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Paving a path to triple-negative breast cancer treatment

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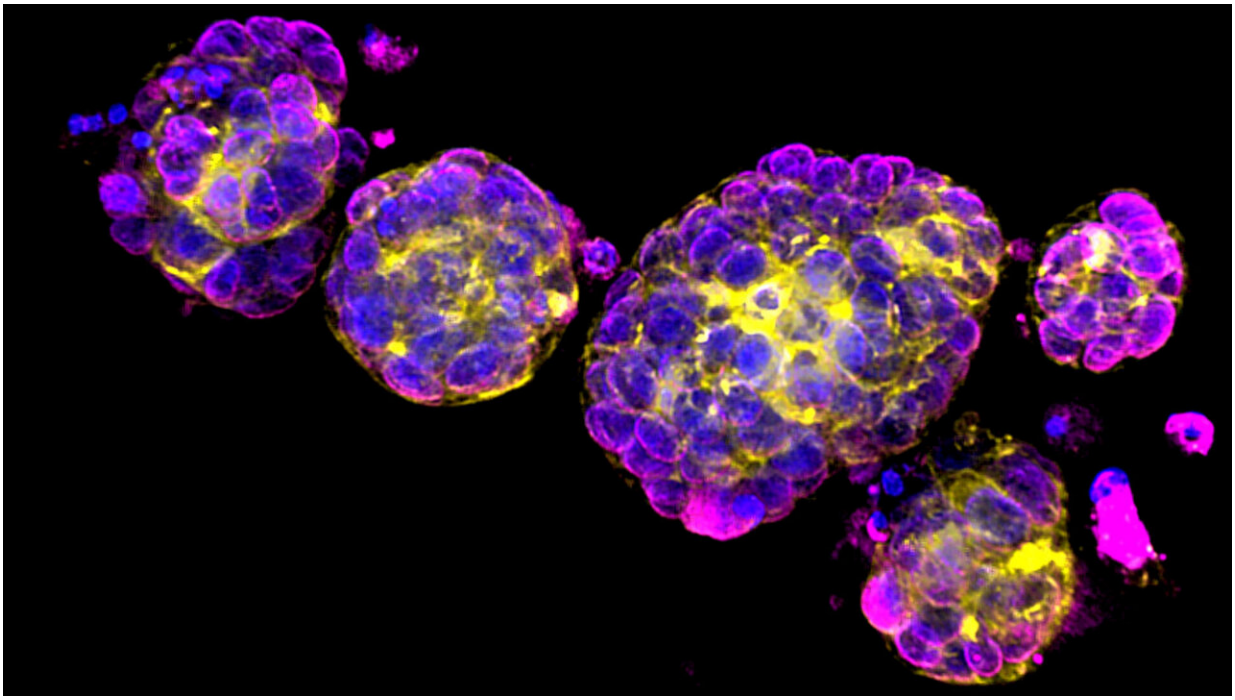

Organoids are tiny clumps of cells that are grown from and resemble tiny 3D organs. The image above shows breast cancer organoids, derived from human patients. Breast cancer cells are labeled in purple, DNA is labeled in blue, and cytoskeleton proteins are labeled yellow. Organoids provide a more natural setting than flat tissue culture dishes to study how cancer cells grow, develop, and can be treated. Credit: Sonam Bhatia/Spector lab/CSHL, 2022

It's the cancer version of "mini me." Cold Spring Harbor Laboratory

(CSHL) Professor David Spector, among others, has developed organoids, which are miniature, three-dimensional copies of cancers. Organoids can be derived from cancer or healthy cells. They allow scientists to study the basic biology of particular types of tumors, then to test specific drugs on those cancers in a dish, instead of in a patient. Recently, Spector, postdoctoral researcher Sonam Bhatia, and collaborators from CSHL and Northwell Health created a biobank of 87 triple-negative breast cancer organoids. The researchers published their work in the journal *Cancer Research*.

The research team, which plans to expand the biobank to over 100 patient-derived samples, conducted extensive tests to ensure the organoids had the same characteristics of the tumors when they were in the patient. They tested that organoids and tumors: (1) had similar genetic variation in their DNA; (2) had similar RNA profiles; and (3) produced tumors, similar to the patients' tumors, when implanted into mice. As Spector explained:

"That was our rationale for approaching this from many different directions, to really develop a comprehensive analysis as to whether these breast tumor organoid models would be good model systems."

Spector's lab is testing various treatments to find weaknesses specific to each tumor. They are developing a library of therapeutics known as antisense oligonucleotides to target RNA molecules active in cancer cells, but not in healthy cells. Spector and his team already have 200 potential targets and will prioritize RNA molecules that are made in the largest amounts.

Spector, whose efforts to improve organoid science might one day allow doctors to use them in a clinic, credited a team of researchers for this effort. He described Bhatia as the "key driver" who brought this "massive undertaking" together.

For her part, Bhatia believed this research would have practical applications.

"This biobank opens up an exciting avenue to use this cutting-edge class of therapeutics with better patient-specific models," Bhatia said. "In the longer-term, these patient-derived organoids can be used to test therapy options outside of the patients, in a dish, and can provide information on what treatments the patient does or does not respond to."

More information: "Patient-derived triple negative breast cancer organoids provide robust model systems that recapitulate tumor intrinsic characteristics", *Cancer Research* (2022). DOI: 10.1158/0008-5472.CAN-21-2807

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