**Jordan P. Hall, Duke University Student**

**Project Title:** ***"Validating the genetic expression of tenascin-C (TNC) and delta-like 1 (Drosophila) in postmortem diffuse intrinsic pontine glioma (DIPG) through proteomic analysis"***

**Research at : National Children's Medical Center, Washington D.C.**

**Mentor: Javad Nazarian, Ph.D**

**Lay Summary**

**Cell signaling is part of a complex communication system that governs basic cellular activities and coordinates cell actions. The ability of cells to perceive and correctly respond to the microenvironment is the basis of development, tissue repair, and immunity. Errors in this cellular information processing are responsible for certain diseases, including cancer. By understanding cell signaling and the pathways through which this signaling is transmitted, diseases may be more effectively treated.**

**The involvement of the Notch signaling pathway in human disease is firmly established. There is increasing evidence that this fundamental pathway is implicated in several malignancies and behaves as either an oncogene (an accelerator) or a tumor suppressor (a brake) depending upon the cellular context. Clearly, under certain circumstances, deregulation of the Notch pathway has been connected with the formation of solid tumors in adults.**

**It is in this regard that the Nazarian laboratory has preliminarily identified two genes, TNC and DLK1, in DIPG patient tissue samples. Experiments have demonstrated the capacity of TNC to stimulate tumor growth by various mechanisms including the promotion of proliferation, the escaping of immuno-surveillance and the influencing of blood vessel formation. Separately, other investigations suggest that DLK1 plays a role in the formation or progression of gliomas. Are TNC and DLK1 the significant genes that modulate and regulate the Notch signaling pathway providing key potential gene targets for therapeutic intervention in DIPG patients? At this point, this is unknown; DIPG is a distinct biologic entity. To pursue a systematic approach, the overexpression of these genes in DIPG patient samples must first be verified.**

**Haigreeva Yedla, Duke University Student**

**Project Title*: Investigating the role of mutant histone proteins in DIPG pathogenesis***

**Research at: Duke University**

**Mentor: Dr. Oren Becher**

**Lay Summary**

**Diffuse Intrinsic Pontine Glioma (DIPG) is the foremost cause of death in children with brain**

**tumors. However, clinical trials for the past thirty years have not identified a single agent that demonstrates efficacy against DIPG. To identify effective therapies for DIPG, we must acquire an in-depth understanding of the complex biology that drives its formation. Recently a novel heterozygous mutation in histone 3.3 or 3.1 was identified in 78% of DIPGs, which results in the substitution of a methionine for a lysine in the 27th amino acid of H3F3a or Hist1Hb respectively suggesting a gain of function mutationi. We hypothesize that studying the function of this mutation will provide novel insights regarding the pathogenesis of DIPG and the identification of potential novel therapies. Recently, we described a genetically engineered mouse model of DIPG using the RCAS/tv-a systemii. We hope to implement this model with the histone mutation; we hypothesize that this modelling system will allow us to assess whether this mutant histone is truly a driver of gliomagenesis and determine its function. Functional characterization of this novel mutant histone is critical for improved understanding of DIPG pathogenesis, especially since 78% of DIPGs have this mutant histone. The RCAS/tv-a system is the ideal tool to determine if this mutant histone is truly a driver of brainstem gliomagenesis.**

**i Wu, G. et al. Nat. Genet. published online (29 January 2012) doi: 10.1038/ng.1102 ii"Becher, O. et al. Cancer Research 70, 2548-2557 (2010)."**