CDB SEMINAR

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Wednesday, July 7, 2010

16:00~17:00 A7F Seminar Room

Wnts and Fgfs, via AKT and MAPK, direct discrete aspects of trigeminal placode development

Summary

Neurogenic placodes are focal thickenings of the embryonic ectoderm that form in the vertebrate head. It is within these structures that the precursors of the majority of the sensory neurons of the cranial ganglia are specified. The trigeminal placodes, the ophthalmic and maxillomandibular, form close to the midbrain-hindbrain boundary and many lines of evidence have shown that signals emanating from this level of the neuraxis are important for the development of the ophthalmic placode. Here, we provide the first evidence that both the ophthalmic and maxillomandibular placodes form under the influence of combined isthmic Wnt and FGF signals. Activated Wnt signals direct early development of the Pax3 expressing ophthalmic placodal field and induce premature differentiation of both the ophthalmic and the maxillomandibular placodes. Similarly, overexpression of Fgf8 directs premature differentiation of the trigeminal placodes. Wnt signals require FGF receptor activity to initiate Pax3 expression and, subsequently, the expression of neural markers, such as Brn3a, within the cranial ectoderm. Furthermore, fibroblast growth factor signaling via the PI3K/AKT pathway is specifically involved in the early regulation of Pax3 expression, whereas, MAPK activity is required to establish early neuronal differentiation within the trigeminal placodes. We demonstrate the identity of inductive signals that are necessary for trigeminal ganglion formation. Together, Wnt and FGF signals are both necessary and sufficient for the establishment and differentiation of the ophthalmic and maxillomandibular placodes and, consequently, the trigeminal ganglion. Precisely how the trigeminal placode interprets different signaling activities, specifically those downstream of the FGF receptor, is currently under investigation.

Data arising from a Wnt screen using a small molecule natural product library will also be discussed, particularly in the context of vesicular acidification requirements and Wnt secretion.

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