BMP - a key signaling molecule in specification and morphogenesis of sensory structures

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Akademisk avhandling

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Abstract
Cranial placodes are transient thickenings of the vertebrate embryonic head ectoderm that will give rise to sensory (olfactory, lens, and otic) and non-sensory (hypophyseal) components of the peripheral nervous system (PNS). In most vertebrate embryos, these four sensory placodes undergo invagination. Epithelial invagination is a morphological process in which flat cell sheets transform into three-dimensional structures, like an epithelial pit/cup. The process of invagination is crucial during development as it plays an important role for the formation of the lens, inner ear, nasal cavity, and adenohypophysis. Using the chick as the model system the following questions were addressed. What signals are involved in placode invagination? Is there any common regulatory molecular mechanism for all sensory placode invagination, or is it controlled by unique molecular codes for each individual placode? Are placode invagination and acquisition of placode-specific identities two independent developmental processes or coupled together? To address this we used in vivo assays like electroporation and whole embryo culture. Our in vivo results provide evidence that RhoA and F-actin rearrangements, apical constriction, cell elongation and epithelial invagination are regulated by a common BMP (Bone morphogenetic protein) dependent molecular mechanism. In addition, our results show that epithelial invagination and acquisition of placode-specific identities are two independent developmental processes.

BMP signals have been shown to be essential for lens development and patterning of the retina. However, the spatial and temporal requirement of BMP activity during early events of lens development has remained elusive. Moreover, when and how retinal cells are specified, and whether the lens plays any role for the early development of the retina is not completely known. To address these questions, we have used gain- and loss-of-function analyses in chick explant and intact embryo assays. Here, we show that during lens development BMP activity is both required and sufficient to induce the lens specific marker, L-Maf. After the L-Maf upregulation the cells are no longer dependent on BMP signaling for the next step of fiber cell differentiation, which is characterized by up-regulation of δ-crystallin expression. Regarding the specification of retinal cells our results provide evidence that at blastula stages, BMP signals inhibit the acquisition of eye-field character. Furthermore, from optic vesicle stages, BMP signals emanating from the lens are essential for maintaining eye-field identity, inhibiting telencephalic character and inducing neural retina cells.

Keywords
BMP signaling, Placode morphogenesis, lens, retina, olfactory, otic