A Tipping Point
In Cancer Research

THE DAMON RUNYON CANCER RESEARCH FOUNDATION IDENTIFIES the nation's most brilliant young scientists and funds research that impacts all cancers. Our scientists include physicians, chemists, and geneticists leading new fields like nanotechnology and transforming traditional ones like radiology. Their innovations have delivered a series of breakthroughs that are revolutionizing cancer research. Below, we offer a snapshot of the range of experts and scientific approaches that are converging to create a tipping point in cancer research.

2011 Annual Report

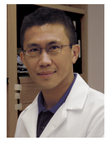
Damon Runyon
Cancer Research
Foundation

Damon Runyon Scientists

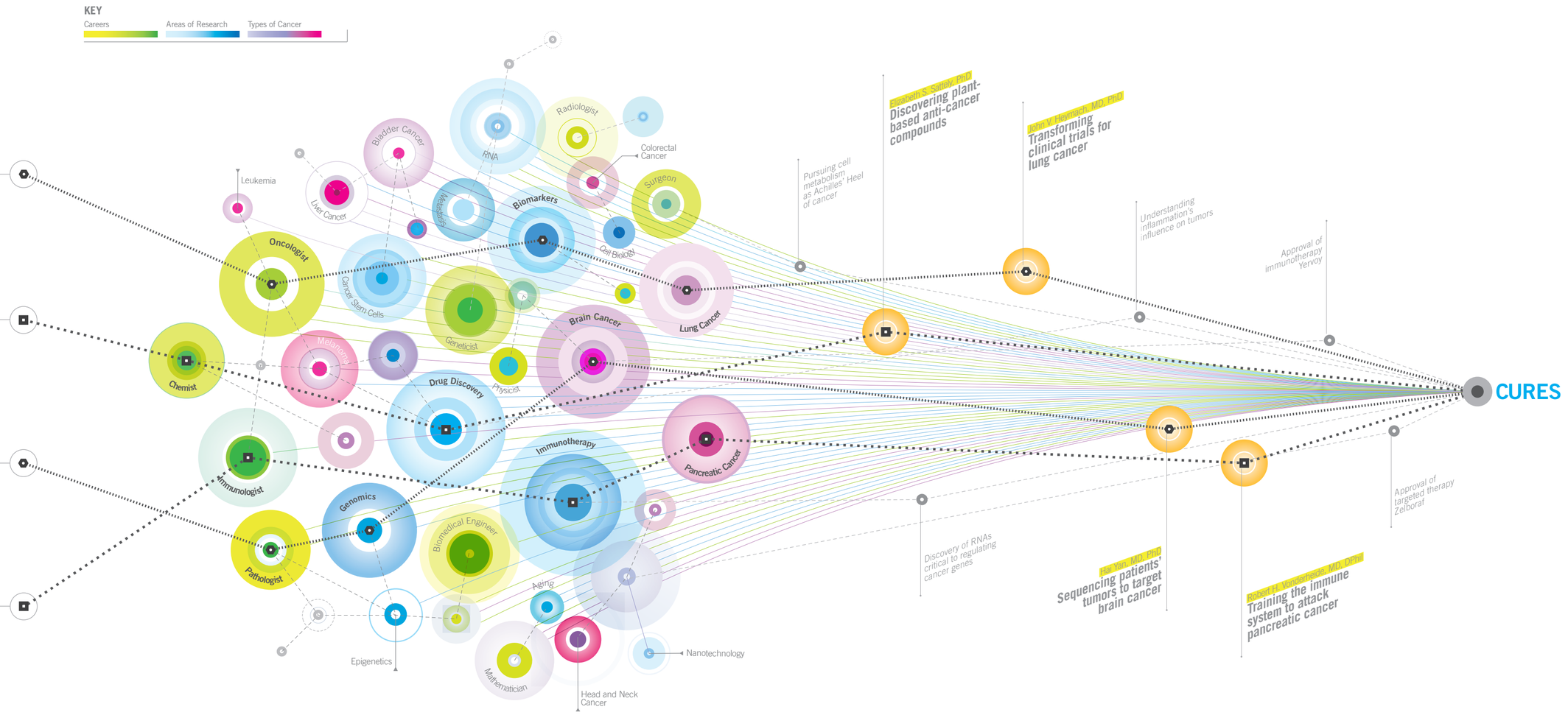
John V. Heymach, MD, PhD
Damon Runyon-Lilly Clinical Investigator '04-'09
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Elizabeth S. Sattely, PhD
Damon Runyon Fellow '08-'10
Stanford University
Stanford, California

Hai Yan, MD, PhD
Damon Runyon Scholar '05-'07
Duke University Medical Center
Durham, North Carolina



Robert H. Vonderheide, MD, DPhil
Damon Runyon-Lilly Clinical Investigator '00-'05
Abramson Family
Cancer Research Institute
University of Pennsylvania
Philadelphia, Pennsylvania



Proof of Progress

Death rates from cancer are decreasing

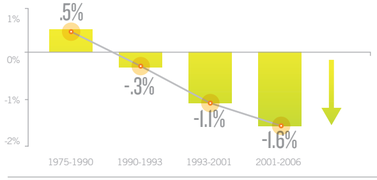


FIGURE: PhRMA. 2011. Annual Change in U.S. Death Rate from Cancer. JPG, from http://www.phrma.org/cancers-decline-death-rates (accessed October 5, 2011).

DATA: Edwards B.K., et al. 2010. Annual Report to the Nation on the Status of Cancer, 1975-2006. Cancer 116, no. 3.

More Americans are surviving cancer and living longer

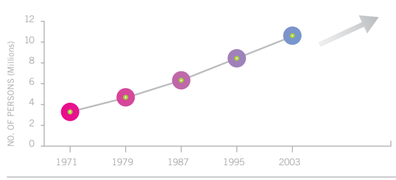


FIGURE: Centers for Disease Control and Prevention. 2011. Morbidity and Mortality Weekly Report: Cancer Survivors-United States, 2007. JPG, http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6009a1.htm#fig1 (accessed October 5, 2011).

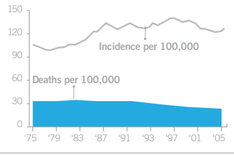
Great strides have been made against some of the most common cancers

BREAST (FEMALE)

Improvements in detection increased incidence rates in the 1980s and 90s, but parallel advances in treatment have resulted in declining death rates since 1969 and increased the overall five year survival rate to 89%.

89% Overall 5-Year Survival Rate

-2.2% 5-Year Mortality Trend



PROSTATE

The introduction of the PSA test brought a spike in incidence rates in the 1990s, but breakthrough therapies have increased the overall five year survival rate to 99%.

99% Overall 5-Year Survival Rate

-3.3% 5-Year Mortality Trend

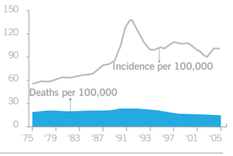


FIGURE: Marshall, E. 2011. Cancer Research and the $90 Billion Metaphor. Science 331, no. 6024. JPG, from http://www.sciencemag.org/content/331/6024/1540.1/suppl/DC1 (accessed October 5, 2011).

DISCOVERING THE TALENT TO DISCOVER THE CURE

Damon Runyon Scientists

Scientists > Research > Breakthroughs

LEVERAGING THIS TIPPING POINT IN CANCER RESEARCH requires an "all hands on deck" approach. It is not enough to focus on a single cancer, type of scientist, field of research, or stage of discovery. Damon Runyon identifies young geniuses across the spectrum. Together, scientists like Beth, John, Hai, and Bob are boldly leading us into a new era of cancer research and bringing us closer to cures.

Elizabeth S. Sattely, PhD

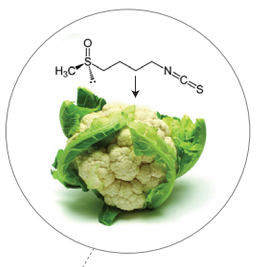
Assistant Professor
Stanford University, Stanford, California

Damon Runyon Fellow '08-'10

"Before the Damon Runyon Fellowship, I didn't appreciate the diversity of backgrounds required to tackle cancer."

Using Chemistry to Identify Natural Anti-Cancer Compounds

Chemist > Drug Discovery > All Cancers



SULFORAPHANE, found in vegetables like cauliflower, is one of many plant compounds being explored for potential anti-cancer properties.

AS PROGRESS IN CANCER RESEARCH accelerates, scientists are drawing from a broader set of disciplines than ever before. Chemists like Elizabeth S. Sattely, PhD, have moved from peripheral players to key collaborators in the pursuit of more effective ways to prevent and treat cancer.

Cancer treatments are comprised of single or multiple chemical compounds. Many of these compounds—like etoposide, frequently used to treat lymphoma and sarcoma, among other cancers—are produced in nature by plants or microbes. "Nature's ingenuity in drug design is what inspired me to study how plants themselves act as synthetic chemists, and how plant products can be used to treat and prevent cancer," Beth says.

Generating a clinically useful amount of a natural compound that is safe to administer as a drug, however, remains a challenge. While completing her doctoral thesis, she and her colleagues at Boston College achieved a breakthrough, discovering a catalyst capable of creating these complex molecules faster and more effectively. Now at Stanford, she is establishing a research program that will harness the rich molecular diversity of plants to improve human health.

"With the sequencing of plant genomes, we're now able to map pathways that are involved in making these helpful molecules. We think this is a key piece of information in understanding how, for example, diet is affecting cancer incidence." That knowledge could help save millions of lives. According to a recent World Cancer Research Fund report, 2.9 million new cancers are linked to diet, obesity and lack of exercise each year.

"One plant family we're looking at, the brassicas (which includes broccoli and Chinese cabbage), contains compounds that affect cell biology and have been shown to have chemopreventative properties. Epidemiological studies have revealed that certain populations that eat plants from this family have a lower incidence of particular cancer types."

"In order to use these compounds against cancer, we have to better understand what's going on in molecular detail. Once we do, we'll have a new way to approach cancer prevention and treatment based on diet and plant products."

John V. Heymach, MD, PhD

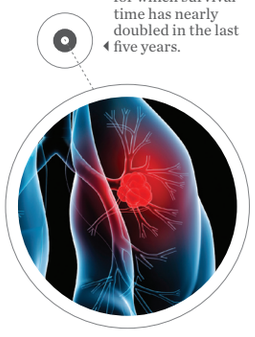
Co-Director of the Thoracic Molecular Pathology Laboratory
The University of Texas MD Anderson Cancer Center, Houston, Texas

Damon Runyon-Lilly Clinical Investigator '04-'09

"Damon Runyon's funding has been invaluable. Their generosity and flexibility allowed us to marry the lab and the bedside, which was essential to developing new biomarkers."

Creating a New Model for Personalized Medicine

Oncologist > Biomarkers > Lung Cancer



A MODEL DEPICTING LUNG CANCER, for which survival time has nearly doubled in the last five years.

IN THE PAST, CANCER PATIENTS received treatment based on the name of their disease. Some patients responded to treatment while others inexplicably did not. We now know that each patient's cancer is unique. The cancer treatments of the future will be based on the biology of each patient's tumor, also known as personalized medicine.

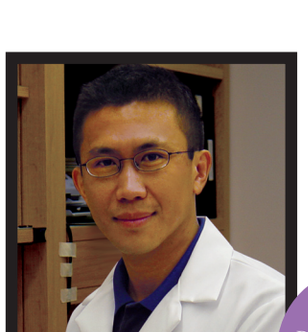
John V. Heymach, MD, PhD, is leading this revolution in cancer research. He has helped create a new model for clinical trials that matches the right drugs to the right patients and speeds the approval process for new therapies.

"We envision a future of matching patients with the most appropriate drug based on the genetic profile of the tumor," John explains. "One of the biggest successes has been the identification of certain mutations that cancers are addicted to. In lung cancer, patients with the EGFR mutation are very responsive to drugs that inhibit the EGFR pathway."

However, EGFR mutations only affect about 12% of non-small cell lung cancer patients. "Until recently, we just haven't had the tools to measure why a drug worked for some but not others," John adds. To address these shortcomings, he and his colleagues launched the pioneering BATTLE trial. "Our hope was to develop biomarkers that could become standard tools for predicting who was going to respond to which drugs."

Focusing on lung cancer, they were able to sharpen the trial's focus and improve its effectiveness by reviewing individual patients' biological data and making adjustments mid-trial. "As the study progressed, we used real-time information from one group to treat the next group of patients with drugs more likely to help them," John explains. The approach worked. "For the first time, we identified biomarkers to predict which patients would be resistant to erlotinib [Tarceva], the standard lung cancer treatment. With these markers, we can more effectively treat patients, lower toxicity, and reduce costs from ineffective treatment."

He is now applying the lessons from BATTLE in new clinical trials focused on overcoming drug resistance. The future looks bright. "We live in a remarkable period. From 1973 to roughly 2005, survival for lung cancer patients increased by less than a month. In the last five years, we've almost doubled that from 7-8 months to 12-14. And there are no signs of that progress abating."



Hai Yan, MD, PhD

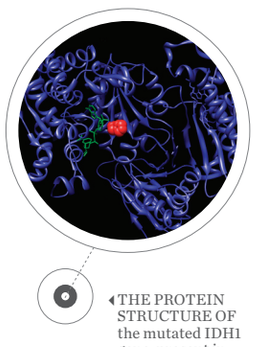
Assistant Professor
Duke University, Durham, North Carolina

Damon Runyon Scholar '05-'07

"My Damon Runyon grant was the first I ever received. I had no name in the field yet, but the award empowered me to find the most important gene in brain cancer."

Sequencing Individual Patients' Tumors to Identify New Drug Targets

Pathologist > Genomics > Brain Cancer



THE PROTEIN STRUCTURE OF the mutated IDH1 gene, present in 70% of gliomas.

HAI YAN, MD, PHD, IS INSATIABLY CURIOUS about the unknown, and has been for most of his life. "When I was a kid in China, I dreamed of being an astronaut or scientist," he recalls, "I became nearsighted when I was 10, so I couldn't fly. But I could be a scientist with glasses!" It is a critical trait for any young researcher taking on the formidable challenge that is glioma, the most common and aggressive type of brain tumor.

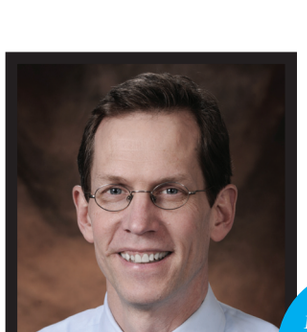
The brain is a complex organ sealed behind the blood-brain barrier, rendering traditional cancer detection and treatment methods ineffective and allowing most brain cancers to go undiagnosed until they are too advanced to treat. Fortunately, new technologies like whole genome sequencing, a lab process that reveals the sequence of DNA in a given tissue, are helping researchers reverse the tide.

In 2008, Hai and his colleagues sequenced nearly 20,000 genes from glioma tumors. The goal was to look through the whole tumor genome and determine what gene mutations were unique to brain cancer cells. They discovered that each tumor contained 40-50 mutated genes, including IDH1, a gene mutated in 70% of glioma. It marked the first time the gene was ever linked to cancer.

In subsequent studies, he confirmed that mutations inIDH1 altered cancer cell metabolism, a vital process that provides tumors energy to grow. Scientists believe that the unique metabolism of cancer cells may be an "Achilles' heel" shared by many forms of the disease. In 2009, researchers at Agios Pharmaceuticals demonstrated that this change in IDH1 produces a unique metabolic chemical not found in normal cells.

"With this knowledge, small molecule drugs may now be designed to target IDH1 mutations," Hai notes, "and this metabolite could be used as a biomarker for screening, possibly before any tumor arises."

Hai truly believes in the power of rigorous science. "Genomics has changed the landscape of cancer research. With unbiased, whole genome sequencing we found a gene that has been elusive for many years; we defined what it is, where it is, and are now trying to answer how to stop it from promoting tumor growth."



Robert H. Vonderheide, MD, DPhil

Associate Professor and Investigator
Abramson Family Cancer Research Institute
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania

Damon Runyon-Lilly Clinical Investigator '00-'05

"The Damon Runyon program truly understood what it took to translate an idea from the laboratory to patients. It made all the difference."

Leveraging the Immune System to Attack Cancer

Immunologist > Immunotherapy > Pancreatic Cancer

EVEN AS HE GRADUATED from Notre Dame with a degree in chemical engineering, Robert H. Vonderheide, MD, DPhil, was already considering a new career. A Rhodes Scholarship allowed him to explore physiology at Oxford University. "That's when I realized that medicine is a type of bioengineering that really excited me. I just couldn't believe the beauty and the power of the immune system."

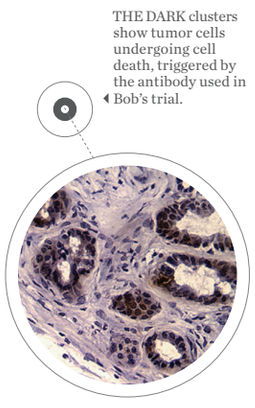
For more than a decade, Bob has been transforming our understanding of how the immune system interacts with and responds to cancer. "My mentor Lee Nadler made it very clear that it was possible for a single person to use immunology to impact patients with cancer. So, I was thinking immunotherapy from the very beginning."

Immunotherapy is a thriving new class of cancer treatments that directs the immune system to fight disease. In the past year, the FDA has approved two immunotherapeutic drugs for types of skin and prostate cancer that have been notoriously difficult to treat, developments that "were only dreams ten years ago," Bob says. "I think the time has come. There is a dam burst of successful immunotherapies based on a decade of experimentation and rigorous science."

This year, Bob and his colleagues at the University of Pennsylvania announced that they had successfully triggered an immune response to attack advanced pancreatic cancer. "Pancreatic cancer is a medical tragedy that we need to do more about, and we found evidence that antibodies targeting the protein CD40 could jumpstart an immune response in some patients."

Bob developed an experimental antibody that was combined with chemotherapy to treat patients with advanced pancreatic cancer in an early phase clinical trial. It extended survival and temporarily forced the tumors into regression for 24% of patients compared to just 5% for those receiving chemotherapy alone. The antibody stimulated macrophages, an immune cell that pancreatic tumors manipulate for protection. The macrophages reversed course, eating away the tumor's supporting tissue. "It is something of a Trojan horse approach. The tumor is still calling in macrophages, but now we've used CD40 to re-educate those macrophages to attack."

Bob is awaiting approval for a new Phase I trial to determine how the antibody can be used for patients with less advanced pancreatic cancer. The antibody has also shown promise against melanoma, with at least one patient in remission after therapy since 2005.



THE DARK clusters show tumor cells undergoing cell death, triggered by the antibody used in Bob's trial.

Damon Runyon Cancer Research Foundation