Understanding what drives breast cancer

Dr Clare Davies

The University of Birmingham's School of Cancer Sciences is pioneering a new approach to breast cancer research, seeking to combat the increasing resistance to treatments of the disease that claims around 11,000 lives annually. The research, funded by the Birmingham Fellowship is seeking to understand a group of enzymes, known as Protein Arginine Methyltranferases (PRMTs), which are elevated in breast cancer patients. The research will explore whether the increased amounts of PRMTs contribute to the development of breast cancer or occur as a consequence of the disease.

Methylation of proteins by PRMTs has been known for over 40 years, but very little is actually known about how they are regulated and contribute to disease. Heightened levels occur in breast cancer sufferers and it is expected that this new research will show they are causative of breast cancer.

What we do know about PRMTs is that their expression levels are elevated in a number of human cancers and breast cancer has been the most studied cancer with regard to these enzymes. One of the main things we need to investigate is alternative strategies in which to treat breast cancer because it often becomes resistant to conventional drugs.

Tamoxifen is widely prescribed to treat ER-positive breast cancer, but in many cases the cancer becomes resistant to the drug in the long-term. This is because cancer cells are 'pretty cunning' and are able to change. Rather than dying, they mutate or develop mechanisms to remove the drug from the cancer cell.

The breast cancer stem cell hypothesis is that there's a sub-set of cells, called cancer stem cells, that are resistant to conventional treatment. This is because they divide very infrequently. Many chemotherapies work by targeting cells that are dividing, thus the majority of the proliferating cancer is destroyed, but the cancer-initiating cells remain. The stem cell hypothesis is not applicable to every tumour, but the stem cell population could be the reason why you get relapse – because conventional drug treatment will hardly ever target the stem cell population. PRMTs are known to be important for maintaining the stem cell population.

This new research, then, will focus on deepening medical scientists' understanding of the role of PRMTs in bolstering cancer stem cells.

Normal breast tissue has pluripotent stem cells, meaning that a single cell population can give rise to all the major specialised cell types of the breast, a process particularly important in pregnancy. Human breast tumours display enrichment for cells that have stem-like properties. Therefore, targeting the cancer stem cell compartment with inhibitors would be a major step forward.

Conventional chemotherapy is incredibly toxic – targeting rapidly dividing healthy cells as well as cancerous ones, resulting in patients suffering stomach problems and hair loss.

By understanding which proteins are modified by PRMTs in cancer cells, maybe we can develop specific inhibitors for them. This would enable us to target the cancer cell and leave others alone. This would make the treatment more powerful and reduce the side effects.

However, researchers still need to understand how these proteins are driving breast cancer, either in the stem cell compartment or in the tumour itself.

What we need to know is whether they are a cause or a consequence of the cancer. The research is still in its infancy, but finding something new could have a positive effect on the lives of a lot of people.

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