New discovery approach accelerates identification of potential cancer treatments

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Researchers at the University of Michigan have described a new approach to discovering potential cancer treatments that requires a fraction of the time needed for more traditional methods.

They used the platform to identify a novel antibody that is undergoing further investigation as a potential treatment for breast, ovarian and other cancers.

In research published online in the *Proceedings of the National Academy of Sciences*, researchers in the lab of Stephen Weiss at the U-M Life Sciences Institute detail an approach that replicates the native environment of cancer cells and increases the likelihood that drugs effective against the growth of tumor cells in test tube models will also stop cancer from growing in humans.

The researchers have used their method to identify an antibody that stops breast cancer tumor growth in animal models, and they are investigating the antibody as a potential treatment in humans.

"Discovering new targets for cancer therapeutics is a long and tedious undertaking, and identifying and developing a potential drug to specifically hit that target without harming healthy cells is a daunting task," Weiss said. "Our approach allows us to identify potential therapeutics in a fraction of the time that traditional methods require."

The researchers began by creating a 3-D "matrix" of collagen, a connective tissue molecule very similar to that found surrounding breast cancer cells in human patients. They then embedded breast cancer cells in the matrix, where the cells grow as they would in human tissue.

The investigators then injected the cancer-collagen tissue composites into mice that then recognize the human cancer cells as foreign tissue. Much in the way that our immune system generates antibodies to fight infection, the mice begin to generate thousands of antibodies directed against the human cancer cells. These antibodies were then tested for the ability to stop the growth of the human tumor cells.

"We create an environment in which cells cultured in the laboratory 'think' they are growing in the body and then rapidly screen large numbers of antibodies to see if any exert anti-cancer effects," Weiss said. "This allows us to select promising antibodies very quickly and then work to identify what the antibody targets on the cancer cell surface."

They discovered a particular antibody, 4C3, that was able to almost completely stop the proliferation of the breast cancer cells. They then identified the molecule on the cancer cells that the antibody targets. Next, Weiss said, the antibody can be further engineered to generate humanized monoclonal antibodies for use in patients as a potential therapeutic.

"We still need to do a lot more work to determine how effective 4C3 might be as a treatment for breast and other cancers, on its own or in conjunction with other therapies," Weiss said. "But we have enough data to warrant further pursuit, and are expanding our efforts to use this discovery platform to find similarly promising antibodies."

More information: A 3D matrix platform for the rapid generation of therapeutic anti-human carcinoma monoclonal antibodies , *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1410996111

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