

"Neuronal subtype specification in the mammalian forebrain"

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A necessary step in the assembly of functional circuits in the nervous system is the generation of multiple neuronal subtypes with unique chemical, morphological and physiological properties. As part of our studies on neuronal differentiation in mice, we have identified two novel members of the LIM-homeodomain family of transcription factors (named Lhx6 and Lhx7) which are specifically expressed in the forebrain, the region of the central nervous system that controls diverse functions such as motor co-ordination and cognition. Lhx6 is expressed in specific subpopulations of GABAergic interneurons in the cortex and deletion of *Lhx6* results in failure of specification and differentiation of a large subpopulation of cortical interneurons. Expression of Lhx7 is restricted to the ventral forebrain and its product is localised in cholinergic interneurons of the striatum and the cholinergic projection neurons of the ventral telencephalon. Moreover, deletion of *Lhx7*, results in severe reduction in the number of acetyl-choline-producing neurons in the forebrain. Our experiments address the mechanisms by which the co-ordinate activity of Lhx6, Lhx7 and other members of the LIM homeodomain family of transcription factors control the generation of GABAergic and cholinergic neurons in the mammalian forebrain. Furthermore, our findings have wider implications on the understanding of neuronal subtype specification and neuronal network formation throughout the nervous system of animals.