

**“Atorvastatin regulates basic helix-loop-helix transcription factor gene expression and neurogenesis after stroke in retired breeder rats”**

**Jennifer Ding, Adams High School, Rochester Hills, MI and Ang Li, Troy High School, Troy, MI – 2005-06 National Team Finalists**

Abstract: Neurogenesis contributes to functional improvement after stroke. Transcription factors with basic helix-loop-helix (bHLH) motif, are essential elements in neurogenesis. Growth factors regulate progenitor cell proliferation and differentiation by altering the balance of expression of various bHLH transcription factors. Here we demonstrate whether atorvastatin treatment enhances neurogenesis after stroke in retired breeder rats. Atorvastatin significantly increased numbers of newly generated neuroblasts, and mammalian achaete-scute homologue-1 (Mash1) expression, which encodes a bHLH transcription factor in the ischemic brain. To further investigate the mechanisms of atorvastatin-induced neurogenesis, experiments were performed on neurospheres derived from retired breeder rat subventricular zone (SVZ) cells. Increased neurosphere formation, cell proliferation, telomerase activity and neuronal differentiation were found in cultured neurospheres treated with atorvastatin compared to non-treatment neurospheres. Atorvastatin increased basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF) expression and upregulated Notch1, Hairy-Enhancer of Split1 (Hes1) and Mash1 gene expression in cultured neurospheres. These data indicate that atorvastatin increases the neural progenitor cell pool and neuronal differentiation in older rats. Atorvastatin upregulation of growth factor expression, influences bHLH signaling, which in turn, facilitates an increase in SVZ neural progenitor cell proliferation and neuronal differentiation.

**“Sexual Selection in *Drosophila*: A Behavioral, Morphological, and Geographic Study”**

**Abhinav Khanna and Benjamin Pollack, Plainview Old Bethpage John F. Kennedy High School, Plainview, NY -- 2005-06 National Team Finalists**

Abstract: Species of the genus *Drosophila* exhibit a fascinating diversification of male specific courtship behavior displays, and have historically been the focus of much discussion in sexual selection and speciation literature (Mayr, 1946; Spieth, 1951; Markow, 1981; Kaneshiro, 1983; Carson, 2002). The first part of this two-phase study examines the role of wing spots in mating. In *Drosophila biarmipes*, males exhibit distinct wing melanin patterns, known as wing spots, which coordinate with a distinct wing display behavior during courtship (Kopp and True, 2002). This study examines the effect of wing spots on mating success by using no-choice and single choice mating tests. The second phase of this study examines sexual selection on island populations of *Drosophila melanogaster* to determine mating propensities on islands as opposed to the widely studied mainland (cosmopolitan) locations by using multiple choice mating tests.

The findings of this study yielded a more complete understanding of how behavioral, morphological, and geographical traits influence sexual selection in *D. melanogaster* and *D. biarmipes*. Females of the *D. biarmipes* species show a strong preference for males with wing spots. This suggests that the wing spots evolved partially due to sexual pressure, and that they are maintained across the species by sexual selection. *D. melanogaster* populations in the Bahamas are showing significant non-random mating with mainland USA populations and exhibit the beginning stages of sexual isolation, while results suggest that there is no isolation among *D. melanogaster* from within the same geographical location. Early stages of incipient speciation were evident with both locations. This study suggests that island populations might have differentiated enough in male traits for the evolution of female local preference.

### **“Simulation of the Spread of the West Nile Virus using STELLA 7.02”**

**Jeffrey Schneider and Mark Schneider, South Windsor High School, South Windsor, CT – 2003-04 National Team Winners**

Abstract: The West Nile Virus (WNV) is one of America’s most seriously growing epidemics. WNV first appeared in North America in 1999. In the past four years WNV has claimed among its victims tens of thousands of birds, thousands of wild and domestic animals and over one hundred humans. This project develops a STELLA 7.02 computer simulation of the WNV transmission process and illustrates the efficacy of various virus control strategies. Model simulation comparisons to the 2000 Staten Island WNV outbreak and Hartford County WNV experience in 2002 indicates that the model captures the dominant phenomenological trends associated with disease transmission including crow mortality and identification of periods of high infection. Sensitivity studies indicate that WNV transmission is affected by the number of infected and disease resistant avians in the area and the number of mosquitoes surviving the winter. Suggestions for further research and model development are also provided

**Mentor:** Mr. David White

### **“Determination of Thrombopoietin Productions Sites Among Peripheral Blood Mononuclear Cells.”**

**Alexander Vinberg and Winston Wang, Manhasset High School, Manhasset, NY -- 2001-02 National Team Finalists**

Thrombocytopenia is a condition that afflicts 40% of all HIV patients, (Ballen et al.; 1992) Thrombocytopenic patients, attributed to low Thrombopoietin levels, experience bruising rashes, and even hemorrhaging and blood vomiting (Won, 2000). Thrombopoietin (TPO) is a cytokine that regulates platelet production, (Schattner, 96).

The main sources of TPO are found in the kidneys, liver and spleen, (Sungaran 97). There is a paucity of research on which cells within the peripheral blood produces TPO. Therefore the purpose of the experiment is to isolate the cells in the peripheral blood, which express the mRNA necessary to make TPO. The peripheral blood contains many different types of lymphocytes, including monocytes (CD14 cells), and progenitor cells (CD34 cells). In order to isolate these cells a new process called Magnetic Cell Sorting (MACS) was used. Once each cell population was isolated, RNA was extracted. Afterward through use of RT-PCR the mRNA from each cell population will be tested for the expression of TPO through gel electrophoresis. To ensure viable cDNA samples from RT-PCR, samples were tested for GAPDH expressions in gel electrophoresis.

A pilot study concluded that TPO was expressed in the peripheral blood RNA. Subsequent successful gel electrophoresis trials showed no expression of TPO in CD34, CD3 and CD22 cells, but there was a 347 basepair Thrombopoietin expression in CD14 cells (monocytes). Contamination was disproven with use of negative controls. All samples displayed strong GAPDH expressions and were therefore viable. In conclusion, CD14 cells (monocytes) are the cells which produce TPO in the peripheral blood.

**“Measles Virus Nucleocapsid Gene Enhances the 1,25-Dihydroxyvitamin-D<sub>3</sub> Sensitivity of Osteoclast Precursors from Patients with Paget’s Disease”**

**Debra Ting Hsuing, Health Careers High School, San Antonio, Texas, 2001-02 National Individual Finalist**

Abstract: Osteoclasts (OCLs) in Paget’s disease (PD) patients contain paromyxovirus-like nuclear inclusions and are hypersensitive to 1,25-Dihydroxyvitamin-D<sub>3</sub> (1,25-(OH)<sub>2</sub>D<sub>3</sub>). This hypersensitivity is also found in OCLs formed from normal human bone marrow cells transduced with the measles virus nucleocapsid gene (MVNP). The objective of this study was to determine if MVNP gene induces a coactivator of VDR that enhances 1,25-(OH)<sub>2</sub>D<sub>3</sub> sensitivity in normal OCL precursors *and* pagetic OCLs.

Measurements of 24-hydroxylase (VDR target gene) mRNA expression in OCL precursors and luciferase reporter activity (using vitamin D and retinoic acid response elements) determined that the 1,25-(OH)<sub>2</sub>D<sub>3</sub> sensitivity of pagetic OCL precursors was VDR mediated, and that MVNP-transduced NIH3T3 cell hypersensitivity to 1,25-(OH)<sub>2</sub>D<sub>3</sub> resulted from preferential transcription of VDR-responsive genes rather than overall enhanced steroid hormone transcriptional response. A 17kDa VDR-binding peptide, TAF<sub>II</sub>17 (a component of the TAF<sub>II</sub>D transcription complex), was identified using a GST-VDR chimeric protein with 1,25-(OH)<sub>2</sub>D<sub>3</sub> –treated cell lysates. TAF<sub>II</sub>17 was expressed at high levels in MVNP-transduced and PD-involved marrow cells, but at low levels in normal marrow and PD-uninvolved marrow cells. Furthermore, TAF<sub>II</sub>17-transduced NIH3T3 cells showed increased 1,25-(OH)<sub>2</sub>D<sub>3</sub> sensitivity. These data indicate that enhanced 1,25-(OH)<sub>2</sub>D<sub>3</sub> sensitivity of pagetic OCLs may be due to MVNP.

**“Overexpressed p35 mediates in soluble Aβ-induced neuronal tau phosphorylation *in vitro*”**

**Reed Shaffner, Astronaut High School, Titusville, Fla. – 2001-02 National Individual Finalist**

Abstract: The creation of an eventual cure or highly effective treatment for Alzheimer’s Disease will require a better understanding of tau hyper-phosphorylation. This paper presents a mechanism for tau hyper-phosphorylation and a treatment that could possibly reduce it. The main focus of this study is to determine the effect of soluble forms of Aβ on Cdk5-mediated AD-like tau phosphorylation.

N2a cells were transfected with a p35 vector (N2a/p35 cells), and following differentiation, these cells were challenged with a Aβ<sub>1-42</sub> peptide (sAβ<sub>1-42</sub>). Results show that Aβ<sub>1-42</sub> at relatively low levels (1 to 5 μM) dose-dependently increases tau phosphorylation at AD-specific phosphoepitopes in differentiated N2a/p35 cells compared to controls, an effect that was blocked by antisense oligonucleotides against p35. sAβ<sub>1-42</sub> –induced tau phosphorylation was concomitant with an increase in both the p25 to p35 ratio and Cdk5 activity (but not protein levels). Additionally, blockade of L-type calcium channels or inhibition of calpain completely abolishes this effect. This abolishment indicates that the calcium inhibitors may offer a treatment route in the future. Taken together, these data indicate that sAβ is a potent activator of the p25/Cdk5 pathway, resulting in promotion of AD-like tau phosphorylation *in vitro*.