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Review

Induction and specification of cranial placodes

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Abstract

Cranial placodes are specialized regions of the ectoderm, which give rise to various sensory ganglia and contribute to the pituitary gland and sensory organs of the vertebrate head. They include the adenohypophyseal, olfactory, lens, trigeminal, and profundal placodes, a series of epibranchial placodes, an otic placode, and a series of lateral line placodes. After a long period of neglect, recent years have seen a resurgence of interest in placode induction and specification. There is increasing evidence that all placodes despite their different developmental fates originate from a common panplacodal primordium around the neural plate. This common primordium is defined by the expression of transcription factors of the *Six1/2*, *Six4/5*, and *Eya* families, which later continue to be expressed in all placodes and appear to promote generic placodal properties such as proliferation, the capacity for morphogenetic movements, and neuronal differentiation. A large number of other transcription factors are expressed in subdomains of the panplacodal primordium and appear to contribute to the specification of particular subsets of placodes. This review first provides a brief overview of different cranial placodes and then synthesizes evidence for the common origin of all placodes from a panplacodal primordium. The role of various transcription factors for the development of the different placodes is addressed next, and it is discussed how individual placodes may be specified and compartmentalized within the panplacodal primordium. Finally, tissues and signals involved in placode induction are summarized with a special focus on induction of the panplacodal primordium itself (generic placode induction) and its relation to neural induction and neural crest induction. Integrating current data, new models of generic placode induction and of combinatorial placode specification are presented.

Keywords: Adenohypophyseal placode; Olfactory placode; Lens placode; Trigeminal placode; Otic placode; Lateral line placodes; Epibranchial placodes; Pituitary; *Xenopus*; Chick; Zebrafish; Mouse; Six1; Six4; Eya; Dlx3; GATA; SoxB1; Irx; ANF; Pitx; Msx; Fox; Tbx; Pax; FGF; BMP; Wnt

Introduction

Vertebrates are distinguished from other deuterostomes by their specialized head with an elaborate brain encased in a cartilaginous or bony skull and with complex paired sense organs such as nose, eyes, and ears. Many of these evolutionary innovations of the vertebrate head originate from only two embryonic tissues, the neural crest, and the cranial placodes, which probably evolved in early vertebrates when these ceased to be filter feeders and adopted a new life style as active predators (Northcutt and Gans, 1983; Gans and Northcutt, 1983; see also Northcutt, 1996, 2005; Baker and Bronner-Fraser, 1997a; Holland and Holland, 1999, 2001; Meulemans and Bronner-Fraser, 2004; Schlosser, 2005).

Neural crest and placodes are specialized domains of the embryonic ectoderm which develop similarly in several respects. Both are very versatile embryonic tissues that give rise to multiple non-epidermal cell types including neurons, glia, and secretory cells. Moreover, the development of both tissues involves cell shape changes; these allow placodal and crest cells to migrate and/or to participate in various morphogenetic movements. Finally, both neural crest and placodes develop from populations of cells near the border of the neural plate.

Beyond these similarities, however, cranial placodes develop in a peculiar fashion quite distinct from the neural crest (reviewed for example in Webb and Noden, 1993; Northcutt, 1996; Baker and Bronner-Fraser, 1997a, 2001; Le Douarin and Kalcheim, 1999; Hall, 1999; Kalcheim, 2000; Santagati and Rijli, 2003; Meulemans and Bronner-Fraser, 2004; Huang and Saint-Jeannet, 2004). First, placodes develop exclusively from cranial ectoderm, whereas the neural crest develops in both

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head and trunk. Second, placodes comprise a quite heterogeneous assembly of structures, which form as focal thickenings of the cranial ectoderm at various stages of embryonic development (mostly after neural tube closure) and later invaginate and/or give rise to a subpopulation of migratory cells. The neural crest, in contrast, is an entirely migratory population of cells, which leaves the neural plate border region prior to or during fusion of the neural folds. Third, the developmental potential of placodes is more restricted than of neural crest. While both tissues give rise to secretory cells, neurons, and glia, only neural crest cells can form cartilage and bone, smooth muscle, and pigment cells. And fourth, with few exceptions, neural crest and placodes express different sets of transcription factors indicating that their development is controlled by different gene regulatory networks.

Compared to the neural crest, which has attracted much attention for its versatility and morphogenetic capacity and has been intensely studied ever since its discovery (reviewed in Baker and Bronner-Fraser, 1997b; Le Douarin and Dupin, 2003; Le Douarin and Kalcheim, 1999; Hall, 1999; Mayor and Aybar, 2001; Mayor et al., 1999; Kalcheim, 2000; Aybar and Mayor, 2002; Knecht and Bronner-Fraser, 2002; Santagati and Rijli, 2003; Meulemans and Bronner-Fraser, 2004; Huang and Saint-Jeannet, 2004), placodal development has long been neglected. The last couple of years, however, have seen a resurgence of interest in placode development, spurred by the discovery of many transcription factors with placode-specific expression and by increasing evidence for a common developmental origin of all placodes from a panplacodal primordium (for reviews, see Baker and Bronner-Fraser, 2001; Schlosser, 2002a, 2005; Streit, 2004; Brugmann and Moody, 2005).

The present review focuses on early aspects of placode development addressing in particular the origin of different placodes from such a panplacodal primordium. After providing an overview of different cranial placodes, I review the evidence for their common origin from a panplacodal primordium. Next, I address the role of various transcription factors for placodal development. I then discuss how different placodes may be specified within this primordium and how the latter is finally divided into distinct placodes. Finally, I consider tissues and signals involved in placode induction, concentrating on generic steps of placode induction and their relation to the induction of neural plate and neural crest. Evolutionary implications of our current view of placode development will not be covered but are reviewed elsewhere (Schlosser, 2005).

Development and derivatives of cranial placodes—an overview

Placodes were first discovered as transitory thickenings of cranial ectoderm (van Wijhe, 1883; Froriep, 1885; von Kupffer, 1891, 1895). The cranial placodes, as understood here, include the adenohypophyseal, olfactory, lens, trigeminal, and profundal placodes, a series of epibranchial and hypobranchial placodes, an otic placode, and a series of lateral line placodes (Fig. 1) (reviewed in Webb and Noden, 1993; Northcutt, 1996; Baker and Bronner-Fraser, 2001; Schlosser, 2002a, 2005; Streit, 2004). Most of these placodes are present in all vertebrates. However, the neurogenic hypobranchial placodes have only been found in amphibians (Schlosser, 2003; Schlosser and Northcutt, 2000; Schlosser et al., 1999), and the number of epibranchial and lateral line placodes differs for different taxa, with lateral line placodes being completely lost repeatedly, for instance, in amniotes (reviewed in Northcutt, 1992, 1993a,b, 1997; Schlosser, 2002b).

All placodes are specialized areas of the cranial non-neural ectoderm (i.e. ectoderm outside of neural plate and neural crest), where cells undergo pronounced cell shape changes (which may result in thickening, invagination, and/or cell delamination) and which give rise to various non-epidermal cell types. As I have discussed elsewhere (Schlosser, 2002a), placodes are often recognizable as thickenings (regions of columnar epithelium), but this is not always the case. It should be noted that there are some other ectodermal areas—including the amphibian hatching gland and cement gland (Drysdale and Elinson, 1992; Sive and Bradley, 1996) as well as the primordia of teeth, feathers, and hairs (Pispa and Thesleff, 2003)—which also give rise to specialized cell types but are not considered as placodes here because they apparently do not share a common developmental origin or bias (see below) with cranial placodes in the strict sense as enumerated above. Hatching and cement glands, for example, develop from the superficial layer of the bilayered amphibian ectoderm (Drysdale and Elinson, 1992; Sive and Bradley, 1996), while cranial placodes arise from its deep layer (Northcutt and Brändle, 1995; Northcutt et al., 1994; Schlosser and Northcutt, 2000).

There are several generic aspects of placode development shared by different placodes and reflected in the coexpression of many genes in different placodes (see below and McCabe et al., 2004). First, placodes are regions of increased cell proliferation compared to the epidermis (Saka and Smith, 2001; Washausen et al., 2005). Second, the development of placodal derivatives often involves cell shape changes and morphogenetic movements (reviewed in Noden, 1991; Webb and Noden, 1993; Northcutt, 1996; Baker and Bronner-Fraser, 2001), allowing placodes to develop into columnar epithelia, to invaginate, and/or to give rise to various types of migratory cells (neuronal, endocrine, or glial precursor cells or lateral line primordia). And third, all placodes with the exception of adenohypophyseal and lens placode are neurogenic (e.g. D'Amico-Martel and Noden, 1983; Ma et al., 1998; Fode et al., 1998; Schlosser and Northcutt, 2000; Andermann et al., 2002; Begbie et al., 2002). The absence of neurogenesis in these two placodes may be due to its active suppression in ectoderm originally biased for a neuronal fate judged by the initial expression and subsequent downregulation of *Xenopus Ngnr-1* in the prospective lens and adenohypophyseal ectoderm (Schlosser and Ahrens, 2004).

Aside from these similarities, however, different cranial placodes develop differently and give rise to different sense organs and ganglia, each with a distinct set of derivative cell types. These are briefly summarized in the following paragraphs and in Fig. 1, which also shows the location of cranial placodes in chick and *Xenopus* embryos.