LBRN Work-in-Progress

INBRE Seminar series

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Tuesday August 27, 2013

10:00 - 11:30AM

Characterization of SwitchI Mutants in Kinesin Kif5A that cause Hereditary Spastic Paraplegia

DR. THOMAS HUCKABA
Department of Biology
XAVIER UNIVERSITY
10:00 AM

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Regulation of Mouse ES Cell Differentiation by Hoxa1: Upstream and Downstream Signaling

EDUARDO MARTINEZ-CEBALLOS
Department of Biology
SOUTHERN UNIVERSITY AND A&M COLLEGE
10:45 AM

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Characterization of SwitchI Mutants in Kinesin Kif5A that cause Hereditary Spastic Paraplegia

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Thomas Huckaba PhD, Department of Biology, Xavier University

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Mentors:

Sunyoung Kim PhD

Department of Biochemistry and Molecular Biology

LSUHSC-NO

Edward Wojcik PhD

Department of Biochemistry and Molecular Biology

LSUHSC-NO

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Hereditary spastic paraplegia is a neurodegenerative disorder that is caused by the progressive loss of neuronal axons in the corticospinal tract. Mutations in Kif5A, the kinesin motor protein that transports cellular cargoes in neurons, cause an autosomal dominant form of hereditary spastic paraplegia. In an effort to better understand the mechanism of this disease, we have characterized the altered biochemical and biophysical properties of human Kif5A proteins harboring disease-causing mutations.

Regulation of Mouse ES Cell Differentiation by Hoxa1: Upstream and Downstream Signaling

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Eduardo Martinez-Celballos PhD, Department of Biological Sciences, Southern University and A&M College

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Mentor:

Konstantin G. Kousoulas PhD

BIOMMED, Department of Pathobiological Sciences

Louisiana State University School of Veterinary Medicine

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The homeobox (Hox) family of transcription factors comprises important regulators of embryonic patterning and organogenesis. In mammals, the Hox genes are located in four separate chromosome clusters, and can be activated sequentially by retinoic acid (RA) in a manner that resembles their positions in the clusters, e.g. 3' genes are activated by RA before 5' genes. In vertebrate embryos, alterations of the normal pattern of Hox gene expression result in homeotic transformations and malformations. In mice, *Hoxa1* has been shown to be required for proper patterning of the early hindbrain and the associated neural crest; however, little is known about the molecular events that regulate the Hoxa1 signaling pathway. Here, we have studied separately upstream and downstream molecular events that regulate Hoxa1 gene activation and function. To first gain insight into the molecular mechanism of *Hoxa1* regulation in mouse ES cells, we sought to determine the effect of RA treatment on the levels of the small noncoding microRNA miR-10a, which is a known repressor of HOXA1 expression in human cells. We observed that miR-10a levels can be upregulated by RA after 24 hours of treatment in ES cells. Furthermore, inhibition of miR-10a in the presence of RA resulted in the upregulation of Hoxa1 protein levels, which indicates that miR-10a is a repressor of *Hoxa1* activation in mouse ES cells. In order to better understand the signaling events that occur downstream of *Hoxa1* activation, we performed ChIP-chip and RNA-seq integrated analyses on wild type vs. Hoxa1-/- ES cells. These analyses identified a group of putative direct Hoxa1 target genes that are known to play important roles during embryonic brain patterning and/or neuronal differentiation. All together, our studies provide an insight into the mechanism of Hoxa1 action in differentiating mouse ES cells.