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Hesx1 antagonises canonical Wnt signalling in anterior forebrain and pituitary gland

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We have previously shown that the activity of the homeobox transcription factor *Hesx1* is required to specify correct forebrain development, possibly through antagonizing canonical Wnt signalling, thus maintaining anterior identity in mouse. *Hesx1* mutants exhibit anterior forebrain truncations of variable severity and in the more sensitive pituitary gland, defects resulting from the over-proliferation of precursors. Mutations in *HESX1* have been identified in patients with hypopituitarism. Our data suggest that the expression of *Hesx1* between 9.5 and 13.5 dpc in the pituitary is crucial to antagonize Wnt signalling in order to temporally regulate proliferation. We have performed conditional gain and loss of function of β-catenin experiments in the *Hesx1* domain, demonstrating that up-regulation of canonical Wnt signalling affects pro-

liferation and terminal differentiation of the Pit1-lineage in the developing gland, leading to an embryonic phenotype similar to that of loss of *Hesx1* and dwarfism in surviving animals. On the other hand, a conditional reduction in Wnt signalling is not sufficient to rescue *Hesx1* mutant pituitary defects however results in a marked improvement of the forebrain defects, confirming the role of *Hesx1* as a canonical Wnt signalling antagonist.

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