'REST' is crucial for the timing of brain development

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Researchers have just shown that the molecule REST acts as an adapter in stem cells, and hope that future studies of REST will contribute to the development of new types of treatments for diseases such as cancer.

Upon fertilisation, a single cell is formed when egg and sperm fuse. Our entire body, with more than 200 specialised cell types and billions of cells are formed from this single cell. It is a scientific mystery how the early stem cells know what cell type to become, but a precise timing of the process is crucial for correct development and function of our body. Researchers across the world chase knowledge about our stem cells, as this knowledge holds great promises for development of treatment against several major diseases. Researchers from BRIC, University of Copenhagen, have just shown that the molecule REST acts as an adapter in stem cells, coupling molecular on-off switches with neural genes and thereby times neuronal development.

"REST secure neuronal genes to be turned off in our stem cells until the correct time point in fetal life, where the molecule is lost and development of the nervous system begins. Our results are very important for the understanding of how genes are turned on and off during fetal development, but also relates to disease development such as cancer. Hopefully, our future studies of REST will contribute to the development of new types of treatments," says Associate Professor and Group Leader at BRIC, Klaus Hansen.

Genetic switches

All our cells contain the same DNA, yet they can develop into specialised cells with different shapes and functions. This ability is due to only selective genes being turned on in for example neuronal cells and other genes in liver cells and skin cells. Postdoc Nikolaj Dietrich from Klaus Hansen's laboratory has been the main driver of the investigation:

"Our results show that REST act as an adapter for the protein complexes called PRCs, connecting these complexes to neuronal genes. The PRCs are genetic switches turning off genes and therefore REST and the PRCs act in concert to shutdown neuronal genes. A similar mechanism has previously been described in fruit flies, but until now, no one has been able to identify such adapter-molecules in humans or other mammals. This has led to various biological hypotheses, but now we are able to show that this genetic mechanism has been conserved trough out evolution," says Nikolaj Dietrich.

Brain damage and brain tumors

REST and PRC are attached to neuronal genes in the early fetal stem cells, keeping neuronal genes turned off. During fetal development, REST disappears in cells that are determined to develop into neuronal cells, whereas the molecule is preserved in other cell types. REST is also preserved in special neuronal stem cells, ensuring that these cells maintain their stem cell properties. This is crucial if we experience damage to our nervous system later in life, as only the neuronal stem cells can repair the damage by giving rise to new neurons and thereby secure vital body functions. However, REST also appears to be associated with a higher risk of cancer:

"An increased amount of REST has been found in the brain tumor form

called neuroblastoma. Some of our results indicate that REST may be involved in cancer, as the molecule can turn off some growth-inhibitory and cancer-protective genes called tumor suppressors. This possible action of REST is the focus of ongoing studies," says Nikolaj Dietrich.

More information: The results have just been published in the international scientific journal *PLoS Genetics*: REST-Mediated Recruitment of Polycomb Repressor Complexes in Mammalian Cells, Dietrich et al. March 1, 2012.

Provided by University of Copenhagen