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Cleveland Clinic researcher awarded $2.6 million grant to create innovative models of colorectal cancer

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Cleveland Clinic researcher Emina Huang, M.D., a colorectal surgeon in the Digestive Disease and Surgery Institute and a staff member in the Lerner Research Institute's Department of Stem Cell Biology and Regenerative Medicine, has been awarded a collaborative five-year, $2.6 million grant from the National Cancer Institute to create innovative models of colorectal cancer that will enhance understanding of how the disease develops and spreads.

This grant - a collaboration between Cleveland Clinic, Duke University and Cornell University - is the newest project funded by NCI's Cancer Tissue Engineering Collaborative (TEC) Research Program. The program supports the development and characterization of state-of-the-art tissue engineered technologies for cancer research. There are only four other TEC-funded research institutions nationwide. NCI is part of the National Institutes of Health.

"I'm very excited to lead a project that brings together some of the top surgeons, researchers and biomedical engineers in their respective fields," said Dr. Huang. "Colorectal cancer affects millions of adults in the United States. In some cases, the five-year survival rate is less than 13 percent. In order to develop effective treatment and prevention therapies for such a serious and complex disease, and deliver them to the patients and families who so desperately need them, we'll need to work collaboratively across specialties and disciplines. With this new project, I think we're well on our way."

Dr. Huang and her team will work to develop three leading-edge models of colorectal cancer that will help researchers uncover the role inflammation, messenger RNA (transcriptome) and epigenetics play in the spread, or metastasis, of colorectal cancer. What is unique about these models is that they will all use human tissues, both from the colon and other sites throughout the body. Studying colorectal cancer using cells from people will maximize the applicability of findings and may speed the time of discovery.

This project is also innovative in that other conditions aside from colorectal cancer--including hypoxia, or lack of oxygen, and altered glucose levels--are reflected in these models. This will help mimic the extreme complexity of the colorectal cancer microenvironment. Additionally, the models are scalable and will allow for comparison between various cell types and combinations within and between the three models.

While Dr. Huang is the principal investigator for the project, each collaborating organization will take the lead on developing one of the three models. Dr. Huang's lab will develop what is called an organotypic model. They will remove native cells from human colons, taken from resected colons and cancerous lesions, and repopulate them with new cells, including healthy cells as well as various types of cancer cells. Studying how the different classes of cells respond will help researchers understand the roles inflammation and cellular invasion and differentiation play in metastasis.

Michael L. Shuler, the Eckert Professor of Engineering at Cornell University, will develop the second model that will utilize new body-on-a-chip technology. This technology will use human cells to create tiny, organ-like structures that simulate the function of a human colon. These structures will be placed on a chip, which mimics the body and explicitly connects the colon to a meme of the liver.

The team at Duke University - led by Professor Xiling Shen, Department of Biomedical Engineering - will validate the two previously described models in an animal metastasis model, with the goal of better understanding how the immune system may play a role in shaping colorectal cancer metastasis.

Dr. Huang co-directs Lerner Research Institute's Center of Excellence in Colon Cancer Metastasis Research. This program brings together top scientists with front-line physicians to speed the translation of lab discoveries into real benefits for patients. The center is currently working on several projects, including examining colon cancer's cellular microenvironment, reversing the effects of angiogenesis, as well as understanding how genetic changes may make colon cancer cells more aggressive in some individuals and how those changes may be reversed. This project is the newest addition to the center's impressive portfolio.

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