

Dream team selected to tackle one of cancer's deadliest forms—pancreatic cancer

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Axial CT image with i.v. contrast. Macrocystic adenocarcinoma of the pancreatic head. Credit: public domain

The Stand Up To Cancer-Cancer Research UK-Lustgarten Foundation Dream Team of top cancer researchers from the United States and the United Kingdom was named here today to launch a fresh attack on

pancreatic cancer, one of the deadliest forms of cancer on both sides of the Atlantic.

Daniel D. Von Hoff, MD, physician-in-chief and distinguished professor at the Translational Genomics Research Institute (TGen) in Phoenix, chief scientific officer at HonorHealth, and professor of medicine at the Mayo Clinic, will lead the team, with Ronald M. Evans, PhD, professor and director of the Gene Expression Laboratory at the Salk Institute for Biological Studies in La Jolla, California, and Gerard I. Evan, PhD, professor and chair of the Department of Biochemistry at the University of Cambridge in the United Kingdom, as the co-leaders.

Stand Up To Cancer (SU2C), Cancer Research UK, and The Lustgarten Foundation selected the team and are providing \$12 million in funding over three years. The team was announced during the 2015 International Conference on Molecular Targets and Cancer Therapeutics sponsored by the American Association for Cancer Research (AACR), the National Cancer Institute, and the European Organisation for Research and Treatment of Cancer. The AACR is SU2C's Scientific Partner and will administer the grant.

Serving as principal investigators on the team are Christopher Heeschen, MD, PhD, lead, Centre for Stem Cells in Cancer and Ageing at the Barts Cancer Institute, Queen Mary University of London; David Propper, MD, a consultant medical oncologist at Barts Cancer Institute and the London NHS Trust; and Joshua D. Rabinowitz, MD, PhD, professor of chemistry and integrative genomics at Princeton University in Princeton, New Jersey.

The team also includes more than two dozen other researchers based in the United States and the United Kingdom, and two advocates, Suzanne Berenger of England and Howard Young of the United States, both of whom are pancreatic [cancer](#) survivors.

Pancreatic cancer typically has a dismal outlook, with a five-year survival rate around 7 percent in the United States and 3 percent in the United Kingdom. It takes the lives of approximately 40,000 people per year in the United States and 8,000 in the United Kingdom. The new Dream Team's research project will focus on reprogramming the biology of cells in [pancreatic tumors](#)—both the cancer cells themselves as well as the surrounding noncancerous cells upon which the cancer cells rely for support—so that the tumors can be stopped. They have found gene networks in pancreatic tumors controlled by genetic 'hot spots' in the DNA called super enhancers (SEs) that are known to control wound repair and tissue regeneration. Unlike the normal system of wound healing that has a shut-off mechanism, in tumors the process remains on, 'hijacked' to drive constant growth.

The SU2C-Cancer Research UK-Lustgarten Foundation Dream Team aims to develop new approaches to reset malfunctioning SEs in pancreatic tumors, thereby dialing up sensitivity to chemotherapy and to anticancer immune cells and pushing pancreatic tumors into lasting remission. To achieve this goal, team members will take a three-pronged approach. They will use cutting-edge technology to analyze pancreatic tumor SE hot spots so that they can understand the biological 'hacking' of normal wound-healing regenerative processes. They will seek to understand how SEs allow cancer cells to obtain nutrients from nearby normal cells, while at the same time avoiding detection by the immune system. They will also initiate clinical trials in pancreatic cancer with a new class of SE-targeted drugs that are geared to enhance chemotherapy and revitalize the immune response. The trials are slated to start in the first year of the Dream Team's funding.

"We are going after pancreatic cancer in a different way," Von Hoff said. "We will use new and existing agents to reprogram the master regulatory biological machinery in cancer cells that drives tumor growth. This machinery comprises molecular complexes of DNA and proteins

that are known as 'super enhancers' for their ability to coordinate the expression of a large number of genes.

"By resetting the malfunctioning genome in both pancreatic tumor cells as well as the surrounding noncancer cells on which the [cancer cells](#) rely for support," Von Hoff said, "the team will try to increase the sensitivity of tumors to chemotherapy and make them vulnerable to the patient's immune response."

"Cancer is a like a wound that does not heal," Evans said, "in part because the super enhancer master switch is stuck in the 'on' position. By deploying a completely new class of drugs, our goal is to reboot the circuit, reprogram the entire cell, and send the pancreatic cancer into durable remission. By thinking differently, we will bring a new approach to defeat this disease."

Gerard Evan described another goal of the research.

"Despite the apparent diversity in pancreatic cancer, there is a remarkable underlying commonality in the biological pathways that drive pancreatic tumors," Evan said. "Our goal is to exploit these commonalities that underlie pancreatic cancer to identify common targets against which to develop more durable, more accurate, and more effective treatments."

A Joint Scientific Advisory Committee (JSAC) composed of highly accomplished researchers and physician-scientists, as well as advocates, conducted a rapid, interactive, and rigorous evaluation of the applications and recommended the team led by Von Hoff and co-led by Evans and Evan for funding.

"Cancer of the pancreas poses some very difficult challenges because the diagnosis is often made at a late stage, and surgery is often impossible,"

said Phillip A. Sharp, PhD, Nobel laureate, institute professor at the David H. Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology, and chairperson of the JSAC. "The Dream Team will bring new insights such as inhibition of novel gene control processes to the battle against this terrible disease."

Cancer Research UK, the largest charitable funder of cancer research in the world, supports a broad range of research to better understand, diagnose, prevent, and treat all cancers. The international collaboration between SU2C and Cancer Research UK launched with a live Stand Up To Cancer telecast on Channel 4 in the United Kingdom in 2012. Through annual telecasts on Channel 4, the U.K. SU2C campaign has generated more than \$35 million to accelerate groundbreaking cancer research in the United Kingdom and abroad. The new Dream Team is the first supported by the transatlantic collaboration between SU2C and Cancer Research UK.

Iain Foulkes, PhD, executive director of research funding for Cancer Research UK, said: "Survival from pancreatic cancer is low; only 7 percent of patients live for five years. Frankly, progress has not been good enough and it's why we have invested \$6 million in this Dream Team. These are among the finest researchers in the world and we're really excited by the potential of their ideas in the fight against this terrible disease."

The Lustgarten Foundation, located in Bethpage, New York, is America's largest nonprofit private funder of pancreatic cancer research dedicated to scientific and medical advancements related to the prevention, diagnosis, treatment, and cure of pancreatic cancer. As a longstanding partner of SU2C, The Lustgarten Foundation's co-funding of this new Dream Team will be the third Dream Team supported by the foundation, bringing the organization's total investment in SU2C's research program to \$12 million.

"Eradicating pancreatic cancer will take a collaborative effort, and private funding plays a critical role in accelerating the development of new clinical trials for this deadly disease," said Kerri Kaplan, executive director and chief operating officer of The Lustgarten Foundation. "This international collaboration will bring together leading global experts in the field of [pancreatic cancer](#) research, and together we will focus on developing new therapies and innovative approaches so patients can benefit and live longer lives."

Provided by American Association for Cancer Research

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