Development of Gustatory Organs and Innervating Sensory Ganglia

Charlotte M. Mistretta¹, Arturas Grigaliunas¹,² and Hong-Xiang Liu¹

¹Department of Biologic and Materials Sciences, School of Dentistry, University of Michigan, Ann Arbor, MI, USA, ²Institute for Biomedical Research, Kaunas University of Medicine, Kaunas, Lithuania and Department of Physics, Mathematics and Biophysics, Kaunas University of Medicine, Kaunas, Lithuania

Correspondence to be sent to: Charlotte M. Mistretta, e-mail: chmist@umich.edu

Key words: fungiform papilla, geniculate ganglion, neurotrophins, sonic hedgehog, taste, trigeminal ganglion

Introduction

Taste function requires neural circuits to transmit gustatory information from taste receptor cells in taste buds, via afferent nerves to the soma of ganglion neurons, and through central ganglion processes into the brainstem. During initial formation, the sensory ganglion neurons have a key situation in establishing receptive fields by extending neurites bidirectionally, to the peripheral taste organs and to central taste nuclei.

Our laboratory is studying functional differentiation of sensory ganglia that innervate the tongue, and morphogenesis and patterning of the tongue and papilla organs. The lingual ganglia and taste papillae initially develop independently, but then become reciprocally dependent as ganglia derive molecular support from gustatory papillae and the papillae require sensory innervation for growth and morphogenesis (Mistretta, 1998). Currently our focus is on the geniculate and trigeminal ganglia, which innervate anterior tongue, and the fungiform papilla taste organs innervated by these ganglia. Geniculate and trigeminal ganglia innervate spatially contiguous, but functionally distinct, sensory organs of the fungiform papilla; the trigeminal neurons innervate lateral papilla epithelium and subserve somatosensation and nociception, whereas the geniculate axons project to central apical papilla epithelium to innervate cells that will form taste buds for gustatory sensation (Mistretta and Hill, 2003).

In this brief paper we summarize some recent work on development of tongue and taste regions, and on early functional phenotypes of the geniculate and trigeminal ganglia.

Peripheral target organs: tongue and taste papillae

The embryonic rat tongue goes through a series of morphological changes from E12 through E19, as the tongue appears as separate tissue swellings on the floor of the developing mandible, and progresses through gustatory papilla acquisition to final filiform papilla emergence (Mistretta, 1972; Mbiene et al., 1997). Using in vitro approaches we have shown that the papillae develop independently of sensory innervation (Mbiene et al., 1997). However, by embryonic day 16 of the 21 day rat gestation, the papillae are well-formed and robustly innervated by chorda tympani (from the geniculate ganglion) and lingual (from the trigeminal) nerves (Mbiene and Mistretta, 1997).

Because nerves are not essential for taste papilla initiation, we turned to study of molecular regulators and hypothesized a role for the morphogen, sonic hedgehog (Shh) (Ingham and McMahon, 2001), in target organ development. With immunoreactions we have found an initial diffuse distribution of Shh in early tongue swellings, and then a close association with papilla placodes (E14) and the formed taste papillae (E15–16) (Liu et al., 2004).

To determine functional roles for Shh in papilla development, we used whole tongue cultures in which fungiform papillae develop with temporal and spatial distributions that match formation in the embryo (Nosrat et al., 2001; Mistretta et al., 2003). Cyclopamine, a steroid alkaloid that specifically disrupts Shh signaling at the receptor, was added to cultures initiated at different stages of tongue or papilla development (Liu et al., 2004). Blocking Shh signaling had widely variant functional effects, including abrogation of tongue formation (E12 cultures); alteration of fungiform papilla size and pattern (E13); and, papilla pattern disruption including fungiform papilla formation on posterior tongue in typically papilla-free regions (E14) (Figure 1). Furthermore, in cultures begun at E16 there were no apparent effects of Shh signal disruption. Shh has, therefore, crucial and stage-specific functions in tongue and taste papilla development.

Epidermal growth factor (EGF) and its receptor (EGFR) are immunolocalized in specific lingual locations that contrast with Shh during tongue and papilla development (Liu and Mistretta, 2004). Adding EGF to tongue cultures decreased the number of fungiform papillae, in a dose dependent manner. Pre-incubation with EGF, followed by culture with EGF plus cyclopamine, prevented the cyclopamine-induced change in papilla pattern.

In summary, our data demonstrate roles for Shh and EGF in papilla development and patterning, and suggest interactions between these proteins in regulating papilla development. This is just the beginning of identifying the cast of molecules that regulate...
We used TTX to learn about sodium channel properties in different neurotrophin conditions. In culture with NGF, all E13 trigeminal neurons that were recorded had TTX-resistant (TTX-R) action potentials (Grigaliunas et al., 2003). In contrast, with BDNF in culture, action potentials from all recorded neurons were TTX-sensitive (TTX-S). For the geniculate ganglion, whether in culture with BDNF or NGF, neurons had TTX-S action potentials.

NGF can up-regulate TTX-R channel transcripts in dorsal root ganglion neurons, and down-regulate expression of TTX-S channels (Black et al., 1997). The absence of TTX-S action potentials in our embryonic trigeminal ganglion neurons sustained with NGF may be attributable to a similar effect.

In summary, trigeminal and geniculate ganglion neurons, at embryonic stages when the tongue and taste papillae are first innervated, already have distinctive electrophysiological properties including differences in sodium channel expression. These intrinsic properties are susceptible to alteration with molecular exposure, providing an avenue for target organ molecules to regulate innervating neurons.

Supported by NIH, NIDCD Grant DC00456.

### References


