Developmental Biology 389 (2014) 28–38

Contents lists available at ScienceDirect

Developmental Biology

journal homepage: www.elsevier.com/locate/developmentalbiology

Neural crest and placode interaction during the development of the cranial sensory system

Ben Steventon [a], Roberto Mayor [b], Andrea Streit [c,*]

[a] Department of Developmental and Stem Cell Biology, Insitut Pasteur, France
[b] Department of Cell and Developmental Biology, University College London, London, UK
[c] Department of Craniofacial Development and Stem Cell Biology, King's College London, London, UK

ARTICLE INFO

Article history:
Received 1 November 2013
Received in revised form
19 January 2014
Accepted 25 January 2014
Available online 31 January 2014

Keywords:
Morphogenesis
Cell fate
Cell migration
Cell movements
Sensory nervous system

ABSTRACT

In the vertebrate head, the peripheral components of the sensory nervous system are derived from two embryonic cell populations, the neural crest and cranial sensory placodes. Both arise in close proximity to each other at the border of the neural plate: neural crest precursors abut the future central nervous system, while placodes originate in a common preplacodal region slightly more lateral. During head morphogenesis, complex events organise these precursors into functional sensory structures, raising the question of how their development is coordinated. Here we review the evidence that neural crest and placode cells remain in close proximity throughout their development and interact repeatedly in a reciprocal manner. We also review recent controversies about the relative contribution of the neural crest and placodes to the otic and olfactory systems. We propose that a sequence of mutual interactions between the neural crest and placodes drives the coordinated morphogenesis that generates functional sensory systems within the head.

Introduction

A key problem during embryonic development is to understand how multiple cell populations coordinate their behaviour as functional organs emerge. The sensory nervous system in the vertebrate head, consisting of the craniofacial ganglia, the eye, ear, lateral line and olfactory organs, clearly illustrates this problem. These structures require the production of a range of specialised cell types that mainly derive from two embryonic cell populations with different properties: the neural crest and placodes. To form functional sensory circuits their development must be tightly coordinated both with one another, and with their targets in the central nervous system (CNS).

Neural crest cells initially derive from the neuroectoderm before undergoing an epithelial-to-mesenchymal transition and migrating along well-defined pathways (Theveneau and Mayor, 2012). The neural crest generates a wide range of cell types including neurons and glia of the peripheral nervous system, cartilage and bone that make up much of the cranial skeleton, endocrine cells, smooth muscle cells and tendons (Le Douarin and Teillet, 1971; Minoux and Rijli, 2010; Dupin et al., 2006; Grenier et al., 2009; Theveneau and Mayor, 2012). The cranial neural crest migrates in three main streams (branchial, hyoid and mandibular), along with a fourth population that migrates into the frontal-nasal region (Fig. 1). Together with the cranial placodes, neural crest cells are thought to have evolved early on in the vertebrate lineage, and both give rise to many vertebrate-specific attributes of the head (Northcutt and Gans, 1983; Northcutt, 2005).

Cranial placodes are thickened regions of ectoderm that include the olfactory, lens, otic, trigeminal and epibranchial placodes (Fig. 1), as well as the recently discovered paratympanic placode in chick (O'Neill et al., 2012). The epibranchial placodes produce cells that directly delaminate to contribute sensory neurons to the distal parts of the VIIth, IXth and Xth cranial nerves (geniculate, petrosal and nodose placodes, respectively) that innervate the taste buds in the oropharyngeal cavity as well as the heart, respiratory system, gastrointestinal tract and external ear. They then relay this information via central projections to the rostral nucleus of the solitary tract in the hindbrain (D'Amico-Martel and Noden, 1983; Schlosser and Northcutt, 2000; Harlow and Barlow, 2007; Harlow et al., 2011). In addition to providing peripheral glial cells (Le Douarin, 1986; Le Douarin et al., 1991), the neural crest contributes sensory neurons to the proximal ganglia that provide general epithelial innervation and project to the spinal trigeminal tract (D'Amico-Martel and Noden, 1983; Harlow et al., 2011; Harlow and Barlow, 2007). This distinction between distal and

* Corresponding author.
E-mail address: andrea.streit@kcl.ac.uk (A. Streit).

http://dx.doi.org/10.1016/j.ydbio.2014.01.021
0012-1606

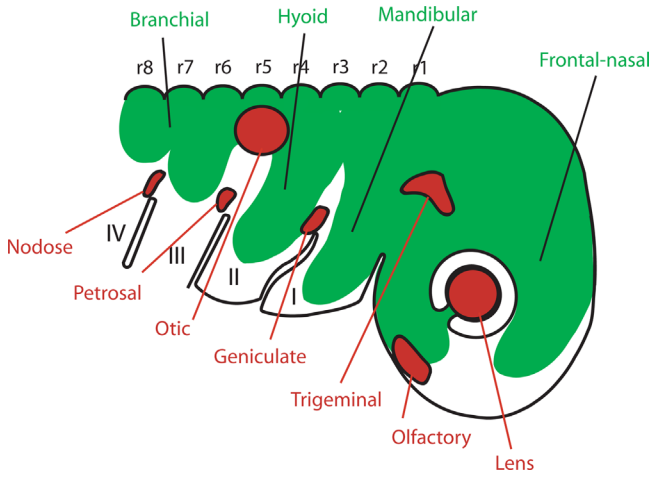

Fig. 1. The neural crest (green) migrates in three main streams: the branchial, hypoid and mandbular neural crest streams. In addition, a fourth population migrates into the frontal-nasal region of the head. A subset of cranial placodes that is discussed in the text is shown in red. Roman numerals are used to number pharyngeal arches. Rhombomeres are numbered r1–r8.

proximal elements of the epibranchial ganglia is difficult to see in *Xenopus* due to the early fusion of the primordia (Schlosser and Northcutt, 2000). The trigeminal ganglia contain sensory neurons derived from both the neural crest and placodes, with the trigeminal placode (the maxillomandibular and ophthalmic placodes in amniotes, profundal and trigeminal placodes in *Xenopus*) contributing predominantly to the distal part of the Vth cranial ganglion, whereas the neural crest produces its proximal components and associated glia (Hamburger, 1961; Lwigale, 2001). Within the epibranchial and trigeminal ganglia, terminal differentiation of placode-derived neurons precedes that of neural crest-derived neurons (D'Amico-Martel and Noden, 1980; D'Amico-Martel, 1982). As a result neural crest cells do not undergo large-scale neuronal production until after the cranial ganglia have fully condensed.

In contrast to these purely neurogenic placodes, the lens, olfactory and otic placodes undergo invagination to form pits or vesicles and contribute to sense organs of the head. The lens is non-neurogenic and differentiates into both lens fibre and lens epithelial cells (Cvekl and Duncan, 2007; Lang, 2004). The olfactory placode forms adjacent to the forebrain and generates odorant and pheromone receptor cells that centrally project to the olfactory and accessory olfactory bulb. It also produces hypothalamic GnRH neurons that are rare in their ability to move from the periphery into the CNS (Murakami and Arai, 1994; Hilal et al., 1996; Mulrenin et al., 1999; Wray, 2002; Toba et al., 2008). In addition, the olfactory placode generates supporting cells and stem cells, which have the unique ability to regenerate olfactory sensory neurons throughout life (Farbman, 1994; Schwob, 2002). The otic placode develops dorsal to the epibranchial placodes, adjacent to the hindbrain and undergoes a complex morphogenesis to generate the inner ear (Chen and Streit, 2013). It gives rise to a large range of cell types, including hair cells, sensory bipolar neurons (which connect hair cells with their central targets) as well as secretory and supporting cells (Riley and Phillips, 2003; Barald and Kelley, 2004; Ohyama et al., 2007).

Anamniote vertebrates have an additional set of lateral line placodes that function to detect movements within the water and electric fields. These placodes generate mechano- and electrosensory cells and their surrounding supporting cells as well as the sensory neurons that innervate them and make up the lateral line ganglia (Northcutt et al., 1995; Modrell et al., 2011a; Gillis et al., 2012). Finally, amniotes have an additional paratympanic placode arising from a molecularly distinct, *Sox2* positive domain just dorsal to the geniculate placode in chick (O'Neill et al., 2007). The paratympanic organ is homologous to the anamniote spiracular organ.

Interactions between neural crest and placode cells and their derivatives is a clear example of how fate specification, differentiation and movement of adjacent cell populations are coordinated to build complex structures. In this review, we summarise our current knowledge of neural crest–placode interactions at various stages of their development. We first review the close positioning of neural crest and placode precursors during neural crest migration and the formation of individualised placodes, before reviewing recent data that shed light on their functional interaction at early stages. We next summarise the experimental evidence for a role of neural crest derivatives in the formation of the cranial ganglia. Finally, we discuss recent controversies on the joint contribution of neural crest and placode cells to the olfactory and otic systems. We propose that repeated and reciprocal interactions between the neural crest and placode cells are not only crucial for the formation of the many vertebrate specific sensory structures, but are also important drivers of head morphogenesis.

Spatial relationship of neural crest and placode precursors during neural crest migration

The cranial placodes arise from a common primordium, the preplacodal region, adjacent to the anterior neural plate (Bhattacharyya et al., 2004; Pieper et al., 2011; Streit, 2002; Xu et al., 2008). This territory splits into individual epithelial thickenings at precise positions next to the developing CNS. Neural crest cells are induced at the neural plate border in a position that initially overlaps with placode precursors, but later are positioned medial to the preplacodal region (Bhattacharyya et al., 2004; Pieper et al., 2011; Streit, 2002; Xu et al., 2008).

The cranial neural crest delaminates from the neuroectoderm and migrates in three distinct streams that correspond to distinct sub-divisions of the neural tube. The first stream emerges at the level of the diencephalon to rhombomere 2 (r2) and populates the frontal-nasal region and the first pharyngeal arch, the second stream arises at r4 populating the second pharyngeal arch, while the third stream arises in r6–8 and later splits to populate the third and fourth pharyngeal arches. R3 and r5 neural crest cells split to join the adjacent streams (for review see Theveneau and Mayor, 2011; Fig. 2B). There are multiple points of contact between the neural crest as it migrates ventrally and placodal precursors, as they split to form distinct placodes from an initially common domain. To assess the potential for functional interactions between the neural crest and placode precursors in driving these processes, we will first briefly describe the spatial relationship of these two populations during neural crest migration.

Pharyngeal arch neural crest migration and the sub-division of the posterior preplacodal region

Otic and epibranchial placodes arise from a common territory in the posterior preplacodal region, which later resolves into individual domains. This territory may also contain paratympanic placode progenitors in amniotes if present (O'Neill et al., 2012) and does include lateral line precursors in anamniotes (Pieper et al., 2011). Changes in gene expression appear to reflect the division into otic and epibranchial placodes: *FoxiI*, *Sox3* and *Pax2* are initially expressed widely, but then become localised to the forming placodes (Abu-Elmagd et al., 2001; Ishii et al., 2001; Ohyama, 2006; Ohyama and Groves, 2004; Streit, 2002; Sun et al.,