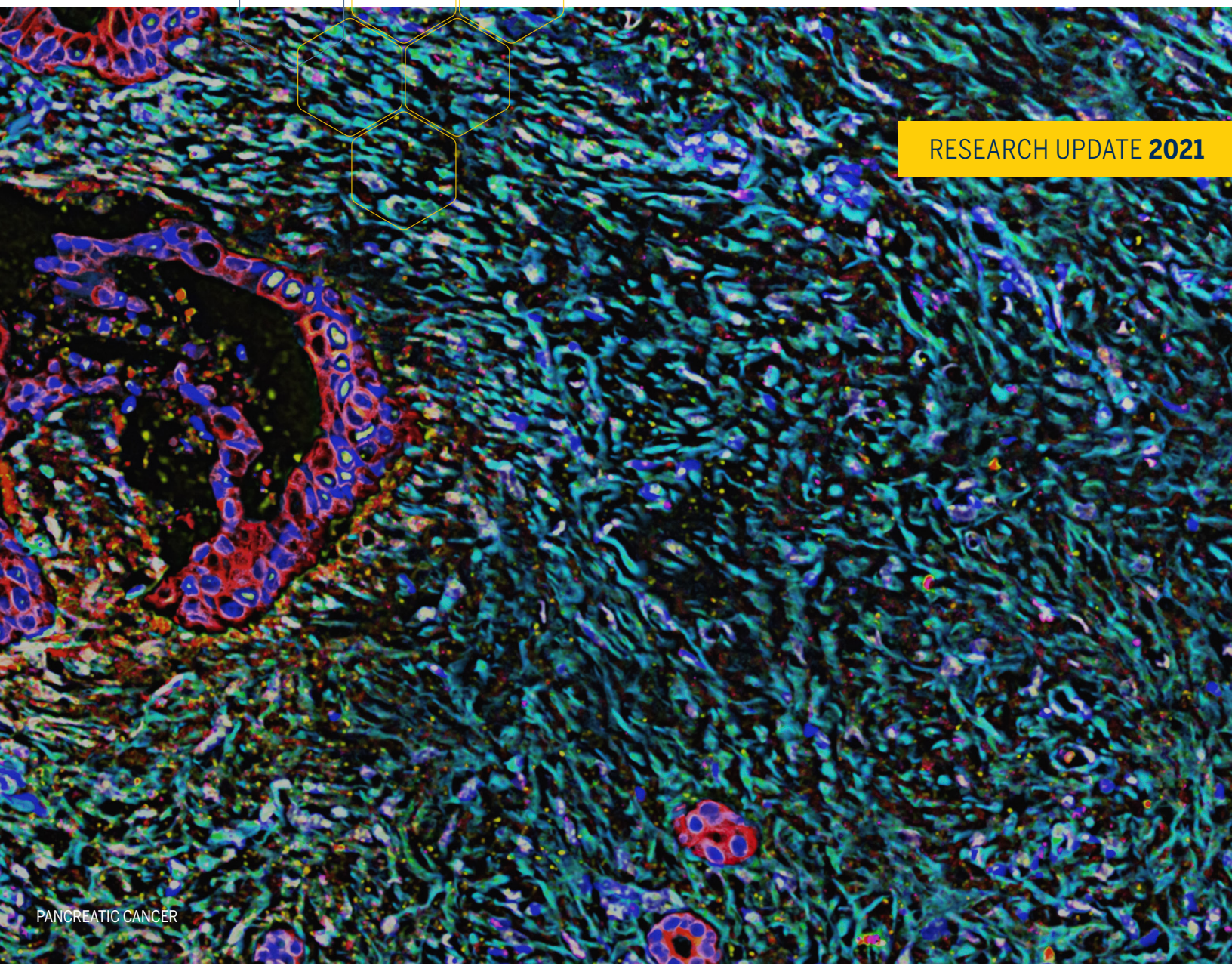
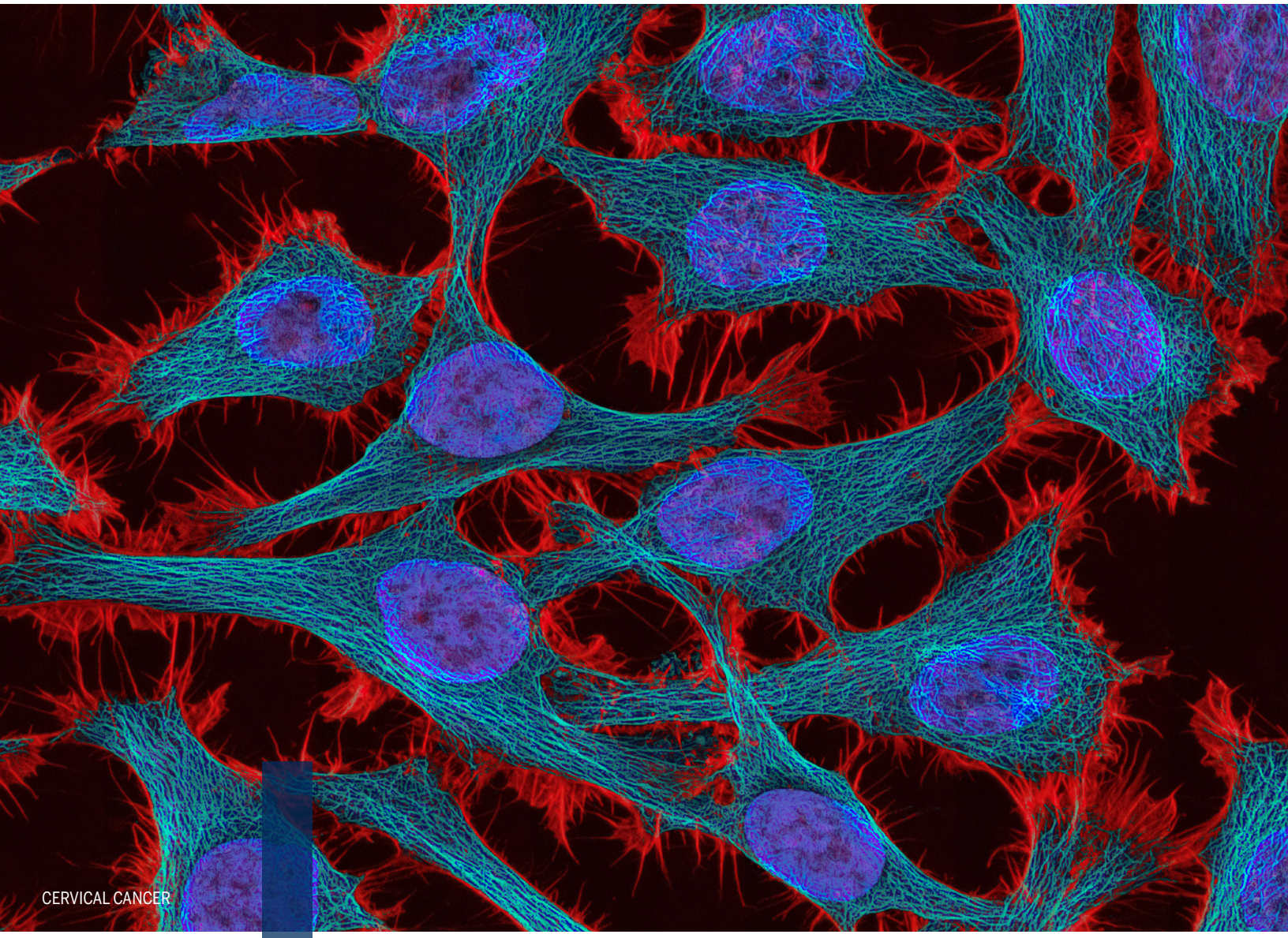
Advancing Cancer Research Toward New Treatments

RESEARCH UPDATE **2021**



PANCREATIC CANCER

FORBES INSTITUTE FOR CANCER DISCOVERY
MICHIGAN MEDICINE



CERVICAL CANCER

"The road to high-risk, high-reward cancer discovery is arduous. It has become our mission, our passion, and our social responsibility. The Forbes family has devoted our time and our philanthropy, investing in a very talented team at the University of Michigan. The Forbes Institute for Cancer Discovery is about hope. It is about promise. And it is about human dignity. We invite everyone to join us as we pursue this mission and work hard to solve these very complex issues." —NATHAN FORBES

Fueling Collaboration to Improve Care for Cancer Patients

Dear Friends:

It is an honor and privilege to serve as the director of the Forbes Institute for Cancer Discovery. One of the great things about our work is that we leverage tremendous talent from across the University of Michigan. Some of our major contributions have resulted from interactions between different schools, as you will see in the stories highlighted in this publication.

At the Forbes Institute, we give grants to projects that involve teams from across disciplines that have the greatest potential to directly impact patients. We have had many successes, and we look forward to exciting things to come.

As we share the progress made by Forbes Scholars in 2021, we also are embarking on the selection process for our 2022 grants. Grants, which are fully funded by philanthropy, are typically $250,000 for one year, and they may be renewed based on progress and potential impact.

Our call for proposals asked for innovative team science projects that emphasize efforts to translate new discoveries and approaches toward clinical applications. We especially encourage high-risk, high-potential proposals that might be too risky or too preliminary to garner support from the National Institutes of Health at this time.

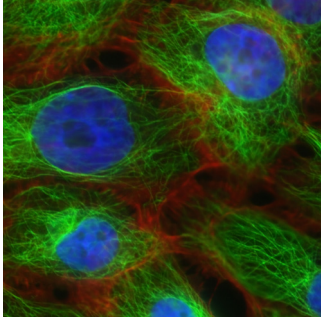
Each proposal is currently going through a competitive peer review process and is being evaluated on:

- Innovation
- Potential impact
- Translational potential
- Transdisciplinary teams, leveraging strengths across U-M
- Milestones and metrics for success
- Sustainability and likelihood for future funding

We will share news of our next group of Forbes Scholars in the months ahead. We appreciate your interest in and support of the Forbes Institute, which is driving the cancer care of the future.

With gratitude and warm regards,

Max S. Wicha, M.D.
Madeline and Sidney Forbes Professor of Oncology
Director, Forbes Institute for Cancer Discovery
Founding Director Emeritus, Rogel Cancer Center



Discovery, Dedication, and Early Detection

A project aimed at saving the lives of breast cancer patients

Justin Colacino, Ph.D.

Sunitha Nagrath, Ph.D.

In 2018, **Justin Colacino, Ph.D.**, the John G. Searle Assistant Professor of Environmental Health Sciences in the School of Public Health, assembled a team of physicians, scientists, and engineers to pursue an ambitious goal: identifying breast cancer cells that are circulating in the blood to develop new targets for breast cancer prevention, diagnosis, and treatment.

"If you can analyze the cancer cells that are present in the blood, instead of relying on invasive biopsies, we can understand the characteristics of the primary tumor and much more," says **Sunitha Nagrath, Ph.D.**, a professor of chemical engineering and a key contributor to the project.

The team has focused on identifying cancer cells in the blood of patients with ductal carcinoma in situ, or DCIS, which is an early-stage cancer that is present in the lining of milk ducts but has not spread to surrounding tissue.

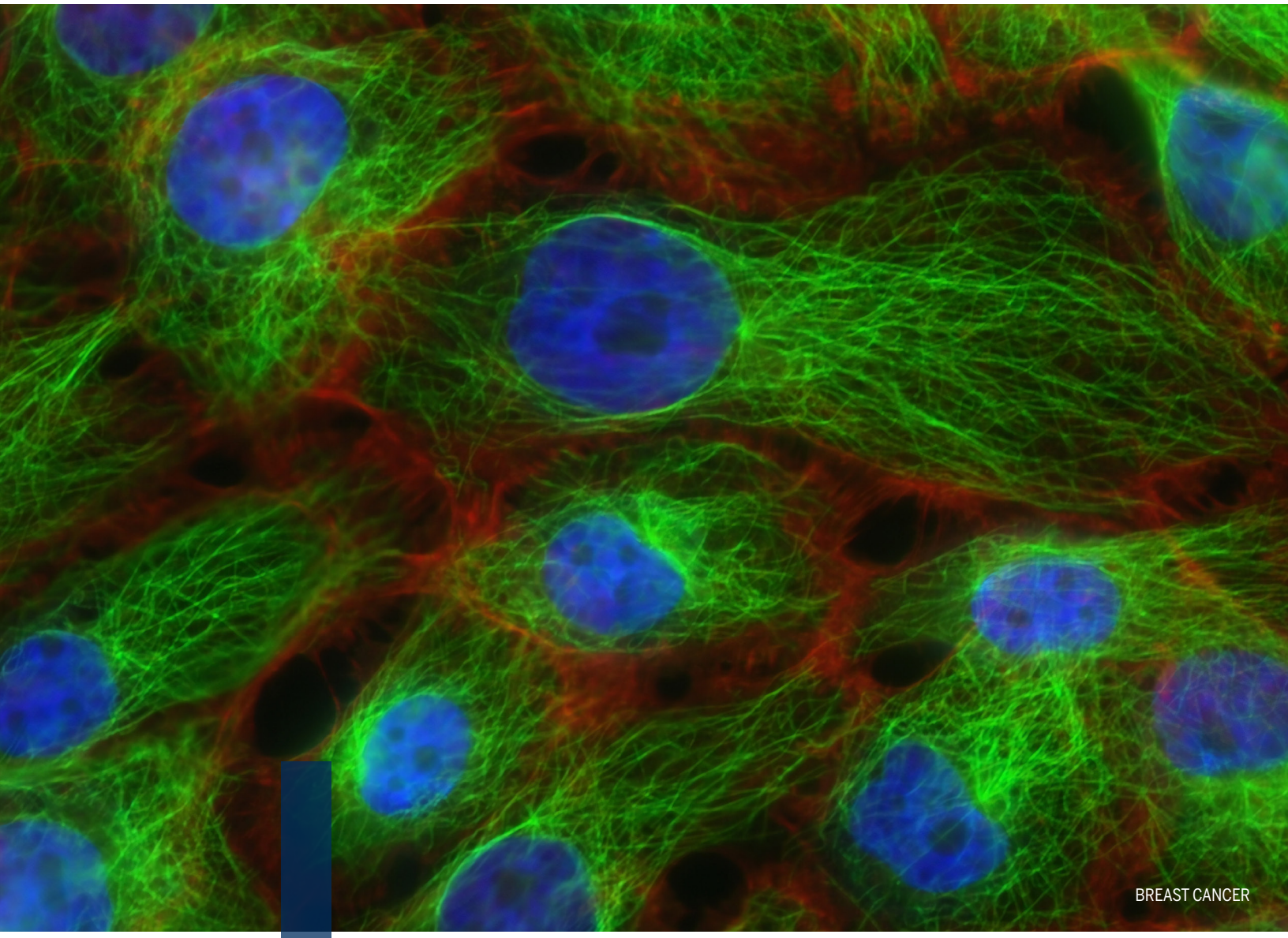
"With generous support from the Forbes Institute, our lab has been able to develop an approach for isolating, capturing, and analyzing the very early disseminated cells from pre-invasive breast cancer," Dr. Nagrath says.

In 2021, the team analyzed the blood of patients with confirmed DCIS and found cancer cells in 50% of samples. "It is very exciting," she says. "We hypothesize that the detection of the cells indicates that patients are at risk for eventual metastasis if we do not intervene."

Today, Drs. Colacino and Nagrath are partnering with colleagues at the Rogel Cancer Center, the University of California San Francisco, the University of Kansas, and the Baylor College of Medicine to construct a large, collaborative, multicenter study. "Our proposal is focused on developing new methods of identifying women who are most at risk of dying from breast cancer following a diagnosis at the earliest stages of the disease," says Dr. Colacino.

"This ends up being a really important health disparities issue, because we know that, in particular, African-American women who are young and diagnosed with this early-stage breast cancer are at much, much higher risk of dying from breast cancer eventually," he says. "But we don't know why, and we don't have a good method to identify them."

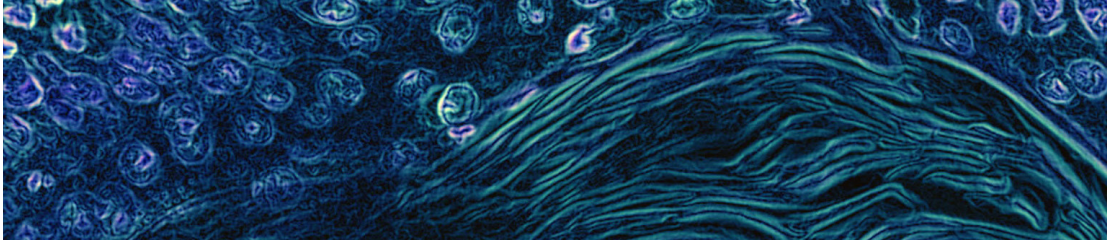
This project may change that, says Dr. Nagrath, who is characterizing the molecular makeup of the cancer cells she captures from the blood. "I strongly believe that a simple blood test can provide a biomarker that tells us who is at risk for more advance cancer, which can save lives. In the age of precision medicine, it is important that we develop state-of-the-art tools to predict cancer recurrence, closely monitor for recurrence, and prevent lethal metastasis."



BREAST CANCER

This project combines expertise from the U-M the College of Engineering and the School of Public Health. It enables us to study pre-invasive breast cancer cells that might be circulating throughout the body and gives us a glimpse of how we might be able to develop new cancer prevention and diagnosis approaches. It embodies what the Forbes Institute is all about.

— ERIC R. FEARON, M.D., PH.D.
Emanuel N. Maisel Professor of Oncology
Director, University of Michigan Rogel Cancer Center



Research Progress and Scholars Update

From Idea to Clinical Trial: Targeting Treatment Resistance in Brain Cancer

Daniel Wahl, M.D., Ph.D.

Forbes Scholar **Daniel Wahl, M.D., Ph.D.**, was among six recipients nationwide of the 2021 Damon Runyon Clinical Investigator Award, which recognizes outstanding early-career physician-scientists working to develop new cancer therapies. An assistant professor of radiation oncology who specializes in treating brain cancer, his research focuses on developing new therapies to overcome treatment resistance in aggressive forms of the disease.

Dr. Wahl's grant from the Forbes Institute is giving brain cancer patients a new option for care. "I was very fortunate to receive research support from the Forbes Institute early in my faculty career," Dr. Wahl says. "We had an idea that small molecules inside the cell called metabolites, things like amino acids or sugars, made brain tumors resistant to radiation and chemotherapy. The Forbes Institute invested in these ideas, and over the last couple of years we have spent a lot of time and effort understanding these links. We have opened a clinical trial for aggressive brain tumors, where we are trying to block these metabolic pathways to make our treatments work better."

Lonnie Shea, Ph.D.

An Inside Job: Studies Show Increasing Promise of Implantable Device

Jacqueline S. Jeruss, M.D., Ph.D.

Lonnie Shea, Ph.D., and **Jacqueline S. Jeruss, M.D., Ph.D.**, were in our first class of Forbes Scholars, winning foundational support to advance an implantable device designed to capture cancer cells attempting to spread from an original tumor. The idea was to detect metastasis as early as possible.

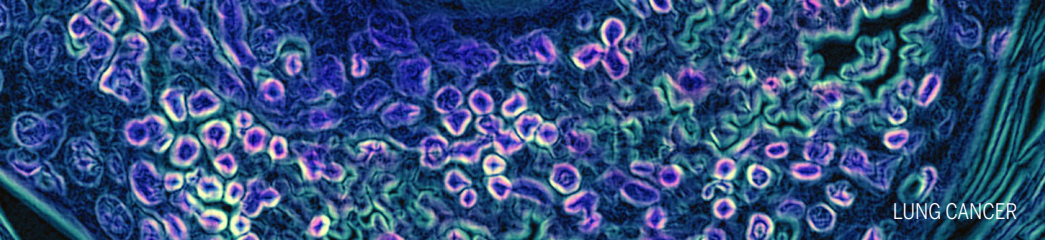
Along with a large team of collaborators, Drs. Shea and Jeruss have made significant progress. In 2021, they published research demonstrating that implantable biomaterial scaffolds could attract pancreatic cancer cells in laboratory models. The scaffolds also enabled researchers to determine whether the attracted cancer cells were of an early-disease form or a late-disease form.

Clifford Cho, M.D.

The scaffolds have shown promise for breast cancer as well. In laboratory models, the scaffolds have been able to recruit metastatic cancer breast cells, while researchers used spectral ultrasound imaging as a non-invasive strategy for detecting and analyzing cells in the scaffolds.

Collectively, the findings suggest that we will be able to capture metastatic tumor cells in the implantable scaffolds and determine the stage of the metastasis, transforming our ability to identify the early spread of cancer.

Dr. Jeruss is associate dean for regulatory affairs as well as a professor of surgery, pathology, and biomedical engineering. Dr. Shea is the Steven A. Goldstein Collegiate Professor of Biomedical Engineering, a professor of chemical engineering, and a professor of surgery.



Progress and Promise: Advancing the Use of Ultrasound Technology Against Cancer

In 2019, **Clifford Cho, M.D.**, was awarded a Forbes Institute grant to determine whether histotripsy — a process developed at U-M that uses focused ultrasound to very precisely destroy tumors — would generate an immune response against cancer.

His research team, which includes colleagues in surgery and biomedical engineering, found that histotripsy stimulated a profound immune response in laboratory models of melanoma and liver cancer. Published in the *Journal for ImmunoTherapy of Cancer*, this research points to a potential new direction for cancer therapy.

When a tumor in the laboratory is treated with histotripsy, it kicks off an immune response at other tumor sites. "Even though the tumor cells are wiped out with histotripsy, the contents of what's left behind are still recognizable so the immune system reacts to that at other tumor sites," Dr. Cho explains.

In a small clinical trial in Spain, histotripsy was found to be safe and well-tolerated, and researchers confirmed that tumors other than the ones directly targeted also shrank or stabilized after treatment.

Today, the University of Michigan is one of eight sites around the country enrolling patients in a much larger clinical trial to evaluate the safety and efficacy of histotripsy to treat liver tumors. Dr. Cho, the C. Gardner Child Professor of Surgery, is co-principal investigator of the #HOPE4LIVER trial. It is sponsored by the U-M startup company HistoSonics, which is commercializing the histotripsy technique.

In a surprise laboratory finding, histotripsy also appears promising in another way. Dr. Cho and his colleagues have found that using residue from a tumor treated with histotripsy like a vaccine seemed to provide some level of protection in laboratory models when cancer is later introduced. The cancer wasn't prevented, but the tumors grew more slowly and had a more potent anti-tumor immune response than normal.

New Clues Toward Treating Pediatric Brain Tumors Harboring Epigenetic Mutation

Common Diabetes Drug Promising Against Rare Childhood Brain Tumor in Laboratory Studies

Glioma Subtype May Hold the Secret to the Success of Immunotherapies

First Inhibitors Against Key Epigenetic Complex Involved in Cancer Developed

Researchers Find First Long Non-Coding RNA to Play a Role in Body's Immune Response

Researchers Develop First-in-Class Inhibitors Against Key Leukemia Protein

Read these stories and more!

Visit "News and Impact" at **rogelcancercenter.org/ForbesInstitute**.

JOIN US! The Forbes Institute for Cancer Discovery was founded by Sidney and Madeline Forbes, long-time Detroit-area philanthropists and dedicated friends and supporters of the University of Michigan. Nathan Forbes represents the family's dedication to high-impact research on the Rogel Cancer Center's National Advisory Board. The Forbes Institute's grants are solely funded by gifts from donors, and the Forbes family invites everyone inspired to advance cancer knowledge toward cures to be a partner in its mission.

For more information or to make a contribution, visit **rogelcancercenter.org/ForbesInstitute** or contact:

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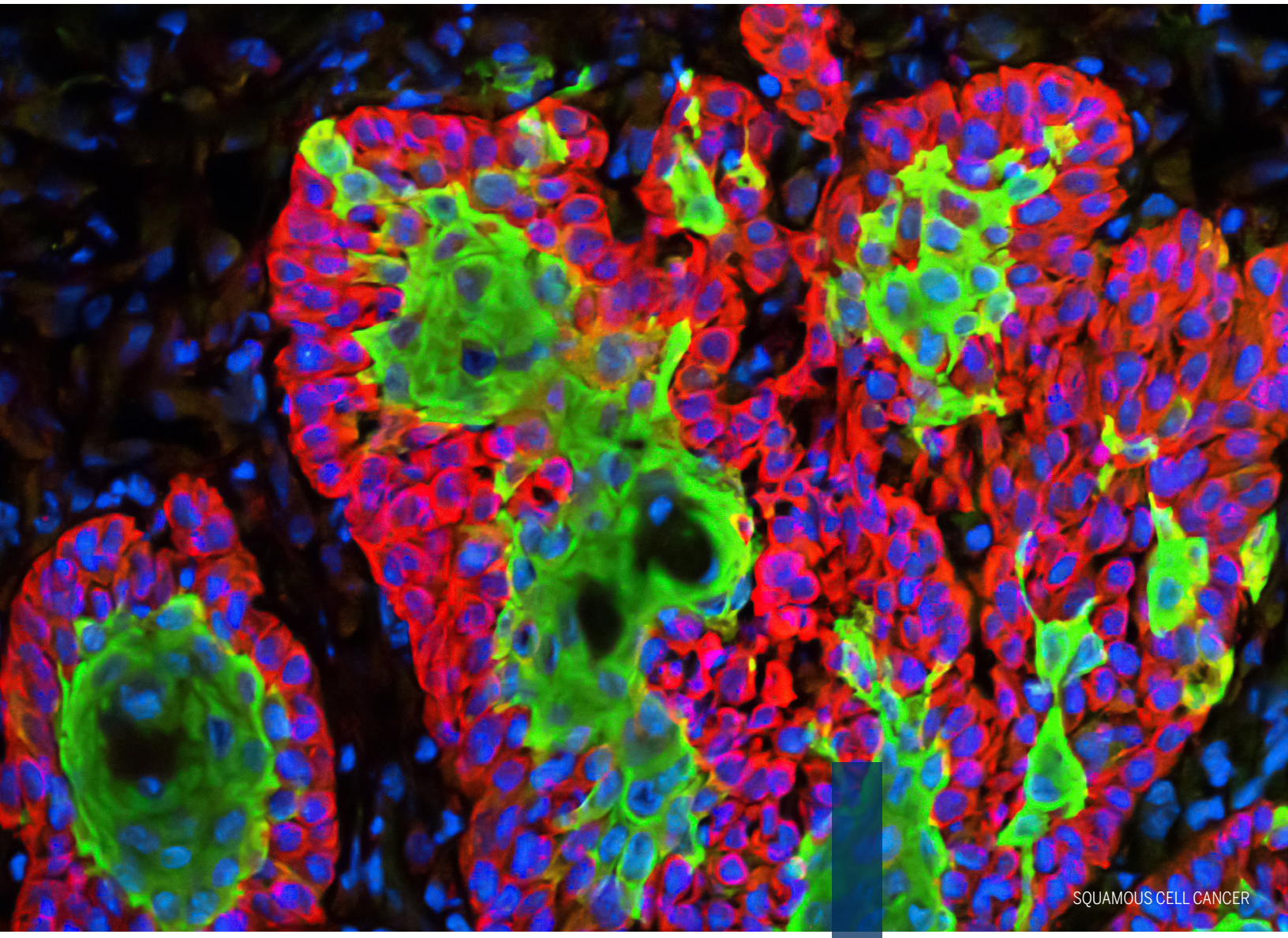

SQUAMOUS CELL CANCER

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