

Driven by Science Powered by Hope

2022 ANNUAL REPORT

BREAKTHROUGHCANCER.ORG

	03
LETTER FROM THE PRESIDENT	04
BOARD OF DIRECTORS	05
SCIENTIFIC ADVISORY BOARD	07
	09
GLIOBLASTOMA	10
OVARIAN CANCER	11
PANCREATIC CANCER	12
DATA SCIENCE HUB	13
BREAK THROUGH CANCER SCIENTISTS	15
	17
DAVID M. LIVINGSTON COLLABORATION AWARD	17
EVENTS	18
LEADERSHIP	19
PHILANTHROPY AND PARTNERSHIP	20
	21



Break *Through* Cancer **empowers outstanding researchers** and physicians to both intercept and find cures for the **deadliest cancers** by stimulating **radical collaboration**.

In 2022, our first full year of operation, we got right to work–developing and underwriting a series of ambitious projects that tackle some of the biggest challenges in cancer care by surmounting longstanding barriers to deep and broad collaboration.

Those projects leverage the capacities of scientific investigators and clinicians at five world-class cancer research organizations: Dana-Farber Cancer Institute, the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, The University of Texas M.D. Anderson Cancer Center, Memorial Sloan Kettering Cancer Center, and the Koch Institute for Integrative Cancer Research at Massachusetts Institute of Technology (MIT).

Read on to learn about Break *Through* Cancer's radical vision, the people pursuing that vision, and the important steps we took in 2022 toward making it a reality.





LETTER FROM THE PRESIDENT



Tyler Jacks, PhD President, Break *Through* Cancer

The Science Begins

If 2021 was the year that Break *Through* Cancer stood up, then 2022 was year it strode forward, boldly. We built an expansive and impressive community of leading cancer researchers and physicians, and empowered them to work as integrated teams.

In April 2022, we announced our first grants: \$50 million to support high-risk, high-reward projects that unite scientists and clinicians from five of the nation's most accomplished cancer research institutions. Those projects have been developed through a novel, collaborative process that identifies potentially transformative ideas, fine-tunes project strategies and research teams, and strives to ensure that the resulting outcomes will benefit the broadest possible range of patients.

We chose to initially focus on intractable cancers: glioblastoma, ovarian cancer, and pancreatic cancer. These diseases share a key characteristic: while each has an unacceptably low survival rate, scientists have identified paths toward break through interventions—if researchers can remove the practical hurdles in their way.

Each member of our project TeamLabs is dedicated to accelerating the pace of discovery and translating those discoveries into new, effective ways to diagnose and treat cancer. Indeed, we believe our model of collaborative science will increasingly enable clinicians and to replace the words "diagnose" and "treat" with "prevent" and "cure."

I encourage you to delve deeply into this Annual Report, learn about our innovative projects and pioneering strategies, and meet some of the extraordinary people who comprise the Break *Through* Cancer community.



BOARD OF DIRECTORS

The Break Through Cancer model leverages the strengths of scientists and clinicians working at the nation's leading cancer research and clinical care organizations. The Board of Directors, comprised of leaders from each of our institutional partners, reflects these organizations' deep commitment to the foundation's vision of radical collaboration and swifter innovation.

Together, we are aiming to transform the way cancer research is done-working to bring every scientific tool and every bright mind to bear in order to prevent, diagnose, and cure some of the deadliest cancers. We believe, passionately, that Break Through Cancer is going to have enormous impact."

William G. Nelson, MD, PhD

Chairman of the Board, Break Through Cancer & Director, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Not only does Break Through Cancer draw together the best scientists and research technologies, it nurtures a collaborative ethos where getting credit-institutionally or individually -for scientific or clinical advances is beside the point. The only thing that matters is whether our patients benefit from those advances."

Laurie Glimcher, MD

President and CEO, Dana-Farber Cancer Institute







Giulio F. Draetta, MD, PhD The University of Texas MD Anderson Cancer Center



Laurie Glimcher, MD Dana-Farber Cancer Institute



Alice Goodwin Commonwealth Foundation for Cancer Research



Elizabeth M. Jaffee, MD, FAACR, FACP

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

David Jaffray, PhD The University of Texas MD Anderson Cancer Center



William G. (Bill) Nelson, V, MD, PhD

Chairman of the Board, Break Through Cancer, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins



William H. Goodwin, Jr Commonwealth Foundation for Cancer Research



David A. Scheinberg, MD, PhD

Memorial Sloan Kettering Cancer Center



William C. Hahn, MD, PhD Dana-Farber Cancer Institute



John Sherman Commonwealth Foundation for Cancer Research



Susan Hockfield, PhD Massachusetts Institute of Technology



Lisa M. DeAngelis, MD Memorial Sloan Kettering

Cancer Center



Tyler Jacks, PhD President, Break Through Cancer, MIT's Koch Institute for Integrative Cancer Research



Matt Vander Heiden, MD, PhD MIT's Koch Institute for Integrative Cancer Research



Break *Through* Cancer's Scientific Advisory Board (SAB) is comprised of distinguished cancer researchers and clinicians affiliated with seven leading academic medical centers. Its members engage in shaping research proposals into honed project plans that are ambitious, feasible, and designed to have broad impact. The SAB remains involved throughout the year, providing feedback and support across the TeamLabs. In addition, the SAB helps shape the composition of each TeamLab, ensuring the correct balance of expertise, perspective, and experience necessary to achieve the project's goals.





"

Just as Break *Through* Cancer has a unique research model, it has a uniquely engaged group of scientific advisors. Each of us is deeply involved in developing projects that are impactful—and in building research teams with the full range of knowledge and tools needed to succeed."

Miriam Merad, MD, PhD

Mount Sinai Endowed Professor in Cancer Immunology, Mount Sinai School of Medicine





Cory Abate-Shen, PhD

Chair, Department of Molecular Pharmacology and Therapeutics, Vagelos College of Physicians and Surgeons, Columbia University



John D. Carpten, PhD Chair, Translational Genomics; Director, Institute of Translational Genomics, Keck School of Medicine, University of Southern California



Timothy Cloughesy, MD Director, Neuro-Oncology Program; Director, Henry Singleton Brain Cancer Research Program, University of California, Los Angeles



Benjamin Haibe-Kains, PhD Senior Scientist, Princess Margaret Cancer Centre, University Health Network; Associate Professor, Department of Medical Biophysics, University of Toronto





Director, Precision Immunology Institute; Director, Mount Sinai Human Immune Monitoring Center, Icahn School of Medicine, Mount Sinai

Dinah Singer, PhD Bethesda, Maryland



Louis M. Staudt, MD, PhD Bethesda, Maryland



Alejandro Sweet-Cordero, MD

Director, Molecular Oncology Initiative, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco



Patricia LoRusso, DO

Associate Cancer Center Director, Experimental Therapeutics, Yale Cancer Center



Frank McCormick, PhD, FRS, DSc (Hon)

Professor, Helen Diller Family Comprehensive Cancer Center; Department of Cellular and Molecular Pharmacology, University of California, San Francisco



E. John Wherry, PhD

Chair, Department of Systems Pharmacology and Translational Therapeutics; Director, Institute for Immunology, Perelman School of Medicine, University of Pennsylvania



Break *Through* Cancer seeks to dramatically accelerate the process of bringing novel and effective treatments to cancer patients, thus saving lives. To achieve that goal, our projects operate in a fundamentally new way. We create TeamLabs–carefully selected teams of scientists, engineers, clinicians, data scientists, and public health professionals from disparate domains. And, instead of standard "divide and conquer" cancer research approaches, TeamLabs work in a highly collaborative and integrated way, prioritizing impact and urgency.

Break *Through* Cancer has committed more than \$50 million to an initial series of projects on four deadly cancer types: glioblastoma, ovarian cancer, pancreatic cancer, and acute myelogenous leukemia. Following are summaries of the projects we launched in 2022.



"

Clinicians, surgeons, engineers, and scientists are coming together in a really intense, focused way with the single goal of making an impact on a particular kind of cancer. I mean, who wouldn't want to be involved in that?

Angela Belcher, PhD MIT's Koch Institute for Integrative Cancer Research



Glioblastoma



"Every time I see a patient and I have to break the news to them, it just gives you a perspective of what we are doing, why are we doing it, and the urgency of the situation."



Sangeeta Goswami, MD, PhD

The University of Texas MD Anderson Cancer Center

TeamLab: Revolutionizing GBM Drug Development Through Serial Biopsies The five-year survival rate for patients with glioblastoma is below 10%. No treatments approved in recent decades have changed that harsh reality–nor have recent major clinical trials.

Revolutionizing Glioblastoma (GBM) Drug Development Through Serial Biopsies

We believe the lack of progress in developing new GBM treatments is due, in part, to the application of traditional clinical trial protocols to brain cancer. Thus, this TeamLab is creating a novel platform for GBM clinical trials.

First, they are making it much easier for patients to participate in early testing of new treatments in the brain. Second, they are taking a series of samples of patients' tumors, blood, and spinal fluid-both before and after treatment-and using cutting-edge techniques to track the drugs' effects in real-time, thus allowing the clinical trial to yield the most information possible.

This platform holds real potential for driving the kinds of breakthroughs that have transformed treatment of other cancers.



Ovarian Cancer

"The words that come to mind are urgency and acceleration. We're trying to move faster. It's not business as usual. And that's what I love about it."



Karen Lu, MD The University of Texas MD Anderson Cancer Center

TeamLabs: Targeting Minimal Residual Disease in Ovarian Cancer and Intercepting Ovarian Cancer Ovarian cancer is the deadliest gynecologic malignancy, primarily because it is often not diagnosed until it has spread to other organs. And even after seemingly successful treatment, the cancer often recurs.

Intercepting Ovarian Cancer

Recent studies show that ovarian cancer often originates as pre-cancerous lesions in the fallopian tubes—and we believe that women who undergo preventive fallopian tube removal have significantly reduced risk of developing ovarian cancer later in life. This simple preventive procedure, called "bilateral salpingectomy," is frequently covered by insurance and has minimal known side effects. The Intercepting Ovarian Cancer TeamLab is developing a national strategy to ensure access to this preventive procedure for women who choose it. The effort will also spur development of more effective methods for diagnosing precancerous fallopian tube lesions.

Targeting Minimal Residual Disease in Ovarian Cancer

While initial treatments often lead to dramatic responses with few or no tumor cells detectable, ovarian cancer often recurs because of a small number of malignant cells resistant to those treatments. This "minimal residual disease" fuels the cancer's recurrence and spread. This TeamLab is working to identify and exploit the vulnerabilities of the residual cancer cells. Then it will test novel therapies—such as nanoparticle-based targeting strategies—to strike those weak points. The ultimate goal is frontline treatment strategies that leave no cancer cells alive.



Pancreatic Cancer



"This is completely changing the landscape of how we do cancer research, because, in some respects, institutions and disciplines don't matter as long as you're focused on the hardest questions in cancer."



Anirban Maitra, MBBS

The University of Texas MD Anderson Cancer Center

TeamLabs: Conquering KRAS in Pancreatic Cancer and Demystifying Pancreatic Cancer Therapies In the U.S., pancreatic cancer kills 50,000 people annually, most within one year of diagnosis. And 90% of patients with pancreatic cancer die within five years.

Conquering KRAS in Pancreatic Cancer

Scientists believe that the KRAS growth-promoting gene is pancreatic cancer's Achilles' heel: block the gene's function, block tumor growth. New KRAS-targeting cancer therapies are starting to become available-but, to date, clinical development has focused on lung and colon cancer.

Now, this TeamLab is working quickly and collaboratively– bridging disciplines, institutions, and sectors–to test a range of KRAS inhibitors for pancreatic cancer, evaluating those drugs both individually and in combination with other therapies.

Demystifying Pancreatic Cancer Therapies

Evidence suggests that the interactions among a variety of cells in a pancreatic tumor's microenvironment help malignant cells survive current treatments. Thus, it is critically important to understand how treatments change the microenvironment. This TeamLab is deploying cutting-edge molecular analytical tools to analyze tumor samples from patients undergoing therapy. This work will provide an unprecedented view into the effects of therapies on the tumor microenvironment, and enable researchers to fine-tune new treatments and drug combinations.



The Data Science Hub

Computational advances have now made it possible to perform comprehensive molecular, immunological, and genetic analysis on nearly any patient's tumor. But such data typically stays within the purview of an individual lab or research institution, resulting in redundancy and missed opportunities.

Break *Through* Cancer's Data Science Hub represents a new approach to data collaboration: unifying large-scale cancer data collection and machine learning by creating a dedicated, state-of-the-art platform. That platform will maximize data sharing and the discovery potential of data generated across Break *Through* Cancer's research portfolio.





"

By bringing data scientists together across all the disease teams, we have a rare opportunity to work and innovate together. And it builds such a community that we have a chance to get to the best advances and best technologies."

Elana Fertig, PhD

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

TeamLabs: The Data Science Hub, Conquering KRAS in Pancreatic Cancer and Demystifying Pancreatic Cancer Therapies





The Data Science Hub team is comprised of 20 world-class leaders who collectively possess deep expertise in creating largescale data infrastructures, developing computational algorithms and methods, and deploying software tools and databases on a global scale.

These data science experts are bringing together the domains of cancer data science, data governance, and data infrastructure to create data solutions that are readily accessible to laboratory scientists and clinicians. By doing so, they are accelerating the pace of discovery.



Break Through Cancer Scientists

Break *Through* Cancer's strategy centers on TeamLabs, comprised of clinical and research faculty at our partner institutions. But our complex projects demand an additional professional resource: a cadre of scientists and engineers whose skills, knowledge, and insights enable them to serve as cross-institutional catalysts for scientific innovation and collaboration.

That's why, in 2022, we appointed our first cohort of Break *Through* Cancer Scientists: a carefully selected group of researchers who possess phenomenal expertise in early diagnostics, single-cell genomics data and materials science, and specific types of cancer. Embedded at our partner institutions and working hand-in-hand with the faculty labs we fund, each of them possesses a stellar reputation, a robust track record of community building and collaboration, and a passion for advancing knowledge in our focal areas of cancer research. We are pleased to introduce them here:



Neelkanth Bardhan, PhD

Based at MIT's Koch Institute for Integrative Cancer Research, Bardhan works with the <u>Intercepting Ovarian Cancer</u> TeamLab, helping design an optical imaging system for highly sensitive detection of early precursor lesions in ovarian cancer. A scientific innovator, his previous research led to three issued U.S. patents and numerous pending patent applications. "This role enables me to use my engineering skills to help design real-world approaches for intercepting ovarian cancer early in its development," says Bardhan. "It also positions me to help forge cross-cutting collaborations that would have been very difficult to achieve in a traditional, siloed research structure."



Sreyashi Basu, PhD

A Research Group Leader at MD Anderson Cancer Center's Immunotherapy Platform, Basu is a member of the <u>Revolutionizing GBM Drug Development</u>. <u>Through Serial Biopsies</u> TeamLab. Currently focusing on immunogenomic profiling as a way to identify immune cell changes in response to therapy and predictive biomarkers of therapeutic benefit, her group previously identified CD73+ immunosuppressive myeloid cells as a resistance mechanism to immune checkpoint therapy in GBM. "This role provides an exciting opportunity to be part of collaborative science across highly acclaimed institutions," says Basu. "I believe that the scientific relationships I am building will help drive success in our TeamLab project and contribute meaningfully toward Break *Through* Cancer's overall mission."





Paola A. Guerrero, PhD

A Research Group Leader at MD Anderson Cancer Center's Pancreatic Cancer Research Center, Guerrero conducts innovative research on patientderived models and biospecimens. Now working with the <u>Conquering</u>. <u>KRAS in Pancreatic Cancer</u> and Demystifying Pancreatic Cancer Therapies TeamLabs, she previously showed that limited biopsies can capture a full range of key cell types, and she identified mechanisms that may enable immune evasion in the tumor microenvironment. "This appointment enables me able to play a leading role in advancing initiatives that can benefit multiple Break *Through* Cancer projects," says Guerrero. "At the same time, it offers an exceptional learning experience: facilitating and engaging with research by an interdisciplinary group of investigators who are working in multiple labs across several institutions."



Thomas R. Pisanic II, PhD

An Associate Research Professor at the Institute for NanoBioTechnology and the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Pisanic has two decades' experience developing new clinical diagnostic approaches, including molecular diagnostic assays for early, noninvasive detection of cancer. Now engaged with the <u>Intercepting Ovarian Cancer</u> TeamLab, he is applying his background in cancer epigenetics to explore how epigenetic alterations contribute to the progression of precursor lesions of the fallopian tube. "This role provides an unprecedented opportunity to work together with the top clinicians, scientists, and engineers in the country, employing a true 'team-based' approach to developing solutions that could dramatically improve the lives of those affected by cancer," says Pisanic. "In addition, the uniquely open Break *Through* Cancer environment will enable me to apply my research tools and expertise to exciting new avenues in translational cancer research."

David M. Livingston Collaboration Award



Our community of people is committed to collaboration and teamwork. In October 2022, we created the David M. Livingston Collaboration Award to recognize individuals whose efforts on behalf of Break *Through* Cancer demonstrate that commitment in an impactful way.

The award was established to honor an extraordinary scientist, caregiver, leader, and friend, David Livingston, who died unexpectedly in 2021. A renowned physician and cancer researcher, Livingston served as Deputy Director of the Dana-Farber/Harvard Cancer Center and the Emil Frei Professor of Genetics and Medicine at Harvard Medical School. His fervent belief in collaboration and teamwork was inspiring, and he was instrumental in helping to conceptualize Break *Through* Cancer's goals and research model. An enduring recognition of his personal and professional legacy– and of his contributions to our foundation–the David M. Livingston Collaboration Award will be given annually to members of our community who are exemplary in pursuing the concept of teamwork that David embodied.

The inaugural award was bestowed upon two individuals who showed remarkable skill and commitment in leading the planning team that developed our Revolutionizing Glioblastoma Drug Development project: **Nathalie Y.R. Agar, PhD**, the Daniel E. Ponton Distinguished Chair in Neurosurgery at Brigham and Women's Hospital and Associate Professor of Neurosurgery and Radiology at Harvard Medical School; and **Michael J. Cima, PhD**, the David H. Koch Professor of Engineering and Professor of Materials Science and Engineering at the Massachusetts Institute of Technology. Their leadership of a long and challenging collaborative decision-making process has been critical to the development of a pioneering project and an extraordinary TeamLab.



Events







From top left clockwise: Staff at 2022 Annual Summit; Summit attendees in Kiawah, South Carolina; Tyler Jacks offering remarks at 2022 Summit; Board of Directors meeting at the Foundry

Leadership



Tyler Jacks, PhD President



Jesse Boehm, PhD Chief Science Officer



Bill Hulme Chief Financial Officer



Michael Noble Chief Data Officer



Kari McHugh Chief Communications Officer



Lisa Schwarz Chief Operating Officer and Chief Philanthropy Officer



Profile of a Philanthropic Partner: The Lustgarten Foundation

"We all share the goal of wanting our science to make a difference in our patients."

David Tuveson, MD, PhD Chief Scientist, The Lustgarten Foundation



From left to right: Tyler Jacks, President of Break *Through* Cancer, Linda Tantawi, CEO of the Lustgarten Foundation; Andrew Rakeman, Vice President of Research, the Lustgarten Foundation

Since its founding in 1998, the Lustgarten Foundation has funded more than \$280 million in research grants and been a leading force in every major advancement in pancreatic cancer research. As the largest private funder of the world's preeminent pancreatic cancer researchers, Lustgarten is driving the pursuit of bold and innovative science toward earlier detection and better treatments.

In 2022, the Lustgarten Foundation and Break *Through* Cancer partnered to maximize interdisciplinary collaboration among scientists in pancreatic cancer research. The Lustgarten Foundation has invested in two TeamLab projects, Conquering KRAS in Pancreatic Cancer and Demystifying Pancreatic Cancer Therapies, bringing teams of researchers from five of the nation's top cancer research centers to boldly tackle two of the biggest challenges in pancreatic cancer care.

The organizations share a common goal-to transform pancreatic cancer into a curable disease.



Break Through Cancer Financials







BREAKTHROUGHCANCER.ORG

