Version 2.0

Abstract

Back to Hit List

Grant Number:	1R01HD039926-01
PI Name:	WOTTON, DAVID
PI Email:	dw2p@virginia.edu
PI Title:	
Project Title:	MOLECULAR ANALYSIS OF TRANSCRIPTIONAL REPRESSION BY TGIF

Abstract: DESCRIPTION (Adapted from the Investigator's Abstract): TGIF (TG-interacting factor) is a member of the TALE family of homeodomain proteins. TALE homeodomain proteins have a three amino acid insertion between helices one and two of the homeodomain, which specifies interactions with other DNA binding proteins. In humans, mutation of TGIF leads to holoprosencephaly, a genetic disorder resulting in profound effects on craniofacial development. TGIF is a transcriptional repressor, which acts in part by recruiting histone deacetylases, and is a transcriptional co-repressor for TGF-beta-activated Smads. In response to TGF-beta, an activated Smad complex enters the nucleus, binds to DNA and interacts either with transcriptional activators, or a co-repressor complex via TGIF. It appears that TGIF acts in distinct transcriptional regulatory pathways: Repressing transcription of TGF-beta-activated genes via Smads and repressing a second set of genes when bound directly to DNA. However, target genes, regulated by direct binding of TGIF are not known. The goal of this project is to understand the mechanism of action of TGIF and its role in transcriptional regulation. Specifically, this project will analyze transcriptional repression by TGIF at the molecular level, and determine and its role in TGF-beta-activated transcription. Target genes for TGIF, and DNA binding proteins, with which TGIF interacts, will be identified. These studies will help us understand how defects in TGIF lead to holoprosencephaly, and shed light on TGF-beta-activated transcriptional regulation, which when perturbed by mutations affecting Smad proteins, contributes to cancer.

Thesaurus Terms:
DNA binding protein, genetic transcription, transcription factor, transforming growth factor amidohydrolase, biological signal transduction, brain, developmental genetics, developmental neurobiology, gene expression, gene induction /repression, gene targeting, genetic regulation, histone, phosphorylation, protein protein interaction, protein structure function, recombinant protein, regulatory gene
high performance liquid chromatography, microarray technology, protein purification, tissue /cell culture, transfection, yeast two hybrid system

Institution:	UNIVERSITY OF VIRGINIA CHARLOTTESVILLE BOX 400195 CHARLOTTESVILLE, VA 22904
Fiscal Year:	2001
Department:	CENTER FOR CELL SIGNALING
Project Start:	09-FEB-2001
Project End:	31-JAN-2006
ICD:	NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
IRG:	OBM