Cyclic transcription of *Hox* genes suggests a link between patterning and the segmentation clock

JÓZSEF ZÁKÁNY, MARIE KMITA, JOSÉ-LUIS DE LA POMPA^{1,} and DENIS DUBOULE*

Department of Zoology and Animal Biology, University of Geneva, Switzerland and ¹EMBL, Mouse Biology Programme, Monterotondo, Roma, Italy * Denis.Duboule@zoo.unige.ch

During mammalian development, transcription of *Hox* genes is activated in presomitic mesoderm with a time sequence that follows the order of the genes along the chromosome. Consequently, newly formed somites contain specific combinations of HOX proteins that define their fates. Here, we show that *Hoxd1* displays transitory stripes of expression within presomitic mesoderm, but not in somites. Stabilization of its transcripts through targeted modification uncovered sustained expression in somites, reminiscent of other *Hox* gene patterns, suggesting that cyclic activation in presomitic mesoderm may be a general phenomenon masked by slow transcript turnover. Accordingly, in addition to *Hoxd1* and *Hoxd3*, we show that the

promoters of both *Hoxb1* and *Hoxd11* transgenes can respond to this regulation. We propose that colinearity is associated with bursts of transcriptional activation of *Hox* genes every time a somite is about to form. This dynamic transcriptional behavior appears to depend upon *Notch* signaling, as mice deficient for the *Su(H)/RBPJk/CBF1* gene, the effector of the *Notch* pathway, showed severely reduced *Hoxd* gene expression in presomitic mesoderm. These results suggest a tight link between *Hox* gene activation and the mechanisms behind the segmentation clock. Such a linkage would coordinate the production of novel segments with their morphological specification.