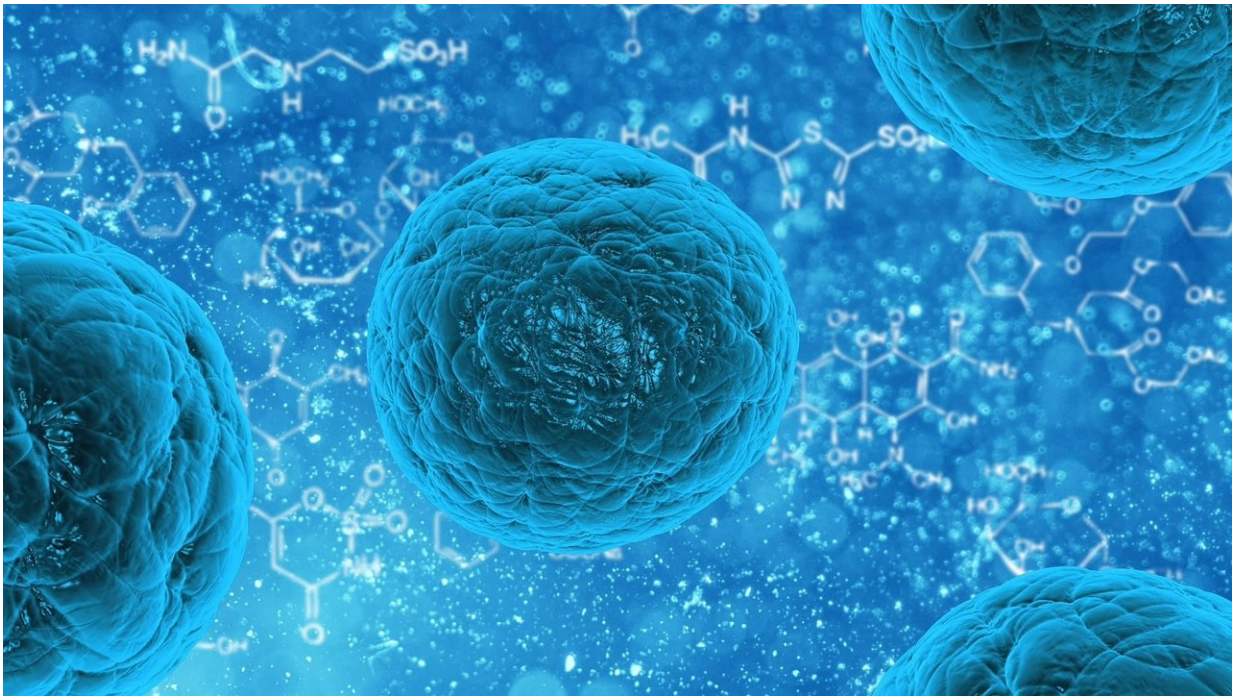
New platform could enable personalized immunotherapy

July 22 2021



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An innovative testing platform that more closely mimics what cancer encounters in the body may allow for more precise, personalized therapies by enabling the rapid study of multiple therapeutic combinations against tumor cells. The platform, which uses a three-dimensional environment to more closely mirror a tumor microenvironment, is demonstrated in research published in

Communications Biology.

"This whole platform really gives us a way to optimize personalized immunotherapy on a rapid, high throughput scale," said Jonathan Dordick, Institute Professor of chemical and biological engineering and member of the Center for Biotechnology and Interdisciplinary Studies (CBIS) at Rensselaer Polytechnic Institute, who led this research. "You can imagine somebody having cancer, and you quickly biopsy the tumor and then you use this biochip platform to identify very quickly—within a day or two—what specific treatment modality might be ideally suited against a particular cancer."

Of particular interest to researchers is the behavior of a specific type of immune cell known as natural killer (NK) cells, which seek out cancer or viruses within the body, bind to their receptors, and excrete an enzyme meant to kill the unwanted cells. The platform studied in this paper allows researchers to compare what happens when the NK cells are left to fight tumor cells on their own versus how they behave when an antibody or cancer drug, or a combination of the two, is added.

The platform is a small two-piece plastic chip that's about the size of a microscope slide. One side of the sandwich chip contains 330 tiny pillars upon which researchers can place an external matrix, made of a gel-like substance, which mimics the mechanical environment of a tumor cell. When cancer cells are placed inside this gel-like structure, they're encouraged to grow into a spheroid shape, much as they would inside the body. The second piece contains 330 microwells within which NK cells can be added in suspension—much as they would flow, untethered inside the body.

At Rensselaer, Dordick collaborated with Seok-Joon Kwon, senior research scientist in CBIS, and Sneha Gopal, who recently received her Ph.D. based, in part, on this study. The Rensselaer team collaborated

with researchers from Konyang University and Medical & Bio Decision Company Ltd. To test this platform, researchers studied two types of breast cancer cells, as well as pancreatic cancer cells, with various combinations of NK cells, two monoclonal antibodies, and an anti-cancer chemotherapy drug.

"You can screen very quickly to determine what combinations of NK cells, antibodies, and chemotherapeutic drugs target the cancer cells within the spheroid geometry," Dordick said. "What really is amazing is we see very significant differences between what happens in that spheroid, within the slots of the chip, versus what would happen in a more traditional two-dimensional cell culture that's often used in the screening."

In the spheroid design, for instance, the chemotherapy drug paclitaxel had little effect on the three types of cancer cells on its own, whereas in a traditional two-dimensional system, Dordick said, the drug may appear to do well. It performed dramatically better when it was combined with both NK cells and an antibody.

"This platform moves researchers closer to personalized medicine," said Deepak Vashishth, director of CBIS. "This work conducted by Professor Dordick and his research group is an excellent example of how we, at Rensselaer, are providing a new angle to human health by developing new approaches at the intersection of engineering and life sciences to enhance cures for diseases such as cancer."

To further the potential use of this tool, Dordick said that it must be tested on a wide range of cancer types, including a tumor microenvironment that consists of multiple different types of cells. In the future, he envisions that the platform has the potential to identify combination therapies that work best against a patient's specific cancer, enabling the identification and delivery of personalized immunotherapy.

More information: Sneha Gopal et al, 3D tumor spheroid microarray for high-throughput, high-content natural killer cell-mediated cytotoxicity, *Communications Biology* (2021). DOI: 10.1038/s42003-021-02417-2

Provided by Rensselaer Polytechnic Institute