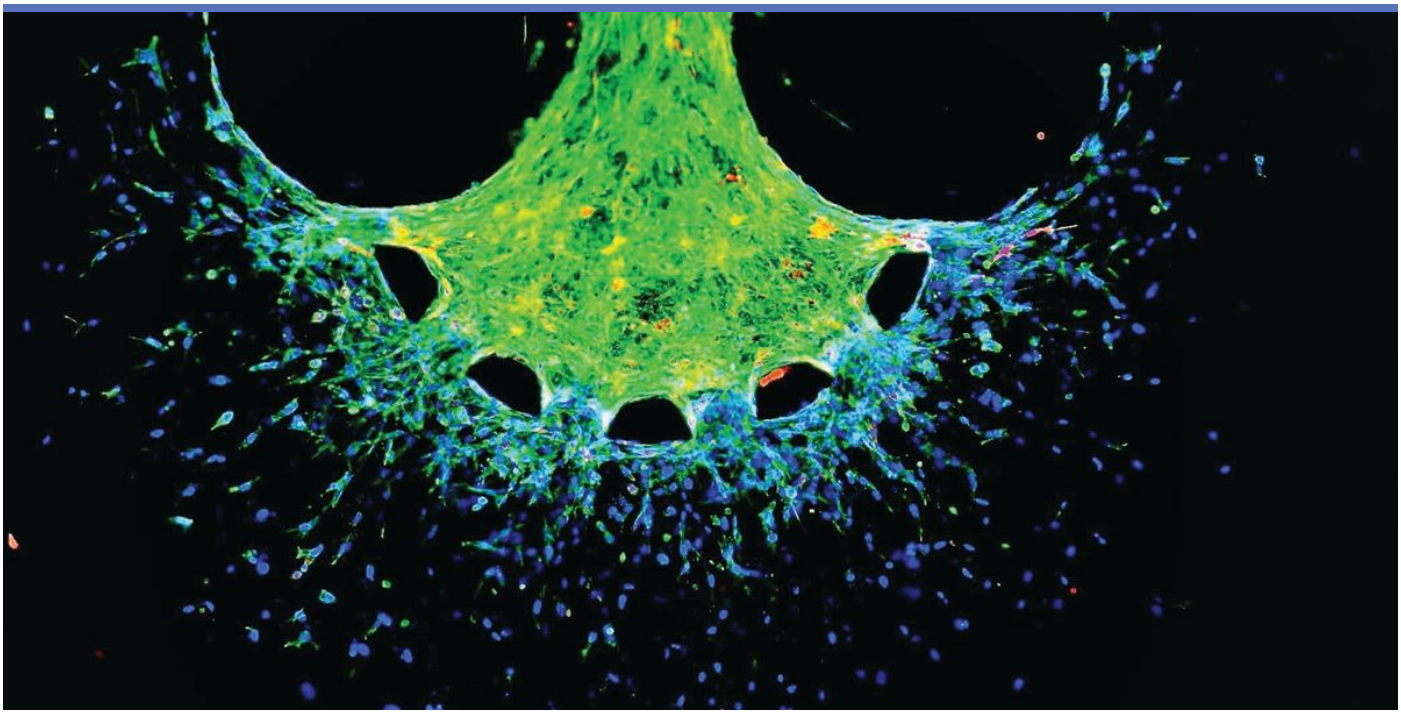
TODAY'S CLINICAL LAB

READ THIS ARTICLE ONLINE



Improving Cancer Therapies with Organ-on-a-Chip Technologies

Can modeling the complexities of disease using organ-on-a-chip platforms help improve cancer therapies?

Jun 02, 2023 JONATHAN KLANE, MSED, CIH, CSP, CHMM, CIT , MIRIAM BERGERET, MSC

If you had to watch both of your uncles die of cancer, including glioblastoma, how might that affect you? Beyond the grief, you might dedicate your life to advancing cancer therapies.

This is exactly what spurred Mehdi Nikkhah, PhD, to dive into biomedical engineering and cancer research to help people with cancer and their families. Now an associate professor of biomedical engineering in the School of Biological and Health Systems Engineering at Arizona State University, Nikkhah researches organ-on-a-chip (OOAC) technologies in the hope of improving cancer therapies.

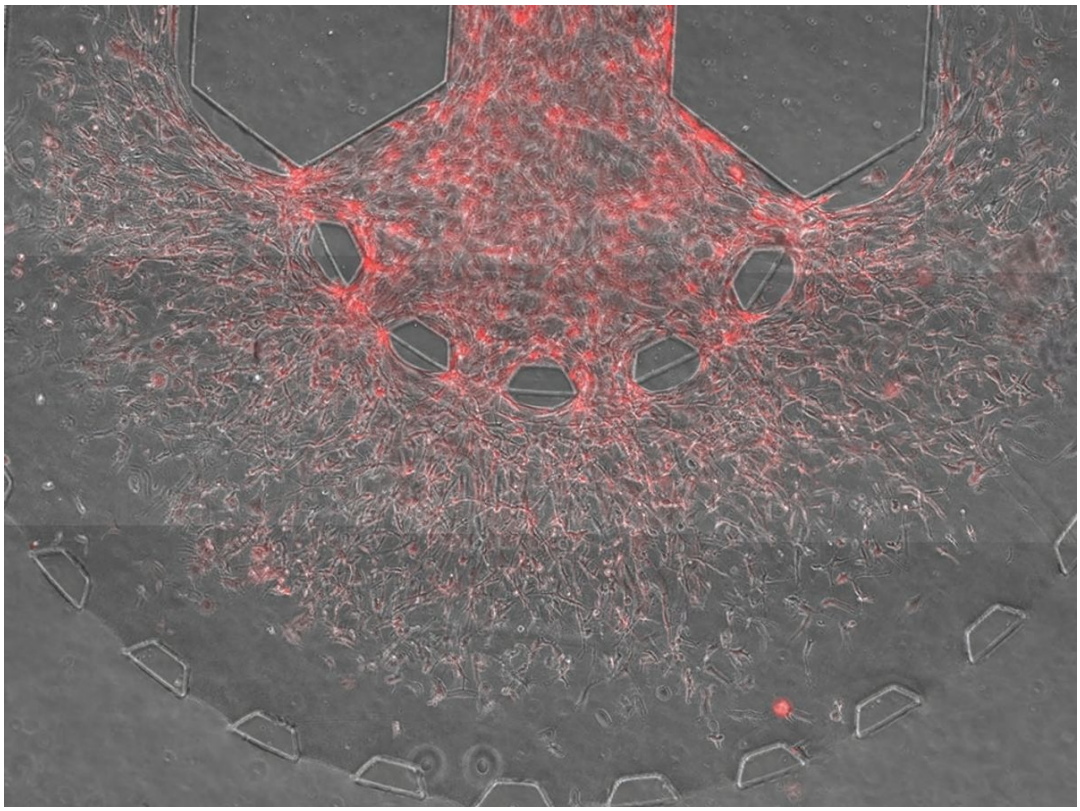
Gaining bioengineering experience

After a start in mechanical engineering, including an initial focus on biomedical engineering robotics, Nikkhah felt the pull toward more patient-focused research on cancer: "My uncles'

cancers (on both my mom and dad's sides) strengthened my motivation to dedicate my research and efforts toward this area," he says.

For his PhD research, he cultured cancer cells 12–15 hours a day but knew there had to be a better approach—one that was more efficient and effective. This focus intensified after one uncle's death from glioblastoma, which his lab now studies.

Designing sophisticated organ-on-a-chip platforms



Phase contrast image of migration of cancer cell—SUM159 (red) into the stromal region within the tumor-on-chip model.

COURTESY OF KALPANA RAVI AND MEHDI NIKKHAH

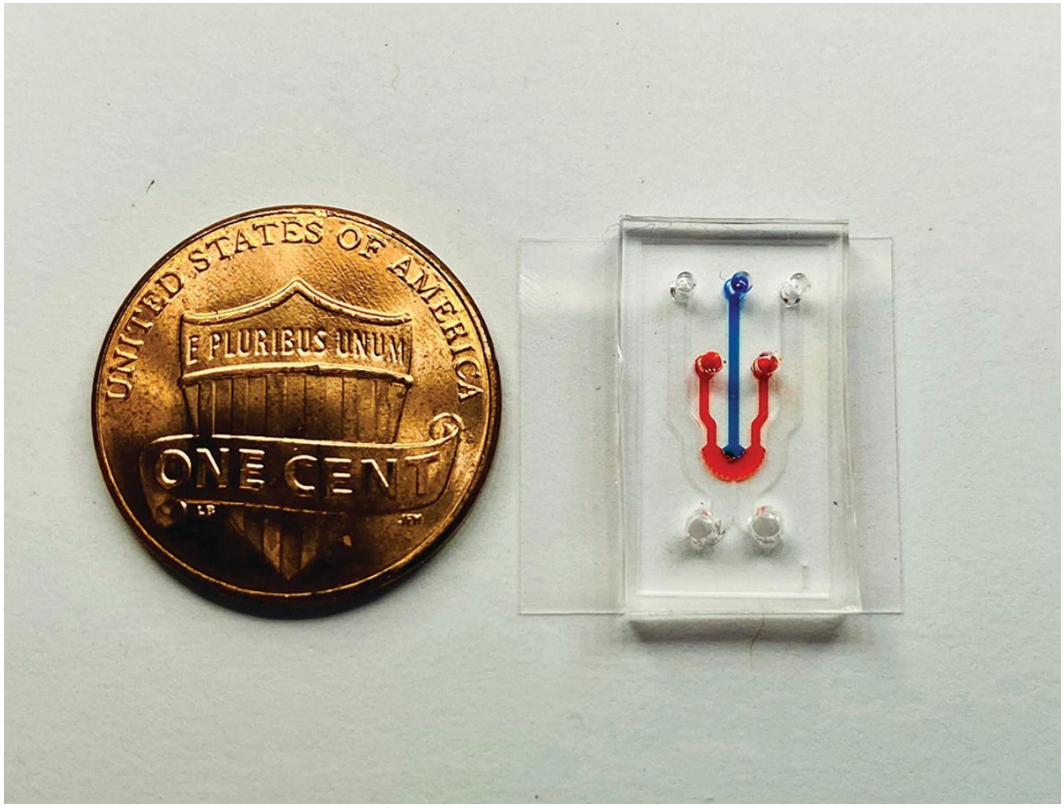
Much of cancer research currently relies on mouse models for preclinical trials, which have limitations—such as inherent differences in biological mechanisms in mice versus humans—that affect therapeutic efficacy, as well as the significant time, resources, and cost needed to take a drug from initial discovery to clinical approval.

Because of these limitations, there is a need to develop alternative cancer research platforms, such as taking cancer cells from an individual's biopsy and placing them onto a chip to model their specific tumor.

For example, we may have a person whose cancer tests positive for three cancer subtypes,

says Nikkhah. Using OOAC technology, researchers and scientists could bypass creating an animal model of the tumor by using cells and tissues (e.g., tumor or stromal cells) from a biopsy to model the tumor on a microchip.

One of his team's driving questions has been, can we model the complexities of the disease landscape on a microchip? These disease landscapes include tumor, cardiac, and vascular disease environments, as well as the microenvironment surrounding myocardial infarctions, i.e., heart attacks.



Photograph of microfluidic tumor-on-chip next to a US penny. Tumor cells embedded with extracellular matrix forms the central tumor region (blue). The stromal region (red) surrounding the tumor region is injected with other cells of the tumor microenvironment.

COURTESY OF KALPANA RAVI AND MEHDI NIKKHAH.

After much work with OOAC innovations, his group and collaborators are seeing progress: "We recently published a high impact manuscript in *Biomaterials* identifying a novel signaling pathway that promotes brain tumor invasion," says Nikkhah. "It is very fulfilling to see my research contributing to the community."

The *Biomaterials* paper describes his lab's 3D micro-engineered model with breast cancer cells, which provided insight into changes in signaling pathways in the tissue extracellular environment during tumor invasion. This work offers a well-controlled tumor microenvironment model that can be used to further investigate signaling cues involved in

tumor invasion and progression.

Collaborating with other clinical researchers

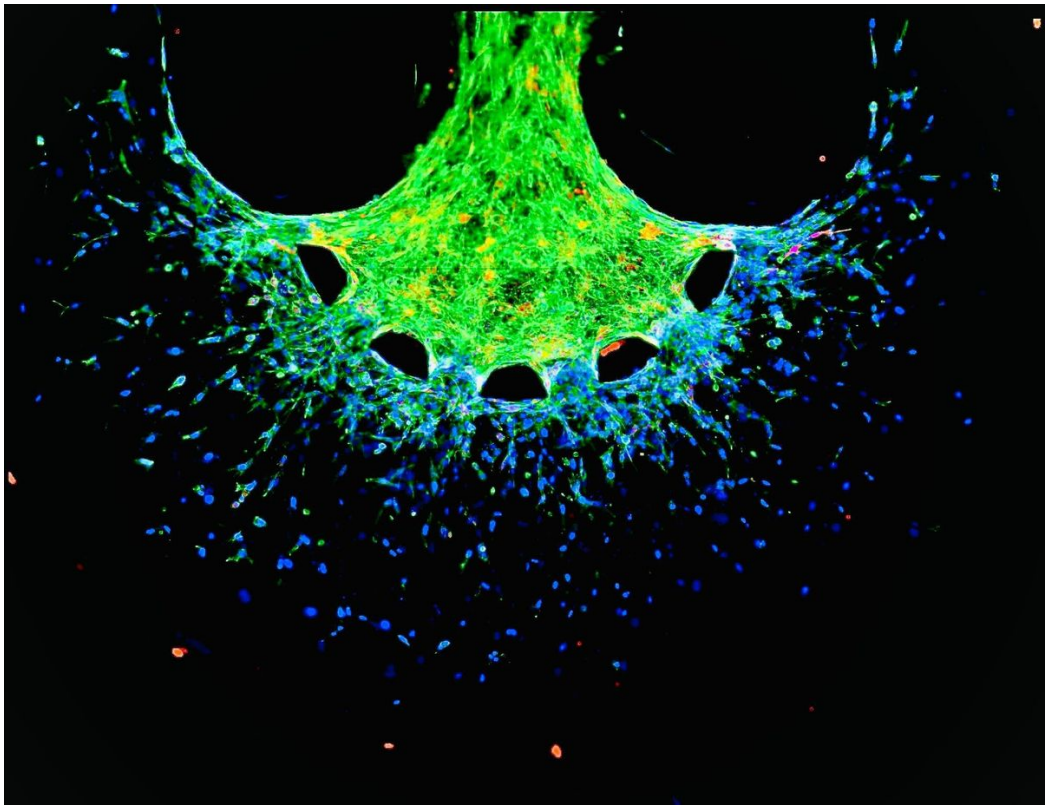
To remain motivated and focused on his research goals, Nikkhah uses what he calls “scientific meditation”—reading and staying mindful of how his research could help others.

He also emphasizes the collaborative nature of his research. For example, his lab has access to breast cancer tissue biopsy samples thanks to Barbara A. Pockaj, MD, a surgical oncologist at the Mayo Clinic of Arizona.

Nikkhah also works with Shwetal Mehta, MS, PhD, a brain tumor researcher and chief operating officer, deputy director, and preclinical co-leader of the Ivy Brain Tumor Center at Barrow Neurological Institute in Phoenix, AZ. Mehta approached Nikkhah a few years ago to collaborate on glioblastoma research using their technology and patient-derived cells.

Ultimately, our paper doesn’t solve the problem of effective tumor modeling, he says, but “it’s one more piece of the puzzle [...] Together, we can find solutions to cancer.”

From bench to beside and vice versa



Z-projection of cytoskeletal staining of invading cancer cells within the tumor-on-chip model (F-actin = green, DAPI = blue).

COURTESY OF KALPANA RAVI AND MEHDI NIKKHAH.

Nikkhah currently has two patents for tumor-on-a-chip technologies, as well as funding from the National Science Foundation for “heart (attack) on a chip.” He also recently secured a five-year National Institutes of Health grant to study brain tumors that he expects will bear fruit. With this funding, he expects to eventually find the answers to these key questions: “How do we go from bench to bedside and vice versa?” and “Can we identify druggable pathways?”

In the past few years, Nikkhah’s work has received much attention. In 2017 and 2020, he won the Phoenix Children’s Hospital Leadership Circle Award for his congenital heart disease work. When asked about his many awards, he says, “making a difference in patients’ lives is what keeps me innovating,” that, and the memories of the two uncles he lost to cancer.