CSU RICRO Administator

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PI	[redacted]
Department	[redacted]
Investigator	(none)
Investigator	(none)
Investigator	(none)
Protocol number	10-014B
Status	Approved
Date of original submission	2010-02-02
Date of initial approval	2010-02-10
Date of most recent approval	2010-02-10
Date of expiration	2011-02-10
Project title	**Role of Cofilin and Wnt Signaling in Neural Crest Development**
Type of project	Extamural funding
Sponsor	NIH
PASS number	[redacted]
Locations of work	[redacted]
Project utilizes Select Agent(s)	No

Overview of Project

Normal morphological development of tissues during embryogenesis requires precise coordination of multiple cellular events such as cell migration and cell differentiation. Aberrant patterning of the nervous system results in severe congenital human diseases such as spina bifida. Prevention or treatment of these diseases requires an understanding of the machinery that controls neural patterning. The actin cytoskeleton is a fundamental cellular scaffold which dictates cell morphology and multiple important dynamic cell processes.

Cofilin is a member of a family of important actin assembly-regulatory proteins. Inactivation of cofilin-1 in mice results in neural tube closure defects, impaired neural crest migration and abnormal neuronal differentiation. The molecular and cellular basis of these developmental defects remains to be determined. We hypothesize that Wnt PCP signaling is coupled to cofilin regulation during vertebrate neural crest development. In this proposal we aim toidentify means by which Wnt signaling and cofilin govern neural crest patterning. We will use the chick as a model system to determine what Wnt activity controls neural crest migration in this vertebrate. Neural crest migration will be directly assessed in situ and in vitro by time lapse microscopy following specific inhibition of non canonical Wnt signaling through expression of dominant negative signaling intermediates or pharmacological inhibition. We will differentiate roles for canonical Wnt signaling versus non

canonical Wnt PCP and Wnt Calcium signaling pathways in neural crest patterning. We will identify Wnt ligands that stimulate neural crest migration and establish their cellular and molecular mechanisms.Cofilin activity in neural crest cells will be evaluated in response to treatments that either disrupt or stimulate Wnt PCP signaling. The role of cofilin and Wnt signaling on neural crest cell migration will be evaluated through 4D fluorescence confocal microscopy live cell imaging. We will analyze migration in whole chick embryos and neural crest explant cultures.

Infectious Agents

Name of Agent	Strains	Used in vitro?	Used in vivo?
Adenovirus	Ad5dl309	Yes at BSL 2	No

Dual use potential: No

Human-origin material

None

Toxins

None

Non-exempt recombinant DNA

cDNAs encoding various vertebrate proteins will be cloned into the AdEasy adenoviral expression system. We will use adenoviral mediated gene transfer to express the different cDNAs in cultured chick embryonic tissues.

- Source(s) of DNA to be expressed: from invertebrates and vertebrate animals including human
- Vector(s) used for delivery: Adenovirus
- Host(s) for expression of rDNA: cultured cells, chick embryonic tissue
- Proteins expressed via rDNA technology: cofilin, LIMK, slingshot, actin, RhoGTPases, PAKs
- NIH Guidelines category of non-exempt rDNA study: III-D-3
- Is the expressed product toxic to vertebrates: YES
- Is a federal permit required for this work: NO
- Is this a gene therapy trial: NO
- Are transgenic animals being generated: NO
- Are transgenic plants being generated: NO

Original IBC Review

The CSU Biosafety Committee has reviewed your project application for: Role of Cofilin and Wnt Signaling in Neural Crest Development (Project 10-014B).

This application was APPROVED AS SUBMITTED.

The IBC greatly appreciated the level of detail provided in this approval request and would like to save it as an example for future applicants.

If you have any questions regarding this approval please contact Christine Johnson at 491-8690 or Chrsitine.Johnson@Colostate.Edu.

Thank you,

Christy