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Abstract

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PI Name:	NISWANDER, LEE A.
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PI Title:	ASSISTANT MEMBER
Project Title:	VERTEBRATE ORGANIZER FORMATION CELL AND MOLECULAR CUES

Abstract: Embryonic organizing centers regulate pattern formation within a developmental field. Organizing centers are established at the boundaries between cells with distinct cellular and molecular properties. Vertebrate embryonic organizing centers include the primitive streak which forms at the junction between embryonic and extraembryonic ectoderm, the roof plate which forms at the junction between the neural tube and dorsal ectoderm, and the apical ectodermal ridge and posterior polarizing mesenchyme of the limb which form near the junction between dorsal and ventral ectoderm. The goal of the studies presented here is to analyze embryonic organizer formation at a cellular and molecular level in the vertebrate embryo. A model system to study the establishment of embryonic organizers is the developing chick limb. Surgical manipulations have defined three major limb organizing centers that direct patterning of the three axes, the apical ectodermal ridge, posterior polarizing mesenchyme (ZPA), and non- ridge ectoderm. Molecular experiments-have identified three signaling molecules, FGF, SHH and WNT that are expressed in these tissues and can substitute for their activities. Interactions among these signaling systems are required for normal limb development. Based on genetic and molecular data in Drosophila and vertebrate expression patterns, three specific hypotheses have been formulated for understanding the cellular and molecular basis of organizer formation and their role in patterning the chick limb. l) The hypothesis will be tested that the limb organizing centers, the ridge and ZPA, are formed by cooperative interaction between dorsal ectoderm and ventral ectoderm. 2) A second hypothesis is that the molecular mechanisms that underlie the cellular interaction can be described in terms of interactions between the WNT and BMP family of signaling molecules. 3) The third hypothesis is that BMPs play important roles in limb patterning, growth regulation, and translation of global patterns into cartilage and bone formation and differentiation. These hypotheses will be tested using a variety of experimental techniques, including heterografting, application of protein, and ectopic expression using retrovirus encoding ligand and mutant receptor constructs. These families of signaling molecules, WNT, BMP, FGF and SHH are likely to be used in other organizing centers in vertebrates and non-vertebrates. Thus, these findings will be relevant to understanding developmental abnormalities reflecting patterning defects

in many systems and many organisms, including humans.

Thesaurus Terms:
biological signal transduction, ectoderm, histogenesis, limb, mesenchyme, molecular biology, vertebrate embryology
cell cell interaction, cell differentiation, cellular polarity, developmental genetics, growth factor, growth factor receptor, protein signal sequence
chick embryo, in situ hybridization, oligonucleotide, restriction endonuclease, tissue /cell culture

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