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Review

A time space translation hypothesis for vertebrate axial patterning

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ABSTRACT

How vertebrates generate their anterior–posterior axis is a >90-year-old unsolved probem. This mechanism clearly works very differently in vertebrates than in Drosophila. Here, we present evidence from the Amphibian Xenopus that a time space translation mechanism underlies initial axial patterning in the trunk part of the axis. We show that a timer in the gastrula's non organiser mesoderm (NOM) undergoes sequential timed interactions with the Spemann organiser (SO) during gastrulation to generate the spatial axial pattern. Evidence is also presented that this mechanism works via Hox collinearity and that it requires Hox functionality. The NOM timer is putatively Hox temporal collinearity. This generates a spatially collinear axial Hox pattern in the emerging dorsal central nervous system and dorsal paraxial mesoderm. The interactions with the organiser are mediated by a BMP–anti BMP dependent mechanism. Hox functionality is implicated because knocking out the Hox1 paralogue group not only disrupts expression of Hox1 genes but also of the whole spatially collinear axial Hox sequence in the early embryo's A–P axis. This mechanism and its nature are discussed. The evidence supporting this hypothesis is presented and critically assessed. Strengths and weaknesses, questions, uncertainties and holes in the evidence are identified. Future directions are indicated.

Contents

1. A time space translation hypothesis for vertebrate axial patterning

How vertebrates make their anterior–posterior (A–P) axis is a >90-year-old unsolved problem [1,2]. This question is possibly close to being solved for Drosophila [3], but definitely not for vertebrates. Despite the lack of progress, the investigations have already yielded at least two directly relevant Nobel prizes (Spemann [1,2], Lewis [4], Nuesslein-Volhard [3]) The underlying mechanism clearly works very differently in vertebrates than in Drosophila. Much evidence indicates that timing is involved in generating the vertebrate anterior–posterior (A–P) axis [10–12]. Our recent findings support this view (Fig. 1).

Here, we present evidence that a time space translation (TST) mechanism (i.e.: a mechanism whereby a temporal sequence of early anterior to late posterior axial gene expression generates the congruent axial spatial sequence) underlies initial vertebrate A–P patterning in the trunk part of the axis. We present evidence that a BMP dependent timer in the gastrula's non organiser mesoderm (NOM) undergoes sequential timed interactions with the BMP

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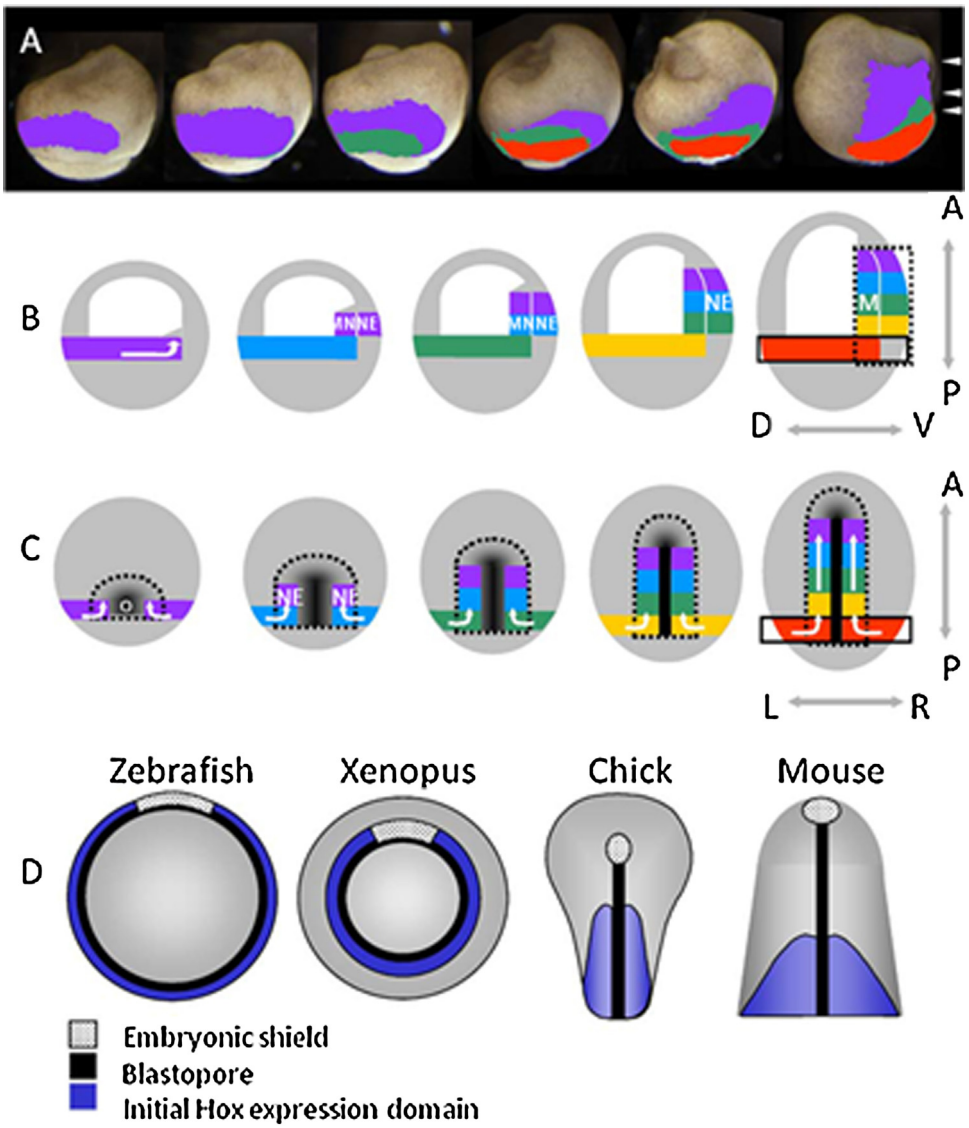

Fig. 1. The time space translation hypothesis (Wacker et al. [6], Durston et al. [7]). (A) False colour representation of expression of an early anterior to late posterior sequence of three axial markers (Hox genes) during Xenopus gastrulation. WISH on external lateral views of sibling embryos for Hoxd-1 (purple), Hoxc-6 (green), Hoxb-9 (red). Digital images were analysed and selected areas labelled with respective false colour and combined in one image. Six gastrula stages (10.5, 11, 11.5, 12, 12.5 and 13) are shown in a lateral external view, anterior up and dorsal to the right. Anterior boundaries of the Hox expression at the end of gastrulation are arrowed. (B) The time space translation hypothesis. Lateral views. Time sequences of lateral views of gastrulae through gastrulation Expression of new A–P markers is initiated in non-organiser mesoderm (NOM) at sequential times (a time sequence of more and more posterior Hox codes in NOM is represented by a spectral colour sequence of differently coloured horizontal bars). Non-organiser mesodermal tissue (depicted by a horizontal coloured bar which is a 2D representation of the 3D broken ring of Hox expression in the marginal zone of the wall of the embryo) moves (flows) toward the Spemann organiser by convergence and then extends anteriorly (arrow). The NOM mesoderm (IM), adjacent to the Spemann organiser involutes and its current A–P positional value (=Hox code) is then transferred to overlying neurectoderm (NE). While the early temporal Hox sequence in the non-organiser mesoderm (differently coloured horizontal bars; outlined by continuous black line in rightmost figures of B and C) is running, cohorts of new cells from this region are continually moved into the range of Spemann organiser (range represented by dashed black line) and their Hox code is then stabilised by an organiser signal. The temporal Hox sequence is thus converted into a spatial AP pattern by continuous morphogenetic movement and stabilisation of timed information by the organiser both in involuted NOM mesoderm (IM) and overlying neurectoderm (NE). The section represents a paraxial level just lateral to the organiser so the organiser is not visible. (C) The time space translation hypothesis: dorsal views. In non-organiser mesodermal (NOM) cells, the Hox sequence is running (differently coloured bars, solid black outline in rightmost figures). From this domain, cells are continuously moved into the influence of the Spemann organiser (dashed blackoutline) by convergence and extension (arrows). The AP pattern arises by sequential posterior addition of new stabilised NOM segments each expressing a different subset of Hox genes. A, anterior; P, posterior; V, ventral; D, dorsal; L, left; R, right. The outer neurectoderm is not shown in this figure because this section is internal, at the level of the dorsal mesoderm.
(D) Time space translation occurs in all vertebrates. Schematic diagrams depicting locations of Spemann organiser, blastopore and initial Hox expression domain in Xenopus and orthologous structures in the zebrafish [39], the chick [40] and the mouse [41] all shown at the beginning of gastrulation. Zebrafish and Xenopus are shown in vegetal views, chick and mouse are shown in dorsal views.

antagonistic Spemann organiser (SO) [1,2]: a structure absent in Drosophila), The interactions occur during and after gastrulation and generate the spatial axial pattern. We present evidence that this mechanism involves Hox collinearity [4] and that it requires Hox functionality [5]. The timer in the NOM mesoderm appears to be Hox temporal collinearity (an early anterior to late posterior time sequence of Hox expression codes). This generates the congruent spatially collinear axial Hox pattern (the same Hox codes arranged sequentially spatially along the axis) in the emerging dorsal central nervous system and dorsal paraxial mesoderm. Hox temporal collinearity thus generates Hox spatial collinearity. The interactions with the organiser are mediated by a BMP–anti BMP dependent mechanism), [6,7] see below and Fig. 1, Text Box 1, Figs. S1A, B. Hox genes thus take a higher place in the A–P patterning cascade