MINI MEDICAL SCHOOL 2007

Genetics of Medicine

Wednesday, November 14, 2007
University of Florida
Health Science Center
8:30am - 3:30pm
Welcome to Mini Medical School 2007!

We are delighted you could join us for a day full of opportunities. Health care professionals and teachers are once again “Partnering for Tomorrow’s Health” by sharing knowledge and insight to better educate the scientists and health care leaders of tomorrow. Join us for a day of “Genetics of Medicine” from the latest research to the clinical applications, and the points in between.

Mini Medical School is an opportunity for middle and high school teachers to experience some of the many facets of the University of Florida College of Medicine, much like a medical or graduate student would. Participants visit clinical and research laboratories, attend lectures, engage in thought provoking discussions, share ideas, and gain an appreciation for the breadth of knowledge and discovery at the University of Florida.

We hope you will find the day enjoyable and educational. Within the University of Florida Health Science Center and Shands at UF, some of the most talented and gifted researchers and clinicians are housed. We are fortunate to be able to spend time with some of them as a sampling of the fascinating work taking place at the University of Florida.

Mini Medical School focused exclusively for teachers is in its seventh year. Your feedback is particularly important in shaping Mini Medical School’s future. The constructive comments received from the evaluations will be a tremendous help in planning for next year. Please complete the evaluation at the end of the day and return it before leaving today.

Mini Medical School 2007 was made possible by the following sponsors:
University of Florida Medical Guild
University of Florida Center for Precollegiate Education and Training
Shands HealthCare

We would like to thank:
Our speakers
Dr. Kevin Brown, Ms. Lisa Brown, Dr. Julie Johnson, Dr. Judith Wubah

The laboratories of
Drs. Baker, Bloom, Bose, Brantly, Bungert, Byrne, Chang, Driscoll, Ghivizzani, Gorbatyuk, Gulig, Lewin, McIntyre, Muzyczka, Renne, Resnick, Sayeski, Weigel-Van Aken, Wu

The UF Medical Guild Volunteers
Timothy Goldfarb, CEO Shands HealthCare

UF CPET
Mike Anthony, Julie Bokor, Sara Day, Mary Jo Koroly, Charles Lawrence, Lauren Pyne

Mini Medical School is coordinated by the UF Center for Precollegiate Education and Training.
The University of Florida Medical Guild was founded in 1959 as a non-profit volunteer organization. Through the fundraising and volunteer efforts of the Guild Members, extraordinary support is made possible for the J. Hillis Miller Health Science Center. The funds support scholarships for students in the College of Medicine and for special projects throughout the Health Science Center and Shands at UF. Through patrons of past Mini Medical School, the Guild has raised over $20,000 for these awards.

Since 1996, when the Guild underwrote Mini Medical School IV, the annual event has attracted participants from school age to retirees. For the past seven years, Mini Medical School has focused on science teachers throughout Florida. It is through these teachers that students will come to know the opportunities available to them through the study of science.

UF CPET is the University of Florida’s “umbrella” for the articulation and transfer of current science, technology, engineering and mathematics (STEM) by linking research faculty and students with K-12 school teachers and students through a variety of campus and statewide programs. For almost half a century, CPET has offered discovery-based learning opportunities for secondary school students and, in more recent years, for teachers. The infrastructure of this University Center allows efficient and effective use of resources to administer programs on campus and throughout Florida. Its programs incorporate bridging activities that include teachers, researchers and industry professionals in preparing and delivering effective STEM education and career opportunities from middle school through graduate school. National and state science education standards govern CPET instructional programs. Activities are designed around National Research Council and Florida criteria for students to learn skills and acquire knowledge, and for developing curricula.

As a Center in Academic Affairs, CPET involves more than 200 UF scientists and engineers annually in its outreach programs. CPET also has an established history of collaborations with local, regional and state schools, and with educational and scientific professional societies. Professional development programs supported by NIEHS, NSF, Woodrow Wilson Foundation and the University of Florida expand the content knowledge, skills, resources, and enthusiasm of in-service teachers. They also forge long-term relationships with researchers that result in converting new expertise into measurably successful new learning modules for students.

Please visit our website at: www.cpet.ufl.edu for more information about our programs.
MINI MEDICAL SCHOOL AGENDA

8:15-8:30am  Registration/ Coffee and Conversation  
Location: Cancer & Genetics Research Complex, Room 133

8:30-9:00am  Welcome  
Ms. Kathryn Seagle, President UF Medical Guild  
Dr. Mary Jo Koroly, Director UF CPET and  
Associate Research Professor, Biochemistry and Molecular Biology  
Location: Cancer & Genetics Research Complex, Auditorium

9:00-9:30am  Mitochondria...The Other Story  
Dr. Judith Wubah  
Assistant Professor  
Department of Anatomy and Cell Biology  
College of Medicine  
Location: Cancer & Genetics Research Complex, Auditorium

10:00-10:30am  Lab Visit One

10:45-11:15am  Lab Visit Two

11:30-12:15pm  Lunch  
Sponsored by Shands HealthCare  
Location: Cancer & Genetics Research Complex, Room 451A/B  
Please take the opportunity to share your teaching practices

12:30-1:00pm  Genetic Counseling  
Lisa Brown, MS, CGC  
University of Florida Cancer Genetics Program  
Department of Hematology/Oncology  
Location: Cancer & Genetics Research Complex, Auditorium

1:15-2:00pm  Pharmacogenomics  
Dr. Julie Johnson  
Professor of Pharmaceutical Sciences  
Director, UF Center for Pharmacogenomics  
Colleges of Pharmacy and Medicine  
Location: Cancer & Genetics Research Complex, Auditorium

2:15-3:00pm  Epigenetics  
Dr. Kevin Brown  
Associate Professor  
Department of Biochemistry and Molecular Biology  
College of Medicine  
Location: Cancer & Genetics Research Complex, Auditorium

3:00-3:30pm  Closing remarks/evaluation  
Location: Cancer & Genetics Research Complex, Auditorium
**Mini Medical School Speakers**

**Kevin Brown, Ph.D.**
Dr. Brown obtained his Ph.D. at the University of Alabama at Birmingham followed by post-doctoral training at Johns Hopkins and NIH. Dr. Brown was an Assistant Professor at LSU Health Sciences Center in the Department of Biochemistry and Molecular Biology and remained there until 2004 when he moved to UF where he is an Associate Professor in Biochemistry and Molecular Biology in the College of Medicine. Dr. Brown’s research interests lie in understanding the factors and mechanisms that maintain stability of the human genome and disease-associated changes in genome structure.

**Julie Johnson, PharmD, FCCP, BCPS**
Dr. Johnson received her B.S. in Pharmacy from the Ohio State University and her Pharm.D. from the University of Texas at Austin. Following her Pharm.D., she completed a post-doctoral fellowship in cardiovascular pharmacology/pharmacokinetics at the Ohio State University. Prior to her appointment at the University of Florida, Dr. Johnson was a faculty member at the University of Tennessee College of Pharmacy. Dr. Johnson is the V. Ravi Chandran Professor of Pharmaceutical Sciences, Professor and Chair of the Department of Pharmacy Practice, Professor in the Colleges of Pharmacy and Medicine, and Director, University of Florida Center for Pharmacogenomics. Dr. Johnson’s research focus is cardiovascular drug pharmacogenomics, and disease-gene associations that may be relevant to pharmacogenomics, and the influence of race/ethnicity on drug response and pharmacogenomics. The majority of her research centers around efforts in hypertension, heart failure, with a primary focus on proteins that are drug targets and the impact of their genetic polymorphisms on drug response and disease.

**Judith Wubah, Ph.D.**
Dr. Wubah recently joined the faculty at the University of Florida in the Department of Anatomy and Cell Biology in the College of Medicine. Dr. Wubah comes to UF from James Madison University in Virginia where she was an Assistant Professor of Biology. She is active in The Teratology Society. Research interests are focused on the causes and biological processes leading to abnormal development and birth defects at the fundamental and clinical level, and appropriate measures for prevention.
MINI MEDICAL SCHOOL SITE HOSTS

**Host: Henry Baker, Ph.D.**  Professor, Molecular Genetics and Microbiology
Dr. Baker’s research focus is in developing gene expression classifiers that can be used to diagnosis illness, predict clinical course and ultimately responsiveness to therapy. Dr. Baker is a participating investigator in Large Scale Collaborative Research Program Inflammation and the Host Response. His laboratory serves as one of three genomic cores for this program. The others are Washington University School of Medicine and the Genomics Center at Stanford University. He is a member of the computational analysis and modeling core of the program. The main goals of this project are using microarrays to determine whether patterns of gene expression from whole blood leukocytes can be used to identify trauma and burned patients at risk of developing MODS. The Baker lab is also dedicated to assisting other researchers interested in applying the tools of functional genomics including microarray technology and bioinformatics to medically important problems.

**Host: Linda Bloom, Ph.D.**  Associate Professor, Biochemistry and Molecular Biology
The general research interests of the Bloom laboratory are in the dynamic protein-protein and protein-DNA interactions that are required to maintain the structure and to preserve the genetic integrity of DNA. Current research is in the general areas of DNA replication and repair, specifically how individual enzymes work to accurately replicate and repair DNA as well as in the coordination and timing of interactions between proteins and between proteins and DNA. Long-term goals are to define molecular mechanisms by which the replication machinery duplicates genomes to support normal cell division, and to define mechanisms by which these enzymes respond to DNA damage that is encountered during replication. Although current work is not directly aimed at developing a cure for a specific disease or disorder, basic research in the area of DNA replication provides the foundation of knowledge on which to make clinical correlations between defects in DNA replication and disease. In addition, the development of therapeutic agents that selectively target the replication machinery of pathogens and the development of diagnostic tools such as PCR require a strong understanding of the biochemistry of DNA replication.

**Host: Himangshu Bose, Ph.D.**  Assistant Professor, Physiology and Functional Genomics
The Bose laboratory is focused on the folding and translocation of mitochondrial proteins that regulate steroid hormone synthesis. Among the proteins imported into mitochondria are enzymes that convert cholesterol into steroid hormones. The steroidogenic acute regulatory protein (StAR) facilitates the movement of cholesterol from the outer to inner mitochondrial membrane. Human StAR mutations cause a lethal disorder of steroidogenesis. StAR’s action is confined to the outer mitochondrial membrane (OMM); in fact, the degree of StAR activity is proportional to the time it resides on the OMM. The laboratory’s goal is to characterize StAR’s entry into mitochondria: to understand StAR’s docking with the OMM, to determine whether it enters the mitochondria through a non-classic import mechanism, to identify proteins involved in that mechanism and to characterize how StAR enters. In addition they seek to understand how StAR binds to, imports, and discharges cholesterol, and how the process of StAR-mediated cholesterol import is related to StAR’s protein import.

**Host: Mark Brantly, M.D.**  Professor of Medicine and Molecular Genetics and Microbiology
Alpha One Foundation Research Professor
Pulmonary, Critical Care, and Sleep Medicine
Dr. Brantly’s research has focused on the development of new treatment modalities. In collaboration with the Powell Gene Therapy Center, some of these efforts have included the use of gene therapy for the treatment of Alpha-1 antitrypsin deficiency. These studies have led to the start of the first Alpha-1 Antitrypsin Deficiency Gene Transfer Research Study in human subjects.

**Host: Jorg Bungert, Ph.D.**  Associate Professor, Biochemistry and Molecular Biology
Dr. Bungert’s research focuses on the analysis of the structure and function of the human beta-globin locus control region (LCR), a powerful DNA regulatory element composed of five DNaseI hypersensitive sites (HS1 to HS5) and located from 8 to 22 Kbp upstream of the human epsilon-globin gene. The LCR regulates the chromatin structure over the beta-globin gene locus and is required for high level globin gene expression throughout erythroid development.
MINI MEDICAL SCHOOL SITE HOSTS

Host: Lung-Ji Chang, Ph.D.  Professor, Molecular Genetics and Microbiology
Retroviruses are RNA viruses that synthesize DNA inside the host cell and then incorporate it into the chromosome by a process called reverse transcription and integration. The Chang lab studies the life cycle of retroviruses, in particular, the retrovirus which causes AIDS, also known as human immunodeficiency virus (HIV). His research focuses on the development of novel gene transfer tools and small animal models for the study of HIV, cancer, vaccines, and immunotherapeutic strategies.

Hosts: Thomas Conlon, Ph.D.  and Denise Cloutier (for Byrne lab)
Barry Byrne, MD, Ph.D.  Professor, Molecular Genetics and Microbiology
Director, Powell Gene Therapy Center (PGTC); Associate Chair of Pediatrics
The Byrne laboratory is actively involved in developing new genetic therapies for cardiovascular disease. In the area of cardiomyopathy, they are studying gene replacement in an autosomal recessive form of fatal cardiomyopathy in children. The disease is the prototype of lysosomal storage disorders leading to skeletal and cardiac muscle weakness. The Byrne laboratory has used AAV vectors to achieve sustained correction of the gene deficiency and correction of the phenotype in natural and transgenic mouse models of the disease. The current therapy is currently being proposed for human clinical trials. Similar therapies are being used to combat cardiac transplantation rejection. Secondly, they are investigating the ability of mesenchymal stem cells to undergo myocardial specification for the purpose of tissue repair in the heart. Finally, several projects are focused on the use of AAV vectors injected into striated muscle to achieve sustained release of therapeutic proteins, including thrombolytic factors and coagulation factors.

Host: Steven Ghivizzani, Ph.D.  Assoc Prof, Depts of Orthopaedics & Rehabilitation and Molecular Genetics
The Orthopaedic Gene Therapy Laboratory, headed by Dr. Ghivizzani, incorporates gene transfer and stem cell technologies to study and develop treatments for musculoskeletal disorders. Scientific investigations focus on the following: the development of gene therapies for arthritis, repair and regeneration of damaged skeletal and connective tissue, the development of gene-based therapies for congenital skeletal conditions, and studies of the pathogenesis and treatment of articular fibrosis.

Host: Marina Gorbatyuk, Ph.D.  (for Lewin lab)
Alfred Lewin, Ph.D.  Professor, Molecular Genetics and Microbiology
Marina Gorbatyuk, Ph.D.  Assistant Research Professor, Molecular Genetics and Microbiology
Gene therapy using ribozymes is one focus of the Lewin laboratory.Ribozymes might be particularly useful in controlling dominant negative genetic diseases—disorders associated with the expression of a single mutant allele. They are designing ribozymes to block retinal degeneration in certain forms of retinitis pigmentosa and have tested these in animal models of this dominant genetic disorder using AAV vectors. They have used AAV-delivered ribozymes to create mouse models of mitochondrial diseases, which are unattainable using transgenic approaches because of embryonic lethality. Work is being done on a similar approach to obtain a faithful animal model of Parkinson Disease and of Age-Related Macular Degeneration.

Host: Paul Gulig, Ph.D.  Professor, Molecular Genetics and Microbiology
Dr. Gulig’s research interests are the molecular pathogenesis of bacterial disease, in particular Vibrio vulnificus, and detection of infectious agents for biodefense. The Gulig laboratory is focusing their studies on how the vibrios replicate so rapidly, how they avoid the host defenses, and how they cause damage in such a short period of time--24 hours after infection. The laboratory is now moving into genome-wide analysis of gene expression to determine the transcriptome of V. vulnificus growing in infected host tissues compared with growth in vitro. In biodefense, the lab is collaborating with researchers at the University of South Florida to develop immunological tools for use in a real time/near real time, fiber optic-based system to detect bacterial and viral agents of bioterrorism.
MINI MEDICAL SCHOOL SITE HOSTS

Host: Paul Kuipers, MS (for Driscoll lab)
Daniel Driscoll, MD Ph.D. Prof & Hayward Prof. of Genetics Research, Pediatrics, Molecular Genetics, and Medicine

The phenomenon of genomic imprinting is the differential modification of the maternal and paternal genetic contributions to the zygote, resulting in the differential expression of parental alleles during development and in the adult. A disturbance in genomic imprinting in humans has been shown to play a role in several birth defects, genetic diseases and cancers. In humans, the most convincing demonstration of an imprinted region is at chromosome 15q11-q13 with a deficiency of the maternal region resulting in the Angelman syndrome (AS) and a deficiency of the paternal region resulting in the Prader-Willi syndrome (PWS). These two syndromes, which share a common chromosomal deletion, are vastly different clinically. The team in Pediatric Genetics has assembled one of the best characterized panels of AS and PWS patients in the world, allowing them to pursue several avenues of research regarding mammalian genomic imprinting. Using AS (paternal allele only) and PWS (maternal allele only), Dr. Driscoll’s group is able to identify differences in DNA methylation, gene expression, DNA replication and chromatin structure between the maternal and paternal alleles in the imprinted 4 megabase 15q11-q13 region.

Host: Lauren McIntyre, Ph.D.
Associate Professor, Molecular Genetics and Microbiology

The McIntyre Lab is developing new methods to help analyze large amounts of data and understand complex problems in genetics and evolution. Similar to Systems Biology, they are largely concerned with whole systems of “omic” data from genomic to proteomic, and apply statistical theory to extend research across DNA, RNA and proteins and model the relationships that result in the phenotype. This area of research has also been referred to as ‘genetical genomics’. Dr. McIntyre studies populations that have available genetic information, from structured populations to natural populations. Beyond examining single populations for data, the McIntyre lab studies the relationship between structured populations and natural populations. Dr. McIntyre’s group also studies the technologies and procedures used in their experiments to understand limitations and ensure that data is accurate to an acceptable margin of error.

Host: Nicholas Muzyczka, Ph.D.
Eminent Scholar, Molecular Genetics and Microbiology

The biochemistry of AAV DNA replication and the development of AAV vectors for gene therapy and delivery are the focus of Dr. Muzyczka’s laboratory. His research focuses on three issues that need to be resolved if AAV vectors are to be useful. First, he is investigating the behavior of AAV in primary cells or whole animals, a topic about which there is little information. Second, he is constructing vectors carrying a variety of promoters to determine if AAV proviruses can supply sufficient expression to correct genetic defects. Third, his lab is testing a number of strategies for improving the methods currently used to grow recombinant AAV viruses are being tested. Dr. Muzyczka is also working on the problem of defining the mechanism of AAV integration.

Host: Rolf Renne, Ph.D.
Associate Professor, Molecular Genetics and Microbiology

Work in Dr. Renne’s laboratory is focused on latent DNA replication and long-term episomal maintenance of Kaposi’s sarcoma-associated herpesvirus (KSHV). The long-term goal is to increase knowledge on the mechanisms by which KSHV successfully establish and maintain latency – potentially these studies can lead to the development of novel therapeutic strategies. Most recently, the Renne laboratory has started working on KSHV-encoded microRNAs (miRNAs). MiRNAs represent a novel class of post-transcriptional regulators, which bind to 3, UTRs of mRNAs and either slow down their translation and/or induce their degradation. It is now known that a large number of DNA viruses also encode miRNAs their by likely modulate the host cellular transcriptome. Currently, Dr. Renne is pursuing a variety of genomics, proteomics, and ribonomics-based approaches to determine host cellular and/or viral genes that may be regulated by KSHV-encoded miRNAs.
As the embryonic progenitors of mature gametes, primordial germ cells (PGCs) play critical roles in both reproduction and embryogenesis. During development, germ cells first appear in the extraembryonic tissues and subsequently migrate to the developing fetal gonad. Recent evidence suggests that primordial germ cells are also responsible for the erasure of epigenetic marks in the germline, and that erasure coincides with gonad colonization. The Resnick laboratory is interested in understanding the mechanisms which regulate these diverse programs in early gonadal germ cells. Recently, the Resnick laboratory united with Cami Brannan’s lab using mouse genetics to investigate mechanisms underlying genetic imprinting in the Prader-Willi / Angelman Syndrome region. Most genes are equally expressed from both the maternal and paternal alleles. However, some genes are imprinted, and are expressed from only one parental allele. Prader-Willi and Angelman Syndromes are clinically distinct, but result from opposite patterns of imprinting of human chromosome 15q11-q13.

Research in the Sayeski laboratory is focused on elucidating the intracellular signaling pathways of the vasoactive peptide, angiotensin II. Angiotensin II is the effector molecule of the renin-angiotensin system and is crucial for maintaining pressure and electrolyte homeostasis in animals. In addition to having hemodynamic effects, angiotensin II can also act as a potent growth factor. Under certain conditions however, the growth promoting effects of angiotensin II can be maladaptive and lead to vascular disease states that are routinely seen in humans. Current studies in the laboratory are aimed at determining the importance of tyrosine kinases in mediating angiotensin II-dependent growth responses and determining whether the catalytic activity of these tyrosine kinases is altered in disease states. A variety of cellular, molecular, genetic and biochemical techniques are used for these studies.

The Division of Cellular and Molecular Therapy consists of a group of investigators having shared interests in both the molecular and cellular biology of AAV and parvovirus B19 as eminently suitable vectors for human gene therapy. It also serves as a reference point for collating the in-flow and out-flow of ideas and materials relevant to application of parvovirus vectors in basic science research and clinical trials on campus as well as elsewhere throughout the scientific community.

Broad research interests are to understand the molecular events responsible for stem cell maintenance, cell fate determination and oncogenic transformation. Dr. Wu is particularly interested in a specific signal transduction pathway mediated by the Notch receptors, the Notch signaling pathway. Notch signaling is one of a few highly conserved cell-fate determination pathways that are essential for the development of almost all tissues. Interestingly, this pathway also has emerging roles in regulating self-renewal of normal and cancer stem cells. Abnormalities in the components of this pathway are associated with a number of developmental disorders and cancer.
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### GENETICS OF MEDICINE

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</table>
MINI MEDICAL SCHOOL EVALUATION FORM

Please complete this form and return before leaving. Feel free to use the back of this sheet if you need more space. Thank you for attending Mini Medical School. We hope you had a wonderful day.

1. Are you a middle school or high school teacher?
   Middle         High
   3=Very informative, 2=Somewhat informative, 1=Not informative
   
2. Was the talk by Dr. Wubah informative? 3 2 1
   a. What did you like best about the presentation?

3. Which number laboratory group were you in? ______________________________
   a. How would you rate the first visit? 3 2 1
   b. What did you like best about the first visit? Would you make any changes?
   c. How would you rate the second visit? 3 2 1
   d. What did you like best about the second visit? Would you make any changes?

4. Is the exchange of “Best Practices” beneficial? How could it be improved?

5. Was the presentation by Ms. Brown informative? 3 2 1
   a. What did you like best about the presentation?

6. Was the afternoon talk by Dr. Johnson informative? 3 2 1
   a. What did you like best about the presentation?

7. Was the afternoon talk by Dr. Brown informative? 3 2 1
   a. What did you like best about the presentation?

8. Will you be able to incorporate what you learned today in your classroom? Yes No

9. How did you hear about the program? (please circle all that apply)
   CPET (Julie Bokor)    SIFT    Science Supervisor    School administrator

10. Do you have any suggestions for improvement?

11. What was you favorite part of the day?

12. Do you have a suggestion for next year’s topic?

13. Please make a ‘one-line’ comment about the program and its value that can be used on the program’s website or in future brochures. (There is no need to provide your name, unless you would like it used with the comment.)