Version 2.0

Abstract

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Grant Number:	1R01HD034538-01A2
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PI Title:	PROFESSOR
Project Title:	NOTCH SIGNALING AND VERTEBRATE LIMB DEVELOPMENT

Abstract: DESCRIPTION (adapted from investigator's abstract): During vertebrate embryogenesis patterning signals emanate from very discrete centers like the Hensen's node, the midbrain-hindbrain junction or, in the case of the limb, the zone of polarizing activity (ZPA) of the apical ectodermal ridge (AER). It has become evident that many of the molecules that control developmental pathways in insects have homologous counterparts in vertebrates. The AER is required for vertebrate limb outgrowth. Formation of the ridge relies on the previous establishment of the dorso-ventral limb axis. The investigator has cloned a gene, r-fng, which is expressed in the dorsal ectoderm and in the ridge. Ectopic expression experiments indicate that r-fng is able to induce additional AERs suggesting that the AER develops from tissue that is expressing high levels of r-fng adjacent to tissue that is not, i.e. a r-fng boundary. A similar mechanism has been proposed in Drosophila, where the fng gene plays a pivotal role in wing development. Identification of the existence of a common signaling process that mediates the formation of the Drosophila wing margin and the vertebrate AER will be quite surprising, even in light of previously demonstrated homologies between the two phylogenetic groups, and it will require the isolation of downstream molecules. In Drosophila, activation of fng induces a cascade of events that results in the activation of the expression of Serrate, Notch, Vestigial, Cut and Wingless at the dorso-ventral boundary. The investigator has cloned chick homologues of Serrate, Notch and Cut and shown they are expressed in the AER. By using wild type and limb mutant embryos, the investigator will study the consequences of disrupting Notch signaling for establishing and positioning the vertebrate AER. The molecules described above are also required during embryogenesis for other processes like neurogenesis and somitogenesis. This suggests that during limb development, somitogenesis, or neurogenesis, a similar combination of genetic building blocks could be used again and again. Understanding the way these genetic bricks interact with each other in order to position and establish the AER will prove to be a rewarding enterprise, not only from the point of view of limb development, but also from a more general perspective of unraveling how evolution has utilized the same combination of molecules to establish other signaling centers during vertebrate development.

Thesaurus Terms:
biological signal transduction, developmental genetics, embryogenesis, gene expression, limb, vertebrate embryology
gene interaction
chick embryo

Institution:	SALK INSTITUTE FOR BIOLOGICAL STUDIES 10010 N TORREY PINES RD SAN DIEGO, CA 92037
Fiscal Year:	1998
Department:	
Project Start:	08-DEC-1997
Project End:	30-NOV-2002
ICD:	NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
IRG:	HED