

MORGELLONS:

INSECT HORMONE ECDYSONE (or its analogs) TRIGGERS GENETIC CHANGES
TO BUILD NEW HAIR, SKIN, NAILS and CAUSE DISEASES

SkizitGesture-2013

Morgellons is a military grade entomological terror weapon being used to torture and kill innocent civilians. The medical community has not been informed about this disease and its complexity keeps it from being properly identified, named, researched and treated. The longer a biological weapon remains untreated, the more time it has to reach its peak lethality. Obstruction by agencies as to its treatment or cure is a part of the military strategy. [1] Textbook of Military Medicine: Medical Aspect of Chemical and Biological Warfare, Use of Biological Weapons, p. 636-658.

<http://www.cs.amedd.army.mil/borden/Portlet.aspx?ID=66cffe45-c1b8-4453-91e0-9275007fd157>

Information about Morgellons cannot be found soon enough. Many people are dying and the deaths are being attributed to other causes — pneumonia or heart and lung problems. Therefore, assistance from any direction is needed. This is my plea to ask at large for any professionals with any training and resources to please help this cause. Also, there are products which people cannot afford that could be donated to them. If there is anyone with funds they could appropriate to needy victims, please contact Skizit at skizit@hushmail.com.

Now, as to the topic of this article, people with Morgellons often have slow healing lesions. These lesions may be caused by microscopic arthropods too small to be seen by the naked eye. Has a doctor said you are delusional because he/she can't see the bugs? Are insects or worms, bacteria, fungus or plants growing in your skin?

Gene therapy makes this possible. What is gene therapy? Gene therapy is the use of DNA as a treatment or cure for disease. It can be used to change or replace genes in animal and plant cells. Various methods are used to insert new genes into cells.

Geneticists have designed a system for use in transgenic animals where the insect ecdysone hormone receptor molecule can be synthesized continuously in the glandular cells of the organism. [2] Campbell, John, Engineering the Human Germline: An Exploration of the Science and Ethics of Altering the Genes We Pass to Our Children, Jan 7, 2000.

Humans have 48(+) kinds of hormone receptors but not the ecdysone receptor, so its gene must be taken from an insect genome. [3] Robinson-Rechavi M., How many nuclear hormone receptors are there in the human genome? Trends Genet, 2001 Oct. 17(10):554-6. <http://www.ncbi.nlm.nih.gov/pubmed/11585645>

The insect hormone receptor from the fly DROSOPHILA MELANOGASTER or other species are incorporated into human cells. [4] D No., Ecdysone-inducible gene expression

in mammalian cells and transgenic mice, Proc Natl Acad Sci USA., 1996 April 16; 93(8): 3346-3351. www.ncbi.nlm.nih.gov/pmc/articles/PMC39610/

The early patent is entitled “Polynucleotide Encoding Insect Ecdysone Receptor.” US 6245531 B1, Polynucleotides are DNA & RNA (biopolymers made of 13 or more nucleotide monomers in a chain). [5]

http://www.patentlens.net/patentlens/patents.html?patnums=US_6245531&language=&patnum=US_6245531&language=en&query=&stemming=&returnTo=quick.html%3Fquery%3D%2528US6723531%2Bin%2Bpublication_number%2529&pid=p0#tab_1

The inventors are: David Hogness, Michael Koelle and William Seagraves. The assignee is the Board of Trustees of Leland Stanford University, Palo Alto, CA. Filed September 30, 1992, Published May 7, 1996. The patent provides for three plasmid cassettes containing genetic instructions. This patent describes the insertion of a molecular switch using the 20-OH ecdysone receptor (or DHR3, E75A or E75B) which is genetically inserted into insects, worms, bacteria, plants and mammals. For more on the patents owned by Stanford related to ecdysone see “RHeoGene and Invitrogen Sign Licensing Agreement for Ecdysone Receptor Technology,”

<http://www.thefreelibrary.com/RHeoGene+and+Invitrogen+Sign+Licensing+Agreement+for+Ecdysone...-a085493921>

Ecdysone is used in biochemistry research as an inducer in transgenic animals where a new gene is introduced into an animal. Adding or removing ecdysteroids from the animal’s DIET turns the gene on or off. This creates a system where food for humans could be laced with the hormone of choice to induce disease and death. [6] Ecdysone-inducible gene expression in mammalian cells and transgenic mice; Proc. Natl. Acad. Sci. USA; Vol. 93, pp. 3346-3351, April 1996, Genetics <http://www.skizit.biz/2012/11/21/what-is-an-expression-system/>

Transgenic means an organism whose genetic material has been altered using genetic engineering techniques. Transgenesis is the process of introducing an exogenous (from another organism) gene called a transgene into a living organism so that the organism will exhibit a new property and transmit that property to its offspring.

Transgenic organisms are able to express foreign genes because the genetic code is similar for all organisms. This means that a specific DNA sequence will code for the same protein in all organisms. Due to this similarity in protein sequence, scientists can cut DNA at these common protein points and add other genes.

VECTORS

DNA that encodes a therapeutic (treatment) protein is packaged within a “vector”. [7] Regulatable Gene Expression Systems for Gene Therapy applications: Progress and Future Challenges, Curr Gene Ther. 2006 August 6(4): 421-438. There may be multiple vectors, perhaps a primary (insect) vector and a secondary vector (bacteria). Once inside

a cell, the DNA becomes expressed by the cellular machinery, resulting in the production of a therapeutic protein, which in turn treats the patient's disease.

Nucleic acid (DNA) encoding a therapeutic protein is placed inside a virus "vector" whose infectious machinery is used to insert the new or therapeutic DNA in the cells of an organism. The nucleic acids (DNA) could be meant to help or harm you, such as a stealth virus, bacteria or any other pathogenic materials in the case of a bioweapon like Morgellons.

Adenovirus is used as a virus vector. Adenoviral vectors can hold large DNA inserts (up to 35 kb). They are human viruses and are able to transduce a large number of different human cell types at very high efficiency. The inside of the virus is scooped out and the genes to be transmitted are put inside. The virus infects the cell and the ecdysone receptor proteins enter the cell nucleus. The ecdysone switch turns the DNA on and it is expressed in the animal. [8] Graham, Lloyd D., Ecdysone-controlled expression of transgenes.

<http://informahealthcare.com/doi/abs/10.1517/14712598.2.5.525>

The ability to administer the vector repeatedly is critical in many treatment protocols so the presence of multiple generations of the animals is important to maintain in the victim. In order to suppress the immune response, the costimulatory interactions required for an immune response to an antigen is blocked, blinding the immune system, making repeat administration possible. [9] Anderson W. French, Human Gene Therapy, Nature, 1998 apr 30,392(6679 Suppl) 25-30.

The process of gene delivery and expression is known as transduction. The vector must be capable of targeting the cell type most appropriate for the disease. To achieve stable, sustained gene expression requires integration of the vector DNA into the host DNA or in a separate structure known as an episome, which is a closed circular DNA molecule that is replicated in the nucleus. [10] Verma, Inder M., Weitzman, Matthew D.; Gene Therapy: Twenty-First Century Medicine, Annu Rev. Biochem. 2005. 74:711-38

NUCLEAR RECEPTORS

What is a nuclear receptor? A nuclear receptor is a protein in cells that senses steroid and thyroid hormones and regulates the expression of specific genes, only when a ligand (hormone) such as ecdysone is present, thereby controlling the development, homeostasis and metabolism of the organism. [11] Evans RM. The steroid and thyroid hormone receptor superfamily. Science. 1988;240 (4854):889-95.

<http://links.jstor.org/sici?sici=0036-8075%2819880513%293%3A240%3A4854%3C889%3ATSATHR%3E2.0.CO%3B2K>

[12] Mangelsdorf DJ, et al. The nuclear receptor superfamily: the second decade. Cell 1995; 83(6): 835-9; <http://Blumberg.bio.uci.edu/reprints/mango-cell-intro.pdf>

The ecdysone receptor (EcR) is a steroid hormone receptor involved in triggering metamorphosis in the fly *Drosophila melanogaster*. A class of steroid hormone called ecdysteroids binds to the receptor EcR. [13] Regulatable Gene Expression Systems for Gene Therapy applications: Progress and Future Challenges.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1629032/>

Steroid hormone receptors are the largest group of transcription factors in the mammalian proteome (list of all proteins in a single cell or organism). The ligands (hormones) of steroid receptors cross epithelial (skin) barriers and plasma membranes (enclose cells) with ease. The hormones bind to their receptors in the cytoplasm (the cell substance between the cell membrane and the nucleus) and these hormone-receptor complexes are then moved to the nucleus where they regulate gene expression.

The intracellular (within the cell) protein receptors usually perform the entire task of transferring genetic material from one cell to another. The hormone-receptor complexes bind to specific sites in the cell's DNA and stimulate the transcription (the process by which mRNA is synthesized from a DNA template resulting in the transfer of genetic information from the DNA molecule to mRNA) of specific genes. mRNA produced in response to hormone stimulation is translated into new protein in the cytoplasm. This new protein could be a pathogen that produces a disease as part of a bioweapon. [14]

www.course-

[notes.org/Biology/Outlines/Chapter_45_Hormones_and_the_Endocrine_System](http://www.course-notes.org/Biology/Outlines/Chapter_45_Hormones_and_the_Endocrine_System)

In insects, ecdysone triggers reproduction, growth, molting & development through the activation of the ecdysone receptor. The receptor is called EcR and is coupled with another protein called Ultraspiracle (USP). [15] Ecdysone-inducible gene expression in mammalian cells and transgenic mice; Proc. Natl. Acad. Sci. USA, Vol. 93, pp. 3346-3351, April 1996 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC39610/pdf/pnas01515-0196.pdf>

The ecdysone receptor senses and responds to the presence of ecdysone, causing a cascade of molecular events controlling the development, homeostasis and metabolism of the organism. The presence of ecdysone triggers the ecdysone receptor. In the absence of ecdysone, nothing happens. This molecular on/off switch is called an Inducible Expression System. Ecdysone has no effect on animals that do not have extra genes inserted so its presence indicates the transgene is working. [16] Inducible control of transgene expression with ecdysone receptor: gene switches with high sensitivity, robust expression, and reduced size; RheoGene, Inc., Norristown, PA, USA; BioTechniques 39:191-200 (August 2005)

http://www.biotechniques.com/multimedia/archive/00004/BTN_A_05392ST01_O_4596a.pdf

WHAT DOES THE INDUCIBLE EXPRESSION SYSTEM DO?

The gene is given a promoter that is active only in the glandular cells of the target organ so a disease could be placed in a particular place in the body, such as the brain, heart,

pancreas, liver, skin, finger nails or hair follicles, but it is possible that the products of gene expression can be seen in the whole organism.

In the ecdysone inducible expression system, DNA is cloned using *E. coli* and other microbial hosts such as *Bacillus subtilis*, *Salmonella*, *Serratia* and various *Pseudomonas* species.

This system uses enhancers or promoters derived from viruses such as SV40, Adenovirus, Bovine Papilloma Virus, polyoma virus, cytomegalovirus and retroviruses such as leukemia virus, Rous sarcoma virus & HIV.

The genes that are switched on could be stealth viruses or any other pathogenic genetic construction, including man-made creations. The ecdysone switch could also be used to turn on dormant viruses.

This system uses reporter molecules such as luciferase (a general term for bioluminescence) so that the presence or location of a desired ligand (hormone) may be easily determined.

The ecdysone system has effects on some kinds of blood cells such as lymphocytes and neutrophils and may regulate the immune system. Also during gene therapy the presence of cytokines in the blood may result in fatigue and in extreme cases, death. Cytokines are regulators of the immune system such as interleukins and interferons. Viral vectors induce an immune response because they express immunogenic epitopes within the organism. The first immune response occurring after vector transfer is cytokines and chemokines secretions at a lesion site. [17] Bessis, N., Immune Responses to gene therapy vectors: influence on vector function and effector mechanisms; Gene Therapy 2004 Vol(): S10-S17. You may have a rash with multiple lesions. Adverse reactions to cytokines are inflammation and/or ulceration or widespread papular eruptions. [18] James, William, et al (2005). Andrews' Diseases of the Skin: Clinical Dermatology. (10th ed.). Saunders.

If you have been inoculated with the Ecdysone Inducible Expression System, you may have ecdysone or other arthropod hormones and receptors in your blood. There may be a blood test for the hormone and its receptor. It would certainly be unusual to ask for one unless your doctor understood that Morgellons victims infected with arthropods, nematodes, plants and parasites were engineered using these techniques.

INFESTATIONS BY ARTHROPODS

An infestation of flies (of the order Diptera) is called Myiasis. There are 38 species of parasitic flies. Myiasis is a condition where flies of the Order Diptera lay eggs in the skin or flesh of a human being or other vertebrate. A vertebrate is an animal with a backbone. Baby flies called larvae (maggots) are born in the flesh of the host and eat living or dead tissue, body fluids and ingested food. The female lays eggs in open wounds, in unbroken skin, in the nose or ears or in food or water. The life cycle consists of the egg, larvae, pupae and adult. When the larvae hatch, they cut through the skin and tunnel through

the host tissue, causing lesions and dangerous infections. [19]

<http://www.morgellonsuk.org.uk/micromyiasis.htm>

An infestation of mites is called Acariasis (of the order Acari). Infestations by nematodes (round worms) are named after the animal. Disease caused by whipworms is called Trichuriasis. Other Morgellons infestations are caused by parasitic wasps, moths, ants, spiders and many other arthropods.

In Morgellons, these animals aggressively lay eggs in the skin. Female mites only have to be fertilized once and they remain fertilized for life. Some female arthropods are born pregnant. These super egg layers may account for the presence of ecdysone being continually in the human body so that DNA changes and reconstruction of organs (skin, hair, nails) can occur.

MORGELLONS EXPERIENCE

Attracting Insects: The presence of insect hormones in the skin may explain why some Morgellon's victims feel that insects are being attracted to them.

Brain Fog: All steroid hormones pass easily through the blood brain barrier so some changes in brain chemistry from foreign DNA may account for the brain fog. The genetic changes induced or "switched on" may target specific organs or systems, including the brain. The possibilities involved in this symptom need further investigation.

Presence of Fibrillar Structures: This system is perfect for the delivery of fibrillar structures found in various diseases such as Alzheimers disease. It can deliver filamenting bacteria and fungus which filament naturally or in reacting to their environment and available food sources. In Morgellons, various bacteria, including E. coli and Bacillus subtilis form colored filaments, indicating how much of the molecules needed to form the fibers is present, therefore they are sensors.

Delivery of man-made materials: It can deliver man-made molecules and hydrogels that form networks and goo of various colors. Hydrogels made entirely of DNA are conjugated with various biological organisms. There are so many materials and structures that Morgellons' victims find in their bodies that for anyone who has not studied the science that created them, there is no way to know what they are. When examined closely, many have their makers' logos, names, addresses and pictures. One patent that describes the encapsulation of polymeric materials is

The article specifically references a patented insecticidal delivery system (United States Patent 4844896). The patent describes a:

"1. Microencapsulated pathogen comprising:

- (i) an insecticidal pathogen including a virus, bacterium, or fungi known to infect insects

- (ii) a polymeric encapsulating agent comprising polyacrylates, polyacrylic acids, polyacrylamides or mixtures thereof;
- (iii) a sunscreensing agent comprising methyl orange, malachite green or its hydrochloride, methyl green, brilliant green, an FDC green, coomassie brilliant blue R, methylene blue HCl salt, brilliant cresyl blue, acridine yellow, and FDC yellow, an FDC red, fluorescein free acid or mixtures thereof."

Self-Assembled Nonviral Vectors: Complexes consist of DNA and cationic (the active ingredient carries a positive charge) lipids or cationic polymers which can be inserted in plasmids or piggybacked on viruses or bacteria. The polymers used in biomedical applications can be found in this article. I printed it but could not locate the link so I'll try to get this posted somewhere if not here soon. [20] Polymers for DNA Delivery, *Molecules* 2005, 10, 34-64.

Multiple Parasites: The animal vectors are parasites that have their own parasites called endoparasites. A host and parasite are called commensal partners. Commensalism is a relationship between individuals of two species in which the smaller commensal species obtains nutrients, shelter, support, or transport from the host without the host benefiting or being harmed.

HUMAN SKIN

Human Skin is an INDEPENDENT PERIPHERAL ENDOCRINE ORGAN which produces hormones and is able to metabolize hormones and to activate and inactivate them. [21] Zouboulis; Christos C.; Human Skin: An Independent Peripheral Endocrine Organ; *Hormone Research* 2000;54:230-242; http://www.klinikum-dessau.de/fileadmin/user_upload/Hautklinik/PDF-Files/110_hormres.pdf

Human skin produces hormones which are released into the circulation and are important for the functions of the entire organism. Therefore, it is the target of ecdysone receptor gene therapy.

Human skin produces insulin-like growth factors and binding proteins, proopiomelanocortin derivatives, catecholamines (norepinephrine and epinephrine), steroid hormones, Vitamin D, retinoids and eicosanoids (prostaglandins, prostacyclins, leukotrienes) from fatty acids. Hormones exert their biological effects on the skin through interaction with receptors for peptide hormones, neurotransmitters, steroid hormones and thyroid hormones.

Some Morgellons victims who have had the disease for a long period, maybe over 8-10 years, report that their hair, skin and nails are completely replaced with diseased tissue with live animals inside, with synthetic materials, odd colors and even glowing or blinking skin. These conditions are made possible through gene delivery to the skin. [22] Trainer, Alison; Alexander, M. Yvonne, Gene delivery to the epidermis; *Human Molecular Genetics* 1997, Vol 6, No. 10. The majority of the epidermis is comprised of keratinocytes. Through the use of keratin promoters, keratinocytes express exogenous genes such as

the coagulation cascade protein Factor IX and growth hormone. The epidermis has a secretory capability, allowing recombinant gene products expressed in the epidermis to be secreted into the circulation, indicating its potential for the creating systemic disorders (spread throughout the body).

GENE THERAPY AS A BIOWEAPON

Gene therapy can be used to induce disease or cure it. The goal of gene therapy as a weapon is to effect a permanent debilitating change in the genetic makeup of the victim. The weapon does not have to be lethal to be effective because incapacitation and confusion may be all the disruption necessary to cause the intended effects. These are the exact effects we see in Morgellons. People are incapacitated with overwhelming multiple pathogens. They lose their health, jobs, families, property and their place in society in order to keep other people from being contaminated.

Gene therapy is used to change the genetic makeup of a person without their knowledge or consent by means of an insect vector. Insects transmit genes via their saliva, reproductive systems or excretory systems. They deliver the hormone, the receptor and the diseases.

Insects carry bacteria which can be used to change your DNA in a process called bactofection. An outgrowth of vaccination was the idea to use attenuated bacteria as carriers to transport plasmid DNA to the nuclei of specific cells. Bactofection can stimulate the production of antibodies from a wide variety of pathogens by releasing plasmid DNA specifically encoded to stimulate the production of a particular antigen, and could even serve as a general vaccination against cancer. Attenuated bacteria like Shigella, Salmonella and Listeria have all been used as bactofection delivery agents. Nanoparticles are also used to deliver DNA. [23] Bacteria Gives Nanoparticles a Ride. http://libna.mntl.illinois.edu/pdf/publications/76.nnano.2007.149.complete_akin.pdf

The genes must enter cells and be stably expressed at the right levels. The genetic control must be extremely precise so that a potentially lethal disease is not released prematurely, but only in response to the trigger. [24] Block, Steven M., Living Nightmares: Biological Threats Enabled by Molecular Biology, p. 64-68 <http://www.stanford.edu/group/blocklab/Block%20New%20Error%20Chapter%202.pdf>

Genetically engineered systems tend to be "leaky". That has changed with the tighter control systems such as the insect hormone ecdysone system. Stealth viruses can remain for long periods without causing detectable harm. They can be contagious, silently spreading throughout a targeted population over an extended time and then triggered.

With the genetic tools of cellular and molecular biology, it is possible to contemplate a disease first, then construct the pathogen necessary to produce it second using the molecular signaling pathways that are critical to the health of humans. The disease might target the immune response, escaping our natural ability to fight it; or it might activate normally dormant genes and wreak havoc in our cells; or it might simply instruct the cells

in our body to commit suicide in programmed cell death (apoptosis). These are the processes which can be triggered with the ecdysone system.

Inducible hormone receptor systems can be used in arthropods, nematodes, plants [25] Development of a tightly regulated and highly inducible ecdysone receptor gene switch for plants through the use of retinoid X receptor [human] chimeras. Transgenic Res. 2007 Oct;16(5):599-612. Epub 2006 Dec 1. <http://www.ncbi.nlm.nih.gov/pubmed/17139530>

[26] Creation of ecdysone receptor chimeras in plants for controlled regulation of gene expression, Mol Gen Gent (1999) 261; 546-552.
<http://link.springer.com/article/10.1007/s004380050999#page-1>

and mammals [27] Ecdysone receptor-based inducible gene expression system; US 7091038 B2. by fusing the nuclear hormone insect receptor to existing hormone receptors.

NUCLEAR HORMONE RECEPTOR PROTEINS AND WHAT THEY DO

Nuclear hormone receptor proteins are activated when bound to specific sequences of DNA. The bound hormone bends the shape of the receptor so that it can attach to its promoter and activate the gene. They serve as on-off switches for copying DNA within the cell nucleus. These switches control the development and differentiation of skin, bone, and behavioral centers in the brain as well as the continual regulation of reproductive tissues.

In the case of the testosterone, the presence of testosterone turns the gene on; remove it and the gene goes silent. Estrogen and other steroid hormones work the same way, each binding its own specific receptor to activate its own hormone-dependent promoters. Even lower animals control gene expression with steroid hormone/receptor systems. For example, ecdysone and ecdysone receptor constitute a system unique to insects. [28] Identification of Ligands and Coligands for the Ecdysone-Regulated Gene Switch. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC18950/>

The ecdysone switch of insects is like a cocked gun that could be triggered to kill cancer cells. The gun is the gene that codes for Diphtheria toxin, a lethal cellular poison. The gene is activated by ecdysone, through an ecdysone-dependent promoter. This promoter will be snipped from an insect genome and pasted in front of the toxin gene.

A two-gene cassette is used to protect against prostate cancer. Gene 1 codes for ecdysone receptor which controls the expression of gene 2, which codes for diphtheria toxin. When ecdysone is present, the toxin gene is expressed in prostate cells and the cells die. The toxin gene is not expressed in any other cells, because no other cells synthesize the ecdysone-dependent transcription factor.

If prostate cancer were ever diagnosed, a man would get an injection of ecdysone. The hormone would activate the ecdysone receptors in his prostate glandular cells, which

would “turn on” the diphtheria gene, resulting in diphtheria toxin that would kill the cells. Ecdysone would be present throughout the body, but only prostate cells would have the ecdysone receptor to which it would bind, because ecdysone is not a natural hormone of humans.

This same cocked gun could be aimed at the breast, pancreas, or other vulnerable tissues. These are germline engineering procedures and strategies that geneticists are using to create transgenic animals and humans.

http://books.google.com/books?id=9VZ6EF_TUw8C&pg=PA13&lpg=PA13&dq=ecdysone+receptor+in+humans&source=bl&ots=IV6SNqv0wV&sig=NmGaKS8RKMjIcAEhR2IyYhbk4&hl=en&sa=X&ei=8nSIUdnKN4uw8ASfrYCIAQ&ved=0CCwQ6AEwADgK#v=onepage&q=ecdysone%20receptor%20in%20humans&f=false

CONSEQUENCES

It is not hard to see how this inducible system could be installed in unsuspecting humans and then switched on at some opportune time to extinguish a portion of the population. The hormones can be put in food and who controls the content of food? If food were scarce and everyone had to be dependent on authorities for food and water, the source of a chemical that induced the switch to be turned on so that whatever pathogen were present in a person’s body would start to create a disease which would incapacitate them. This system provides a tight control on a population of helpless citizens.

“Ashes and diamonds, foe and friend, we will all equal in the end.” – Roger Waters, Pink Floyd

OTHER INDUCIBLE EXPRESSION SYSTEMS

<http://www.patentlens.net/daisy/promoters/271/272/g3/1465.html>

Other patents related to steroid-responsive promoters

There is an increasing number of patent documents related to the steroid/retinoid/thyroid receptor superfamily and their multiple applications, which are beyond of the scope of this report. The disclosure of the European application EP 1112360 A1 discusses several patent applications and patents related to this topic. As such, it is a good reference to those who would like to assess the patent landscape in this field in a much broader context.

The following list of patent documents refers to chimeric inducible receptors that combine domains from steroid-responsive promoters such as glucocorticoid, mineralocorticoid, and estrogen, among others. Some of them also combine receptors that can respond to both steroid and metal compounds making it a doubly inducible promoter system. Finally, ecdysone receptors isolated from different insects and new receptors based on the retinoic acid receptor are also included. In no way do these documents represent the total number of patents directed to this extensive topic, but they give an idea of the diverse applications in this field of technology.

ELECTROMAGNETIC INDUCIBLE EXPRESSION SYSTEMS

Once Inducible Expression Systems are in the body, it may be possible to start them working via electromagnetic frequencies which would be a reason for radiating a person in their home.

<http://www.amazon.com/frequency-electromagnetic-field-induction-expression/dp/1243491094>

Low Frequency Electromagnetic Field Induction of Heat Shock Gene Expression: Promoter for Targeted Gene Therapy.—[Paul H Frisch](#)

Advances in the knowledge of gene function coupled with advanced laboratory techniques to manipulate and alter genetic material have evolved into a new direction of potential cancer treatment. Research at Memorial Sloan-Kettering Cancer Center (Li, et al., 2003) has demonstrated that the Ku70 gene fragment can be placed in the anti-sense orientation under the control of a heat-inducible (hsp70) promoter, and be activated through heat shock exposure at temperatures ranging from 42°C-45°C. The Ku heterodimer, consisting of two subunits, Ku70 and Ku80, is a member of a family of DNA repair proteins that repairs damaged DNA in order to preserve the integrity of the genome. The heat shock-induced expression of anti-sense Ku70 RNA attenuates the Ku70 protein expression limiting the repair process sensitizing tumors to ionizing radiation. Application of the temperatures necessary to thermally induced hsp response presents significant limitations to the actual clinical treatment scenario. As an alternative static or low frequency electromagnetic fields could provide an innovative and noninvasive method of consistently and uniformly initiating the cellular heat shock response and stress protein hsp70 expression. This thesis research focused on the investigation of utilizing electromagnetic fields to initiate a cellular stress response, acting as a promoter, enabling the development of a targeted gene therapy. Initial experiments confirmed that low frequency electromagnetic fields, could induce hsp70 heat shock expression, however the order of magnitude of the response was significantly smaller than presented by Yanagida (Yanagida, et al., 2000), raising questions of the robustness as response. Experiments examined the possibilities of bias's influencing the hsp70 expression through the potential introduction of thermal effects and/or potential changes in chemical toxicity. These experiments indicated that the potential biasing parameters, of chemical toxicity and heat, did not directly influence the observed hsp70 expression, within our validation experiments. However, concerns about whether electric fields could be applied within a clinical environment directed the research to look more closely at the magnetic field components. The significant clinical advantages of using magnetic fields, led to a series of experiments designed to look at hsp70 response resulting from a pure static magnetic field exposure. These experiments isolated the magnetic field induced hsp70 response, without any electric field components, thermal induction, or changes in chemical toxicity. Experimental data indicated an approximate 3 fold increase in hsp70 response as compared to the no exposure control. This represented response levels on the order of approximately 25-30% that of the thermally induced heat shock hsp70 response, at exposure times of 48 hours. Comparison of the hsp70 response to that measured from electrochemical cell exposures indicates a similar level of response, further indicating that the static magnetic field exposure might be a

preferred clinical approach. A follow-up series of experiments focussed on addressing and analyzing overall genomic expression as a function of magnetic field exposure. Using Affymetrix GeneChip technology, two replicates of the magnetic field exposure, indicated changes in expression (up regulated) of the heat shock genes, and further identified alternative genes, such as Cysteine rich protein 61 and avian myelocytomatosis viral (v-myc) oncogene. These genes could potentially act as candidate promoters for gene therapy applications.

<http://www.thefreelibrary.com/RHeoGene+and+Invitrogen+Sign+Licensing+Agreement+for+Ecdysone...-a085493921>

Business Editors & Health/Medical WritersBIOWIRE2KSPRING HOUSE, Pa.-(BW HealthWire)-May 7, 2002

Agreement grants Invitrogen nonexclusive, worldwide rights

to manufacture and sell Ecdysone-Inducible Expression research kits

RHeoGene today announced it has negotiated an agreement to grant Invitrogen (Carlsbad, CA) a nonexclusive, worldwide sublicense for sales of Invitrogen's Ecdysone-Inducible Expression System and related products for research purposes only.

RHeoGene holds an exclusive license to Stanford University patents U.S. 5,514,578, 6,245,531 and EP Patent 0517805 that cover sales and use of certain ecdysone-based products.

Invitrogen has been manufacturing and selling its Ecdysone- Inducible Expression System under a separate license since 1996. Under its license from RHeoGene, Invitrogen will continue to provide Ecdysone-Inducible Expression System products to academic, **government**, industrial, and clinical institutions for research purposes. Customers wishing to use ecdysone receptor-based gene expression systems for commercial purposes should contact RHeoGene for a commercial license.

"This licensing agreement is the first external validation of the importance of RHeoGene's exclusive license to the intellectual property encompassed by these Stanford patents after broader claims to U.S. 5,514,578 were granted," said Tom Tillett, RHeoGene Executive Vice President for Operations.

The Stanford patents are directed to genes that encode insect-based ecdysone receptors from a broad range of insect species and methods for regulating gene expression in host cells. The patent coverage includes ecdysone receptor (EcR) genes originating from *Drosophila*, the basis of **Invitrogen's Ecdysone-Inducible Expression System**. The patents are based on the pioneering research of Dr. David Hogness, Emeritus Munzer Professor of Developmental Biology and Biochemistry at Stanford University. RHeoGene's exclusive license to these patents encompasses all uses outside of plants,

including cell-based assays, genomics, proteomics, **gene therapy**, cell culture/fermentation, **transgenic animals**, and biosensors.

Financial terms were not disclosed.

RHeoGene is the source for advanced applications, products, and technologies that manage gene expression. Seamlessly integrating biology and chemistry applications that deliver precise management of gene regulation, RHeoGene focuses on delivering customized inducible gene expression technology systems to advance proteomics, drug discovery, biotherapeutics production, and **human gene therapy**. RHeoGene's operations are located in Spring House, Pa., and Charlottesville, Va. For more information, visit www.rheogene.com.

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