



Neuroscience Center of Excellence

SEMINAR

“Astrocyte Regulation of Vascular Remodeling: Insight from a Novel Crystallin Mutation”

DEBASISH SINHA, Ph.D.

Wilmer Eye Institute
Baltimore, MD

Astrocytes are known to be indispensable for initial formation of the retinal vasculature; our studies with the *Nuc1* rat provide novel evidence that these cells are also essential in the retinal remodeling process. *Nuc1* is a spontaneous mutation in the Sprague-Dawley rat originally characterized by nuclear cataracts in the heterozygote and microphthalmia in the homozygote. The *Nuc1* allele results from mutation of the β A3/A1-crystallin gene, which in the neural retina is expressed only in astrocytes. We demonstrate striking structural abnormalities in *Nuc1* astrocytes with profound effects on the organization of intermediate filaments. Our data suggest, for the first time, that β A3/A1-crystallin is essential for the normal functioning of astrocytes and has a critical role in mediating vascular remodeling. A second severe de novo mutation arose spontaneously in our colony of *Nuc1* Sprague Dawley rats. Since the hind limbs of the affected animals were abducted so severely that they did not effectively support the animal's weight, the condition was named *frogleg*. The mutation is autosomal recessive and maps to chromosome 1q36-q37. A striking feature of the *frogleg* mutation is a dramatic reduction in brain size and volume, however, the body weight, which is typically lower in neonatal *frogleg* rats, normalizes after several months. Rats homozygous for the *frogleg* mutation display a marked increase in the ventricular size and possible gliosis. Our laboratory strives to understand the role of glial cells in health and disease and uses rodent mutants as highly reproducible genetic tools for examining the events governing proper glial cell development.

**Monday November 5, 2007 12:00pm, 8th Floor Neuroscience Center
Conference Room, LSU Lion's Building, 2020 Gravier Street
New Orleans**