The development of newborn olfactory bulb interneuron regulated by the various odors.

Sei-ichi Yoshihara

Laboratory for Molecular Biology of Neural System, Advanced Medical Research Center, Nara Medical University

Sensory input has been shown to regulate development in a variety of species and in various structures, including the retina, cortex and olfactory bulb (OB). Within the mammalian OB specifically, the development of dendrites in mitral/tufted cells is well known to be odorevoked activity-dependent. However, little is known about the developmental role of sensory input in the other major OB population of the GABAgenic interneurons, such as granule cells and periglomerular cells. Here, we identified, with DNA microarray and in situ hybridization screenings, a trophoblast glycoprotein gene, 5T4, whose expression in a specific subtype of OB interneurons is dependent on sensory input. 5T4 is a type I membrane protein, whose extracellular domain contains seven leucine-rich repeats (LRR) flanked by characteristic LRR-N- and C-flanking regions, and a cytoplasmic domain. 5T4 overexpression in the newborn OB interneurons facilitated their dendritic arborization even under the sensory inputdeprived condition. By contrast, both 5T4 knockdown with RNAi and 5T4 knockout with mice resulted in a significant reduction in the dendritic arborization of 5T4⁺ granule cells. Further, we identified the amino-acid sequence in the 5T4 cytoplasmic domain that is necessary and sufficient for the sensory input-dependent dendritic shaping of specific neuronal subtypes in the OB. Thus, these results demonstrate that 5T4 glycoprotein contributes in the regulation of activity-dependent dendritic development of interneurons and the formation of functional neural circuitry in the OB.