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Towards a synthetic view of axis specification mechanisms in vertebrates: insights from the dogfish

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Abstract

The genetic mechanisms, which control axis specification, apparently extensively diverge across vertebrates. In amphibians and teleosts, they are tightly linked to the establishment of an early dorso-ventral polarity. This polarity has no equivalent in amniotes, which unlike the former, retain a considerable plasticity for their site of axis formation until blastula stages and rely on signals secreted by extra-embryonic tissues for the establishment of their early rostro-caudal pattern. In order to better understand the links between these seemingly highly divergent mechanisms, we have used an evo-devo approach, aimed at reconstructing the gnathostome ancestral state and focussed on a chondrichthyan, the dogfish *Scyliorhinus canicula*. A detailed molecular characterization of the dogfish embryo at blastula and gastrula stages highlights striking similarities with all vertebrate model organisms including amniotes. It suggests the presence in the dogfish of territories homologous to the hypoblast and extra-embryonic ectoderm of the latter, which may therefore reflect the primitive condition of jawed vertebrates. In the ancestral state, these territories are specified at opposite sides of an early axis of bilateral symmetry, homologous to the dorso-ventral axis of amphibians and teleosts, and aligned with the later forming embryonic axis, from head to tail. Amniotes have diverged from this pattern through a posterior expansion of extra-embryonic ectoderm, resulting in an apparently radial symmetry at late blastula stages. These data delineate the broad outlines of the gnathostome ancestral pattern of axis specification and highlight an unexpected unity of mechanisms across jawed vertebrates. They illustrate the complementarity of comparative and genetic approaches for a comprehensive view of developmental mechanisms themselves. ***To cite this article: M. Coolen et al., C. R. Biologies 332 (2009).***

Résumé

Vers une synthèse des mécanismes de spécification des axes chez les vertébrés : apport d'un chondrichtyen. Les mécanismes génétiques impliqués dans la spécification des axes embryonnaires semblent différer profondément entre les organismes modèles des vertébrés, amniotes d'une part, poisson-zèbre et xénope d'autre part. Afin de mieux comprendre leur unité sous-jacente, nous avons utilisé une approche évolution-développement, visant à reconstruire l'état ancestral chez les gnathostomes et ciblée sur un chondrichtyen, la roussette *Scyliorhinus canicula*. Une caractérisation détaillée de l'embryon de roussette aux stades blastula et gastrula met en évidence des similitudes frappantes non seulement avec les amphibiens et les téléostéens mais également, de façon plus inattendue, avec les amniotes. Elle suggère en particulier la présence chez la roussette de territoires homologues à des territoires extra-embryonnaires chez ces derniers, l'ectoderme extra-embryonnaire et l'hypoblaste. Chez la roussette,

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ces deux territoires sont cependant spécifiés à des pôles opposés d'un axe de symétrie bilatérale précoce, clairement apparenté à l'axe dorso-ventral des amphibiens et des téléostéens. Les amniotes ont divergé de ce patron ancestral par une expansion postérieure de l'ectoderme extra-embryonnaire, conduisant à une symétrie apparemment radiale de ce tissu au stade blastula. Ces données esquissent les grandes caractéristiques de l'état ancestral des gnathostomes au cours du développement précoce et mettent en évidence une unité inattendue des mécanismes dans ce taxon. Elles illustrent la complémentarité des approches comparatives et génétiques pour une approche synthétique des mécanismes du développement. ***Pour citer cet article : M. Coolen et al., C. R. Biologies 332 (2009).***

Keywords: Dogfish; *Scyliorhinus canicula*; Chondrichthyan; Gnathostome; Embryonic polarities; Gastrulation; Ancestral pattern

Mots-clés : Roussette ; *Scyliorhinus canicula* ; Chondrichtyen ; Gnathostome ; Polarités embryonnaires ; Gastrulation ; Patron ancestral

Since their emergence in the 1980s, developmental genetics have mainly relied on the study of a handful of model organisms, *Drosophila* and *C. elegans* in protostomes, the mouse, chick, xenopus and zebrafish in deuterostomes. The focus on these sole species has clearly led to major advances in our understanding of the complex molecular and cellular mechanisms that gradually shape the embryo during ontogeny. However, as comparative data accumulate, limitations inherent to this strategy become more and more obvious. A major caveat is related to the absence of a systematic assessment of the evolutionary conservation of the mechanisms characterized in model organisms. This results in frequent overgeneralizations, that tend to consider processes identified in a single species as general to a whole taxon, in the absence of any explicit argument. Another one is that as any extant species, model organisms have independently diverged from ancestral patterns, each along his lineage. This divergence process can considerably obscure the relationships between the developmental processes characterized in each model organism. In the absence of unambiguous morphological conservation, comparisons of molecular patterns or interactions have opened new possibilities to alleviate this difficulty. However, the frequent recruitments of gene regulatory networks and signaling pathways, now known to repeatedly occur during evolution, make conclusions based on this sole criteria extremely hazardous. Comparisons at the broad evolutionary scale, such as those between Drosophila and vertebrates, are obviously faced with these limitations. But the same kind of difficulty can arise in comparisons between much more closely related species, as exemplified by the mechanisms of early axis specification, which apparently substantially diverge across vertebrates. This review first aims at an overview of the main characteristics of this process in vertebrate model organisms. We then show how an evo-devo approach, relying on the detailed molecular characterization of a chondrichthyan, the dogfish *Scyliorhinus canicula*, provides insight into the underlying unity of these apparently diverse mechanisms.

1. The genetic control of axis specification in the vertebrates: a difficult synthesis

In all vertebrates, the embryonic axis proper, from head to tail, is laid down during gastrulation. As in all bilaterians, this axis is endowed with two polarities, antero-posterior and dorso-ventral (left-right asymmetries appearing later, at advanced stages of gastrulation). However, bilaterality is established at much earlier stages of development. A first polarized axis (animal/vegetal), conserved across vertebrates, is thus inherited from the oocyte, while the second one results from a radial symmetry breaking event, which may involve different mechanisms depending on the species considered. Deciphering the mechanisms of axis specification in vertebrates thus implies answering two main questions: Which are the molecular mechanisms responsible for the establishment of the earliest polarities observed? And second, which is the link between these polarities and those of the embryo proper? Studies conducted in amphibians or teleosts on the one hand, and in amniotes on the other hand, lead to substantially different views.

In xenopus, which has long been the vertebrate reference for this process, radial symmetry is broken upon fertilization. Sperm entry thus triggers a microtubule-directed movement, which results in the displacement of vegetal maternal determinants towards the opposite pole of the egg [1]. At this location, these determinants initiate a succession of inductive events, ultimately leading to Spemann organizer formation. The canonical Wnt signaling pathway is central in this process, even though other signals may also be involved [2]. The organizer/ab-organizer axis thus formed is traditionally termed dorso-ventral, both because of the dorsalizing effects mediated by the organizer during gastrulation