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Researchers identify key enzyme that regulates the early growth of breast cancer cells

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New University of Georgia research, published this week in the early online edition of the journal *Proceedings of the National Academy of Sciences,* has found that blocking the action of an enzyme called GnT-V significantly delays the onset and spread of tumors in mice with cancer very similar to many cases of human breast cancer.

When the GnT-V enzyme activity in the cells was increased in mammary gland cells, they increased proliferation and began to take on many characteristics of cancer cells. Using a mouse model of human breast cancer, tumors appeared when the enzyme was deleted, but onset was delayed an average of 10 weeks in the mice.

"In human terms," said Michael Pierce, director of the UGA Cancer Center and study co-author, "the corresponding delay would be many months and maybe years. You basically are slowing everything down and keeping the cancer from forming and progressing very early." Slowing the pace of the cancer could eliminate its spread to other organs, keeping it localized where it could be treated successfully, Pierce explained.

The researchers, lead by Hua-Bei Guo, assistant research scientist in the department of biochemistry and molecular biology in the Franklin College of Arts and Sciences, stimulated breast cancer formation in mouse mammary glands by over-expressing a her-2 protein that is a growth receptor on the cell surface. The researchers note that over-

expression of her-2 is associated with 25 to 30 percent of human breast cancers.

The GnT-V enzyme makes glycans, which are sugars on the cell surface that change in defined ways when the cell becomes cancerous. Glycans are released from the cell as glycoproteins, making them a promising early-detection marker in blood. The researchers studied a glycan made by GnT-V that appears when normal breast cells become cancerous. The GnT-V glycan product is found on her-2 and other receptors and acts to regulate the number of cancer stem cells in the tissue. The number of these cancer stem cells determines how rapidly the cancer will form and develop.

"Glycans often are ignored by scientists, because they're very complicated and present unusual problems to identify and understand," said Pierce. "This study is an example of how particular glycans that are present on various cell receptors can actually modulate the onset of tumor formation. That may give us new drug targets and new ways to kill the cancer cells specifically."

The finding of Guo and the research team at UGA's Complex Carbohydrate Research Center that the elimination of a glycan-synthesizing enzyme significantly reduced the population of breast cancer stem cells is unprecedented, they note.

"That population of cells appears to drive breast tumor formation in many cases," said Pierce, who also is UGA's Mudter Professor in Cancer Research, "and our research suggests that glycans may be potential targets to kill them selectively."

Pierce likened the cancerous stem cells to the queen of an ant colony. "You can try to get rid of the anthill, but it will just come back if you don't kill the queen," Pierce said. "If we can target those cancer stem

cells for elimination, that would be the most effective treatment."

Provided by University of Georgia