New discovery expected to significantly change biomedical research

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File illustration photo shows a dish of stem cell cultures in a lab. US researchers said Monday they have discovered how to keep tumor cells alive in a lab, generating buzz in the scientific community about a potential breakthrough that could transform cancer treatment.

In a major step that could revolutionize biomedical research, scientists have discovered a way to keep normal cells as well as tumor cells taken from an individual cancer patient alive in the laboratory — which previously had not been possible. Normal cells usually die in the lab after dividing only a few times, and many common cancers will not grow, unaltered, outside of the body.

This new technique, described today online in the American Journal of Pathology, could be the critical advance that ushers in a new era of personalized cancer medicine, and has potential application in

regenerative medicine, says the study's senior investigator, Richard Schlegel, M.D., Ph.D., chairman of the department of pathology at Georgetown Lombardi Comprehensive Cancer Center, a part of Georgetown University Medical Center.

"Because every tumor is unique, this advance will make it possible for an oncologist to find the right therapies that both kills a patient's cancer and spares normal cells from toxicity," he says. "We can test resistance as well chemosensitivity to single or combination therapies directly on the cancer cell itself."

The research team, which also includes several scientists from the National Institutes of Health, found that adding two different substances to cancer and normal cells in a laboratory pushes them to morph into stem-like cells — adult cells from which other cells are made.

The two substances are a Rho kinase (ROCK) inhibitor and fibroblast feeder cells. ROCK inhibitors help stop cell movement, but it is unclear why this agent turns on stem cell attributes, Schlegel says. His co-investigator Alison McBride, Ph.D., of the National Institute of Allergy and Infectious Diseases, had discovered that a ROCK inhibitor allowed skin cells (keratinocytes) to reproduce in the laboratory while feeder cells kept them alive.

The Georgetown researchers — 13 investigators in the departments of pathology and oncology — tried ROCK inhibitors and fibroblast feeder cells on the non-keratinocyte epithelial cells that line glands and organs to see if they had any effect. They found that both were needed to produce a dramatic effect in which the cells visibly changed their shape as they reverted to a stem-like state.

"We tried breast cells and they grew well. We tried prostate cells and their growth was fantastic, which is amazing because it is normally

impossible to grow these cells in the lab," Schlegel says. "We found the same thing with lung and colon cells that have always been difficult to grow."

"In short, we discovered we can grow normal and tumor cells from the same patient forever, and nobody has been able to do that," he says. "Normal cell cultures for most organ systems can't be established in the lab, so it wasn't possible previously to compare normal and tumor cells directly."

The ability to immortalize cancer cells will also make biobanking both viable and relevant, Schlegel says. The researchers further discovered that the stem-like behavior in these cells is reversible. Withdrawing the ROCK inhibitor forces the cells to differentiate into the adult cells that they were initially. This "conditional immortalization" could help advance the field of regenerative medicine, Schlegel says.

However, the most immediate change in medical practice from these findings is the potential they have in "revolutionizing what pathology departments do," Schlegel says.

"Today, pathologists don't work with living tissue. They make a diagnosis from biopsies that are either frozen or fixed and embedded in wax," he says. "In the future, pathologists will be able to establish live cultures of normal and cancerous cells from patients, and use this to diagnose tumors and screen treatments. That has fantastic potential."

Provided by Georgetown University Medical Center