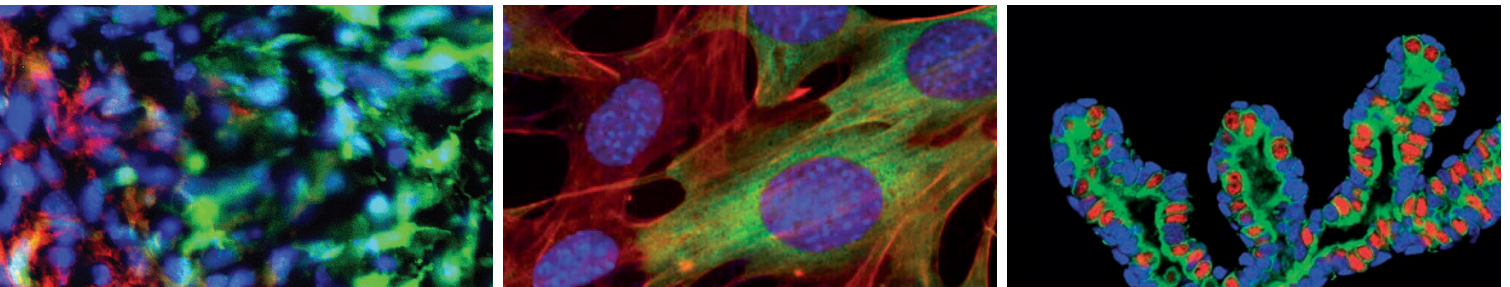


## YEAR TWO UPDATE

Fall 2020



*Thank you for your generosity to the Conquering Cancer Initiative. This report features the Initiative's progress in cancer research, the launch of new programs and continued momentum of exciting projects—all made possible thanks to your partnership.*

Cancer is unlike other diseases. Most conditions have external causes—bacteria, viruses, injury—but cancer often comes from inside us. Cells go rogue, divide recklessly, invade other tissues and spread throughout the body. They do things normal cells cannot do. Cancer is secretive, terrifying. The word itself evokes fear. It grows unobserved, recodes itself to escape treatment and co-opts normal biology to keep growing. To add to its complexity, cancer is not one disease but many—hundreds, perhaps thousands.

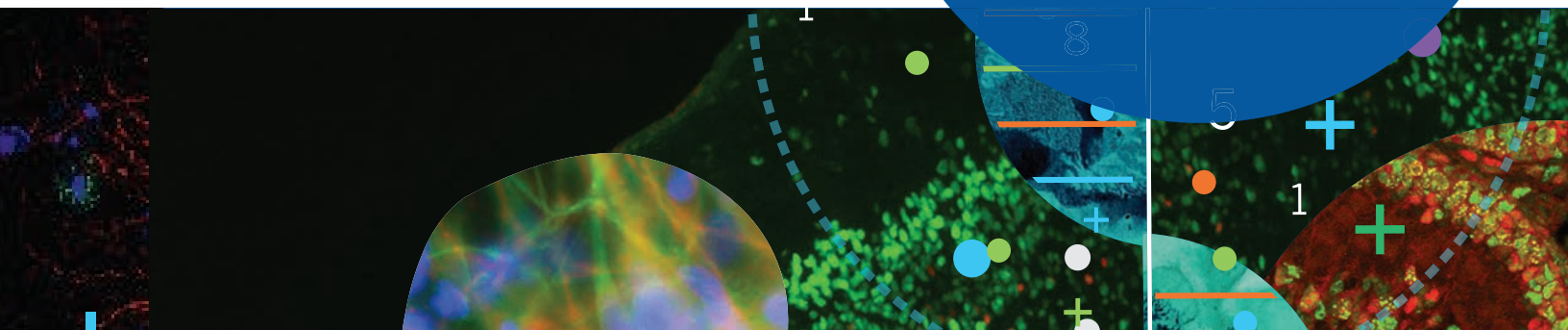
*According to the  
American Cancer Society,  
the global burden  
is expected to grow to*

**27.5 million**  
new cancer cases

*and **16.3 million**  
cancer deaths*

*by **2040***

*simply due to the growth and  
aging of the population.*



# OUR APPROACH

**In 2018, Salk's NCI-designated Cancer Center—one of the first such centers in America—launched the Conquering Cancer Initiative.**

The Conquering Cancer Initiative is a scientific and philanthropic initiative to bring scientists in more than 30 labs together to harness new strategies against deadly cancers: pancreatic, ovarian, lung, brain (glioblastoma), colon cancer and triple-negative breast. As part of the Initiative, Salk researchers are uncovering vulnerabilities in these cancers and developing novel methods to attack tumors and leave healthy tissues alone. This year, the Conquering Cancer Initiative will be highlighting scientific research addressing colon cancer due in part to the dramatic increase of cases.

## PEOPLE



### Welcome Assistant Professor Daniel Hollern

This year, the Salk Institute recruited Daniel Hollern as an assistant professor in the Salk Cancer Center. Hollern comes to Salk from the University of North Carolina at Chapel Hill, where he was a postdoctoral fellow. His lab will focus on triple-negative breast cancer and collaborate with Salk's NOMIS Center for Immunobiology and Microbial Pathogenesis. Hollern takes a multi-disciplinary approach to investigate responses to cancer therapies, immune cell dynamics and the mechanisms controlling tumor growth. In order to improve treatment strategies for cancer patients, he will leverage functional genomics and experimental biology to study the anti-tumor immune response. Hollern earned his PhD in cell and molecular biology from Michigan State University and is the recipient of numerous awards.

## OUTREACH

The Bench-to-Bedside-to-Bench lecture series was created to showcase physician-scientists who pair patient and clinical perspectives with cutting-edge areas of cancer disease research. Despite using leading-edge molecular tools to target druggable pathways, scientists working at the lab bench aren't always privy to the real-world limitations of inhibitor treatments and the subsequent toxicities that patients may experience. Eric Collisson, MD, from UC San Francisco Helen Diller Comprehensive Cancer Center, explored this connection and shared insights in clinical oncology and his collaborations with Salk scientists.

### New Bench-to-Bedside-to-Bench Seminar Series

*With support from Susan and David Mandel and the Salk Cancer Center Director's Fund, the new Bench-to-Bedside-to-Bench Series was launched on August 20 with a virtual event. The next Seminar Series will take place in March 2021.*

# GOALS of the Conquering Cancer Initiative

## Increase the number of promising clinical research projects translated into new therapies

- Based on research from the labs of Professors **Tony Hunter**, holder of the Renato Dulbecco Chair, and **Ronald Evans**, holder of the March of Dimes Chair, trials have been developed to examine new therapeutic possibilities for pancreatic cancer as well as for other forms of solid tumors/cancers more broadly.
- Professors **Reuben Shaw**, holder of the William R. Brody Chair, **Evans** and **Clodagh O'Shea**, Howard Hughes Medical Institute Faculty Scholar and holder of the Wicklow Chair, have been deeply focused on new therapeutics to enter clinical trials in the next 5 years.

## Increase collaborations and build clinical alliances

Over the last two years, numerous new collaborations have been initiated:

- Children with aggressive neuroblastoma have poor cure rates despite intensive treatment, and new treatments are needed. Collaborators **Hunter** and Peter Zage, MD/PhD, a pediatric oncologist at Rady Children's Hospital, are studying cells to control the function of proteins required for neuroblastoma growth and survival. Results could lead to new types of treatment, improved success of neuroblastoma therapy and improved chances of survival for children with neuroblastoma.
- Endometrial cancer is the fourth-most common cancer in women and the most commonly diagnosed gynecologic cancer. Assistant Professor **Diana Hargreaves** teamed up with UC San Diego gynecologic oncologist Ramez Eskander, MD, to study the epigenetic signature of endometrial cancer in order to reveal potential genetic "driver" activity based on modifications at regulatory sequences affecting gene expression. Their studies will help develop a classification system based on epigenetic features, which will improve diagnosis and help identify novel treatment strategies for endometrial cancer.
- **Shaw**, in collaboration with UC San Diego oncologist Hatim Husain, MD, believes that autophagy (a type of cellular recycling) allows lung cancer cells to evade cell death in response to chemo- and targeted therapies, causing therapeutic resistance. They will test a new drug known as an autophagy inhibitor in the first-of-its-kind study for the treatment of lung cancer.

## Identify cancer biomarkers and develop early detection tools

- **Hunter** discovered how a signaling protein called LIF (leukemia inhibitory factor) is a useful biomarker in pancreatic cancer and may be an excellent therapeutic target to defeat this deadly form of cancer. Research from labs of Hunter and Assistant Professor **Dannielle Engle** has identified new biomarkers of pancreatic cancers that have the potential to identify individuals at risk for developing these cancers. The inability to detect these cancers early when interventions can be most effective is the primary reason they are so deadly.

## Ensure researchers' shared access to cutting-edge technology

- Professor **Juan Carlos Izpisua Belmonte**, holder of the Roger Guillemin Chair, developed a new genome-editing technology that can be expanded for use in a broad range of gene mutation conditions.
- Professor **Alan Saghatelian**, holder of the Dr. Frederik Paulsen Chair, developed a lipidomic (fat-related) technology that is leading to the discovery of new cancer biomarkers.
- Professor **O'Shea** is developing "designer" adenoviruses that can destroy cancer cells once they enter those cells.

## Support the next generation of cancer researchers

- We provide educational and career enhancement opportunities to doctoral and postdoctoral trainees to ensure the next generation of cancer researchers. In addition to providing mentees opportunities to engage in experiences that enhance their knowledge of cancer science and translate their work to the clinic, our goals include offering targeted training in emerging technologies; presentations on various aspects of cancer therapy such as pathology, spatial imaging, molecularly-targeted trials and tumor boards; modern drug discovery techniques courses; numerous seminars and symposia; and a grant-writing tutorial series.

*If you are interested in supporting one of these programs, please contact Salk External Relations at [giving@salk.edu](mailto:giving@salk.edu)*



## Progress in EMERGING RESEARCH

### Glioblastoma Multiforme

Glioblastoma multiforme (GBM) is the most lethal form of brain cancer and remains largely resistant to treatment. Salk scientists are actively working to find new and more effective treatments. Professor **Satchin Panda** found a surprising new target: components of the body's circadian clock may control how and when nutrients get into GBM tumor cells and allow a therapeutic window to treating this deadly disease. Using a compound that activates two circadian switches as a tool, his lab showed effective inhibition and improved survival in animal models of GBM.

### Triple-Negative Breast Cancer

The labs of Professors **Martin Hetzer**, holder of the Jesse and Caryl Philips Chair and **Geoffrey Wahl**, holder of the Daniel and Martina Lewis Chair, have identified how expression of the Nup93 gene inversely correlates with the survival of triple-negative breast cancer patients. The researchers identified Nup93 as a contributor of triple-negative breast cancer cell invasion and highlights potential novel targets for the development of anti-metastatic therapies.

### Ovarian Cancer

Ovarian cancer is often diagnosed late, when the cancer has already spread. **Izpisua Belmonte** uncovered several genes that could be used as biomarkers and could point to therapeutic targets for diagnosing and treating age-associated ovarian diseases, such as ovarian cancer. A better understanding of the ovarian environment as well as the mechanisms of healthy aging could inform new therapies.

### Pancreatic Cancer

Pancreatic cancer is a highly lethal malignancy and will soon become the second-leading cause of cancer-related death, due to a perfect storm of tumor resistance pathways. **Evans** is investigating the possible convergence of the pancreatic cancer epigenome and tumor-microenvironment-activated cancer cells as a potential therapeutic target.

A multi-investigator collaborative team including Ronald Evans, Tony Hunter, Reuben Shaw, Geoffrey Wahl, Susan Kaech, Edward Stites, Dannielle Engle and Michael Downes are working to find new therapeutic approaches for pancreatic cancer survival and overcome how pancreatic cancer uniquely evades cancer therapies. For more information, please visit [www.salk.edu/conqueringcancer](http://www.salk.edu/conqueringcancer)

Over the past year, Salk scientists  
have made groundbreaking discoveries.

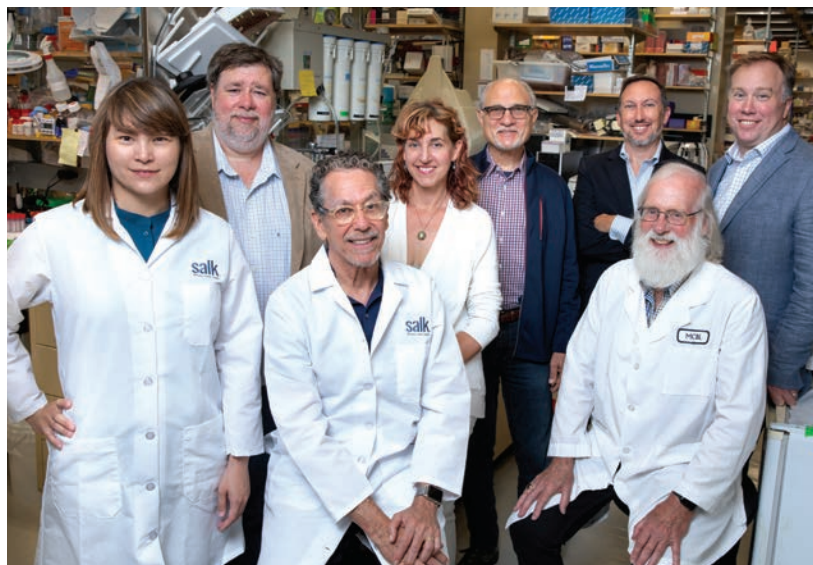
### Lung Cancer

Lung cancer is the number one cause of cancer deaths per year. **Shaw** led a team investigating non-small cell lung cancers (85 percent of total cases), which often contain a mutated gene called LKB1, and recently discovered precisely why inactive LKB1 results in cancer development. The surprising results highlight how LKB1 communicates with two enzymes that suppress inflammation in addition to cell growth, to block tumor growth. The study emphasizes the need to gain a deeper understanding of key cellular processes in order to reveal novel vulnerabilities that can be exploited to selectively kill cancer cells.

### Colon Cancer

Colon cancer is the third-most common cancer. Some patients with a certain gene mutation benefit from a chemotherapy drug called cetuximab, although the reason why the drug works in these patients was unknown. Assistant Professor **Edward Stites**, MD/PhD, holder of the Hearst Foundation Developmental Chair, combined computational biology with experimental investigations to discover the mechanism for why these patients respond to cetuximab, which will help doctors identify more effective treatment plans for people diagnosed with colon cancer.

Additionally, in a separate exciting paper last year, **Evans** not only discovered a mechanism for how high-fat diets may increase colon cancer risk but also showed a candidate therapy that reversed those effects.



# Conquering Cancer

## FUNDING PRIORITIES

### Conquering Cancer Initiative Strategic Fund

The Conquering Cancer Initiative Strategic Fund provides support for the highest priorities outlined in the Conquering Cancer Initiative Strategic Plan. Projects may include purchasing critical equipment to keep up with the pace of technology, seed funding for laboratory research and pilot projects, and bridge funding.

### Recruitment

To keep attracting, retaining and recognizing the world's top cancer researchers, we must be able to offer ongoing support of their innovative research. New endowed faculty chairs and postdoctoral fellowships will enable us to attract and retain the best scientists who conduct foundational, also known as basic, research. Endowments ensure the long-term sustainability of science innovation for researchers and their teams.

### Emerging Research

Private philanthropy is pivotal for breakthroughs in our research efforts to treat and eradicate cancer. In research, the most important discoveries are often not those we would predict, but unexpected observations that must be explored. Research funds provide opportunities for scientists to develop concepts that otherwise would be difficult, if not impossible, to develop.

### Cancer Center Director's Fund

This fund will support training, seminars, scientific advisory board activities, symposia and training programs for high school students interested in careers in science and medicine, hosting undergraduates in research laboratories for internships during the summer, and providing support for graduate students, postdoctoral scientists and research fellows. Thanks to the dollar-for-dollar challenge made possible by Corinne Mentzelopoulos, every dollar to the Director's Fund will be doubled, up to \$1 million.

### Translational Discovery Fund

The Translational Discovery Fund provides starter funds that will support projects specifically focused on the translation of laboratory and/or clinical research into new interventions that improve outcomes for patients. Particular focus will be on the development of new therapies (medications, nutrition, behavioral interventions, etc.) or diagnostics, new approaches to prevention or translation of knowledge. This funding is critical for the long-term growth of The Cancer Center at the Salk Institute.

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*"Since the Salk Cancer Center's inception, our researchers have been taking a collaborative, multidisciplinary approach to understanding the fundamental underpinnings of cancer. By working across scientific fields, we are finding what different cancers have in common, knowledge that will have a cascading impact on our ability to treat all cancers, including the deadliest ones."*

— **REUBEN SHAW** Professor and Director of Salk Cancer Center, William R. Brody Chair

We invite you to join us for this upcoming virtual special event.  
*The presentation will be 30 minutes, followed by Q&A.*

## SAVE THE DATE

**Monday, November 16, 2020 / 1 pm PST**

### **Power of Science: Conquering Pancreatic Cancer**

featuring Professor Ron Evans, March of Dimes Chair

Join us for a live episode of the Power of Science Lecture Series featuring **Ron Evans, PhD**, who will be sharing clinical trial updates on pancreas cancer research breakthroughs including immunotherapy and a vitamin D derivative. Pancreatic cancer is a devastating disease with only 8% of patients surviving more than five years. As part of the Conquering Cancer Initiative, the research team at the Salk Institute are working on breakthrough discoveries that are redefining diagnoses and treatment.

To register for the Power of Science:  
Conquering Pancreatic Cancer, please visit:  
**[www.salk.edu/evans-registration](http://www.salk.edu/evans-registration)**

To make a gift online, please visit:  
**[www.salk.edu/donate-to-cancer](http://www.salk.edu/donate-to-cancer)**

To mail in a check, please mail to:  
Salk Institute  
Conquering Cancer  
10010 N Torrey Pines Road  
La Jolla, CA 92037

## Thank you for your support of Salk's Conquering Cancer Initiative

As donors, you contribute to the Initiative's success, and we are exceptionally grateful for your commitment and dedication.



**Conquering Cancer Advisory Committee:** (From left) Eve Benton, Scott Dailard, Susan Pidgeon Mandel, Tim Schoen, Genta Luddy, Reuben Shaw, Rita Ryu, Sandy Liarakos (Not pictured: Ellen Chodorow and Heather Slosar)

*The Salk Institute has been ranked as one of the top 5 nonprofit institutions in the world focused on the life sciences and one of the top 10 nonprofits generally, according to a 2019 Nature Index report.*

To give through your IRA, retirement fund or Donor Advised Fund: Please contact Cheryl Dean at [cdean@salk.edu](mailto:cdean@salk.edu)

For help with donations, fundraising or questions about supporting the Salk Institute: please contact Salk Institute, External Relations at [giving@salk.edu](mailto:giving@salk.edu) or (858) 453-4100  
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For the ninth consecutive year, the Salk Institute earned the highest ranking from Charity Navigator, America's largest independent evaluator of nonprofit charities. This exceptional designation, highlighting the Institute's attention to fiscal accountability and transparency, is awarded to only three percent of the more than one million charities evaluated.

The Salk Institute is a 5013C tax-exempt organization (EIN: 95-2160097) and your gift is tax-deductible within the guidelines of U.S. law.