Reprogramming cell identity in the pituitary gland

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A team of researchers at the IRCM, supervised by Dr. Jacques Drouin, reprogrammed the identity of cells in the pituitary gland and identified critical mechanisms of epigenetic cell programming. This important discovery, published yesterday by the scientific journal *Genes & Development*, could eventually lead to new pharmacological targets for the treatment of Cushing's disease.

Dr. Drouin's team studies the pituitary gland, which is the master gland located at the base of the skull that secretes hormones to control all other glands of the endocrine system. Disruption of pituitary functions has dire consequences on growth, reproduction and metabolism.

Within the pituitary gland, each hormone is produced by cells of a different lineage. Unique cell identities are created by cell-specific genetic programs that are implemented during development. Appropriate cell programming is a critical process that needs to be harnessed in order to exploit the therapeutic benefits of stem cell research.

In their work, the IRCM researchers showed that the transcription factor Pax7 has pioneering abilities, meaning that it is able to open the tightly-packed chromatin structure of specific regions of the genome. This unmasking of a subset of the genome's regulatory sequences changes the genome's response to differentiation signals such that different cell types are generated.

"We reprogrammed the identity of pituitary cells by using the Pax7 gene

in order to create two different types of cells," says Lionel Budry, former student in Dr. Drouin's laboratory and first author of the article. "This allowed us to show that the Tpit protein produces different cell lineages according to the presence or absence of Pax7, and its impact on chromatin organisation."

Cushing's disease is caused by small tumours of the pituitary gland that produce excessive amounts of hormones. For patients with this disease, the abnormal hormone production can lead to hypertension, obesity, diabetes and osteoporosis.

"For approximately 10% of patients suffering from Cushing's disease, we found that the disease-causing tumours contain cells that express the Pax7 protein," explains Dr. Drouin, Director of the Molecular Genetics research unit at the IRCM. "No effective pharmacological treatment currently exists for Cushing's disease. This discovery could ultimately lead to the development of such treatment, based on tumour growth inhibition by hormones, similarly to what is already done for other pituitary tumours like lactotrope adenomas."

More information: genesdev.cshlp.org/content/26/20/2299.abstract

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