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Nectin-1 spots regulate the branching of olfactory mitral cell dendrites

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ABSTRACT

Olfactory mitral cells extend lateral secondary dendrites that contact the lateral secondary and apical primary dendrites of other mitral cells in the external plexiform layer (EPL) of the olfactory bulb. The lateral dendrites further contact granule cell dendrites, forming dendrodendritic reciprocal synapses in the EPL. These dendritic structures are critical for odor information processing, but it remains unknown how they are formed. We recently showed that the immunoglobulin-like cell adhesion molecule nectin-1 constitutes a novel adhesion apparatus at the contacts between mitral cell lateral dendrites, between mitral cell lateral and apical dendrites, and between mitral cell lateral dendrites and granule cell dendritic spine necks in the deep sub-lamina of the EPL of the developing mouse olfactory bulb and named them nectin-1 spots. We investigated here the role of the nectin-1 spots in the formation of dendritic structures in the EPL of the mouse olfactory bulb. We showed that in cultured *nectin-1*-knockout mitral cells, the number of branching points of mitral cell dendrites was reduced compared to that in the control cells. In the deep sub-lamina of the EPL in the *nectin-1*-knockout olfactory bulb, the number of branching points of mitral cell lateral dendrites and the number of dendrodendritic reciprocal synapses were reduced compared to those in the control olfactory bulb. These results indicate that the nectin-1 spots regulate the branching of mitral cell dendrites in the deep sub-lamina of the EPL and suggest that the nectin-1 spots are required for odor information processing in the olfactory bulb.

1. Introduction

The olfactory bulb is composed of a few thousand glomerular modules, each of which receives converging axonal inputs from olfactory sensory neurons expressing the same type of odorant receptor (Mombaerts et al., 1996; Mori et al., 1999; Mori and Sakano, 2011) (Fig. 1A). An individual olfactory mitral cell projects an apical primary dendrite (apical dendrite) to a single glomerulus, receives olfactory sensory inputs within the glomerulus, and projects an axon to the olfactory cortex (Nagayama et al., 2014). Additionally, individual mitral cells project several long lateral secondary dendrites (lateral dendrites) tangentially with appropriate branching patterns, which are in direct apposition with the lateral and apical dendrites of other mitral cells and connected with granule cell dendritic spines to form dendrodendritic reciprocal synapses. In response to odor stimulation, mitral cells belonging to different but co-activated glomerular modules show synchronized spike activities at gamma-range frequency (40–100 Hz), which are thought to play important roles in the olfactory cortex for the perception, learning, and memory of the odor objects (Beshel et al., 2007; Nagayama et al., 2014; Shepherd et al., 2004). Proper dendritic connections lead to the formation of dendrodendritic reciprocal synapses between mitral cell lateral dendrites and granule cell dendrites in the deep sub-lamina of the external plexiform layer (EPL) that are responsible for the generation of gamma-synchronized

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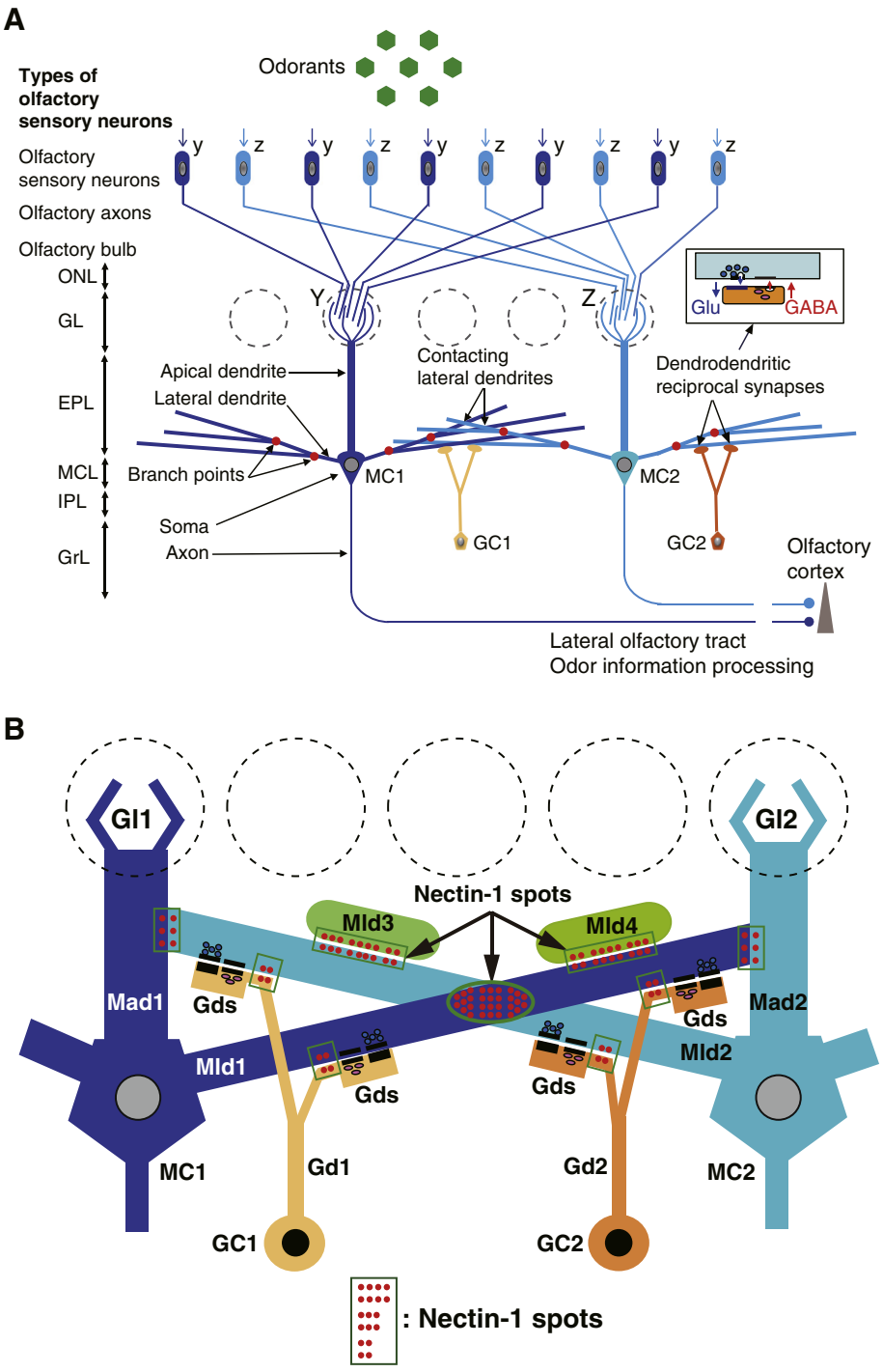

Fig. 1. Schematic representations of basic odor information processing in the olfactory bulb and the localization of nectin-1 spots. (A) Putative types of olfactory sensory neurons and the glomeruli on which their axons are converging are represented by y and z, and Y and Z, respectively. Odorants (green hexagons) simulate an ensemble of glomeruli (Y, Z). Mitral cells (MC1 and MC2) belonging to the corresponding activated glomerulus generate action potentials that are propagated not only along axons but also along lateral dendrites. The propagated action potentials on lateral dendrites activate excitatory elements of reciprocal synapses (mitral-to-granule synapses) to release glutamate (Glu), which induces excitatory post synaptic potential on dendritic spines of granule cells. Specific subsets of granule cells that are activated by mitral cells belonging to co-activated glomeruli generate spikes that propagate along whole dendritic trees to activate inhibitory elements of reciprocal synapses (granule-to-mitral synapses) inducing GABA release. (B) Schematic representation of the symmetric localization of nectin-1 (red dots, nectin-1 spots) between mitral cell lateral dendrites, mitral cell lateral and apical dendrites, and between mitral cell lateral dendrites and granule cell dendrites in the deep sub-lamina of the EPL. Green ellipsoid and rectangles show clusters of the nectin-1 spots. ONL, olfactory nerve layer; GL, glomerular layer; EPL, external plexiform layer; MCL, mitral cell layer; IPL, internal plexiform layer; GrL, granule cell layer; MC, mitral cell; Mld, mitral cell lateral dendrite; Mad, mitral cell apical dendrite; GC, granule cell; Gd, granule cell dendrite; Gds, granule cell dendritic spine.
The figure and legend are modified from an article by Inoue et al.

outputs from mitral cells (Beshel et al., 2007). The lateral extent of dendritic trees from a single mitral cell is much wider than that from a single granule cell. Thus, the arrangement and extent of overlapping of mitral cell lateral dendrites as well as dendrodendritic synapses formed between mitral cell lateral dendrites and granule cell dendrites are key determinants for efficient odor information processing derived from