Version 2.0

Abstract

Back to Hit List

Grant Number:	1R01HD037909-01
PI Name:	MOENS, CECILIA B.
PI Email:	cmoens@fhcrc.org
PI Title:	ASSISTANT MEMBER
Project Title:	GENETIC MECHANISMS OF HINDBRAIN SEGMENTATION

Abstract: DESCRIPTION (Adapted from the applicant's abstract): The establishment of functional neural circuits in the vertebrate central nervous system depends on the correct partial positioning of distinct neural cell types. In the hindbrain this is facilitated by the appearance of segments, or rhombomeres, that act as lineage-restricted compartments in which developmental programs are reiterated. Hindbrain neural crest contributes to the structural and neuronal components of the head and neck, and disruption of the early patterning of the hindbrain results both in neurological and craniofacial defects in humans. The long-term goal of this research is to understand how hindbrain segmentation is established, how segments acquire distinct identities and how these identities result in the specification of functionally distinct neuronal cell types. The zebrafish, suited to both genetic analysis and experimental embryology, is used as a model system in which to address these questions. Lazarus and valentino are zebrafish hindbrain segmentation genes that were identified in a screen for zebrafish mutants in which hindbrain patterning is disrupted. The proposed experiments use these mutants to address the genetic and molecular basis of head segmentation as follows: (1) Genetic analysis of lazarus will address whether its function is required within the hindbrain or in the periphery to bring about global segmentation in the head. Positional cloning will establish its molecular mechanism and its position in the hierarchy of hindbrain segmentation. (2) The role of valentino in hindbrain segmentation will be studied by identifying molecular partners with which it interacts in order to subdivide rhombomeres 5 and 6 from their common precursor in the presumptive hindbrain. (3) The hypothesized role of Eph receptors and their ligands in mediating repulsive cell-cell interactions in the hindbrain will be examined by assaying the effects of Eph and ephrin expression on the characteristic behaviors of valentino and lazarus mutant cells in genetic mosaics.

Thesaurus Terms:
developmental genetics, developmental neurobiology, rhombencephalon
gene expression, gene mutation, nonmammalian vertebrate embryology, transcription factor
molecular cloning, zebrafish

Institution:	FRED HUTCHINSON CANCER RESEARCH CENTER BOX 19024, 1100 FAIRVIEW AVE N SEATTLE, WA 98109
Fiscal Year:	1999
Department:	
Project Start:	01-AUG-1999
Project End:	31-MAY-2004
ICD:	NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
IRG:	ZRG1