ALLIANCE FOR CANCER GENE THERAPY’S MARATHON MAN: DR. MICHAEL T. LOTZE

At age six, Michael Lotze drew pictures of himself with a stethoscope around his neck and his mother was thrilled that young Michael would clearly follow in the footsteps of her father, Michael's grandfather, and become a valued Western Pennsylvania general practitioner. What Michael's mother could not predict was that soon after receiving his medical degree from Northwestern University Feinberg School of Medicine within the Honors Program in Medical Education, and launching training in surgery, he traded his scalpel and stethoscope for a microscope and laboratory, beginning a journey leading to breakthrough cell and gene therapy in the fight against cancer.

BLENDING SCIENCE—MYSTERY—HOPE

A science for Cancer Gene Therapy (ACGT) founding Scientific Advisory Council member Dr. Michael T. Lotze is Professor of Surgery and Bioengineering, Vice Chair of Research within the Department of Surgery; Assistant Vice Chancellor Health Sciences at Pittsburgh Clinical Medicine, and Director of Strategic Partnerships within the University of Pittsburgh. He has worked in the field of Immunology and Clinical medicine for over 35 years and believes that a fundamental understanding of cancer biology and immunology is essential to making progress in Oncology. He is the co-inventor of 10 patents in dendritic cell vaccines and antigen discovery and serves as Associate Editor of the Journal of Immunotherapy. He has over 500 publications in peer-reviewed journals.

In tandem with all of Michael Lotze’s outstanding scientific accomplishments, he has completed 60 marathons in seven countries and will compete in the New York City Marathon for the third time in 2011! How does his love for long-distance running connect with his passion for scientific cancer research? "It stimulates the mind and body, it creates a deep understanding of focus, it motivates the attainment of goals and it allows one to establish objectives that are beyond immediate reach. I have been involved in cancer research and the field of Immunotherapy for over 35 years. The challenges, mysteries, setbacks, victories and the hope are all marathons. In scientific research you must go the distance, never half way.”

ZENO’S PARADOX: THE TORTOISE AND THE HARE!

Dr. Lotze says, “Setting goals brings to mind Zeno’s Paradox.” Zeno’s Paradoxes are a set of problems generally thought to have been devised by Zeno of Elea to support Parmenides’ (Ancient Greek Philosopher) doctrine that all is one. That which is in locomotion must arrive at the halfway stage before it arrives at the goal. Says Lotze, “If you set your goal as successively reaching in intervals the halfway point, you will never get to the finish line! In cell and gene therapy research you must go the distance or you will be diverted time and again by Zeno’s Paradox!”

THE CANCER MYSTERY “FIGHTING FIRE WITH FIRE”

Gene Therapy: Gene therapy is the replacement or modification of a defective or missing gene. One area of gene therapy is immunotherapy in which researchers genetically modify a patient’s immune cells so they recognize antigens produced by cancer cells, thus destroying them and eliminating the tumor. T-cells: A type of white blood cell that is of key importance to the immune system and is at the core of adaptive immunity, the system that tailors the body’s immune response to specific pathogens. T-cells are like soldiers who search out and destroy the targeted invaders.

“When I began my career, cancer was a great mystery. There was little or no biological understanding of the disease. The good news today is that some of that mystery has been lifted. We now know that cancer is fundamentally a disease of the genes and of cells. We have also come to understand that cancer cell and gene therapy is really about fighting fire with fire. It is about introducing through immunology, modified genes and killer cells (T-cells) that kill cancer cells!”

“The very beginning of gene therapy and the first clinical trials were cooked up by Michael Blaese and me. Dr. Michael Blaese was then in the Metabolism Section of the NCI and subsequently, Chief of the Clinical Gene Therapy Branch of the National Human Genome Research Institute. Dr. Blaese had been very interested in immune deficiencies and thought that gene therapy might be a way to cure some of these disorders. Since we were already giving T-cells to cancer patients, we talked about developing a new protocol that marked the T-cells as a strategy to purposely launch genetic manipulation of the cell, which eventually became the first gene therapy.”

Injecting cells with a treated human gene at first met with extraordinary resistance. In the 1960s, the Cambridge, Massachusetts City Council actually outlawed the science at both M.I.T. and Harvard University laboratories. The modern period of cell therapy started in the 1970s and gene therapy in the 1990s. Dr. Lotze adds, “We have come a long way. We have now seen the first approved cell therapy for the treatment of some prostate cancers. However, there as yet is no approved gene therapy for cancer treatment in the United States. Everything remains in trials. It is exciting indeed that Dr. Carl June’s breakthrough clinical trials at the University of Pennsylvania, funded by ACGT, suggest that gene and cell therapy is going to soon be very much a part of modern therapy.”

“EXCEEDING ALL EXPECTATIONS!”

ACGT Research Fellow Dr. Carl June and his team at the University of Pennsyl- vania’s Abramson Cancer Center and Perelman School of Medicine have made great strides in the treatment of advanced CLL (chronic lymphocytic leu- kemia), the most common type of the blood disease that strikes 13,000 people in the U.S. and kills 4,300 every year. The treatment uses genetically modified versions of the patient’s own T-cells, and has shown remission for up to a year in a small group of patients, several of whom are in complete remission. The protocol, which involves removing the patient’s white blood cells and modifying them, then infusing the new cells back into the patient’s body following chemotherapy, provides a tumor-attack roadmap for the treatment of leukemia and other cancers including those of the lung and ovaries and myeloma and melanoma. This is the first demonstration of the use of gene transfer therapy to create “serial killer” T-cells aimed at cancerous tumors. “Within three weeks, the tumors, which were several pounds each, had been obliterated in a way that was much more complete than we ever expected,” said senior author Carl June.
One of the more difficult tasks confronting attorneys who consil creative artists is explaining such terms as “compilation,” “collective work,” and “derivative work,” all separately defined in the first section of the Copyright Act. This column will try to explain “compilation” and “collective work.”

Under the Copyright Act, a “compilation” is a work formed by the collection in assembling of pre-existing materials or data that are selected, coordinated, or arranged in such a way that the resulting work as a whole constitutes an original work or authorship. The term “compilation” includes collective works (emphasis added).

A “collective work” is a work such as a periodical issue, anthology, or encyclopaedia, in which a number of contributions, constituting separate and independent works in themselves, are assembled into a collective whole.

Other examples of collective works are: magazines, software programs, collections of songs by third parties and retrospective collections of a particular artist’s films. The resulting “collection” may become a separately-protectable work, if certain requirements are met.

Keep in mind the phrase in the first section of the Copyright Act, original work of authorship. How difficult is it to establish originality? The case law seems to say that originality is not difficult to establish at all. It depends on the act of selection and editing, which the courts have held to be a “highly creative endeavor.” On the other hand, where there is no originality — where the selection process is purely mechanical, as in the simple al-phabetical arrangement of names in a phone book — copyright protection will be much more difficult to obtain.

In short, artists, editors, film producers and publishers seeking copyright protection for “compilations” or “collective works,” will stand a much better chance if there is selection, coordination or arrangement sufficient to constitute an original work of authorship. The considered selection of prints of a certain artist, or of several stories of a prolific author, would satisfy the selection, coordination or requirement of the Copyright Act. On the other hand, the arrangement of a list of 10,000 names in alphabetical order would almost certainly not satisfy this requirement.

We will deal with the ambiguities of “derivative works” in the next article.

“Compilations” and “Collective Works”