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Shh Signaling and Regulatory Gene Expression in Mouse Taste Buds

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Introduction

In mammals, taste buds arise from local epithelium and are maintained by continuous cell renewal (Beidler and Smallman, 1965; Farbman, 1980; Delay et al., 1986; Stone et al., 1995). The life span of taste cells is estimated to be ~10 days. Denervation causes the degeneration of taste buds, indicating that the taste nerves trophically maintain the taste buds. It is assumed that cell proliferation, differentiation and death for taste buds are regulated in a coordinated fashion. However, the mechanism of each process in taste buds remains to be clarified.

Shh signaling in taste buds

Sonic hedgehog (Shh) is an evolutionarily conserved intercellular signaling molecule and Patched1 (Ptc) is its receptor (Ingham and McMahon, 2001). Shh signaling is known to mediate various inducative events, including cell proliferation and differentiation, in animal development. We have examined the expression of Shh signaling-related genes in taste buds of adult mice. The expression of Shh was found in the basal cells in taste buds, and Ptc expression was observed in the surrounding region of the Shh expression (Figure 1; Miura et al., 2001). This Shh and Ptc expression pattern was observed in every taste papilla (Figure 2). While Ptc expression itself can indicate the tissues responding to Shh during development (Goodrich et al., 1996; Marigo et al., 1996), the expression of Shh target gene Gli1 was also observed in almost same region where Ptc was expressed, indicating that the cells responded to Shh signal (Figure 1). Analysis of BrdU incorporation showed mitotic cells were observed mainly in Ptc-expressing region, while mitotic cells in and around taste buds have been thought to contain the taste bud progenitors (Beidler and Smallman, 1965; Delay et al., 1986). In addition, the expression of a downstream gene of Shh, Nkx2.2, was observed in a subset of taste cells (Miura et al., 2003). Nkx2.2 is a homeobox, which is induced by Shh in the ventral region of neural tube and is required for the specification of ventral neuron (Briscoe et al., 2000). These data raise the possibility that Shh signal may be involved in taste cell differentiation and that Nkx2.2-expressing cells in taste buds might be derived from the Ptc-expressing cells, which received Shh signal. The transection of cranial nerve IXth caused the

Figure 1  The expression of Shh, Ptc and Gli1. The expression of Shh was restricted to the basal cells in taste buds. Ptc was observed in the basal side of the epithelial cell around Shh expression. The expression of Gli1 was observed in almost same region where Ptc was expressed. Scale bar indicate 50 µm.

Figure 2  The expression of Ptc in taste papillae and soft palate. (A) Circumvallate papilla; (B) foliate papilla; (C) fungiform papilla; (D) soft palate. In order to detect the Ptc expression with high sensitivity in whole mount, Ptc+/– mice, in which part of Ptc exon I and all of exon II were replaced with lacZ gene, were used, and the Ptc expression was detected by X-gal staining (Goodrich et al., 1996). (A–C) The lingual epithelia were peeled off by collagenase and elastase treatment and used for staining. Ptc expression was observed in every taste bud. Scale bars indicate 50 µm.

Figure 3  Hypothetical cell lineage in taste buds. Shh may be involved in expression of Ptc and Nkx2.2. Type II cell may be derived from type III cell, while some of type III cell may be in type III cell state throughout cell life. (See text for further details.)
rapid loss of Shh expression in the basal cells in taste buds of circumvallate papillae, suggesting the possible involvement of Shh signaling in the taste bud maintenance (Miura et al., 2001).

Regulatory genes in taste buds and possible cell lineage

On the other hand, most Nkx2.2-expressing taste cells co-expressed Mash1, a bHLH transcription factor required for neuronal differentiation in CNS and olfactory epithelium (OE) (Miura et al., 2003). We have previously reported that, in taste buds, the expression of Mash1 segregated with those of taste reception-related genes, gustducin and T1R2, and that Mash1 expression preceded taste reception-related gene expressions during development (Kusakabe et al., 2002). Based on these data, we speculated that gustducin- and T1R2-expressing cells might be derived from Mash1-expressing cells. The expression of NeuroD in gustducin-expressing cells (Suzuki et al., 2002) appears to be consistent with this idea by consideration of the sequential expression of bHLH transcription factors in neuronal differentiation in olfactory epithelium: Mash1 is expressed in the early phase, and induces the expression of the other bHLH genes including NeuroD (Cau et al., 2002). Based on ultrastructural characteristics, the taste bud cells have been categorized into four cell types—basal cell, type I (dark) cell, type II cell and type III (light) cell—and some immunohistochemical markers have been shown to correlate with each cell types: gustducin and NCAM are specific for type II and type III, respectively (Yee et al., 2001). However, it is not clear whether these cell types represent separate cell lineages or transient cell states of one cell lineage (Pumplin et al., 1997; Delay et al., 1986). We found almost of all Mash1-expressing taste cells were NCAM-positive (unpublished data). Therefore, the hypothesis that gustducin-expressing cells derived from Mash1-expressing cells proposes the possible cell lineage of type II cell from type III cell. Mash1 and NeuroD are bHLH factors critical for neuronal differentiation, while Type I cell has been considered as a glia-like cell (Lindemann, 1996; Lawton et al., 2000). Recently, the expression of genes related to Delta-Notch signaling in taste buds has been reported (Seta et al., 2003). This signaling is known to be involved in neuron–glia cell fate determination, and therefore it may be possible for the Delta-Notch signaling to be involved in a cell-fate choice between neuron-like cell and glia-like cell in taste buds. Our hypothesis of taste cell lineage is summarized schematically in Figure 3.

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References


