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The cell's 'personal space:' A controlling factor in maintaining healthy tissue

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Cells in normal tissue seem to have "personal space" issues. They know how much space they like, and if things get too tight, some cells are forced to leave.

Researchers from Huntsman Cancer Institute (HCI) at the University of Utah have found that normal epithelium tissue ejects living cells to maintain a steady population and ease overcrowding. This discovery has the potential to reveal what goes awry in cancer when cells do not turnover, but instead pile up. The research results appeared online April 15, 2012 in the journal *Nature*.

The epithelium is the tissue layer that forms the outer and inner surfaces of the body, including the skin and the lining of the gastrointestinal tract. Many types of cancer originate in the epithelium.

Earlier studies showed that dying cells are pushed out of the epithelium, or extruded, when researchers purposely trigger cell death in the lab. "But it wasn't clear what factors caused cells to die in normal tissues," said Jody Rosenblatt, Ph.D., assistant professor in the Department of Oncological Sciences at the University of Utah School of Medicine and an HCI investigator.

In one experiment, cells were cultured on a stretched elastic base. After the culture was well-populated with cells, the base was allowed to return to its original size, which meant the cells had much less room. "We found that overcrowding—too many cells occupying a limited space—

makes some cells leave the tissue to give the remaining cells enough room," said Rosenblatt.

Another experiment in the series used a zebrafish model to show that when a key stretch-activated channel controlling cell extrusion is blocked, cell masses form where cells failed to extrude. The same type of increased cell density without extrusions was observed in sections of colon polyps, compared to normal colon tissue.

"In the polyps, which are precursors to colon cancer, there's a similar pile-up of cells," said Rosenblatt. "If they behaved as normal colon tissue, we would have seen cells extrude, but polyps don't seem to do it. We don't know why yet; that will be investigated in further research.

"This is a basic discovery for which there may be exciting implications for diseases like asthma or colitis where too much cell death leads to poor barrier function and for cancer where there is not enough cell death," she added. "More studies are needed even to figure out what those implications may be."

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