UBC expert immobilizes tiny structures linked to metastatic breast cancer

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Although breast cancer treatment has made great strides, around 5,000 Canadian women are still expected to succumb to the disease in 2019 alone. And it's not the breast tumour that will kill them; it's the spread of the cancer cells to other sites—a process called metastasis.

Karla Williams, a professor in the faculty of pharmaceutical sciences at UBC and the Canada Research Chair in Oncology is researching potential treatments for metastatic breast cancer (MBC) by studying invadopodia—structures in cancer cells that are thought to play a key role in the spread of the disease. We ask her about her early findings and what they could mean for women with MBC.

Why is metastatic breast cancer so challenging to treat?

Metastatic breast cancer is cancer that has spread to other organs, often the bones, lungs and brain. Despite effective treatment of the primary tumour, some women will still end up with metastatic disease. It's very, very difficult to treat because we don't know very much about how it spreads and how it grows in what should be foreign soil. There are thousands of women in Canada living with MBC and unfortunately many of them will die from this disease.

That said, the research on invadopodia is showing some promise in understanding metastatic breast cancer. Invadopodia—podia is Latin for feet—are tiny structures that stick out from the cancer cell. They seem to kick their way through tissue, out into the bloodstream and into other sites, enabling cancer cells to implant themselves outside their original location in the breast.

In our lab, we're looking at how certain proteins can spur the growth of these structures and help them move around the body. We're also studying what drives the growth of the cancer cells when they arrive at their secondary location. I was recently fortunate to receive a $600,000 grant from the Susan G. Komen Foundation to further support this research.

What have you learned so far?

We've established that GABA, a common molecule in the brain, functions as a critical energy source for invadopodia. We described this in a paper we published in January. Invadopodia are capable of sensing GABA and using it to support the spread of breast cancer. This could have implications for how we prevent or possibly treat metastatic breast tumours in the brain.

We're currently focusing on using CRISPR to edit out a gene—Tks5—that's essential for invadopodia formation. We've found that breast cancer cells lacking the Tks5 gene can't form invadopodia. We've used these cells in a mouse model to generate a breast tumour and found that the cancer cells aren't breaking through into the lymphatic system and spreading into other organs—they're effectively being neutralized. We're excited by this breakthrough.

What does this mean for women with MBC?

We're hoping that our Komen-funded project will figure out exactly when and how invadopodia support metastatic disease. This will help us determine when targeting them will give the biggest impact to patient outcomes.

After that we will look for drugs that can target these "feet". We'll start by testing commonly used therapeutics that are already on the market and can stop the cancer cells from walking around the body and setting up new homes.

If we can do all these, we can stop more women with breast cancer from progressing to MBC.

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