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How a particular gene protects against aggressive breast cancer

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Women with an inactive Wnt5a gene run a higher risk of aggressive breast cancer. In a transatlantic collaboration between Karolinska Institutet and Weill Cornell Medicine in New York scientists have discovered how Wnt5a prevents tumour development. The study is published in the periodical *PLOS Genetics*.

Breast cancer is globally the most common form of cancer in women, with 7,800 women in Sweden alone having been diagnosed with the disease in 2013 and the number of new cases rising by an annual two per cent.

Previous large studies have shown that women who have an inactive Wnt5a gene are at greater risk of developing aggressive breast cancer.

Inhibits ability

An active Wnt5a gene, on the other hand, inhibits the ability of cells to propagate and form tumours. The precise mechanism behind this phenomena has been unclear, but now the researchers have found an explanation. The building blocks of the human body are made up of proteins manufactured in our cells in protein factories called ribosomes. The creation of ribosomes – ribosomal biogenesis – is a highly complex process that consumes 60 to 80 per cent of a cell's total energy. Tumour cells, which divide more often than normal cells, need more proteins and therefore more ribosomes in order to continue the mitotic process.

Ribosomal biogenesis is controlled by the RNA-polymerase I (Pol I) enzyme complex, which is overactive and uncontrolled during cancer.

"Our research group has discovered that an active Wnt5a gene regulates and inhibits Pol I activity and with it ribosomal biogenesis in breast cancer cells, which inhibits cell growth and division," explains Theresa Vincent, research group leader at Karolinska Institutet's Department of Physiology and Pharmacology and at Weill Cornell Medicine's Department of Physiology and Biophysics.

New treatment

Their results show why drugs that mimic the activity of the Wnt5a gene could lead to a new treatment for aggressive breast cancer.

"We also show that breast cancer patients with an active Wnt5a live longer than those without," continues Dr Vincent. "With a better understanding of ribosome biology we will be able to design new types of drug able, hopefully, to combat aggressive breast cancer tumours and possibly other forms of cancer too."

More information: Randall A. Dass et al. Wnt5a Signals through DVL1 to Repress Ribosomal DNA Transcription by RNA Polymerase I, *PLOS Genetics* (2016). DOI: 10.1371/journal.pgen.1006217

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