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PITUITARY GLAND

Understanding pituitary development

New research has identified PROP1 as a key component of pituitary stem cell differentiation. These findings could have implications for understanding the aetiology of hypopituitarism and lead to novel therapeutics.

"In humans, mutations in *PROP1* cause progressive hormone loss, and the basis for this wasn't understood," explains corresponding author Sally Camper. Previous work suggested that all hormone-producing cells in the pituitary gland are derived from PROP1-expressing progenitors, which indicates that PROP1 is involved in regulating pituitary stem cells. Camper and colleagues decided to investigate this finding further to try and improve understanding of combined pituitary hormone deficiency (CPHD) and identify a set of *PROP1* target genes that might be implicated in CPHD of unknown aetiology.

The researchers conducted genome-wide analysis of PROP1 DNA binding and its effects on gene expression in mutant mice, isolated mouse stem cells and engineered mouse cell lines. They found that a normal number of pituitary stem cells can only be established with *Prop1* expression, which is also needed for these cells to behave in a normal way. Furthermore, in the mutant stem cells, many of the genes that depend on PROP1 were involved in epithelial–mesenchymal transition-like processes. Therefore, PROP1 seems to be essential for maintenance of the stem cell pool and stimulating progenitor cells to differentiate. "We think the progressive loss of hormones in humans with *PROP1* mutations may be due to exhaustion of stem cell pools," says Camper.

The team are now collaborating with other researchers to screen candidate genes for mutations in patients with CPHD. "There is great interest in harnessing stem cell therapy for treatment, but many challenges remain," concludes Camper. "Nevertheless, we have advanced our understanding of basic pituitary stem cell biology."

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ORIGINAL ARTICLE Pérez Millán, M. I. *et al.* PROP1 triggers epithelial–mesenchymal transition-like process in pituitary stem cells. *eLIFE* http://dx.doi.org/10.7554/eLife.14470 (2016)