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Review

Gene duplications and the early evolution of neural crest development

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ABSTRACT

Neural crest cells are an important cell type present in all vertebrates, and elaboration of the neural crest is thought to have been a key factor in their evolutionary success. Genomic comparisons suggest there were two major genome duplications in early vertebrate evolution, raising the possibility that evolution of neural crest was facilitated by gene duplications. Here, we review the process of early neural crest formation and its underlying gene regulatory network (GRN) as well as the evolution of important neural crest derivatives. In this context, we assess the likelihood that gene and genome duplications capacitated neural crest evolution, particularly in light of novel data arising from invertebrate chordates.

Contents

1. Introduction

There is extensive variation in gene number and genome size throughout animals [1]. Within the chordates, there is significant evidence that vertebrates, but not closely related invertebrates, have gone through two whole genome duplications [2–4]. Similar to this increase in gene number, there is general agreement that there was a significant increase in complexity during the early evolution of vertebrates [5]. Anatomical complexity is difficult to quantitate, but the number of cell types and genes are increased in the vertebrates compared with non-vertebrate chordates [5–7].

One key source of new vertebrate cell types and new anatomical structures was via the evolution and elaboration of neural crest cells. Neural crest cells are a multipotent, transient cell type that originates in the neural–epidermal border region, migrates away from the dorsal neural tube to diverse sites in the embryo, and differentiates into multiple characteristic cell types with disparate roles, as varied as neuroglial and mesenchymal cells. The 'bona fide' neural crest (defined by cell position, behavior, and early gene expression of similar genes) is shared by all vertebrates, and generally thought to have evolved during the early origins of the vertebrates.

These two things – genome duplication and origin of the neural crest – both occurred in early vertebrate evolution. If two rounds of genome duplication took place about when the neural crest went through its most significant expansion in complexity, this raises the intriguing possibility that there may be a causal relationship between gene (and genome) duplication and the advent/expansion

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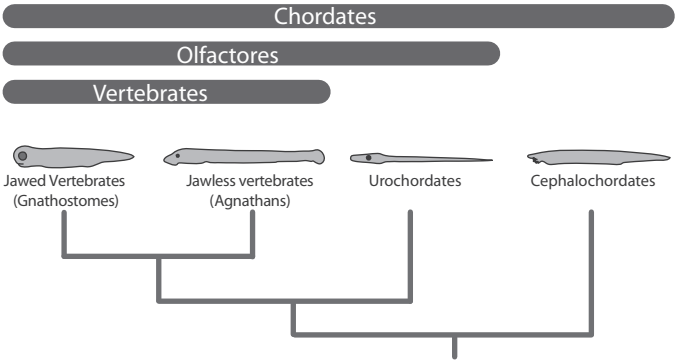

Fig. 1. Phylogeny depicting interrelationships between selected chordate taxa. The name of each monophyletic group is shown above a schematic cladogram.

of the neural crest, which in turn promoted vertebrate complexity [2]. One might expect there to be considerable support for such a relationship. Some data are consistent with this scenario but most are either vague or unsupportive [8–10].

In this review, we discuss evidence related to gene duplication and the origin and diversification of neural crest, and address key missing comparative developmental data that will be essential for producing a balanced view of neural crest evolution. We focus particularly on the early development of the neural crest, and on early evolution of vertebrates. In addition, we review literature regarding the possibility of a rudimentary neural crest-like cell population in non-vertebrate chordates. Together, these issues are central to interpreting of the origins of neural crest.

2. Chordate phylogeny and evolution

Within the vertebrates, there is an important distinction between jawed vertebrates (gnathostomes) and jawless vertebrates (agnathans, or cyclostomes), the latter including living lamprey and hagfish species (for a recent review, see [11]). The living gnathostomes and agnathans lineages segregated during early vertebrate evolution, making the agnathans the last remnants of a once diverse group of fishes with a distinct developmental architecture [12]. Precisely which aspects of agnathan soft-tissue anatomy and development are indicative of primitive vertebrate traits is difficult to assess, since the agnathans have some specialized anatomical features (esp. in feeding structures). Identification of shared derived traits between gnathostomes and agnathans has been a crucial source of information about these early vertebrates [11,12].

All chordates share a dorsal notochord and somites, among other similarities [13]. Careful morphological and sequence-based assessments have converged on a consensus model of the interrelationships between the major chordate phyla, including the vertebrates, the urochordates (e.g. ascidians such as *Ciona intestinalis*), and the cephalochordates (e.g. the lancelet *Branchiostoma floridae*) [14,15] (see Fig. 1). Vertebrates are the sister group of Tunicates, and together they comprise a group called the olfactores [14]. The sister group of the olfactores are the cephalochordates [14]. Larval ascidians and amphioxus are thought to reflect the anatomical complexity of early chordates, and they are important groups for comparative analyses within the phylum [16,17].

3. Chordate evolution and gene duplication

Separate lines of study have identified an increase in genome size between invertebrate chordates and vertebrates [2–4,18,19]. Genome duplications might correlate with and have been implicated in the acquisition of vertebrate novelty, though paleontological data suggest anatomical evolution was gradual [9]. Comparisons between chordates suggested that two rounds of duplication occurred in early vertebrates [2,16,18]. Data from lamprey are less clear. One scenario suggests ancestral agnathans had one genome duplication before separating from gnathostomes [2,18]. Elucidation of when the second gnathostome genome duplication took place relative to the divergence of gnathostomes and agnathans is important for understanding vertebrate evolution. However, it is likely that early vertebrates and some aspects of neural crest emerged amid a background of gene duplication. Microevolutionary studies suggest that partial redundancy between the duplicated paralogues might somewhat weaken selection on them, facilitating the spread of genetic changes that can lead to subfunctionalization or neofunctionalization, rather than degradation [20].

Changes in the neural crest certainly involved evolution of gene regulatory novelty. The early formation of neural crest is in large part due to the action of genes that most likely were coopted from use in other tissues, mostly the mesoderm [21,22]. The precise role of gene duplications in triggering the formation of the neural crest can be very difficult to test. It has not yet been possible to comprehensively address the extent of cis-regulatory evolution [16,23,24] due to the lack of genomic information, and tests of protein functionality between these groups are only beginning [25].

In order to determine the extent to which gene duplication has played a role in neural crest evolution, it is necessary to understand both the key morphological and cell behavioral events that characterize the neural crest, and to understand how they are controlled by underlying gene regulatory networks (GRNs) [22,23,26].

4. Neural crest

The neural crest is an important embryonic cell population that originates at the border between neurogenic ectoderm and non-neural ectoderm. Later, these multipotent precursors reside within the dorsal neural tube and then migrate away to diverse sites, giving rise to many derivative cell types [27–29]. For a historical overview, please refer to [28]. Cellular derivatives have been studied extensively in different vertebrate model species, and include neurons and glia of the peripheral nervous system and mesenchymal cells like craniofacial cartilage and smooth muscle [5].

It is important to note that while there are particular characteristic neural crest cell fates, many of them have been secondarily modified or lost in some vertebrates. Comparisons between species are an important means to infer which particular aspects of neural crest are truly ancestral for the group, and comparative support is essential to infer when particular cell types emerged.

Here, we review the embryology and developmental genetics of neural crest formation within gnathostome vertebrates. We then discuss the status of the neural crest regulatory networks in lampreys and ascidians, both of which are in crucial phylogenetic positions for inferring aspects of early neural crest evolution. For comprehensive reviews of pertinent molecular and experimental details, please see [30–34].

4.1. Neural crest formation and intrinsic gene regulatory networks

Based on studies in a few model vertebrates, neural crest development can be parsed into several key steps: (a) specification of the neural plate border, (b) specification of the neural crest, (c) emigration from the neural tube and migration to distinct sites, and (d) progressive differentiation [22,26–28]. Each of these steps hypothetically can be described by modules of a gene regulatory network