Stress can control our genes

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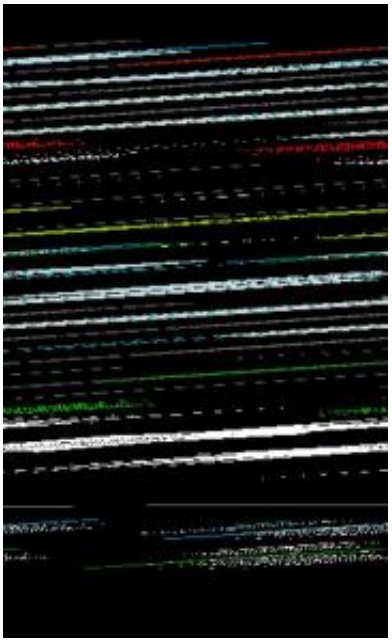

Stress-factors signal to the enzyme MSK and cause activation of silenced genes. Credit: Lise Rudkjær/Katrine Sonne-Hansen

Stress has become one of the major disease states in the developed world. But what is stress? It depends on from where you look. You may experience stress as something that affects your entire body and mind, the causes of which are plentiful. But if we zoom in on the building bricks of the body, our cells, stress and its causes are defined somewhat differently. Stress can arise at the cellular level after exposure to pollution, tobacco smoke, bacterial toxins etc, where stressed cells have to react to survive and maintain their normal function. In worst case

scenario, cellular stress can lead to development of disease.

Researchers from Dr.Klaus Hansen's group at BRIC, University of Copenhagen, have shown that external factors can stress our cells through the control of our genes. "We found that stress-activating factors can control our genes by turning on certain genes that were supposed to be silenced. It is very important that some genes are on and others are off in order to ensure normal foetal development and correct function of our cells later in life" says Dr. Klaus Hansen.

Simmi Gehani, PhD-student in the Hansen group, found that exposing human cells to a stress-activating compound turned on silenced genes. Even brief changes in gene activation can be disastrous during foetal development as establishment of correct cellular identity can be disturbed in our cells. But altered gene activity can also have consequences in the adult body. "For example, one could imagine that prolonged stress causes nerve cells in the brain to produce hormones and other signalling molecules they do not normally produce and this can disturb normal brain function" says Simmi Gehani.

The Hansen research group is very interested in understanding how our genes are turned on and off. "We know that different protein complexes can associate with specific proteins (histones) to which DNA is wound around and thereby determine whether the genes are active or inactive. Small chemical groups can cause protein complexes to bind to histones and these can control gene activity" says Dr. Klaus Hansen. The researchers have studied in detail a complex called PRC2.

PRC2 can attach small chemical groups - methyl groups - to the histones. Protective complexes can bind to the histones when this marker is present and the genes are turned off. Their new results show that the protective complexes are lost and selected genes turned on when cells are exposed to external stress factors. The reason why the complexes are lost

is that the stress factors instruct an enzyme named MSK to attach another chemical group - a phosphate group - to the histones neighbouring the methyl group. The phosphate group neutralises the effect of the methyl group and turns specific genes on.

"The consequence is that genes that should be turned off are now active and this may disturb cellular development, identity and growth" says Simmi Gehani. This means that without damaging our genetic code external stress factors can control the activity of our genes.

The results are published today in the renowned international journal *Molecular Cell*.

Provided by University of Copenhagen