Newly discovered enzyme implicated in the spreading of cancer

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"We hope our new knowledge will make it easier to find a substance that can prevent cancer spreading," says Professor Pål Falnes (left) and the principal person behind the study, former postdoc, Stefan Kernstock. Credit: Yngve Vogt

Enzyme hunters at UiO have discovered the function of an enzyme that is important in the spreading of cancer. Cancer researchers now hope to inhibit the enzyme.

The new discovery could be groundbreaking for patients with metastasised cancer, in other words cancer that is spreading seriously. Enzyme hunters at the University of Oslo have discovered the function of an enzyme that causes cancer cells to spread.

"The enzyme may help cancer cells survive. We have shown that cells that lack the enzyme grow more slowly than normal cells. Our findings

may be important in relation to treating cancer. We hope our new knowledge will make it easier to find a substance that can prevent cancer spreading. One can envisage a cancer medicine consisting of bespoke inhibitors of the enzyme," says Professor Pål Falnes of the Institute for Molecular Biosciences at the University of Oslo. The research was conducted as a collaboration with Oslo University Hospital. The results were recently published in *Nature Communications*.

Hunting for enzymes

Hunting enzymes is very laborious work. To understand enzymes the researchers require detailed knowledge about the genetic material and proteins.

The human genome consists of more than 20,000 genes. Genes are codes for proteins. They contain recipes for how the proteins should be put together in long chains consisting of 20 different types of building blocks, called amino acids. Today, researchers understand the function of only half of the proteins in our cells.

Many proteins are enzymes. Enzymes are catalysts. They ensure that biochemical reactions in cells keep going.

Pål Falnes researches unknown enzymes. To achieve this he is joined by researchers with backgrounds from biochemistry, genetics, bioinformatics and cell biology.

Marking of proteins

The researchers must also be on the front line of epigenetics. Epigeneticists study how genes can be turned on and off and how epigentic information can be passed on from one generation to the next.

This information can be affected by external stimuli such as the environment and lifestyle.

Our genome is a long chain that consists of four different building blocks: adenine, thymine, guanine and cytosine. The order of these building blocks constitutes the genetic information.

Our genome is packed together with a certain type of protein called histones. There are a number of enzymes in the cell that can add and remove epigenetic markers to both histones and in the DNA to turn genes on and off. One type of marker is methyl molecules, which consist of a few hydrogen and carbon atoms.

The special enzyme that the researchers at UiO have discovered the function of may also fix such methyl markers to histones, but their main job is to attach such markers to another, very important protein.

Cancer spreading

In 2011, a German group of researchers from Heidelberg University established that the newly discovered enzyme is important in relation to a cancer cell's ability to spread and invade other tissue.

However, it was the researchers at the University of Oslo who revealed the enzyme's properties.

"Even though this is a big breakthrough, we still know little about how the enzyme stimulates cancer to spread and how important it really is. It may be that the enzyme affects the epigenetic methyl markers in cancer cells in such a way that the tumour becomes more aggressive," says Falnes.

Professor Jonathan Sleeman in the German group of researchers told

Apollon that the results of the Oslo group are very exciting because they reveal how the enzyme functions.

From yeast to human cells

Molecular biologists often used single celled organisms, such as yeast or bacteria, to determine the function of enzymes. The problem was that the enzyme the UiO researchers have discovered the function of does not exist in such model organisms. The principal person behind the study, Stefan Kernstock, former postdoc at UiO and now employee of the biotechnology company Sero, has therefore conducted the research directly using human cells. He had to develop a completely new biochemical method in order to discover the special enzyme.

The innovation company Inven2 at UiO and the university hospitals have submitted an application to patent the method.

"We hope an international actor will buy and distribute the product. This will enable more people to conduct research on this enzyme," says Inven2's business developer, Kristin Sandereid.

Reversed properties

Pål Falnes has hunted for the functions of unknown enzymes since 2000. 10 years ago he discovered how one enzyme repairs damaged genes. This gained quite a bit of attention.

While the enzyme he is researching now covers a protein with methyl molecules, the enzyme he was researching then does precisely the opposite. It removes harmful methyl molecules from the DNA string. Since then, researchers have discovered that this mechanism is also used by a series of proteins that remove epigenetic methyl markers.

Eight new enzymes

Enzyme hunters at UiO have recently also shed light on a further eight unknown enzymes in people. The results also indicate that these enzymes use methyl markers to change certain proteins.

"Some of these enzymes may be important for cancer and other diseases."

Falnes's research group is now going to study these enzymes more closely.

Provided by University of Oslo