UBC discovery may lead to 'smart' therapies for breast, ovarian cancer

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New non-toxic and targeted therapies for metastatic breast and ovarian cancers may now be possible, thanks to a discovery by a team of researchers at the University of British Columbia.

In a collaboration between UBC stem cell and cancer scientists, it was found that a protein called podocalyxin – which the researchers had previously shown to be a predictor of metastatic breast cancer – changes the shape and adhesive quality of tumour cells, affecting their ability to grow and metastasize. Metastatic cancer is invasive cancer that spreads from the original site to other sites in the body.

The discovery demonstrated that the protein not only predicted the spread of breast cancer cells, it likely helped to cause it. The findings were recently published online by the Public Library of Science.

"We believe we've found a new important culprit in metastatic breast cancer, which opens up an entirely new avenue of cancer research," says Calvin Roskelley, an associate professor of cellular and physiological science who specializes in breast cancer and is co-senior principal investigator. "The culprit is hiding in plain sight on the surface of tumour cells, so we are now developing "smart" molecules to block its function. The ultimate goal is to generate new targeted, non-toxic treatments – very different from the standard 'slash and burn' chemotherapy."

The researchers found that podocalyxin significantly expands the non-

adhesive face of cells, allowing individual cells to brush aside adhesion molecules situated between tumour cells. The "freed" cells then move away from the original site to form new tumours at other sites. Also, the protein causes tumour cells to sprout microvilli, or hair-like projections, that may help propel cancer cells to other sites.

In addition, when the protein expands the non-adhesive face of cells it drags along with it a second protein called NHERF-1 – a protein shown by others to be implicated in cell growth and invasion. The researchers now believe the mechanism applies to difficult-to-treat invasive breast and ovarian cancers.

"We're now tapping into what causes the characteristic cell shape changes seen in cancerous tumours and possibly how these cells grow and metastasize. It gives us a whole new target for therapy," says Assoc. Prof. of Medical Genetics and stem cell expert Kelly McNagny, co-senior principal investigator. "If we can block the protein, we may be able to stop the spread of cells."

Post-doctoral Fellow Julie Nielsen, of UBC's Biomedical Research Centre, and PhD student Marcia Graves of the Dept. of Cellular and Physical Sciences, were instrumental in designing and executing the research experiments, he adds.

Next steps involve advancing the research in animal models, designing antibodies to block the function of the protein and working with the UBC-based Centre for Drug Research and Development to identify new therapies to combat metastasizing cancer.

The researchers say information from this discovery may speed development of new therapies to within 10 years.

In 2006, more than 22,000 women were diagnosed with breast cancer

and 5,300 died of it, according to estimates from the Canadian Breast Cancer Foundation. The Canadian Cancer Society estimates that approximately 2,300 new cases of ovarian cancer were diagnosed and about 1,600 women died from the disease in 2006.

Source: University of British Columbia