Cornell University
College of Veterinary Medicine

First proven origin of ovarian cancer could unlock earlier detection in other human cancers

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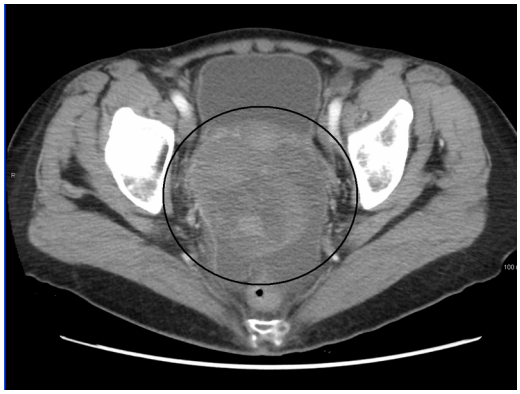
The most common and aggressive type of ovarian cancer, ovarian carcinoma, leaves a dark trail. Science has learned too little and most women learn too late to treat the deadly disease. Now Cornell scientists have found ovarian carcinoma's first proven origin cells and uncovered clues for finding similar sources of other cancers. Published in Nature in March 2013, the study opens paths for new screening methods to detect cancer earlier and increase treatment chances in the ovaries and beyond.



A very large ovarian cancer as seen on CT

Most organs have stem-cells, which help healing and development, but many cancers start when such cells go astray. Using a novel cell location technique never before used in ovaries, the Cornell study uncovered a nest (niche) of particularly cancer-prone stem cells at an area in the ovaries where different tissue types meet. It provides the most direct proof yet that vulnerable stem cells can nest near such tissue junctions, which occur throughout the body.

"Poor understanding of ovarian cancer's development has posed the biggest roadblock to helping its victims," said Dr. Alexander Nikitin, pathology professor at Cornell's College of Veterinary Medicine and leader of the Cornell Stem Cell Program. "We have found what is very likely to be the source of cells from which ovarian carcinoma arises, as well as the strongest suggestion yet that cancer-prone stem cells can nest in tissue junctions. This could spur new discoveries of cancer-prone stem cell niches throughout the body, revealing new ways to screen for and diagnose several different cancers."

A woman's risk of getting aggressive ovarian cancer in her lifetime is about 1 in 72, according to the American Cancer Society. Once diagnosed, 70% will die within five years. No good screening tests exist, but uncovering a specific location that seeds it could let people catch it earlier and change those chances for the better.

Nikitin's lab found the new cancer-prone stem cell niche using direct lineage tracing, a new technique that labels and tracks cells. The niche, found near the junction of the ovaries and the uterine tube (also known as the Fallopian tube), houses stem cells that regenerate the ovarian surface epithelium, a cover that opens when females ovulate and must grow back each time.

But Nikitin's team found that these cells turned cancerous when two important tumor suppressor genes p53 and Rb were deleted. These genes have been shown to be inactive in human ovarian carcinoma. Nikitin's lab had previously

Stem cells expressing stem cell marker ALDH1 (red) and retaining proliferation label BrdU (green) in the hilum region of the ovary

proven that properly functioning p53 and Rb protected against ovarian carcinoma development in the mouse.

The new study showed that newly discovered stem cells without p53 and Rb grew faster and showed more aggressive metastatic behavior compared to more mature cells. Nikitin is now working on leveraging his lab's discoveries to find cancer-prone stem cells at similar junction areas in human ovaries and other places where two different types of tissue converge, such as the esophagus and stomach, anus and rectum, and different parts of the uterus. Such junctions are breeding grounds for tumors.

"Until now, we have had no explanation for why so many tumors form at junction sites," said Nikitin. "Our study suggests new undiscovered stem cell niches might occur beyond the ovaries. It's likely to lead scientists to search for similar cancer-prone stem cell niches at other junctions, which could lead to specific diagnostic screening tests to detect cancers earlier."