

approach may provide more precise ages for lithosphere stabilization, and may distinguish stabilization from later events of crust–mantle disturbance, such as the vertical migration of melts.

Another piece of the puzzle for reconstructing craton formation has come from xenoliths of basalt composition called eclogites, which form a small percentage of the mantle and contain some types of diamonds². These eclogites (and their diamonds) are thought to have formed after craton stabilization, either by intrusion of magmas or by recycling into the mantle of basaltic crust that formed earlier. The stable isotope compositions (including carbon and oxygen) of these eclogite xenoliths support a recycled origin, as the values obtained are similar to those in altered basalts from the sea floor. However, rhenium–osmium ages for the formation of these eclogites are about 500 million years older than the (presumably) surrounding mantle rocks¹. This surprising result may be an artefact of the analytical technique, which may give mixed ages for mantle rocks rather than the age of their original formation, as mentioned above.

There is much speculation about how cratons formed and evolved. A commonly held view is that the processes operating deep in the Earth to form the lithosphere in Archaean times were fundamentally different from those forming the lithosphere today. The Earth's mantle was much hotter in the Archaean, and this caused large-scale melting, with relatively iron-rich magmas adding to the crust and the complementary

magnesium-rich residue forming the buoyant mantle layer of the Archaean lithosphere. There is evidence⁹ from distinctive layered mantle lithosphere in some cratons that large mantle plumes (upwelling blobs of very hot, deep mantle material) provided not only the source of heat for this melting, but also the material that separated into the magmas and residue that formed Archaean cratons.

The Kaapvaal project has provided an unprecedented seismic context for xenolith studies of cratons in southern Africa. Such a context is needed to complement the understanding gleaned from xenoliths in other cratonic regions, such as Siberia, and in the Slave Craton in Canada. ■

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Developmental biology

Clocks and Hox

Clifford J. Tabin and Randy L. Johnson

Segmentation is a key feature of many animals. New molecular studies add to our understanding of how vertebrate segments form and how this process is linked to the genes that make each segment unique.

In vertebrates, the spine, ribcage and breastbone are derived from repeated blocks of tissue that begin as identical units in early development and are then modified into unique shapes with different purposes. Some segments, for example, allow the head to move; some are sites of attachment for the muscles involved in breathing; and some protect the organs in the chest. To produce such a body plan, there must be mechanisms both for generating the segments and for giving each its distinct identity. For vertebrates, the task of producing repeated units seems to be controlled partly by a molecular clock in the unsegmented paraxial mesoderm — the tissue from which the units arise. The identity of the units is controlled by the differential expression of genes known

as Hox genes in a nested pattern from the head to the tail¹. Writing in *Cell*, Dubrulle *et al.*² and Zákány *et al.*³ suggest that these processes are causally connected.

Simply put, segmentation in vertebrate embryos occurs as follows. On each side of the neural tube (which forms the spinal cord) is a strip of unsegmented ('presomitic') mesoderm. Cells from this tissue progressively bud off, contributing to somites — the units of cells that will later develop into vertebrae and associated muscles. This differentiation process occurs in a wave that moves gradually from the head to the tail (that is, down the anterior–posterior axis), with presomitic mesoderm in front of the wave and somites in its wake.

The molecular and genetic mechanisms

that control vertebrate segmentation are not yet understood, but emerging evidence supports a long-standing theory known as the 'clock-and-wavefront' model⁴ (Fig. 1). In this model, an autonomous developmental timer (the segmentation clock) interacts with a molecular wavefront of differentiation, which converts information from the clock into spatial information. The model has received support from the discovery of several genes whose expression patterns oscillate in the presomitic mesoderm with the same periodicity as that of somite formation (reviewed in ref. 5).

Dubrulle *et al.*² now provide evidence that the wavefront may correspond to a sharp gradient of fibroblast growth factor-8 (FGF-8) protein within the presomitic mesoderm. Grafting experiments in chick embryos² showed that presumptive somites –I to –V (see Fig. 1) are fixed with respect to their anterior–posterior polarity and boundaries. But the tissue posterior to somite –V is not yet fixed in this way. Dubrulle *et al.* show that this 'undetermined' zone of the presomitic mesoderm corresponds to a posterior domain of high FGF-8 expression.

Dubrulle *et al.* also found that widespread, forced expression of FGF-8 is sufficient to keep the cells of the presomitic mesoderm in an immature, undifferentiated state. Moreover, when FGF-8 protein was applied locally to one part of the presomitic mesoderm, a series of small somites formed. However, the total number of somites remained the same, because a larger-than-normal somite developed posterior to the smaller ones. Conversely, when signalling from FGF-8 was blocked, larger somites formed. How can these results be explained?

The authors' detailed observations² of oscillating gene expression show that forced FGF-8 signalling does not affect the segmentation clock itself. Rather, their data suggest that an interaction between FGF-8 signalling and the clock controls somite size, possibly by specifying the location of boundaries between presumptive somites. So, the clock determines when the boundaries form, and the gradient of FGF-8 determines where. When more FGF-8 is applied to the embryo, the FGF-8 gradient continues further than normal in the anterior direction, and more presomitic mesodermal cells are prevented from contributing to somites. But each somite is programmed to develop at the same time as usual, so each somite ends up containing fewer cells and is therefore smaller. Conversely, blocking FGF signalling shifts the determination front in the posterior direction, and so more cells are allocated to each somite behind the front. This interpretation is consistent with a role for FGF signalling in mediating the wavefront component of the clock-and-wavefront model (Fig. 1).

Once somites have formed, they must

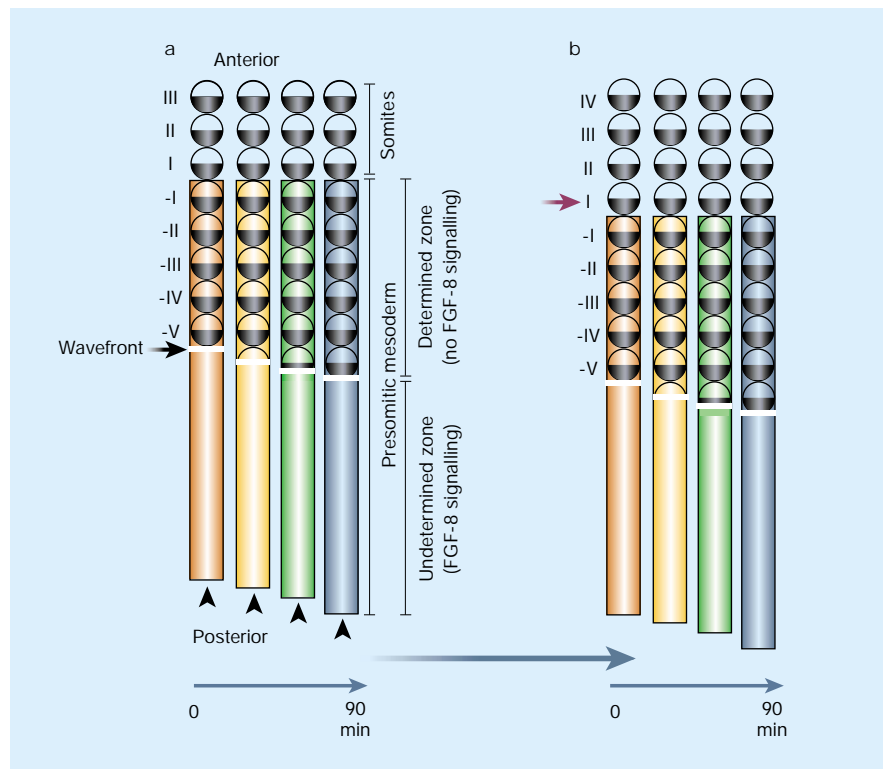


Figure 1 The 'clock-and-wavefront model' of segmentation and patterning in vertebrates. Each vertebra is derived from the fusion of derivatives of an anterior half-somite (transparent semicircles) and of a posterior half-somite (black semicircles). The somites themselves are formed from presomitic mesoderm, in which gene expression oscillates, producing a segmentation 'clock'. The presomitic mesoderm is maintained at a constant length by addition of cells at its posterior end. **a**, The boundary between somites is specified by the interaction of a wavefront of differentiation with the presomitic mesoderm at the start of a new clock cycle (red). This interaction specifies the mesodermal cells as anterior in the first half of the cycle (red and yellow) and posterior in the second half (green and blue). **b**, At the same time as a new cycle begins, a new somite (purple arrowhead) is formed at the anterior end of the presomitic mesoderm. The oscillation of gene expression is regulated, at least in part, by components of the Notch signalling pathway. Signalling from fibroblast growth factor-8 (FGF-8) sets the location of the undetermined zone; the wavefront corresponds to the boundary between cells that express FGF-8 and cells that do not².

express the appropriate complement of Hox genes, which determine the nature of the somites. The ability to manipulate somite size, and hence the number of somites in a given region, allowed Dubrulle *et al.* to investigate whether the boundaries of Hox-gene expression follow somite number or absolute anterior–posterior position. The answer is that the embryo seems to count somites to set the boundaries of Hox expression.

Zákány *et al.*³ suggest that the coordination of Hox-gene expression with segmentation requires the molecules of the segmentation clock. They found that several Hox genes are activated in the presomitic mesoderm in mice at the location where the next somite will form. This region coincides both spatially and temporally with a wave of expression of *lunatic-fringe*, a gene that is cyclically expressed in presomitic mesoderm and is controlled by signalling from Notch — a component of the segmentation clock. So it seemed that Hox expression might likewise be regulated by the clock. The authors

confirmed this by showing that mice with a mutation in a protein downstream of Notch fail to activate significant levels of Hox expression in the presomitic mesoderm. At minimum, this provides a mechanism for aligning the levels of Hox expression with the

Planetary science

Gases make a rare appearance

Typhoon Lee

The unexpected discovery of noble gases within silicate pockets in a primitive meteorite is hard to explain. Could they have been captured from the solar wind streaming from the young Sun?

The five noble gases — helium, neon, krypton, argon and xenon — are rather aloof. They neither react with other elements to form solids nor condense easily. Although they are quite abundant in the Universe, their strong preference to remain gaseous means that their concentrations in

segments, as Hox-gene expression is triggered up to the sharp boundary formed by the action of the clock and wavefront. Once a particular Hox gene is activated by the clock, its anterior boundary of expression is maintained at the level of the somite that was formed at the time the gene was switched on.

These studies^{2,3} provide convincing evidence of a link between activation of Hox genes and segmentation. It seems that once Hox genes are activated by the clock in the presomitic mesoderm, they maintain their expression boundaries in somites and their derivatives. So the time at which a Hox gene is activated establishes its boundary of expression in the embryo. But it is not clear why one Hox gene is activated rather than another in a given clock cycle. As there are more somites than Hox genes, the mechanism must be more complicated than 'one somite, one Hox gene'. The activation of Hox genes follows the physical order of the genes on the relevant chromosome, and this 'temporal co-linearity' depends on the release of the DNA containing the Hox genes from a repressive configuration⁶. The data discussed here suggest that Notch signalling is involved in periodic activation of the expression of unrepressed Hox genes. The details of how the release from repression is coordinated with the segmentation clock will be the next piece of the puzzle.

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