Cancer cells can poison normal cells

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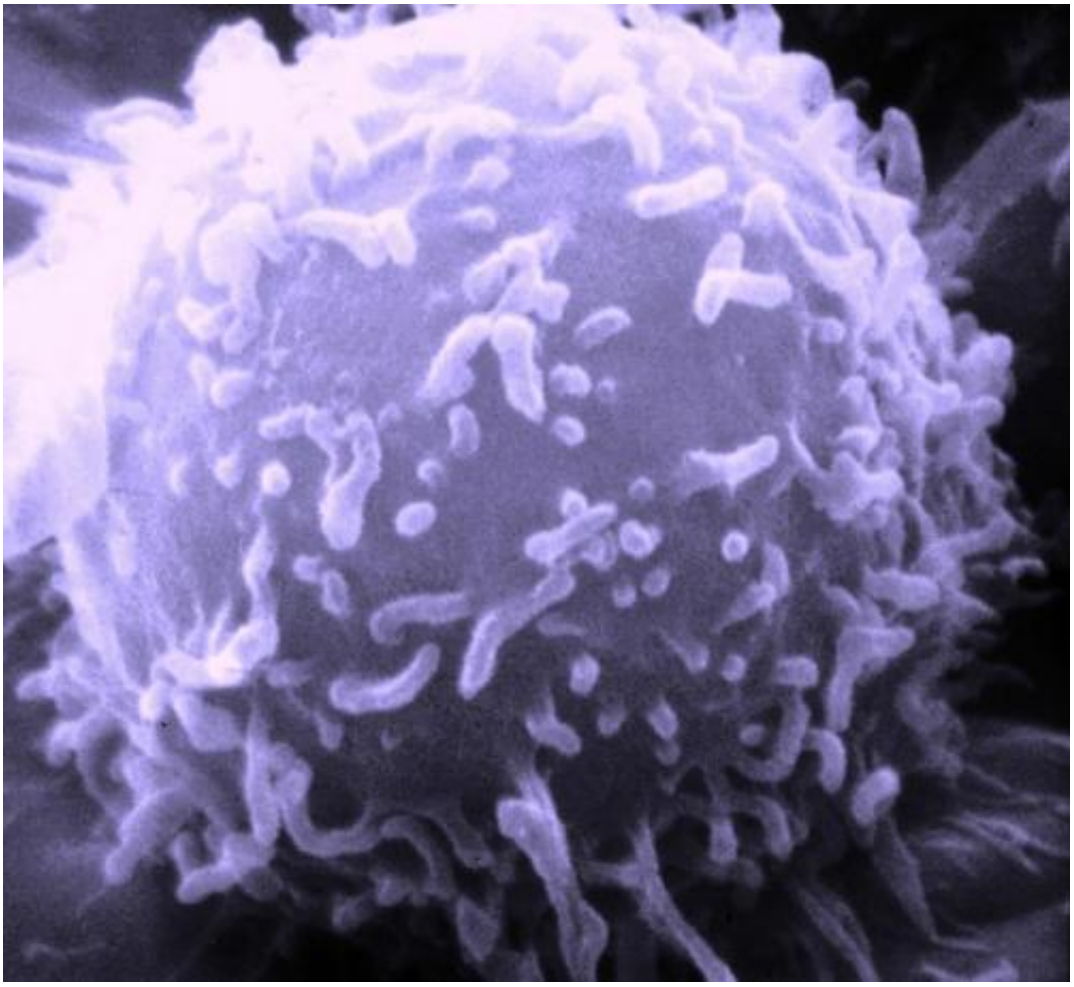

Electron microscopic image of a single human lymphocyte. Credit: Dr. Triche National Cancer Institute

Cancer cells are continuously produced in our bodies, where most of them are recognized by our immune systems and destroyed. Some,

however, escape this innate surveillance system and find a place to survive and grow.

Several factors expelled by tumor cells are concentrated in the area immediately surrounding the tumor, called the tumor microenvironment. While it is established that these factors support and enhance cancer cell growth and multiplication, it was not known whether these factors influence neighboring normal cells.

Now a team of researchers from the University of Delaware, Nemours/A.I. duPont Hospital for Children, St. Joseph's Hospital and Medical Center in Phoenix and Therapy Architects LLC in Wilmington, Delaware, has reported that cancer cells can actually cause neighboring normal cells to become cancerous. The research is documented in the current online edition of the *Journal of Cell Science*.

The researchers used a three-dimensional co-culture system where they grew normal cells and cancer cells together, mimicking the situation inside the body.

They found that cancer cells produce an enzyme—a protease—which splits a cell-cell adhesion molecule called E-cadherin from normal cells. The action of the protease liberates the segment of E-cadherin that projects outside the cells. This segment, designated soluble E-cadherin, or sE-cad, then associates with a signaling molecule called epidermal growth factor receptor on normal cells and converts them to cancerous cells.

"The serum of adult cancer patients contains high levels of sE-cad," says Pratima Patil, who received her doctorate in biological sciences from the University of Delaware earlier this year. "Our finding documents that tumor cells modify normal epithelial cells, disrupting their cellular architecture, and use them as accomplices to generate sE-cad, which is

known to facilitate tumor progression."

Ayyappan Rajasekaran, University of Delaware adjunct professor in materials science and engineering and president of Therapy Architects, says this is the first time research has demonstrated that a cancer cell can sequentially induce early and late stages of cancer development in neighboring normal cells—a fundamental finding that can inform future studies.

"Like bacteria and viruses, cancer cells have the potential to infect normal cells and promote cancer progression," he adds.

This finding opens up new cancer research areas, including determining how cancer cells interact with neighboring normal cells and promote cancer development.

From a clinical perspective, the discovery raises the question of whether reducing sE-cad levels in cancer patients will slow the progression of cancer and improve treatment options.

"These future studies should give a new dimension to our understanding of cancer development and treatment," Rajasekaran says.

More information: "Carcinoma Cells Induce Lumen Filling and EMT in Epithelial Cells by soluble E-cadherin-Mediated Activation of EGFR," *Journal of Cell Science*, 2015.

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