Ovarian cancer cells hoard iron to fuel growth

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Cancer cells tend to hoard iron, and researchers at UConn Health have found that iron may be playing a critical role in fueling the cells' growth through increased fatty acid synthesis. Credit: Yesenia Carrero/UConn Illustration

An unexpected link between iron and fatty acids may be juicing the

metabolism of ovarian cancer cells, report UConn Health researchers in the July 1 issue of *OMICS: A Journal of Integrative Biology*. The findings could suggest new avenues of research for cancer treatments.

Ovarian cancer is the fifth leading cause of cancer deaths in women ages 35 to 74, and about one in 75 women will be diagnosed with it in their lifetime, according to the National Ovarian Cancer Coalition.

Cancer cells tend to hoard iron, and ovarian cancer cells in particular. They take in more iron than normal cells, and they release less of it. UConn Health postdoctoral fellow in computational biology Anna Konstorum, director of the Center for Quantitative Medicine Reinhard Laubenbacher, and their colleagues wondered why. Perhaps cancer cells' iron habit was a weakness doctors could use against the disease.

To figure out what the cancer cells were using the iron for, Konstorum analyzed data from four different publicly available datasets. Two of them contained cells from advanced ovarian cancers and their immediate environment in the body; a third dataset contained both normal and cancerous tissue from ovarian cancer patients but not the cancers' environment; and a fourth contained just stem cells from ovarian cancers and normal tissue. The researchers hoped that, because each dataset contained slightly different information, finding the same pattern in all of them would be significant. And indeed, one unusual pattern appeared in all four of Konstorum's analyses. Altered iron uptake seemed to be connected to increased fatty acid production. Fatty acid production tends to be increased in cancer cells, and the researchers thought the connection to iron could be significant.

"Iron may be playing a critical role in increased fatty acid synthesis in cancer. No one knew that before," Konstorum says. Fatty acids are essential building blocks for cell walls and for the messages cells send each other. Prostaglandins, for example, are messenger molecules that

alert other cells and cause inflammation. Inflammation is also associated with cancer. Prostaglandins are made from arachidonic acid, one of the fatty acids whose metabolism that Konstorum's analysis connected to iron levels.

"When you read about cancer, it's almost always about genetics. But it's only recently that people have begun to think about metabolism; what cells do, instead of how they're made," says Laubenbacher.

Konstorum, Laubenbacher, and their colleagues found three major pathways connecting increased iron to increased fatty acids. The first encourages cells to import more fatty acids. The second affects iron-binding enzymes that can build other molecules from fatty acid building blocks. The third also affects iron-binding enzymes, in this case the enzymes that control the levels of mono- and poly-unsaturated fatty acids in the cell.

The researchers are currently working with UConn Health's Torti lab to test whether the connections they identified in the data affect living cancer cells.

More information: Anna Konstorum et al. A Systems Biology Approach to Understanding the Pathophysiology of High-Grade Serous Ovarian Cancer: Focus on Iron and Fatty Acid Metabolism, *OMICS: A Journal of Integrative Biology* (2018). DOI: 10.1089/omi.2018.0060

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