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Developmental regulatory targets of the homeobox transcription factor HESX1

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The homeobox gene Hesx1 codes for a transcriptional repressor that is expressed during mouse development in the prospective forebrain and Rathke's pouch, the primordium of the anterior pituitary. Work from our laboratory has shown that Hesx1 plays a role in the normal patterning of anterior forebrain by preventing the activation of posterior neural markers. In the anterior pituitary, Hesx1 has been shown to regulate normal cell proliferation of pituitary progenitor cells. Several lines of evidence suggest that Hesx1 is required to antagonize the activation of Wnt/beta-catenin signalling. The interaction of HESX1 with several co-repressors and with DNMT1 (DNA Methyltransferase 1) has been proposed to underlie HESX1 molecular activity. To date, however, HESX1 target genes remain essentially unknown. To gain further knowledge into the molecular function of HESX1, we have combined microarray gene expression profiling with chromatin immunoprecipitation-on-chip technology for the identification of direct HESX1 genetic targets. For this analysis we have used embryonic stem cells, where Hesx1 is normally transcribed, translated and imported into the nucleus. The role of DNA methylation in normal forebrain and pituitary gland development is being studied by combining molecular with genetic approaches. Data from these analyses are presented here.

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