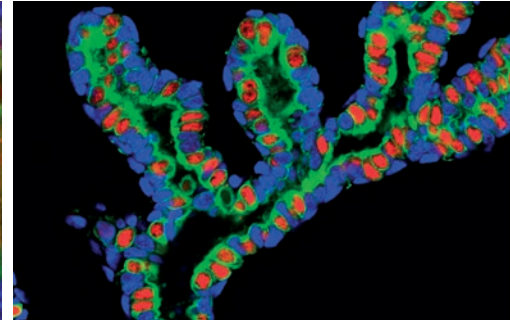
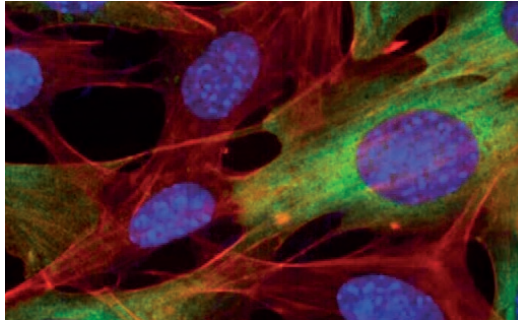
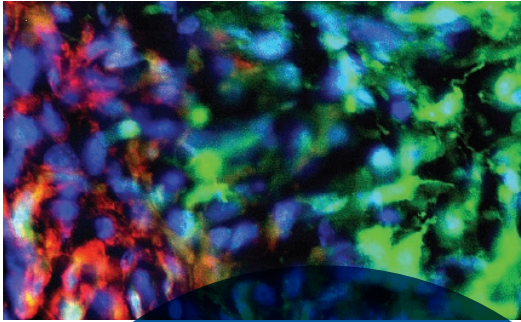


# YEAR THREE UPDATE

Fall 2021



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

## Message from the Cancer Center Director

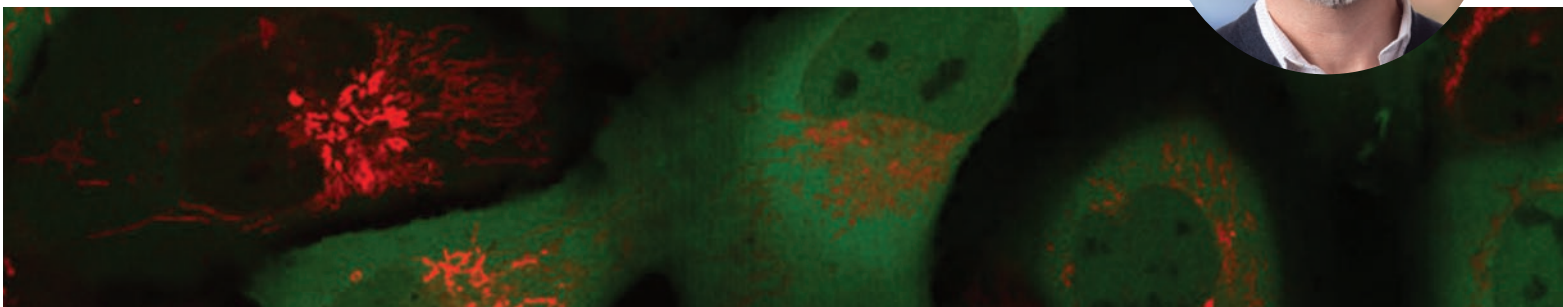
In spite of the challenges, trials and tribulations of the last 18 months from COVID-19, cancer has not stopped. As cancer researchers, we cannot stop bringing the fight to cancer, and will continue to push to develop new therapeutics, to identify targets, and to work collaboratively to mix expertise in different disciplines to come up with truly unexpected breakthroughs that lead to future medicines.

The Salk Cancer Center has been expanding its number of professors and scientists during the COVID-19 pandemic, and we join with our colleagues across the country to advance new research discoveries and push new potential treatments towards the clinic. The world witnessing the importance of biomedicine in fighting the pandemic has made it clear how essential modern science is to fighting off both new and ancient diseases, from simple viruses to the most complex and deadly cancers.

We appreciate your partnership and thank you for your support.

### **REUBEN SHAW, PhD**

Professor and Director of the Salk Cancer Center,  
William R. Brody Chair



## Cancer Metabolism: Cutting Cancer's Fuel Lines

To continue growing, tumors must constantly find new food sources. Scientists have known for more than a century that tumors rewire their metabolism to get more energy. However, it's only in the past few years that researchers have recognized what a powerful weapon metabolism can be. Professors Susan Kaech and Reuben Shaw are leading a collaborative Salk effort to exploit the connection between cancer and metabolism and uncover new therapeutic strategies. The effort launched in September 2021 with the Salk Cancer Summit hybrid event, where Salk researchers shared how they are cutting cancer's fuel lines to attack deadly tumors.

Like normal cells, tumors rely primarily on glucose for energy, but should glucose run short, tumors are able to rewire themselves to use alternative sources of fuel. The team at Salk believes it can take away these sources one at a time, for example by targeting mitochondria, the cells' power stations, or autophagy, the cellular recycling system. The metabolism strategies that the team at Salk is working on shows great promise and underscores Salk's overall approach: identify cancer's many vulnerabilities and exploit



From left: Tim Schoen (moderator), Reuben Shaw, Susan Kaech, Christian Metallo, Satchin Panda, Christina Towers and Daniel Hollern.

them. Because each patient's disease is different, these approaches can be mixed and matched based on a tumor's genetic profile.

Watch the video at: [www.salk.edu/cancer210901](http://www.salk.edu/cancer210901)

## Outreach: Our Bench-to-Bed-side-to-Bench Seminar

With support from Susan and David Mandel and the Salk Cancer Center Director's Fund, seminars took place virtually in March and September. The first lecture showcased a physician-scientist, Christine Lovly, MD, PhD, from the Vanderbilt-Ingram Cancer Center, who pairs her patient and clinical perspectives with her cutting-edge areas of cancer disease research. Clinical researchers' observations about the nature and progression of a disease through direct patient care can feed into and drive basic science investigations, where scientists working at the lab bench can then integrate their discoveries in molecular biology back to the clinic. Lovly shared insights into how her clinical oncology practice directly informs her research in understanding and developing improved therapeutic strategies for her patients with lung cancer. The second lecture featured Olufunmilayo I. Olopade, MD, FACP, human genetics



Olufunmilayo I. Olopade, MD



Christine Lovly, MD, PhD

director from the University of Chicago, who treats patients with familial breast cancer. Olopade discussed the goal of retooling precision oncology for equity in cancer care and how genetics and environmental or lifestyle factors, can vary by race or ethnicity and impact breast cancer incidence. For more information, please visit [www.salk.edu/conqueringcancer/benchtobedsidetobench](http://www.salk.edu/conqueringcancer/benchtobedsidetobench).

## New Salk Cancer Researchers



### Christina Towers, PhD

In 2020, the Salk Institute welcomed Assistant Professor Christina Towers, a top researcher in the field of cancer biology. Towers joined Salk's renowned NCI-Designated Cancer Center from the University of Colorado Denver Anschutz Medical Campus to examine how cancer cells recycle both their own nutrients and the power-generating structures called mitochondria in order to survive. Despite being at an early stage of her career, Towers is already the recipient of a number of prestigious awards. The Salk Institute received a matching \$1 million gift from the BioMed Realty Management Team that was used to fund Towers' recruitment and will support her research and that of the Salk Cancer Center. This gift was spearheaded by BioMed Realty's President and CEO, Tim Schoen, who is a Salk trustee and chairman of the Institute's Conquering Cancer Initiative Advisory Committee. For more information about the BioMed Realty Management Match, visit [www.salk.edu/conquering-cancer-initiative](http://www.salk.edu/conquering-cancer-initiative).



### Christian Metallo, PhD

The Salk Institute welcomed Professor Christian Metallo from the University of California San Diego. Metallo received his BS degree from the University of Pennsylvania and his MS and PhD from the University of Wisconsin-Madison. Metallo uses a bioengineering approach to map interconnected metabolic networks to uncover disease-causing pathways that lead to diseases like cancer, obesity and eye diseases. These pathways can be targeted using therapeutic candidates or dietary manipulations to improve health. As a committed educator, Metallo fosters a better understanding of biochemistry and metabolism through his outreach programs, conducting hands-on activities and lectures to teach concepts related to his research aimed at sparking interest in engineering and science among high school students.

*"The Salk Cancer Center aims to push back the boundaries of fundamental understanding of cancer and use that knowledge to develop new therapeutics. By being bold, by being innovative and by being collaborative, we hope to turn the tide against cancer."* **REUBEN SHAW, PhD** Professor and Director of the Salk Cancer Center, William R. Brody Chair



# Excellence in Research



In April 2021, Assistant Professor **Dannielle Engle** was selected as the first recipient of the **Lustgarten Foundation-AACR Career Development Award for Pancreatic Cancer Research in Honor of Ruth Bader Ginsburg**, the late Supreme Court Justice and women's rights pioneer. This award is given to one young researcher nationwide and, as the inaugural awardee, Engle will receive \$300,000 over three years to fund her lab's research into understanding how we can intercept the signals causing pancreatic cancer to metastasize and become so deadly. In October 2020, Engle also received a New Investigator Award from the Tobacco-Related Disease Research Program, which will grant \$1 million over three years to examine how tobacco use promotes cellular changes that lead to pancreatic cancer.

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Assistant Professor **Jesse Dixon** was awarded a **National Cancer Institute** research grant to study the impact of structural variants on 3D genome organization in cancer as part of the NIH Common Fund's 4D Nucleome program in collaboration with Professor Joseph Ecker's lab at Salk.

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Assistant Professor **Edward Stites** was awarded \$500,000 by **The Conrad Prebys Foundation** as part of its inaugural round of grants which will support Stites' project investigating how specific FDA-approved drugs function against three types of melanoma mutations, which drive approximately 80 percent of melanomas. Stites, who is a physician-scientist and the Hearst Foundation Developmental Chair, combines mathematical and computational approaches with experimental cancer biology to identify strategies to convert failed oncology therapeutics into effective agents. He also received a five-year NIH Director's New Innovator Award as part of the NIH High-Risk, High-Reward Research Program for innovative research from early career investigators.

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Professor **Susan Kaech**, director of the NOMIS Center for Immunobiology and Microbial Pathogenesis and holder of the NOMIS Chair, and Professor Alan Saghatelian, holder of the Dr. Frederik Paulsen Chair in the Clayton Foundation Laboratories for Peptide Biology, have been named **2020 Fellows of the American Association for the Advancement of Science (AAAS)**, the world's largest general scientific society and publisher of the journal *Science*.

In August, **Diana Hargreaves** was promoted to the rank of associate professor for her notable contributions in epigenetic regulation, which make specific regions of our DNA accessible to the machinery of cells. Hargreaves, who holds the Richard Heyman and Anne Daigle Endowed Developmental Chair, was awarded the **Pew-Stewart Scholar for Cancer Research** in 2019 and the **American Cancer Society Research Scholar Award** in 2020 to support her work on a better understanding of the causes, diagnosis and treatment of cancer.

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Professor **Reuben Shaw**, director of Salk's Cancer Center, showed that proteins in familial Parkinson's disease are controlled by cancer-fighting enzymes that are disrupted in lung cancer. This new work detailed in April 2021 suggests that metformin (a common type 2 diabetes drug that can suppress cancer), may also help restore function in patients with neurodegenerative disease. This study illustrates a common genetic and biochemical pathway in the body that helps fight cancer, diabetes and neurodegenerative diseases.

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Professor **Ronald Evans**, director of the Salk Institute's Gene Expression Laboratory and March of Dimes Chair in Molecular and Developmental Biology, was awarded the **2021 Asan Award in Basic Medicine by the Asan Foundation**. The award, which totals \$250,000, recognizes "medical scientists who have achieved remarkable accomplishments in the fields of basic and clinical medicine to promote human health," according to the Asan Foundation. Evans is the first international recipient of the Asan Award in Basic Medicine.

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In November 2020, three Salk Cancer Center professors (**Joseph Ecker**, **Rusty Gage** and **Reuben Shaw**) made the prestigious list of **"Most Influential Scientific Minds"** due to their cumulative life publications being in the top 1 percent by citations by Clarivate Analytics in the past year. Citations are a formal reference to a previous publication that have a bearing on the subject of the new publication; so this accolade is taken as a metric of how influential a scientist's body of work is on impacting and extending the frontiers of knowledge in their field(s).

## Impact of Vitamin D on Pancreatic Cancer

Pancreatic cancer is the third-leading cause of cancer-related deaths in the United States and carries one of the worst prognoses of any cancer. Despite clinical efforts, five-year survival rates have barely improved over the last three decades and currently hover around eight percent. The only treatment with curative potential is surgical resection; however, this is not an option for the majority of patients who present with metastatic disease at the time of diagnosis.

Therapeutic resistance in pancreatic cancer is thought to be due to an extensive tumor-associated cellular support network (or “stroma”), comprising large numbers of aberrantly activated fibroblasts and immune cells. This stromal network acts as both a physical barrier that prevents the effective delivery of drugs and an

immunological barrier that limits the actions of many therapeutics, including chemotherapies and immune checkpoint inhibitors.

The work from Ronald Evans’ lab assessed how stromal remodeling therapies, including VDR (vitamin D receptor) agonists and super-enhancer targeting BET inhibitors, impact these immune cell populations in regard to both their frequency and function with pancreatic tumors. The Evans lab has begun to test the ability of stromal remodeling therapies to sensitize pancreatic tumors to otherwise ineffective immunotherapies, such as immune checkpoint inhibitors. During the past year, Evans and other scientists have made significant progress towards the goals of comprehensively describing the immune environment in pancreatic cancer and exploring how stromal remodeling therapies can be employed to harness the immune system for curing this disease. The therapies are currently being tested in clinical trials.

### Science with Soul

After receiving the devastating diagnosis of pancreatic cancer last December, Sarah Crossley, together with her husband Stephen (both based in the U.K.), contacted the Salk Institute to learn more about the pancreatic cancer research program. Stephen had searched across the globe for the latest treatments before learning about Professor Ronald Evans and his current studies in a vitamin D treatment. Sarah has had a long career with the Wiley Publishing Company and their Women in Leadership and Women in Technology groups, of which Sarah is a member. She selected Salk for their fall fundraising effort, engaging their global employee base as well as matching donations dollar for dollar to support pancreatic cancer research at Salk.



Above: Sarah and Stephen Crossley with their three daughters.

*“Dr. Evans epitomizes someone who has ‘science with soul’ with his dedication and passion for helping patients with pancreatic cancer.”*

**STEPHEN CROSSLEY**

# What Does It Mean to Be an NCI Cancer Center?

The National Cancer Institute (NCI) is the federal government's primary agency for cancer research and training and is the largest funder of cancer research in the world. Through its Cancer Centers Program, which is responsible for accrediting high performance cancer centers, the NCI provides grant funding to select cancer centers throughout the country. The NCI is the only extramural funding program of the National Institutes of Health that still includes on-site reviews of applicants. An official cancer center designation by the NCI is the highest federal rating a cancer center can achieve. This is bestowed upon the nation's top cancer centers in recognition of their innovative research and leading-edge treatments and is the gold standard for cancer programs.

When the NCI was formed, the Salk Institute was the second-designated cancer center and has held the designation continuously since 1972. Every five years, the Salk Cancer Center undergoes a rigorous and intensive evaluation of our research programs and related activities, such as community outreach and education efforts.

There are currently 71 NCI-Designated Cancer Centers (most are affiliated with university medical centers) that interconnect the NCI's initiatives for studying and preventing cancer. Seven, including the Salk Cancer Center, are Basic Laboratory Cancer Centers that are primarily focused on laboratory research and often conduct preclinical translation while working collaboratively with other institutions to apply these laboratory findings to new and better treatments. For more information about NCI-Designated cancer centers, please visit [www.cancer.gov/about-nci](http://www.cancer.gov/about-nci).

## Translation Fund

Last year, the Salk Cancer Center launched a Translation Fund Award Program, managed by the Office of Technology Development (OTD). The award supports translational research for innovations with the potential to have a meaningful clinical impact for cancer patients. The goal of the Salk Translation Fund is to build a translational culture at Salk, bolster patentable discoveries into de-risked, valuable assets that will be partnered with industry for further translation, and foster Salk's continued success of driving discoveries to benefit the public good. Particular focus is on the development of new therapies (medications, nutrition, behavioral interventions, etc.) or diagnostics, and new approaches to prevention or translation of knowledge.

## 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.

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

To support the program, please contact Lisa Cashman, Director, External Relations at [lcashman@salk.edu](mailto:lcashman@salk.edu) or **(858) 453-4100 x1227 | [WWW.SALK.EDU/GIVE-TO-CANCER](http://WWW.SALK.EDU/GIVE-TO-CANCER)**



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**For ten consecutive times, 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.

[WWW.SALK.EDU/CONQUERINGCANCER](http://WWW.SALK.EDU/CONQUERINGCANCER)