NOTE: This is the first in a series of articles profiling the Research Fellows of the Alliance for Cancer Gene Therapy, Inc., a national non-profit public charity based in Connecticut

ALLIANCE FOR CANCER GENE THERAPY RESEARCH STAR: ***CLODAGH O'SHEA, PH.D.***

Photo: Courtesy of SALK

From Ice Axe to Laboratory

"For me, it's about the moment when you know you're the only person who has ever discovered something new and unique. It's extraordinary!"

Introducing Clodagh O'Shea, Ph.D. -- Clodagh is an assistant professor at the USCD Salk Institute for Biological Studies, Molecular and Cell Biology Laboratory, La Jolla, California. Her avocation is technical ice and rock climbing! Clodagh is an Alliance for Cancer Gene Therapy (ACGT) Research Fellow and the recipient of a multi-year research grant from the nationally renowned Stamford, Connecticut based not-for-profit foundation. Her area of research is developing viral therapies for many different types of cancer.

O'Shea is a native of Ireland having completed her undergraduate work at University College in Cork Ireland in Biochemistry and Microbiology. She is the first member of her family to attend college. She further distinguished herself at Imperial College/Imperial Cancer Research Fund, Lincoln's Inn Fields, London, England where she received her Ph.D in Immunology. She then completed four years of post-doctoral work at the University of California San Francisco in Oncology. She has been published in dozens of medical journals.

While at the Imperial College in England she heard founding ACGT Scientific Advisory Council member Frank McCormick speak and Clodagh became convinced that cancer cell and gene therapy in her words, " Could change the world." That lecture charted the future course for O'Shea. Dr. Frank McCormick is currently the incoming president of the American Association of Cancer Research (AACR) and the David A. Wood Distinguished Professor of Tumor Biology and Cancer Research at the University of California San Francisco.

"FOCUS AND WILL KEEP ME GOING"

Clodagh is among a group of young research scientists funded by ACGT who see discovering new treatments and finding a possible cure for cancer as a daily quest requiring a laser-like focus not unlike climbing a sheer ice face in the Andes or Patagonia. Does being an ice climber and a scientific researcher share much in common? "Actually I think about it all the time. They are not dissimilar. It is looking at big challenges along the way, some you do not expect, and being able to break them down into individual steps. It takes a lot of mental commitment, focus and the will to keep going."

In ice climbing the most challenging and difficult face is a W17. The technical description of a W17 is sustained and overhanging with no rests, extremely rare, near mythical! Not at all unlike the challenges that face researchers like Clodagh in the fight against cancer.

Alliance for Cancer Gene Therapy was founded in 2001 by Greenwich, Connecticut residents Barbara and her late husband Edward Netter. Barbara succeeded Edward as president in 2011. A decade ago, the Netter's daughter-in-law died of breast cancer and as the Netter's witnessed the ravages of the cancer itself and the devastating effects of chemotherapy and radiation treatments they became determined to find a means to discover a new approach to cancer treatment and therapies.

Cancer cell and gene therapy is a highly complex and scientific pursuit that works on the basic premise of finding a way to make the human cell in-hospitable to the creation and multiplication of cancer cells. The development of the breast cancer drug Herceptin nearly 20 years ago was accomplished through early genetic and cancer cell research.

Barbara Netter shares her husband's vision. "We are driven by our mission to support the extraordinary potential offered by cell and gene-based therapies to accelerate effective and safe treatment of all types of cancer. We have never wavered from our belief that molecular medicine is the new paradigm to treat cancer and that the source of cancer, the genes, is where research should be focused. It is our hope and belief that the answers lie in the hands of brilliant researchers like our Clodagh O'Shea."

COULD THE COMMON COLD VIRUS BE THE PATH TO A CURE?

A recipient of the 2007 ACGT Young Investigator Award, Dr. O'Shea describes her work: "Most commonly used cancer chemotherapies are little more than DNA poisons that slow down tumor growth but do not ultimately cure patients. Chemotherapy also has devastating side effects. There is a desperate need to identify new drugs and combinations of therapies that abate cancer cells while leaving normal cells unharmed." Dr. O'Shea's approach is to employ the help of a small DNA virus, called adenovirus, (the common cold virus), to understand and treat cancer.

Recently, research has shown that in every human cancer there is a tumor suppressor gene, p53 that is inactivated due to mutations or loss. Yet there is still no effective therapy to treat patients based on the loss of p53 because it is extremely challenging to tackle something that is no longer there. However, it

has been discovered that just like cancer cells, the cold virus relies on inactivating these same suppressor genes to reproduce in infected cells.Dr. O'Shea's research focuses on using these viruses to multiply only in the tumor cell and implode them from the inside out. The most important finding so far is that the adenovirus brings along another protein that neutralizes the loss of p53 through a completely different mechanism. By understanding this pathway and the virus mechanism, new viruses are being genetically engineered. These viruses can selectively kill tumor cells and also reawaken the immune system to recognize that a tumor is present which needs to be eradicated, both locally and at sites of distant metastases. It proves that science can be serendipitous. By studying one thing, Dr. O'Shea's lab not only found what they were looking for, but in addition, something completely unexpected.

"YOU HAVE TO AIM HIGH"

What keeps this adventurous young research fellow passionate about science? "Scientific research is a celebration of life at its deepest level. To understand even the slightest pathway to treatments and possible cures for cancer and to be able to share that information with others is an amazing experience. Like climbing, once you begin you can never be negative. Even in the slow going you understand that every step forward counts because it increases your knowledge and confidence. While in the laboratory knowing that I can actually help someone by using that acquired knowledge is uplifting and encourages me to keep moving. I know that my work as a research scientist will eventually relieve suffering through new and break-through therapies. You have to aim high, right? It's a huge problem to tackle and I don't even care if we are going to be foot soldiers or captains. That's not what is important to me. It's the battle itself and if I can contribute in any way I'll feel that it's been worth it."

Why does ACGT refer to their young Research Fellows as Research-Stars? Margaret Cianci of Riverside, Connecticut has been ACGT's Executive Director since its founding. "These researchers first and foremost are incredibly well qualified. Before even applying to ACGT for grant support they have dedicated their lives to their education and the field of science. They undergo a rigorous multi-step scientific review process overseen by the prestigious ACGT Scientific Advisory Council. They have attained Research-Star status in our minds because they have separated themselves from the pack by being committed to trying new approaches where no-one has traveled before. Their passion and dedication is inspiring. While not every new idea is successful, we at ACGT believe that taking risks and encountering new scientific frontiers is the approach that will eventually solve the cancer puzzle, piece by piece."

Clodagh O'Shea's research could impact the treatment of many different cancers and ACGT has, over the past ten years, awarded in excess of 22-million dollars in grants for work on cancer cell and gene therapy dealing with all forms of cancer including lymphoma, lung, ovarian and brain cancers. Those grants have attracted an additional 58-million dollars in complimentary funding. Seventeen human trials have been approved with over 100 cancer patients participating. Other ACGT Fellows are conducting research at MD Anderson, Houston, Texas, Stanford University, Stanford, California, Dana Farber/Harvard Cancer Center, Boston, Massachusetts, Memorial Sloan-Kettering Cancer Center, New York, New York, University of Chicago, Chicago, Illinois, Mayo Clinic Cancer Center, Rochester, Minnesota, Johns Hopkins University, Baltimore, Maryland and University of Pennsylvania, Philadelphia, Pennsylvania among others.

"I AM OPTIMISTIC"

When asked about a time line for a cancer cure breakthrough O'Shea shared this perspective. "I am an optimist with a dash of realism. I think that we will see certain cancers going from a terminal disease to a treatable chronic condition within the next twenty years. The treatment of certain leukemia's is an excellent example of that transition. I think for certain tumors we will see potential cures within the short term. These include treatment of early detected breast and lung cancers while others such as brain cancer will be more difficult. We need to further understand how to use viruses through cell and gene therapy in combination with other drugs as was the case in the development of the HIV cocktail treatment. For example, can we capitalize on the advances in our understanding of cancer and therapeutic viruses by using new genome assembly technologies to create optimized tumor killing viruses? The genome elements of viral cancer therapies could be designated as individual Lego pieces and then, just as a child plays with Legos, used to assemble different combinations until the different cocktails are developed to treat various cancers.

"Cancer research is an ongoing daily project that requires tremendous resources," says O'Shea. "It is discouraging to see Federal cutbacks in funding. Like a climbing expedition you can get there but you need tremendous support to accomplish your goals. We are dealing with cancer and all bets have to be on the table so that we can attain these goals in a way that we can willingly and aggressively take the necessary risks to find answers."

It is not surprising to discover that Clodagh, the ice climbing ACGT Research-Star is a caring person. She is also a sharing person. In the small print in her curriculum vitae you read. "Mentor, masters and doctoral students, Biological Sciences, University of California, San Diego, and Outstanding Mentor, Siemens Westinghouse Competition in Math Science and Technology."

O'Shea continues to climb the difficult, unknown and rewarding route to a potential cure for cancer while at the same time she's securing climbing rope and encouraging the work of others. □

MEET CLODAGH O'SHEA

On April 19, 2012 The Alliance for Cancer Gene Therapy will celebrate its tenth anniversary and honor its co-founder, Edward Netter, (left) at a New Frontiers Tribute dinner at the Hyatt Regency in Greenwich.

At the evening's reception guests will have the opportunity to meet Clodagh O'Shea and her colleague ACGT Research Fellows along with all of the members of the ACGT Scientific Advisory Council who will gather from throughout the nation.

You will find complete details of the mission and accomplishments of The Alliance for Cancer Gene Therapy at www.acgtfoundation.org.