Research improving breast cancer treatment by targeting tumor initiating cells

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A Kansas State University professor's research on breast cancer stem cells may help improve survival rates by preventing cancer recurrence and metastasis—the major causes of death among breast cancer patients.

Anna Zolkiewska, associate professor of biochemistry and molecular biophysics, has received a four-year $1.245 million grant from the National Cancer Institute—at the National Institutes of Health—to study a promising breast cancer marker called ADAM12. The grant is titled "ADAM12 in breast tumor initiating cells."

The grant currently is the biggest National Cancer Institute commitment to fund a single investigator at Kansas State University. Zolkiewska also is completing a three-year $444,000 grant from the National Institutes of Health for research on mutations in the ADAM12 gene.

Zolkiewska's research focuses on breast tumor initiating cells, called BTICs, which also are known as cancer stem cells. These cells drive breast tumor progression and tumor recurrence or metastasis.

"Our studies strive to produce new research and diagnostic tools for detection of breast tumor initiating cells and to develop new therapies to target these cells," Zolkiewska said.

While current treatments for breast cancer—such as surgery, chemotherapy and radiation therapy—can destroy the majority of tumor cells, these treatments cannot eradicate cancer stem cells. Current

treatments also have many negative side effects.

"The problem is that cancer stem cells are present in very low amounts," Zolkiewska said. "They are difficult to detect. But we know that they exist and they are practically resistant to chemotherapy and radiation therapy."

Even when chemotherapy appears to work, breast tumor initiating cells can cause tumors to re-emerge or metastasize to bones, lungs or the brain.

"Once metastasis occurs, the chances to cure the patient decrease dramatically," Zolkiewska said. "It is absolutely critical to be able to identify cancer stem cells and to find more effective treatments against them."

Zolkiewska is focusing on ADAM12, which a member of the ADAM family of cell-surface disintegrin-metalloproteases. Unlike other current cancer markers—which are found in both healthy and cancerous tissues—ADAM 12 is not expressed in healthy human mammary glands. Zolkiewska's work suggests that ADAM12 is induced precisely in breast cancer stem cells.

"We might be able to use ADAM12 to develop targeted therapies to eradicate cancer stem cells with less side effects, which is of great importance," Zolkiewska said. "Ultimately, we hope we can improve the quality of life for breast cancer patients."

The research can provide clinicians with better diagnostic tools for breast cancer, new cancer prevention strategies and improved treatment options. ADAM12 can be used with existing markers for improved detection, isolation and characterization of breast tumor initiating cells in the laboratory.

Long term, Zolkiewska wants to understand exactly how ADAM12 functions in cancer stem cells at the molecular level. She also wants to better understand how breast tumor initiating cells differ from other breast tumor cells.

"We are especially grateful to the Johnson Cancer Research Center at Kansas State University because they have provided us with support for preliminary work," Zolkiewska said. "Preliminary data are absolutely critical to obtain major grants from the National Institutes of Health. The center has really helped us over the years."

Zolkiewska's research team includes Hui Lui, postdoctoral researcher; Sara Duhachek Muggy, doctoral student in biochemistry, Manhattan; and Yue Qi, doctoral student in biochemistry, China. Zolkiewska also is a member of the University of Kansas Cancer Center and collaborates with the University of Kansas Medical Center.

Zolkiewska and her team will present their research at the prestigious Gordon Research Conference in May in Tuscany, Italy.

Provided by Kansas State University