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Review

Establishing the plane of symmetry for lumen formation and bilateral brain formation in the zebrafish neural rod

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ABSTRACT

The lumen of the zebrafish neural tube develops precisely at the midline of the solid neural rod primordium. This process depends on cell polarisation and cell rearrangements, both of which are manifest at the midline of the neural rod. The result of this cell polarisation and cell rearrangement is an epithelial tube that has overt mirror-symmetry, such that cell morphology and apicobasal polarisation are mirrored across the midline of the neural tube. This article discusses how this mirror-symmetry is established and proposes the hypothesis that positioning the cells' centrosomes to the midline of the neural rod is a key event in organising this process.

Contents

1. Symmetry and the neural tube

The zebrafish brain and spinal cord is built from a bilaterally symmetric neural tube. The basic symmetric shape and the balance between cell numbers on the left and right sides of the neural tube will be critical for the formation of a correctly functioning bilateral brain and spinal cord. The embryo must therefore employ mechanisms that ensure this symmetry develops correctly and is maintained during the process of neural lumen formation. Throughout our studies of zebrafish neural tube formation we have been struck by the role that symmetry may play in defining where the lumen forms within the initially solid neural rod. We originally noted that a specialised mode of cell division generated mirror-symmetric daughters around the plane of the nascent lumen [1]. More recently we described how the plane of the nascent lumen appears to organise a mirror-symmetric microtubule cytoskeleton within individual cells that transiently span the midline of the neural rod [2]. In this article we will attempt a synthesis of our data and ideas about how symmetry is generated during lumen formation.

Bilateral symmetry is the most apparent type of symmetry seen in animal body plans. To identify structures with bilateral symmetry, you need to define a plane of reflection. As pointed out by Weyl [3] in the diagram in Fig. 1, the two points P and P′ mean nothing in relation to each other until their symmetry is revealed by

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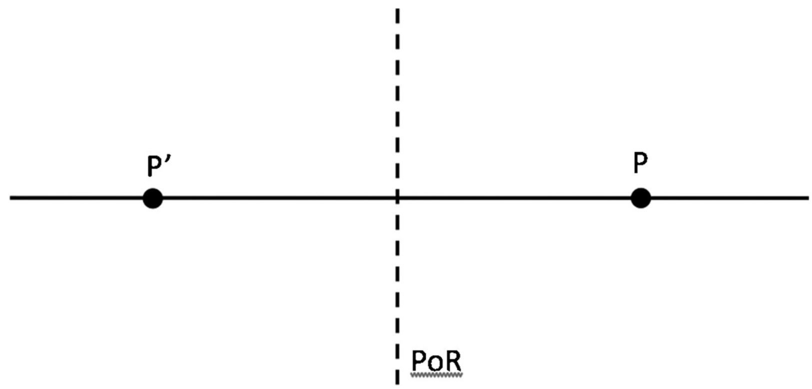

Fig. 1. The points P and P′ can only be understood as symmetric when described in relation to the dotted line which is the plane of reflection (PoR). Diagram adapted from Weyl [3].

the plane of reflection PoR [3]. Such a plane of reflection or 'mirror' clearly develops at the midline of the zebrafish neural rod prior to lumen formation. This is recognisable both molecularly as the proteins required to assemble the lumen surface accumulate at this plane, and also (slightly later) morphologically as an interface between cells on the left and cells on the right side of the rod (Fig. 2). We propose that, during morphogenesis of the neural tube, cells must recognise where to assemble this plane of reflection (in other words identify the midline of the neural rod) and then organise their shape, their internal cytoskeleton and their cell–cell junctions in order to arrange themselves mirror-symmetrically around that plane. This raises the following questions: how is the mirror placed in the correct location and how do cells respond to it in order to generate symmetry around it? Teleost neurulation provides a tractable model in which to investigate this question. Recent work in our lab has led us to believe that the establishment of a plane of reflection (mirror-symmetry) occurs at subcellular levels, is defined by integrating cell–cell and cell–tissue interactions and provides one of the keys to the establishment of bilateral symmetry at the tissue level in the zebrafish central nervous system [2].

2. Establishing the plane of symmetry in the neural rod

The neural rod of the zebrafish embryo develops from the neural keel after the cells of the neural plate have converged towards the dorsal midline of the embryo [4,5]. Throughout the plate and keel stages the neural primordium is a bilaterally symmetric structure but there is not yet a precise morphologically identifiable plane of symmetry at the midline, since, even after cells have converged at neural keel and early rod stages, cells from the left and right sides interdigitate across the midline. We suggest that at these early stages the neural primordium is bilaterally symmetric but not yet precisely mirror-symmetric. The interdigitation of cells across the midline must be resolved by cell rearrangements before the left and right sides can separate to form a lumen via tissue cavitation. A distinct morphological plane of symmetry thus only appears in the neural rod as its cells rearrange themselves into two columns of elongated cells that meet at the midline plane in preparation for lumen formation (Fig. 3). At the same time as cells are resolving their interdigitation they are transforming into an apicobasally polarised epithelial tube. Thus cell rearrangement and apicobasal polarisation appear to be intimately linked, and this results in our ability to recognise the plane of mirror symmetry not only by the morphological interface between cells of the left and right sides of the rod, but also by the molecular assembly of polarity proteins such as Pard3 at this interface [1].

3. Mirror-symmetric divisions across the plane of the midline drive cell rearrangement

One of the characteristic cell behaviours that occurs at the plane of reflection in the zebrafish neural rod is cell division, and a number of studies support the view that cell division plays a dominant role in establishing mirror symmetry and organising lumen formation in this system. Cell division is in many ways a mirror-symmetric event. An early example of this is given by Guenter Albrecht-Buehler who studied 3T3 cells dividing in culture and found that a significant proportion of daughter cells have mirror-symmetric patterns of actin bundles and moved mirror symmetrically after completing division [6]. He hypothesised that there might be a "relationship between the universally found bilateral symmetry of organisms and the mirror symmetry between certain daughter cells" [6] but he could not suggest a way in which this mirror-symmetry at the cellular level could be transferred to and maintained at the tissue level, stating that "the perfect mirror-symmetry of the mitotic spindle can hardly be expected to

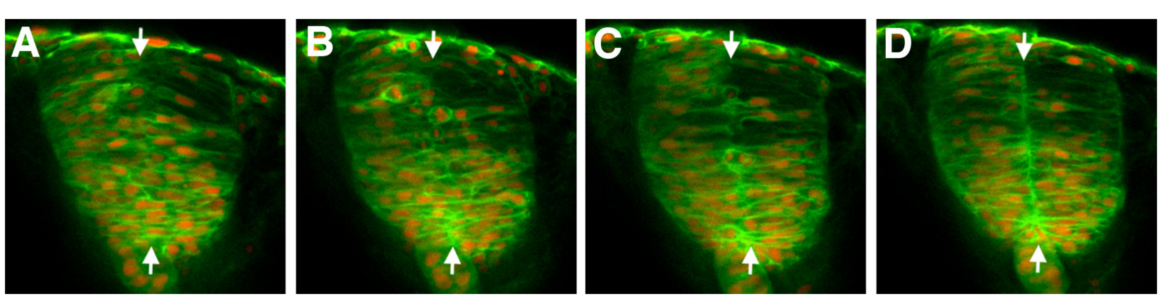

Fig. 2. Four frames from a time-lapse movie showing neural rod development in the transverse plane. In A cells from left right sides of the rod interdigitate across the neural midline (arrowed) and a plane of reflection is not visible. By frame D the cells have rearranged such that left and right cells now meet at the midline rather than intersecting it. Thus by frame D the plane of reflection is visible as this morphological interface.

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