Breast cancer impersonates neurons to invade the brain

- 20:00 06 January 2014 by **Alyssa Botelho**
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Women with breast cancer often enjoy several years in remission, only to then be given the devastating news that they have developed brain tumours. Now we are finally starting to understand how breast cancer cells are able to spread undetected in the brain: they masquerade as neurons and hijack their energy supply.

For every tumour that originates in the brain, 10 arrive there from other organ systems. Understanding how tumours spread, or metastasise, and survive in the brain is important because the survival rate of people with brain metastases is poor – only a fifth are still alive a year after being diagnosed.

Rahul Jandial, a neurosurgeon at the City of Hope Cancer Center in Duarte, California, wanted to explore how breast cancer cells are able to cross the blood-brain barrier and escape destruction by the immune system.

"If, by chance, a malignant breast cancer cell swimming in the bloodstream crossed into the brain, how would it survive in a completely new, foreign habitat?" Jandial says. He and his team wondered if breast cancer cells that could use the resources around them – neurotransmitters and other chemicals in the brain – would be the ones that survived and flourished.

To test the idea, they took samples of metastatic breast cancer cells from the brains of several women and grew them in the lab. They compared the expression of proteins involved in detecting and absorbing GABA – a common neurotransmitter that neurons convert into energy – in these cells with what happens in non-metastatic breast cancer cells.

Masters of disguise

Sure enough, the breast cancer cells taken from the brain expressed a receptor for GABA, plus a transporter protein that brings GABA into the cell, and a host of other compounds that convert GABA into energy. In this way, the metastatic tumour cells had in effect disguised themselves as neurons. No such machinery was seen in the non-metastatic breast cancer cells.

"The idea that metastasising cells can adopt a new identity, shielding them from intrinsic defence mechanisms, is very exciting and suggests that cancer cells are likely more plastic than previously suspected," says Ellen Carpenter, a neuroscientist at the University of California, Los Angeles, who was not involved in the work. "I think this is likely a tremendous advance in breast cancer research."

But understanding the neuronal disguise – a mechanism that other cancers may be using to spread in the brain, says Jandial – requires further work. For example, it's not clear whether breast cancer cells evolved the GABA machinery by chance over time, or somehow acquired it from their environment.

Still, Jandial hopes the results will lead to new chemotherapies based on existing drugs for

brain cancers or neurodegenerative disease, or help us discover novel drugs to treat tumours that spread to the brain.

Journal reference: *PNAS*, DOI: 10.1073/pnas.1322098111