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Studies on the Role of Cux1 in Regulation of the Onset of Joint Formation in the Developing Limb

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Abstract

Joint formation, the onset of which is characterized by the segmentation of continuous skeletal rudiments into two or more separate elements, is a fundamental aspect of limb pattern formation, playing a critical role in determining the size, shape, and number of individual skeletal elements. Joint formation is initiated by conversion of differentiated chondrocytes at sites of presumptive joints into densely packed nonchondrogenic cells of the joint interzone. This conversion is accompanied by loss of Alcian blue-staining cartilage matrix and downregulation of cartilage-specific gene expression. Here, we report that *Cux1*, which encodes a transcription factor containing a homeodomain and other DNA-binding motifs, is highly expressed at all of the discrete sites of incipient joint formation in the developing limb concomitant with conversion of differentiated chondrocytes into interzone tissue. Moreover, differentiated limb chondrocytes in micromass cultures infected with a *Cux1* retroviral expression vector are converted into nonchondrogenic cells which exhibit loss of Alcian blue cartilage matrix and downregulation of cartilage-specific gene expression as occurs at the onset of normal joint formation. These results suggest that Cux1 is involved in regulating the onset of joint formation by facilitating conversion of chondrocytes into nonchondrogenic cells of the interzone.

Keywords

joint development; Cux1; cartilage; skeletal development; limb development; pattern formation

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