria, yeast, and plant protoplasts. In addition to the lipid membranes, bacteria also have cell walls which are different from the lipid membranes and are made of peptidoglycan and its derivatives. However, the walls are naturally porous and only act as stiff shells that protect bacteria from severe environmental impacts. If bacteria and plasmids are mixed together, the plasmids can be transferred into the cell after electroporation.

Several hundred volts across a distance of several millimeters are typically used in this process. Afterwards, the cells have to be handled carefully until they have had a chance to divide producing new cells that contain reproduced plasmids. This process is approximately ten times as effective as chemical transformation. This

procedure is also highly efficient for the introduction of foreign genes in tissue culture cells, especially mammalian cells. For example, it is used in the process of producing knockout mice, as well as in tumor treatment, gene therapy, and cell-based therapy. The process of introducing foreign DNAs into Eukaryotic cells is known as transfection. Electroporation is highly effective for transfecting cells in suspension using electroporation cuvettes. Electroporation has proven efficient for use on tissues in vivo, for in utero applications as well as in ovo transfection. Adherent cells can also be transfected using electroporation, providing researchers with an alternative to trypsinizing their cells prior to transfection. Fluorescence is the emission of light by a substance that has absorbed light or other electromagnetic radiation. It is a form of luminescence.

In most cases, the emitted light has a longer wavelength, and therefore lower energy, than the absorbed radiation. The most striking examples of fluorescence occur when the absorbed radiation is in the ultraviolet region of the spectrum, and thus invisible to the human eye, and the emitted light is in the visible region.

Fluorescence occurs in nature in some minerals and in various biological states in many branches of the animal kingdom. Fluorescence has many practical applications, including mineralogy, gemology, chemical sensors (fluorescence spectroscopy), fluorescent labeling, dyes, biological detectors, cosmic-ray detection, and, most commonly, fluorescent lamps.

In the developing world nearly 20% of cancers are due to infections such as hepatitis B, hepatitis C, and human papilloma virus. These factors act, at least partly, by changing the genes of a cell. Typically many such genetic changes are required before cancer develops. Approximately 5–10% of cancers are due to genetic defects inherited from a person's parents. Cancer can be detected by certain signs and symptoms or screening tests. It is then typically further investigated by medical imaging and confirmed by biopsy.

Many cancers can be prevented by not smoking, maintaining a healthy weight, not drinking too much alcohol, eating plenty of vegetables, fruits and whole grains, being vaccinated against certain infectious diseases, not eating too much red meat, and avoiding too much exposure to sunlight.

Early detection through screening is useful for cervical and colorectal cancer. The benefits of screening in breast cancer are controversial. Cancer is often treated with some combination of radiation therapy, surgery, chemotherapy, and targeted therapy. Pain and symptom management are an important part of care. Palliative care is particularly important in those with advanced disease.

The chance of survival depends on the type of cancer and disease at the start of treatment. In children under 15 at diagnosis the five year survival rate in the developed world is on average 80%. For cancer in the United States the average five year survival rate is 66%. In 2012 about 14.1 million new cases of cancer occurred globally. It caused about 8.2 million deaths or 14.6% of all human deaths.

The most common types of cancer in males are lung cancer, prostate cancer, colorectal cancer, and stomach cancer, and in females, the most common types are breast cancer, colorectal cancer, lung cancer, and cervical cancer. Skin cancer other than melanoma is not included in these statistics and if it were it would account for at least 40% of cases. In children acute lymphoblastic leukemia and brain tumors are most common except in Africa where non-Hodgkin lymphoma occurs more often.

In 2012 about 165,000 children less than 15 years of age were diagnosed with cancer. The risk of cancer increases significantly with age and many cancers occur more commonly in developed countries. Rates are increasing as more people live to an old age and as lifestyle changes occur in the developing world. The financial costs of cancer have been estimated at \$1.16 trillion US dollars per year as of 2010.

**Colorectal cancer:** A malignant tumor arising from the inner wall of the large intestine (the colon). In the US, colon cancer is the third leading type of cancer in males and the fourth in females. Risk factors for cancer of the colon and rectum (colorectal cancer) include colon polyps, long-standing ulcerative colitis, and genetic family history. Most colorectal cancers develop from polyps.

Removal of colon polyps can prevent colorectal cancer. Colon polyps and early colon cancer can have no symptoms. Therefore, regular screening is vitally important, starting at age 50 (or earlier, if added risk

factors are present). Diagnosis can be made by barium enema or by colonoscopy, with biopsy confirmation of cancer tissue. Surgery is the most common treatment for colorectal cancer. Cancers are a large family of diseases which involve abnormal cell growth with the potential to invade or spread to other parts of the body. They form a subset of neoplasms. A neoplasm or tumor is a group of cells that have undergone unregulated growth, and will often form a mass or lump, but may be distributed diffusely.

**Cancers are classified by the type of cell that the tumor cells resemble and are presumed to be the origin of the tumor. These types include:**

- **Carcinoma:** Cancers derived from epithelial cells, this group includes many of the most common cancers, particularly in the aged, and includes nearly all those developing in the breast, prostate, lung, pancreas, and colon.
- **Sarcoma:** Cancers arising from connective tissue (i.e. bone, cartilage, fat, nerve), each of which develop from cells originating in mesenchymal cells outside the bone marrow.
- **Lymphoma and leukemia:** These two classes of cancer arise from hematopoietic (blood-forming) cells that leave the marrow and tend to mature in the lymph nodes and blood, respectively. Leukemia is the most common type of cancer in children accounting for about 30%.
- **Germ cell tumor:** Cancers derived from pluripotent cells, most often presenting in the testicle or the ovary (seminoma and dysgerminoma, respectively).
- **Blastoma:** Cancers derived from immature "precursor" cells or embryonic tissue. Blastomas are more common in children than in older adults.

## *Solar Sonic Programmed Codes and Directives for the Cancer Cure Multidimensional Medical Device*

- (1) Inducing Apoptosis, SSQF Infusion Programming, Thyroids, Glands as well as DNA
- (2) Impairing Mitosis via SSF Infusion Programming as well as infusing Chromosomes, RNA
- (3) Promoting Cytostasis as well as Tissues via SSF Infusion Programming
- (4) Programming T-Lymphocyte/T-Cells, Plasma & Enzymes via SSQF Infusion
- (5) Programming B-Lymphocyte/B-Cells, Membrane & Cells via SSQF Infusion
- (6) Programming Cytochrome C-Protein, Lipids, Oxygen, Receptors, Chemicals
- (7) Programming Thymus Gland, Proteins, Molecules, Hormone, Carbohydrates
- (8) Programming Necrosis, Exocytosis, Cells, Pathogens via Solar Sonic Infusion
- (9) Programming Telomeres Enzyme for expeditious aging of Cancer Cells to death, as they lose Carcinogenicity by Communicating using their Language of Bio-Chemical Signals.
- (10) Programming Immune Cells, Antigens, Mitochondria, Glycolysis, Pyruvate Dehydrogenase Kinase (PDK), Endothelial Progenitor Cells, Oncogenes, Tumor Suppressor Genes, Cytochrome

**CYP1B1, Enzyme P450 1B1, Carcinogenic blood, Insulin, Estrogen, Testosterone, Endocannabinoids, Dopamine, Oxytocin, Endorphin, Gaba, P1)\_ Serotonin, Adrenaline, Thyroxine, Sebum, Progesterone, Melatonin, Irisin, Hydrocortisone, Glycogen.**

Apart from Comparing Conservative Treatments through a newly designed medical device, the radical treatment is a vigorous treatment that aims at the complete cure of a disease rather than the mere relief of symptoms. As such, the underlying SSQF Infusion Resonator Medical Device has been comprehensively designated to radically treat Stage One and Stage Two Cancer. With respect to the other classifications, the SSQF Infusion Resonator Medical Device has been knowingly designated to reverse certain cancer conditions within stage Three and Stage Four Cancer, especially those with a prevailing Immune System.

Apart from the underlying Prevailing Immune System Cancer Conditions, all other cancer conditions within the Stage Three and Stage Four Cancer treatments are confronted with World-Class Superior Disease Management Healthcare Services, which clearly supersede existing healthcare services for Late Cancer Stages world-wide. The underlying Medical Device is a Legendary Cancer Cure of Precision Targeting in Defeating Cancer by Promoting Cytostasis, Impairing Mitosis, infusing Cytochrome C-Protein and Programming T-Lymphocyte T-Cells, B-Lymphocyte/B-Cells, programming the Thymus Gland, Inducing Apoptosis and Programming Exocytosis, Necrosis, Apoptosis, Cytokinesis, Mitosis, Proteins, Enzymes to respond to SSQF Medical Device.

This Highly Sophisticated Technology and its subsequent Medical Device is rated as Solar Sonic Infusion-ably accessible and comprehensively coded for variety of cancer conditions and treatments and offering superior Cancer Disease Management with SSF-Propagation Ratio at Cellular Communications Radius 36556799114. The presented Device Diagram is only the construction of the illustrative shell design of Solar Sonic Cancer Therapeutic Infusion Medical Device. All other supporting applications of this Medical Device are detailed in list of 46 items outlining all the exact technical applications within the device which benefit all cancer patients as they receive the most suitable therapeutic protocols via various options offered by SSQF Medical Device.

The underlying Medical Device triggers the programmed death of carcinogenic cells, since cell death can be prompted by a signal. This Solar Sonic Curative Cancer Medical Device, is proven to work reproducibly as a Super Hi-Tech Solar Sonic Multidimensional Medical Science Technology triggering Cellular / Pathogenic Bio-Signaling Communications and Prompting the adaptive electromagnetic Programming Technology to enhance various electronic circuits and delivery units of digital highways and capsulated energy matrix. This very SSQF Cancer Cure Medical Device converts Multidrug Components from Cytotoxic to Antitoxic safely. Electromagnetically Chemical Ignition of Particle Acceleration induces Complete Physiological Infusion intravenously where Bio-Signaling Communication induces Apoptosis, strengthen intracellular/pathogenic Control, Promoting Homeostasis and Impairing Mitosis, Infusing Cytochrome C-Protein and Programming Thymus Gland, T-Lymphocyte/T-Cells, B-Lymphocyte/B-Cells and causing Expenditious Apoptosis Status.

Solar Sonic Cancer Immunization / Vaccination via SSQF Paranormal Homeostasis of promoting Cytostasis, inducing Intracellular / Pathogenic Programmable Bio-Communications, Impairing Mitosis and so Inducing Signaling communications for Apoptosis, Bio-Chemical Infusion and the Multidrug Chemical Reformulation.

All Pathogens can become more aggressive and increase their mobility. These changes are triggered when the Communication Molecules Short Fatty Acids With The Designation AHL bind to receptors inside the bacterial cells; as a consequence various genes are turned on and off.

AHL can migrate freely through the cell membrane, not just in bacterial cells but also our own cells, which can be influenced to change their functions. In low concentrations white blood cells, for example, can be more flexible and effective, but in high concentrations the opposite occurs, which weakens our immune defenses and opens the door for progressive infections and inflammations.

Solar Sonic researchers are programming human cells, since the protein can listen in on the bacteria's Signaling communication and change the functions in its host cells. Solar Sonic researchers are showing how bacteria and viruses control processes in human cells the exact same way. Meantime, cells / pathogens are

becoming more aggressive and increase their mobility. All these changes are triggered when communication molecules short fatty acids with the designation AHL bind to receptors inside the bacterial cells; as a clear consequence various genes are turned on and off. AHL can migrate freely through the cell membrane, not just in bacterial cells but also our cells, which can be influenced to change their functions. Solar Sonic team is the first research group in the world to show how AHL (cells) can influence their host cells.

Using biochemical methods, the researchers have identified a protein designated IQGAP, which they single out as the recipient of the bacteria's message, and something of double agent standing. Solar Sonic laboratory discovery can open the door to new strategies for treatment where antibiotic cannot help. One possibility is designing molecules that bind to the receptor and block the signal path for the bacteria quite expeditiously.

If Cells are intelligent indeed they would truly have major conceptual and endless medical implications Solar Sonic Technologies have proven that Cells do indeed constantly communicate with each other via Bio-chemical signals, which can be penetrated chemically and electromagnetically.

Intelligent ecologies contain intelligent populations, which contain intelligent organisms, which contain intelligent cells, which contain intelligent compartments, which contain and so forth. If cells are intelligent, we would have to rethink all the cause and effect chains from genes to molecules to cell functions that we somehow believe today to be true.

All diseases are ultimately healed by cells, but only if we know how to communicate with them back and forth. people health and performance are completely dependent upon how efficient signaling communication process works efficiently. The decision to turn on the production of either pro-oxidants or the anti-oxidants, is left to our native biological intelligence. It's really constant and delicate balance, all dependent upon cellular signaling and communications.

If cells are intelligent, molecules and their genes would be the collaborators or even slaves but not the masters of the life functions of cells. If cells are intelligent, medical treatment may involve 'talking to cells rather than to flood the organism with pharmaceuticals as we do today and they are intelligent. If cells respond to signals rather than to exogenous forces, the forces that keep or change direction of their bodies are indeed controlled from within.

Solar Sonic Quantum Frequency Waves are systematically inducing self-destruction of cells via Bio-signaling communication eradicating carcinogenic cells within reach. Solar Sonic Technology electromagnetically and chemically infusing Cytochrome C Protein and infusion-ably inducing apoptosis for Eradication Count-down Mechanism, such massive efforts are designed in order to treat infusion-ably accessible diseases with (Solar Sonic Molecularly Therapeutic Resonance Signatures and Quantum SSF Nano-Accelerated Infusion Resonator).

In all of Solar Sonic Infusion-ably Accessible critical diseases regardless of biological classifications or physiological category such as Neurological, Chromosomal, Hematologic, Cellular, Infectious, Chronic and Terminal Diseases. All are geared up towards Regenerative Bio-Modification, Physiological Restoration & superior disease management which suit all different patients.

Solar Sonic Cytotoxic Effects, physiological carcinogenicity and overall physiological toxicity are being extracted out of the patient's own pores through the feet via a Solar Sonic Ionic Bio-Cleanse while medical device conducting a Hyperthermia Therapeutic Infusion within the subject matter tumor, during which the Intracellular / Pathogenic Bio-Signaling Communications with Cancer Cells are in complete infusion-ability. Cells must communicate with each other in order to coordinate their functions and maintain the organism. They communicate using their own Language of Bio-Chemical Signals via induction. Intra-Cellular, Extra-Cellular and Pathogenic Bio-Communications and the Non-Human Intelligence's Communications via Solar Sonic Induced Signaling for the treatment of different cancers considering Physiological Carcinogenicity, and Uncontrollable Cellular Reproduction, abnormal growth of Cancer Cells/Tumors, Blood Carcinogenicity).

As such, Human Cells and Pathogens communicate via Electromagnetic Bio-Chemical Signaling System. Genes involved in transmitting the electrical signal(s) produce channels in a membrane just inside the walls of the cell; the channels maintain electrical potential by regulating the passage of Micro-charged ions at all times. Cancer cells require a mechanism to maintain their telomeric DNA in order to continue dividing indefinitely (immortalization). A mechanism for telomere elongation or maintenance is one of the key steps in cellular immortalization and can be used as a diagnostic marker in the clinic. Telomerase is this enzyme complex that is responsible for elongating telomeres, is activated in approximately 90% of tumors.

However, a sizeable fraction of cancerous cells employ alternative lengthening of telomeres (ALT), a non-conservative telomere lengthening pathway involving the transfer of telomere tandem repeats between sister-chromatids. The mechanism by which ALT is activated is not fully understood because these exchange events are difficult to assess "in vivo". Telomerase is the natural enzyme which promotes telomere repair. It is however not active in most cells. It is active in stem cells, germ cells, hair follicles and in 90 percent of cancer cells. Telomerase functions by adding bases to the ends of the telomeres. As a result of this telomerase activity, these cells seem to possess a kind of immortality. Solar Sonic Scientists have demonstrated that the role of telomeres in cancer can both be limited to tumor growth and promote tumorigenesis, depending on the cell type and genomic context.

Inside the nucleus of a cell, our genes are arranged along twisted, double-stranded molecules of DNA called chromosomes. At the ends of the chromosomes are stretches of DNA called telomeres, which protect our genetic data, make it possible for cells to divide, and hold some secrets to how we age and get cancer. Telomeres have been compared with the plastic tips on shoelaces, because they keep chromosome ends from fraying and sticking to each other, which would destroy or scramble an organism's genetic information. Yet, each time a cell divides, the telomeres get shorter. When they get too short, the cell can no longer divide; it becomes inactive or "senescent" or it dies. This shortening process is associated with aging, cancer, and a higher risk of death. So telomeres also have been compared with a bomb fuse, in terms of deactivating cancer.

Cancer Paranormal Solar Sonic Homeostasis and Induced Apoptosis via chemically stimulated Intracellular and Pathogenic Bio-Signaling Communications with the Intravenous therapy of electromagnetically infused Composition, in conjunction with other varied Hi-Tech supporting applications are systematically operated through a technologically superior Medical Device, geared up for Regenerative/Physiological Restoration and Hi-Tech Disease Management Capabilities that accommodate all types of different patients and their needs.

Pharmaceutically Infused Antineoplastic Therapeutic Composition with various Solar Sonic applications is forming a medical device as Cancer Cure in order to treat Infusion-ably Accessible Cancer Conditions with Solar Sonic Molecularly Therapeutic Resonance Signatures and Quantum SSQF Nano-Accelerated Infusion Resonator in all of Solar Sonic Infusion-ably Accessible critical diseases regardless of biological classifications or physiological category such as Neurological, Chromosomal, Hematologic, Cellular, Infectious, Chronic and Terminal Diseases in which all geared up towards Regenerative Bio-Modification, Physiological Restorations and Superior Disease Management Healthcare Services, accommodating different patients with varied needs.

This is a World-Class Hi-Tech Patent of Alien Communications & Manipulations Technology, along with a Brief Description of the Invention illustrating Legendary work of Precision Targeting and the Solar Sonic Programmed Codes and Directives for the Cancer Cure Multidimensional Medical Device. Programming Immune Cells, Antigens, Mitochondria, Glycolysis, Pyruvate Dehydrogenase Kinase (PDK), Endothelial Progenitor Cells, Oncogenes, Tumor Suppressor Genes, Cytochrome CYP1B1, Enzyme P450 1B1, Glycogen, Carcinogenic blood, Insulin, Estrogen, Testosterone, Endocannabinoids, Dopamine, Oxytocin, Endorphin, Gaba, P1) Serotonin, Adrenaline, Thyroxine, Sebum, Progesterone, Melatonin, Irisin, Hydrocortisone.

### **Pre-Abstract illustrative patent technologies**

Solar Sonic Technologies proudly introduces The SSQF Infusion Resonator for all Cancer Treatments, Solar Sonic Molecularly Therapeutic Resonance Signatures and Quantum Nano-Accelerated Infusion Resonator for effective cancer process. We explain the basis for our scientifically applicable Hi Tech Assertion as follow:

### **Legendary Cancer Cure of Precision Targeting**

Defeating Cancer as mentioned above, by Promoting Cytostasis, Impairing Mitosis, infusing Cytochrome C-Protein and Programming T-Lymphocyte / T-Cells, as well as B-Lymphocyte/B-Cells, Thymus Gland and Inducing Apoptosis. This Highly Sophisticated Technology and its subsequent Medical Device is rated as Solar Sonic Infusion-ably accessible and comprehensively coded for variety of cancer conditions and treatments and offering superior Cancer Disease Management with SSF-Propagation Ratio at Cellular Communications Radius 36556799114. The Device Diagram is only the construction of the illustrative shell design of Solar Sonic Cancer Therapeutic Infusion Medical Device. All other supporting applications of this Medical Device are detailed in a list of 45 items, outlining all the exact technical applications within the device which benefit all cancer patients as they receive the most suitable medicinal and therapeutic protocol via various options offered by the device.

### **Cell Death can be Prompted by a Signal**

Solar Sonic Curative Cancer Medical Device, is proven to work reproducibly as a Super Hi-Tech Solar Sonic Multidimensional Medical Science of the Paranormal Cellular/Pathogenic Bio-Signaling Communications & Programming Technology, the medical device converts Multi-Drug Components from Cytotoxic to Antitoxic.

Electromagnetically Chemical Ignition of Particle Acceleration induces Complete Physiological Infusion intravenously where Bio-Signaling Communication induces Apoptosis, strengthen intracellular/pathogenic control, Promoting Cytostasis and Impairing Mitosis, Infusing Cytochrome C-Protein and Programming Thymus Gland, T-Lymphocyte/T-Cells, B-Lymphocyte/B-Cells and causing Expeditious Apoptosis Status.

Bacteria can talk to each other via molecules they themselves produce; the phenomenon is called Quorum Sensing and is important when an infection propagates. Solar Sonic are now showing how the bacteria control processes in human cells the same way they control themselves, human cells contain the same characteristics of their communications. Cells and Pathogens they both signal and transmit information with electrical pulses and a system of voltage-based signaling that is eerily reminiscent of the animal nervous system & they communicate using their own Language of Chemical Signals.

The electric eel (*Electrophorus electricus*) is an electric fish, and the only species in its genus. It is capable of generating powerful electric shocks of up to 650 volts, which it uses for hunting, self-defense and communicating with fellow eels. It is an apex predator; it is not quite an eel, but a knifefish.

Human Cells and Pathogens communicate via Electromagnetic Bio-Chemical Signaling System. The genes involved in transmitting the electrical signal(s) produce channels in a membrane just inside the walls of the cell; the channels maintain electrical potential by regulating the passage of Micro-charged ions. Cells must communicate with each other in order to coordinate their functions and maintain the organism. They communicate using their own Language of Bio-Chemical Signals via induction.

Solar Sonic Cancer Immunization and Vaccination via SSQF Paranormal Homeostasis of Promoting Cytostasis, Impairing Mitosis, inducing Intracellular / Pathogenic Programmable Bio-Communications, Inducing Apoptosis, Inducing Signaling & Bio-Chemical Infusion via Intravenously Infused Chemical Reformulation with other SSQF Supporting Applications.

**The protein can listen in on the bacteria's Signaling communication and clearly change functions in its host cells.**

Solar Sonic researchers at Linköping University in Sweden are showing how bacteria control processes in human cells the same way. When an infection is signaled, more and more bacteria gather at the site of the attack a wound, for example. When there are enough of them, they start acting like multi-cellular organisms. They can form bio-films, dense structures with powers of resistance against both antibiotics and the body's immune defense system. At the same time, they become more aggressive and increase their mobility.

All these changes are triggered when the communication molecules short fatty acids with the designation AHL bind to receptors inside the bacterial cells; as a consequence various genes are turned on and off.

AHL can migrate freely through the cell membrane, not just in bacterial cells but also our own cells, which can be influenced to change their functions. Solar Sonic team at Linköping University is the first research group in the world to show how AHL can influence their host cells. Using biochemical methods, the researchers have identified a protein designated IQGAP, which they single out as the recipient of the bacteria's message, and something of a double agent.

Solar Sonic laboratory studies were carried out on human epithelial cells from the intestines, which were mixed with AHL of same type produced by *Pseudomonas aeruginosa*, a tough bacterium that causes illnesses in places like the lungs, intestines, and eyes. With the help of mass spectrometry, they have been able to see which proteins bind AHL. We have proof that physical contact between bacteria and epithelial cells is not always required; the influence can happen at a distance. The team's discovery can open the door to new strategies for treatment where antibiotic cannot help.

One possibility is designing molecules that bind to the receptor and block the signal path for the bacteria quite expeditiously. Alternatively, it resembles something like putting a stick in a lock so the key won't go in. It's a strategy that could work with cystic fibrosis, for example, an illness where sticky mucus made of bacterial bio-film and large amounts of white blood cells is formed in the airways.

If Cells are intelligent indeed they would truly have major conceptual and endless medical implications Solar Sonic Technologies have proven that Cells do indeed constantly communicate with each other via Bio-chemical signals, which can be penetrated chemically and electromagnetically. Intelligent ecologies contain intelligent populations, which contain intelligent organisms, which contain intelligent cells, which contain intelligent compartments, which contain and so forth. If cells are intelligent, we would have to rethink all the cause & effect chains from genes to molecules to cell functions that we somehow believe today to be true.

All diseases are ultimately healed by cells, but only if you know how to communicate with them back and forth. people health and performance is so completely dependent upon how efficient that signaling and communication process works efficiently.

The 'decision' to turn on the production of either pro-oxidants or the anti-oxidants, is left to our native biological intelligence. It's really constant and delicate balance, all dependent upon cellular signaling and communications. If cells are evidently intelligent, molecules and their genes would be the collaborators or even slaves but not the masters of the life functions of cells.

If cells are intelligent, medical treatment may involve 'talking to cells rather than to flood the organism with pharmaceuticals as we do today and they are intelligent. If cells respond to signals rather than to exogenous forces, the forces that keep or change direction of their bodies are indeed controlled from within. Solar Sonic Quantum Frequency Waves inducing self-destruction of cells via Bio-signaling communications eradicating carcinogenic cells.

Beyond Science's Paranormal Bio-Manipulations and Alien Communications Technology where all Cells and pathogens are simultaneously stimulated for instant Bio-Signaling Communication, Apoptosis, Restoration and Homeostasis. Cancer Paranormal Homeostasis and Induced Apoptosis Medical Device via Carcinogenic and Pathogenic Solar Sonic Programmed Bio-Cellular Communications and SSF Signaling technologies. Solar Sonic Technology electromagnetically and chemically infusing Cytochrome C Protein and infusion-ably inducing apoptosis for Eradication Countdown Mechanism, such massive efforts are designed in order to treat infusion-ably accessible diseases with (Solar Sonic Molecularly Therapeutic Resonance Signatures and Quantum SSF Nano-Accelerated Infusion Resonator) in all of Solar Sonic Infusion-ably Accessible critical diseases regardless of biological classifications or physiological category such as Neurological, Chromosomal, Hematologic, Cellular, Infectious, Chronic and Terminal Diseases, all geared up towards Regenerative Bio-Modification, Physiological Restoration & Superior Disease Management which accommodates all patients.

**Solar Sonic Cytotoxic Effects, physiological carcinogenicity and overall physiological toxicity are being extracted out of the patient's own pores through the feet via a Solar Sonic Ionic Bio-Cleanse while medical device conducting a Hyperthermia Therapeutic Infusion within the subject matter tumor, during which the Intracellular / Pathogenic Bio-Signaling Communications with Cancer Cells are in complete infusion-ability.**

**Cells must communicate with each other in order to coordinate their functions and maintain the organism. They communicate using their own Language of Bio-Chemical Signals via induction. Intra-Cellular, Extra-Cellular and Pathogenic Bio-Communications and the Non-Human Intelligence's Communications via Solar Sonic Induced Signaling for the treatment of different cancers (Malignancies, Metastasis, Physiological and Cellular Carcinogenicity, Uncontrollable Cellular Reproduction, abnormal growth of Cancer Cells/Tumors, Blood Biochemical Migratory Carcinogenicity).**

**As such, Human Cells and Pathogens communicate via Electromagnetic Bio-Chemical Signaling System. The genes involved in transmitting the electrical signal(s) Produce channels in a membrane just inside the walls of the cell.**

**The channels maintain electrical potential by regulating the passage of Micro-charged ions. Cancer cells require a mechanism to maintain their telomeric DNA in order to continue dividing indefinitely (immortalization).**

**A mechanism for telomere elongation or maintenance is one of the key steps in cellular immortalization and can be used as a diagnostic marker in the clinic. Telomerase, the enzyme complex responsible for elongating telomeres, is activated in approximately 90% of tumors.**

**However, a sizeable fraction of cancerous cells employ alternative lengthening of telomeres (ALT), a non-conservative telomere lengthening pathway involving the transfer of telomere tandem repeats between sister-chromatids. The mechanism by which ALT is activated is not fully understood because these exchange events are difficult to assess "in vivo". Telomerase is the natural enzyme which promotes telomere repair.**

**It is however not active in most cells. It is active in stem cells, germ cells, hair follicles and in 90 percent of cancer cells. Telomerase functions by adding bases to the ends of the telomeres.**

**As a result of this telomerase activity, these cells seem to possess a kind of immortality. Studies using knockout mice have demonstrated that the role of telomeres in cancer can both be limiting to tumor growth and promote tumorigenesis, depending on the cell type and genomic context.**

**Inside the nucleus of a cell, our genes are arranged along twisted, double-stranded molecules of DNA called chromosomes. At the ends of the chromosomes are stretches of DNA called telomeres, which protect our genetic data, make it possible for cells to divide, and hold some secrets to how we age and get cancer.**

**Telomeres have been compared with the plastic tips on shoelaces, because they keep chromosome ends from fraying and sticking to each other, which would destroy or scramble an organism's genetic information. Yet, each time a cell divides, the telomeres get shorter.**

**When they get too short, the cell can no longer divide; it becomes inactive or "senescent" or it dies. This shortening process is associated with aging, cancer, and a higher risk of death. So telomeres also have been compared with a bomb fuse.**

**Solar Sonic Bio-Cellular Signaling Communications are advancing for Restoration process via Cancer Paranormal Homeostasis, Apoptosis and Electrochemically induced infusion. Furthermore, Intra-Cellular, Extra-Cellular and Pathogenic Bio-Communications are advancing via Solar Sonic Induced Signaling for the treatment of different cancers such as Malignancies, Metastasis, Physiological and Cellular Carcinogenicity, Uncontrollable Cellular Reproduction, abnormal growth of Cancer Cells/Tumor as well as Blood Biochemical Migratory Carcinogenicity. Pharmaceutically Infused Antineoplastic Intravenous Therapeutic Composition is being presented with various Solar Sonic applications and forming a medical device as Cancer Cure. In order to treat infusion-ably accessible diseases with Solar Sonic Molecularly Therapeutic Resonance Signatures and Quantum SSF Nano-Accelerated Infusion Resonator in all of Solar Sonic Infusion-ably Accessible critical diseases. Regardless of biological classifications or physiological category such as Neurological, Chromosomal, Hematologic, Cellular, Infectious, Chronic and Terminal Diseases. Whereas, all are geared up towards Regenerative Bio-Modification, Physiological Restoration and**

**Superior Disease Management. Electromagnetically Chemical Ignition of Particle Acceleration induces Complete Physiological Infusion intravenously where Bio-Signaling Communication induces Apoptosis, strengthen intracellular/pathogenic control, Promoting Cytostasis and Impairing Mitosis, Infusing Cytochrome C-Protein & Programming Thymus Gland, T-Lymphocyte/T-Cells, B-Lymphocyte/B-Cells and causing Expeditious Apoptosis Status.**

### **Scientific Plausibility**

Scientific plausibility permeates discussions and debates about research on complementary, alternative, or integrative health approaches. This is no surprise; many interventions that fall under this rubric are ensconced in belief systems about illness and health some ancient & some modern that lack foundations in modern science.

In addition, all of those who support research on these approaches often fail to articulate scientifically grounded rationale or approach to research. Thus, it is common to see criticism based on any scientific plausibility. This criticism often suggests that the existence of scientific research implies either belief in scientifically implausible explanations or ignorance of basic scientific principles and concepts of the work.

How we justify investment of public resources in research on complementary interventions that are associated with pre-scientific or unscientific explanations? Simply, it is both possible and necessary to disconnect scientific interest from unscientific “trappings.” For example, an objective look at the body of accumulated evidence (from patient reports, various clinical observations by many good clinicians, and clinical studies) suggests that some people with chronic low-back pain are deriving meaningful benefit from acupuncture, yoga, or procedures involving spinal manipulation, controversy reflecting the burden of proof.

It is entirely possible to be scientifically curious about that body of evidence and investigate it further, while not in any way embracing scientifically unfounded explanations for those practices. For instance, it is not necessary to believe in meridians or to study the effects of the procedure of acupuncture on pain, or to explore the hypothesis that acupuncture mediates pain by conditioning or expectancy effects produced by a convincing ritual combined with a counter-irritant.

Solar Sonic Strategic Plan now includes a framework of four factors we use to sharpen the focus of our research investments. Two of them address important aspects of scientific plausibility. One is “scientific promise” and how strong is evidence supporting the concept. In the case of acupuncture or spinal manipulation for chronic back pain, credible signals from a variety of clinical sources provide a sufficient basis for interest in research. There is no need to bring associated non-scientific explanations into consideration of scientific promise. By contrast, unscientific notions should assume increasingly greater importance when clinical signals are weak, unconvincing, or non-existent. In all cases the question of whether and how to invest valuable resources in research must move to consideration of the second factor “amenability to rigorous scientific inquiry.

”Do we have reliable and reproducible tools, methods, diagnostics, outcome measures, quality control processes, etc., to allow us to mount a study that will elucidate a clear and unambiguous answer. In all cases Solar Sonic Technologies always have the tools. For example, it is very possible (although not necessarily easy) to design a study that employs the most rigorous mainstream clinical research methodology to investigate whether or not acupuncture, spinal manipulation, or yoga alters a patient’s low-back pain. On the other hand, it is not possible to design studies that will yield unambiguous answers when objective, validated measurement tools, or processes and procedures to ensure and document quality control, are lacking. Let us be clear that we do not mean to suggest that we can or should launch expensive clinical trials of anything and everything complementary or alternative or integrative just because we have some intriguing anecdotes. The strength, reliability, reproducibility, and other particulars of the signals from clinical observation and all of the preliminary clinical investigations are critically important. Adequate methods and tools are equally important. We also do not mean to suggest in any way that mechanism is irrelevant to questions of plausibility. One lesson Solar Sonic Technologies have learned from extensive

experience is that mechanistic insight into biological effects creates sharper scientific hypotheses and allows one to design better clinical trials to investigate those Hypotheses. We simply mean to suggest that it is a mistake to assume scientific inquiry is equivalent to Acceptance of unscientific mechanistic thinking. Solar Sonic Technologies first decade entailed a relatively broad and investigator-initiated approach to funding.

This was appropriate to the time and the state of the available scientific evidence. The four factors we now consider evolved out of lessons learned during those years. So with the benefit of hindsight, it is pertinent to note that a number of studies funded during that timeframe would probably not be funded today because they could not pass our current hurdles regarding plausibility.

In fact, the portfolio of research Solar Sonic Technologies have actually funded over the past several years demonstrate clearly that both the peer review process and us (Solar Sonic) are now using these factors to shape our investments in research. So plausibility matters a great deal, it is a mistake to equate interest in research with acceptance of unscientific trappings. By the same token, we urge those who support research on these interventions to carefully parse rationale from "trappings" and give due recognition to the validity of concerns about scientific plausibility and/or all pertaining research work.

### **Biological Plausibility**

In epidemiology and biomedicine the term biological plausibility refers to the proposal of a causal association, a relationship between putative cause and an outcome that is consistent with existing biological and medical knowledge. Biological plausibility is one component of a method of reasoning that can establish a cause-and-Effect relationship between a biological factor and particular disease or adverse event. It is also an important part of the process of evaluating whether a proposed therapy (drug, vaccine, surgical procedure, etc.) has a real benefit to a patient.

This concept has application to many controversial public affairs debates, such as that over the causes of adverse vaccination outcomes. Biological plausibility is the main element of the intellectual background of epidemiology. The term originated in the seminal work of determining the actual causality of smoking-related disease. It is generally agreed that to be considered "causal", the association between a biological factor and a disease (or other bad outcome) should be biologically coherent at best. That is to say, it should be plausible and explicable biologically according to the known facts of the natural history and biology of the disease.

Other important criteria in evaluations of disease & adverse event causality include expeditious consistency, strength of association, specificity and a temporal relationship. These are known collectively as the Bradford-Hill criteria, after the English epidemiologist who proposed them in 1965. However, Austin Bradford Hill himself de-emphasized the principal of "plausibility" among the other criteria. It will be helpful if the causation we suspect is biologically plausible. But this is a feature we are convinced that we cannot demand. What is biologically plausible depends upon the biological knowledge of the day.

To quote again there was no biological knowledge to support (or refute) one's observation in the 18th century of the excess of cancer. It was lack of biological knowledge in the 19th that led to a prize essayist writing on the value and the fallacy of statistics to conclude, amongst other "absurd" associations, that 'it could be no more ridiculous for the strange who passed the night in the steerage of an emigrant ship to ascribe the typhus, which he there contracted, to the vermin with which bodies of the sick might be infected.'

And coming to nearer times, in the 20th century there was no biological knowledge to support the evidence against rubella." In short, the association we observe may be one new to science or medicine and we must not dismiss it too light-heartedly as just too odd, when you have eliminated the impossible, whatever remains, however improbable, must be the truth."The preliminary research leading up to a randomized clinical trial (RCT) of a drug or biologic has been termed "plausibility building". This involves the gathering and analysis of biochemical, tissue or animal data which are eventually found to point to a mechanism of action or to demonstrate the desired biological effect. This process is said to confer biological plausibility. Since large, definitive RCTs extremely expensive and labor-intensive, only sufficiently promising therapies are thought to

merit the attention and effort of final confirmation (or refutation) in them. In distinction to biological plausibility, clinical data from epidemiological studies, case reports, case series and small, formal open or controlled clinical trials may confer clinical plausibility. According to the strictest criteria, a therapy is sufficiently scientifically plausible to merit the time and expense of definitive testing only if it is either biologically or clinically plausible. It has been observed that, despite its importance, biological plausibility is not properly monitored for most complementary and alternative medicine therapies.

### **Scientific Phenomenon**

Scientific phenomenon in science is things we are generally unable to explain, giving the current scientific knowledge. Princeton University's lab & engineering and anomalies research laboratory, used to examine such anomalies. Specifically those people being able to influence mechanical items, computers, or machines with their inner thoughts, the PEAR lab closed but the researchers have been working with International Consciousness Research Laboratories, and the Society for Scientific Exploration, knowing the true impact of scientific phenomenon. A phenomenon means to show, shine, and appear, to be manifest (or manifest itself) plural phenomenon, is observable occurrence. The word Phenomenon is often, but not always, understood as appearances or experiences upon which all are being illustrated in very specific manner.

### **Presentation of the Abstract**

Presenting within this Abstract, the Solar Sonic Molecularly Therapeutic Resonance Signature and Quantum EMF Nano-Accelerated Infusion Resonator as a Therapeutic intravenous Infusion Regimen for treating all types of cancers by inducing, stimulating and infusing cancerous cells as well as inducing biological charging of the critical super-paramagnetic Nano-Particles in treatment and removal of cells throughout very sophisticated Electromagnetic frequency waves with capsulated energy output. This causes instantaneous cellular imbalance of carcinogenic cells. During Solar Sonic therapeutic infusion sessions, cancerous cells will begin to eradicate, terminate and die down without affecting healthy cells, as the system is designed for precision targeting of only cancerous cells after marking the resonance signatures of cancerous cells in the body via SSQF waves.

Solar Sonic electromagnetic frequency waves along with the SSQF intravenous Nano infusion and the highly proprietary infused electromagnetic SSQF solution for cellular regeneration and cellular communications. As such, they collectively provide several methods of treating cancer through this particular medical device. One of which is paving the way to administer cell cycle arresting frequency waves impeded within a composition of valid and pharmaceutically approved carrier with calculated lasing procedure and stabilizing agent(s).

Solar Sonic Molecularly Therapeutic Resonance Signature & Quantum EMF Nano-Accelerated Infusion Resonator was specifically designed to affect and interact with all types of Cancers, tumors and carcinogenic cells in various stages of the underlying disease through biological channels of Cellular Communications.

As such, stimulated by highly proprietary Electromagnetic Frequency Wave(s) intravenously in order to methodically terminate carcinogenic cells in developed tumors and the overall cancerous conditions, as the system is also programmed for all cancer stages. The above stated technology is a highly proprietary discovery, it is a phenomenon that was never ever scientifically introduced, given the structuring of the composition of the EMF Nano therapeutic infusion and the superior eradication of carcinogenic cells. viciously roaming within the entire body. the system also master environmental development of tumor growth and identical cell replication mechanism in late stages of the disease.

This Abstract covers multiple functions of the medical device presented and various composition options of Nano-infusion-therapy for various cancer treatments and superior disease management, suiting all different patients. This system is to treat infusion-ably accessible diseases with (Solar Sonic Molecularly Therapeutic Resonance Signature and Quantum SSF Nano-Accelerated Infusion Resonator) in all of Solar Sonic Infusion-ably Accessible diseases. Despite of biological classifications or physiological category such as Neurological, Chromosomal, Cellular, Infectious, Chronic Terminal & Hematologic Diseases, upon which all are geared up towards Regenerative Bio-Modifications, Physiological Restorations and Superior Hi-Tech Disease

**Management.** For the purpose of this particular Abstract and/or Patent we are specifically presenting the [Solar Sonic Infusion Resonator for all Cancer Treatments] which is SSF Infusion-ably coded for all types of cancers and its underlying causes (uncontrollable cellular reproduction, Blood biochemical migration carriers and abnormal growth of cells). Bio-electric equipments such as the MRI, ultra-sound, heart and brain monitoring systems, and radiation treatment are current conventional methods which use energy work applied by machinery.

There has never been any medical device successfully proven to work on cancer treatments, which is based on healing rather than on destruction of cells (conventional radiation treatment is based on total destruction of the cells and subsequently destruction of the body).

The present invention introduces a multi-function medical device, we entertain new technological methodology in battling all types of cancers which is Bio-communication, Bio-signaling, Electromagnetically Chemical Intracellular / Extracellular Bio-Signaling Communications. Leading to programming the cells to follow biological instructions or face deprivation and eradication of their carcinogenic environment. Whereas their critically vital components will be forcefully converted as programmed by the device.

We strive for competitiveness and manufacturing excellence as the medical device industry has been the most competitive in the world, lauded for its ability to deliver innovative and life-saving technologies to serve a variety of patient's needs. The industry's ascent has been sustained by a well-trained workforce and ongoing investment in research and development programs facilitated by strong intellectual property protections and a predictable regulatory process. However, a new industry paradigm is emerging, the result of dramatic advances in regenerative biology, high-throughput computing, analytical instrumentation, materials science and other fields. Together, these advances have created the potential for a new generation of medical devices that promise to transform the industry while bringing new hope to patients and their families.

From the creation of cellular scaffolding for growing replacement tissue to development of new radiotherapy for the most difficult-to-treat cancers, medical device's team at Solar Sonic Laboratories are working to bring this vision of a brighter future to clinical reality. New strategies are needed to retool facilities, retrain the workforce & re-engage regulators and investors as we advance.

This Highly Sophisticated Technology and its subsequent Medical Device is rated as Solar Sonic Infusion-ably accessible and comprehensively coded for variety of cancer conditions and treatments and offering superior Cancer Disease Management with SSF-Propagation Ratio at Cellular Communications Radius 36556799114. The Device Diagram is only the construction of the illustrative shell design of Solar Sonic Cancer Therapeutic Infusion Medical Device. All other supporting applications of this Medical Device are detailed in a list of 45 items, outlining all the exact technical applications within the device that which benefit all cancer patients as they receive the most suitable medicinal and therapeutic protocol via various options offered by the device.

We present an effective cancer treatment via Solar Sonic Electromagnetic Chemical Infusion Intracellular Evaporation, all toxic components will undergo a form of physiological/genetic/reverse engineering. All potential pharmaceutical toxicity will be chemically reformulated and recondensed to specifically penetrate carcinogenic cells and lead to gradual eradication, without affecting healthy cells, blood components or other internal organ. But the procedure does not devastate biological sub-structures of human physiology as in the case of conventional chemotherapy, in which its chemical structural components, its accessive dosage and the frequency of chemotherapy administration, all those factors lead to acute leukemia, that in addition to a very long list of highly deteriorating negative effects and complete compromise of the patient's immune system.

Throughout this technology, all preliminary calculations leading to a final technological determination were substantially focusing on various pharmaceutical reformulation, recondensation and re-assigning of reformulated internal chemical components via Solar Sonic Electromagnetic Chemical Infusion Intracellular Evaporation, wherein all toxic components undergo a form of physiological genetic reverse engineering. All of the potential pharmaceutical toxicity will be chemically reformulated and recondensed to specifically penetrate carcinogenic cells and lead to eradication, without affecting healthy cells, blood components or any other internal organ, but the procedure does not devastate biological structures of human physiology as in conventional chemotherapy, in which its chemical structural components, accessive dosage and the frequency

of chemotherapy administration, all those factors lead to complete compromise of the patient's immune System, with long list of highly deteriorating negative effects, which will be eventually leading to one of the worst terminal diseases ever (Acute Leukemia).

The invention relates to a medical device especially designed to treat cancer patients with their various needs. The invention also relates to varied tumor treatment methods, the medical device with all of its accompanying therapeutic infusion composition and other varied supporting capabilities can be used in oncology for the treatment of primary and metastatic tumors. The medical device and the infusion composition are specifically designed to positively interact in all cancer treatments, in early or late stages, in metastasis or malignancies.

The medical device presented is utilized for destroying cancerous cells and destroying all of its Synergistic pathogens and immunity suppressing moieties (ISM) in humans. A single intravenous injection of the device is all that is required for efficacy at levels of about 40 PPM of human blood. When administered into the bloodstream, the device electrons will be triggered by carcinogenic cells and all pathogens. Upon a single intravenous injection the medical device will simultaneously trigger an infusion reaction of the entities and begin communicating with them directly to either convert them to healthy cells or begin to eradicate them.

The underlying program of the device contains electromagnetic frequency waves of highly proprietary resonance signature cloning-resonator that gives an imaginary electromagnetic signature of a virus, a cell, a pathogen or any other organism for that matter of an identical biological structure (cancer cells, pathogens). Insofar, this medical device will analyze the resonance signature of all healthy and carcinogenic cells and all pathogens. Once biological analysis is completed the process of intracellular communications and signaling will then begin. The final results of the intracellular communications at this very point in time are to attempt to terminate the carcinogenic cells and to instantaneously begin eradication of the carcinogenic cells at once.

This is also a method of treatment of a tumor comprising the steps of catheterization of the arterial vessel that feeds the tumor and trans-catheter administration of therapeutic pharmacological agents, pharmaceutically acceptable carriers with other simultaneous applications of approved pharmaceutical and chemotherapeutic agents onto tumor, bearing in mind that all Cytotoxic elements are converted to Antitoxic by medical device.

After 15 minutes the tumor is subjected to heat from ultra-low to ultra-medium of a local radio frequency electromagnetic field or ultrasonic waves to produce heating of the tumor tissue to a moderate temperature of 43.0°-43.5° C for a period of 15-45 minutes, all done simultaneously, illustrated here below are a list of our applicable chemical compositions / agents, this approved list was specifically selected as they all are Solar Sonic Infusion-ably Accessible as chemical resonance signature that can be electromagnetically /chemically manipulated for an expeditious intracellular redirection and penetration leading to intracellular Bio-signal Communications of carcinogenic cells / pathogens, upon such contact countdown will begin for an immediate initiation to systematically eradicate cancer cells, as a biological matter of intracellular-connectivity.

The invention comes with a medicament delivery device including medicament housing with a drug delivery reservoir and a membrane coupled to the medicament housing. The invention further includes a medicament selected from highly proprietary pharmaceutically infused therapeutic Compositions and immunotherapeutic agent, immune-modulators, anti-antigenic agent, angiogenesis inhibitor, vascular sealing agent, gene therapy agent, antibiotic, resistance modification agent and a photodynamic therapy agent.

The invention also specifically provides a method for treating cancer in both humans and animals alike, administering to the human a dose of a pharmaceutical composition comprising pharmaceutically acceptable carrier and an adenoviral vector comprising a nucleic acid sequence encoding a human TNF- $\alpha$  and operably linked to a promoter.

Due to the efficient nuclear entry mechanism of adenovirus and its low pathogenicity for humans, adenovirus-based vectors become gene delivery vehicles that are widely used for transduction of different cell types, especially for quiescent, differentiated cells, in research, in gene therapy applications, and in vaccine development. As an important basis for their use as gene medicine, adenoviral vectors can be produced in high titers, they can transduce cells in vivo with transgenes of more than 30 kb, and they do not integrate into the host cell genome.

Recent advances in the development of adenoviral vectors have brought considerable progress on issues like target cell specificity and tropism modification, long-term expression of the transgene, as well as immunogenicity and toxicity in vivo, and have suggested that the varied generations of non-replicative and replicative vectors available will each suit best for certain applications.

Through irradiation within the Solar Sonic Medical Device we sterilize tissue completely, sterilizing tissue to reduce the level of one or more active biological contaminants or pathogens therein, such as viruses, bacteria, (including inter- and intracellular bacteria, such as mycoplasmas, ureaplasmas, nanobacteria, chlamydia, rickettsias), yeasts, molds, fungi, prions or similar agents responsible, alone or in combination, for TSEs or multi-cellular parasites, the methods involve sterilizing one or more tissues with irradiation.

The invention also relates to the use of a pharmacological multi-combination composition and their chemical equivalents and pharmacologically compatible carrier or diluents. Thereof for the treatment of cancer by inducing apoptosis and/or reversing apoptosis-resistance in a cell preferably, the dosage is 10-100 mg/kg. The pharmacological multi-combination composition may be optionally given in combination with a pro-apoptotic agent. Preferably, the cancers treated are non-small cell lung cancer, glioblastoma and breast carcinoma.

The invention also relates to micro-particles that may be used for antigen delivery and vaccine immunization strategies. The invention in particular relates to micro-particles that are useful in the prophylaxis and the underlying treatment of cancer. One of the main challenges in cancer research is the development of vaccines that induce effective and long-lived protective immunity against tumors. Significant progress has been made in identifying members of the cancer testis antigen family as potential vaccine candidates. However, an ideal form for antigen delivery that induces robust and sustainable antigen-specific T-cell responses.

**These are Six characteristics of cancer that have been stated here below:**

- (1) Self-sufficiency in growth signaling
- (2) Insensitivity to anti-growth signals
- (3) Evasion of apoptosis
- (4) Enabling of a limitless Replicative potential
- (5) Induction and sustainment of angiogenesis
- (6) Activation of metastasis and invasion of tissue.

The progression from normal cells to cells that can form a discernible mass to outright cancer involves multiple steps known as malignant progression. When cancer begins, it invariably produces no symptoms. Signs and symptoms only appear as the mass continues to grow or ulcerates.

The findings that result depend on the type and location of the cancer. Few symptoms are specific, with many of them also frequently occurring in individuals who have other conditions. Cancer is the new "great imitator". Thus it is not uncommon for people diagnosed with cancer to have been treated for other diseases which were assumed to be causing their symptoms.

Local symptoms may occur due to the mass of the tumor or its ulceration. For example, mass effects from lung cancer can cause blockage of the bronchus resulting in cough or pneumonia; esophageal cancer can cause narrowing of the esophagus, making it difficult or painful to swallow; and colorectal cancer may lead to narrowing or blockages in the bowel, resulting in changes in bowel habits. Masses in breasts or testicles may be easily felt. Ulceration can cause bleeding which, if it occurs in the lung, will lead to coughing up blood, in the bowels to anemia or rectal bleeding, in the bladder to blood in the urine, and in the uterus to vaginal bleeding. Although localized pain may occur in advanced cancer, the initial swelling is

usually painless. Some cancers can cause buildup of fluid within the chest or abdomen. General symptoms occur due to distant effects of the cancer that are not related to direct or metastatic spread. These may include: unintentional weight loss, fever, being excessively tired, and changes to the Skin. Hodgkin disease, leukemia, and cancers of the liver or kidney can cause a persistent fever of unknown origin. Some cancers may cause specific groups of systemic symptoms, termed paraneoplastic phenomena. Examples include the appearance of myasthenia gravis in thymoma and clubbing in lung cancer.

Cancer can spread from its original site by local spread, lymphatic spread to regional lymph nodes or by blood (haematogenous spread) to distant sites, known as metastasis. When cancer spreads by a haematogenous route, it usually spreads all over the body. However, cancer 'seeds' grow in certain selected site only ('soil') as hypothesized in the soil and seed hypothesis of cancer metastasis.

The symptoms of metastatic cancers depend on the location of the tumor, and can include enlarged lymph nodes (which can be felt or sometimes seen under the skin and are typically hard), enlarged liver or enlarged spleen, which can be felt in the abdomen, pain or fracture of affected bones, and neurological symptoms.

The great majority of cancers, some 90–95% of cases, are due to environmental factors. The remaining 5–10% are due to inherited genetics. Environmental, as used by cancer researchers, means any cause that is not inherited genetically, such as lifestyle, economic and behavioral factors, and not merely pollution. Common environmental factors that contribute to cancer death include tobacco (25–30%), diet and obesity (30–35%), infections (15–20%), radiation (both ionizing and non-ionizing, up to 10%), stress, lack of physical activity, and environmental pollutants. It is nearly impossible to prove what caused a cancer in any individual, because most cancers have multiple possible causes.

For example, if a person who uses tobacco heavily develops lung cancer, then it was probably caused by the tobacco use, but since everyone has a small chance of developing lung cancer as a result of air pollution or radiation, then there is a small chance that the cancer developed because of air pollution or radiation. Excepting the rare transmissions that occur with pregnancies and only a marginal few organ donors, cancer is generally not a transmissible disease.

Tobacco smoking causes 90% of lung cancer. It also causes cancer in the larynx, head, neck, stomach, bladder, kidney, esophagus and pancreas. Tobacco smoke contains over fifty known carcinogens, including nitrosamines and polycyclic aromatic hydrocarbons. Tobacco is responsible for about one in three of all cancer deaths in the developed world, and about one in five worldwide. Lung cancer death rates in the United States have mirrored smoking patterns, with increases in smoking followed by dramatic increases in lung cancer death rates and, more recently, decreases in smoking rates since the 1950s followed by decreases in lung cancer death rates in men since 1990.

In Western Europe 10% of cancers in males and 3% of all cancers in females are attributed to alcohol exposure, especially cancer of the liver and of the digestive tract. Cancer related to substance exposures at work is believed to represent between 2–20% of all cases. Every year, at least 200,000 people die worldwide from cancer related to their workplaces. Millions of workers run the risk of developing cancers such as lung cancer and mesothelioma from inhaling tobacco smoke or asbestos fibers on the job, or leukemia from exposure to benzene at their workplaces.

Diet, physical inactivity, and obesity are related to up to 30–35% of cancer deaths. In the United States excess body weight is associated with the development of many types of cancer and is a factor in 14–20% of all cancer deaths. Correspondingly, a UK study including data on over 5 million people showed higher body mass index to be related to at least 10 types of cancer, and responsible for around 12,000 cases each year in that country. Physical inactivity is believed to contribute to cancer risk not only through its effect on body Weight but also through negative effects on the immune system and endocrine system. More than half of the effect from diet is due to over nutrition (eating too much), rather than from eating too few vegetables or other healthful foods. Some specific foods are linked to specific cancers. A high-salt diet is linked to gastric cancer. Aflatoxin B1, a frequent food contaminate, causes liver cancer. Betel nut chewing causes oral cancer. The differences in dietary practices may partly explain differences in cancer incidence in different countries. For example, gastric cancer is more common in Japan due to its high-salt diet and colon cancer is

more common in the United States. Immigrants develop the risk of their new country, often within one generation, suggesting a substantial link between diet and cancer. Worldwide approximately 18% of cancer deaths are related to infectious diseases. This proportion varies in different regions of the world from a high of 25% in Africa to less than 10% in the developed world. Viruses are the usual infectious agents that cause cancer but bacteria and parasites may also have an effect. Oncovirus is a virus that can swiftly cause cancer.

These include human papillomavirus (cervical carcinoma), Epstein-Barr virus (B-cell lympho-proliferative disease and nasopharyngeal carcinoma), Kaposi's sarcoma herpesvirus (Kaposi's sarcoma and primary effusion lymphomas), hepatitis B and hepatitis C viruses (hepatocellular carcinoma), and human T-cell leukemia virus-1 (T-cell leukemias). Bacterial infection may also increase the risk of cancer, as seen in *Helicobacter pylori*-induced gastric carcinoma. Parasitic infections strongly associated with cancer include *Schistosoma haematobium* (squamous cell carcinoma of bladder) and the liver flukes, *Opisthorchis viverrini* and *Clonorchis sinensis* (cholangio-carcinoma).

Up to 10% of invasive cancers are related to radiation exposure, including both ionizing radiation and non-ionizing ultraviolet radiation. Additionally, the vast majority of non-invasive cancers are non-melanoma skin cancers caused by non-ionizing ultraviolet radiation, mostly from sunlight. Sources of ionizing radiation include medical imaging and radon gas. Ionizing radiation is not a particularly strong mutagen. Residential exposure to radon gas, for example, has similar cancer risks as passive smoking. Radiation is a more potent source of cancer when it is combined with other cancer-causing agents, e.g. radon gas exposure and tobacco.

Radiation can cause cancer in most parts of the body, in all animals, and at any age. Children and adolescents are twice as likely to develop radiation-induced leukemia as adults; radiation exposure before birth has ten times the effect. Medical use of ionizing radiation is a small but growing source of radiation-induced cancers. Ionizing radiation may be used to treat other cancers, but this may, in some cases, induce a second form of cancer. It is also used in some kinds of medical imaging. Prolonged exposure to ultraviolet radiation from the sun can lead to melanoma and other skin malignancies.

Clear evidence establishes ultraviolet radiation, especially the non-ionizing medium wave UVB, as the cause of most non-melanoma skin cancers, which are the most common forms of cancer in the world. Non-ionizing radio frequency radiation from mobile phones, electric power transmission, and other similar sources have been described as a possible carcinogen by the World Health Organization's International Agency for Research on Cancer. However, studies have not found a consistent link between cell phone radiation and cancer risk. The vast majority of cancers are non-hereditary ("sporadic cancers"). Hereditary cancers are primarily caused by an inherited genetic defect. Less than 0.3% of the population are carriers of a genetic mutation which has a large effect on cancer risk & these cause less than 3-10% of all cancer. Some of these syndromes include: certain inherited mutations in the genes BRCA1 and BRCA2 with a more than 75% risk of breast cancer and ovarian cancer, and hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome) which is present in about 3% of people with colorectal cancer, among others.

Some substances cause cancer primarily through their physical, rather than chemical, effects on cells. A prominent example of this is prolonged exposure to asbestos, naturally occurring mineral fibers which are a major cause of mesothelioma, which is a cancer of the serous membrane, usually the serous membrane surrounding the lungs. Other substances in this category, including both naturally occurring and synthetic asbestos-like fibers such as wollastonite, attapulgite, glass wool, and rock wool, are believed to have similar effects. Non-fibrous particulate materials that cause cancer include powdered metallic cobalt and nickel, and crystalline silica (quartz, cristobalite, and tridymite). Usually, physical carcinogens must get inside the body (such as through inhaling tiny pieces) and require years of exposure to develop cancer.

Physical trauma resulting in cancer is relatively rare. Claims that breaking bones resulted in bone cancer, for example, have never been proven. Similarly, physical trauma is not accepted as a cause for cervical cancer, breast cancer, or brain cancer. One accepted source is frequent, long-term application of hot objects to the body. It is possible that repeated burns on the same part of the body, such as those produced by kanger and kairo heaters (charcoal hand warmers), may produce skin cancer, especially if carcinogenic chemicals are also present. Frequently drinking scalding hot tea may produce esophageal cancer. Generally, it is believed that the cancer arises, or a pre-existing cancer is encouraged, during the process of repairing the trauma,

rather than the cancer being caused directly by the trauma. However, repeated injuries to the same tissues might promote excessive cell proliferation, which could then increase the odds of a cancerous mutation. It is controversial whether chronic inflammation can directly cause mutation. It is recognized, however, that inflammation can contribute to proliferation, survival, angiogenesis and migration of cancer cells by influencing the microenvironment around tumors.

Furthermore, oncogenes are known to build up an inflammatory pro-tumorigenic microenvironment. Some hormones play a role in the development of cancer by promoting cell proliferation. Insulin-like growth factors and their binding proteins play a key role in cancer cell proliferation, differentiation and apoptosis, suggesting possible involvement in carcinogenesis. Hormones are important agents in sex-related cancers such as cancer of the breast, endometrium, prostate, ovary, and testis, and also of thyroid cancer and bone cancer. For example, the daughters of women who have breast cancer have significantly higher levels of estrogen and progesterone than the daughters of women without breast cancer.

These higher hormone levels may explain why these women have higher risk of breast cancer, even in the absence of a breast-cancer gene. Similarly, men of African ancestry have significantly higher levels of testosterone than men of European ancestry, and have a correspondingly much higher level of prostate cancer. Men of Asian ancestry, with the lowest levels of testosterone-activating and rostanediol glucuronide, have the lowest levels of prostate cancer. Other factors are also relevant: obese people have higher levels of some hormones associated with cancer and a higher rate of those cancers.

Women who take hormone replacement therapy have a higher risk of developing cancers associated with those hormones. On the other hand, people who exercise far more than average have lower levels of these hormones, and lower risk of cancer. Osteosarcoma may be promoted by growth hormones. Some treatments and prevention approaches leverage this cause by artificially reducing hormone levels, and thus discouraging hormone-sensitive cancers. Cancer is fundamentally a disease of tissue growth regulation failure. In order for a normal cell to transform into a cancer cell, the genes which regulate cell growth and differentiation must be altered. The affected genes are divided into two broad categories.

Oncogenes are genes which promote cell growth and reproduction. Tumor suppressor genes are genes which inhibit cell division and survival. Malignant transformation can occur through the formation of novel oncogenes, the inappropriate over-expression of normal oncogenes, or by the under-expression or disabling of tumor suppressor genes. Typically, changes in many genes are required to transform a normal cell into a cancer cell. Genetic changes can occur at different levels and by different mechanisms. The gain or loss of an entire chromosome can occur through errors in mitosis. More common are mutations, which are changes in the nucleotide sequence of genomic DNA. Large-scale mutations involve the deletion or gain of a portion of a chromosome. Genomic amplification occurs when a cell gains many copies (often 20 or more) of a small chromosomal locus, containing one or more oncogenes and adjacent genetic material.

Translocation occurs when two separate chromosomal regions become abnormally fused, often at a characteristic location. A well-known example of this is the Philadelphia chromosome, or translocation of chromosomes 9 and 22, which occurs in chronic myelogenous leukemia, and results in production of the BCR-abl fusion protein, an oncogenic tyrosine kinase. Small-scale mutations include point mutations, deletions, and insertions, which may occur in the promoter region of a gene and affect its expression, or may occur in the gene's coding sequence and alter the function or stability of its protein product.

Disruption of a single gene may also result from integration of genomic material from a DNA virus or retrovirus, leading to the expression of viral oncogenes in affected cell and its descendants. Replication of the enormous amount of data contained within the DNA of living cells will probabilistically result in some errors (mutations). Complex error correction and prevention is built into the process, and safeguards the cell against cancer. If significant error occurs, the damaged cell can "self-destruct" through programmed cell death, termed apoptosis. If the error control processes fail, then the mutations will survive and be passed along to daughter cells. Some environments make errors more likely to arise and propagate, they can include the presence of disruptive substances called carcinogens, repeated physical injury, heat, ionizing radiation, or hypoxia.

**The errors which cause cancer are self-amplifying and compounding, for example:**

- (1) A mutation in the error-correcting machinery of a cell might cause that cell and its children to accumulate errors more rapidly.
- (2) A further mutation in an oncogene might cause the cell to reproduce more rapidly and more frequently than its normal counterparts.
- (3) A further mutation may cause loss of a tumor suppressor gene, disrupting the apoptosis signaling pathway and resulting in the cell becoming immortal.
- (4) A further mutation in signaling machinery of the cell might send error-causing signals to nearby cells.

The transformation of normal cell into cancer is akin to a chain reaction caused by initial errors, which compound into more severe errors, each progressively allowing the cell to escape the controls that limit normal tissue growth. This rebellion-like scenario becomes an undesirable survival of the fittest, where the driving forces of evolution work against the body's design and enforcement of order. Once cancer has begun to develop, this ongoing process, termed clonal evolution, drives progression towards more invasive stages.

Characteristic abilities developed by cancers are divided into a number of categories. Six categories were originally proposed, in a 2000 paper called "The Hallmarks of Cancer" by Douglas Hanahan and Robert Weinberg: evasion of apoptosis, self-sufficiency in growth signals, insensitivity to anti-growth signals, sustained angiogenesis, limitless replicative potential, and metastasis.

Classically, cancer has been viewed as a set of diseases that are driven by progressive genetic abnormalities that include mutations in tumor-suppressor genes and oncogenes, and chromosomal abnormalities. However, it has become apparent that cancer is also driven by epigenetic alterations.

Epigenetic alterations refer to functionally relevant modifications to the genome that do not involve a change in the nucleotide sequence. Examples of such modifications are changes in DNA methylation (hypermethylation and hypomethylation) and histone modification and changes in chromosomal architecture (caused by inappropriate expression of proteins such as HMG A2 or HMG A1). Each of these epigenetic alterations serves to regulate gene expression without altering the underlying DNA sequence. These changes may remain through cell divisions, last for multiple generations, and can be considered to be epimutations (equivalent to mutations). Epigenetic alterations occur frequently in cancers. As an example, Schnekenburger and Diederich listed protein coding genes that were frequently altered in their methylation in association with colon cancer. These included 147 hypermethylated and 27 hypomethylated genes. Of the hypermethylated genes, 10 were hypermethylated in 100% of colon cancers, and many others were hypermethylated in more than 50% of colon cancers.

While large numbers of epigenetic alterations are found in cancers, the epigenetic alterations in DNA repair genes, causing reduced expression of DNA repair proteins, may be of particular importance. Such alterations are thought to occur early in progression to cancer and to be a likely cause of the genetic instability characteristic of cancers.

Reduced expression of DNA repair genes causes deficient DNA repair. When DNA repair is deficient DNA damages remain in cells at a higher than usual level and these excess damages cause increased frequencies of mutation and/or epimutation.

Mutation rates increase substantially in cells defective in DNA mismatch repair or in homologous recombinational repair (HRR). Chromosomal rearrangements and aneuploidy also increase in HRR defective cells. Higher levels of DNA damage not only cause increased mutation, but also cause increased epimutation. During repair of DNA double strand breaks, or repair of other DNA damages, incompletely cleared sites of repair can cause epigenetic gene silencing.

Deficient expression of DNA repair proteins due to an inherited mutation can cause increased risk of cancer. Individuals with an inherited impairment in any of 34 DNA repair genes have an increased risk of cancer, with some defects causing up to a 100% lifetime chance of cancer ( p53 mutations).

Germ line DNA repair mutations are noted, with an arrow indicating their contribution to DNA repair deficiency. However, such germline mutations (which cause highly penetrant cancer syndromes) are the cause of only about 1 percent of cancers. In sporadic cancers, deficiencies in DNA repair are occasionally caused by a mutation in a DNA repair gene, but are much more frequently caused by epigenetic alterations that reduce or silence expression of DNA repair genes.

Many studies of heavy metal-induced carcinogenesis show that such heavy metals cause reduction in expression of DNA repair enzymes, some through epigenetic mechanisms. In some cases, DNA repair inhibition is proposed to be a predominant mechanism in heavy metal-induced carcinogenicity. In addition, there are frequent epigenetic alterations of the DNA sequences coding for small RNAs called microRNAs (or miRNAs). MiRNAs do not code for proteins, can "target" protein-coding genes and reduce their expression.

Cancers usually arise from an assemblage of mutations and epimutations that confer a selective advantage leading to clonal expansion. Mutations, however, may not be as frequent in cancers as epigenetic alterations. An average cancer of the breast or colon can have about 60 to 70 protein-altering mutations, of which about 3 or 4 may be "driver" mutations, and the remaining ones may be "passenger" mutations. As pointed out above under genetic alterations, cancer is caused by failure to regulate tissue growth, when the genes which regulate cell growth and differentiation are altered. It has become clear that these alterations are caused by both DNA sequence mutation in oncogenes and tumor suppressor genes as well as by epigenetic alterations.

The epigenetic deficiencies in expression of DNA repair genes, in particular, likely cause an increased frequency of mutations, some of which then occur in oncogenes and tumor suppressor genes. Metastasis is the spread of cancer to other locations in the body. The new tumors are called metastatic tumors, while the original is called the primary tumor. Almost all cancers can metastasize. Most cancer deaths are due to cancer that has spread from its primary site to other organs (metastasized).

---

Metastasis is very common in the late stages of cancer, and it can occur via the blood or the lymphatic system or both. The typical steps in metastasis are local invasion, intravasation into the blood or lymph, circulation through the body, extravasation into the new tissue, proliferation, and angiogenesis.

Different types of cancers tend to metastasize to particular organs, but overall the most common places for metastases to occur are the lungs, liver, brain, and the bones. Most cancers are initially recognized either because of the appearance of signs or symptoms or through screening. Neither of these lead to a definitive diagnosis, which requires the examination of a tissue sample by a pathologist. People with suspected cancer are investigated with medical tests. These commonly include blood tests, X-rays, CT scans and endoscopy.

Most people are distressed to learn that they have cancer. They may become extremely anxious and depressed. The risk of suicide in people with cancer is approximately double the normal risk. Cancers are classified by the type of cell that the tumor cells resemble and is therefore presumed to be the origin of the tumor. These types include:

- (1) **Carcinoma:** Cancers derived from epithelial cells. This group includes many of the most common cancers, particularly in the aged, and include nearly all those developing in the breast, prostate, lung, pancreas, and colon.
- (2) **Sarcoma:** Cancers arising from connective tissue (bone, cartilage, fat, nerve), each of which develop from cells originating in mesenchymal cells outside the bone marrow.
- (3) **Lymphoma and leukemia:** These two classes of cancer arise from hematopoietic (blood-forming) cells that leave the marrow and tend to mature in the lymph nodes and blood, respectively. Leukemia is the most common type of cancer in children accounting for about 30%.
- (4) **Germ cell tumor:** Cancers derived from pluripotent cells, most often presenting in the testicle or the ovary (seminoma and dysgerminoma, respectively).
- (5) **Blastoma:** Cancers derived from immature "precursor" cells or embryonic tissue. Blastomas are more common in children than in older adults.

Cancers are usually named using -carcinoma, -sarcoma or -blastoma as a suffix, with the Latin or Greek word for the organ or tissue of origin as the root. For example, cancers of the liver parenchyma arising from malignant epithelial cells is called hepatocarcinoma, while a malignancy arising from primitive liver precursor cells is called a hepatoblastoma, and a cancer arising from fat cells is called a liposarcoma.

For some common cancers, the English organ name is used. For example, the most common type of breast cancer is called ductal carcinoma of the breast. Here, the adjective ductal refers to the appearance of the cancer under the microscope, which suggests that it has originated in the milk ducts.

Benign tumors (which are not cancers) are named using -oma as a suffix with the organ name as the root. For example, a benign tumor of smooth muscle cells is called leiomyoma (the common name of this frequently occurring benign Tumor in the uterus is fibroid).

Confusingly, some types of cancer use the -noma suffix, examples including melanoma and seminoma. Some types of cancer are named for the size and shape of the cells under a microscope, such as giant cell carcinoma, spindle cell carcinoma, and small-cell carcinoma. The tissue diagnosis given by the pathologist indicates the type of cell that is proliferating, its histological grade, genetic abnormalities, and other features of the tumor. Together, this information is useful to evaluate the prognosis of the patient and to choose the best treatment. Cytogenetics and immuno-histochemistry are other types of testing that the pathologist may perform on the tissue specimen. These tests may provide information about the molecular changes (such as mutations, fusion genes, and numerical chromosome changes) that have happened in the cancer cells, and may thus also indicate the future behavior of the cancer (prognosis) and best treatment.

Cancer prevention is defined as active measures to decrease the risk of cancer. The vast majority of cancer cases are due to environmental risk factors, and many, but not all, of these environmental factors are controllable lifestyle choices. Thus, cancer is considered a largely preventable disease. Greater than 30% of cancer deaths could be prevented by avoiding risk factors including: tobacco, overweight / obesity, an insufficient diet, physical inactivity, alcohol, sexually transmitted infections, and air pollution. Not all environmental causes are controllable, such as naturally occurring background radiation, and other cases of cancer are caused through hereditary genetic disorders, thus it is not possible to prevent all cases of cancer.

While many dietary recommendations have been proposed to reduce the risk of cancer, the evidence to support them is not actually definitive at the present time. The primary dietary factors that increase risk are obesity and alcohol consumption; with a diet low in fruits and vegetables and high in red meat being implicated but not confirmed. A 2014 meta-analysis did not find a relationship between fruits and vegetables and cancer. Consumption of coffee is associated with a reduced risk of liver cancer.

Studies have linked excessive consumption of red or processed meat to an increased risk of breast cancer, colon cancer, and pancreatic cancer, a phenomenon which could be due to the presence of carcinogens in meats cooked at high temperatures. Dietary recommendations for cancer prevention typically include an emphasis on vegetables, fruit, whole grains, and fish, and an avoidance of processed and red meat (beef, pork, lamb), animal fats, and refined carbohydrates.

The concept that medications can be used to prevent cancer is attractive, and evidence supports their use in a few defined circumstances. In the general population, NSAIDs reduce the risk of colorectal cancer, however due to the cardiovascular and gastrointestinal side effects they cause overall harm when used for prevention. Aspirin has been found to reduce the risk of death from cancer by about 7%. COX-2 inhibitor may decrease the rate of polyp formation in people with familial adenomatous polyposis, however it is associated with the same adverse effects as NSAIDs. Daily use of tamoxifen or raloxifene has been demonstrated to reduce the risk of developing breast cancer in high-risk women.

The benefit versus harm for 5-alpha-reductase inhibitor such as finasteride is not clear. Vitamins have not been found to be effective at preventing cancer, although low blood levels of vitamin D are correlated with increased cancer risk. Whether this relationship is causal and vitamin D supplementation is protective is not determined. Beta-Carotene supplementation has been found to increase lung cancer rates in those who are high risk. Folic acid supplementation has not been found effective in preventing colon cancer and may increase colon polyps. It is unclear if selenium supplementation has an effect. Vaccines have been developed that prevent infection by some carcinogenic viruses. Human papillomavirus vaccine (Gardasil and Cervarix) decreases the risk of developing Cervical Cancer. The Hepatitis B vaccine prevents infection with hepatitis B virus and thus decreases the risk of liver cancer. The administration of human papillomavirus and hepatitis B

vaccinations is recommended when resources allow. Unlike diagnosis efforts prompted by symptoms and medical signs, cancer screening involves efforts to detect cancer after it has formed, but before any noticeable symptoms appear. This may involve physical examination, blood or urine tests, or medical imaging. Cancer screening is currently not possible for many types of cancers, and even when tests are available, they may not be recommended for everyone. Universal screening or mass screening involves screening everyone. Selective screening identifies people who are known to be at higher risk of developing cancer, such as people with a family history of cancer.

Several factors are considered to determine whether the benefits of screening outweigh the risks and the costs of screening. These factors include:

- (1) Possible harms from the screening test: for example, X-ray images involve exposure to potentially harmful ionizing radiation.
- (2) The likelihood of the test correctly identifying cancer.
- (3) The likelihood of cancer being present: Screening is not normally useful for rare cancers.
- (4) Possible harms from follow-up procedures.
- (5) Whether suitable treatment is available.
- (6) Whether early detection improves treatment outcomes.
- (7) Whether the cancer will ever need treatment.
- (8) Whether the test is acceptable to the people: If a screening test is too burdensome (for example, being extremely painful), then people will refuse to participate.
- (9) Cost of the test.

The U.S. Preventive Services Task Force strongly recommends cervical cancer screening in women who are sexually active and have a cervix at least until the age of 65. They recommend that Americans be screened for colorectal cancer via fecal occult blood testing, sigmoidoscopy, or colonoscopy starting at age 50 until age 75. There is insufficient evidence to recommend for or against screening for skin cancer, oral cancer, lung cancer, or prostate cancer in men under 75. Routine screening is not recommended for bladder cancer, testicular cancer, ovarian cancer, pancreatic cancer, or prostate cancer.

The U.S. Preventive Services Task Force recommends mammography for breast cancer screening every two years for those 50–74 years old; however, they do not recommend either breast self-examination or clinical breast examination. A 2011 Cochrane review came to slightly different conclusions with respect to breast cancer screening stating that routine mammography may do more harm than good. Japan screens for gastric cancer using photofluorography due to the high incidence there. Genetic testing for individuals at high-risk of certain cancers is recommended. Carriers of these mutations may then undergo enhanced surveillance, chemoprevention, or preventative surgery to reduce their subsequent risk. Many treatment options for cancer exist, with the primary ones including surgery, chemotherapy, radiation therapy, hormonal therapy, targeted therapy and palliative care. Which treatments are used depends upon the type, location, and grade of the cancer as well as the person's health and wishes. The treatment intent may be curative or not curative.

As to the consideration of Chemotherapy, it is the treatment of cancer with one or more cytotoxic anti-neoplastic drugs (chemotherapeutic agents) as part of a standardized regimen. The term encompasses any of a large variety of different anticancer drugs, which are divided into broad categories such as alkylating agents and antimetabolites. Traditional chemotherapeutic agents act by killing cells that divide rapidly, one of the main properties of most cancer cells.

Targeted therapy is a form of chemotherapy which target specific molecular differences between cancer and normal cells. The first targeted therapies to be developed blocked the estrogen receptor molecule, inhibiting the growth of breast cancer. Another common example is the class of Bcr-Abl inhibitors, which are used to treat chronic myelogenous leukemia (CML). Currently, there are targeted therapies for breast cancer, multiple myeloma, lymphoma, prostate cancer, melanoma and other cancers.

The efficacy of chemotherapy depends on the type of cancer and the stage. In combination with surgery, chemotherapy has proven useful in a number of different cancer types including: breast cancer, colorectal cancer, pancreatic cancer, osteogenic sarcoma, testicular cancer, ovarian cancer, and certain lung cancers. The overall effectiveness ranges from being curative for some cancers, such as some leukemia, to being ineffective, such as in some brain tumors, to being needless in others, like most non-melanoma skin cancers.

The effectiveness of chemotherapy is often limited by toxicity to other tissues in the body. Even when it is impossible for chemotherapy to provide a permanent cure, chemotherapy may be useful to reduce Symptoms like pain or to reduce the size of an inoperable tumor in the hope that surgery will be possible in the future. As to the consideration of Radiation therapy, it involves the use of ionizing radiation in an attempt to either cure or improve the symptoms of cancer.

It works by damaging the DNA of cancerous tissue leading to cellular death. To spare normal tissues (such as skin or organs which radiation must pass through to treat the tumor), shaped radiation beams are aimed from several angles of exposure to intersect at the tumor, providing a much larger absorbed dose there than in the surrounding, healthy tissue. As with chemotherapy, different cancers respond differently to radiation therapy. Radiation therapy is used in about half of all cases and the radiation can be from either internal sources in the form of brachytherapy or external sources. Radiation is typically used in addition to surgery and or chemotherapy but for certain types of cancer, such as early head and neck cancer, may be used alone. For painful bone metastasis, it has been found to be effective in about 70% of people.

Surgery is the primary method of treatment of most isolated solid cancers and may play a role in palliation and prolongation of survival. It is typically an important part of making the definitive diagnosis and staging the tumor as biopsies are usually required. In localized cancer surgery typically attempts to remove the entire mass along with, in certain cases, the lymph nodes in the area.

For some types of cancer this is all that is needed to eliminate the cancer. Palliative care refers to treatment which attempts to make the person feel better and may or may not be combined with an attempt to treat the cancer. Palliative care includes action to reduce the physical, emotional, spiritual, and psycho-social distress experienced by people with cancer. Unlike treatment that is aimed at killing cancer cells, the primary goal of palliative care is to improve the person's quality of life.

People at all stages of cancer treatment should have some kind of palliative care to provide comfort. In some cases, medical specialty professional organizations recommend that people and physicians respond to cancer only with palliative care and not with cure-directed therapy. This includes:

- (1) People with low performance status, corresponding with limited ability to care for themselves.
- (2) People who received no benefit from prior evidence-based treatments.
- (3) People who are not eligible to participate in any appropriate clinical trial people for whom the physician sees no strong evidence that treatment would be effective.

Palliative care is often confused with hospice and therefore only involved when people approach end of life. Like hospice care, palliative care attempts to help the person cope with the immediate needs and to increase The person's comfort. Unlike hospice care, palliative care does not require people to stop treatment aimed at prolonging their lives or curing the cancer. Multiple national medical guidelines recommend early palliative care for people whose cancer has produced distressing symptoms (pain, shortness of breath, fatigue, nausea) or who need help coping with their illness. In people who have metastatic disease when first diagnosed, oncologists should consider a palliative care consult immediately. Additionally, an oncologist should consider a palliative care in any person has less than 12 months of life even if continuing aggressive treatment.

A variety of therapies using immunotherapy, stimulating or helping the immune system to fight cancer, have come into use since 1997, and this continues to be an area of very active research. Cancer has a reputation as a deadly disease. About half of people receiving treatment for invasive cancer (excluding carcinoma in situ and non-melanoma skin cancers) die from cancer or its treatment. Survival is worse in the developing world, partly because the types of cancer that are most common there are at present harder to treat than those associated with the lifestyle of many developed countries. However, the survival rates vary dramatically by type of cancer, and by the stage at which it is diagnosed, with the range running from the great majority of people surviving to almost no one surviving as long as five years after diagnosis. Once a cancer has metastasized or spread beyond its original site the prognosis normally becomes much worse. Those who

survive cancer are at increased risk of developing a second primary cancer at about twice the rate of those never diagnosed with cancer. The increased risk is believed to be primarily due to the same risk factors that produced the first cancer, partly due to the treatment for the first cancer, and potentially related to better compliance with screening. Predicting either short-term or long-term survival is difficult and depends on many factors. The most important factors are the Particular kind of cancer and the patient's age and health.

People who are frail with many other health problems have lower survival rates than otherwise healthy people. A centenarian is unlikely to survive for five years even if The treatment is successful. People who report a higher quality of life tend to survive longer. People with lower quality of life may be affected by major depressive disorder and complications from cancer treatment and/or disease progression that both impairs their quality of life and reduces their quantity of life.

Additionally, patients with worse prognoses may be depressed or report a lower quality of life directly because they correctly perceive that their condition is likely to be fatal. In 2008, approximately 12.7 million cancers were diagnosed (excluding non-melanoma skin cancers and other non-invasive cancers), and in 2010 nearly 7.98 million people died. Cancers as a group account for approximately 13% of all deaths each year with the most common being: lung cancer (1.4 million deaths), stomach cancer (740,000 deaths), liver cancer (700,000 deaths), colorectal cancer(610,000 deaths), and breast cancer (460,000 deaths). This makes invasive cancer the leading cause of death in the developed world and the second leading cause of death in the developing world.

Over half of cases occur in the developing world. Deaths from cancer were 5.8 million in 1990 and rates have been increasing primarily due to an aging population and lifestyle changes in the developing world. The most significant risk factor for developing cancer is old age.

Although it is possible for cancer to strike at any age, most people who are diagnosed with invasive cancer are over the age of 65. According to cancer researcher Robert A. Weinberg, "If we lived long enough, sooner or later we all would get cancer." Some of the association between aging and cancer is attributed to immunosenescence, errors accumulated in DNA over a lifetime, and age-related changes in the endocrine system. The effect of aging on cancer is complicated with a number of factors such as DNA damage and inflammation promoting it and a number of factors such as vascular aging & endocrine changes inhibiting it.

Some slow-growing cancers are particularly common. Autopsy studies in Europe and Asia have shown that up to 36% of people have undiagnosed and apparently harmless thyroid cancer at the time of their deaths, and that 80% of men develop prostate cancer by age 80. As these cancers did not cause the person's death, identifying them would have represented over-diagnosis rather than useful medical care. The three most common childhood cancers are leukemia (34%), brain tumors (23%), and lymphomas (12%). In the United States cancer affects about 1 in 285 children. Rates of childhood cancer have increased by 0.6% per year Between 1975 to 2002 in the United States and by 1.1% per year between 1978 and 1997 in Europe. Death from childhood cancer have decreased by half since 1975 in the United States. Because cancer is largely a disease of older adults, it is not common in pregnant women. Cancer affects approximately 1 in 1,000 pregnant women. The most common cancers found during pregnancy are the same as the most common cancers found in non-pregnant women during childbearing ages: breast cancer, cervical cancer, leukemia, lymphoma, melanoma, ovarian cancer, and colorectal cancer.

### **The Present Invention**

The invention relates to a process/composition for the diagnosis or killing of cancer cells and inactivation of susceptible bacterial, parasitic, fungal, and viral pathogens by chemically generating heat, and/or free radicals or hyperthermia-inducible immunogenic determinants by using mitochondrial uncoupling agents, especially 2,4 dinitrophenol and, their conjugates, in combination with other drugs, hormones and cytokines. The present invention also has the capabilities to prognosticate cancer.

Further provided are therapeutic infusion compositions, processes and systems to prognosticate cancer, agitate, and cause very early developed carcinogenic cells to Bio-communicate and Bio-signal for proper logistical information and necessary data as a direct result from such aggressively systematic Bio-Signaling and Intracellular Communications with cancer cells, by the end of which a detection, diagnosis and the best treatment can be assigned by the system.

The present invention also illustrates a laser accelerator driven electronic brachy-therapy system, device, and method for particle based treatment of a tumor or other human diseases and conditions is disclosed. In an embodiment, a particle-based electronic brachytherapy device can include an applicator (catheter) and a high energy particle, such as but not limited to, laser plasma accelerator.

The laser plasma accelerator can be a compact, miniature laser-based plasma accelerator with a voltage gradient suitable to generate particles having energies in the range of 570 MeV. Electrons, protons, and heavy ions with acceleration gradients of 30 GeV/m to 200 GeV/m can be obtained through Solar Sonic Cancer Cure Medical Device via laser plasma accelerator, circuit equivalents, integrated circuits and central delivery unit of energy output fluctuations. The present invention also relates to therapeutic compositions for treating cancer or preventing the growth of cancer cells, tumor growth, in a subject.

The present invention relates to methods for treating cancer, inhibiting tumor growth, in a subject who has become resistant to treatment, by administering to a subject an effective amount of a proteasome inhibitor and an effective amount of therapeutic agent, chemotherapeutic agent. The present invention further relates to methods for purging bone marrow, removing cancer cells from Bone marrow, by exposing the bone marrow cells to a proteasome inhibitor and a therapeutic agent, and a chemotherapeutic agent.

The present invention also promotes methods for improving the efficiency of electroporation protocols and methods to enhance the permeabilized state, to improve the intracellular delivery of therapeutic substances, involve the use of at least one agent which is capable of prolonging the permeability of the cell membranes in the tissue exposed to an electroporation-inducing electrical field. The present invention also contains an anti adhesion therapy which uses the compound as a mediator or inhibitor of adhesion proteins and angiopoietins. It inhibits excess adhesion and inhibits cell attachment. It modulates angiogenesis. The compounds also use as mediator of cell adhesion receptor, cell circulating, cell moving and inflammatory.

This invention provides a method of synthesizing new active compounds for pharmaceutical uses including cancer treatment, wherein the cancers comprise breast, leukocytic, liver, ovarian, bladder, prostatic, skin, bone, brain, leukemia, lung, colon, CNS, melanoma, renal, cervical, esophageal, testicular, splenic, kidney, lymphatic, pancreatic, stomach and thyroid cancers.

The present invention also relates to novel photoactivable rhodamine derivatives for enhancing high quantum-yield production and singlet oxygen generation upon irradiation with light while maintaining desirable differential retention of rhodamine between normal and cancer cells, said derivatives are selected from the group consisting of dibromorhodamine dibromo-6-amino-3-imino-3H-xanthen-9-yl-benzoic acid methyl ester hydrochloride; dibromorhodamine dibromo-6-amino-3-imino-3H-xanthen-9-yl-benzoic acid ethyl ester hydrochloride; and photoactivable derivatives; whereby photoactivation of the derivatives induces cell killing while unactivated derivatives are substantially non-toxic to cells.

Also, the present invention relates to the use of photoactivable derivatives of the present invention for photodynamic therapy of a cancer patient by destroying human cancer cells, wherein appropriate intracellular levels of the derivatives are achieved and irradiation with light of a suitable wavelength is applied.

The present invention also relates to a method for the photodynamic therapy of a patient suffering from leukemias, disseminated multiple myelomas or lymphomas. The present invention also concerns methods and compositions for forming anti-cancer chemical complexes using Solar Sonic Anti-Cancer Multidimensional electrochemical therapeutic infusion technologies.

In preferred embodiments, the anti-cancer chemical complex comprises an antibody moiety that binds to dendritic cells, such as an anti-CD74 antibody or antigen-binding fragment thereof, attached to an AD (anchoring domain) moiety and a xenoantigen, such as CD20, attached to a DDD (dimerization and docking domain) moiety, wherein two copies of the DDD moiety form a dimer that binds to the AD moiety, resulting in the formation of the SSQF Chemical Complex. The anti-cancer chemical complex is capable of inducing

an immune response against xenoantigen expressing cancer cells, such as CD138<sup>neg</sup>CD20<sup>+</sup> MM stem cells, and inducing apoptosis of and inhibiting the growth of carcinogenic cells and eliminating the cancer cells.

The present invention also presents an antibody for targeted induction of Apoptosis, CDC and ADCC mediated killing of Cancer cells, TBL-CLN1, is disclosed. The antibodies, TBL-CLN1, are monoclonal antibodies which can specifically target and bind to the epitope of SEQ ID expressed on cancer cells which further leads to killing of cancer cells. TBL-CLN1 is not conjugated to toxin or cytotoxic molecules, and provides selective killing of cancer cells just by binding to cancer cell surface.

The present invention also illustrates that biological organism suffering from cancer can be treated by administering a cancer cell cycle arresting drug; optionally administering a microtubule stabilizing agent; and exposing the cell cycle arrested cells to mechanical vibrational energy, the method selectively induces apoptosis in cancer cells. The Present invention also relates to multiple targeting protocols and methods of treating all cancer at all stages, Wherein a pharmaceutical composition made from 'Mycobacterium (M<sub>w</sub>) is found to be useful in the management of cancer. We have now found that the same therapeutic agent is useful in management of cancer. The use of Mycobacterium W containing formulations is associated with decrease in burden of cancer tissue, decreasing systems associated with cancer and improving quality of life.

It also improves tolerance to other therapies. The present invention also relates to the use of dichloroacetate and chemical equivalents thereof for the treatment of cancer by inducing apoptosis or reversing apoptosis-resistance in a cell. Preferably, the dosage is 10-100 mg/kg. Preferably, sodium dichloroacetate is selected from the Active Solar Sonic Infusion-ably Accessible Pharmacological Agents. Dichloroacetate may optionally be given in combination with a pro-apoptotic agent and/or a chemotherapeutic agent. Preferably, the cancers treated are non-small cell lung cancer, glioblastoma and breast carcinoma.

The present invention also provides a combined frequency therapy and hyperthermia therapy including inducing hyperthermia in at least a portion of a target area, a tumor or targeted cancerous cells. Bio-molecules labeled with at least one radionuclide suitable for radiotherapy are provided and introduced into a patient; targeted frequency absorption enhancers provided and introduced into a patient; and a hyperthermia generating frequency signal is directed toward the target cells, warming the radionuclide-labeled bio-molecules and target frequency absorption enhancers bound to target cells.

Targeted frequency absorption enhancers may, in a manner of speaking, add one or more frequency absorption frequencies to cells in the target area, which permit a hyperthermia generating frequency signal at that frequency or frequencies to heat the targeted cells. Bio-molecules labeled with at least one radionuclide suitable for radiotherapy may be used for both radiotherapy and as frequency absorption enhancers for the hyperthermia generating frequency signal.

The present invention also comprises a charged particle beam path coupling an injector, synchrotron accelerator, beam transport system, targeting system, and/or patient interface method and apparatus. Preferably, the injector comprises: a negative ion beam source, a two phase ion source vacuum system, an ion beam focusing lens, and/or a tandem accelerator.

Preferably, the synchrotron comprises turning magnets, edge focusing magnets, magnetic field concentration magnets, winding and correction coils, flat magnetic field incident surfaces, and/or extraction elements. Preferably, the synchrotron, beam transport system, targeting system, and patient interface combine to allow multi-axis/multi-field irradiation, where multi-axis control comprises control of horizontal and vertical beam position, beam energy, and/or beam intensity and multi-field control comprises control of patient rotation and distribution of delivered energy in and about the tumor in a time controlled, targeted, accurate, precise, dosage controlled, and/or efficient manner.

The present invention also relates to the use of phytocannabinoids, either in an isolated form or in the form of a botanical drug substance (BDS), as a prophylactic or in the treatment of cancer. Typically the cancer to be treated is a cancer of the: prostate, breast, skin, glioma, colon, lung or a bone or lymph metastasis. The

phytocannabinoids is safely used in combination with other Solar Sonic cancer treatment methodologies. The present invention also relates to compositions of immunotoxins, Monoclonal antibody, CD22, CD25, interleukin. More particularly this invention relates to the use of antibody to potentiate the vital activity of the immunotoxins for treatment of cancer. Immunotoxins are antibody-toxin bifunctional molecules that rely on intracellular toxin action to kill target cells.

Target specificity is determined via the binding attributes of the chosen antibody. Mostly, but not exclusively, immunotoxins are purpose-built to kill cancer cells as part of novel treatment approaches. Other applications for immunotoxins include immune regulation and the treatment of viral or parasitic diseases. Here we discuss the utility of protein toxins, of both bacterial and plant origin, joined to antibodies for targeting cancer cells.

The invention presents a method for treating a patient suffering from cancer comprising administering to said patient an amount of a cell cycle arresting drug sufficient to synchronize cell cycles of a plurality of cancer cells in said patient; and subjecting said cells to mechanical vibrational energy, wherein the cell cycle arresting drug from the group consisting of: gemcytabine, cisplatin, carboplatin, cyclophosphamide, topoisomerase inhibitor, etoposide, 5-fluorouracil, doxorubicin, methotrexate, hydroxyurea, and 3'-azido-3'-deoxythymidine, wherein the mechanical vibrational energy is ultrasound energy having a frequency of about 50 megahertz to about 2 gigahertz, wherein the exposure to mechanical vibrational energy is repeated or sustained over a period of at least one typical cell cycle.

The invention provides a method of treating a patient suffering from cancer comprising administering to said patient an amount of a cell cycle arresting drug sufficient to synchronize cell cycles of a plurality of cancer cells in the patient; administering to the patient a microtubule stabilizing agent; and exposing the patient to mechanical vibrational energy, wherein the microtubule stabilizing agent is selected from the group consisting of: taxanes, magnetic taxanes; coumarins, magnetic coumarins, and combinations thereof, wherein the microtubule stabilizing agent is selected from the group consisting of paclitaxel, docetaxel, magnetic derivatives thereof, and combinations thereof, wherein the cell cycle arresting drug is selected from the group consisting of: gemcytabine, cisplatin, carboplatin, cyclophosphamide, topoisomerase inhibitor, etoposide, 5-fluorouracil, doxorubicin, methotrexate, hydroxyurea, and 3'-azido-3'-deoxythymidine.

Wherein the cell cycle arresting drug is gemcytabine and the microtubule stabilizing agent is a taxane, a coumarin, magnetic derivatives, and combinations thereof, wherein the mechanical vibrational energy is ultrasound energy having a frequency of 50 megahertz to about 2 gigahertz, wherein exposure to mechanical vibrational energy is repeated or sustained over a period of one typical cell cycle and exposure to mechanical Vibrational energy is performed at least 60 minutes after administration of the cell cycle arresting drug, wherein the microtubule stabilizing agent is administered from a drug eluting implant, wherein the implant is a drug eluting stent.

The invention provides a process for treating a patient suffering from cancer comprising administering to said patient an amount of a cell cycle arresting drug sufficient to synchronize cell cycles of a plurality of the cancer cells in said patient; administering to the said patient radiation therapy sufficient to stabilize microtubule assembly in said cancer cells; and subjecting said cancer cells to mechanical vibrational energy.

The invention provides a method of treating a patient suffering from cancer comprising administering to said patient a cancer cell cycle arresting amount of gemcytabine; administering a microtubule stabilizing agent selected from the group consisting of taxanes, coumarins, magnetic derivatives thereof, and combinations thereof; and exposing the patient to mechanical vibrational energy of frequency of about 50 megahertz to about 2 gigahertz, wherein the microtubule stabilizing agent is selected from the group consisting of paclitaxel, docetaxel, magnetic derivatives thereof, and combinations thereof.

The invention provides a method of treating a patient suffering from cancer comprising administering to said patient an amount of a cell cycle arresting drug sufficient to synchronize cell cycles of a plurality of cancer cells in patient; administering to the patient a magnetic microtubule stabilizing agent; applying a localized Magnetic field to increase the concentration of magnetic microtubule stabilizing agent at a predetermined

location in the patient; and exposing the patient to mechanical vibrational energy, wherein the magnetic microtubule stabilizing agent is a magnetic taxane or a magnetic coumarin, wherein the mechanical vibrational energy is ultrasound energy of frequency of about 50 megahertz to about 2 gigahertz, wherein the ultrasound energy is administered to the patient by an intracorporeal device.

The invention provides method for treating a cancer associated with hyperpolarized mitochondria which comprising: selecting a patient having a cancer comprising hyperpolarized mitochondria and/or an elevated survivin to Kv1.5 protein ratio relative to a normal control; and administering to said patient in need thereof a therapeutically effective amount of dichloroacetate (DCA) or an acid or salt thereof, wherein the intended dichloroacetate or acid or salt thereof is a salt of dichloroacetic acid.

Wherein the dichloroacetate or acid or salt thereof is sodium dichloroacetate, wherein the cancer comprising hyperpolarized mitochondria and/or an elevated survivin to Kv1.5 protein ratio relative to a normal control is selected from the group consisting of non-small cell lung cancer, glioblastoma and breast carcinoma, wherein the dichloroacetate or acid or salt thereof is administered in the form of a pharmaceutical composition comprising dichloroacetate or acid or salt thereof and a pharmaceutically acceptable carrier, wherein the dichloroacetate or acid or salt thereof is administered orally, wherein 10-100 mg/kg of DCA or acid or salt thereof is administered per day, wherein 10-100 mg/kg of DCA or acid or salt thereof is administered twice per day.

Wherein a dose is 25-50 mg/kg, wherein a dose is 25-50 mg/kg, wherein the dichloroacetate or acid or salt thereof is administered in combination with another pro-apoptotic agent and/or chemotherapeutic agent, and/or other cancer therapy, wherein the administering of an effective amount of dichloroacetate or acid or salt thereof induces apoptosis and/or reverses apoptosis resistance in a cancer cell of the patient, wherein the administering of an effective amount of dichloroacetate or acid or salt thereof inhibits proliferation of cancer cells of the patient, wherein the administering of an effective amount of dichloroacetate or acid or salt thereof decreases level of survivin in a cancer cell of the patient.

Wherein the administering of an effective amount of dichloroacetate or acid or salt thereof increases level of Kv1.5 protein in a cancer cell of the patient, wherein the administering of an effective amount of dichloroacetate or acid or salt thereof increases level of apoptosis-inducing factor (AIF) in a cancer cell of the patient, wherein the administering of an effective amount of dichloroacetate or acid or salt thereof increases level of H<sub>2</sub>O<sub>2</sub> in a cancer cell of the patient, wherein cancer cells, but not normal or non-cancerous cells, of the patient are affected by the administration of dichloroacetate or acid or salt thereof, wherein the dichloroacetate or acid or salt thereof has the formula CH(Cl<sub>2</sub>)-COO-X, wherein X is selected from the group consisting of Na<sup>+</sup>, K<sup>+</sup>, CH<sub>3</sub> and OH, wherein the dichloroacetate or acid or salt thereof has the formula CH(Cl<sub>2</sub>)-COO<sup>-</sup>K<sup>+</sup>.

The invention also provides a method for delivering a therapeutic substance to a region of tissue in a patient comprising: providing a therapeutic substance to a patient in need of said substance; establishing electrical Field which encompasses a region of tissue within said patient; exposing said region of tissue to said electrical field for a time and under conditions sufficient to permit the permeation of said substance across the cell membranes of cells located within said region of tissue; and administering to said patient at least one agent which is capable of prolonging the permeability of the cell membranes in the tissue exposed to said electrical field in a manner so that said agent does not contact said region of tissue until after the tissue's exposure to the electrical field.

The invention also provides a method for delivering a therapeutic substance as recited in claim wherein said agent comprises at least one compound which temporarily decreases cell membrane fluidity. A method for delivering a therapeutic substance as recited in claims wherein said agent comprises a steroid. A method for delivering a therapeutic substance as recited in claims wherein said agent comprises at least one member selected from the group consisting of dexamethasone, prednisone, methylprednisolone, progesterone, Angiotensin II and Vitamin E.

The invention also provides a method for delivering a therapeutic substance as recited in claims wherein said agent comprises at least dexamethasone. A method for delivering a therapeutic substance as recited in claims wherein said therapeutic substance is provided to the patient by direct administration to the region of tissue within said patient. A method for delivering a therapeutic substance as recited in claims.

Wherein said therapeutic substances are provided to the patient by systemic administration. A method for delivering a therapeutic substances as recited in claims wherein said therapeutic substances are provided to the patient by a combination of systemic administration. A method for delivering a therapeutic substance to a region of tissue located in a patient wherein said tissue has been exposed to an electroporation-inducing electrical field, the improvement comprising: Contacting said tissue after it has been exposed to said electrical field with at least one agent which is capable of prolonging the permeability of the cell membranes in the tissue exposed to said electrical field. A method for delivering a therapeutic substance as recited in claims wherein said agent comprises at least one compound which temporarily decreases cell membrane fluidity.

A method for delivering a therapeutic substance as recited in claims wherein said agent comprises a steroid. A method for delivering a therapeutic substance as recited in claims wherein said agent comprises at least one member selected from the group consisting of dexamethasone, prednisone, methylprednisolone, progesterone, Angiotensin II and Vitamin E. A method for delivering a therapeutic substance as recited in claims wherein said agent comprises at least dexamethasone.

A method for delivering a therapeutic substance as recited in claims wherein said therapeutic substance is provided to the patient by direct administration to the region of tissue within said patient. A method for delivering a therapeutic substance as recited in claims wherein said therapeutic substance is provided to the patient by systemic administration to the patient. A method for delivering a therapeutic substance as recited in claims wherein said therapeutic substance is provided to the patient by a combination of systemic administration to the patient and direct administration to the region of tissue within said patient.

The invention also provides a method for treating multiple myeloma or breast cancer in a subject wherein the subject's multiple myeloma or breast cancer cells are resistant to treatment with a proteasome inhibitor, comprising administering to the subject an effective amount of a second proteasome inhibitor and an effective amount of a therapeutic agent, wherein the therapeutic agent is doxorubicin, such that the multiple myeloma or breast cancer is treated, wherein the treatment of cancer is due to the inhibition of tumor growth, wherein the proteasome inhibitor and/or the second proteasome inhibitor is PS-341.

Wherein the second proteasome inhibitor is administered prior to the administration of the therapeutic agent, simultaneously with the administration of the therapeutic agent, or after the administration of the therapeutic agent, wherein the second proteasome inhibitor inhibits NF- $\kappa$ B activity or abolishes cell adhesion mediated drug-resistance, Wherein the administration of an effective amount of the second proteasome inhibitor and an effective amount of the therapeutic agent results in cancer cell death, apoptosis of cancer cells, or modulation of the response to genotoxic stress, wherein the second proteasome inhibitor modulates a DNA-dependant protein kinase, wherein the second proteasome inhibitor and the therapeutic agent are administered intravenously, intraperitoneally.

Wherein the second proteasome inhibitor is administered at a dose of about 0.001 mg/m<sup>2</sup> body surface area/day to about 4.0 mg/m<sup>2</sup> body surface area/day, wherein the treatment of cancer is due to the inhibition of tumor growth, wherein the proteasome inhibitor and/or the second proteasome inhibitor is PS-341, wherein the second proteasome inhibitor is administered prior to the administration of the therapeutic agent, simultaneously with the administration of the therapeutic agent, or after the administration of the therapeutic agent.

Wherein the second proteasome inhibitor inhibits NF- $\kappa$ B activity or abolishes cell adhesion mediated drug-resistance, wherein the administration of an effective amount of the second proteasome inhibitor and an effective amount of the therapeutic agent results in cancer cell death, apoptosis of cancer cells, or modulation

of the response to genotoxic stress, wherein the second proteasome inhibitor modulates a DNA-dependant protein kinase, wherein the second proteasome inhibitor and the Therapeutic agent are administered intravenously, intraperitoneally, or orally, wherein the proteasome inhibitor and the second proteasome inhibitor are the same, wherein the proteasome inhibitor and the second proteasome inhibitor are the same, wherein the proteasome inhibitor and the second proteasome inhibitor are different, wherein the proteasome inhibitor and the second proteasome inhibitor are different.

Finally, while clinical goals are focused on the development of novel cancer treatments, much has been learned about toxin action and intracellular pathways. Toxins are considered both medicines for treating human disease and probes of cellular function. Immunotoxins are proteins contain a toxin along with an antibody or growth factor that binds specifically to target cells. Nearly all protein toxins work by enzymatically inhibiting protein synthesis. And so, for the immunotoxin to work, it must bind to and be internalized by the target cells, and the enzymatic fragment of the toxin must translocate to the cytosol. Once in the cytosol, 1 molecule is capable of killing a cell, making immunotoxins some of the most potent killing agents. Various plants and bacterial toxins have been genetically fused or chemically conjugated to ligands that bind to cancer cells. Among the most active clinically are those that bind to hematologic tumors.

At present, only 1 agent, which contains human interleukin-2 and truncated diphtheria toxin, is approved for use in cutaneous T-cell lymphoma. Another, containing an anti-CD22 Fv and truncated Pseudomonas exotoxin, has induced complete remissions in a high proportion of cases of hairy-cell leukemia. Refinement of existing immunotoxins and development of new immunotoxins are underway to improve the treatment of cancer. In a preferred embodiment, the inventive method further comprises administering a dose of one or more therapeutic pharmacological agents, a pharmaceutically acceptable carrier with other simultaneous applications of approved pharmaceutical agents and chemotherapeutic agents onto the area of the tumor to a patient over the therapeutic period.

Illustrated here below is a list of our applicable chemical agents and compositions, this approved list was specifically selected as they are all Solar Sonic Infusion-ably Accessible as chemical resonance signatures that can be electromagnetically /chemically manipulated for an expeditious intracellular redirection as well as penetration leading to intracellular Bio-signal Communications of carcinogenic cells / pathogens, upon which a magnificent cellular eradication count-down will begin for immediate biological initiation to systematically eradicate cancer cells.

Any suitable therapeutic pharmacological agents can be used in the inventive method. Suitable Agents are the ones that are Solar Sonic Infusion-ably accessible and compatible to the patient's present condition and needs. Solar Sonic Laboratories have systematically divided the most suitable therapeutic pharmacological agents to be intravenously infused into all cancer patients into Seven Substantial Group List (SSGL), each group represents certain types of cancer. There are also Chemical Common Denominators (CCD) which trigger Intra-Cellular/Extra-Cellular Cross-Links Communications of endless physiological connectivity matrix. Within the Seven Substantial Group List, Solar Sonic Technologies provide absolute cancer cure. Natural tissues are composed of functionally diverse cell types that are organized in spatially complex arrangements. Organogenesis of complex tissues requires a coordinated sequential transformation process, with individual stages involving time-dependent expression of cell-cell, cell-matrix, and cell-signal interactions in three dimensions.

The common theme of temporal-spatial patterning of these cellular interactions is also observed in other physiological processes, such as growth, development, wound healing, and tumor migration. The "precursor tissue analog" (PTA) applies the temporal-spatial patterning theme to tissue engineering. The goal of PTA in tissue engineering is not to fabricate the final transplantable tissue but rather to guide the dynamic organization, maturation, and remodeling leading to the formation of normal and functional tissues. We show the critical design principles of PTA. Structural, mechanical, physiological requirements of the PTA as a temporary scaffold must be met by a fabrication method with flexibility. The fabrication incorporating biological materials like living cells/plasmid DNA has been addressed. Second, the PTA concept is considered suitable for future tissue engineering and the use of undifferentiated stem cells, and may possess a capability.

Solar Sonic Technologies have perfected the science of Electromagnetically Bio-Chemical Intracellular and pathogenic communication and signaling, to the extent that we can affect intracellular and pathogenic programming, signaling, Pathogenic communication and manipulation leading to Homeostasis or Apoptosis.

Fiber-Optic Micro-needle is utilized with Solar Sonic Cancer Cure Device to deliver pharmacologically infused composition or for the swift delivery of advanced Nano-particles or entertaining as such Solar Sonic DNA and Cell Reprogramming Via Epigenetic Information swiftly Delivered by Magnetic Fields, Sound Vibration and Coherent Hydrogen Molecules.

Solar Sonic Laser Needles and pulsed electromagnetic fields for the administration of the SSF Therapeutic Infusion Composition Protocols for the absolute eradication of carcinogenic cells, intracellular/pathogenic Bio-communications, Bio-restoration and regenerative human physiology via SSF Paranormal Homeostasis and Induced Apoptosis.

Solar Sonic Therapeutic Infusion Medical Device chemically promotes Pulsed Suppression of Mitochondria-K<sup>+</sup> Channel Axis in Cancer, Inducing Apoptosis and Inhibiting Cancer Growth. Solar Sonic Curative Cancer Medical Device, is proven to work reproducibly as a Super Hi-Tech Solar Sonic Multidimensional Medical Science of the Paranormal Cellular/Pathogenic Bio-Signaling Communications and Programming Technology, the medical device converts Multi-Drug Components from Cytotoxic to Antitoxic. Solar Sonic Cancer Immunization and Vaccination via SSQF Paranormal Homeostasis of Promoting Cytostasis, Impairing Mitosis, inducing of Intracellular and Pathogenic Programmable Bio-Communications, Inducing Apoptosis, Inducing Signaling and Bio-Chemical Infusion via Intravenously Infused Chemical Reformulation with other SSQF Supporting Applications.

### **Principal Claims of the invention**

Defeating Cancer by Promoting Cytostasis, Infuse Cytochrome C-Protein, Program T-Lymphocyte / T-Cells, B-Lymphocyte/B-Cells, Thymus Gland and Inducing Apoptosis. This is beyond Science and Paranormal Bio-Manipulations and Alien Communications Technology where all Cells and pathogens are simultaneously stimulated for instant Bio-Signaling Communication, Apoptosis, Restoration and Homeostasis. Solar Sonic Cytotoxic Effects, physiological carcinogenicity and the overall toxicity are being extracted out of the patient's own pores through the feet via a Solar Sonic Ionic Bio-Cleanse. That occurs while the medical device conducting a Hyperthermia Therapeutic Infusion within the tumor and Intracellular/Pathogenic Bio-Signaling Communications with Cancer Cells.

Solar Sonic Laser Needles and pulsed electromagnetic fields are permeating for the administration of the SSF Therapeutic Infusion Composition Protocols for the eradication of carcinogenic cells. The intracellular and pathogenic Bio-communications, and regenerative human physiology via SSF Paranormal Homeostasis and Induced Apoptosis are leading the way in combating pathogens. Solar Sonic Therapeutic Infusion Medical Device Electrochemically promotes Pulsed Suppression of Mitochondria-K<sup>+</sup> Channel Axis in Cancer, Inducing Apoptosis and Inhibiting Cancer Growth.

The decision to turn on the production of either pro-oxidants or the anti-oxidants, is left to our native biological intelligence. It's really constant and delicate balance, all dependent upon cellular signaling and communications. If cells are intelligent indeed it would have major conceptual and medical implications. If cells are intelligent, we would have to rethink all the cause and effect chains from genes to molecules to cell functions that we somehow believe today to be true.

If cells are intelligent, molecules and their genes would be the collaborators or even slaves but not the masters of the life functions of cells. If cells are intelligent, medical treatment may involve 'talking to cells rather than to flood the organism with pharmaceuticals as we do today and they are intelligent. If cells respond to signals rather than to exogenous forces, the forces that keep or change the direction of their bodies must be controlled from within.

Solar Sonic Quantum Frequency Waves induce self- destruction of cells via Bio-signaling communications eradicating carcinogenic cells. Solar Sonic Curative Cancer Medical Device, is proven to work reproducibly as a Super Hi-Tech Solar Sonic Multidimensional Medical Science of the Paranormal Cellular/Pathogenic Bio-Signaling Communications & Programming Technology, the medical device converts Multi-Drug Components from Cytotoxic to Antitoxic.

### **Field of the invention**

Treatment of cancer has traditionally been approached through chemotherapy, coupled with radiotherapy for primary elimination of leukemias, neoplasms and tumors. In contrast, surgery has been used to remove solid tumors. Therapy involves both curative and palliative leading to cure and reduction of suffering of the Patient. Immunotherapeutic methods have also been found to be effective against a restrictive range of tumors of mesodermal origin suggesting that the immune system is capable of preventing or capable of delaying the growth of tumors in certain cases. Traditionally BCG vaccine is used for boosting of immunity of individuals with cancer. This has not been well accepted as a mode of therapy due to inconclusive results. The only accepted method of BCG is to use it for bladder cancer by way of intravesicular therapy. The disadvantage associated with use of BCG is practical development of systemic tuberculosis caused by BCG. This is related to the fact that BCG contain live organism and they can be pathogenic to immunocompromised host.

The present invention relates to a medical device especially designed to treat cancer patients with their various needs. The invention also relates to varied tumor treatment methods, the medical device with all of its accompanying therapeutic infusion composition and other supporting capabilities can be used in oncology for the treatment of primary and metastatic tumors. The medical device and the infusion composition are specifically designed to positively interact in all treatments related to cancer, either early or late stages, metastasis & malignancies.

The present invention relates to the design and generation of dendritic cell-based, in vivo antigen targeting vaccines for therapy of cancer, such as multiple myeloma. In preferred embodiments the vaccines are generated by the SSQFV method, in which effector moieties are attached to anchoring domain, derived from AKAP proteins and dimerization and docking domain moieties derived from protein kinase A (PKA). SSQFV complexes are generated when dimerization and docking domain moieties spontaneously dimerize and bind to an anchoring domain moiety, resulting in a complex with a 2:1 stoichiometry between-linked effectors.

In more preferred embodiments, the effector moieties comprise a humanized anti-CD74 antibody and a tumor-associated xenoantigen, such as a CD20 xenoantigen. In most preferred embodiments, the anti-CD74 antibody is an hLL1 antibody. The SSQFV/CC constructs are of use for preparation of pharmaceutical compositions, for generation of chemical complex against cancers, such as multiple myeloma (MM), and for induction of an immune response against tumor antigen-expressing cells, such as CD20 positive cancer cells in patients with multiple myeloma or other CD20-expressing cancers.

The present invention also relates to the a process for treating a biological organism in which a cell cycle arresting drug is administered to the organism to produce synchronized cells, optionally the microtubules within the synchronized cells are stabilized by means of microtubule stabilizing agent & synchronized cells with the optionally stabilized microtubules are then contacted with mechanical vibrational energy, such as ultrasound energy. Multiple myeloma (MM) is a hematological malignancy characterized by clonal proliferation of neoplastic plasma cells in the bone marrow. Although responsive to many chemotherapeutic agents, MM remains largely incurable and the majority of patients ultimately relapse.

Recently, a small population of clonotypic B cells, that do not express the characteristic plasma cell surface antigen CD138 but do express the B cell antigen CD20, was identified from both MM cell lines and primary bone marrow of MM patients. This small population of cells is resistant to multiple clinical anti-myeloma drugs and is capable of clonogenic growth in a 3-D culture model and is capable of differentiation into MM cells in vitro and in engrafted NOD/SCID mice during both primary and secondary transplantation. It has been suggested that these CD138<sup>neg</sup>CD20<sup>+</sup> cells represent the putative multiple myeloma cancer stem cells.

Like other cancer stem cells, MM cancer stem cells are refractory to multiple chemotherapeutic drugs and responsible for tumor re-growth and relapse. Strategies and approaches that could selectively target and eradicate cancer stem cells, such as MM stem cells, are needed. Due to the multiple drug resistance in cancer stem cells, immunotherapy and vaccination may offer a potential modality to eradicate these cells, particularly after standard therapies and/or stem cell transplantation, the time when tumor load is greatly reduced.

A need exists for effective compositions and methods of immunotherapy and vaccination targeted to treatment of multiple myeloma, particularly those capable of inducing an immune response against and inhibiting or eradicating MM cancer stem cells. A further need exists for effective compositions and methods of immunotherapy and vaccination targeted to treatment of cancers in general. The present invention also relates to the field of immunotherapy for cancers, and more particularly to monoclonal antibodies which specifically target an epitope expressed on cancer cells.

Cancer is a class of diseases which occurs because cells become immortalized; they fail to heed customary signals to turn off growth which is a normal function of remodeling in the body that requires cells to die on cue. Apoptosis or programmed cell death, can become defective, when this happens malignant transformation can take place. The immortalized cells grow beyond their normal limits and invade adjacent tissues. The malignant cells may also metastasize and spread to other locations in the body via the bloodstream or lymphatic system. Cancer cells often form a mass known as a tumor.

There are about 200 different types of cancer; the cancers can start in any type of body tissue although many cancers will metastasize into other body tissues. There are many different causes of cancer and these include; carcinogens, age, genetic mutations, immune system problems, diet, weight, lifestyle, environmental factors such as pollutants, some viruses for example the human papilloma virus (HPV) is implicated in cervical cancer and some bacterial infections are also known to cause cancers. There are many different treatment options for cancer and the treatment sought is often determined by the type and stage of the cancer.

Treatment options include; chemotherapeutic drug treatment, hormonal drug treatment, radiotherapy, surgery, complementary therapies and combinations thereof. Prostate cancer is the most common type of cancer in men and accounts for 24% of all UK male cancers. In 2006 there were over 35,000 new cases of prostate cancer diagnosed in the UK alone. The prostate is a gland in the male reproductive system and symptoms of cancer in the prostate can include pain, difficulty urinating, problems with sexual intercourse and erectile dysfunction. Prostate cancer may metastasize to the bones and or lymph nodes. Treatment options for prostate cancer include surgery, radiation therapy, and Chemotherapy and hormone treatment.

Hormone treatment usually involves treatment with an anti-androgen such as cyproterone acetate, flutamide or bicalutamide, either alone or in combination with a chemotherapeutic agent. These treatments work to stop the production of testosterone (androgen) which can slow down tumor growth or even shrink the tumor.

While the prostate cancer cells are responding to anti-androgens, they are referred to as 'hormone-sensitive' prostate cancer. Unfortunately, after a few years of treatment with anti-androgens the prostate cancer stops responding to hormone treatment and is termed 'hormone-insensitive' prostate cancer, and at this stage the cancer growth cannot be controlled by the hormone treatment.

In order to test the effectiveness of different compounds in the treatment of either hormone-sensitive or hormone-insensitive prostate cancer two different cell lines can be used. The cell line LNCaP is hormone-sensitive prostate cancer cells which were derived from a supraclavicular lymph node metastasis in a 50 year.

The cell line DU-145 is hormone-insensitive prostate cancer cells which were derived from a brain metastasis. It is known that expression levels of both cannabinoid receptors, CB1 and CB2, were significantly higher in CA-human papillomavirus-10 (virally transformed cells derived from adeno-carcinoma of human prostate tissue), and other human prostate cells LNCaP, DU-145, PC3, and CWR22RN1 than in human prostate epithelial and PZ-HPV-7 (virally transformed cells derived from normal human prostate tissue) cells.

Additionally it is known that WIN-55,212-2 (mixed CB1/CB2 agonist) treatment with hormone sensitive LNCaP cells resulted in a dose- (1-10 Mmol/L) and time-dependent (24-48 hours) inhibition of cell growth. Blocking of CB1 and CB2 receptors by their antagonists SR141716 (CB1) and SR144528 (CB2) significantly prevented this effect.

These results suggested that WIN-55,212-2 or other cannabinoid receptor agonists could be developed as novel therapeutic agents for the treatment of prostate cancer. Cannabis has been ascribed to be both a carcinogen and anti-cancer agent. In particular smoking cannabis is known to be carcinogenic as the cannabis smoke contains at least 50 different known carcinogenic compounds, many of which are the same substances found in smoked tobacco. One of these carcinogens, benzopyrene is known to cause cancer as it alters a gene called p53, which is a tumor suppressor gene. Cannabis contains the substance tetrahydrocannabinol (THC) which has been shown to cause benzopyrene to promote the p53 gene to change. Researchers however have discovered that some cannabinoids, including THC and cannabidiol (CBD) are able to promote re-emergence of apoptosis so that some tumors will heed the signals, stop dividing, and die. The process of apoptosis is judged by observation of several phenomena including: reduced cellular volume, condensation of nuclear chromatin, changes in distribution of phospholipids in plasma membrane phospholipids, and cleavage of chromatin into DNA fragments called DNA ladders. Another method by which tumours grow is by ensuring that they are nourished: they send out signals to promote angiogenesis, the growth of new blood vessels.

Cannabinoids may turn off these signals as well. Cannabinoids have been shown to have an anti-proliferative effect on different cancer cell lines. The cannabinoids THC, THCA, CBD, CBDA, CBG and CBC and the cannabinoid BDS THC and CBD were tested on eight different cell lines including DU-145 (hormone-sensitive prostate cancer), MDA-MB-231 (breastcancer), CaCo-2 (colorectal cancer) and C6 (glioma cells).

The data for each cannabinoid in each different type of cancer varied but generally the best data were observed with CBD or CBD BDS. The IC50 values for all the cannabinoids on the DU-145 were quite high inferring that none of the cannabinoids tested were particularly effective in the inhibition of hormone-insensitive prostate cancer. Several transient receptor potential (TRP) channels have been implicated in survival, growth and spread of prostate and other cancers. TRPM8 is expressed in sensory neurons, where it responds to cold and to cooling agents, notably menthol, but it is also abundantly expressed in the prostate. In particular TRPM8 is over-expressed in hormone-sensitive prostate cancer cells, expression of TRPM8 is almost completely ablated once the cancer becomes hormone-insensitive and in patients receiving anti-androgen therapy. Expression of TRPM8 is stimulated by androgens in hormone-sensitive prostate cancer cell lines (LNCaP). There is evidence that expression of TRPM8 is required for survival of prostate cancer cells. The mechanism of such an action of TRPM8 is likely to relate to its ability to modulate intracellular calcium, and possibly even the distribution of calcium within the cell. The latter point may be important because of the localization of TRPM8 in the prostate cancer cell.

While found on the cell membrane, it is also found on the endoplasmic reticulum; thus any potential therapeutic agent which targets the TRPM8 receptor must be able to gain good access to the intracellular space. The endogenous cannabinoid anandamide has been shown to antagonise TRPM8. The authors also showed stimulation of CB1 receptors transiently antagonised TRPM8 receptors expressed on the same cells.

Different binding potentials of the cannabinoid-containing plant extracts at the TRPA1 and TRPM8 channels are described. The diseases/conditions to be prevented or treated include: neuropathic pain, inflammation, vasoconstriction or cancer. The TRPM8 receptor has also been found in breast, colon and skin cancers. It has been shown that CBD is able to down-regulate the expression of the DNA binding protein inhibitor, Id-1 in human breast cancer cells. The CBD concentrations effective at inhibiting Id-1 expression correlated with those used to inhibit the proliferative and invasive phenotype of breast cancer cells. CBD was able to inhibit Id-1 expression at the mRNA and protein level in a concentration-dependent fashion. CBD has also been shown to inhibit human cancer cell proliferation and invasion through differential modulation of the ERK and ROS pathways and that sustained activation of the ERK pathway leads to down-regulation of Id-1 expression. It was also demonstrated that CBD up-regulates the pro-differentiation agent, Id-2.

Using a mouse 4T1 cell line and a model of metastatic breast cancer, CBD significantly reduced metastatic spread. As such CBD may represent a promising treatment of breast cancer in patients with secondary tumours. Recent evidence indicates that CBD is a GPR55 antagonist; this raises the possibility that this receptor may underlie the effects of CBD on breast and other tumour cells. GPR55 couples to G12/13 and the downstream activation of the RhoA, rac1 and cdc42 small GTPases; this pathway is crucial in cytoskeletal reorganisation and cell migration. Increased G12/13 expression has been found in early stage human breast cancer cells taken by biopsy and inhibition of G13 decreases the level of breast cancer cell metastasis in vivo. The anti-proliferative effects of CBD have also been evaluated on U87 and U373 human glioma cell lines. The anti-proliferative effect of CBD was correlated to induction of apoptosis, as determined by cytofluorimetric analysis and single-strand DNA staining, which was not reverted by cannabinoid antagonists. In addition CBD, administered s.c. to nude mice at the dose of 0.5 mg/mouse, significantly inhibited the growth of subcutaneously implanted U87 human glioma cells.

It was concluded that CBD was able to produce a significant anti-tumour activity both in vitro and in vivo, thus suggesting a possible application of CBD as a chemotherapeutic agent. CBD caused a concentration-dependent inhibition of the migration of U87 glioma cells, quantified in a Boyden chamber. Since these cells express both cannabinoid CB1 and CB2 receptors in the membrane, the group also evaluated their engagement in the anti-migratory effect of CBD.

Cannabinoids have been shown to play a fundamental role in the control of cell survival / cell death. It has been reported cannabinoids may induce proliferation, growth arrest, or apoptosis in a number of cells, including neurons, lymphocytes, and various transformed Neural and non-neural cells, and that cannabinoids induce apoptosis of glioma cells in culture and regression of malignant gliomas in vivo.

A pilot clinical study of THC in patients with recurrent glioblastoma multiforme has been conducted. This pilot phase I trial consisted of nine patients with recurrent glioblastoma multiforme who were administered THC intra-tumourally. The patients had previously failed standard therapy (surgery and radiotherapy) and had clear evidence of tumor progression. The primary end point of the study was to determine the safety of intracranial THC administration. They also evaluated THC action on the length of survival and various tumour-cell parameters. Median survival of the cohort from the beginning of cannabinoid administration was 24 weeks (95% confidence interval).

In particular the cancer to be treated is a brain tumour, more particularly a glioma; more particularly still a glioblastoma multiforme (GBM). The non- cannabinoid chemotherapeutic agent may be a selective estrogen receptor modulator or an alkylating agent. The literature and corresponding patent applications demonstrate the general usefulness of cannabinoids in the area of cancer research and treatment.

It is an object of the present invention to find improved and / or alternative cancer therapies. To this end a platform of data representing the use of isolated phytocannabinoids and phytocannabinoid botanical drug substances (BDS) in different aspects of the treatment of cancer is provided and the results extrapolated to identify groups of phytocannabinoids, whether isolated or in the form of a BDS, which appear more promising than others in specific treatments.

These results suggest that electroporation may provide a feasible method for the transfection of genetic material into living cells in tissue. The use of electroporation therapy for the transmembrane delivery of therapeutic substances is dependent on achieving two necessary and sufficient conditions in the region to be treated:

(I). Adequate concentration of therapeutic substance must be present in the extracellular space, and  
(II). Threshold level electrical fields must be generated throughout the target tissue. While a significant amount of research has been performed demonstrating the utility of electroporation in the treatment of various animal and human tumor models. There is limited understanding regarding the best methods for the clinical application of electroporation therapy. In the field of cancer treatment, delivery of therapeutic substances is made more difficult by the anatomical characteristics of solid tumors such as non

uniform vasculature and high interstitial pressure. These properties make it difficult to achieve uniform, high concentrations of therapeutic substances within the tumor. The tortuous, non-uniform vasculature prevents blood borne substances from reaching all parts of the tumor. Due to high interstitial pressures, maintaining the necessary concentrations of drug within the tumor is also difficult, because this pressure gradient causes substances to be forced back into the vasculature or carried by convection to the exterior of the tumor. The nature of current chemotherapeutic drugs also limits their effectiveness. While administration of drugs into the vasculature provides excellent distribution, systemic dosages of therapeutic substances are limited by their toxic side effects.

Therefore, a higher concentration of therapeutic substance cannot be achieved simply by increasing the systemic dosage, without serious risk of harm to the patient. Given the problematic nature of delivering high levels of therapeutic substance to solid tumors, electroporation therapy seems well suited to the treatment of these cancers.

However, methods must be employed to ensure that sufficient levels of therapeutic substance is present in the interstitial space when the permeabilizing pulses are delivered.

Because membrane permeability occurs as a result of exposing a cell to threshold level electric field strengths, an electroporation therapy is dependent on propagating these fields throughout a target region of tissue and allowing concentrations of the desired substances to accumulate intracellularly.

Thus, it is considered desirable to provide a means for increasing the amount of therapeutic substance which accumulates in the cells of electroporated tissue.

### **Disclosure of the Invention**

The invention provides methods to facilitate the intracellular delivery of substances via electroporation. In particular, these methods can be applied to improve benefit derived from the application of electroporation therapy to diseased tissue. The invention provides for delivering a therapeutic substance to a predetermined location in a patient comprising providing a therapeutic substance to a patient in need of the substance, establishing an electrical field which encompasses a predetermined region of tissue within the patient.

Exposing the tissue to the electrical field for a time and under conditions sufficient to permit the permeation of the substance across the cell membranes of cells located within the region of tissue, and contacting the tissue with at least one agent which is capable of prolonging the permeability of the cell membranes in the tissue exposed to the electrical field. Use of the invention facilitates the transport of certain therapeutic substances to their site of action, inside the cell. Even under unfavorable conditions, such as low concentrations of therapeutic substance within the target tissue and substance with a large or irregularly shaped molecular structure, the present techniques can be effective in the delivery of therapeutic substances.

In one aspect, this invention provides a method for the concentration of therapeutic substances within a diseased region of tissue. Utilization of this technique improves the efficacy of electroporation mediated delivery while minimizing side effects associated with the administration of cytotoxic substances. A further aspect of this invention provides a method for the use of substances capable of prolonging the permeabilized state of the cell membrane, dramatically improving the intracellular delivery of therapeutic substances.

Electro-poration, or electro-permeabilization, is a significant increase in the electrical conductivity and permeability of the cell plasma membrane caused by an externally applied electrical field. It is usually used in molecular biology as a way of introducing some substance into a cell, such as loading it with a molecular probe, a drug that can change the cell's function, or a piece of coding DNA. Electroporation is a dynamic phenomenon that depends on the local trans-membrane voltage at each point on the cell membrane. It is generally accepted that for a given pulse duration and shape, a specific transmembrane voltage threshold exists for the manifestation of the electroporation phenomenon (from 0.5 V to 1 V). This leads to the definition of an electric field magnitude threshold for electroporation ( $E_{th}$ ).

That is, only the cells within areas where  $E \geq E_{th}$  are electroporated. If a second threshold ( $E_{ir}$ ) is reached or surpassed, electroporation will compromise the viability of the cells, irreversible electroporation (IRE). In molecular biology, the process of electroporation is often used for the transformation of bacteria, yeast, and plant protoplasts. In addition to the lipid membranes, bacteria also have cell walls which are different from the lipid membranes and are made of peptidoglycan and its derivatives.

However, the walls are naturally porous and only act as stiff shells that protect bacteria from severe environmental impacts. If bacteria and plasmids are mixed together, the plasmids can be transferred into the cell after electroporation. Several hundred volts across a distance of several millimeters are typically used in this process.

Afterwards, the cells have to be handled carefully until they have had a chance to divide producing new cells that contain Reproduced plasmids; this process is approximately ten times as effective as chemical transformation. This procedure is also highly efficient for the introduction of foreign genes in tissue culture cells, especially mammalian cells.

For example, it is used in the process of producing knockout mice, as well as in tumor treatment, gene therapy, and cell-based therapy. The process of introducing foreign DNAs into eukaryotic cells is known as transfection. Electroporation is highly effective for transfecting cells in suspension using electroporation cuvettes. Electroporation has proven efficient for use on tissues in vivo, for in utero applications as well as in ovo transfection. Adherent cells can also be transfected using electroporation, providing researchers with an alternative to trypsinizing their cells prior to transfection.

### **Description of the Invention**

Antibody for targeted induction of Apoptosis, CDC & ADCC mediated killing of Cancer Cells, TBL-CLN1"FD2LD of invention. The present invention relates to the field of immunotherapy for cancers, and more particularly to monoclonal antibodies which specifically target an epitope expressed on cancer cells.

Solar Sonic Curative Cancer Medical Device, is proven to work reproducibly as a Super Hi-Tech Solar Sonic Multidimensional Medical Science of the Paranormal Cellular/Pathogenic Bio-Signaling Communications & Programming Technology, the medical device converts Multi-Drug Components from Cytotoxic to Antitoxic.

Defeating Cancer by Promoting Cytostasis, Impairing Mitosis, Infusing Cytochrome C-Protein, Programming T-Lymphocyte/T-Cells, B-Lymphocyte/B-Cell, Thymus Gland & Inducing Apoptosis. Solar Sonic Cancer Immunization and Vaccination via SSQF Paranormal Homeostasis of Promoting Cytostasis, Impairing Mitosis, the inducing of Intracellular / Pathogenic Programmable Bio-Communications, Inducing Apoptosis, Inducing Signaling & Bio-Chemical Infusion via Intravenously Infused Chemical Reformulation with other SSQF Supporting Applications.

Solar Sonic Quantum Frequency Waves inducing self- destruction of cells via Bio-signaling communications eradicating carcinogenic cells. Pharmaceutically Infused Antineoplastic Intravenous Therapeutic Composition with various Solar Sonic applications, forming a medical device as Cancer Cure. Solar Sonic Antineoplastic Medical Device, supported by an electromagnetically infused pharmaceutical composition for Intracellular/Pathogenic Infusion Therapy.

Cancer Paranormal Solar Sonic Homeostasis and Induced Apoptosis via chemically stimulated Intracellular and Pathogenic Bio-Signaling Communications with the Intravenous therapy of electromagnetically infused (SSQFIT) Composition, in conjunction with other varied Hi-Tech supporting applications which are systematically operated through a technologically superior Medical Device, geared up towards Regenerative Physiological Restorations and Hi-Tech Disease Management Capabilities that accommodate all types of different patients and their needs.

## Background of the Invention

Important breakthroughs in cancer therapy include clinical application of antibodies. The therapeutic strategy relies on the deliberate and selective induction of apoptosis or killing by antibody-dependent cell-mediated cytotoxicity (hereinafter referred to as ADCC) and complement-dependent cytotoxicity (hereinafter referred to as CDC) of malignant cells. Importantly, therapy-resistance in cancer is frequently associated with de-regulation in the mechanisms that control apoptosis. However, cancer cells are often reliant on these molecular aberrations for survival. Therefore, selective induction of apoptosis, CDC and ADCC in cancer cells but not normal cells is a challenge to be addressed. Induction of apoptosis in tumor cells by tumor necrosis factor [TNF]-related apoptosis-inducing ligand (hereinafter referred to as TRAIL) is a promising therapeutic principle in oncology. Programmed cell death, known as apoptosis, is an essential cellular homeostasis mechanism that ensures correct development and function of multi-cellular organisms.

The pivotal importance of correct execution of apoptosis is apparent from the many human diseases with aberrancies in apoptosis, including cancer. One possible treatment for cancer involves monoclonal antibodies (mAb) that bind only to cancer cell-specific antigens and induce an immunological response against the target cancer cell. Such mAb could also be modified for delivery of a toxin, radioisotope, cytokine or other active conjugate. It is also possible to design bispecific antibodies that can bind with their fragment antigen binding (hereinafter referred to as Fab) regions both to target antigen and to a conjugate or effector cell.

Monoclonal antibody drugs are a relatively new innovation in cancer treatment. While several Monoclonal antibody drugs are available for treating certain cancers, the best way to use these new drugs isn't always clear. The immune system attacks foreign invaders in our body, but it doesn't always recognize cancer cells as enemies. A monoclonal antibody can be directed to attach to certain parts of a cancer cell. In this way, the antibody marks the cancer cell and makes it easier for the immune system to find. Monoclonal antibody developed to the specific cancer cell surface target can kill the cell with or without toxin attached just by binding to cell surface target.

The antibody can initiate lysis of the cancer cell through apoptosis, CDC and ADCC. Monoclonal antibody therapy can be used to destroy malignant tumor cells and prevent tumor growth by blocking specific cell receptors or by delivering a conjugated toxin. There is a need for an antibody which can selectively target and induce killing of cancer cells. Paclitaxel is a complex diterpenoid that is widely used as an anti-mitotic agent; it consists of a bulky, fused ring system and an extended side chain that is required for its activity.

“Taxane Anticancer Agents: Basic Science and Current Status,” The aqueous solubility of paclitaxel is relatively low, estimates of paclitaxel solubility vary widely, ranging from about 30 micrograms per milliliter and about 7 micrograms per milliliter to less than 0.7 micrograms per milliliter. The molecular weight of paclitaxel is in excess of 700; this relatively high molecular weight is one factor according to the well-known “rule of 5,” contributes to paclitaxel poor water solubility. It is an object of this invention to provide such an agent, in particular, and in one embodiment, it is an object of this to provide a magnetic anti-mitotic composition that can be directed to be more toxic to cancer cells than normal cells.

Furthermore, and in another embodiment, it is another object of this invention to provide a delivery system that will provide a chemotherapeutic agent at a high concentration for a sustained period of time but not at such a high concentration that a substantial number of normal cells are injured beyond repair. It is yet another object of this invention to provide a process for treating a biological organism in which the water soluble anti-mitotic agent may be used to both synchronize certain cells and immobilize the microtubules within such cells. Important breakthroughs in cancer therapy include clinical application of antibodies. The therapeutic strategy relies on the deliberate and selective induction of apoptosis or killing by ADCC and CDC of malignant cells. Importantly, therapy-resistance in cancer is frequently associated with de-regulation in the mechanisms that control apoptosis. However, cancer cells are often reliant on these molecular aberrations for survival. Therefore, selective induction of apoptosis, CDC and ADCC in cancer cells but not normal cells is a challenge to be addressed.

Induction of apoptosis in tumor cells by TRAIL (tumor necrosis factor) related apoptosis-inducing ligand) is a promising therapeutic principle in oncology. Programmed cell death, known as apoptosis, is an essential cellular homeostasis mechanism that ensures correct development and function of multi-cellular organisms. The pivotal importance of correct execution of apoptosis is apparent from the many human diseases with aberrancies in apoptosis, including cancer. One possible treatment for cancer involves monoclonal antibodies (mAb) that bind only to cancer cell-specific antigens and induce an immunological response against the target cancer cell. Such mAb could, also be modified for delivery of a toxin, radioisotope, cytokine or other active conjugate. It is also possible to design bispecific antibodies that can bind with their Fab regions both to target antigen and to a conjugate or effector cell. Monoclonal antibody drugs are a relatively new innovation in cancer treatment. While several monoclonal antibody drugs are available for treating certain cancers, the best way to use these new drugs isn't always clear.

The immune system attacks foreign invaders in our body, but it doesn't always recognize cancer cells as 2011/000133 enemies. A monoclonal antibody can be directed to attach to certain parts of a cancer cell. In this way, the antibody marks the cancer cell and makes it easier for the immune system to find. Monoclonal antibody developed to the specific cancer cell surface target can kill the cell with or without toxin attached by binding to cell surface target. The antibody can initiate lysis of the cancer cell through apoptosis, complement dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC). Monoclonal antibody therapy can be used to destroy malignant tumor cells and prevent tumor growth by blocking specific cell receptors or by delivering a conjugated toxin. There is needs for an antibody which can selectively target and induce killing of cancer cells. At present the principal tumor treatment methods include surgical, chemotherapeutic, and radiation approaches. Surgical approach is efficient in cases of early diagnosis and smaller tumors without remote metastases. Large, advanced tumors may be removed only in rare cases, and this approach is often impossible.

The preferred method of conservative treatment of malignant tumors includes selective chemotherapy performed by injection of antitumor preparations into the blood vessels that supply the tumor, or directly into the tumor tissue or peritumoral region. Known in the art is the method of treatment of malignant kidney tumors including chemoembolization of arterial network of the diseased kidney using an oil solution containing 100 mg of the anticancer substance Dioxadet, followed by occlusion of the main branch of the renal artery by a metal coil. Such chemoembolization leads to a reliable increase in the corrected indices of 3- and 5-year cumulative survival in patients with inoperable cancer of kidney parenchyma to  $33.0 \pm 6.9\%$  and  $24.5 \pm 6.75\%$  respectively, in comparison with the convenient embolization methods without a chemotherapeutic component, where these indices are  $10.6 \pm 4.2\%$  and  $0\%$ .

However, gradually increasing intoxication caused by tumor decomposition sharply aggravates the patient's condition. Besides this, along with the tumor degradation products, tumor cellular elements are liberated into The venal bloodstream and lymphatic system, and may cause metastases. Known in the art is a method of treatment of malignant liver tumors which includes embolization of the hepatic artery by a metal coil after the injection of Dioxadet (30-50 mg) dissolved in 6-9 ml of Myodil into its arterial branches.

Intra-arterial infusion of chemo-therapeutic agents provides better results as compared to intraportal infusion, since malignant tumors of the liver are supplied mainly by the arterial blood system. Therefore the intra-arterial injection received wider application. According to the inventors' data, remissions last up to 6-8 months, and one-year survival in patients with unresectable malignant tumors was 56.2%. The duration of remissions reported in the world medical literature for selective chemotherapy is 4-12 months. Anticancer substances are known to be toxic, especially when used systemically.

The use of oil solutions somewhat reduces the general intoxication of the body due to retarded supply of a chemotherapeutic agent from an oil into tissues around the tumor. However, in spite of this fact, the decomposition of tumor tissue induced by chemotherapeutics, especially in bulky tumors, leads to sufficiently high intoxication and therefore worsens the general condition of a patient. Localization of an oil solution of chemotherapeutic agent in the tumor tissue for a period of 20-25 days often proves insufficient for the complete death of tumor cells. This disadvantage is further increased by the fact that oil solution eventually dissipates from the tumor. It brings about the need of repetitive intraorganous injections of a preparation

and, as a consequence, yet more increase of intoxication. Known in the art is also a method of treatment of hepatomas by chemoembolization using ferromagnetic particles followed by hyperthermia. Chemotherapeutic agent is administered into hepatic artery within the mixture containing a solution of carboxymethylcellulose or dextrane in a saline aqueous medium, and magnetically soft substance, metal iron, in the form of particles 30-50  $\mu\text{m}$  in size.

The composition is confined within the tumor area by a local magnetic field. Hyperthermia is performed by induction heating of the magnetic particles. However, the large size of particles necessary for efficient induction heating (30-50  $\mu\text{m}$ ) causes occlusion of the precapillary zone of the tumor. Therefore the prerequisites are created for preservation of viable parts of the tumor. Magnetically soft material may migrate out of the tumor area and dissipate in the course of tumor degradation. This phenomenon may lead to undesirable micro-embolizations. The use of water-based solutions of chemotherapeutic agents is known to provide a less pronounced prolongation effect because of the faster diffusion into tissues with consequent washing out of the organ. This process is increased by preserved organ blood flow.

The dissipation of ferromagnetic from the tumor area is inconvenient for monitoring the tumor in remote periods and excludes the possibility of repeated hyperthermia procedures that may prove necessary. All said reasons increase probability of the tumor recurrence. Known in the art is also the experimentally tested method of reduction of the tumor mass, based on the delivery into a tumor of magnetically hard ferromagnetic material using magnetic field, with consequent heating of the tumor at the expense of heat emitted by this ferromagnetic when placed into low-frequency oscillating electromagnetic field. However, the said method employs heat treatment of a tumor alone, which, as evidenced by many reported data, is insufficient for complete necrosis and death of tumor cells. Therefore, none of the known methods can provide necrosis of the tumor lesion without considerable intoxication and the risk of metastatic off spread.

### **Object of the Invention**

The principal object of this invention is to provide a method for targeted and selective killing of cancer cells, wherein the killing' may be induced by apoptosis, ADCC and CDC of cancer cells. Another object of the invention is to provide a method for selective elimination of cancer cells without affecting the normal cell, population.

### **Summary of the invention**

It is therefore the main objective of the present invention to reduce the probability of recurrence of a tumor and of the off spread of metastases. Another objective of the invention is to reduce systemic toxicity of the treatment. The main and other objectives are achieved by the method for tumor treatment which involves first catheterization of the vessel that supplies a tumor of interest. Then, a suspension of a magnetically hard ferromagnetic substance in an oil solution of oil-soluble antitumor agent is injected through the catheter under fluoroscopic control and, at the same time, local magnetic field is applied onto the tumor-bearing area.

After 1-3 days the tumor is subjected to oscillating power field selected from ultrahigh radio frequency electromagnetic field and the field of ultrasonic contraction waves until the temperature of 43.0°-43.5° C. is reached within the tumor, this temperature is maintained for 5-45 minutes. In cases of large size tumors it is preferable, according to the invention, to reduce the blood flow in the tumor-feeding blood vessel after the administration thereto of the said suspension.

The magnetically hard ferromagnetic substance preferably includes non-toxic non-corrosive iron containing material such as strontium hexaferrite ( $\text{SrO} \cdot 6\text{Fe}_2\text{O}_3$ ) in the form of particles 0.5-7  $\mu\text{m}$  in size, which allow the ferromagnetic to penetrate also into capillary part of a tumor vasculature. According to the invention, the application of local magnetic field serves not only to confine the embolization within the tumor area, but also to form a compact, porous body of the ferromagnetic particles held together by magnetic forces, owing to the high residual magnetism of the hard ferromagnetic material. Such a compact magnetic system can withstand considerable hydrostatic pressure and provides reliable retention of the liquid phase of the

embolizate within the tumor vasculature for a long time, without recanalization and dissipation of both ferromagnetic and liquid phase throughout the body. Therefore the antitumor agent is uniformly distributed within the tumor, while its systemic concentration is strongly reduced, and therapeutic index is improved. This advantage is supported by the delivery of the antitumor agent in the form of an oil solution which is better retained within the embolizate due to its Immiscibility with tissue and body fluids. Thus, the stability of embolizate within the whole tumor-feeding vasculature in combination with prolonged chemotherapy and hyperthermia of a tumor reduces the proportion of viable tumor cells, prevents their migration outside the embolized area and therefore decreases the metastatic off spread.

The antitumor agent, as well as the products of tumor tissue degradation, are prevented from migration outside the tumor focus; therefore toxic effects of the antitumor chemotherapeutic agent and of the tumor degradation products are substantially reduced. In accordance with one embodiment of this invention, there is provided a process for treating a biological organism in which a cell cycle arresting drug is administered to the organism to produce synchronized cells, optionally the microtubules within the Synchronized cells are stabilized by means of a microtubule stabilizing agent, and the synchronized cells with the optionally stabilized microtubules are then contacted with mechanical vibrational energy.

The present invention also discloses methods and compositions for vaccines against cancer stem cells, such as MM stem cells, that are prepared using the SSQF method. The SSQF technique has been used to generate a variety of stable and defined complexes suitable for in vivo applications. In preferred embodiments, the SSQF complexes comprise an anti-CD74 antibody or antigen binding fragment thereof, such as the hLL1 antibody, attached to a dimerization and docking domain or anchor domain moiety. The dimerization and docking domain moieties spontaneously dimerize and each dimer binds to an anchoring domain moiety. In more preferred embodiments, a complementary moiety is attached to a CD20 xenoantigen, as described, resulting in formation of SSQF complexes comprising anti-CD74 moieties and CD20 xenoantigen moieties. However, the skilled artisan will realize that depending on the cancer, a different xenoantigen and/or antibody or antibody fragment may be utilized. The antibody component directs the SSQF complex to antigen presenting cells (APCs), such as dendritic cells (DCs), while the xenoantigen component is processed to invoke an immune response against cells expressing the target antigen.

The sequences of various CD20 xenoantigens suitable for use in the anti-cancer vaccine SSQF complex are known in the art, such as the murine CD20 sequence. Other CD20 amino acid sequences of potential use are readily available to the skilled artisan through well-known public databases as the NCBI protein database.

Although the murine CD20 sequence is recited herein, the skilled artisan will realize that CD20 amino acid sequences are known and readily available from a wide variety of species and can be incorporated into the anti-cancer vaccine SSQF complex. However, the skilled artisan will realize that other tumor-associated antigens (TAAs) are known in the art and may be utilized in the SSQF complexes to induce an immune response against tumors expressing different TAAs.

The skilled artisan will further realize that other known antibodies or antigen-binding fragments thereof may potentially be incorporated into the anti-cancer vaccine SSQFV constructs. In preferred embodiments, the Antibody binds to an antigen expressed by APCs, more preferably dendritic cells. A variety of antigens associated with dendritic cells are known in the art, including but not limited to CD209 (DC-SIGN), CD34, CD74, CD205, TLR 2, TLR 4, TLR 7, TLR 9, BDCA-2, BDCA-3, BDCA-4, and HLA-DR.

In preferred embodiments, the target antigen is CD74. However, other types of target antigen are known to be associated with dendritic cells and anti-cancer vaccine SSQF constructs incorporating antibodies that target any such alternative antigen may be utilized in the claimed methods and compositions. In some embodiments, the anti-cancer vaccine SSQF comprise an anti-CD74 antibody or antigen-binding fragment thereof and another anti-dendritic cell antibody or fragment. The use of chimeric antibodies is preferred because they possess human antibody constant region sequences and therefore do not elicit as strong a human anti-mouse antibody (HAMA) response as murine antibodies. The use of humanized antibodies is even more preferred, in order to further reduce the possibility of inducing a HAMA reaction. As discussed below, techniques for humanization of murine antibodies by replacing murine framework and constant region

sequences with corresponding human antibody framework and constant region sequences are well known in the art and have been applied to numerous murine anti-cancer antibodies. Antibody humanization may also involve the substitution of one or more human framework amino acid residues with the corresponding residues from the parent murine framework region sequences. As also discussed below, techniques for production of human antibodies are also well known and such antibodies may be incorporated into the subject anti-cancer vaccine constructs.

In certain embodiments, the anti-cancer vaccine SSQFV constructs may be administered in combination with at least one therapeutic agent administered before, simultaneously with or after the anti-cancer vaccine construct. In preferred embodiments, the therapeutic agent is administered before the anti-cancer vaccine.

However, in alternative embodiments, the therapeutic agent may be co-administered with or even conjugated to the SSQFV construct. Any therapeutic agent known in the art, as discussed in more detail below, may be utilized in conjunction with an anti-cancer vaccine SSQFV, including but not limited to radionuclides, immunomodulators, anti-angiogenic agents, cytokines, chemokines, growth factors, hormones, drugs, prodrugs, enzymes, oligonucleotides, siRNAs, pro-apoptotic agents, photoactive therapeutic agents, cytotoxic agents, chemotherapeutic agents, toxins, other antibodies or antigen binding fragments thereof.

In a preferred embodiment, the therapeutic agent is a cytotoxic agent, such as a drug or a toxin. Also preferred, the drug is selected from the group consisting of nitrogen mustards, ethylenimine derivatives, alkyl sulfonates, nitrosoureas, gemcitabine, triazines, folic acid analogs, anthracyclines, taxanes, COX-2 inhibitors, pyrimidine analogs, purine analogs, antibiotics, enzyme inhibitors, epipodophyllotoxins, coordination complexes, vinca alkaloids, substituted ureas, methyl hydrazine derivatives, adrenocortical suppressants, hormone antagonists, endostatin, taxols, camptothecins, SN-38, doxorubicins /analogs, Antimetabolites, alkylating agents, antimetotics, anti-angiogenic agents, tyrosine kinase inhibitors, mTOR inhibitors, heat shock protein (HSP90) inhibitors, proteasome inhibitors, HDAC inhibitors, pro-apoptotic agents, methotrexate, CPT-11, and a combination thereof.

In another preferred embodiment, the therapeutic agent is a toxin selected from the group consisting of ricin, abrin, alpha toxin, saporin, ribonuclease (RNase), DNase I, Staphylococcal enterotoxin-A, pokeweed antiviral protein, gelonin, diphtheria toxin, Pseudomonas exotoxin, and Pseudomonas endotoxin and combinations thereof, or an immunomodulator selected from the group consisting of a cytokine, a stem cell growth factor, a lymphotoxin, a hematopoietic factor, a colony stimulating factor (CSF), an interferon (IFN), a stem cell growth factor, erythropoietin, thrombopoietin and a combinations thereof.

In other embodiments the therapeutic agent is a photoactive therapeutic agent selected from the group consisting of chromogens and dyes. Alternatively, the therapeutic agent is an enzyme selected from the group consisting of malate dehydrogenase, staphylococcal nuclease, delta-V-steroid isomerase, yeast alcohol dehydrogenase, alpha-glycerophosphate dehydrogenase, triose phosphate isomerase, horseradish peroxidase, alkaline phosphatase, asparaginase, glucose oxidase, beta-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, glucoamylase and acetylcholinesterase.

Such enzymes may be used, for example, in combination with prodrugs that are administered in relatively non-toxic form and converted at the target site by the enzyme into a cytotoxic agent. In other alternatives, a drug may be converted into less toxic form by endogenous enzymes in the subject but may be reconverted into a cytotoxic form by the therapeutic enzyme.

Although in preferred embodiments, the anti-cancer vaccine SSQFV complexes are of use for therapy of multiple myeloma, the skilled artisan will realize that a CD20/anti-CD74 construct may potentially be of use for other types of diseases, such as other forms of CD20<sup>+</sup> cancer like B-cell lymphoma, B-cell leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, follicular lymphoma, mantle cell lymphoma, small lymphocytic lymphoma, diffuse B-cell lymphoma, marginal zone lymphoma, Burkitt lymphoma, Hodgkin's lymphoma or non-Hodgkin's lymphoma.

Where a tumor-associated xenoantigen other than CD20 is used, the skilled artisan will realize that any type of cancer with an associated TAA may be targeted using the SSQFV. Still other embodiments relate to DNA sequences encoding fusion proteins, such as antibody-DDD or xenoantigen-DDD fusion proteins or antibody-AD or xenoantigen-AD fusion proteins, vectors and host cells containing the DNA sequences, and methods of making fusion proteins for the production of anti-cancer vaccine SSQFV constructs.

Related embodiments include fusion proteins of use for making anti-Cancer Vaccine SSQFV constructs, antibody-DDD or xenoantigen-DDD fusion proteins or antibody-AD or xenoantigen-AD fusion proteins. In alternative embodiments, the subunit components of the SSQFV complex may be formed by chemical cross-linking of, an antibody or antibody fragment and a DDD peptide, or a CD20 xenoantigen and an AD peptide for example.

In still other embodiments, the diagnostic agent is a fluorescent labeling compound selected from the group consisting of fluorescein isothiocyanate, rhodamine, phycoerytherin, phycocyanin, allophycocyanin, o-phthaldehyde and fluorescamine, a chemiluminescent labeling compound selected from the group consisting of luminol, isoluminol, an aromatic acridinium ester, an imidazole, an acridinium salt and an oxalate ester, or a bioluminescent compound selected from the group consisting of luciferin, luciferase and aequorin.

### **Detailed Description of the Invention**

The embodiments herein and the various features and advantageous details thereof are explained more fully with reference to the non-limiting embodiments. Descriptions of well-known components and processing techniques are omitted so as to not unnecessarily obscure the embodiments herein. The examples used herein are intended merely to facilitate an understanding of ways in which the embodiments herein may be practiced and to further enable those of skill in the art to practice the embodiments herein.

Accordingly, the examples should not be construed as limiting the scope of the embodiments herein. It is to be understood that the present disclosure is not limited in its application to the details of construction and the arrangement of components set forth in the following description. The present disclosure is capable of other embodiments and of being practiced or of being carried out in various ways.

Also, it is to be understood that the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting. Embodiments of the present invention are directed towards An antibody and, a method for targeting and killing of cancer cells including; Colon cancer, Multiple Myeloma and Non-Hodgkin's lymphoma cancer cells. The main focus of the present invention is to selectively target and kill cancer cells by monoclonal antibodies produced against a unique surface antigen over expressed on Colon cancer (CC), Multiple Myeloma(MM) and Non-Hodgkin's Lymphoma (NHL) cancer cells.

According to a non limiting aspect, the invention focuses on enhancing the immunogenicity of surface antigen by adding a cysteine residue to the carboxyl end of the 14 amino acid long extra- cellular antigenic peptide epitope. Tumor necrosis factor receptors (TNFR) are single transmembrane- spanning glycoproteins that bind cytokines and trigger multiple signal transduction pathways. Tumor necrosis factor (TNF) is a pro-inflammatory cytokine whose role is established in the pathogenesis of malignant diseases like cancer.

TNF has been found to have a pro-cancerous effect and gene polymorphisms which increase or decrease TNF production results either in increased risk or protective effect on a number of different cancers and precancerous diseases including gastric cancer, lymphoma and cervical cancer, certain TNFR member proteins are expressed on specific cancer cells.

TNF has been detected in a number of different tumor types such as ovarian and breast tissue as well as hematological malignancies. Both mRNA expression and TNF protein has been found in human epithelial ovarian tumor cells as well as within the infiltrating macrophages. The p55 TNFR has also been detected within ovarian tumor cells and infiltrating macrophages but not stromal macrophages while the p75 TNFR has only been found within the infiltrating macrophages. In chronic B cell lymphocytic leukemia, increased

TNF levels were found at all stages with a progressive increase in serum TNF levels in relation to the disease. TNF is a cytokine that is produced early in the inflammatory cascade and has been shown to promote carcinogenesis. TNF has a wide range of activities in cancer.

**Systematic list of essential components of Solar Sonic Carcinogenic and Pathogenic Bio-Cellular Communications for systematic treatment of cancer via Bio-Signaling Induction & Stimulation, which all are gearing up for timely Bio-Restoration process:**

- (1).The construction of biomedical shell/device to host varied functions & Hi-Tech capabilities.
- (2).The main component of the device is “Solar Sonic Therapeutic Infusion Composition Mix”.
- (3).Solar Sonic Electromagnetic Frequency Waves with Bio-Signaling Pulsations for initiation.
- (4).Solar Sonic Bio-connectivity for viewing all biological channels of blood, cells and vital signs.
- (5).Solar Sonic Multi-channeling Bio-Detoxification throughout Bio-Cellular Communications
- (6).Solar Sonic Hyperthermia heat-regulating mechanism unit to maintain normal metabolism.
- (7).Therapeutic Laser for Hormonal Immunotherapy (Angiogenesis Inhibitors & Deregulated Proteins)
- (8).Molecularly Quantum Scalar Wave Laser infused with SSQF Low Electric Field Therapies.
- (9).SSF High Gravity Infusion Pump for EMF Quantum Lasing Nutritional Immunotherapy.
- (10).Solar Sonic Quantum Lasing Antidote Therapeutic Infusion (For Cellular Targeting Cleanse).
- (11).Pulsed Electromagnetic Field Resonator for programmable Bio-Cellular Communications
- (12).Total Restoration of physiological Resonance Signatures via SSF low velocity therapeutic infusion for Solar Sonic Carcinogenic & Pathogenic Bio-Cellular Communications/Bio-signaling

**This very medical device was simply designed to execute specific Bio-Medical Directives, some of which are:**

1. SSF Reversal of Carcinogenicity/Pathogenicity that damage the genome & disrupt cellular metabolic processes
2. Programmable electromagnetic chemical infusion to remove the total physiological Toxicity of cancer patients
3. Rebuilding Immune system of cancer patients by programming cells, tissue, gland, hormone, Thyroid, protein
4. Programming protein telomerase to emit continuous electromagnetic toxic resonance signature to cancer cells
5. Maximum tolerated dose, which is the highest dose that does not produce serious or fatal adverse effects.
6. Solar Sonic Electromagnetic Chemical Infusion Intracellular Evaporation (chemical values internal shifting).
7. Intracellular Bio-communications & Bio-signaling capabilities to initiate systematic eradication of cancer cells.

8. **Pathogenic Bio-communications & Bio-signaling capabilities to initiate systematic eradication of all pathogens.**
9. **Regenerative restorations of internal tissues, cells, glands, hormones & balancing out blood / immune system.**
10. **Device causes Internal Electromagnetic Chemical Infusion Intracellular Evaporation for instant Bio-shiftings.**
11. **Device physiologically capable of communicating with all human organs via Solar Sonic Resonance Signature.**
12. **Device convert/redirect/expel Toxic Chemical as form of physiological genetic reverse engineering in the body.**
13. **SSF Physiological distribution systems of intravenous liquid oxygen, SSQF Soft Laser and Heat Bio-delivery.**
14. **Solar Sonic Technology chemically and electromagnetically infusing Cytochrome C-Protein and programming Apoptosis for eradication countdown mechanism, whereas carcinogenic cells lose all their environmental essentials.**
15. **A Mitochondria-K<sup>+</sup> Channel Axis Is Suppressed in Cancer and Its Normalization Promotes Apoptosis and Inhibits Cancer Growth, we therefore we cause its chemical therapeutic infusion, supported by direct EMF effect.**
16. **Device is capable of injecting cancer cells with imaginary (sensory) accessive flow of highly oxygenated blood, since cancer cells are proven to be anaerobic, such injection will be done via various Solar Sonic Electromagnetic Chemical Infusion Intracellular Evaporation, whereby the Solar Sonic Phenomenon of physiological genetic reverse engineering will simultaneously occur, at the end of which gradual rate of cancer cells eradication countdown will literally begin.**
17. **Solar Sonic Laser Needles and pulsed electromagnetic fields in the administration of the SSF Therapeutic Infusion Composition Protocols for the absolute eradication of carcinogenic cells, intracellular/pathogenic Bio-communications, regenerative human physiology via Paranormal Homeostasis and Induced Apoptosis for Bio-restorations. Laser needle delivers the intended medicine to eradicate cancer & it interacts with all units.**

#### **Essential Compartments of the SSF-Medical Device:**

- (1).The construction of biomedical shell/device to host varied functions & Hi-Tech capabilities.
- (2).The main component of the device is Solar Sonic Therapeutic Infusion Composition Mix.
- (3).Solar Sonic Electromagnetic Frequency Waves with Bio-Signaling Pulsations for initiation.
- (4).Solar Sonic Bio-connectivity for viewing all biological channels of blood, cells & vital signs.
- (5).Solar Sonic Multi-channeling Bio-Detoxification throughout Bio-Cellular Communications
- (6).Hyperthermia heat-regulating mechanism for normal metabolism & warming up the tumor.
- (7).Therapeutic Laser for Hormonal Immunotherapy (Angiogenesis Inhibitors/Deregulated Proteins).
- (8).Molecularly Quantum Scalar Wave Laser infused with SSQF Low Electric Field Procedures.
- (9).SSF High Gravity Infusion Pump for EMF Quantum Lasing Nutritional Immunotherapy.

- (10).Solar Sonic Quantum Lasing Antidote Therapeutic Infusion (For Cellular Targeting Cleanse).
- (11).The Pulsed Electromagnetic Field Resonator for programmable Bio-Cellular Communications
- (12).Total Restoration of Resonance Signatures via SSF low velocity therapeutic infusion for Solar Sonic Carcinogenic and Pathogenic Bio-Cellular Communications & induced Bio-signaling.
- (13).Solar Sonic Molecularly Quantum Frequencies & Pulsed Electromagnetic Frequency Waves.
- (14).Solar Sonic Infusion Particle Acceleration to evaluate mass/properties of Atomic Nucleus
- (15).The Scattering Photons Infusion Pump for Hydrogen Peroxide, Substantial Minerals/Vitamins.
- (16).Scattering Photons, Protons & Electrons via Oxygenation/Ozonation Gravity Infusion Pump.
- (17).Solar Sonic Biochemical Cleanse, paving for complete Detoxification orally & intravenously.
- (18).Invention Device is equipped with advanced electronic linkage capabilities & miscellaneous.
- (19).Invention Device is equipped with Molecular Metric beam for Bio-element dimensionalities.
- (20).Invention Device is equipped with Photon, Proton & Electron Infusion Therapy Capabilities.
- (21).Invention Device is equipped with the advanced infrared signature capabilities/directed energy.
- (22).Invention Device is equipped with advanced radio waves and signal penetration capabilities.
- (23).SSF-Penetration Capabilities of zero gravity dimensionalities, making cancer cells fall dead.
- (24).Invention Device is equipped with Solar Sonic Multi-wave Cellular Penetration Capabilities.
- (25).Invention Device is equipped with the Molecularly Quantum Laser Capabilities & miscellaneous.
- (26).Invention Device is equipped with Solar Sonic customized/coded signals, waves, beams, rays.
- (27).Invention Device is equipped with infrasonic signal integration & cellular penetration circuit
- (28).Device is equipped with customized converter/transmitter/transducer/capacitor/transceiver.
- (29).IV Pharmaceutical Photonic Needle/sensing circuits initiating Bio-signaling communication
- (30).Sensing/Removal Capabilities of chemicals, pathogens, toxins, heavy metals & free-radicals.
- (31).Device is equipped with highly SSF magnetic conduction transmitters/transducers/capacitors.
- (32).Device is equipped with radioactive sensing circuit & SSQF-Radiation Detection / Treatment
- (33).Device is equipped with Ultra sensitive detection cameras & Bio-Storage/Retrieval/Recording
- (34).Device is equipped with controlling of blood chemistry/thinning & Blood Oxygenation IV
- (35).Anti Gravity Fittings, magnetic sheets, coils, magnetic design box for better SSF- Signaling.
- (36).Electromagnetic cooling/heating systems with anti gravity tubes & major SSF miscellaneous.
- (37).Highly sensitive Progress monitors with led lights, solar filters & major SSF miscellaneous.
- (38).Laser filters, Photonic filters, sonic filters and Anti-gravity magnetic foam-shields & sensors.

- (39).Biomedical Integrated circuits & major miscellaneous for operating system chips/turnkey.
- (40).Hyper sonic amplifier, ultra sonic amplifier, sonic metric converter, multi-system sensors.
- (41). Multi-faceted distribution system, air suctioning, air blowing, air pressure, air compression.
- (42).Solar Sonic Multi-Channeling Biological Cleanse System for extracting Carcinogenic Debris
- (43).Solar Sonic Highly Proprietary Intracellular Software, Hardware & Bio-connectivity viewing systems
- (44).SSQF Capacitors, Transducers, Voltage Regulators, Sonic Agitators, Photonic Agitators, Sonic laser, infrared transducers, high magnetic transceivers, transducers, capacitors, regulators.
- (45).Solar Sonic Laser Needles and pulsed electromagnetic fields in the administration of the SSF Therapeutic Infusion Composition Protocols for the absolute eradication of carcinogenic cells, intracellular/pathogenic Bio-communications and regenerative human physiology via Paranormal Homeostasis and Induced Apoptosis for Bio-restorations. The Laser needle of the medical device delivers the intended medicine to eradicate cancer & it interacts with all units.
- (46).Solar Sonic Therapeutic Infusion Medical Device chemically promotes Pulsed Suppression of Mitochondria-K<sup>+</sup> Channel Axis in Cancer, Inducing Apoptosis and Inhibiting Cancer Growth. The mitochondria is a natural cancer fighting human organelle, the mitochondria is never a cell, it is an organelle. It certainly cannot be accurately characterized as a cancer fighting cell, since its primary function is to provide nucleoside triphosphates such as ATP for cell structure. However, Solar Sonic Laboratories were able to precisely program the mitochondria organelle to communicate with carcinogenic cells and systematically cause their irreversible eradication and the inevitable methodical deprivation to cancer cells from vital carcinogenic environment.

**In light of the above mentioned, we therefore further Claim as follows:**

We present a medical device and a pharmaceutically acceptable carrier for therapeutic infusion in cancer treatments. We present this medical device for selectively removing a target cell, pathogen, or virus expressing a binding partner on its surface, the device comprising various Solar Sonic Circuits, wherein the SSQF Circuit comprises a magnetic filter comprising a magnet capable of generating a magnetic field sufficient to capture magnetic nanomaterials in the magnetic field and a removable, magnetizable substrate capable of capturing magnetic nanomaterials; and a pump in fluid communication with the magnetic filter, wherein the pump moves fluid through the Solar Sonic Circuit. The device of claim, wherein the magnetizable substrate is a screen, the device of claim, further comprising a reservoir in fluid communication with the magnetic filter, the device of claim, further comprising a mixing chamber between the reservoir and the magnetic filter and in fluid communication with the reservoir and the magnetic filter, the device of claim further comprising a heater for heating fluid moving through the device.

The device of claim further comprising a management component in electrical communication or wireless communication with the pump for monitoring or maintaining flow rate of the fluid, the device of claim, further comprising a management component in electrical communication or wireless communication with the heater for maintaining the fluid at a predetermined temperature, the device of claim, wherein the magnetizable substrate is removable from the magnetic filter, the device of claim, wherein the reservoir and magnetizable substrate are sterilizable, the device of claim wherein the reservoir systematically comprises superparamagnetic nanoparticles functionalized with a first binding partner that binds to the binding partner on the surface of the target cell, pathogen or virus, the device of claim, wherein the binding partner on the target cell comprises a tumor specific antigen or fragment thereof capable of binding to the first binding partner. The device of claim, wherein the first binding partner on the superparamagnetic nanoparticles is selected from the group consisting of nucleic acid aptamers, peptide aptamers, pseudo peptide, synthetic ligands selected for the target, and antibodies or antigen binding

fragments thereof. A method for removing a target cell, organism, or virus from a subject in need of treatment, comprising removing a biofluid from the patient and transporting the biofluid into the device passing the mixture of the superparamagnetic nanoparticles and biofluid through the magnetic filter, and either returning the filtrate to the reservoir or the patient, wherein the target cell is a cancer cell, the method of claim, further comprising administering replacement fluids to the subject.

The method of claim, wherein the biofluid is a fluid selected from the group consisting of blood, blood serum, cerebrospinal fluid, lymph, and peritoneal fluid. An method for removing a target cell, organism, or virus from a subject in need of treatment, comprising removing a biofluid from the patient and transporting the biofluid into the device of any one of claims, passing the mixture of the superparamagnetic nano-particles and biofluid through the magnetic filter, and either returning the filtrate to the reservoir or the patient, wherein the target cell is an infected cell. The method of claim, wherein infected cell is infected by a virus, bacterium, protozoan, or fungus, the method of claim further comprising administering replacement fluids to the subject wherein the binding partner on the superparamagnetic nanoparticles is selected from the group consisting of nucleic acid aptamers, peptide aptamers, pseudo peptide, and synthetic ligands selected for the target.

A method for removing a target cell organism, or virus from a subject comprising obtaining a biofluid from the subject; transporting the biofluid into the device of passing a mixture of the superparamagnetic nano particles and biofluid through the magnetic filter. A method for removing nanomaterials having magnetic properties from a subject comprising obtaining a biofluid containing a nanomaterial having magnetic properties from the subject; transporting the biofluid into the device of any one of claims wherein nanomaterials in the biofluid are captured by the magnetic filter, and either returning the filtrate to the reservoir or the patient.

A method of treating or managing cancer comprising administering to a patient a pharmaceutical composition comprising an effective amount of mycobacterium W or constituents of mycobacterium W Wherein the method is for decreasing the burden of cancer tissues, a method of claim, wherein the method is for improving the cancer treating effect of radiotherapy or chemotherapy.

The method of claim, wherein the method is for reducing the side-effects of radiotherapy or chemotherapy wherein the side effects are mostly hematological side effects, the method of claim, wherein the side effects are reduced to avoid postponement of chemotherapy, the method of claim, wherein the side effects are leucopenia, thrombocytopenia, anaemia, nausea, vomiting or mucositis, wherein the mycobacterium W is dead mycobacterium w, wherein the mycobacterium w has been killed by a physical method, wherein the physical method is the application of heat, wherein the heat is applied by means of autoclaving. Wherein the pharmaceutical composition comprises constituents of mycobacterium w that have been obtained by sonication, wherein the pharmaceutical composition comprises constituents of mycobacterium w that have been obtained by extraction.

The method of claims wherein the constituents of mycobacterium W have been extracted by organic solvents and wherein the organic solvents are selected from the group consisting of chloroform, ethanol, methanol, acetone, phenol, isopropyl alcohol, acetic acid, urea and hexane. A method of improving the quality of life in a patient suffering from cancer comprising: administering to a patient a pharmaceutical composition comprising an effective amount of mycobacterium w or constituents of mycobacterium w. Wherein the improvement in quality of life is obtained in the absence of other modes of treatment, wherein the improvement in quality of life is obtained with the addition of other modes of treatment. A method of amelioration of symptoms associated with cancer comprising: administering to a patient a pharmaceutical composition comprising an effective amount of mycobacterium W or constituents of mycobacterium W.

Moreover, we herein also presenting an assembly comprised of a device, wherein said device comprises a substrate and, disposed over such substrate, nanomagnetic material and mageto-resistive material, wherein:

(a) Said nanomagnetic material has a saturation magnetization of from about 2 to about 3000 electromagnetic units per cubic centimeter, and

(b) Said nanomagnetic material is comprised of nanomagnetic particles with an average particle size of less than about 100 nanometers, wherein the average coherence length between adjacent nanomagnetic particles is less than 100 nanometers.

The assembly as recited wherein said magneto-resistive material, when exposed to a direct current field of 1.5 Tesla and a radio frequency field of 64 megahertz increase its resistance by at least two orders of magnitude, wherein said device is a medical device, wherein said medical device is comprised of a first therapeutic agent, wherein said first therapeutic agent is an anti-cancer drug, wherein said nanomagnetic material has average particle size of less than about 20 nanometers and a phase transition temperature of less than about 200 degrees Celsius, wherein said assembly further comprises a cytotoxic radioactive material, wherein said assembly is comprised of a material that is absorbable in living tissue.

The therapeutic assembly as recited wherein said material that is absorbable in living tissue is selected from the group consisting of polyester amides from glycolic acids, polyester amides from lactic acids, polymers and copolymers of glycolate, polymers and copolymers of lactate, and polydioxanone, wherein said medical device is comprised of a polymeric material, wherein said polymeric material is comprised of said first therapeutic agent, wherein said polymeric material is comprised of a second therapeutic agent, wherein said polymeric material is comprised of a third therapeutic agent, wherein said polymeric material is a drug-eluting polymer, wherein said polymeric material is a synthetic absorbable copolymer formed by copolymerizing glycolide with trimethylene carbonate, wherein said polymeric material is selected from the group of silk, polyester, polytetrafluoroethylene, polyurethane silicone-based material, and polyamide.

The assembly as recited in claim, wherein said therapeutic agent is selected from the group consisting of antithrombogenic agents, antiplatelet agents, prostaglandins, thrombolytic drugs, antiproliferative drugs, antirejection drugs, antimicrobial drugs, growth factors, anticalcifying agents, and mixtures thereof, wherein said reservoir is formed by a polymer selected from the group consisting of polyurethanes and its copolymers, silicone and its copolymers, ethylene vinylacetate, thermoplastic elastomers, polyvinylchloride, polyolefins, celluloses, polyamides, polytetrafluoroethylenes, polyesters, polycarbonates, polysulfones, acrylics, and acrylonitrile butadiene styrene copolymers, wherein said polymeric material is a bioabsorbable polymer selected from group consisting of poly (L-lactic acid), polycaprolactone, poly (lactide-co-glycolide) Poly (hydroxybutyrate), poly (hydroxybutyrate-co-valerate), polydioxanone, polyorthoester, polyanhydride, poly (glycolic acid), poly (D,L-lactic acid), poly (glycolic acid-co-trimethylene carbonate), polyphosphoester, polyphosphoester urethane, poly(amino acid), cyanoacrylate, poly(trimethylene carbonate), poly (iminocarbonate) copoly (ether-ester), polyalkylene oxalate, polyphosphazenes, and mixtures thereof.

Wherein said polymeric material is a biomolecule, wherein said biomolecule is selected from the group consisting of fibrin, fibrogen, cellulose, starch, collagen, and hyaluronic acid, wherein said polymeric material is selected from the group consisting of polyolefin, acrylic polymer, acrylic copolymer, vinyl halide polymer, vinyl halide copolymer, polyvinyl ether, polyvinylidene halide, polyvinylketone, polyvinyl aromatic polymer, copolymers of vinyl monomer, acrylonitrile-styrene copolymer, ethylene-vinyl acetate copolymer, polyamide, Alkyd resin, polyoxymethylene, polyimide, polyether, epoxy resin, rayon, rayon-tracetate, cellulose, cellulose acetate, cellulose butyrate, cellulose acetate butyrate, cellophane, cellulose nitrate, cellulose propionate, cellulose ether, and carboxymethyl cellulose, wherein said first therapeutic agent is selected from the group consisting of glucocorticoids, heparin, hirudin, tocopherol, angiopeptin, aspirin, ACE inhibitors, growth factors, oligonucleotides, antiplatelet agents, anticoagulant agents, antimetabolic agents, antioxidants, antimetabolite agents, and anti-inflammatory agents, wherein a heterobifunctional photolytic linker is bonded to said polymeric material, wherein said first therapeutic agent is a vasoreactive agent, wherein said vasoreactive agent is a nitric oxide releasing agent, wherein said polymeric material is comprised of a multiplicity of microcapsules, wherein said polymeric material is a mixture of fibrinogen and thrombin.

Wherein said polymeric material is a multi-layered polymeric material, wherein said polymeric material is a porous polymeric material, wherein said polymeric material has a thermal processing temperature of less than about 100 degrees Celsius, wherein said polymeric material is comprised of a porosigen, wherein said porosigen is selected from the group of microgranules of sodium chloride, lactose, sodium heparin, polyethylene glycol, polyethylene oxide/polypropylene oxide copolymer, and mixtures thereof, wherein said

polymeric material is a thermoplastic polymer, wherein said polymeric material is an elastomeric polymer, wherein said polymeric material is in the form of a layer of material with a thickness of from about 0.002 to about 0.02 inches, wherein said polymeric material is a controlled release polymer, wherein said controlled release polymer is comprised of a congener of an endothelium-derived bioactive composition.

Wherein said congener of an endothelium-derived bioactive agent is selected from the group consisting of nitric oxide, nitric L-arginine, sodium nitroprusside, and nitroglycerine, wherein said polymeric material is a transparent polymeric material wherein said polymeric material is a hydrophobic elastomeric material, wherein said polymeric material is a hydrophilic polymer, wherein said first therapeutic agent is a water-soluble therapeutic agent, wherein said first therapeutic agent is an anti-microtubule agent that impairs functioning of microtubules, wherein said anti-microtubule agent is paclitaxel, wherein said polymeric material is a pH-sensitive polymer, wherein said pH-sensitive polymer is selected from the group consisting of poly(acrylic acid), poly(aminocarboxylic acid), poly(acrylic acid), poly(methyl acrylic acid), cellulose acetate phthalate, hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate, cellulose acetate trimellitate, and chitosan, wherein said polymeric material is a temperature-sensitive polymer, wherein said polymeric material is a thermogelling polymer.

The assembly also shows as recited, wherein said thermogelling polymer is selected from the group consisting of poly(-methyl-N-n-propylacrylamide), poly(-methyl-N-n-propylacrylamide), poly(N-n-propylacrylamide), poly(N-methyl-N-isopropylacrylamide), poly(N-n-propylmethacrylamide), poly(N-isopropylacrylamide), poly(N,n-diethylacrylamide), poly(N-isopropylmethacrylamide), poly(N-cyclopropylacrylamide), poly(N-ethylmethacrylamide), poly(N-methyl-N-ethylacrylamide), poly(N-cyclopropylmethacrylamide), and poly(N-ethylacrylamide), hydroxypropyl cellulose, methyl cellulose, hydroxypropylmethyl cellulose, as well as ethylhydroxyethyl cellulose, wherein the average particle size of such nanomagnetic particles is less than about 15 nanometers, wherein said nanomagnetic material has a saturation magnetization of at least 2,000 electromagnetic units per cubic centimeter, wherein said nanomagnetic material has a saturation magnetization of at least 2,500 electromagnetic units per cubic centimeter, wherein said particles of said nanomagnetic material have a squareness of from about 0.05 to about 1.0.

Wherein particles of said nanomagnetic material are at least triatomic, being comprised of a first distinct atom, a second distinct atom, and a third distinct atom, wherein said first distinct atom is an atom selected from the group consisting of atoms of actinium, americium, berkelium, californium, cerium, chromium, cobalt, curium, dysprosium, einsteinium, erbium, europium, fermium, gadolinium, holmium, iron, lanthanum, lawrencium, lutetium, manganese, mendelevium, nickel, neodymium, neptunium, nobelium, plutonium, praseodymium, promethium, protactinium, samarium, terbium, thorium, thulium, uranium, and ytterbium, wherein said first distinct atom is a cobalt atom, wherein said particles of nanomagnetic material are comprised of atoms of cobalt and atoms of iron wherein said first distinct atom is radioactive cobalt atom.

Wherein said particles of nanomagnetic material are comprised of a said first distinct atom, said second distinct atom, said third distinct atom, and a fourth distinct atom, wherein said particles of nanomagnetic material are comprised of a fifth distinct atom, wherein said particles of nanomagnetic material have a squareness of from about 0.1 to about 0.9, wherein said particles of nanomagnetic material have a squareness is from about 0.2 to about 0.8, wherein said particles of nanomagnetic material have an average size of less than about 3 nanometers.

Wherein said particles of nanomagnetic material have an average size of less than about 15 nanometers, wherein said particles of nanomagnetic material have an average size is less than about 11 nanometers, wherein said particles of nanomagnetic material have a phase transition temperature of less than 46 degrees Celsius, wherein said particles of nanomagnetic material have a phase transition temperature of less than about 50 degrees Celsius, wherein said nanomagnetic material has a coercive force of from about 0.1 to about 10 Oersteds, wherein particles of nanomagnetic material have a relative magnetic permeability of from about 1.5 to about 2,000, wherein particles of nanomagnetic material have a saturation magnetization of at least 100 electromagnetic units per cubic centimeter. Wherein said particles of nanomagnetic material have a saturation magnetization of at least about 200 electromagnetic units (emu) per cubic centimeter, wherein particles of nanomagnetic material have a saturation magnetization of about 1,000 electromagnetic units per

cubic centimeter, wherein said particles of nanomagnetic material have a coercive force of from about 0.01 to about 5,000 Oersteds, wherein said particles of nanomagnetic material have a coercive force of from about 0.01 to about 3,000 Oersteds, wherein said particles of nanomagnetic material are disposed within a film that has a heat shielding factor of at least 0.2, wherein said particles of nanomagnetic material have a relative magnetic permeability of from about 1 to about 500,000, wherein said particles of nanomagnetic material have a relative magnetic permeability of from about 1.5 to about 260,000, wherein said assembly is comprised of antithrombogenic material, wherein said particles of nanomagnetic material have a mass density of about 0.001 grams per cubic centimeter.

Wherein said particles of nanomagnetic material have a mass density of at least about 1 gram per cubic centimeter, wherein said particles of nanomagnetic material have a mass density of at least about 3 grams per cubic centimeter, wherein said particles of nanomagnetic material have a mass density of at least about 4 grams per cubic centimeter, wherein said second distinct atom has a relative magnetic permeability of about 1.0, wherein said second distinct atom is an atom selected from the group consisting of aluminum, antimony, barium, beryllium, boron, bismuth, calcium, gallium, germanium, gold, indium, lead, magnesium, palladium, platinum, silicon, silver, strontium, tantalum, tin, titanium, tungsten, yttrium, zirconium, magnesium, and zinc, wherein said third distinct atom is an atom selected from the group consisting of argon, bromine, carbon, chlorine, fluorine, helium, hydrogen, iodine, krypton, oxygen, neon, nitrogen, phosphorus, sulfur, and xenon, wherein said third distinct atom is nitrogen, wherein said nanomagnetic particles are represented by the formula  $A_xB_yC_z$ , wherein A is said first distinct atom, B is said second distinct atom, C is said third distinct atom, and  $x+y+z$  is equal to 1, wherein said nanomagnetic particles are comprised of atoms of oxygen, wherein said nanomagnetic particles are comprised of atoms of iron, wherein said atoms of iron are atoms of radioactive iron, wherein said nanomagnetic particles are comprised of atoms of cobalt.

Wherein said nanomagnetic material is disposed within a ceramic binder, wherein said ceramic binder is selected from the group consisting of a clay binder, an organic colloidal particle binder, and a molecular organic binder, wherein said nanomagnetic material is disposed within a synthetic polymeric binder, wherein said nanomagnetic material is disposed within a fiber, wherein said nanomagnetic material is disposed within a fabric, wherein said particles of nanomagnetic material are disposed within an insulating matrix, wherein said particles of nanomagnetic material are present in the form of a coating with a thickness of from about 400 to about 2000 nanometers, wherein said coating has a thickness of from about 600 to about 1200 nanometers.

Wherein said coating has a morphological density of at least about 98 percent, wherein said coating has a morphological density of at least about 99 percent, wherein said coating has a morphological density of at least about 99.5 percent, wherein said coating has an average surface roughness of less than about 100 nanometers, wherein said coating has an average surface roughness of less than about 10 nanometers, wherein said coating is hydrophilic, biocompatible, hydrophobic and presenting various methods therein, one of which is a method of eliciting an immune response in a subject directed against a polypeptide sequence selected from the above listed pharmacological groups and acceptable carriers, comprising, administering to the subject an immunologically sufficient amount of a polypeptide sequence selected from the above listed Pharmacological groups and acceptable carriers. The system is a method of treating cancer comprising, administering a therapeutically effective amount of antibody that binds to a polypeptide, wherein said cancer is selected from a group consisting of Multiple Myeloma, Colon Cancer and Non-Hodgkin's Lymphoma. Use of an antibody that binds to a polypeptide sequence selected from the above listed pharmacological groups and acceptable carriers in treating cancer. The use of an antibody as claimed, wherein said cancer is selected from a group consisting of Multiple myeloma, Colon cancer and Non-Hodgkin's lymphoma. The SSQF technology, presents a medical device and pharmacologically infused therapeutic composition complex of claims, wherein the xenoantigen is selected from the group consisting of:

Carbonic anhydrase IX, alpha-fetoprotein,  $\alpha$ -actinin-4, ART-4, B7, BAGE, CA125, CAMEL, CAP-1, CASP-8/m, CCCL19, CCCL21, CD1, CD1a, CD2, CD3, CD4, CD5, CD8, CD11A, CD14, CD15, CD16, CD18, CD19, CD20, CD21, CD22, CD23, CD25, CD29, CD30, CD32b, CD33, CD37, CD38, CD40, CD40L, CD45, CD46, CD52, CD54, CD55, CD59, CD64, CD66a-e, CD67, CD70, CD74, CD79a, CD80, CD83, CD95, CD126, CD133.

**The invention is also a process for treating a biological organism, comprising the steps of:**

- (a) Administering a cell cycle arresting drug to said organism, thereby producing synchronized cells within such organism,
- (b) administering a microtubule stabilizing drug to said organism, thereby producing synchronized cells whose microtubules have been stabilized within said organism, and
- (c) Contacting said synchronized cells whose microtubules have been stabilized with mechanical vibrational energy

Wherein said mechanical vibrational energy has an excitation source frequency in the range of from about 1 hertz to about 10 Gigahertz, wherein cell cycle arresting drug synchronizes tumor cells with respect to cell cycle progression, wherein said cell cycle arresting drug is selected from the group consisting of gemcitabine, cisplatin, carboplatin, cyclophosphamide, topoisomerase inhibitor, etoposide, 5-fluorouracil, doxorubicin, methotrexate, hydroxyurea, 3'-azido-3'-deoxythymidine, and mixtures thereof, wherein said cell cycle arresting drug is gemcitabine, wherein said cell cycle arresting drug synchronizes said cells in metaphase, wherein said cell cycle arresting drug synchronizes said cells in anaphase, wherein at least about 30 percent of said cells are synchronized in metaphase, wherein 50 percent of said cells are synchronized in metaphase.

Wherein at least about 70 percent of said cells are synchronized in metaphase, wherein said mechanical vibrational energy is ultrasound, wherein said synchronized cells are contacted with said ultrasound only after at least 25 minutes after said cell cycle arresting drug has been administered to said organism, wherein said synchronized cells are contacted with said ultrasound only after at least 60 minutes after said cell cycle arresting drug has been administered to said organism, wherein synchronized cells are contacted with said ultrasound only after at least 240 minutes after said cell cycle arresting drug has been administered to said organism, wherein said synchronized cells are contacted with said ultrasound only after at least 48 hours after said cell cycle arresting drug has been administered to said organism, wherein said microtubule stabilizing drug is a laulimalid microtubule stabilizing agent, wherein said microtubule stabilizing drug is a coumarin compound, wherein said ultrasound has a frequency of from about 270 to about 420 kilohertz.

Wherein said ultrasound has an intensity of from about 10 to about 30 watts per square meter, wherein said microtubule stabilizing drug is paclitaxel, wherein said ultrasound has a frequency of from about 50 megahertz to about 2 gigahertz, wherein said ultrasound has a frequency of from about 100 megahertz to about 1 gigahertz, wherein the power of said ultrasound is at least about 0.01 watts per square meter, wherein the power of said ultrasound is at least about 0.1 watts per square meter, wherein said ultrasound has a frequency of from about 100 kilohertz to about 500 kilohertz, wherein said ultrasound has a frequency of from about 110 to about 200 kilohertz, wherein said ultrasound has a frequency of from about 130 to about 170 kilohertz, wherein the power of said ultrasound is from about 1 to about 30 watts per square meter, wherein the power of said ultrasound is from about 5 to about 15 watts per square meter.

**Characteristic abilities developed by cancers are divided into a number of categories, SSQF is creating several programs for each one to induce Apoptosis and/or trigger Metabolic Homeostasis:**

- (1). Evasion of Apoptosis
- (2). Sustained Angiogenesis
- (3). Limitless Replicative Potential
- (4). Evasion of Immune Destruction

- (5). Self-sufficiency in Growth Signals
- (6). Insensitivity to Anti-Growth Signals
- (7). Reprogramming of Energy Metabolism
- (8). Metastasis & Unrestricted Carcinogenic Pathways

### **How does the Hi-Tech phenomenon works**

Solar Sonic Multidimensional Quantum Frequency Infusion Technologies have been proven to Generate and Convert Energies into all forms of Matter and Antimatter with Solar Sonic Frequency Pulse, promoting Stimulation and Manipulation. It grants the ability to infuse Matter and Antimatter with Ultra Solar Sonic rearranged cellular particles and resonant energetic matrix via calculated triggering mediums. Thereby creating cellular shifts in molecular structures, regenerative signatures, energy navigational pathways, element vibration matrix and object migratory routes of energetic forces. Such an extent that impedes and emits rearranged infused energy structures with sonically photonic spin-ratio. Thereby, forming redirected zero point energy to net energy matrix ratio which exceed all known energy efficiencies or any conductively regenerative matrix. Such an energetic phenomenon that defies all the laws of physics beyond expectations.

Solar Sonic Effects use special frequency arrays to decode and extract Logistical Data contained in the holographic matrix of the universe as the Unified Field. At the core of Solar-Sonic-Discovery is a complex matrix of light, heat, sound, reflection, refraction, attenuation, kinetics, and resonance. These matrices obey the mathematical principals of frequencies. All vibration frequencies are mathematically represented on a graph as a waveform as all matters visible or invisible emits unique frequency signatures.

Solar Sonic possesses intellectual knowledge, crucial frequency array coding technology and algorithms that Together detect, capture, emit, enhance and modulate any waveform frequency. Such Effects generate results when the master waveforms are manipulated and sonically photonic configured within specific proprietary parameters where it produces two events. The first event is "IPAST Image Penetration and Stimulation Technology", which is matrix imaging of the elected target and override its physical entity with compatible elements, enhancing its resolution with multidimensional imaging technology and dominating its elements.

It is then penetrated and stimulated with the Matrix Effect, uncovering volumes of quantum data. The second event is "FPAST Frequency Penetration And Stimulation Technology", FPAST inserts frequencies that penetrate and stimulate other waveforms, such as Any Organism, Atoms, Cells, Molecules, Particles, Air, Water, Heat, Sonic-Patterns, Solar-Patterns. As well as Ultrasonic, Infrasonic, Hypersonic, Supersonic and Solar-Sonic, thereby greatly enhancing and enriching the data gathered and strengthening its principal extraction potential in a very methodical manner. Whereas all the bonding of frequency patterns enriching tremendously within massive Frequency Matrix Cycle for optimum molecular structures, Cellular Communications, Pathogenic Signaling, Metabolic Homeostasis and other proprietary modalities and substantial quantum logistical data, which are substantially critical for determining tools of communications.

Solid tumors, including the aggressive primary brain cancer glioblastoma multiforme, develop resistance to cell death, in part as a result of a switch from mitochondrial oxidative phosphorylation to cytoplasmic glycolysis. This metabolic remodeling is accompanied by mitochondrial hyperpolarization. We tested whether the small-molecule and orphan drug dichloroacetate (DCA) can reverse this cancer-specific metabolic and mitochondrial remodeling in glioblastoma. Freshly isolated glioblastomas from 49 patients showed mitochondrial hyperpolarization which was rapidly reversed by DCA.

DCA therapy also inhibited the hypoxia-inducible factor-1 $\alpha$ , promoted p53 activation, and suppressed angiogenesis both *in vivo* and *in vitro*. The dose-limiting toxicity was a dose-dependent, reversible peripheral neuropathy, and there was no hematologic, hepatic, renal, or cardiac toxicity. Indications of clinical efficacy were present at a dose that did not cause peripheral neuropathy and at serum concentrations of DCA sufficient to inhibit the target enzyme of DCA, pyruvate dehydrogenase kinase II, which was highly expressed in all glioblastomas.

Metabolic modulation may be a viable therapeutic approach in the treatment of glioblastoma. The function of the apoptotic pathway in cancer cells is extremely critical for all cancer research and for all new inventions in treating cancer. The intrinsic (self) and extrinsic (from the outside) pathways of cell suicide are activated by mitochondrial cytochrome C release, which cascade with other enzymes activating the caspase 8, 9 pathways which cleave all the cells protein, killing it. However, a cancer cell, being a cancer cell, will have this pathway cut off--irreversibly--simply because it otherwise would have been killed before it became cancer.

The extrinsic pathway will be cut off due to faulty receptors or cascading proteins, and the intrinsic pathway--even if the mitochondria are "activated" and cytochrome C is released, because the cell either won't listen to the death signal that has an amplification of repressors to the apoptotic signal (BCL2, BCL XL), or the DNA coding for the proteins necessary to carry out the caspase activity of cleaving proteins has been mutated/deleted/rendered non-functional.

Unfortunately, the first step toward cancer is an immortalizing event. Later, come proto-oncogene mutations leading to uncontrolled division. This means, the mitochondrial apoptotic pathway is destroyed. It isn't simply dormant, waiting to be turned on. It's like being asked to drive a car when it's missing nearly all its parts, and has other parts that are deformed and beyond functional.

In human bodies there is a natural cancer fighting human cell, the mitochondria, but they need to be triggered to be effective. Scientists used to think that these mitochondria cells were damaged and thus ineffective against cancer. So they used to focus on glycolysis, which is less effective in curing cancer and more wasteful. The drug manufacturers focused on this glycolysis method to fight cancer. This DCA on the other hand doesn't rely on glycolysis instead on mitochondria; it triggers the mitochondria which in turn fights the cancer cells. The side effect of DCA is also reactivates a process called apoptosis. Mitochondria contain an all-too-important self-destruct button that can't be pressed in cancer cells. Without it, tumors grow larger as cells refuse to be extinguished. Fully functioning mitochondria, thanks to DCA, can once again die. With glycolysis turned off, the body produces less lactic acid, so the bad tissue around cancer cells doesn't break down and seed new tumors.

### **A Mitochondria-K<sup>+</sup> Channel Axis is Suppressed in Cancer and its Normalization Promotes Apoptosis and Inhibits Cancer Growth**

The unique metabolic profile of cancer (aerobic glycolysis) might confer apoptosis resistance and be therapeutically targeted. Compared to normal cells, several human cancers have high mitochondrial membrane potential and low expression of the K<sup>+</sup> channel Kv1.5, both contributing to apoptosis resistance.

Dichloroacetate (DCA) inhibits mitochondrial pyruvate dehydrogenase kinase (PDK), shifts metabolism from glycolysis to glucose oxidation, decreases, increases mitochondrial H<sub>2</sub>O<sub>2</sub>, and activates Kv channels in all cancer, but not normal, cells; DCA upregulates Kv1.5 by an NFAT1-dependent mechanism. DCA induces apoptosis, decreases proliferation, and inhibits tumor growth, without apparent toxicity. Molecular inhibition of PDK2 by siRNA mimics DCA. The mitochondria-NFAT-Kv axis and PDK are important therapeutic targets in cancer; the orally available DCA is a promising selective anticancer agent.

**In addition to the foregoing extensive data already furnished within the previous pages, we further proceed to Claim additional work with respect to our Cancer Therapeutic Infusion Medical Device as follows:**

Solar Sonic Technologies have perfected the science of Electromagnetically Bio-Chemical Intracellular and pathogenic communication and signaling, to the extent that we can affect cellular programming, signaling, reprogramming, cellular communications and manipulations leading to either Homeostasis or Apoptosis. Apoptosis is the death of cells which occurs as a normal and controlled part of an organism's growth or development. Apoptosis is the process of programmed cell death (PCD) that may occur in multi-cellular organisms. Biochemical events lead to characteristic cell changes (morphology) and death. These changes include blebbing, cell shrinkage, nuclear fragmentation, chromatin condensation, and chromosomal DNA fragmentation. In contrast to necrosis which is form of traumatic cell death that results from cellular injury?

Necrosis is the death of most or all of the cells in an organ or tissue due to disease, injury, or failure of the blood supply. Necroptosis is a programmed form of necrotic cell death and Necrotic cell death has been considered a form of passive cell death. Mitotic catastrophe is an event in which a cell is destroyed during mitosis. This is believed by some to occur as a result of an attempt at aberrant chromosome segregation early in mitosis, or as a result of DNA damage later.

Mitosis is a type of cell division that results in two daughter cells each having the same number and kind of chromosomes as the parent nucleus, typical of ordinary tissue growth. Cytostasis is the inhibition of cell growth and multiplication. Cytostatic refers to a cellular component or medicine that inhibits cell growth. Cytostasis is an important prerequisite for structured multi-cellular organisms.

However, the discovery that TNF alpha mediated necrosis can be inhibited by a specific inhibitor of RIP1 kinase, necrostatin-1, led to the concept of Necroptosis; in general apoptosis confers advantages during an organism's lifecycle. For example, the separation of fingers and toes in a developing human embryo occurs because cells between the digits undergo apoptosis. Unlike necrosis, apoptosis produces cell fragments called apoptotic bodies that phagocytic cells are able to engulf and quickly remove before the contents of the cell can spill out onto surrounding cells and cause damage. Between 50 and 70 billion cells die each day due to apoptosis in the average human adult. For an average child between the ages of 8 and 14, approximately 20 billion to 30 billion cells die a day. Research in and around apoptosis has increased substantially since the early 1990s. In addition to its importance as a biological phenomenon, defective apoptotic processes have been implicated in an extensive variety of diseases. Excessive apoptosis causes atrophy, whereas an insufficient amount results in uncontrolled cell proliferation, such as cancer. Nanotechnology can be applied in a variety of bio-medical and bio-engineering proceedings and is called Nano-medicine.

Magnetic nano-particles of different sizes with tailored surface chemistry are used in a routine setting for cell Separation and in as magnetic resonance imaging contrast agents, hyperthermia and drug delivery, for SSF applications these particles coated by different materials to receive biocompatibility. One major hurdle that underlies the use of nano-particles in the treatment of diseases is the problem of getting the particles to a specific body compartment; Solar Sonic Laboratories have completely solved that.

A potential benefit of using these particles is the application of external magnetic fields/gradients to focus the particles to the particular site in the body and to hold them until the therapy is complete. All these efforts point to an aim in which drugs are only delivered to specific sites and at therapeutic levels. Magnetic drug targeting, in which magnetic nano-particles bound to a chemotherapeutic agent and concentrated in a tumor region by an external magnetic field after intra-arterial injection could be a promising tool in cancer therapy. Intracellular distributions of the anticancer drug doxorubicin (DR) and nucleic acid dyes 4',6-diamidino-2-phenylindole (DAPI) and ethidium (E) bromide were investigated and modified by Solar Sonic Laboratories. By visual inspection, it was observed that yeast cell culture was heterogeneous in stainability by DAPI, DR E.

There were different dynamics of staining by each dye. It was explained by the specifics of permeability of the cell envelopes for each substance, resulting from combination of at least two factors. The first one is the diffusion barrier of the cell wall and plasma membrane; the second is associated with the system of

nonspecific drug resistance, providing energy-dependent excretion of cationic organic molecules from the cell. The fluorescence of DAPI in the cells made a clear pattern of "spots & dots". The spots and dots corresponded to the nuclear and the mitochondrial DNA, subsequently respond to SSF Bio-communications.

A different pattern of fluorescence was seen for DR and E. While large spots, most probably representing nuclei, were well discerned, the entire region of mitochondria exhibited diffuse uniform glow. Upon joint treatment of cells with DAPI + DR or DAPI + E, both patterns were seen. We describe the osteomimetic and mesenchymal properties of cancer cells and relate this to our tendency to metastasize to bone. Cancer cells are thought to originate from epithelial cells in the epithelium, and the question arises how cancer cells of epithelial origin can adopt osteomimetic properties.

If we study osteomimetic properties in greater detail, we find that cancer cells of the primary tumor site already show osteomimetic features even in those cancer cells or types that seldom metastasize to the bone. Most known human carcinomas show an increased expression of osteopontin, osteocalcin and sialoprotein, which are bone-specific proteins. Thus the expression of bone Specific proteins by primary tumour cells is not just restricted to cancer cells metastasizing to bone but a general feature of the malignant phenotype. Moreover, cancer cells in the primary tumour site express various enzymes commonly expressed by osteoclasts too, such as TRAP, MMP-9 Cath-K and carbonic anhydrase, and the vacuolic H<sup>+</sup>-ATPase.

These features do not accord with the assumed epithelial character of cancer cells in the primary site. Preosteoclastic behaviour is also reflected in the functional properties of cancer cells, that is: matrix-resolving properties, hormone / neuronal dependence, coupling with mesenchymal cells, migrating and transmigrating properties, neurogenetic properties, trafficking to the bone, immune deviation, sensitivity to antirheumatics, bisphosphonates, polyphenols and steroids. When preosteoclasts fuse to osteoclasts they over-express certain intracellular signaling pathways which are likewise over-expressed in cancer cells during their proliferation. When we compare the surface markers of cancer cells with those of osteoclasts and their myeloid lineage progenitors, we detect multiple correspondences.

The following clusters of differentiation commonly expressed by myeloid, including preand osteoclast cells, are surface markers of various cancer cells as well: CD9, CD10, CD11b, CD13, CD14, CD24, CD26, CD31, CD34, CD35, CD36, CD37, CD40, CD44, CD46, CD 47, CD49, CD51, CD53, CD54, CD55, CD56, CD59, CD61, CD63, CD68, CD71, CD73, CD75, CD80/86, CD 81, CD87, CD90, CD97, CD 98, CD 105, CD115, CD117, CD151, CD133, CD147, CD163, CD164, CD166, CD184, CD200.

Beside the above cited clusters of differentiation expressed by both cancer and myeloid lineage cells, a multiplicity of other surface markers exist, of which we will name only the following: TLRs, RANK, ADAM, DAP12, OSCAR, MAC387, DC-STAMP, NK1 receptor, BMP receptor, Protease activated receptor-1 TRAF- and calcitonin receptors. The calcitonin receptors along with TRAP are specific osteoclast Markers. These surface markers are not expressed by epithelial cells, demonstrating that cancer cells, even in their primary site, are more closely related to the various stages of myeloid cells, passing from stem cells to monocyte progenitor cells, dendritic cells, macrophages through to osteoclasts.

Due to epithelial markers, cancer cells seem likely to be of epithelial origin. But certain cells of the myeloid lineage, the Langerhans cells, usually adopt epithelial markers as well. Langerhans cells show a high level of epithelial surface markers CD326 (EpCAM), CD 227(Mucin1) and E-Cadherin in the epidermis, through which they are connected with keratinocytes. Whether they may also adopt a local cytokeratin scaffold has not so far been ascertained to our knowledge. MTA transgenic mice offer further evidence that myeloid lineage cells in the epidermis, rather than epithelial cells, are required for carcinogenesis. The mice are deficient in MHC-II positive cells in the epidermis, and Langerhans cells or any other myeloid cells are therefore completely absent in the epidermis. These mice are resistant to squamous cell carcinoma induction in the skin, which can be explained by the hypothesis that cells of myeloid origin, rather than epithelial cells alone, are a prerequisite for carcinogenesis. On the basis of phenotypic features, functional characteristics and intracellular signalling-specific activities, we hypothesize that cancer cells originate from the myeloid lineage. Cancer cells can be seen as different stages of the myeloid lineage, from bone marrow stem cells through monocytes to pre- and osteoclasts with the additional feature of malignancy.

We can conclude that the osteomimetic properties of cancer cells are inherent properties of these cells and consequently cannot be interpreted as an epiphenomenon or as opportunistic features for the sole purpose of metastasis in the bone. Whether the fusogenic properties of macrophages and preosteoclasts or their plasticity allow them to adopt local cytokeratin characteristics, and how these aspects may be connected with their malignancy, is the subject of intense research by various research groups. If there is a transition between the different phenotypes of cancer cells, it is more epithelial-myeloid transition and less epithelial-mesenchymal transition.

Hypericin a photosensitive pigment occurs in the plant *Hypericum perforatum* L. It is a substance which, Thanks to its exceptional properties, has attracted for the decades interest of experts in the field of biology and medicine. Attention is given to its anti-retroviral, antidepressant, anti-inflammatory, antineoplastic, and antibacterial effects. Nowadays, however, scientists are mainly interested in the hypericin-mediated photodynamic therapy (PDT) as a promising anticancer therapy.

The only comprehensive genotoxicological study, aimed at the detection of nonphotoactivated hypericin genotoxicity assessment was accomplished in Solar Sonic laboratory on different genetic model systems. Previously we compared the potential genotoxic effect of non-photoactivated and photoactivated hypericin and their potential DNA protective effects. It was proved that non-photoactivated hypericin did not exhibit genotoxic or antigenotoxic effects.

Moreover, our research was aimed at evaluation of the photoactivated hypericin induction damages to DNA using selected test systems enabling to assess growth inhibition, viability and apoptosis of selected cancer, noncancer and stem cells. A recombinant fungal compound Ostreolysin induces anti-proliferative and proapoptotic effects on colon cancer cell many compounds with extraordinary chemical structures and brilliant bioactivities have been identified from marine organisms.

We will illustrate the fascinating natural products as anti cancer drugs we have been investigating, data consists of two topics:

- (1). Development of eribulin from halichondrin B
- (2). Identification and characterization of novel antitumor natural products, lyngbyacycloamides

Halichondrin B was isolated from the black sponge, *Halichondria okadai*. Interestingly, this polyether macrolide exhibited antitumor activity both in vitro and in vivo. The mechanism of action of halichondrin B was shown to be a novel one that disrupts the polymerization dynamics of tubulin, which makes this Natural product an interesting candidate for the treatment of cancer. However, the difficulty of collecting sufficient material (only 12.5 mg from 600 kg of sponge) impaired studies for its development.

The complete synthesis of halichondrin B represented a breakthrough. The total synthesis also facilitated the structure-activity relationship study, and which revealed that the activity resides in the macrocyclic lactone C1-C38 moiety. Ultimately, the moiety derivative was approved for the treatment of breast cancer in several countries and is now available on the market as anti-cancer drug Halaven. Cyanobacteria are photosynthetic prokaryotes and that are widely distributed throughout marine and terrestrial environments.

Members of the marine cyanobacteria genus *Lyngbya* are known to synthesize structurally interesting and biologically active secondary metabolites. Recently, my research group has purified new compounds lyngbyacyclamides A and B. The biological activities of these cyclic peptides are quite unique, since they show toxicity against B16 melanoma cells. And our study revealed that these compounds inhibit the ERK (Extracellular signal-regulated kinase) activity. Efforts to synthesize these molecules are currently in progress so that we can elucidate the mechanism of action in more detail. Role of Vitamin D Binding Protein-derived Macrophage Activating Factor (GcMAF) in the immunotherapy of cancer. There has been much recent interest in the role of the vitamin D axis in the immunotherapy of cancer. The vitamin D axis includes vitamin D, vitamin D receptor (VDR) and vitamin D-binding protein (VDBP; also known as Gc-globulin) that is the precursor of the Gc globulin-derived Macrophage Activating Factor a protein that proved effective as an anticancer agent in a variety of experimental and spontaneous tumours.

The interest for administering GcMAF to humans derives from the observation that different chronic pathologies such as cancer, HIV infection and systemic lupus erythematosus show elevated level of serum alpha-N-acetylgalactosaminidase (Nagalase), an enzyme that degrades VDBP resulting in the loss of MAF precursor activity with consequent impaired immune response.

Consequently, MAF precursor activity and serum Nagalase activity have been used as diagnostic indices for a variety of cancer patients and as prognostic indices during radiation therapy, surgical resection of tumors and GcMAF therapy of tumor bearing mice. The well demonstrated anti-cancer efficacy of GcMAF can be ascribed to different biological properties of the molecule that include activation of tumoricidal macrophages, inhibition of tumor-induced angiogenesis and direct inhibition of cancer cell proliferation, migration and metastatic potential. In the present study, we demonstrate that GcMAF-activated macrophages induce the apoptosis of human breast cancer cells and inhibit their proliferation *in vitro*.

Macrophages (cell line Raw 264.7, HPA Culture Collection) were activated by culturing them in the presence of 100 ng/ml GcMAF for 72 h prior to addition to the human breast cancer cell culture (cell line MCF-7, HPA Culture Collection). Cell cultures were fixed and stained with Haematoxylin Eosin or with Papanicolau staining after 18 and 40 h of co-incubation. It could be swiftly observed that GcMAF-activated macrophage surrounded MCF-7 cells and emitted pseudopods that appeared to "search for" contact with the cancer cells.

MCF-7 cells in contact with activated macrophages showed a significantly altered morphology with large and irregular cytoplasm and with nuclei where the chromatin appeared fragmented, almost as if the cells were undergoing apoptosis. In many fields the GcMAF-activated macrophages appeared to disaggregate the MCF-7 cytoplasm. These results are consistent with the recent observation that underlines the therapeutic potential of manipulating macrophage activation in breast cancer and provide a rationale to suggest clinical trials exploiting the potential of GcMAF in the immunotherapy of human cancer.

Human epidermal growth factor receptor 2 (ErbB2) is a transmembrane oncoprotein that is over expressed in breast cancer. A successful therapeutic treatment is a monoclonal antibody called Trastuzumab which interacts with the ErbB2 extracellular domain (ErbB2-ECD). A better understanding of the detailed structure of the receptor-antibody interaction is indeed of prime interest for the design of more effective anticancer therapies.

For this purpose, we have used molecular dynamics simulation (MD) at the atomistic and coarse grained scales. These methodologies can provide fine details about the molecular interactions between these proteins and give useful information to understand its biological action. The atomistic scale simulations performed on the ECD / Trastuzumab Fab complex. In addition to the established interaction between the Trastuzumab Fab and the ErbB2 domain IV epitope, a nascent interaction between domain II and the constant fragments of the Fab antibody is observed.

This additional interaction is facilitated by genuine hinge movement at the domain III/domain IV interface<sup>1</sup>. On the other hand, the coarse grained simulations were performed on the full ErbB2 receptor including the lipid bilayer, using experimental information and homology modeling, a structural analysis of the influence exerted by the monoclonal antibody on the full receptor was carried out. Multi-microsecond simulations arrived to structures of protein complexes compatible with experimental observations.

The ErbB2 ectodomain as well as the intracellular domain approached the bilayer surface, as can be observed on the two molecular representations. However, the Trastuzumab Fab hindered the approximation of the ECD to the membrane, whereas the antibody effect is less notorious on the cytoplasmic domain, where the signaling cascade starts. These findings support the idea that the main bioactive action of Trastuzumab is on the extracellular fragment, at least on the ErbB2 monomer. Antitumor activities of medicinal mushrooms appeared to be attributable to an immune-modulating action of their polysaccharides and polysaccharides-related complex in immune system. These polysaccharide-related compounds demonstrate their potent and unique properties as biological response modifiers (BRM). It is considered that immune-modulating polysaccharides from edible and medicinal mushrooms could augment or complement a desired immune system to maintain a health condition in a host.

Cytokines play important roles in a regulation of immune responses via cytokine networks and signaling pathways. Then, normal immune responses could contribute to preventing from cancer and immune-deficiency diseases. In this study, we examined an immune-modulating action of polysaccharide fractions from novel medicinal mushroom, *Grifola gargal*, which is known as an edible mushroom in south region in Chile, against macrophages, and their tumorcidal effects.

The fruiting bodies of *G.gargal* cultivated at Solar Sonic Laboratories were used. The lyophilized sample was extracted with hot water, and then a crude extract was obtained, and then it was separated by Sephacryl gel permeation chromatography. The monocyte cell-line, THP-1 was induced differentiation to a macrophage by PMA, then stimulated with various concentrations of each fraction.

After incubation, cytokine proteins and mRNAs produced in the macrophages were examined by western blotting and qRT-PCR, respectively. Moreover, after HeLa cells were co-cultivated with the stimulated cells, a tumorcidal effect was examined. A crude extract of *G. gargal* induced to activate a macrophage. And then, it was shown that a growth of HeLa was inhibited by co-cultivation with it. We obtained three fractions from a crude extract. A polysaccharide fraction (Mw 400 kDa) showed the strongest immunomodulating effect on cytokines productions. These cytokines were recognized as type 1, inflammatory, cytokine, such as TNF-, IL-1, IL-6, and IL-12. Moreover, we also elucidate that other polysaccharide-related complex (Mw 20 kDa) played as a same immunomodulator.

It was shown that a hot water extract from *G. gargal* possessed a tumorcidal activity against HeLa. And, polysaccharide and polysaccharide-related complex fraction from it showed an immune-modulating effect on inflammatory cytokine production from stimulated macrophages. These results suggested that *G. gargal* induced a tumorcidal action of macrophages via type 1 cytokines network. It can be considered that *G. gargal* become a source of a novel medicinal material. Glycosylation is one of the major post-translational modifications of biotherapeutics that depends on the cell line used for production.

By establishment of the GlycoExpress toolbox (GEX) we generated a set of Glyco-engineered human cell lines for the high yield production of fully human glycoproteins to optimize the glycosylation of antibodies and non antibody biotherapeutics. Among other non antibody molecules three glycooptimized antibodies are presently in clinical development and further in the pipeline. Two of these are Biobetter antibody molecules directed against approved targets and glycooptimized with respect to manifold improvement of anti-cancer activity, half-life elongation, and removal of immunogenic components and broadening of the patient and indication coverage.

The clinical outcome of the antibodies Cetuximab and Trastuzumab is largely depending on the FcRIIIa allotypes where only less than 20% of the patients which are homozygous for the Valin allotype on position aa158 (V/V) show a drastically better clinical outcome than patients where the Phenylalanin (F) is present either heterozygous (F/V) or homozygous (F/F).

The receptor is present on natural killer cells (NK cells) which are involved in antibody dependent cellular anti tumor cytotoxicity (ADCC) and are thought to be the effector cells for cancer cell killing. Based on glycooptimization by production in GlycoExpress the ADCC activity of CetuGEX, which is an improved 2<sup>nd</sup> generation GEX-glycooptimized antibody of ErbituxR, is improved by ~10-fold for patients carrying the V/V allotype and up to 250 fold for the other allotypes (>80% of patients). Thereby all allotypes reach an anti tumor activity about 10-fold higher than that of the V/V allotype with conventional non-GEX-glycooptimized antibodies. Therefore an improved antitumor activity and clinical outcome is expected for all patients as well as a broadening of the patient spectra. In addition, CetuGEX revealed a ~1.5-2 fold improvement of serum half live in PK studies within cynomolgus monkeys due to the optimization of its sialylation. The mean terminal serum elimination half-life of CetuGEX was 110 hours while the terminal half-life of ErbituxR was 67.5 hours, respectively, resulting in an improved area under the curve for the CetuGEX molecule. Moreover, while ErbituxR induces severe hypersensitivity reactions that are caused by its nonhuman foreign Galili epitope (Gal-Gal carbohydrate structures due to the production in mouse myeloma cells) CetuGEX will not since structures are not present on CetuGEX. TrasGEX is a Trastuzumab similarly GEX-glycooptimized as CetuGEX with a 10- 140 fold improved ADCC suitable for all patient ADCC receptor allotypes. PankoMab-GEX is a highly potent anti-tumor antibody for up to 100% of the patients of Ovarian, Breast NSCLC and

other endometrial cancers. It is directed against a combined carbohydrate-protein epitope specific for tumors combining tumor-specificity towards *de novo* carbohydrate tumor antigen/high affinity towards protein part. All these antibodies are in Phase I/II clinical development and preliminary data from Phase I indicate high clinical potency of the drugs. In contrast to the classical stem cell theory that proposes that there is a small subpopulation of cancer cells with stem cell properties, we have proposed the stemness phenotype model (SPM) as an alternative model. The SPM proposes that all cancer cells have stem cell properties and thus all of cancer stem cells are potentially tumorigenic.

### **Therefore, to cure cancer, all cancer cells should be eliminated at once**

Following this hypothesis, we developed in a two phase treatment (2PT) where in the first phase cells exposed to conventional anticancer drugs, followed by second phase treatment with salinomycin. Our result showed that several conventional anticancer drugs eliminate the bulk of cancer cells but there is fraction of surviving cells that adopt a senescence-like state. Regarding gliomas, we found glioma cells resistant to the clinically useful anticancer drugs temozolomide (TMZ), carmustine (BCNU), and lomustine (CCNU) survive and adopt a senescent-like state.

In second phase, a low concentration (0.5  $\mu$ M) of salinomycin prevented the regrowth and partially eliminated these surviving cells. All together, the SPM and the 2PT may provide the basis for a more rational approach to develop effective anticancer therapies for gliomas and this varied strategy can be extrapolated to other tumors. Cancer stem cells (CSCs) usually stays in the stationary phase so that they are resistant against the ordinal Chemotherapies because these treatments are effective to growing cells, upon some stimuli or environmental alterations, CSCs are activated & induced proliferation, then finally form secondary cancer cells. If we could modulate stem cell-like properties of CSCs by small organic molecule, it is expected that we could eliminate cancers from human body.

According to the recent studies of Solar Sonic Laboratories, stem cells possess a molecular mechanism that guarantees undifferentiated state while they can proliferate well. One of the factors related to this mechanism is transcription factor, Hairy and Enhancer of Split 1 (Hes1). This helix-loop-helix type transcriptional repressor is expressed in all undifferentiated cells, and inhibits differentiation.

For example, forced expression of Hes1 in fibroblasts results in the resistance to myogenesis, which in turn, repression of Hes1 expression facilitates differentiation. In the case of cancer cells, it was shown that expression level of Hes1 is 5~50 times higher in all the cell lines of rhabdomyosarcome or cancer cells derived from patients. Thus, it is expected that Hes1 inhibitor could take stem celllike property away from CSCs through induction of their differentiation, Hes1 functions through association with a co-repressor, Grocho /transducing-like Enhancer of Split (Gro/TLE) family of proteins.

The most important thing is that a Trp-Arg-Pro-Trp (WRPW) motif of C-terminus of Hes1 is required and sufficient for the binding to Gro/TLE. We speculated a WRPW motif mimicking compound binds to Hes1 binding site of Gro/TLE, interfere the association between Hes1 and Gro/TLE, and then inhibit Hes1 function. We take some advatages in this idea for three reasons: the motif is 1) only four amino acids long, 2) composed of characteristic amino acids, and 3) shown to be turn conformation. at Pro residue.

These features prompted us to design, synthesis, and evaluate the WRPW motif mimic. For our study, we selected benzodiazepine scaffold to mimic the turn structure, and prepared 10 compounds. To evaluate the efficacy of these compounds, we can employ a luciferase reporter assay because Hes1 is a transcription factor.

Briefly, introduction of Hes1 expression vector into the cells results in decrease of Luc activity because of transcriptional repression activity of Hes1 when using Luc plasmid containing actin promoter and Hes1 binding site, N-Box. In the presence of active compound, Luc activity should be restored by inhibiting the interaction between Hes1 and Gro/TLE. We tested 10 compounds by luciferase assay, and found that one of the compound exhibited the activity. Docking study between the compound and Gro/TLE suggested several improvement points to increase activity. According to this, synthesis of second-generating compounds is now in progress.

In the recent years the research on various natural compounds has attracted extensive attention of scientists due to their potential usefulness in chemoprevention and treatment of cancer and some degenerative diseases. Because the prevention is better than cure, an emphasis has been given to find and chemically/ biologically describe the new potential natural compounds which could help mostly in the chemoprevention. Therefore, a study of the influence of the plant extracts on human body is of great importance. In the following research the modulatory effects of the aqueous extract from *Armoracia rusticana* (horseradish) (AE) was studied. This perennial herb belongs to Brassicaceae family and it is widely used.

Firstly, we studied the molecular mechanisms underlying a potential antioxidant activity of AE using four assays: the DPPH assay, OH radicals scavenging assay, DNA-nicking assay and reducing power assay. Secondly, we aimed at the antigenotoxic/modulatory effect of an aqueous extract from *A. rusticana*, by the pre-treatment and post-treatment of H<sub>2</sub>O<sub>2</sub>-treated human lymphocytes. We focused on pre-treatment and post-treatment by AE as a way of hydrogen peroxide-induced oxidative DNA damages modulation using the alkaline Comet assay. It was proved that pre-treatment caused a significant reduction of the DNA damages, and AE acted as a desmutagen due to its antioxidant activities. Pro-apoptotic effect of photo-activated hypericin A549 cell line.

Hypericin is a substance isolated from *Hypericum perforatum* L. It is mainly known for its beneficial effects on human body such as antibacterial, anti-inflammatory, anti-depressant effects. Solar Sonic researchers have shown an increasing interest in hypericin mediated photodynamic therapy which is known for its tumour-seeking ability/minimal toxicity in dark. Our objective was to determine the effects of different concentrations of photoactivated hypericin to inhibit the growth of the A549 cell line and also to determine the mechanism inducing this effect.

Our results show that growth inhibition of hypericin treated and Subsequently photoactivated A549 tumor cells are dependent upon the systematic concentration of hypericin which is caused by reduced viability and increased apoptosis of monitored cells. It is however noteworthy to state that Ugonin K induces Apoptosis of human skin cancer cells by reactivating mediated signal pathways.

Skin cancer is divided into two groups by histological features – nonmelanoma skin cancers (NMSC) and Melanoma. Cutaneous basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of NMSC are almost 75% among human skin malignancy cancer. Ugonin K isolated from *Helminthostachys zeylanica*, inhibited the growth of human skin cancer cells, especially in the case of treatment of SCC25 and BCC.

The cytotoxicity results show that ugonin K expressed less toxic to human keratinocytes (HaCaT cells) and human skin fibroblasts (Hs68 cells) than BCC cells, suggesting that ugonin K may have potential to be developed effective drugs for skin cancer cells without damaging skin normal cells.

After treatment with ugonin K in BCC cells, cell cycle arrested in S-G<sub>2</sub>/M phase with a markedly increased apoptotic sub- G<sub>1</sub> peak, the expression of p53 and p21 revealed a more significant increased than the untreated control. In addition, ugonin K was found to increase reactive oxygen species generation on SCC25 and BCC cells. In this study, we expected ugonin K has potential for an effective and specific drug to cancer cell, can minimize the damage to normal cell and provide a better therapeutic method to skin carcinoma.

Leukemia is the general term for some different types of blood cancer. There are four main types of leukemia called: Acute lymphoblastic (lymphocytic) leukemia (ALL), Acute myeloid (myelogenous) leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid (myelogenous) leukemia (CML). It is important to know that patients are affected and treated differently for each type of leukemia. These four types of leukemia do have one thing in common; they begin in a cell in the bone marrow. The cell undergoes a change and becomes a type of leukemia cell. The first job is to form myeloid cells.

Myeloid leukemia can begin in these cells. The second job is to form lymphocytes, which are a part of the immune system. Lymphocytic leukemia can arise in these cells. The leukemia is called lymphocytic or lymphoblastic if the cancerous change takes place in a type of marrow cell that forms lymphocytes. The leukemia is called myelogenous or myeloid if the cell change takes place in a type of marrow cell that normally goes on to form red cells, some kinds of white cells and platelets. For each type of leukemia, patients

are affected and treated differently. ALL and AML (acute leukemias) are each composed of young cells, known as lymphoblasts or myeloblasts. These cells are sometimes called blasts. Acute leukemias progress rapidly without treatment. Patients who relapse after treatment and Patients who continue treatment after remission (maintenance), a carefully conducted clinical trial may provide the best available therapy.

Currently, Solar Sonic Laboratories are infusing some new drugs, those new drugs called "molecular targeted therapies, which increase life expectancy and quality of life of patients, such as Imatinib (Gilevec) and Nilotinib (Tasigna) that directly attack the malignant cells without harming healthy ones with this treatment, patients no longer suffer the aggressive therapies with traditional treatments such as radiotherapy and chemotherapy, allowing patients to continue with their daily activities while enjoying a good health with good quality of life. The chronic myeloid leukemia (CML) is a malignant disease of the blood and bone marrow progressive and slow that occurs in middle age, with the highest incidence between 35 and 55 years of age.

Knowing the secrets of how the virus functions and reproduces itself, a process called its life cycle can help Solar Sonic scientists design new drugs that are more effective at suppressing the virus & have fewer side effects. Viruses cannot reproduce without the aid of a living cell. Although HIV can infect a number of cells in the body, the main target is an immune cell called a lymphocyte, precisely a CD4 helper cell, a type of T-cell.

T-cells are an important part of the immune system because they help facilitate the body's response to many common but potentially fatal infections. Without enough T-cells, the body's immune system is unable to defend itself against many infections. By ways that are not yet understood, HIV's life cycle directly or indirectly causes a reduction in the number of T-cells in the body and resulting in increased risk of infections.

After HIV enters the body through unsafe sex, contaminated needles, and blood transfusions or from mother to child (vertical or perinatal transmission) it comes in contact with its favorite host cell - the T-cell. When this happens, HIV will hijack the host cell's cellular machinery to reproduce thousands of copies of it. HIV has to complete many steps in order for this to happen. At each step of HIV's life cycle, it is possible to design a drug that will stop the virus. Designing drugs to interfere with specific steps in the viral life cycle is called rational drug design.

#### **Solar Sonic Technologies in detection and treatment of Bladder cancer through Clinical Trials**

Solar Sonic Clinical Trials were extensively conducted over the years, we proceeded to cover bladder cancer clinical trials as an example for the purpose of illustrating biomedical innovations in ophthalmology and cancer diagnostics.

We therefore had previously announced that a blinded, multi-center clinical study of the non-invasive test for detecting bladder cancer in urine, successfully achieved the study's primary endpoint for effectively detecting the recurrence of bladder cancer in subjects with a history of the disease.

The urine test successfully identified cancerous cells in urine samples in patients with a history of the disease, with reported sensitivity of 84.4% and specificity of 82.7% for the study's primary endpoint.

The technology is being developed by Solar Sonic Laboratories as cancer diagnostics subsidiary, and allows an accurate diagnosis of cancerous and precancerous cells, based on a unique combination of color and morphology by utilizing a proprietary kit containing unique extract and dyes.

Solar Sonic Laboratories are extremely pleased with these results showing high sensitivity and specificity and believe that they provide a foundation upon which regulatory approval can be secured and be a second indication for use of the technology platform.

There is a clinical need for a better test for the up to 80 percent of patients with bladder cancer whose cancer recurs, since many of the currently available tests are clinically suboptimal, invasive or expensive. Based on these strong clinical results, we believe that Solar Sonic Laboratories are in turn considered viable promising solutions for the millions of patients with bladder cancer, and have the potential for diagnosing additional cancer indications.

The blinded clinical study was conducted in nine medical centers in Africa, where urine samples from 360 subjects with a history of bladder cancer were tested. The study population included 114 healthy subjects and about 246 patients currently suffering from the disease. The results of the urine tests were compared with results from biopsy or cystoscopy, in cases where biopsies were not taken. The results also indicated that the urine test's negative predictive value (NPV), defined as the probability that a patient having a negative result doesn't suffer from the disease, was 98.5%.

In addition to its high sensitivity for advanced stage tumors and high-grade malignancy, the test was also found to exhibit high sensitivity for early stage tumors and low-grade malignancies, which are difficult to identify using other non-invasive tests currently available on the market. These findings indicate that the method is adequately sensitive for the purpose of accurate and early detection of the recurrence of the disease. Solar Sonic Laboratories have determined that the study results were quite encouraging. The accuracy of this novel assay appears to be superior over any available non-invasive test, suggesting a potential to supplant some or all of the cystoscopies required for bladder cancer surveillance.

This is indeed great news for patients with history of bladder cancer, which may change their management. The secondary endpoint showed that the sensitivity of other non-invasive comparator tests, urine cytology, BTA stat and NMP22 Bladder-Check, was 50.0%, 68.8% and 17.4%, respectively. These findings further underscore the potential of the test as an accurate, reliable and a non-invasive tool for monitoring the recurrence of bladder cancer.

Solar Sonic also plans to utilize reimbursement existing codes for monitoring bladder cancer recurrence and will continue to advance the technology for the diagnosis of additional cancer indications. Bladder cancer is the fourth most prevalent cancer among males in the U.S. and the seventh most prevalent among males worldwide, with nearly 430,000 new case of the disease diagnosed globally in 2012. The rate of recurrence is the highest of all cancers and ranges from 50% to 80%.

According to U.S. clinical guidelines, patients with a history of urinary bladder cancer are required to undergo three to four tests per year to monitor disease recurrence in the first two years immediately following treatment, and one test annually in the years that follow. Because of high recurrence rates, the cost of diagnosing and treating bladder cancer is among the highest of all cancers. Solar Sonic technology allows an accurate diagnosis of cancerous cells, based on unique combination of color and morphology.

The technology may be implemented in screening tests and monitoring tests of disease recurrence in cancer patients after being treated. Solar Sonic Laboratories have proven the efficacy in diagnosing cervical cancer and bladder cancer in the framework of clinical trials, and estimates that the technology underlying the products may be implemented for use in additional cancer indications. The cervical cancer detection screening diagnostic test kit is in the initial commercial stage and has recently completed a clinical trial to prove its ability to monitor bladder cancer recurrence, while the underlying Solar Sonic Technologies are also adapted for other types of cancer as well, after a long history of extensively vigorous clinical trials in Africa.

In a separate experiment consisted of only Six patients at a moderate stage 2 from twelve different cancer categories and were put on the Solar Sonic Protocol treatments as explained in this paper. 6 patients had glioblastoma (brain) 6 patients had Kidney cancer, 6 patients had liver cancer, 6 patients had abdominal cancer, 6 patients had Thyroid cancer, 6 patients had ovarian cancer, 6 patients had bladder cancer, as well as 6 patients had prostate cancer, 6 patients had colon cancer, 6 patients had breast cancer, 6 patients had Pancreatic cancer, 6 patients had Testicular cancer, 6 patients had Bone Cancer, 6 patients had blood cancer.

We have elected to illustrate only the Glioblastoma clinical trial, we prospectively secured baseline and the serial tumor tissue for Glioblastoma and had developed patient-specific cell lines and putative stem cells (CD133+, nestin+ cells), and treated each patient with oral DCA for up to 18 months. DCA depolarized mitochondria, increased mitochondrial reactive oxygen species, and induced Apoptosis in GBM cells, as well as in putative GBM stem cells, both in vitro and in vivo. In post treatment procedures, they had dramatically improved and the outcome can be summarized whereas all of their tests were quite normal, where we reference CBC tests were quite normal (RBCs / WBCs/ Plts), and Hemoglobin (Hgb), Hematocrit (Hct). Additionally their Chemistry panel reports were all normal where their blood chemistry panels (metabolic

profiles) have shown Normal Fats and Normally balanced Proteins Ratios, Normal Sugar (glucose), normally balanced Electrolytes (like potassium, magnesium, sodium, and calcium), normally balanced Enzymes, Normal Leukocyte Count 3,300 to 8,700 WBCs per microliter (mcL) with normal reading of lymphocytes or monocytes. All tests had hematocrit range from 38% to 48%. The hemoglobin (Hgb) level measures the amount of the protein in RBCs that actually carries the oxygen. If the level of hemoglobin is low the body works much harder to deliver oxygen to tissues throughout the body.

Their Hgb had range from 12.6 to 16.1 grams per deciliter. They had a normal range for platelet count, were approximately from 150,000 to 350,000 platelets per mcL. They had normal Neutrophils and their Absolute Neutrophil Count (ANC) had ranged from 2,500 to 6,000 neutrophils. The Solar Sonic Glioblastoma Clinical Trial had been announced for a sufficient period of time of which 6 people joined in and had signed release forms, their medical records were detailed on their way into the study. Glioblastoma had started as a single tumor and a few random symptoms at first. As the cancer progresses, a conglomeration of tumors had developed in different areas around the brain. More symptoms had cropped up, with some of them linked to a tumor in a particular part of the brain. The treatment was really focused on stopping the growth of the tumor and making the patient as comfortable as possible while attempting to prolong life through radiation and chemotherapy. Glioblastoma is always fatal, but we had insisted on fighting.

#### **Solar Sonic software considered complete medical device as follows:**

- 
1. Software used to plan cancer treatment doses and to control the setting of oncology treatment devices
  2. Software used within the overall design and manufacturing processes of the medical devices
  3. Software used to measure and calculate the anatomical sites of the body to facilitate the irradiation of surgical intervention
  4. Software embedded in an implanted pulse generator device
  5. Software used to transmit administrative data such as a patient's name and address

This above matter highlights the increasing prevalence and complexity of software in the medical industry, but also underscores the difficulty of determining if the software is a medical device and, if applicable, which classification rule to apply under the European Medical Device Directive MDD 93/42/EEC. Many critical functions performed by medical devices are directed by software, and because software is not a visible product, sometimes, we lose sight of its importance. This is an extreme, but it emphasizes both how pivotal software is to the function of some medical devices and the consequences of software failure.

#### **Software and Medical Devices explicitly suggest the following categories of medical devices as follows:**

1. Software intended for analysis of patient data generated by a medical device with a view to diagnosis and monitoring
2. Software intended for use by patients to diagnose or treat a physical or medical ailment (condition or disease)
3. Software that is a component and integral part of a medical device

#### **Which Classification for Medical Device Software?**

The MDD 93/42/EEC, Annex IX makes provisions for software that functions as a medical device. Basically, it states that any software that drives a device or influences the use of a device falls automatically in the same classification. Clearly, software may be viewed as a medical device or an accessory to a medical device or as a

component and integral part of a medical device (automatically in the same class as the medical device and subject to the conformity assessment of medical device). The function of the software guides the classification of the software medical device. If the software is a medical device, it may be classified as Class I; however, if software medical device is an integral component of a device as indicated above, it assumes the classification of the device. For example, software that is part of a Class III medical device is viewed as a Class III device.

### **Software Is Viewed as an Active Medical Device**

This may be another concept that is difficult to reconcile and reasonably well explained by the NB-MED guidance, which states: "Operation of software requires electrical energy and software functions by converting this energy by means of interfaces and/or actuators, which are parts of the programmable electrical medical system." The NB-MED guidance document is interesting, because it attempted to delineate some of the inadequacies of the European regulations with regards to software. Fortunately, the proposed revisions to the Medical Device Directive and the Directive for Active Implantable Medical Devices (AIMD) attempt to resolve these omissions.

### **Software as Medical Devices with a Measuring Function**

One last nuance that should be discussed briefly is that potential Class I medical device software may be subject to classification as a Class I medical device with a measuring function. And, if the software now is viewed as such, Notified Body involvement is required for CE Marking. The Guidance MEDDEV 2.1.5, Medical Devices with a Measuring Function may be relevant to some software. Software with a measuring function must meet a few characteristics: measure quantitatively a physiological function or anatomical parameter; measurement displayed in legal units or other acceptable units as described within European Directive 80/181/EEC; and the intended purpose implies accuracy, and failing to comply with the "measurement" could result in a significant adverse effect on the patient's health and safety.

**To determine the proper European route to compliance for our software, we consider the following questions:**

- What is the intended use of the software?
- Does the intended use of the software designate it as a medical device? (The software provides instructions for an instrument for the purpose of diagnosis, prevention, monitoring, treatment or alleviation of disease.)
- If yes, is the software a component of a medical device? (The software drives or influences the use of the device.) If yes, the software assumes the class of the device.
- Is the software an independent device or accessory? If yes, does the software have a measuring function? If yes, perhaps the device is Class I measuring.

### **Revision of European MDD and AIMD**

It is widely accepted that software is either a pivotal medical device or a component of a medical device. The revisions to the Medical Device Directive and AIMD reflect the issues regarding software and provide explicit references and clarification. In the revised Medical Device Directive, the preamble specifically describes software and acknowledges the "growing importance of software in the field of medical devices." It is proposed that software be referenced in the definition of the medical device and a statement included that software may be used with The medical device. The following sentence will be added to Annex IX: "Stand alone software is considered to be an active medical device." In the AIMD, the Essential Requirement on software will be elaborated to discuss software validation and development lifecycle, risk management, validation and verification. Many ancillary topics also deserve mention. Conformity Assessment procedures require consideration of the development lifecycle; procedures for document control and configuration

management; and control of combinations between software versions and intended hardware. Published software medical device standards (not an exhaustive list) include IEC 62304, Medical Device Software-Software Life Cycle Processes, ISO/IEC 90003 and IEC 60601 series. Software is a component of many complicated medical devices or is an independent medical device or accessory, and as such, it is important for manufacturers to appreciate that their software may require CE Marking.

Alternating electric fields, generated by insulated electrodes, have been reported to exhibit inhibitory effect on the growth rate of a variety of human and rodent tumor cell lines as well as malignant tumors in animals. This non-thermal effect selectively affects dividing cells while quiescent cells are left intact. There are 2 modes of action for these anti-tumoric effects: (i) arrest of cell proliferation, and (ii) destruction of cells while undergoing division. Both effects were observed when such fields were applied for 24 hours to cells undergoing mitosis that is oriented along the field direction.

The 1st mode of action is manifested by interference with the proper formation of the mitotic spindle, while the 2nd mode of action results in rapid disintegration of the dividing cells. Both effects are consistent with the computed directional forces exerted by these specific fields on charges and dipoles within the dividing cells. In-vivo treatment of tumors in C57BL/6 and BALB/c mice resulted in significant slowing of tumor growth and extensive destruction of tumor cells within 3 to 6 days. These findings showed the potential applicability of alternating electric fields as a novel therapeutic modality for malignant tumors.

Electric tumor treating fields (ETTF), also known as alternating electrical field therapy, are low-intensity (1 to 2 V/cm), intermediate-frequency (100 to 200 kHz), alternating electric fields employed for the treatment of malignant tumors. This novel treatment modality has shown promise in pilot clinical trials in patients with advanced stage solid tumors including glioblastoma (GBM). Current published evidence is primarily from a single investigator group. The findings of a pilot clinical trial examining the effects of ETTF in 10 patients with recurrent GBM.

Median time to progression (TTP) in these patients was 26.1 weeks and median overall survival (OS) was 62.2 weeks. The authors noted that these TTP and OS values were more than double the reported medians of historical control patients. No device-related serious adverse events (AEs) were seen after more than 70 months of cumulative treatment in all of the patients. The only device-related AE observed was a mild-to-

Moderate contact dermatitis beneath the field delivering electrodes. We concluded that ETTF are a safe and effective new treatment modality that effectively slows down tumor growth in-vitro, in-vivo, as well as in human cancer patients.

We evaluated the safety, tolerability, and effectiveness of ETTF treatment in patients with locally advanced or metastatic solid tumors using the NovoTTF-100A device. A total of 6 patients were heavily pre-treated with several lines of therapy; no additional standard treatment option was available to them. Electric tumor treating field treatments using continuous NovoTTF-100A lasted minimum of 14 days and was well-tolerated.

No related serious AEs occurred. Outcomes showed 1 partial response of a treated skin metastasis from a primary breast cancer, 3 cases where tumor growth was arrested during treatment, and 1 case of disease progression. One mesothelioma patient experienced lesion regression near ETTF with simultaneous tumor stability or progression in distal areas. The number of patients in this study was small, the lack of therapy toxicity and the effectiveness observed in data gathered to date indicate the potential of ETTF as a new Treatment modality for solid tumors, thus, warranting further investigation. The findings of 20 GBM patients who were treated with ETTF for a median duration of 1 year. No ETTF-related systemic toxicity was observed in any of these patients, nor was an increase in temozolomide toxicity seen in patients receiving combined treatment.

In newly diagnosed GBM patients, combining ETTF with temozolomide treatment led to a progression-free survival of 155 weeks and OS of 39+ months. We concluded that these results suggest that combining ETTF with chemotherapeutic cancer treatment may increase chemotherapeutic efficacy and sensitivity without increasing treatment related toxicity. Recent reviews indicated the ETTF is a promising approach for the treatment of GBM and non-small cell lung cancer. We noted that novel treatment approaches in recurrent [GBM] include anti-angiogenic agents (bevacizumab and cilengitide)& ETTF (NovoTTF). Furthermore, we reviewed in-vitro and in-vivo pre-clinical studies, showing the activity of ETTF both as a monotherapy as well as in combination with several cytotoxic agents. We also summarized the clinical experience with ETTF, mainly in 2 indications: (i) recurrent GBM: in a prospective randomized phase III trial, ETTF was compared

with best standard care (BSC, including chemotherapy): ETTF significantly improved median OS compared with standard therapy (7.8 versus 6.1 months) for the patients treated per protocol. Importantly, quality-of-life was also better in the ETTF group (ii) a phase II study of second-line treatment of non-small cell lung cancer, where ETTF was administered concomitantly with pemetrexed.

This combination resulted in an excellent median OS of 13.8 months. Interestingly, the progression-free survival (PFS) within the area of the ETTF was 28 weeks; however, outside the ETTF the PFS was only 22 weeks. This is an important finding because it can be assumed that in the same patient the higher tumor control within the TTF fields area was a specific effect of TTF fields. Median OS was 13.8 months and 1-year survival was 57 %; 6 patients (14.6 %) had a radiological partial remission and 16 patients had stable disease (39 %).

We stated that these results are promising and compare well with matched historical controls treated with pemetrexed alone in second-line treatment. The authors stated that the proof of concept of ETTF has been demonstrated in the pre-clinical setting, and the clinical data seem promising in various tumor types. The side effects of ETTF were minimal and in general consisted of skin reaction to the electrodes.

We indicated that there are a number of ways in which ETTF could be further evaluated, for example, in combination with chemotherapy, as a maintenance treatment, or as a salvage therapy if radiotherapy or surgery is not possible. We concluded that while more clinical data are clearly needed, ETTF is an emerging and promising novel treatment concept.

The system is intended as treatment for adult patients (22 years of age or older) with histologically confirmed glioblastoma multiforme (GBM), following histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

The first randomized clinical study of electric tumor treatment fields did not reach its primary end-point of improved survival compared to active chemotherapy. This study was funded and sponsored by the device manufacturer; Novocure, Ltd. Subjects for this study were age 18+ years with histologically confirmed glioblastoma (World Health Organization grade IV astrocytoma) with radiologically disease progression.

Patients had a Karnofsky performance status greater than or equal to 70 percent, and adequate hematologic, renal and hepatic function (absolute neutrophil count greater than or equal to 1000/mm<sup>3</sup>, hemoglobin greater than or equal to 100g/L, platelet count greater than or equal to 100,000/mm<sup>3</sup>, serum creatinine level less than or equal to 1.7 mg/dL, total serum bilirubin less than or equal to the upper limit of normal and liver function values less than three times the upper limit of normal. Prior therapy must have included radiotherapy (with / without concomitant and/or adjuvant temozolomide).

Patients with infra-tentorial tumor location were excluded, as were patients with implanted electronic medical devices (Pace-Maker, programmable ventriculo-peritoneal shunt). Patients were randomized in a 1:1 ratio to receive NovoTTF-100A without chemotherapy or physician's choice of active chemotherapy (active control).

Chemotherapy agents considered as best standard of care (BSC) during the study included platinum-based chemotherapy (i.e., carboplatin); nitrosureas; procarbazine; combination of procarbazine, lomustine and vincristine; temozolomide; and bevacizumab. For patients assigned to Novo-TTF, uninterrupted treatment was recommended; although patients were allowed to take treatment breaks of up to an hour, twice per day, for personal needs (e.g. shower).

In addition, patients assigned to Novo-TTF were allowed to take 2–3 days off treatment at the end of each of 4 week (which is the minimal required treatment period for TTF therapy to reverse tumor growth). A period of 28 days of treatment with ETTF was considered 1 full treatment course. The primary end point of the study was overall survival. Secondary end points included progression free survival rates at 6-months; median time to progression (TTP), 1-year survival rate; quality-of-life; and radiological response. Subjects were seen in clinic monthly, and magnetic resonance imaging (MRI) was performed after 2, 4 and 6 months from initiation of treatment and subsequent MRIs were done according to local practice until disease progression.

Medical follow-up continued for 2 months after disease progression. Monthly telephone interviews with the subjects' caregivers were used to evaluate subject mortality rates. A total of 28 clinical centers enrolled 237 adult subjects with 120 subjects randomized to the NovoTTF treatment group and 117 subjects randomized to the BSC group. A total of 30 subjects never started on trial (4 in the treatment group and 26 in the BSC

group); 207 subjects started on trial, with 79 % discontinuation rate (n = 47 deaths; n = 49 deterioration of condition; and n = 68 study requirements of 2 additional clinic visits after disease progression were completed). Consent was withdrawn before completing 2 months of post-progression follow-up in 20 subjects. Adverse events led to 20 additional subject withdrawals.

Non-compliance with follow-up was attributed to 3 subjects. The proportions were similar between the NovoTTF-100A group and the BSC group of subjects who did not complete the protocol-defined follow-up due to withdrawal of consent, non-compliance, or AEs. An average of 4.2 months of TTF treatment per subject was completed for the 116 subjects in the active treatment cohort. Complete vital statistics were known for 93 % (221 subjects) at the end of the study. There were 202 known deaths and 19 subjects (ETTF = 9; BSC = 10) were still alive 6 months after the last subject was randomized. Sixteen (7 %) subjects were lost to follow-up.

The trial did not reach its primary end-point of improved survival compared to active chemotherapy. In addition, differences in response rates, progression-free survival at 6 months, and reduction in risk of death were not statistically significant. Quality of life analyses favored ETTF therapy in most domains. The differences in median overall survival between patients in the NovoTTF-100A group and the BSC group were not statistically significant.

The median OS is 6.3 months (95 % confidence interval [CI]: 5.6 to 7.8) in the NovoTTF-100A group and 6.4 months (95 % CI: 5.2 to 7.4) in the BSC group (log rank p = 0.98; Wilcoxon p = 0.72). The hazard ratio is 1.0 (95 % CI: 0.76 to 1.32) (test for proportional hazards p = 0.45). In the active chemotherapy control arm of the trial, survival was not significantly affected by the choice of chemotherapy. The survival curve for the two treatment groups appeared to be very similar during the first 12 months of followup. Between 12 and 24 months, the survival curves separated slightly in favor of the BSC control group.

There were no statistically significant differences in secondary endpoints of one-year survival, progression-free survival, radiologic response rates, and median time to tumor progression (TTP). Mild to moderate contact dermatitis on the scalp beneath the transducer arrays occurred in 16% of ETTF patients. Patients receiving active control chemotherapy experienced toxicity related to pharmacologic mechanism of the agents used: gastrointestinal (30% vs. 8%), hematological (19% vs. 4%) and infectious (12% vs. 4%).

Longitudinal Quality of Life (QOL) was available in only 27 percent of subjects (63 patients) who remained on study therapy for three months and for whom QOL data were available. In the domains of global health and social functioning, no meaningful differences between chemotherapy and ETTF were observed. However, cognitive, emotional & role functioning favored ETTF, physical functioning favored chemotherapy.

Symptom scale analysis is in accordance to treatment-associated toxicity; appetite loss, diarrhea, constipation, nausea and vomiting were directly related to the chemotherapy administration. Increased pain/fatigue was reported in the chemotherapy-treated patients and not in the ETTF treatment. Commenting on the trial by Solar Sonic Laboratories stated that the study was designed for superiority; Although well conducted, it might not have shown it for a limited compliance in the ETTF group. Stated that, even with this limitation, the trial has shown at least equivalence of ETTF to chemotherapy, with a decreased toxicity and increased quality of life favoring ETTF.

The manufacturer has initiated a subsequent randomized clinical trial enrolling diagnosed glioblastoma patients after completion of standard radiochemotherapy, parallel to starting the adjuvant or maintenance temozolomide chemotherapy. Patients randomized to the experimental arm will receive ETTF in addition to maintenance temozolomide. Comprehensive Cancer Network has a Category 2B recommendation to consider the use of ETTF for persons with local, diffuse or multiple recurrences of glioblastoma. Electric tumor treating field's technology is also being studied as a treatment for other solid tumors (e.g., melanoma and non-small cell lung cancer). However there is a paucity of published evidence from randomized controlled trials examining the long-term safety and effectiveness of ETTF as a treatment of tumors.

The anti-mitotic effect of tumor treating fields (TTFields) therapy has been demonstrated in multiple cell lines when the appropriate frequency was utilized. A phase III trial of TTFields monotherapy compared to active chemotherapy in recurrent glioblastoma patients established that TTFields therapy is associated with minimal toxicity, better quality of life, and comparable efficacy to chemotherapy. Ongoing and future trials will evaluate TTFields in newly diagnosed glioblastoma, solid tumor brain metastases, non-small cell lung cancer, and ovarian and pancreatic cancers.

**Efficacy is the capacity to produce an effect: It has different specific meanings in different fields. In medicine, it is the ability of an intervention or drug to produce a desired effect. In medicine, efficacy indicates the capacity for beneficial change (or therapeutic effect) of a given intervention (e.g. a drug, medical device, surgical procedure, or a public health intervention). If efficacy is established, an intervention is likely to be at least as good as other available interventions, to which it will have been compared. Comparisons of this type are typically made in 'explanatory' randomized controlled trials, whereas 'pragmatic' trials are used to establish the effectiveness of an intervention.**

**When talking in terms of efficacy vs. effectiveness, effectiveness relates to how well a treatment works in the practice of medicine, as opposed to efficacy, which measures how treatment works in clinical trials/laboratory studies. In pharmacology, efficacy ( $E_{max}$ ) refers to the maximum response achievable from a drug. Intrinsic activity is a relative term that describes a drug's efficacy relative to a drug with the highest observed efficacy. Effectiveness refers to the ability of a drug to produce a beneficial effect.**

**A distinction is made between 'method' effectiveness which describes the effect achievable if the drug was taken as prescribed and 'use' effectiveness which is the effect obtained under typical use circumstances when adherence is not 100%. The widely used intention to treat method of analyzing clinical trials provides estimates of 'use' effectiveness which are typically biased compared with 'method' effectiveness. Efficacy is the magnitude of response with respect to the  $K_d$ .**

**Cancers are usually named using -carcinoma, -sarcoma or -blastoma as a suffix, with the Latin or Greek word for the organ or tissue of origin as the root. For example, cancers of the liver parenchyma arising from malignant epithelial cells is called hepatocarcinoma, while a malignancy arising from primitive liver precursor cells is called a hepatoblastoma, and a cancer arising from fat cells is called a liposarcoma.**

**For some common cancers, the English organ name is used. For example, the most common type of breast cancer is called ductal carcinoma of the breast. Here, the adjective ductal refers to the appearance of the cancer under the microscope, which suggests that it has originated in the milk ducts.**

**Benign tumors (which are not cancers) are named using -oma as a suffix with the organ name as the root. For example, a benign tumor of smooth muscle cells is called a leiomyoma (the common name of this frequently occurring benign tumor in the uterus is fibroid).**

**Confusingly, some types of cancer use the -noma suffix, examples including melanoma and seminoma. Some types of cancer are named for the size and shape of the cells under a microscope, such as giant cell carcinoma, spindle cell carcinoma, and small-cell carcinoma.**

**In 2008, approximately 12.7 million cancers were diagnosed (excluding non-melanoma skin cancers and other non-invasive cancers), and in 2010 nearly 7.98 million people died. Cancers as a group account for approximately 13% of all deaths each year with the most common being: lung cancer (1.4 million deaths), stomach cancer (740,000 deaths), liver cancer (700,000 deaths), colorectal cancer (610,000 deaths), and breast cancer (460,000 deaths).**

**This makes invasive cancer the leading cause of death in the developed world and the second leading cause of death in the developing world. Over half of cases occur in the developing world. Deaths from cancer were 5.8 million in 1990 and rates have been increasing primarily due to an aging population and lifestyle changes in the developing world. The most significant risk factor for developing cancer is old age. Although it is possible for cancer to strike at any age, most people who are diagnosed with invasive cancer are over the age of 65.**

**"If we lived long enough, sooner or later we all would get cancer." Some of the association between aging and cancer is attributed to immune-senescence, errors accumulated in DNA over a lifetime, and age-related changes in the endocrine system.**

**The effect of aging on cancer is complicated with a number of factors such as DNA damage and inflammation promoting it and a number of factors such as vascular aging and endocrine changes inhibiting it. Some slow-growing cancers are particularly common. Autopsy studies in Europe and Asia have shown that up to 36% of people have undiagnosed and apparently harmless thyroid cancer at the time of their deaths, and that 80% of men develop prostate cancer by age 80. As these cancers did not cause the person's death, identifying them would have represented over-diagnosis rather than useful medical care.**

**Solar Sonic Laboratories have comprehensively concluded that:**

- 1). Communication does not take place principally in the visible Newtonian world but in the subatomic world
- 2). Cells and DNA communicate by means of vibratory frequencies.
- 3). The brain perceives the world and registers it by means of wave pulses.

The Cytochrome C complex is a small heme protein found loosely associated with the inner membrane of the mitochondrion. It belongs to the cytochrome c family of proteins. Cytochrome c is a highly water soluble protein, unlike other cytochromes, with a solubility of about 100 g/L and is an essential component of the electron transport chain, where it carries one electron. It is capable of undergoing oxidation/reduction, but does not bind oxygen. It transfers electrons between Complexes III (Coenzyme Q - Cyt C reductase) and IV (Cyt C oxidase). In humans, cytochrome c is encoded by the CYCS gene. Cytochrome c is a component of the electron transport chain in mitochondria. The heme group of cytochrome c accepts electrons from the bc<sub>1</sub> complex and transfers electrons to the complex IV. Cytochrome c is also involved in initiation of apoptosis. Upon release of Cytochrome c to the cytoplasm, the protein binds apoptotic protease activating factor-1 (Apaf-1). Cytochrome c can catalyze several reactions such as hydroxylation and aromatic oxidation, and shows peroxidase activity by oxidation of various electron donors such as 2,2-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid) (ABTS), 2-keto-4-thiomethyl butyric acid and 4-aminoantipyrine. Cytochrome c is a highly conserved protein across the spectrum of species, found in plants, animals, and many unicellular organisms. This, along with its small size (molecular weight about 12,000 daltons), makes it useful in studies of cladistics.

Its primary structure consists of a chain of about 100 amino acids. Many higher order organisms possess a chain of 104 amino acids. The cytochrome c molecule has been studied for the glimpse it gives into evolutionary biology. Its amino acid sequence is highly conserved in mammals differing by only a few residues. For example, the sequences of cytochrome c in humans are identical to that of chimpanzees (our closest relatives) illustrated here below quite comprehensively as follows:

- (1). Class I includes the lowspin soluble cytochrome c of mitochondria and bacteria. It has the heme-attachment site towards the N terminus of histidine and the sixth ligand provided by a methionine residue towards the C terminus.
- (2). Class II includes the highspin cytochrome c'. It has the heme-attachment site closed to the N terminus of histidine.
- (3). Class III comprises the low redox potential multiple heme cytochromes. The heme c groups are structurally and functionally nonequivalent and present different redox potentials in the range 0 to -400 mV.
- (4). Class IV was originally created to hold the complex proteins that have other prosthetic groups as well as heme c.

Cytochrome C is suspected to be the functional complex in so called LLLT: Low-level laser therapy. In LLLT, red light and some near infra-red wavelengths penetrate tissue in order to increase cellular regeneration. Light of this wavelength appears capable of increasing activity of cytochrome C, thus increasing metabolic activity and freeing up more energy for the cells to repair the tissue.

Cytochrome C is also an intermediate in apoptosis, a controlled form of cell death used to kill cells in the process of development or in response to infection or DNA damage. Cytochrome C binds to cardiolipin in the inner mitochondrial membrane, thus anchoring its presence and keeping it from releasing out of the mitochondria and initiating apoptosis.

While the initial attraction between cardiolipin and cytochrome C is electrostatic due to the extreme positive charge on cytochrome C, the final interaction is hydrophobic, where a hydrophobic tail from cardiolipin inserts itself into the hydrophobic portion of cytochrome C. During the early phase of apoptosis, mitochondrial ROS production is stimulated, and cardiolipin is oxidized by a peroxidase function of cardiolipin–cytochrome C complex. The hemoprotein is detached from mitochondrial inner membrane and can be extruded into the soluble cytoplasm via pores in outer membrane.

**The invention presents a process for initiating apoptosis in a cancer cell comprising:**

- (a) Contacting the cell with a cell cycle arresting drug; and
- (b) Contacting said cell with mechanical vibrational energy.

Wherein the cell cycle arresting drug is selected from the group consisting of: gemcytabine, cisplatin, carboplatin, cyclophosphamide, topoisomerase inhibitor, etoposide, 5-fluorouracil, doxorubicin, Methotrexate, hydroxyurea, and 3'-azido-3'-deoxythymidine, wherein the mechanical vibrational energy is ultrasound energy having a frequency of about 50 megahertz to about 2 gigahertz, wherein the exposure to mechanical vibrational energy is repeated or sustained over a period of at least one typical cell cycle, wherein the step of contacting the cell with mechanical vibrational energy is repeated or sustained over a period of at least one typical cell division. The process of claims, further comprising a step of synchronizing tubulin assembly in the cell, wherein the step of synchronizing tubulin assembly is effected by exposing the cell to a microtubule stabilizing agent and/or radiation, and the step is performed prior to contacting the cell with mechanical vibrational energy, wherein the microtubule stabilizing agent is selected from the group consisting of taxanes, coumarins, and combinations thereof.

It is imperative that in the practice of this invention, patients be selected and evaluated prior to treatment. Recommended patient inclusion and exclusion criteria include:

- (1) Patients have a definitive histopathologic or other laboratory confirmed diagnosis of their disease;
- (2) The disease or condition should be responsive to intracellular hyperthermia treatment;
- (3) Patients should have a Karnofsky score of 70% or greater;
- (4) Not be pregnant;
- (5) Weight should be within 45% (+/-) of ideal body weight and patients must weigh at least 35 kg;
- (6) There should be no history or findings of anhidrosis, scleroderma, ectodermal dysplasia, Riley-Day Syndrome, arthrogryposis multiplex, extensive psoriasis, serious dysrhythmias, malignant hyperthermia or neuroleptic malignant syndrome, pheochromocytoma, hypocalcemia, repeated episodes of hypoglycemia, chronic or recurrent venous thrombosis, alcoholism, renal failure, cirrhosis, untreated hyperthyroidism, anaphylaxis associated with heat or exercise-induced cholinergic type urticaria, exercise or heat induced angioedema, schizophrenia, catatonia, seizure disorders, emotional instability, Parkinson's disease, brain irradiation, cystic fibrosis, unstable angina pectoris, congestive heart failure, patients with cardiac pacemakers, severe cerebrovascular disease, spinal cord injury, severe pulmonary impairment, hereditary muscle disease such as Duchenne type muscular disease, central core disease of muscle, myotonia congenita, King-Denborough syndrome, Scwanry-Jampol syndrome, or osteogenesis imperfecta. As a critical reminder, it is noteworthy to state that, the above mentioned pre-treatment evaluation will be subject to the discretion of the treating physicians.
- (7) No immediate use of drugs that impair the body's heat dissipation mechanisms such as phenothiazines, anticholinergics, antihistamines, antiparkinsonians, glutethimide, hallucinogens, lithium, cocaine or other illicit drug use, monamine oxidase inhibitors, sympathomimetics, phencyclidine, opioids, phenylephrine, INH, tricyclic antidepressants, withdrawal from dopamine agonists, or cardiovascular drugs that clinically impair cardiac output or thermoregulatory vasodilation such as high doses of  $\beta$ -blockers, vasodilators, or calcium channel blockers; and,

(8) The patient should not be anemic or otherwise have reduced oxygen absorbing; carrying or utilizing capacity. Pretreatment evaluation should include a complete medical history and physical examination focused on the selection criteria listed above. Laboratory evaluation should include pulmonary function tests-if indicated, full hematological survey with hemostatic profile, EKG, liver function tests, serum biochemical profile, thyroid panel, serum creatinine, calcium, phosphate, and stress-EKG or exercise-multigated radionucleotide ejection scan on patients whose cardiac ejection fraction is suspect not to be greater than 45% with probable deterioration on exercise.

While clinical exceptions to entry laboratory values may exist, the following laboratory data should be a benchmark guide for initiation of treatment: hemoglobin  $\geq 11.0$  g/dl for men and  $\geq 10.0$  g/dl for women, platelet count  $\geq 75.00$  platelets/mm<sup>3</sup>, bilirubin  $\leq 2 \times$ ULN (ULN=upper limit of normal), ALT (SGPT)  $\leq 2 \times$ ULN, AST (SGOT)  $\leq 2 \times$ ULN, pancreatic amylase  $< 1.5 \times$ ULN, neutrophil count  $\geq 1,000$  cells/mm<sup>3</sup>. Serum electrolytes and K<sup>+</sup> should be well within normal limits, as hypokalemia decreases muscle blood flow, cardiovascular performance, and sweat gland function. More generally, the method outlined above is to be tailored to an individual patient.

As set forth above, the DNP may be administered by intravenous infusion. Alternatively, the route of administration may also be orally, rectally or topically. The frequency and optimal time interval between administrations is individualized and determined by measuring VO<sub>2</sub>, as well as other parameters. For example, various laboratories, x-ray, CAT scan, MRI, PET scan, HIV load, CD4<sup>+</sup> lymphocyte counts, HSP expression, prostatic specific antigen (PSA) and other surrogate markers of clinical outcome can establish the VO<sub>2</sub>, frequency and duration of therapy.

One treatment, or treatments as frequent as every day, or every other day, as far apart as 1 year or longer may be required for sustained beneficial results. The optimal VO<sub>2</sub>, temperature, duration, and frequency between treatments will probably vary from patient to patient and the specific disease or condition being treated. One skilled in the art would be able to modify a protocol within the present invention, in accordance with standard clinical practice, to obtain optimal results.

For example, the HIV relationships between viral load, CD4<sup>+</sup> lymphocyte counts, presence of opportunistic infections and clinical status of the patient can be used to develop more optimal regimes of DNP administration. Applicants' studies have revealed that the methods of the present invention can be effective in the diagnosis and treatment of a wide range of disease states and conditions in which uncoupler induced hypermetabolism, hyperthermia, oxidative stress and their sequela, play a beneficial role.

To those skilled in the art, it is also encompassed that a variety of different veterinary, as well as medical, applications for treatment and diagnosis can be practiced with the present invention. It is envisioned that DNP, or other uncouplers, may also be administered with other compounds used to treat infectious, malignant or other diseases. Examples of other agents include antifungal, antibacterial, antiviral or anti-neoplastic drugs, cell differentiating agents, and, various biologic response modifiers. Examples of anti-fungal agents include Amphotericin B, Griseofulvin, Fluconazole (Diflucan), Intraconazole, 5 fluoro-cytosine (Flutocytosine, 5-FC), Ketatoconazole and Miconazole.

Examples of anti-bacterial agents include antibiotics, such as those represented from the following classifications: beta lactam rings (penicillins), macrocyclic lactone rings (macrolides), polycyclic derivatives of naphthacene-carboxamide (tetracyclines), amino sugars in glycosidic linkages (aminoglycosides), peptides (bacitracin, gramicidin, polymixins, etc.), nitrobenzene derivatives of dichloroacetic acid, large ring compounds with conjugated double bond systems (polyenes), various sulfa drugs including those derived from sulfanilamide (sulfonamides, 5-nitro-2-furanyl compounds (nitrofurans), quinolone carboxylic acids (nalidixic acid), fluorinated quinolones (ciprofloxan, enoxacin, ofloxacin, etc.), nitroimidazoles (metroidazole) and numerous others.

These antibiotic groups are examples of preferred antibiotics, and examples within such groups include: peptide antibiotics, such as: Bacitracin, bleomycin, cactinomycin, capreomycin, colistin, dactinomycin, gramicidin A, enduracitin, amphomycin, gramicidin J, mikamycins, polymyxins, stendomycin, actinomycin; aminoglycosides represented by streptomycin, neomycin, paromycin, gentamycin, ribostamycin, tobramycin, amikacin; lividomycin beta lactams represented by benzylpenicillin, methicillin, oxacillin, hetacillin, piperacillin, amoxicillin and carbenacillin; lincosaminides represented by clindamycin, lincomycin, celesticetin, desalicytin; chloramphenicol; macrolides represented by erythromycins, lankamycin, leucomycin, picromycin; nucleosides such as 5-azacytidine, puromycin, septacidin and amicitin; phenazines

represented by myxin, lomofungin, iodine; oligosaccharides represented by curamycin and everninomycin; sulfonamides represented by sulfathiazole, sulfadiazine, sulfanilamide, sulfapyrazine; polyenes represented by amphotericins, candicidin and nystatin; polyethers; tetracyclines represented by doxycyclines, minocyclines, methacyclines, chlortetracyclines, oxytetracyclines, demeclocyclines; nitrofurans represented by nitrofurazone, furazolidone, nitrofurantoin, furium, nitrovin and nifuroxime; quinolone carboxylic acids represented by nalidixic acid, piromidic acid, pipemidic acid and oxolinic acid. Antiviral agents that can be used with DNP include: interferons  $\alpha$ ,  $\beta$  and  $\gamma$ , amantadine, rimantadine, arildone, ribavirin, acyclovir, abacavir, vidarabine (ARA-A) 9- $\beta$ -D-ribofuranosyl-2,3-dihydroxy-2-propoxy methylguanine (DHPG), ganciclovir, enviroxime, foscarnet, amplexigen, podophyllotoxin, 2,3-dideoxythymidine (ddC), iododeoxyuridine (IDU), trifluorothymidine (TFT), dideoxyinosine (ddi), d4T, 3TC, Zidovudine, efavirenz, protease inhibitor, such as indinavir, saquinavir, ritonavir, nelfinavir, amprenavir & specific antiviral antibodies. Anti-cancer drugs that can be used with DNP include, but are not limited to, various cell cycle-specific agents represented by structural analogs or antimetabolites of methotrexate, mercaptopurine, fluorouracil, cytarabine, thioguanine, azacitidine; bleomycin peptide antibiotics, such as podophyllin alkaloids including etoposide (VP-16) and teniposide (VM-26); and various plant alkaloids such as vincristine, vinblastine, and paclitaxel. Anti-neoplastic cell cycle-nonspecific agents such as various alkylating compounds such as busulfan, cyclophosphamide, mechlorethamine, melphalan, altretamine, ifosfamide, cisplatin, dacarbazine, procarbazine, lomustine, carmustine, lomustine, semustine, chlorambucil, thiotepa and carboplatin.

Anticancer antibiotics and various natural products and miscellaneous agents that can be used with DNP include: dactinomycin, daunorubicin, doxorubicin, plicamycin, mitomycin, idarubicin, amsacrine, asparaginase, quinacrine, retinoic acid derivatives (tretinoin), phenylacetate, suramin, taxotere, tenizolamide, gencytabine, amonafide, streptozocin, mitoxanthrone, mitotane, fludarabine, cytarabine, cladribine, paclitaxel (taxol), tamoxifen, and hydroxyurea, etc. DNP can also be administered with various hormones, hormone agonists and biologic response modifying agents which include, but are not limited to:

Flutamide, prednisone, ethinyl estradiol, diethylstilbestrol, hydroxyprogesterone caproate, medroxyprogesterone, megestrolacetate, testosterone, fluoxymesterone and thyroid hormones such as di-, tri- and tetraiodothyronine. The aromatase inhibitor, amino glutethimide, the peptide hormone inhibitor octreotide and gonadotropin-releasing hormone agonists such as goserilin acetate and leuprolide can also be used with DNP. Biologic response modifiers such as various cytokines, interferon alpha-2a, interferon alpha-2b, interferon-gamma, interferon-beta, interleukin-1, interleukin-2, interleukin-4, interleukin-10, monoclonal antibodies (anti-HER-2/neu humanized antibody), tumor necrosis factor, granulocyte-macrophage colony-stimulating factor, macrophage-colony-stimulating factor, various prostaglandins, phenylacetates, retinoic acids, leukotrienes, thromboxanes and other fatty acid derivatives can also be used with DNP.

### **List of Solar Sonic Six Groups of Medicinal / Therapeutic / Pharmacological Agents that are electro-chemically applicable within SSQF Medical Device:**

#### **Solar Sonic Infusion-ably Compatible Pharmacological Group One:**

Phosphoprotein p53, Ifosfamide, Mitomycin C, Carmustine, Psoralen, Adenovirus, Antigens, immunotoxins, Monoclonal Antibody, Interleukin, Epitope, Idiotypes, Allergen, Superantigen, Tolerogen, Immunoglobulin, Alpha-Lactalbumin, Quercetin, p53 tumour suppressor gene, BI811283 Small Molecule Inhibitor, BRCA1, BRCA2, Gene Suppressors, Oncogenes Suppressors, SSFD Programmable Nucleotide Sequence of Genomic DNA, SSFD Programmable chromosomes, SSFD Genomic De-amplification, SSFD Programmable Mitosis, Solamargine, Prostacyclin, Ruthenium, SSFD Genomic De-amplification, SSFD Re-programmable coding sequence, HPV, HBV, Sipuleucel-T (Provenge).

#### **Solar Sonic Infusion-ably Compatible Pharmacological Group Two:**

Tumor Hypoxia Promoters, Apoptosis Signaling Pathway SSF Promoter, SSFD Modifiers of inappropriate expression of proteins HMGA2 or HMGA1, HRR Defective Cells Modifiers, SSF Micro RNAs Modifiers,

Tamoxifen, Raloxifene, 5-Alpha-Reductase Inhibitor, SSF Infused Vitamin D, Folic acid, Beta-Carotene, Gardasil Vaccine, Cervarix Vaccine, Human papillomavirus Vaccine, Hepatitis B/C Vaccine, Neem Extract, Antimetabolites, Alkylating Agents, Anthracyclines, Taxanes, Epothilones, Histone Deacetylase Inhibitors, Topoisomerase Inhibitors, Kinase Inhibitors, Nucleotide Analogs, Precursor Analogs, Iontophoresis, pro-apoptotic agents, Peptide, Antibiotics, Probiotics, HPV, HBV, Sipuleucel-T (Provenge).

**Solar Sonic Infusion-ably Compatible Pharmacological Group Three:**

Retinoids, Vinca Alkaloids, Diindolylmethane, hydrogen peroxide, Cesium Chloride, Naphthalene Carboxylic dibromorhodamine, Peroxymonosulfuric Acid, Sodium Dichloroacetate, Theobromine, BC534, BC538, CD22, CD25, CD20, CD74, CD138<sup>neg</sup>CD20<sup>+</sup> MM Stem Cells, SUMO Proteins, Rhodamine, Sun Flowers Extract, xanthen, Benzoic acid, Solamargine, Hydrochloride, Anti Acid, isoquinoline carboxylic acid amides, Citric Acid, Ascorbic Acid, Pyridoxine Hydrochloride, Antioxidant Mycobacterium w' (M<sub>w</sub>), oxalic Acid Dihydrate, Vitamin B-17, Phytocannabinoids, Tannic Acid, Amino Acids, Sodium Dichloroacetate, Theobromine, CD74, BC534, BC538, CD22, CD25, CD20, HPV, HBV, Sipuleucel-T (Provenge).

**Solar Sonic Infusion-ably Compatible Pharmacological Group Four:**

Dibromorhodamine, Peroxymonosulfuric Acid, xanthen, Benzoic acid, Solamargine, Hydrochloride, Anti Adhesion Agents, Liquid Oxygen, Wip1 inhibitors, Angiopoietins, Antidote, Morpholinomethyl, Acid, Anti Oxidants, Antisense proteins, Sodium Oxalate, Oxoisoindolin, piperidine, Proteasome Inhibitors, Nutrients, prostacyclin, Photodynamic Agents, derivatives, Nucleic Acid, Senecioid, Crotonoyl, Dimethylartyloyl, Cinnamoyl, Pentenoyl, Hexanoyl, Benzoyl, Ethylbutyryl, hydroxyl, Acetyl, Crotonoyl, Hexahydroxyolean, Angelic Acid, phosphorus oxychloride, phosphorus trichloride, thionyl chloride, tigloyl chloride, Oxalyl chloride, Angeloyl chloride, Hard Cactus Extract, Hard Succulent Extract, Grapefruit seed oil Extract,

**Solar Sonic Infusion-ably Compatible Pharmacological Group Five:**

Whole Marijuana Plant Extract, Inhibitors of adhesion proteins, Inhibitors of Angiopoietins, Cancer Anti-Resistance SSF Agents, Estrogen Receptor Modifier, Angiogenesis Inhibitors, Enzymatic Domains Inhibitors, Tyrosine kinase Inhibitors, Imatinib, Gefitinib, HER2/neu Antibody, Trastuzumab, Rituximab, Estrogens, Anti-CD20 Antibody, Estrogen Modifiers, Testosterone Modifier, Hormone Agonists, Progestogens, Taxanes, Angiogenesis Inhibitors, Bevacizumab, Morphine, Oxycodone, Antiemetics, Ondansetron, Aprepitant, Vinca Alkaloids, Opioids, Anti-tumor antibiotics, Antiviral Agents, Corticosteroids, Differentiating Agents, Anti-Estrogens, Aromatase inhibitors, Progestins, Anti-androgens, Gonadotropin-releasing hormone (GnRH),

**Solar Sonic Infusion-ably Compatible Pharmacological Group Six:**

Monoclonal antibody therapy drugs, Provenge Vaccine, Immunomodulating drugs, Mitotic Inhibitors, Epothilones, Estramustine, Topoisomerase inhibitors, Antimetabolites, Anti-microtubule agents, Cytotoxic antibiotics, Topoisomerase inhibitors, Antibody-Drug Conjugates, SSF Infused Nanoparticles, Cytostatic Drugs, Alkylating Agents, Anthracyclines, Cytoskeletal Disruptors, Epothilones, Histone Deacetylase Inhibitors, Topoisomerase Inhibitors, Kinase Inhibitors, Nucleotide Analogs, Precursor Analogs, Peptide Antibiotics, Platinum-Based Agents, Retinoids, Vinca Alkaloids, opiate, insulin, Hydrochloride, Biologically Intensive Phototherapeutic Agents, Highly illuminating Biological Agents, Heat-borne Biological Agents, Anti-Heat Borne Biological Agents, HPV, HBV, Sipuleucel-T (Provenge).

For the handling of each pharmaceutical drug mentioned above, the Medical Device remains the same, the Vaccine remains the same, but the selected Electromagnetically Biochemical Signaling Communication Frequency is not the same as far as the electrochemical infusion of each individual pharmaceutical drug for

the sole treatment of cancer and carcinogenic cells. For each specific pharmaceutical drug mentioned above and is being handled biochemically, what is being initiated differently from chemical to chemical is the initiation of a completely independent Electromagnetically Biochemical Signaling Communication Frequency in order to impede and emit energetic resonance signature. This energy infuses chemically based pharmaceuticals as the Six groups mentioned above, in which they are being handled as chemicals and furthermore as Bio-chemical Machinery in order to penetrate, impede and emit Electromagnetically Chemical Energy directly into the intracellular and extracellular Sub-Structure(s).

#### **Solar Sonic Technologies in detection and treatment of Bladder cancer through Clinical Trials**

Solar Sonic Clinical Trials were extensively conducted over the years, we proceeded to cover bladder cancer clinical trials as an example for the purpose of illustrating biomedical innovations in ophthalmology and cancer diagnostics.

We therefore had previously announced that a blinded, multi-center clinical study of the non-invasive test for detecting bladder cancer in urine, successfully achieved the study's primary endpoint for effectively detecting the recurrence of bladder cancer in subjects with a history of the disease.

The urine test successfully identified cancerous cells in urine samples in patients with a history of the disease, with reported sensitivity of 84.4% and specificity of 82.7% for the study's primary endpoint.

The technology is being developed by Solar Sonic Laboratories as cancer diagnostics subsidiary, and allows an accurate diagnosis of cancerous and precancerous cells, based on a unique combination of color and morphology by utilizing a proprietary kit containing unique extract and dyes.

Solar Sonic Laboratories are extremely pleased with these results showing high sensitivity and specificity and believe that they provide a foundation upon which regulatory approval can be secured and be a second indication for use of the technology platform.

There is a clinical need for a better test for the up to 80 percent of patients with bladder cancer whose cancer recurs, since many of the currently available tests are clinically suboptimal, invasive or expensive. Based on these strong clinical results, we believe that Solar Sonic Laboratories are in turn considered viable promising solutions for the millions of patients with bladder cancer, and have the potential for diagnosing additional cancer indications.

The blinded clinical study was conducted in nine medical centers in Africa, where urine samples from 360 subjects with a history of bladder cancer were tested. The study population included 114 healthy subjects and about 246 patients currently suffering from the disease. The results of the urine tests were compared with results from biopsy or cystoscopy, in cases where biopsies were not taken. The results also indicated that the urine test's negative predictive value (NPV), defined as the probability that a patient having a negative result doesn't suffer from the disease, was 98.5%.

In addition to its high sensitivity for advanced stage tumors and high-grade malignancy, the test was also found to exhibit high sensitivity for early stage tumors and low-grade malignancies, which are difficult to identify using other non-invasive tests currently available on the market. These findings indicate that the method is adequately sensitive for the purpose of accurate and early detection of the recurrence of the disease. Solar Sonic Laboratories have determined that the study results were quite encouraging. The accuracy of this novel assay appears to be superior over any available non-invasive test, suggesting a potential to supplant some or all of the cystoscopies required for bladder cancer surveillance. This is indeed great news for patients with history of bladder cancer, which may change their management. The secondary endpoint showed that the sensitivity of other non-invasive comparator tests, urine cytology, BTA stat and NMP22 Bladder-Check, was 50.0%, 68.8% and 17.4%, respectively. These findings further underscore the potential of the test as an accurate, reliable and a non-invasive tool for monitoring the recurrence of bladder cancer. Solar Sonic also plans to utilize reimbursement existing codes for monitoring bladder cancer recurrence and will continue to advance the technology for the diagnosis of additional cancer indications. Bladder cancer is the fourth most prevalent cancer among males in the U.S. and the seventh most prevalent among males

worldwide, with nearly 430,000 new case of the disease diagnosed globally in 2012. The rate of recurrence is the highest of all cancers and ranges from 50% to 80%.

According to U.S. clinical guidelines, patients with a history of urinary bladder cancer are required to undergo three to four tests per year to monitor disease recurrence in the first two years immediately following treatment, and one test annually in the years that follow.

Because of high recurrence rates, the cost of diagnosing and treating bladder cancer is among the highest of all cancers. Solar Sonic technology allows an accurate diagnosis of cancerous and precancerous cells, based on unique combination of color and morphology. The technology may be implemented in screening tests and monitoring tests of disease recurrence in cancer patients after being treated. Solar Sonic Laboratories have proven the efficacy in diagnosing cervical cancer and bladder cancer in the framework of clinical trials, and estimates that the technology underlying the products may be implemented for use in additional cancer indications. The cervical cancer detection screening diagnostic test kit is in the initial commercial stage and has recently completed a clinical trial to prove its ability to monitor bladder cancer recurrence, while the underlying Solar Sonic Technologies are also adapted for other types of cancer as well, after a long history of extensively vigorous clinical trials in Africa.

In a separate experiment consisted of only Six patients at a moderate stage 2 from twelve different cancer categories and were put on the Solar Sonic Protocol treatments as explained in this paper. 6 patients had glioblastoma (brain) 6 patients had Kidney cancer, 6 patients had liver cancer, 6 patients had abdominal cancer, 6 patients had Thyroid cancer, 6 patients had ovarian cancer, 6 patients had bladder cancer, as well as 6 patients had prostate cancer, 6 patients had colon cancer, 6 patients had breast cancer, 6 patients had Pancreatic cancer, 6 patients had Testicular cancer, 6 patients had Bone Cancer, 6 patients had blood cancer.

We have elected to illustrate only the Glioblastoma clinical trial, we prospectively secured baseline and the serial tumor tissue for Glioblastoma and had developed patient-specific cell lines and putative stem cells (CD133+, nestin+ cells), and treated each patient with oral DCA for up to 18 months. DCA depolarized mitochondria, increased mitochondrial reactive oxygen species, and induced Apoptosis in GBM cells, as well as in putative GBM stem cells, both in vitro and in vivo.

In post treatment procedures, they had dramatically improved and the outcome can be summarized whereas all of their tests were quite normal, where we reference CBC tests were quite normal (RBCs / WBCs/ Plts), and Hemoglobin (Hgb), Hematocrit (Hct). Additionally their Chemistry panel reports were all normal where their blood chemistry panels (metabolic profiles) have shown Normal Fats and Normally balanced Proteins Ratios, Normal Sugar (glucose), normally balanced Electrolytes (like potassium, magnesium, sodium, and calcium), normally balanced Enzymes, Normal Leukocyte Count 3,300 to 8,700 WBCs per microliter (mcL) with normal reading of lymphocytes or monocytes.

All tests had hematocrit range from 38% to 48%. The hemoglobin (Hgb) level measures the amount of the protein in RBCs that actually carries the oxygen. If the level of hemoglobin is low the body works much harder to deliver oxygen to tissues throughout the body. Their Hgb had range from 12.6 to 16.1 grams per deciliter. They had a normal range for platelet count, were approximately from 150,000 to 350,000 platelets per mcL. They had normal Neutrophils and their Absolute Neutrophil Count (ANC) had ranged from 2,500 to 6,000 neutrophils. The Solar Sonic Glioblastoma Clinical Trial had been announced for a sufficient period of time of which 6 people joined in and had signed release forms, their medical records were detailed on their way into the study. Glioblastoma had started as a single tumor and a few random symptoms at first. As the cancer progresses, a conglomeration of tumors had developed in different areas around the brain. More symptoms had cropped up, with some of them linked to a tumor in a particular part of the brain. The treatment was really focused on stopping the growth of the tumor and making the patient as comfortable as possible while attempting to prolong life through radiation & chemotherapy. Glioblastoma is always fatal, but we had insisted on fighting.

**Closing Statement of the Solar Sonic Cancer Cure Medical Device Invention and its Patent:**

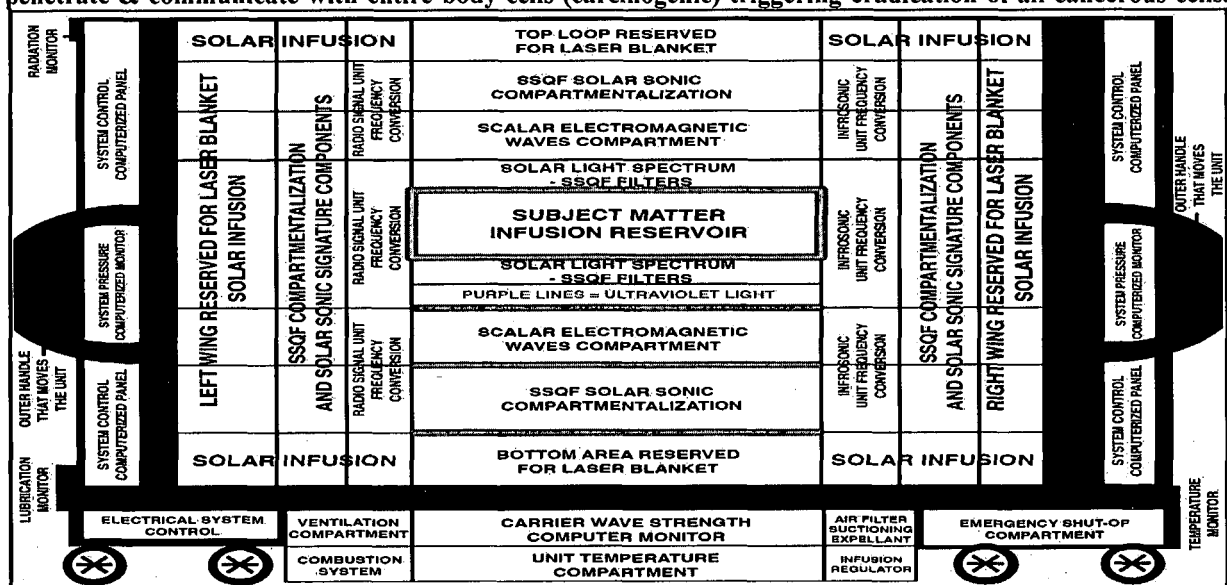
The use of this invention should be under the strict direction of a qualified and specialized team to insure safety and effectiveness. The treatment team remains with the patient throughout the procedure to insure that safe and controlled dosages of patient, which are being administered by monitoring real time changes in V<sub>O</sub><sub>2</sub>, metabolic rate, temperature, respiratory rate, heart rate, urine output and clinical status of the patient. This invention is practiced in controlled steps so as to attain a predetermined V<sub>O</sub><sub>2</sub> and plateau of infusion time for a particular session of any given cancer condition.

For example, in cases were heat dissipation mechanisms do not have to be blocked, the specialized team will periodically recheck V<sub>O</sub><sub>2</sub>, heart rate, blood pressure, CAT scan, MRI, etc., and other laboratory and clinical parameters to insure continued safety and efficacy of SSQF Cancer Therapeutic Infusion Procedure. It is preferred that the specialized team undergo a training period in the use of this invention prior to its administration to human patients.

Within the Solar Sonic Cancer Device there shall be Peripherally Inserted Central Catheter, PICC IV access is secured at the bend of the elbow for Surgery Dehydration, Nutrition, Shock, Imaging, Blood Transfusion, Chemotherapy, Medication Administration, Solar Sonic Controlled Infusion Therapy for Chemical Reformulation, Either intravenously or intrathecally depending on cancer area and the overall Computer Command as a direct delivery of Solar Sonic Antineoplastics to the Central Nervous System and assessing Toxicity and Ultra-Structural Data for Computer Chemical Re-modifications.

This SSQF Cancer Therapeutic Infusion Device has 46 Medical Characteristics, that are the administration of the technological capabilities and that must become a precisely collective training mission before any attempt to operate this Solar Sonic Multidimensional Superior group of Technologies, resonating within just one medical device.

This Highly Sophisticated Technology and its subsequent Medical Device is rated as Solar Sonic Infusion-ably accessible and comprehensively coded for Various Cancer Treatments, offering superior Cancer Disease Management with SSQF-Propagation Ratio at Cellular Communications Radius 36556799114, that of which penetrate & communicate with entire body cells (carcinogenic) triggering eradication of all cancerous cells.



This presented Cancer Device Diagram is only the Construction of the illustrative Shell Design of Solar Sonic Cancer Therapeutic Infusion Medical Device. All other supporting applications of this Medical Device are detailed in list of 46 items outlining the technical applications in the device which benefit all cancer patients as they receive the most suitable therapeutic protocols via various options offered by the SSQF Medical Device.

### Principal claims of the invention

1. Defeating cancer by promoting cytostasis, infusing cytochrome C-Protein, programming T-Lymphocyte/ T-Cells, B-Lymphocyte/ B-Cells, thymus gland and inducing apoptosis. This is beyond science and paranormal bio-manipulations and alien communications technology where all cells and pathogens are simultaneously stimulated for instant bio-signaling communication, apoptosis, restoration and homeostasis.
2. Solar sonic cytotoxic effects, physiological carcinogenicity and the overall toxicity are being extracted out of the patient's own pores through the feet via a solar sonic ionic bio-cleansc. That occurs while the medical device conducting a hyperthermia therapeutic infusion within the tumor & intracellular/pathogenic bio-signaling communications with cancer cells.
3. Solar sonic laser needles and pulsed electromagnetic fields are permeating for the administration of the solar sonic frequency SSF therapeutic infusion composition protocols for the eradication of carcinogenic cells. The intracellular and pathogenic bio-communications and regenerative human physiology via SSF paranormal homeostasis and induced apoptosis are leading the way in combating pathogens. Solar sonic therapeutic infusion medical device electrochemically promotes pulsed suppression of mitochondria-K<sup>+</sup> channel axis in cancer, inducing apoptosis and inhibiting cancer growth.
4. The decision to turn on the production of either pro-oxidants or the anti-oxidants is left to our native biological intelligence. It's really constant and delicate balance, all dependent upon cellular signaling and communications. If cells are intelligent indeed it would have major conceptual and medical implications. If cells are intelligent, we would have to rethink all the cause and effect chains from genes to molecules to cell functions that we somehow believe today to be true.
5. If cells are intelligent, molecules and their genes would be the collaborators or even slaves but not the masters of the life functions of cells. If cells are intelligent, medical treatment may involve talking to cells rather than to flood the organism with pharmaceuticals as we do today and they are intelligent. If cells respond to signals rather than to exogenous forces, the forces that keep or change the direction of their bodies must be controlled from within.
6. Solar sonic quantum frequency waves induce self-destruction of cells via bio-signaling communications eradicating carcinogenic cells. Solar sonic curative cancer medical device is proven to work reproducibly as a super hi-tech solar sonic multidimensional medical science of the paranormal cellular/ pathogenic bio-signaling communications & programming technology; the medical device converts multi-drug components from cytotoxic to antitoxic.

# INTERNATIONAL SEARCH REPORT

International application No PCT/IB2015/000426
---

**A. CLASSIFICATION OF SUBJECT MATTER**  
 INV. A61K31/00 A61M5/00 A61K45/00  
 ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 A61K A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 EPO-Internal, EMBASE, BIOSIS, CHEM ABS Data, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>"www.solarsonicdiscovery.com - web archive of 22.12.2007",            web.archive.org,            22 December 2007 (2007-12-22),            XP055223598,            Retrieved from the Internet:            URL:https://web.archive.org/web/20071222070328/http://www.solarsonicdiscovery.com/            [retrieved on 2015-10-26]            page 3            page 5            page 8 - page 9            page 15 - page 16            page 21 - page 23            page 25 - page 26            -----</p>	1-6

Further documents are listed in the continuation of Box C.       See patent family annex.

\* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&amp;" document member of the same patent family</p>
---	---

Date of the actual completion of the international search  <b>3 November 2015</b>	Date of mailing of the international search report  <b>09/11/2015</b>
---	---

Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  <p style="text-align: center; font-size: 1.2em;">Langer, Oliver</p>
--	---

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2015/000426

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-6

Treatment of cancer

1.1. claim: 1

Defeating cancer by promoting cytostasis, infusing cytochrome C-Protein, programming T-Lymphocyte/ T-Cells, B-Lymphocyte/ B-Cells, thymus gland and inducing apoptosis. This is beyond science and paranormal bio-manipulations and alien communications technology where all cells and pathogens are simultaneously stimulated for instant bio-signaling communication, apoptosis, restoration and homeostasis.

1.2. claim: 2

Solar sonic cytotoxic effects, physiological carcinogenicity and the overall toxicity are being extracted out of the patient's own pores through the feet via a solar sonic ionic bio-cleanse. That occurs while the medical device conducting a hyperthermia therapeutic infusion within the tumor & intracellular/pathogenic bio-signaling communications with cancer cells, as far as not already covered by invention 1, sub-invention 1.

1.3. claim: 3

Solar sonic laser needles and pulsed electromagnetic fields are permeating for the administration of the solar sonic frequency SSF therapeutic infusion composition protocols for the eradication of carcinogenic cells. The intracellular and pathogenic bio-communications and regenerative human physiology via SSF paranormal homeostasis and induced apoptosis are leading the way in combating pathogens. Solar sonic therapeutic infusion medical device electrochemically promotes pulsed suppression of mitochondria-K channel axis in cancer, inducing apoptosis and inhibiting cancer growth, as far as not already covered by invention 1, sub-inventions 1 or 2.

1.4. claim: 4

The decision to turn on the production of either pro-oxidants or the anti oxidants is left to our native biological intelligence. It's really constant and delicate balance, all dependent upon cellular signaling and communications. If cells are intelligent indeed it would have major conceptual and medical implications. If cells are intelligent, we would have to rethink all the cause and effect chains from genes to molecules to cell functions that we somehow believe today to be true, as far as not already

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

covered by invention 1, sub-inventions 1, 2 or 3.

1.5. claim: 5

If cells are intelligent, molecules and their genes would be the collaborators or even slaves but not the masters of the life functions of cells. If cells are intelligent, medical treatment may involve talking to cells rather than to flood the organism with pharmaceuticals as we do today and they are intelligent. If cells respond to signals rather than to exogenous forces, the forces that keep or change the direction of their bodies must be controlled from within, as far as not already covered by invention 1, sub-inventions 1, 2, 3 or 4.

1.6. claim: 6

Solar sonic quantum frequency waves induce self-destruction of cells via bio-signaling communications eradicating carcinogenic cells. Solar sonic curative cancer medical device is proven to work reproducibly as a super hi tech solar sonic multidimensional medical science of the paranormal cellular/ pathogenic bio-signaling communications & programming technology; the medical device converts multi-drug components from cytotoxic to antitoxic, as far as not already covered by invention 1, sub-inventions 1, 2, 3, 4 or 5.

---