

# Newsletter



## WV-INBRE Holds 4<sup>th</sup> Annual Summer Research Symposium

The 4<sup>th</sup> Annual Summer Research Symposium of the WV-INBRE was held August 4<sup>th</sup> on the campus of Marshall University in Huntington, WV. The program consisted of oral presentations in the morning session by students and faculty, a luncheon for participants and a poster session in the afternoon (see page 3). Thirty summer interns completed their



summer research program by presenting their research in oral and poster formats. Presentations were also made by faculty and students from the predominantly undergraduate institutions of the WV-INBRE. Over 90 students and faculty from the WV-INBRE institutions across the state of West Virginia attended.

**Rick A. Kittles,**  
Ph.D., Associate Pro-

fessor in the Department of Molecular Virology, Immunology & Medical Genetics, Ohio State University, was the keynote speaker and spoke on the topic **“Race, Genetic Ancestry and Health Disparities: Real or Imagined Differences”**. Dr. Kittles’ research interests are in genetic effects on complex diseases such as prostate cancer, and on personality traits, and skin color. He earned a bachelor's degree in biology from the Rochester Institute of Technology in 1989 and a doctorate in biological sciences from George Washington University in 1998. Dr. Kittles then went to Howard University where he helped establish the National Human Genome Center. As co-director of molecular genetics at Howard University, he directed large-scale, high throughput genotyping and DNA sequencing projects. Dr. Kittles also coordinated a national cooperative network to study the genetics of hereditary prostate cancer in the African American community. He also co-founded African Ancestry, Inc., a private company that provides DNA testing services for determining shared African genetic ancestry to individuals and genealogists around the world. His work on tracing the genetic ancestry of African Americans has brought to focus many issues, new and old, which relate to race, ancestry, identity, and group membership. Dr. Kittles has published numerous articles and book chapters on prostate cancer in the African American population, race, and health disparities.

### Institutions of the WV-INBRE

#### *Lead Universities*

Marshall University  
West Virginia University

#### *Network Research Institutions (NRIs)*

Fairmont State University  
West Liberty State College  
West Virginia State University  
Wheeling Jesuit University

#### *Network Outreach Institutions (NOIs)*

Alderson-Broaddus College  
Bluefield State College  
Concord University  
Davis & Elkins College  
Shepherd University  
West Virginia Wesleyan College

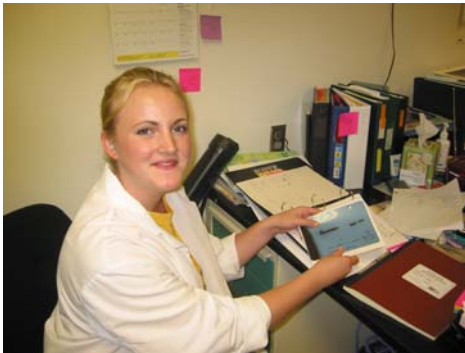
### Inside this issue:

Working in the Lab Photos	2
Symposium Agenda	3
Poster Presentations Titles	4-6
Comments from Interns	6
Poster Presentation Photos	7
Dr. Jarrett Aguilar	8
Bioinformatics Workshop	8
FSU Biomedical Seminar	9
Steering Committee Members	10-11

Supported by:



**Working in the Labs During the 2005 Summer Research Program**



Cara Henry—Bethany College



Coben Thorn—Concord University



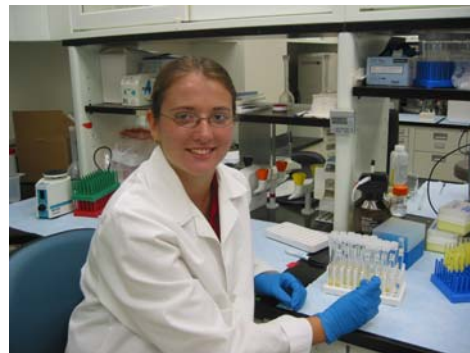
Holly Dudash—Wheeling Jesuit University



Kevin Roush—Alderson-Broaddus College



Matt Thorn—Fairmont State University



Mellisa Leach—West Virginia Wesleyan College



Richard Herrington—Fairmont State University



Sara Lilly—University of Charleston

**Program for the  
West Virginia IDeA Network of Biomedical Research Excellence  
SUMMER RESEARCH SYMPOSIUM  
Marshall University, Huntington, WV  
August 4, 2005**

**Drinko Library – Room -#402**

9:00 – 9:10 AM: Dr. Gary Rankin, Principal Investigator, WV-INBRE - **Opening Remarks**

**Oral Presentations by WV-INBRE Participants**

9:10 – 9:35 AM: Dr. Jarrett Aguilar, West Liberty State College - **“Molecular Dynamics Studies of Active Site/Substrate and Substrate/Substrate Interactions of CYP 2C9”**

9:35 – 10:00 AM: Dr. Albert Magro, Fairmont State University - **“Induction of Apoptosis in Glioblastoma and Breast Cancer Cells by the Inhibition of PPAR- $\alpha$  and FLAP”**

10:00 – 10:25 AM: Dr. Robert Warburton, Shepherd University - **“Proteomics of H-2K<sup>b</sup> & H2K<sup>b</sup> Mutant Antigenic Peptides”**

10:25 – 10:45 AM: **BREAK**

10:45 – 11:05 AM: Bernard Boswell, WV-INBRE Alumni Speaker; First Year Graduate Student in Biomedical Sciences, WVU School of Medicine - **“Control of Cytoskeletal Functions by Caspase-8”**

11:05 – 11:20 AM: Cara Henry, Bethany College, Summer intern - **“Levels and Location of Active  $\beta$ -Catenin and its Partner Proteins in B-16 Mouse Melanoma Cells in Response to Retinoic Acid”**

11:20 – 11:35 AM: Mellisa Leach, West Virginia Wesleyan College, Summer intern” – **“Evaluating Tobacco Smoking's Influence on Alpha-1-acid Glycoprotein Binding of Docetaxel”**

**Guest Speaker**

11:35 – 12:25 PM: Dr. Rick Kittles, Department of Molecular Virology, Immunology & Medical Genetics, Ohio State University - **“Race, Genetic Ancestry and Health Disparities: Real or Imagined Differences”**

**Lunch**

12:25 – 1:30 PM **Memorial Student Center, John Marshall Room**

**Poster Session**

1:30 – 3:30 PM **Memorial Student Center, Alumni Lounge**

WV- INBRE participants will present posters describing their research activities.

Forty poster presentations were made at the 2005 Summer Research Symposium. Participants included interns from the Summer Research Program and faculty and students from the predominantly undergraduate colleges and universities whose research is supported by the WV-INBRE.

Presenters are underlined, summer interns are **bolded**, and their summer mentors are in *italics*. Project Investigators with WV-INBRE- supported research are noted by \*.

THE LOSS OF NITRIC OXIDE PRODUCTION CORRELATES WITH THE INABILITY OF OBESE ZUCKER RATS ON A HIGH FAT DIET TO RESIST SALT-SENSITIVE HYPERTENSION. **Kristen Barbour**, Ryan Morrison, Elsa Mangiarua, *William McCumbee*

UTILIZATION OF LIPID RAFTS BY TYPE-III SECRETION SYSTEMS. **Tara Braithwaite**, Jennifer Salazar, *Joan Olson*

DICLOFENAC NEPHROTOXICITY IN ISOLATED RENAL CORTICAL CELLS FROM MALE FISCHER 344 RATS. **Sophia N. Brown**, Dianne K. Anestis, Lauren L. Richards-Waugh, *Gary O. Rankin*

PRODUCTION OF ALEXA FLUOR488-LABELED REOVIRUS AND CHARACTERIZATION OF TARGET CELL BINDING, REPLICATION COMPETENCE, AND IMMUNOGENICITY OF LABELED VIRIONS. **Ryan Busch**, Ronald Fecek, Hong Lin, Kasturi Pal, Cynthia A. Cunningham, Christopher F. Cuff

EFFECT OF GROWTH CONDITIONS IN *PSEUDOMONAS AERUGINOSA* ON ALGINATE PRODUCTION AND ANTIBIOTIC SENSITIVITY. **Danielle H. Carroll**, Vonya M. Eisinger, *Hongwei D. Yu*

DETECTION OF SINGLE NUCLEOTIDE POLYMORPHISMS WITHIN APOB AND MTP: RELATION TO CARDIOVASCULAR DISEASE. **Brandi D. Connors**, Amanda D. Magers, Amy L. Clark, Robert Kreisberg\*

IDENTIFYING CANDIDATE GENES FOR ACORN STUDIES. **Mary E. Davis**

UPREGULATION OF MANGANESE SUPEROXIDE DISMUTASE PROTEIN AND ACTIVITY BY ALL-TRANS RETINOIC ACID (ATRA): POTENTIAL ROLES OF NFkB AND RETINOIC ACID RECEPTORS (RAR). **Tabetha Davis**, Carla Cook, Michelle Humphrey, Aileen Marcelo, Mariella Tassone, *Kelley Kinningham*, Doug Spitz

OXIDATIVE STRESS AND ANTIOXIDANT TREATMENT IN TIBIALIS ANTERIOR MUSCLE OF AGED RATS. **Holly J Dudash**, Michael J. Ryan, Robert G. Cutlip, *Stephen E. Alway*

MOLECULAR DYNAMICS STUDY OF DAPSONE IN THE ACTIVE SITE OF CYTOCHROME P450 2C9 AND THE CORRELATION OF HYDROGEN BONDING. **J. Leighann Fry**, Zachary R. Hartman, Jarrett S. Aguilar\*

THE ROLE OF GLYCOGEN SYNTHASE KINASE 3B IN NEURONAL CELL DEATH. **Daniel Gallagher**, Cuiling Ma, *Jia Luo*


MOLECULAR DYNAMICS STUDIES OF CYTOCHROME P450 2C9 AND THE EFFECTS OF HYDROGEN BONDING ON THE ORIENTATION OF DAPSONE. Zachary R. Hartman, **Becky L. Gardner**, Jarrett S. Aguilar\*, Rebecca James

NITRIC OXIDE SYNTHASE ACTIVITY IN KIDNEY TISSUE OF HYPERTENSIVE RATS. **Christopher R. Gar-ton**, Sandeep Joshi, *Pedram Ghafourifar*, William McCumbee

MOLECULAR DYNAMICS STUDIES OF HYDROGEN BONDING ON THE METABOLISM OF FLURBIPROFEN IN THE ACTIVE SITE OF CYP 2C9. **Zachary R. Hartman**, Jarrett S. Aguilar\*, Rebecca E. James

LEVELS AND LOCATION OF ACTIVE  $\beta$ -CATENIN AND ITS PARTNER PROTEINS IN B-16 MOUSE MELANOMA CELLS IN RESPONSE TO RETINOIC ACID. **Cara Henry**, *Beverly C. Delidow*





Continued from page 4

THE CAVEOLIN PROFILE IN U266 MULTIPLE MYELOMA CELLS. **Richard Herrington**, Kelly Bailey , and *Jun Liu*

THE IMMUNOTOXIC EFFECT OF A MIXTURE OF ATRAZINE AND ISOXAFLUTOLE. **Emily D. Heston**, *Kathleen Brundage*

INHIBITORY EFFECTS OF Y-27632 AND ML-9 ON CONTRACTILE-INDUCED MYOSIN LIGHT CHAIN PHOSPHORYLATION IN THE SPRAGUE DAWLEY RAT AORTA. **Brenda M. Hill**, Sean Thatcher, Kevin M. Rice, Robert Harris\*, Eric. R. Blough, and *Gary L. Wright*

SINGLE NUCLEOTIDE POLYMORPHISM (SNP) ALLELIC DISCRIMINATION OF APOLIPOPROTEIN C II AND APOLIPOPROTEIN C III. **Brian Huggins**, Amanda D. Magers, Amy L. Clark, Robert Kreisberg\*

BILE ACIDS INHIBIT LIPOGENIC GENE EXPRESSION BY STIMULATING MITOGEN ACTIVATED-PROTEIN KINASE ACTIVITY. **Nicholaos G. Kalathas**, Saswata Talukdar, Brad *Hillgartner*

ROLE OF NITRIC OXIDE IN CR (VI)-INDUCED APOPTOSIS. **Peninnah Kumar**, N. Azad, L. Wang, *Y. Rojanasakul*

EFFECTS OF OXIDATIVE STRESS ON GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) mRNA REGULATION. **Jacob J. Lea**, *Lisa M. Salati*

EVALUATING TOBACCO SMOKING'S INFLUENCE ON ALPHA-1-ACID GLYCOPROTEIN BINDING OF DO-CETAXEL. **Mellisa D. Leach**, *William Petros*

IDENTIFICATION OF GENES CONTRIBUTING TO OBESITY- ASSOCIATED CARDIOVASCULAR DISEASE (OCARD). **Huey Miin Lee**, Mark R. Flood\*, Dana Calica, Bonnie Freeman, Melinda Huff, Sarah Dodson, Amy Clark, Amanda Magers, Robert Kreisberg\*, Mary Davis, Paulette Wehner, Todd L. Green, Donald A. Primerano, James Denvir, Liping Wei, Yulia Dementieva

CELL-CELL ATTACHMENT PROTEIN (CADHERINS) EXPRESSION IN NON-MALIGNANT AND MALIGNANT MOUSE MELANOCYTES. **Sara E. Lilly**, *Richard M. Niles*

SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN APOA AND HL: RISK FACTORS FOR CARDIOVASCULAR DISEASE. **Kathleen E. McIntyre**, Amy L. Clark, Amanda D. Magers, Robert Kreisberg\*

EFFECT OF GENOTYPIC SEX ON THE RESPONSE TO FASTING IN MICE. **Justin R. Morgan**, Nancy Llanza, *Stan Hileman*

MYELOID PROGENITOR CELL ANALYSIS OF HLB STRAIN MICE USING FLOW CYTOMETRY AND THE CFC ASSAY. **Kelli A. Morrison**, Jennifer M. Napper, *Vincent E. Sollars*

MOLECULAR DYNAMICS STUDIES OF CYTOCHROME P450 2C9 AND THE CORRELATION OF PI STACKING AND STERIC HINDRANCE OF MUTATED RESIDUES. Zachary R. Hartman, **Angela G. Niehaus**, Jason J. Cox, Jarrett S. Aguilar\*

ACUTE STRETCH TRIGGERS UPREGULATION OF PROLIFERATIVE PROTEINS IN HEALING MOUSE SKIN. **Mary E. Prescott**, Carl D. Shrader, *Frank D. Reilly*

Continued from page 5

COMPARISON OF S-ADENOSYL-L-METHIONINE (SAmE) AND N-ACETYLCYSTEINE (NAC) EFFECT ON ACETAMINOPHEN-MEDIATED INDUCTION OF TOXICITY. **Ashleigh L. Prince**, Marcus V. Terneus, *Monica A. Valentovic*

POLYMERS IN *E. COLI* DERIVED FROM STREPTOCOCCAL COLLAGEN-LIKE PROTEINS SCL1 AND SCL2. **Kevin Roush**, Clayton Caswell, Runlin Han, Ewa Lukomska, Antoni Zwiefka, *Slawomir Lukomski*

USE OF H19-7 CELLS AS A POTENTIAL FUNCTIONAL MODEL FOR THE HIPPOCAMPUS. **Jeremy Smith**, *Todd Green*, Lawrence Grover

INTERACTION OF HISTAMINE AND SELECTED METABOLITES WITH HEME PROTEINS. **Zechary C. Smith**, Jaroslava Miksovska, Rob Hayes, *Carl Gruetter*

ANGIOGENIC RESPONSE OF PERIPHERAL NERVE ENDOTHELIAL CELLS IN DIABETIC NEUROPATHY. **Kimberly D. Snodgrass**, Ava Dykes, Sean Thatcher, Ryan Morrison, Ben Dalton, Liliana Berti-Mattera, *Elsa Mangiarua*

DETECTION OF GENOMIC MARKERS FOR CARDIOVASCULAR DISEASE; SINGLE NUCLEOTIDE POLYMORPHISMS IN APOLIPOPROTEIN E. *Chris Taylor*, Amanda Magers, Amy Clark, and Robert Kreisberg\*

INSULIN RESISTANCE IS A STRONGER PREDICTOR OF MICROVESSEL RAREFACTION THAN HYPERTENSION IN OBESE ZUCKER RATS. **Coben D. Thorn**, *Jefferson C. Frisbee*

DOES EXPRESSION OF DIFFERENT MUTANT HUMAN SOD1 PROTEINS IN *S. CEREVISIAE* CAUSE MITOCHONDRIAL DEFECTS IN YEAST BY A COMMON MECHANISM LEADING TO ALS? **Matthew J. Thorn**, *Michael R. Gunther*

DEVELOPMENT OF AUTOIMMUNE DISEASE IN NZB/W F1 MICE EXPOSED TO PROPANIL. **Stacey A Velkovich**, *Rosana Schafer*

ROLE OF MAP KINASE IN GROWTH HORMONE SIGNALING IN RAT HIPPOCAMPUS. **Melanie Ward**, *Lawrence Grover*, Todd Green

Comments From The Student Interns  
About The Summer Program

“I changed my mind about applying to Medical School. I am going to apply for a PhD in Biomedical sciences. I didn’t really think I would enjoy research this much.”

“The program was very well coordinated. Every aspect was helpful, not only in doing research, but seeing how research and graduate studies are done. We were given an opportunity to see what being a graduate student would be like, with the amount of work and school that will be needed. I would highly recommend this program to anybody interested in doing research.”

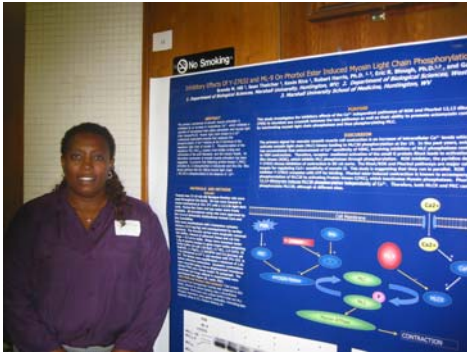
“I just cannot believe how much I have learned in this short span of time, plus my professor and graduate student that I worked with were fantastic.”

“This experience has changed my attitude toward research. I’ve learned a lot about my research topic and about research in general the last couple months.”

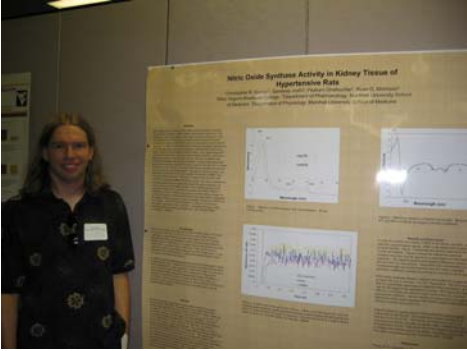
“It was rewarding, I came away knowing a lot more than I arrived with. I also learned lots of new information to help me.”

“I had a very rewarding experience in my lab, and it is going to help me in whatever I decide to do in the future.”

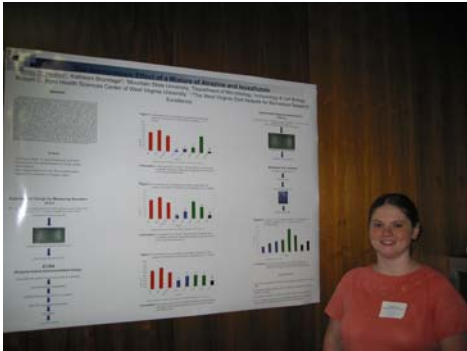
**Summer Symposium Poster Presentations  
August 4, 2005**



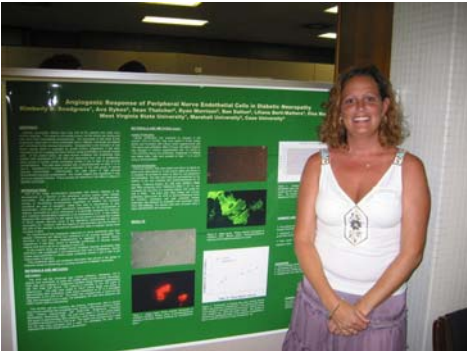
Brenda Hill—West Virginia State University



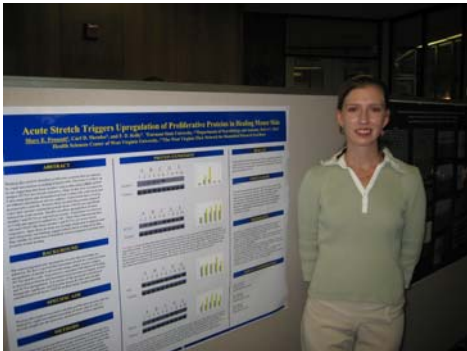
Chris Garton—West Virginia Wesleyan College



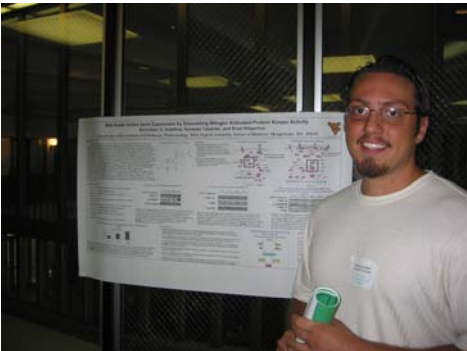
Emily Heston—Mountain State University



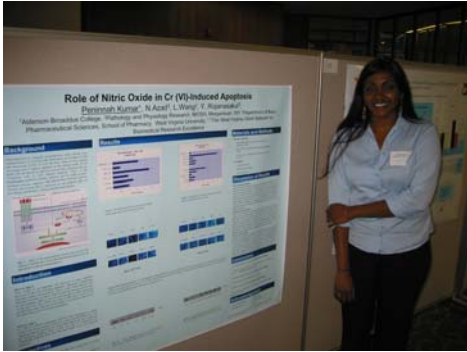
Kimberly Snodgrass—West Virginia State University



Mary Prescott—Fairmont State University



Nick Kalathas—Shepherd University



Penny Kumar—Alderson-Broaddus College



Sophia Brown, West Virginia State University and mentor Dr. Gary Rankin

## WV-INBRE Researcher Uses Molecular Modeling to Study the Active Site of Cytochrome P450 2C9



Dr. Jarrett S. Aguilar, Assistant Professor of Chemistry at West Liberty State College, has been involved with the WV-INBRE program since its inception. He participated as a faculty fellow for two years under the mentorship of Dr. Peter Gannett at the West Virginia University School of Pharmacy when the program was titled WV-BRIN. During that time he began working on molecular modeling projects involving conformations of substrates within the active site of cytochrome P450 2C9. These projects led to co-authorship of a manuscript published in the journal *Biochemistry*, volume 43, pages 7207-7214, 2004.

Currently Dr. Aguilar is a Project Investigator of the WV-INBRE grant. The research that he is conducting is molecular modeling of the active site of cytochrome P450 2C9 and the relationship of dapsone on activation within the active site. The cytochrome P450 enzymes mediate the metabolism of various xenobiotic and endogenous compounds. Many drug-drug interactions are caused by the effect of one of the drugs on the activity of the P450 isoforms involved in the metabolism of the second drug. Some isoforms demonstrate atypical kinetics for the metabolism of certain substrates. It has been suggested that simultaneous binding of two substrates in the active site (a two-site model) is responsible for most atypical kinetic profiles. Dapsone and structurally related substrates have been shown to activate CYP2C9 metabolism of flurbiprofen, naproxen, and piroxicam. The kinetic data suggest both substrate and activator are present in the active site.

These studies concern molecular dynamics calculations involving substrate/active site and substrate/substrate interactions within the active site. Successful completion of the project will provide insight into the mechanism of activation of CYP2C9 metabolism of flurbiprofen, naproxen and piroxicam by dapsone using computational techniques. This method may also be a useful tool in determining if a two-site model can explain all categories of atypical kinetics. The results of these computational studies will provide a method by which harmful and/or beneficial drug-drug interactions can be predicted with computational tools prior to costly, time intensive *in vivo* studies. It will also have a significant impact in the area of drug and drug helper design.

The research being conducted in Dr. Aguilar's lab has been beneficial to the students at West Liberty State College. Thus far, ten students have been provided with valuable research experience in the field of molecular modeling and cytochrome P450 isoforms. Over the past three months he and three students have attended the International Cytochrome P450 conference in Dallas and participated in a molecular modeling workshop. He was a presenter at the annual WV-INBRE symposium and his students displayed posters of their research. His students also presented posters of their research at the West Liberty State College SURE symposium, where one student was an invited speaker for their research. Dr Aguilar has stated that "The WV-INBRE program has been a very rewarding program for me and our students at West Liberty State College".

Research is continuing with hopes to attend and present their findings at a national meeting as well as have another publication from this ongoing project in the near future.

### Bioinformatics Workshop Held

Bioinformatics workshop, **Accelrys GCG 11 SeqLab® and SeqWeb 3® Unveiled and Revealed** held at Marshall University July 25-27 featured the newest release of the Accelrys GCG program suite. Twenty WV-INBRE participants learned the features of the programs, including sequence analysis, PCR primer design and selection tools, sequence comparison (two at a time, or multiple sequence comparisons), evolutionary analysis of sequences, prediction of secondary structure of nucleic acid sequences, and finding motifs in protein sequences.

A new module, SeqMerge®, provides tools to assemble sequence fragments into genes or even genomes. These include the ability to view and align trace files directly from automatic sequencers, mask low-quality ends and vector contamination, and view and edit of questionable calls from automatic sequencers. The finished sequence can then be used with other GCG programs, for example, to compare the sequence to other organisms, predict protein sequence and search for structural motifs.

The new version—Accelrys GCG 11 SeqLab® and SeqWeb 3® are available to all WV-INBRE institutions via accounts at both Marshall University and West Virginia University. The WV-INBRE website contains details on how to get an account.



## Fairmont State University Biomedical Seminar Series

During the past spring semester, Fairmont State University held a Biomedical Speakers Program with faculty and students from the WV-INBRE making research presentations. The participants, their seminar titles and dates of presentations are listed.

- March 24     **Robert Kreisberg, Ph.D.**  
Professor of Biology, West Liberty State College  
**Amy Clark**  
Graduate Student, Fairmont State University
- Presentation: **“Do Triglycerides Have a Role in Heart Disease?”**
- March 31     **Cynthia Cunningham, Ph.D.**  
Technical Director, Flow Cytometric Core Facility  
Research Faculty, West Virginia University Health Science Center
- Presentation: **“Flow Cytometry: Your Cells Never Looked so Good”**
- April 5       **Stephen E. Alway, Ph.D., FACSM**  
Associate Professor and Director of Graduate Studies, Laboratory of Muscle  
Biology and Sarcopenia, Division of Exercise Physiology  
West Virginia University School of Medicine
- Presentation: **“The Role of Apoptosis in Muscle Loss with Disuse and Aging”**
- April 14     **Yehenew Agazie, Ph.D.**  
Assistant Professor, Department of Biochemistry & Molecular Pharmacology  
West Virginia University School of Medicine
- Presentation: **“The Role of SHP2 in Receptor Tyrosine Kinase Signaling and its  
Implication in Cancer”**
- April 21     **Stephen Graber, Ph.D.**  
Associate Professor, Department of Biochemistry & Molecular Pharmacology  
West Virginia University School of Medicine
- Presentation: **“Fantastic Voyage II: Marveling over Molecular Mechanisms”**
- April 26     **Steven Frisch, Ph.D.**  
Professor, Department of Biochemistry & Molecular Pharmacology  
West Virginia University School of Medicine
- Presentation: **“Cell Adhesion and Apoptosis”**

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Principal Investigator

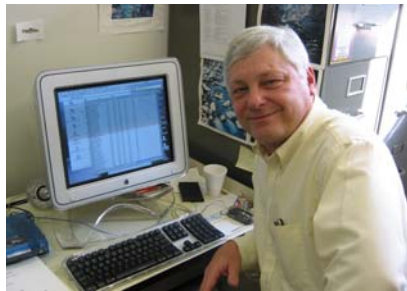


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Vickie Sanders, M.A.  
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