Scientists develop method to keep surgically-removed prostate tissue alive

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The new technique could not only enhance research of prostate biology and cancer, but also hasten the creation of individualized medicines for prostate cancer patients, the investigators say. Previous attempts to culture live prostate tissues resulted in poor viability and lost “tissue architecture,” the researchers note, making them less than useful for research or therapy development.

“Our technique could help scientists more accurately predict how living prostate tissues respond to therapy,” says Marikki Laiho, M.D., Ph.D., director of the division of Molecular Radiation Sciences at Johns Hopkins. “It holds promise for testing anticancer drugs that work best.”

For the study, published in the November 1 issue of *Cancer Research*, the scientists refined their multistep tissue culture technique and performed experiments to test the tissues’ viability and utility in research. Laiho worked with Stanford University researcher Donna

Peehl, Ph.D., to pilot the technique in a research project completed in 2007.

Customarily, pathologists store tissue samples in paraffin wax, which kills the tissue, resulting in samples that are essentially frozen in time. In many research laboratories, scientists experiment with prostate cancer cells that have been grown in flasks filled with nutrients and kept under strict temperature conditions. But these cells are not connected together in the tightly knit architecture of tissue that exists in the actual prostate gland.

“Tissue architecture may hold clues to why certain therapies work and others fail, and may be a better model of the intact, in vivo prostate gland,” says Laiho, who is the Willard and Lillian Hackerman Professor of Radiation Oncology at Johns Hopkins.

Laiho says that one key to success for the international team was to work with surgeons and pathologists to speed up delivery of tissue samples to the pathology lab from the operating room.

At the pathology lab, scientists cut thin slices of prostate specimens taken from 18 patients who had undergone surgery on the prostate gland at the Helsinki University Central Hospital or The Johns Hopkins Hospital during 2007-2009.

Specimen slices had to be a precise thickness to allow cells throughout the tissue to maintain a healthy exchange of gases and growth factors.

Then, Laiho and her team placed the tissues in a liquid solution comprised of a complex mix of 64 separate ingredients to maintain the proper chemical and nutritional support for the biological functions in the tissue.

The scientists validated the presence of biomarkers specific for each type of cell within the prostate tissues to ensure that they were viable.

The scientists caution that although their method gives them a more "real-life" model of the prostate with live tissue samples, it comes at a cost: – even with support, the tissues are short-lived, and experiments on fresh specimens must be completed within one week, which may be too short for some types of research.

The Hopkins-Helsinki team has already used their tissue-culture technique to measure levels of proteins known to repair DNA damage caused by carcinogens and other environmental agents. They found that one of these proteins – p53 – is not activated consistently enough to repair DNA damage. They also found that one of the first proteins to arrive on the DNA repair scene – H2AX – is activated at expected levels in all but one of the architectural compartments in prostate tissue. Low levels of H2AX were found in the so-called "luminal" compartment of prostate tissue, in the part of the prostate gland that produces secretions to protect sperm cells.

Laiho says the tissue-culture technique was a key component of understanding which DNA repair proteins may or may not be activated in different parts of prostate tissue and could help scientists develop therapies that target these DNA repair proteins.

The Hopkins and Helsinki investigators plan to use their new tissue-culture technique to test the response of experimental drugs on prostate cancer tissues.

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