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Building the Vertebrate Spine

OLIVIER POURQUIÉ, Howard Hughes Medical Institute and Stowers Institute for Medical Research

The vertebrate body can be subdivided along the antero-posterior (AP) axis into repeated structures called segments. This periodic pattern is established during embryogenesis by the somitogenesis process. Somites are generated in a rhythmic fashion from the paraxial mesoderm and subsequently differentiate to give rise to the vertebrae and skeletal muscles of the body. Somite formation involves an oscillator-the segmentation clock-whose periodic signal is converted into the periodic array of somite boundaries. This clock drives the dynamic expression of cyclic genes in the presomitic mesoderm and requires Notch and Wnt signaling. Microarray studies of the mouse presomitic mesoderm transcriptome reveal that the segmentation clock drives the periodic expression of a large network of cyclic genes involved in cell signaling. Mutually exclusive activation of the Notch/FGF and Wnt pathways during each cycle suggests that coordinated regulation of these three pathways underlies the clock oscillator. In humans, mutations in the genes associated to the function of this oscillator such as *Dll3* or *Lunatic Fringe* result in abnormal segmentation of the vertebral column such as those seen in congenital scoliosis. Whereas the segmentation clock is thought to set the pace of vertebrate segmentation, the translation of this pulsation into the reiterated arrangement of segment boundaries along the AP axis involves dynamic gradients of FGF and Wnt signaling. The FGF signaling gradient is established based on an unusual mechanism involving mRNA decay which provides an efficient means to couple the spatio-temporal activation of segmentation to the posterior elongation of the embryo. Another striking aspect of somite production is the strict bilateral symmetry of the process. Retinoic acid was shown to control aspects of this coordination by buffering destabilizing effects from the embryonic left-right machinery. Defects in this embryonic program controlling vertebral symmetry might lead to scoliosis in humans. Finally, the subsequent regional differentiation of the precursors of the vertebrae is controlled by *Hox* genes, whose collinear expression controls both gastrulation of somite precursors and their subsequent patterning into region-specific types of structures. Therefore somite development provides an outstanding paradigm to study patterning and differentiation in vertebrate embryos.