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## **Acknowledgements**

On behalf of the Academic Affairs Committee of the Graduate Student Council, we especially thank the following for their sponsorship of the 2009 Graduate Student Research Symposium:

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Dear Vanderbilt Community,

Welcome to the 23<sup>rd</sup> Annual Graduate Student Research Symposium! Thank you for attending and please take full advantage of today's oral presentations running continuously from 9am-4pm and our single poster session from 11am-1pm.

The diversity and quality of the research being done by graduate students at Vanderbilt is reflected by the submissions received for this year's event. Over one hundred individuals from twenty-eight departments are participating. We urge you to use this collection of abstracts to guide you through GSRS 2009.

After each session you attend, please take time to fill out a survey. This not only helps us as we look forward to next year's event, but it also enters your name into our drawing for one of several door prizes.

This year we are pleased to include a keynote address by Dr. Susan Basalla entitled, "What Every Graduate Student Should Know About Jobs Outside Academia" to occur at 4:10pm in Ballroom C of the SLC. A free copy of her co-authored book *So What Are You Going To Do With That? Finding Careers Outside Academia* will be distributed to the first 150 guests. We hope you will join us for both the keynote address and reception immediately following.

Thank you again for your attendance and enjoy the day!

Sincerely,

The Academic Affairs Committee of the Graduate Student Council

Hui-Yiing Chang  
Marquicia Pierce  
Michael Tidwell  
Jennifer Whisenant  
Molly Brown, Vice President of Academic Affairs

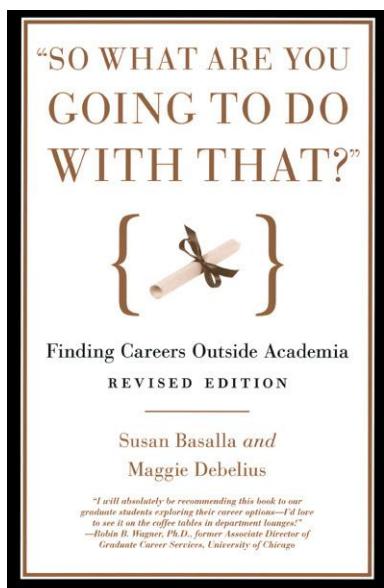
# **Graduate Student Research Symposium Keynote Address**

## **“What Every Graduate Student Should Know About Jobs Outside Academia”**

**Keynote begins at 4:10pm in Ballroom C. Reception and book signing to follow.**

The academic job market is fickle and slow. Why not keep your options open by exploring careers outside academia while you wait? Learn about alternatives to adjuncting and how to avoid the job-hunting mistakes that graduate students most frequently make. Basalla offers real-life examples and practical step-by-step advice for M.A.’s and Ph.D.’s seeking fulfilling work outside academia.

**Susan Basalla, Ph.D., co-author of *So What Are You Going To Do With That? Finding Careers Outside Academia***



Graduate schools churn out thousands of Ph.D.’s and M.A.’s every year. The chances of an academic landing a tenure-track job seem to shrink as student loan debt grows. What’s a frustrated would-be scholar to do? Can a non-academic job really be rewarding—and will anyone want to hire a grad-school refugee?

With “So What Are You Going To Do With That?” Susan Basalla and Maggie Debelius—Ph.D.’s themselves—answer those questions with a resounding “Yes!” Full of concrete advice for anyone contemplating the jump from scholarship to the outside world, “So What Are You Going To Do With That?” covers topics ranging from interview etiquette to translating skills learned in the academy into terms an employer can

appreciate. Packed with stories from real people who have made this daunting—but potentially rewarding—transition, and written with a deep understanding of both the joys and difficulties of academic life, this fully revised edition will be indispensable for any graduate student or professor who has ever flipped through the want ads and wondered, “What if?”

**A free copy of Dr. Basalla’s co-authored book will be distributed to the first 150 guests!**

## **Graduate Student Research Symposium**

March 30, 2009

## Schedule of Events

*All presentations are allotted 20 minutes—15 minutes for the presentation and 5 minutes for Q&A*

**8:30-9:00am—Registration, Front Lobby**

## **9:00—Presentations, Session 1**

## **Ballroom A—Tumorigenesis & Cancer Therapy**

Moderator: Kimberly Boelte (Graduate Student, Department of Cancer Biology)

- AKT activation in HNSCC predicts survival and correlates with HPV status..... Xinyuan Lu  
JAK3 Mutations May Be Tumor Progression Events in Adult T-cell Leukemia/Lymphoma..... Natalina Elliott  
The role of Bid in the ATR-mediated DNA damage signaling pathways..... Yang Liu  
Development of a Lymphedema Symptom Checklist in Head and Neck Cancer Patients..... Jie Deng

## **Ballroom B—The Dynamic Host-Pathogen Interaction: How Host & Infectious Agent respond to each other**

Moderator: Megan Johnson (Graduate Student, Department of Microbiology & Immunology)

- Long-range distal elements within the Ifng locus.....Patrick Collins  
*Staphylococcus aureus* heme oxygenases are differentially regulated during infection.....Michelle Reniere  
Sodium chloride induces increased antibiotic resistance in *Acinetobacter baumannii*.....Indriati Hood  
PD-1 is highly expressed on dominant CTL clonotypes over time and.....Joseph Conrad  
during varying levels of antigen exposure

## **Ballroom C— Radical Agrarianisms**

Moderator: Amanda Hagood (Department of English)

- |  |                    |
|--|--------------------|
| Convivial Communities: An Agrarian Alternative to Violent Empire.....                | Timothy Eberhart   |
| Notes Toward a Radical Agrarianism.....  | Charles Sentell    |
| Farming the Future: Agrarianism, Utopia, and the Challenges Ahead.....               | John Morrell       |
| Fractal hegemony: ethnoecological model for hunter-gatherers of the rain forest..... | Gerson Levi-Mendes |

## **Board of Trust—Structural Biology**

Moderator: Andrew Morin (Graduate Student)

- Moderator: Andrew North (Graduate Student)

Structure and Functional Analysis of the U-Box Domain of.....Kyle Nordquist  
E4B reveals Unique Monomeric Assembly

Structural Insights into RPA Architecture and Function from Heteronuclear NMR Spectroscopy.....Chris Brosey

CryoEM guided de novo Protein Fold Elucidation.....Steffen Lindert

Move it, move it: The 1.85 Å crystal structure and mechanism of a.....Timothy D. Panosian  
phosphopentomutase from *Bacillus cereus*

**Meeting Room#1—Department of Economics, complete schedule from 9-4pm on p.8**

**10:45**—Presentations, Session 2

## **Ballroom B—Target Cell Selection and Replication Mechanisms of Mammalian Reoviruses**

Moderator: Bernardo Mainou (Post-doc, Department of Pediatric Infectious Disease)

- Molecular determinants of reovirus binding to cell-surface sialic acid.....Johnna Allen  
Identification of reovirus cell-tropism determinants in replication protein  $\mu 2$ .....Laura Ooms  
Identification of Cellular Proteins that bind Mammalian Reovirus RNA:.....Charles Martinez III  
A Role for Editing Enzymes?

## **10:45—Presentations, Session 2, continued**

### **Ballroom C—Feminist Food Politics**

Moderator: Brooke Ackerly, Ph.D. (Assoc. Professor, Political Science)

- Performing Troubling Practices of Hope: Community Food Systems Work in Congregations.....Kate Lassiter  
Family Farm: Redomesticating U.S. Agriculture in Barbara Kingsolver's.....Amanda Hagood  
Animal, Vegetable, Miracle  
Getting to the Root: Structural Racism as a Root Cause of.....Claire McKeever  
Food Insecurity in Nashville's Urban Areas

### **Board of Trust—Computational Structural Biology**

Moderator: Nils Woetzel (Graduate Student)

- Docking antidepressants into the human serotonin transporter.....Steven Combs  
Ligand residues and ligand rotamer libraries: extending side chain.....Gordon Lemmon  
rotamer sampling to small molecules  
Improve fold recognition by using a word-based alignment algorithm in BCL::Align.....Sten Heinze

## **11:00-12:00—Poster Session 1, Ballroom A**

*Refreshments, Ballroom A.*

- Determination of Functionalization Efficiency of Gold Nanoparticles.....Charleson Bell  
Engineering a Nanoporous Carbon Adsorbent for Separation of Light Gases from Air.....Amanda Furtado  
Injectable, Biodegradable, Porous Polyurethane Scaffolds for Tissue Regeneration.....Andrea Hafeman  
Triadin deletion Alters Calcium Sparks in Murine Cardiomyocytes.....Fredrick Hilliard  
Updating objects in visual short-term memory.....Philip Ko  
IDPicker 2.0: Improved Protein Assembly with High Discrimination Peptide Identification Filtering.....Zeqiang Ma  
Gene expression correlates of spontaneous physical activity and BMI in the motor cortex and striatum....Amanda Mitchell  
Fabrication and Optical Applications of Nanostructured Vanadium Dioxide.....Joyeeta Nag  
Does Understanding of Social Cues Affect Toddlers' Ability to Learn From People on Video?.....Kate O'Doherty  
Speech recognition and subjective ratings with wireless speech transmission via hearing aids.....Erin Picou  
Structure of DNA glycosylase AlkD reveals a new architecture for locating and excising alkylpurines.....Emily Robinson  
Toward a General Active Cannula Model.....Caleb Rucker  
Visual attention in deaf, unilaterally hearing-impaired and hearing adults.....Hollea Ryan  
Multi-Resolution Comparison of Single-Shot EPI, 3DFFE, and PRESTO for fMRI at 7T.....John Sexton  
Effects of Sensitivity Encoding and Physiological Noise on Temporal Signal Stability and fMRI at 7T.....John Sexton  
Quantitative or Qualitative Differences with DIMCAT, Applied to Differences in Successful Intelligence.....Stijn Smeets  
Separation and Reproducibility of Touch Activations in.....Elizabeth Ann Stringer  
Areas 3b and 1 within the Primary Somatosensory  
Getting a "Feel" for Dynamic Systems.....Jenna Toennies  
Superhydrophobic films: Biomimeting water repellency.....Juan Tuberquia  
Cervical Cancer Detection with Raman Spectroscopy.....Elizabeth Vargas

## **12:00—Presentations, Session 3**

### **Ballroom B—Advances in Nanotechnology & Materials Science**

Moderator: Steve Vilt (Graduate Student)

- Origin of Colossal Ionic Conductivity in YSZ-STO Superlattices.....Timothy Pennycook  
Convection Heat Transfer of Water-based Alumina Nanofluids .....Nicholas Roberts  
The theoretical isosteric heat of adsorption in the Henry's law region for carbon nanopores.....Jian Liu  
Chemical Vapor Deposition of Aluminum Oxide Thin Films.....Benjamin Schmidt  
Using a Novel Single Source Precursor

### **Ballroom C—Preparing Tomorrow's Teachers for Today's Students**

Moderator: Emily Bigelow (Student, Teaching & Learning)

- Second Language Acquisition Theory and Teacher Preparation for English Language Learners.....Mikel Cole  
Mobility & Reading Achievement: A Multi-level Analysis.....Kelly Puzio  
Professional Development: When Preparation is Not Enough.....Christopher Keyes  
The Place for Narrative: Literacy Instruction for African American students.....Emily Bigelow  
Beyond the Digital Divide: Reviewing the Intersections of New Literacies and Issues of Diversity....Nathan Phillips

**12:00—Presentations, Session 3 continued**

**Board of Trust—Cannibal Corpses and other Abominations: what the undead tell us about ourselves**

Moderator: Mike Tidwell (Graduate Student, Department of Anthropology)

The Dubious Comfort Provided: Zombies and Mortuary Ritual.....	Mike Tidwell
The Virgin-Vampire: Transcending the Limits of Traditional Sexual Ethics.....	Natalie Wigg-Stevenson
Spawns of the Golem: From the Monstrous to the Heroic.....	Chris Paris
Between Earth and Hell: The Living in Hell and the Dead on Earth.....	James Grady
When the Man Comes Around: The Inescapable Eschaton in.....	Linzie Treadway
Zack Snyder's Dawn of the Dead (2004)	

**12:00-1:00pm—Poster Session 2, Ballroom A**

*Refreshments served, Ballroom A.*

The Wnt modulator sFRP2 enhances mesenchymal stem cell wound repair.....	Maria Paula Alfaro
In vitro and in vivo studies of cPLA2 involvement in VEGF mediated retinal neovascularization.....	Josh Barnett
Role of RGS2 in myeloid cells and tumor vascularization.....	Kimberly Boelte
Effect of Dyslipidemia on Natural Killer T Cell Activation.....	Nicole Braun
Discovery of a highly M <sub>5</sub> -preferring muscarinic acetylcholine receptor allosteric potentiator.....	Thomas Bridges
Regulation of cell adhesion and motility: a novel function of arrestin proteins.....	Whitney Cleghorn
The Role of NKT Cells in the Pathogenesis of Obesity and Type 2 Diabetes.....	Curtis Gabriel
Rewiring the murine hepatitis virus replicase polyprotein to function with a single papain-like prot.....	Mark Gadlage
Cortical regulation of medium spiny neuron dendritic spine loss in a parkinsonian rat model .....	Bonnie Garcia
YAP signaling plays a role in TGF-beta activation of epithelial plasticity.....	Lin Ge
New iNKT cell phospholipid reactivity revealed after release from negative selection by inhibiting N .....	Laura Gordy
G-protein mediated regulation of $I_{Ca}$ and catecholamine release in adrenal chromaffin cells.....	Mark Jewell
Characterization and antiparkinsonian effects of novel positive allosteric modulators of mGluR4.....	Kari Johnson
Bone Marrow Derived Cells Incorporate in the Prostate During Regrowth Following Castration.....	Veronica Placencio
Immune Defenses of Xenopus laevis Against a Fungus Linked to Global Amphibian Declines.....	Jeremy Ramsey
Type III Transforming Growth Factor- $\beta$ Receptor regulates proliferation and apoptosis in epicardial cells....	Nora Sanchez
MDs on the move: The ecological and psycho-political validity of the African medical brain drain.....	Benjamin Siankam
The lupus susceptibility locus Sle3 is not sufficient to accelerate atherosclerosis in LDLr <sup>-/-</sup> mice.....	Nekeithia Wade
ATF4 regulates chondrocyte proliferation and differentiation during limb development.....	Weiguang Wang
by activating <i>Indian Hedgehog</i> transcription	
Mtgr1 is a tumor modifier in inflammatory carcinogenesis in the colon.....	Caitlyn Whitten

**2:00—Presentations, Session 4**

**Ballroom A—Aspects of Astronomy and Astrophysics**

Moderator: Sonali Shukla (Graduate student, Department of Physics & Astronomy)

Understanding X-ray emission from the plasmas of young stars.....	Sonali Shukla
Search for Star-Disk Interaction Among the Strongest X-ray Flaring Stars.....	Alicia Aarnio
in the Orion Nebula Cluster	
The Search for HI Clouds in Nearby Galaxy Groups.....	Katie Chynoweth
Characteristics of the most massive stars in NGC346 in the small magellanic cloud.....	Thompson Le Blanc
X-Ray/Infrared Characteristics of T Tauri Stars.....	William Teets

**Ballroom B— Translational Biology: From Bench to Bedside**

Moderator: Jennifer Whisenant (Graduate Student)

Formation and Metabolism of 15-deoxy-D <sup>12,14</sup> -prostaglandin J <sub>2</sub> (15-d-PGJ <sub>2</sub> ) in Vivo.....	Klarissa Hardy
Caenorhabditis elegans as a model to study mechanisms of methylmercury toxicity.....	Kirsten Helmcke
BMP signaling regulates eNOS expression and function in the murine pulmonary vasculature.....	Jonathan Lowery
Foxd3 Regulates Neural Crest Multipotency and Self-Renewal.....	Nathan Mundell
Parametric Variation with the Reference Region Model for.....	Mary Loveless
Dynamic Contrast Enhanced MRI (DCE-MRI)	
Functional characterization of an intronic epilepsy mutation in the GABRG2 gene.....	Mengnan Tian

**2:00**—Presentations, Session 4 continued

**Ballroom C— The Metabolic Syndrome**

Moderator: Bonnie Surmi (Graduate Student, Department of Molecular Physiology & Biophysics)	
Characterization of <i>Gulo</i> knockout mice on Vitamins C & E double deficient diet.....	Marquicia Pierce
Leptin-Mediated Macrophage Chemotaxis into Adipose Tissue.....	Dario Gutierrez
Macrophage Inflammatory Protein-1 $\alpha$ Has a More Significant Role in.....	Bonnie Surmi
Diet Induced Obesity in Hyperlipidemic LDLR-/- Mice than in Normolipidemic Mice	
Assessment of Energy Expenditure and Substrate Utilization in Obese and.....	Joshua Squiers
Normal Weight Patients with Heart Failure	

**Board of Trust—Ideology, Identity and Consciousness: the power of ideas through history**

Moderator: Tamara Lewis (Graduate Student, Graduate Department of Religion)	
Anglo-Africans and Cosmopolitans: Staging Race and Nation on the Eve of the Civil War.....	Derrick Spires
Colonial Propaganda and Rebellion: The Ideology of Dissent in Late 17th Century Maryland.....	Kevin Vanzant
The Orders of Queen Elizabeth I to Export Blacks from England in Religious Context.....	Tamara Lewis
Radical Roots: Identity and Consciousness in the Southern Black.....	Selena Sanderfer
Territorial Separatist Movements, 18	
Whose Land is it Anyway? Insight into Questions of Ownership in Genesis 47:13-26.....	Brandon Simonson

**4:00**—Presentations, Session 5

**Board of Trust— Literature and Language Acquisition and Assessment**

Moderator: Kathryn Guillot (Graduate Student, Department of Hearing & Speech Sciences)	
"Ki petit semme petit quelt:" Old French Romance in the Language Classroom.....	Rachel Early
Norm-referenced assessment? What are we assessing?.....	Kathryn Guillot
Phonological Awareness Development: Kindergarten Children's Segmentation and.....	Krystal Werfel
Representation of Consonant Blends	
(Strategies of) Spatial Disorientation in Mark Z. Danielewski's House of Leaves.....	Lucas Faugere

**4:10pm**—Keynote Address, Ballroom C

**"What Every Graduate Student Should Know About Jobs Outside Academia"**  
by Susan Basalla, Ph.D.

The first 150 guests will receive a free copy of Dr. Basalla's co-authored book, *So What Are You Going To Do With That? Finding Careers Outside Academia*

Reception and book signing to follow, *Ballroom A*

**9:00–4:00pm** Department of Economics, Meeting Room #1

The Department of Economics will be holding presentation panels in Meeting Room #1 according to the following schedule:

**Session 1: Empirical Microeconomics, 9-10.30 am**

Trade Liberalization and Skilled Migration: Substitutes or Complements?..... Omolola Soumonni  
Slum Clearance and Urban Renewal in the United States, 1949-1974....William J. Collins and Katharine L. Shester  
Overworking to win the case: representing cases in court and young lawyers' hours of work.....Rosa Ferrer  
Employer-Employee Match and Statistical Discrimination.....Yariv Fadlon

**Session 2: Microeconomic Theory, 10:45-12:00pm**

Redundant disclosure of product information.....Roger Crawford  
Enhancing transportation security against terrorist attacks.....Sunghoon Hong  
A Characterization of Pairwise Nash Stable Networks.....Valeska Groenert

**Session 3: Macroeconomics, 1:15-2:30 pm**

Everyday Low Prices and Temporary Price Reductions.....P.J. Glandon and Matthew Jaremski  
So Far Away?: Distance vs. Firm Risk in Determining Banknote Exchange Rates.....Matthew Jaremski  
Real effects of the New England Monetary Experiment.....Caleb Stroup

**Session 4: Econometrics and Measurement, 2:45-4 pm**

Consistent rank selection in co-trending and co-breaking models.....Zhengfeng Guo and Mototsugu Shintani  
A Class of Association Sensitive Multidimensional Welfare Indices.....Suman Seth  
Dynamic Treatment Effects and Optimal Dynamic Treatment Assignments.....Heng Chen

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**Affiliated Events— Department of English Conference**

Friday, April 3<sup>rd</sup>

Sarratt 216/220

The following first-year graduate students in the Department of English will be delivering presentations at the conference:

Michael Aljewicz  
Elizabeth Barnett  
Heather Freeman  
Caroline Hovanec  
Amanda Johnson  
Chris Pexa  
Donika Ross

Abstracts can be found starting on p.13

## **GSRS 2009 Participant Abstracts: Presentation Panels (alphabetical order by panel title)**

### **Advances in Nanotechnology & Materials Science**

- 1) Origin of Colossal Ionic Conductivity in YSZ-STO Superlattices  
Timothy Pennycook—Department of Physics & Astronomy

An eight order of magnitude increase in the ionic conductivity of yttria-stabilized zirconia (YSZ) has recently been demonstrated in YSZ/strontium titanate (STO) epitaxial heterostructures. YSZ is the preferred electrolyte for solid oxide fuel cells (SOFC), in which the ionic conductivity is the major factor limiting the energy conversion efficiency. A colossal increase in the ionic conductivity, therefore, goes a long way towards increasing SOFC practicality by increasing efficiency overall and reducing the operating temperature necessary for efficient operation. In the heterostructures, thin layers of YSZ are sandwiched between STO. The STO induces a large 7% expansive in-plane strain on the YSZ. Simulated annealing using density functional theory reveals that this strain produces a new structure with a disordered O sublattice in both pure ZrO<sub>2</sub> and YSZ. The theoretical mean square transverse variation of the Zr positions in the new structure at 360K are consistent with the unusually large strain contrast observed in atomic resolution scanning transmission electron microscopy images of the material. Quantum molecular dynamics simulations show the disordered O atoms in strained bulk YSZ to be dramatically more mobile than in the cubic fluorite structure, suggesting that the large strain is the origin of the colossal ionic conductivity observed experimentally.

- 2) Convection Heat Transfer of Water-based Alumina Nanofluids  
Nicholas Roberts—Department of Mechanical Engineering

Nanofluids are solutions of a small fraction of suspended nanoparticles in a bulk fluid. Nanofluids have shown great promise as heat transfer fluids over typically used bulk fluids and fluids with micron sized particles. The nanoparticles do not settle in the fluid and do not cause clogging or damage to surfaces that is seen with micron sized particles. In the current work we compare the performance of different mass loadings and particle sizes of water-based alumina nanofluids in a single heated tube to pure water. The convection coefficients of the fluids are calculated over a range of flow rates by applying a constant heat flux and measuring temperatures along the length of the tube. The size of the nanoparticles in the study is varied from 10 nm to 30 nm. Results show a moderate enhancement in thermal conductivity and convection heat transfer coefficients in the laminar flow regime over that of pure water.

- 3) The theoretical isosteric heat of adsorption in the Henry's law region for carbon nanopores  
Jian Liu—Department of Chemical & Biomolecular Engineering

The isosteric heat of adsorption in the Henry's law region is calculated as a function of the pore width of cylindrical and spherical carbon nanopores. Maximum isosteric heat of adsorption is obtained for six gas molecules, including argon, methane, carbon dioxide, hydrogen, helium, and nitrogen for both cylindrical and spherical nanopores. In addition, the results of cylindrical carbon nanopores are compared with adsorption data of single-wall carbon nanotubes from literature. We determine the pore width where isosteric heat of adsorption is a maximum for both geometries. Unified linear relationships between the pore widths of maximum isosteric heat of adsorption and the specific fluid-fluid Lennard-Jones parameters are discovered for all the six gas molecules. The influence of surface mean curvature on the isosteric heat of adsorption are investigated as well.

- 4) Chemical Vapor Deposition of Aluminum Oxide Thin Films Using a Novel Single Source Precursor  
Benjamin Schmidt—Department of Chemical and Biomolecular Engineering

Aluminum oxide films are used as dielectrics, diffusion barriers, and UV absorbers. Common chemical vapor deposition (CVD) precursors trimethylaluminum and aluminum tri-isopropoxide suffer from requiring oxygen sources and having low vapor pressures, respectively. Dimethylaluminum isopropoxide (DMAI) combines benefits of each, resulting in an oxygen-containing liquid precursor with high vapor pressure. In this work, films have been deposited by high vacuum thermal CVD using DMAI on Si(100) substrates in the range 350–550 deg C. All films contain excess oxygen, but the oxygen:aluminum ratio approaches stoichiometry with increasing substrate temperatures. Carbon incorporation increases with temperature, up to 8% at 550 deg C.

XPS analysis of C1s spectrum indicates enhanced carbon-aluminum bonding within films at high deposition temperatures. Initial stage deposition on hydrophobic and hydrophilic surfaces has also been investigated by spectroscopic ellipsometry. Electrical characterization will be discussed, with the goal of obtaining process-property-performance relationships.

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### **Aspects of Astronomy and Astrophysics**

1) Understanding X-ray emission from the plasmas of young stars

Sonali Shukla—Department of Physics & Astronomy

High-resolution X-ray observations over long integration times have advanced our understanding of the X-ray emitting plasmas of young stars. We have identified and are analyzing a sample of nine stars from the Chandra X-ray Observatory archives observed with the High Energy Transmission Grating Spectrometer (HETGS) spanning the various evolutionary phases (classical, weak-lined, post-T Tauri and main sequence) of young stars. We have identified flaring and quiescent periods, based on overall X-ray luminosity, for several of the stars. By measuring the X-ray line fluxes from these stars, we are able to discern temperatures and densities that indicate the physical characteristics of the X-ray emitting plasmas. Of the analysis thus far, the temperature and density diagnostics for these stars indicate that the dominant X-ray emission from different epochs are produced by plasmas of varying temperatures and densities.

2) Search for Star-Disk Interaction Among the Strongest X-ray Flaring Stars in the Orion Nebula Cluster

Alicia Aarnio—Department of Physics and Astronomy

The Chandra Orion Ultradeep Project observed hundreds of young, low-mass stars undergoing highly energetic X-ray flare events. The 32 most powerful cases have been modeled, with the astonishing result that the magnetic structures responsible for these flares can be many stellar radii in extent. Perhaps these large magnetic loops represent the type of magnetic star-disk interaction often envisaged in magnetospheric accretion scenarios. We have modeled the observed spectral energy distributions (SEDs) of these stars in order to determine whether there is circumstellar disk material situated close enough to the stellar surface for interaction with the observed large magnetic loops. Our SEDs span a wavelength range of 0.3-24 microns, allowing us to determine the structure of dusty circumstellar material out to  $>10$  AU from the stellar surface. For most stars in our sample, the available data are sufficient to strongly constrain the location of the inner edge of the dusty disks. Three stars have SEDs consistent with inner disks within reach of the observed magnetic loops. Eight may have gas disks interior to the dust disk and extending within reach of the magnetic loops, but we cannot confirm this with the available data. The remaining fifteen stars appear to lack significant disk material within reach of the stellar magnetosphere. Our results indicate that while a few of the energetic X-ray flares exhibited by the sample stars could possibly arise from a magnetic star-disk interaction, approximately half of these are associated with free-standing magnetic loops anchored only to the stellar surface.

3) The Search for HI Clouds in Nearby Galaxy Groups

Katie Chynoweth—Department of Physics & Astronomy

I will present the most recent results from my study of neutral hydrogen (HI) in nearby galaxy groups. These observations are part of a Green Bank Telescope HI study of nearby groups of galaxies, searching for HI clouds in the galaxy groups and along the filaments between the groups. This study will give important insights into the processes of galaxy group formation and evolution, trace the remains of recent galaxy interactions, and constrain models of the High Velocity Clouds (HVCs) that are found around the Milky Way. By observing galaxy groups that span the range of interaction and merger activity, we will explore the number density of HI clouds in relation to the level of recent merger activity.

4) Characteristics of the most massive stars in NGC346 in the small magellanic cloud

Thompson Le Blanc—Department: Physics & Astronomy

It is known that stars are born in large stellar nurseries, deep within clouds of gas and dust. First generation clusters of stars are nurtured in a hydrogen-rich environment, a low-metallicity stellar nursery. However,

clouds that have seen various episodes of birth and death are high in metallicity due to the high quantities of heavy metals spewed into this medium from dying stars. How does star and cluster formation differ in these low and high metallicity environments? The goal of this project is to derive the Spectral Energy Distributions (SEDs) for ~ 1000 stars in the NGC346 region of the Small Magellanic Cloud (SMC), for which photometric observations are available in four filters in order to make an accurate census of the stellar content.

### 5) X-Ray/Infrared Characteristics of T Tauri Stars

William Teets—Department of Physics & Astronomy

I will discuss a current project involving observations of several T Tauri stars using the Chandra X-Ray Observatory. The talk will also touch on the goals of another project in the works that uses the Hubble Space Telescope to observe this stellar type in the infrared.

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### **Cannibal Corpses and other Abominations: what the undead tell us about ourselves**

#### 1) The Dubious Comfort Provided: Zombies and Mortuary Ritual

Mike Tidwell—Department of Anthropology

The modern, flesh-eating zombie has seen immense popularity since the release of *Night of the Living Dead* in 1968, yet the idea of the dead feeding off the living is not new. Folklore from China, the Andes, Indonesia and Europe warn about the dangers that follow when the dead are handled improperly. Modern zombies and these other undead are a way of working out symbolically certain primate intuitions, particularly feelings of uneasiness and fear that surround decomposing human bodies. Simply stated, humans are simultaneously repulsed by a corpse, yet also prone to thinking about it as a person with feelings and desires. By tracing the genealogical origins of zombie films, I will demonstrate the psychological connection between modern zombies and mortuary practices. For example, careful examination Romero's *Night of the Living Dead* reveals that the film is not mute on the topic of mortuary ritual, but in fact constitutes a morality tale for the critical importance of properly handling the dead.

#### 2) The Virgin-Vampire: Transcending the Limits of Traditional Sexual Ethics

Natalie Wigg-Stevenson—Graduate Department of Religion

The appeal of vampire narratives lies in their exuberance; they promise eternal life without the burden of traditional sexual mores. With vampires, eternal desire maps onto immortality in the infinite construction of hyper-sexualized, hyper-selves. Their performance of absolute freedom and transcendence of human finitude without the confines of traditional religiosity captivates us.

Stephanie Meyer's *Twilight* series deconstructs this paradigm. Her vampires sublimate their desires for human blood, for unbridled passion, for existential freedom to integrate into human society. Thoroughly domesticated, they feed on animal meat rather than human blood, live in hetero-normed relationships, and construct recognizably nuclear families. The main vampire character, Edward, even waits until he is married to have sex. These are vampires bound tightly by traditional Christian (here, denominationally Mormon) sexual mores.

I argue that in eschewing the sexually liberal mores of vampire narratives, Meyer reveals not the value of traditional Christian sexual ethics, but rather their limits. Edward, the virgin-vampire, is also the first vampire to use his eternal life to practice strict limitations on his self-construction rather than to further it. He is not a hundred-and-ten year old living in a seventeen year old body. He is believably seventeen. While many contemporary theologians imagine new possibilities for Christian sexual ethics that celebrate desire and its relationship to human flourishing, we would do well to understand this *Twilight* phenomenon of conservative sexuality; both for how it has gripped countless sexual imaginations and for how it maps the dangers at the borders we are seeking to transcend.

#### 3) Spawns of the Golem: From the Monstrous to the Heroic

Chris Paris—Graduate Department of Religion

In Jewish legend golems lie somewhere between the monstrous and the heroic. Their living dead status and soulless existence as champions of the innocent make them both the damned and the scourge of the damnable.

Many have observed connections between golems and other creatures such as zombies, the Frankenstein monster, and even robots and cyborgs. More recently a number of books have explored the Jewish origins of comic book artists and writers, pointing to the golem as the prototype for such characters as the Incredible Hulk, the Thing, Superman, and other heroes. All of these spawns of the golem reveal the legendâ€™s potential for good and evil, highlighting the assurance that comes from their guardianship and the fear that arises from their power.

Many see these misunderstood monsters as defenders of the weak when the greater good is pitted against great evil. Against the backdrop of Hitler and Nazi Germany, heroic champions with the power of the golem like Captain America and Superman arise. The monster becomes the hero, but the fear remains that this power may be controlled by another. Therefore every Superman or golem needs its Kryptonite. Within the pages of comic books, we see the struggle of humanity through the eyes of superhumans endowed with the invincibility of the golem, struggling to save souls even as they try to avoid losing their own souls.

#### 4) Between Earth and Hell: The Living in Hell and the Dead on Earth

James Grady—Department of Philosophy

Why has the modern cinematic zombie, as opposed to the classic voodoo zombie, been so enduringly able to horrify. I argue that the plausibility required for it has its roots, and its ancient paradigm, in the Christian version of the notion of separable souls/bodies – the angel/beast dichotomy of human nature -- as most vividly rendered in the medieval theological context by the idea of unforgivable sin (which results in the IMMEDIATE transportation of the soul to hell, the body living out its full life animated by a demon, a doctrine given full representation in the Inferno). Ultimately I argue that zombies, despite being so implausible on their face, speak to a relic that persists in the Christianity which so permeates western culture. The idea of an animated corpse is perhaps more terrifying now, precisely because that element to which it speaks is almost entirely subconscious.

#### 5) When the Man Comes Around: The Inescapable Eschaton in Zack Snyder's Dawn of the Dead (2004)

Linzie Treadway—Department of Religion

Zack Snyder's remake of the 1978 cult classic Dawn of the Dead follows the lives of a group of people struggling to survive after an unknown virus brings about a worldwide threat to human civilization in the form of flesh-eating zombies. The film primarily focuses on Ana, a nurse in Milwaukee, who awakes one morning to witness a recently zombified child attack her husband, who then dies and revives only to try to kill her as well. In fighting to stay alive, she and a small remnant take refuge in the local mall, where they form a community and eventually make a break for the nearby islands by boat, only to find them infested with the undead as well. Virtually every aspect of the filmâ€”the peaceful suburban setting, the age and background of those infected, the religiously charged names such as Fort Pastor and Hallowed Grounds, as well as a televangelistâ€™s interpretation of the situation as Godâ€™s punishment for sinâ€”leaves the viewer with the striking notion that this plague is not an isolated incident from which humanity can recover, but rather an imminent and inescapable cataclysm marking the end of days. Even the music is weighted, from the apocalyptic â€œThe Man Comes Aroundâ€ in the opening credits, the suggestions to â€œcome on, get down with the sicknessâ€ and â€œget ready to dieâ€ in the idyllic middle, and â€œPeople Who Diedâ€ in the final scene, suggesting that no one will escape this impending eschatological end.

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## Computational Structural Biology

#### 1) Docking antidepressants into the human serotonin transporter

Steven Combs—Department of Chemistry

The human serotonin transporter (hSERT) is a transporter responsible for the reuptake of serotonin (5ht) from the synapse. In order to combat depression, several antidepressants have been developed that block the function of SERT. Unfortunately, the crystal structure of hSERT has yet to be solved. We have built a comparative model of hSERT based off of the crystal structure from Aquifex aeolicus of the leucine transporter (LeuT). In this study, both stereo isomers of citalopram has been docked into the homology model of hSERT using RosettaLigand. The results have been analyzed in light of the experimental data. We suggest mutations to interrogate the identified binding modes.

**2) Ligand residues and ligand rotamer libraries: extending side chain rotamer sampling to small molecules**  
Gordon Lemmon—Department of Chemical & Physical Biology

Predicting the interaction between proteins and small molecules is an important goal in computational structural biology. Ligand docking applications make such predictions and can be used to predict how a putative drug will react with its target protein, or how a mutation in a protein might affect its function. Simple docking predictions treat both ligand and protein as rigid-bodies. However ligands and proteins are flexible and predicting their interaction will require modeling that flexibility. In order to efficiently model protein flexibility, amino acid side chains are represented by rotamer libraries. Side chain conformations are sampled from those libraries. I am extending this concept for ligands, by representing ligands as ligand fragments. I generate ligand rotamer libraries that describe the probable conformations of these fragments. By using ligand rotamer libraries, ligand docking predictions improve with minimal increase in computation time.

**3) Improve fold recognition by using a word-based alignment algorithm in BCL::Align**  
Sten Heinze—Department of Chemistry

Similar amino acid sequences fold into similar three dimensional structures. Fold recognition takes advantage of this by predicting the structure for a sequence based on similar amino acid sequences whose folds have been determined. Structural information can be extracted from matched, or aligned, portions of the sequence of unknown structure to sequences of known structures. BCL::Align is a tool for multiple sequence alignment and fold recognition employing a dynamic programming algorithm. Its advantage is a unique customizable scoring function resulting in excellent accuracy for both alignments and fold recognition. However, the dynamic programming algorithm renders BCL::Align computationally intense so it cannot be used for efficient fold recognition. By extending BCL::Align with a blast-like word-based alignment algorithm, the time for calculating an alignment can be drastically reduced. Word-based algorithms use series of short non-overlapping subsequences of the query sequence to identify highly similar regions in the target sequence. If an exact match is found, the alignment is extended in both directions from the position of the match, thus eliminating unnecessary comparisons. The word-based alignment algorithm will speed up the alignment and enable fold recognition, while continuing to use of the highly accurate scoring function.

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### **Department of English Conference**

**1) The Divergence of Albany and Edgar: Analyzing the Connection of Identity and Political Power in a Comparison of Quarto and Folio Versions of King Lear**  
Michael Alijewicz

Cross textual interpretative comparisons of Shakespeare's Folios and Quartos have generally been confined to arguments for good, bad, or conflated versions of the texts. This critical tendency ignores the interpretive potential offered in comparing the two versions of the text. This paper will treat Quarto and Folio versions of King Lear as equally valid in order to make a cross textual analysis centering on the lines of Edgar and Albany, especially the famous and interpretively important last lines regarding the dead march of Lear's dead bed (V.iii). Viewing the transfer of lines between these two characters in the two versions of the play reveals an intimate connection of power and identity in both versions, ultimately offering Edgar in the Folio as a shrewder manipulator of appearances, whereas the Quarto attempts to put Albany forward as a man who begins, but fails, to understand the power derived from demonstrably false appearances. With Lacan's ideas about the unifying power derived from creating a false identity in mind, and Judith Butler's conception of identity play as a source of political power as a guide, this paper will offer Edgar's performance in the Folio as ultimately more successful as a manipulator of identity and therefore, political player. Albany does not approach Edgar's awareness, but the lines he speaks in the Quarto do suggest that the connection between identity and power is key to understanding how the play operates.

**2) Dido and Teddy: The Sacrificial Secret**  
Elizabeth Barnett—Department of English

The reader of Theodore "Teddy" Roosevelt's rollicking, self-assured "Hunting the Grisly," first published in *The Wilderness Hunter* in 1885, will quickly notice a pattern to his hunts. In each, Roosevelt

portrays himself (or a male proxy) as a tough guy who loves “the spice of danger” (637), the bear as either a worthy adversary or a worthless beast, and nature as a knowable field to be named, analyzed, and conquered with either a gun, a pen, or both. But I will argue that the serial retelling of the hunt undermines Roosevelt’s avowed rationality and his creation of a stable, masculine identity. The killing, killing, killing suggests an obsessive need both produced and obscured by the macho naturalist facade.

To approach this unacknowledged presence in the text, I will consider “Hunting the Grisly” alongside Virgil’s *The Aeneid*, which also features frequent animal killings, though of an avowedly different sort. I will suggest that the “hunts” Roosevelt participates in and describes reveal the unspeakable urges that accompany the rational ideology of white masculine American hegemony. In both *The Aeneid* and “Hunting the Grisly,” animals are natural, unquestioned victims. But I will attempt to sketch the ways in which their deaths matter, to suggest that killing can never be “just” killing.

### 3) Illness and Incoherent Bodies in *Pale Horse, Pale Rider*

Caroline Hovanec—Department of English

Katherine Anne Porter’s *Pale Horse, Pale Rider* addresses the impact of World War I and the 1918 influenza pandemic on a small American town. The novel’s portrayals of illness and health, particularly through Miranda’s fevered dreams, work to collapse war and disease, as well as life and death, into indistinguishable reflections of each other. This is not to say that disease becomes merely a metaphor for war, but rather than conflating the two makes certain similarities between them evident, particularly the way in which both visit a violent fragmentation onto the human body and the social body. Yet the novel reveals an ambivalence about this bodily fragmentation, because it also functions as a means of survival. The soldiers Miranda visits in the hospital, returned from war with bandaged limbs and rough hands, are nevertheless alive while most of their compatriots have been killed; Miranda, whose delirium dissociates her consciousness from any awareness of her extremities or her sensory perceptions, nonetheless realizes that she is alive “with a peculiar lucidity and coherence.” It is Adam, the strong and healthy young man who boasts of never having an illness or injury, who never falters in his enactment of social codes, who dies of the flu. Adam’s death is an historically sound plot point—the 1918 flu, which triggered an overreaction of the immune system, tended to be more virulent in young healthy people than in the elderly or the very young with weakened immune responses. Yet his death also calls into question the ideal of bodily integrity, particularly in a society that sends its most physically able men to be slaughtered in a brutal kind of warfare. In this paper I will examine this dialectic of coherent and incoherent bodies in Porter’s novel, tracing the connections between a pathogen that turns the body against itself and the fractured bodies that survive.

### 4) Amanda Johnson—Department of English

This paper focuses on the role of the imagination in the construction of the state in the Romantic period, focusing on the later works of William Hazlitt. In “On the Spirit of Monarchy,” Hazlitt describes the relationship between the royal subject and the monarch as one in which the subject, which he describes as a submissive slave figure, imagines himself in the place of the master or monarch, and in turn, the monarch imagines himself in the place of the submissive. This model could be seen as a mutual projection of two consciousnesses, fostering a sympathy that maintains the power relationships at the basis of the monarchical state. On the other hand, the motions of projection could also suggest a single consciousness oscillating between two subject-positions, effacing the existence of an Other. Similar effacement occurs in *Liber Amoris*, a thinly-disguised memoir of Hazlitt’s love affair with Sarah Walker. This effacement or negation of the Other suggests that the ability to imagine oneself in the place of another is in fact a function of power, something that originates in the masters to justify his dominance by obliterating the slave’s subjectivity. Thus, any form of sympathetic imagination along a vertical axis, between the dominated and the dominant, is itself a fiction. This paper looks at how at Hazlitt’s later writings on power in erotic and monarchical relationships revises his ideas of politics and metaphysics as expressed in earlier writings, and signals a consolidation of Romantic thought on subjectivity and the aesthetics of power.

## **Econometrics and Measurement**

- 1) Consistent rank selection in co-trending and co-breaking models  
Zhengfeng Guo and Mototsugu Shintani—Department of Economics

This paper proposes several nonparametric cointegrating and co-trending rank selection criteria based on the sample variances of the first difference and the level of a time series. The criteria considered have a preferable model-free property and are invariant to scale transformation. All the suggested procedures are easily implemented and consistent under reasonable conditions. Monte Carlo experiments suggest that the finite sample performance of the new procedures is quite satisfactory.

- 2) A Class of Association Sensitive Multidimensional Welfare Indices  
Suman Seth—Department of Economics

The last few decades have seen increased theoretical and empirical interest in multidimensional measures of welfare. This paper develops a two-parameter class of multidimensional welfare indices that are sensitive to inter-personal inequality. A concern for inter-personal inequality in the multidimensional framework can be of two types. The first one pertains to the spread of each dimensional achievement across the population, as would be reflected in the multidimensional version of the usual Lorenz criterion. The second one regards correlation across dimensions, reflecting the key observation that inter-dimensional association may alter evaluation of individual as well as overall inequality. Most existing welfare indices are, however, either completely insensitive to any type of inequality or are only sensitive to the first. The class of indices developed in this paper is characterized by a set of natural axioms, and it is shown that other multidimensional indices, such as the ones developed by Bourguignon (1999) and Foster, Lopez-Calva, and Szekely (2005), are subclasses of this new broader class. Finally, essential statistical tests are constructed to verify the reliability of these indices.

- 3) Dynamic Treatment Effects and Optimal Dynamic Treatment Assignments  
Heng Chen—Department of Economics

Two Main Objectives:

First, find a simple efficient estimator to estimate dynamic treatment effects.

Right now in economics literature of estimating dynamic treatment effects, people only use G-algorithm estimator (Robins 1994) whose efficiency is not fully discussed. However in epidemiology, Robins et.al (2000) invent the inverse-probability-of-treatment-weighted estimator (IPTW), which is still not noticed in economics field. Since IPTW estimator's intuition is similar to treatment effect estimator with weighting, which raise the efficiency of an estimator in Hahn (1998) and Hirano et.al (2003). Hence I would like to come up with some simple efficient estimator for dynamic treatment effects following Hahn (1998) and Hirano et.al (2003). Furthermore, I would like to analyze efficiency of the stabilized- inverse-probability-of-treatment-weighted estimator (Robins et.al 2000), which has better empirical features.

Second, find the optimal dynamic treatment assignments, which maximize the mean response at the end of the final time interval.

Murphy (2003) and Robins (2004) have proposed models and developed semiparametric methods for making inference about the optimal treatment assignments in a multi-interval trial, while in economic literature people still focus on the single interval optimal treatment assignment and follow the parametric approaches. Murphy (2003) and Robins (2004) define the assignments rules recursively and use "regret" function (optimal blip function) to find the optimal rule and estimation of model parameters.

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## **Empirical Microeconomics**

- 1) Trade Liberalization and Skilled Migration: Substitutes or Complements?  
Omolola Soumonni—Department of Economics

Incorporating varying skill levels of labor (highly educated workers versus less educated workers) as factors of production in the standard factor endowments model foresees that with more trade, highly skilled workers will migrate from the country that is relatively endowed in educated workers (higher income) to the country that is

relatively more endowed in unskilled labor (lower income). However, Feenstra and Hanson (1997) and Markusen and Venables (1998) find that trade and investment liberalization increases the relative demand for skilled labor in both the developing and developed country, broadens the wage gap between both countries, and increases factor movements from the lower income to the higher income nation.

The goal of this paper is to address empirically the unresolved issue of whether trade and skilled immigration are substitutes or complements. Of particular interest is the effect of trade liberalization on skilled versus unskilled migration patterns when countries differ in relative factor endowments and size. Docquier and Marfouk (2005) create a dataset that shows considerable migration outflows among the highly educated, a phenomenon mostly observed for a number of Latin American and African countries. This paper attempts to identify the role of trade in the movement of skilled worker from over 100 countries to three main regions in 1990 and 2000: America, Europe, and Oceania<sup>1</sup>. Preliminary analysis of a sample of 20 countries shows a positive correlation between trade and skilled migration for any given destination region.

## 2) Slum Clearance and Urban Renewal in the United States, 1949-1974

William J. Collins and Katharine L. Shester—Department of Economics

In Title I of the National Housing Act of 1949, Congress launched an ambitious plan to rid America's cities of their slums. Policymakers hoped that local government agencies, with federal financial assistance, could assemble, clear, and then sell parcels of land in "blighted" urban areas for redevelopment. The goals of Title I were broad: to reduce substandard, crowded housing that was considered a breeding ground for crime; to stem the suburban migration of middle and upper class whites; and to increase tax revenues for local governments through property value appreciation. As such, Title I was the federal government's most direct effort to boost the economic prospects of American cities by destroying slums and encouraging new investment. To our knowledge, there are no systematic, econometric studies of the program's economic impact on the participating cities. This paper uses cross-city variation in the intensity of urban renewal program participation (measured in terms of funding or area covered) to gauge the effects of the program on a variety of economic outcomes that correspond to the program's broad goals.

## 3) Overworking to win the case: representing cases in court and young lawyers' hours of work

Rosa Ferrer—Department of Economics

Using survey data from the "After the JD" study, I test whether representing cases in court induces young lawyers to work more hours. Young lawyers representing cases in court might have incentives to work more hours because, considering that the trial outcome is an important source of information about lawyers' skills, winning or losing a case might have a considerable impact on their careers. Once controlling for salary, educational background and some other demographic variables, I estimate the average treatment effect between lawyers that are directly involved in court cases (treatment group) and the rest of lawyers working in law firms (control group). I find that young lawyers who usually appear in court as first or second chair on a case work nearly five hours more per week than other young lawyers also working in law firms. This result also holds when the dependent variable is hours of work minus hours expected to work, which allows me to control for unobservable heterogeneities and to address possible selection concerns.

## 4) Employer-Employee Match and Statistical Discrimination

Yariv—Department of Economics

Abstract: I show that premarket skill level (measured by AFQT) can explain at most 35% of the discrimination coefficient for men in the NLSY97. This result suggests that most of the racial wage gap explained at adulthood. Therefore, when looking at the decision made by employer-employee in the labor market, I find that the return to skill is higher if a worker has the same race as the employer (match). This suggests that employers read a signal of productivity more accurately at the time of employment when workers are of the same race.

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<sup>1</sup> Asia and Oceania form one destination location in Docquier and Marfouk's (2005) dataset.

## Feminist Food Politics

- 1) Performing Troubling Practices of Hope: Community Food Systems Work in Congregations  
Kate Lassiter—Graduate Department of Religion

Food is vital for human existence. Yet, USDA reports from 2005 indicate that 35.5 million persons, including 12.6 million children, live in households which are food insecure, representing roughly 1 in 10 households in the U.S. or 10% of the population. Moreover, national-level data shows that poverty and hunger are linked, prevalent in rural areas, among non-white Hispanic and African-American households, and especially among single female headed households. Addressing issues of hunger have taken many forms throughout the years, but have tended to focus on the acts of distribution of food through non-profit or faith-based organizations or else have centered on the discourse of food stamps and the WIC program at the national level. Both are dominated by a rhetoric of charity, not justice.

Congregations more specifically largely engage in acts of food charity. Yet, as Americans have become more familiar with the work of community food activists and their terms—"local, sustainable, organic"—a handful of congregations have pursued programs of social ministry focused on practicing justice with their communities. While these practices, or models, of community food work are nonetheless positive steps to enacting a politic of hope in changing community food systems, they also fail to adequately address the ways that food insecurity affects those consistently marginalized. In my presentation I will provide an introduction to the dominant model of food charity and various models of social ministry unfolding from the increase in greenwashed consumer rhetoric, and then a critique. Lastly I will present several aspects of models that can be of use to congregations as they try to more fully live out their social justice missions.

- 2) Family Farm: Redomesticating U.S. Agriculture in Barbara Kingsolver's Animal, Vegetable, Miracle  
Amanda Hagood—Department of English

This presentation examines Barbara Kingsolver's bestselling *Animal, Vegetable, Miracle* (2007)—a "œlocavore" memoir which details the author's family's attempt to grow most of their own food on their rehabilitated family farm in rural Virginia—through the lens of genre. Part manifesto and part practical guide, the book anchors itself in a sustained mediation upon the family's experience of the local agricultural year, but reaches out to engage wide-ranging political questions of U. S. agribusiness, suburbanization, environmental crisis, and political culture wars. Co-authored by Kingsolver's husband and elder daughter, the book not only challenges longstanding critical assumptions about the reactionary conservatism of agrarian literature, but also suggests, through its multiple narrative voices, that the political movement of which the family considers itself a part thrives upon a plurality of beliefs and an ongoing negotiation between them, rather than a single ideological stance. Ultimately, I argue, *Animal, Vegetable, Miracle* offers a broad approach to food activism, one that pairs the consumerist model of activism that predominates much of local food movement with a directive—and detailed instructions—for developing other social, ecological, and cultural relationships with the food system.

- 3) Getting to the Root: Structural Racism as a Root Cause of Food Insecurity in Nashville's Urban Areas  
Claire McKeever—Department of Religion

Racism within institutions and in public policy making leads to the unequal distribution of resources to individuals and to communities in Middle Tennessee. Barriers of race, language, socio-economic status, religion and age separate our community, resulting in crippling economic, health, and education disparities that compound and perpetuate one another. For example, Nashville food mapping data compiled by Tennessee State University in 2003 identifies three Nashville neighborhoods, Edgehill, North Nashville and East Nashville, as "food deserts" due to an absence of full service grocery stores and an abundance of convenience stores and fast food restaurants (Padgett, n.d.). These primarily African-American neighborhoods are also characterized by a higher-than-average number of persons living below the poverty rate and a higher-than-average number of residents relying on public transportation, two factors that compound the negative health impacts of living in an unhealthy food environment.

While the statutory basis for racism and discrimination has been acknowledged and addressed to some extent, lingering unexamined and unacknowledged practices and policies in our systems and institutions have the effect of perpetuating racial and ethnic disparities in multiple realms (e.g., employment, health, housing, etc.). Thus, I will present on how our traditional faith-based models of community organizing can and

should be both reexamined and redefined when dealing with issues of dismantling racist practices and policies within Nashville's food deserts, as well as how faith based organizations and churches can actively work to co-create and co-labor along with minority community groups already engaged in the work of food justice.

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### **Ideology, Identity and Consciousness: The Power of Ideas through History**

1) Anglo-Africans and Cosmopolitans: Staging Race and Nation on the Eve of the Civil War  
Derrick Spires—Department of English

This paper explores the different constructions of race and nation behind the editorial styles of two antebellum periodicals: *Weekly Anglo-African* and *Pine and Palm*. Published by Thomas Hamilton from 1859 to 1861, the *Weekly Anglo-African* aimed to become the printed link between African Americans across the U.S., “a paper in which to give vent to our opinions and feelings, in which to compare notes with each other, in which to discuss the best plans to pursue, to sympathize if suffering come, to rejoice if victory come.” Towards this end, Hamilton remained neutral throughout brewing debates over various emigration schemes to Haiti, central Africa, and elsewhere. Instead the paper printed arguments representing all angles from would-be leaders like Henry Highland Garnet as well ordinary subscribers like “Lizzie.” The resulting effect, with Hamilton’s framing the debate as amongst a family of readers, was an African American (or Anglo-African) national identity. James Redpath, the official “General Agent of Emigration” to Haiti, bought the *Weekly Anglo-African* in 1861, renaming it the *Pine and Palm* in May of that year. For Redpath, the paper symbolized his vision of “Cosmopolitan Government of the Future...superceding Nationalities and rendering war unnecessary.” Redpath and his correspondents actively promoted emigration to Haiti and placed the republic at the center of this democratic revolution and as the national home of all people of African decent in the U.S. Ultimately, this paper asks: how does each publication, reflect and negotiate the complications of the national and racial identities they create and/or foster?

2) Colonial Propaganda and Rebellion: The Ideology of Dissent in Late 17th Century Maryland  
Kevin Vanzant—Department of History

The English colonies in the 17th century were dependent on consistent migration for their survival. In the mainland colonies, this migration would be predominantly comprised of young, single Englishmen. Historians have attempted to shed light on the details of this massive immigration, focusing on the origins and the final destinations of this early migrating population. The most difficult question to answer, however, concern the perceptions and thinking of these early Atlantic travelers. What for these men was the promise of the “New World,” and how did they see their role in the emerging English empire?

This paper attempts to construct a colonial ideology that reaches beyond the colonial planners and the leading colonists. The paper will look at one colony, Maryland, and how its leaders advertised the colony through promotional literature. Using the promises of the promotional literature as a backdrop, the paper will then examine various dissident documents from the colony. The intention is to find some resonance between these two genres and thereby construct a colonial ideology of the average colonist, the foundations of which traveled with the colonists to the “New World.” With this ideology in mind, the contests over power in the early colonies appear not to be a power struggle within one political ideology, but a contest between two different conceptions of colonial government and society. The end result in Maryland would be a unique relationship between the people and their leaders.

3) The Orders of Queen Elizabeth I to Export Blacks from England in Religious Context  
Tamara Lewis—Graduate Department of Religion

This paper investigates the two late sixteenth and early seventeenth century Elizabethan orders to export blacks from England. While finding that the orders themselves were not executed based on economic and political exigencies, contrary to the conclusions of scholars who find that race was not integral to the contextual and cultural meaning of the documents, this article finds that the language (particularly in the 1601 proclamation) serves to differentiate persons not only on the basis of race or color, but also on the status of faith. One's physical or biological status becomes equated with one's interior or spiritual being. This effectively defines race as ontological difference. In short, the language of 1601 Elizabethan edict reflects the early modern notion that black (or blackamoor) was equivalent to unchristian or non-believing person. Hence

although the proclamations did not result in the wholesale expulsion of black persons from England in the late sixteenth century or early seventeenth century, they do reflect the most concise racial symbolic differentiation to date in official English documents, a view that would have later ramifications in the course of later history.

**4) Radical Roots: Identity and Consciousness in the Southern Black Territorial Separatist Movements, 18**  
Selena Sanderfer—Department of History

This paper examines identity and consciousness among lower class black separatists in the South from 1865 to 1892. After the Civil War some lower class black southerners rationalized territorial separatism as the most viable means to secure economic livelihoods and civil rights. Southern freedmen advocated this radical ideology when seeking to emigrate from the South to Liberia or migrate to all black settlements in the Kansas. This paper examines the formation of a separatist identity in relation to issues of class and race in the southern context. It also addresses issues regarding collective consciousness and nationalism among movement participants. The late nineteenth century separatist movements by black southerners were at the forefront of black protest in the United States. The tendency to remove lower class black Southerners from the most radical aspects of black thought during this period is a gross misrepresentation. The study of these southern grassroots movements offer researchers an alternative view regarding the development of radical black thought and are an important consideration when attempting to understand the black protest tradition in the United States.

**5) Whose Land is it Anyway? Insight into Questions of Ownership in Genesis 47:13-26**  
Brandon Simonson—Graduate Department of Religion

This paper examines the ideological implications behind the concept of ownership in Genesis 47:13-26, a short famine story that takes place in Egypt, and sets out to provide insight into the question, “who owns the land?” This paper employs several methods of exegesis in order to approach the pertinent themes of ownership in this passage.

An understanding of the text and its traditional interpretations will illuminate the problems associated with these traditional interpretations of ownership. Once these problems are located, we can begin to deconstruct the concept of ownership.

Then, by using appropriate methods of textual criticism, we will learn what constitutes land ownership in this passage. For example, a word in this text has traditionally been translated “bodies,” but we will determine, after thorough examination, that “dead bodies” is a much more accurate translation of the word used by the people of Egypt in this passage. Ownership will take on new meaning after the people describe themselves in this way. This new meaning leads us to the ideological critique, where we will ask the following question: what happens when we read the text through the eyes of the displaced people?

Ultimately, the insight into the questions of ownership gathered in this study will provide a new way to understand this passage and the concept of ownership in the cultural context of this story. This paper will bring us a little closer to understanding what it means to own when we ask the question, “whose land is it anyway?”

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### **Literature and Language Acquisition and Assessment**

**1) "Ki petit semme petit quelt:" Old French Romance in the Language Classroom**  
Rachel Early—Department of French and Italian

Too often, we tend to separate the teaching of foreign language from the teaching of literature. Recently, theories on second-language acquisition have suggested that this separation is not only unnecessary but detrimental to language students. Relying on this kind of research, I would like to present a concrete example of how a teacher might use a text-based approach to second-language learning. In particular, I will concentrate on a short passage from the twelfth-century Old French romance *Perceval*, by ChrÃ©tien de Troyes. By discussing this passage's specific linguistic features, I hope to show how integrating literary texts into the language classroom can give students a richer and more holistic view of language at an early stage in the acquisition process.

**2) Norm-referenced assessment? What are we assessing?**  
Kathryn Guillot—Department of Hearing & Speech Sciences

Norm-referenced instruments are widely used in evaluating the language skills of preschool children to make diagnostic decisions. In studies of low income preschoolers from Nashville, TN, Qi, Kaiser and colleagues reported that the mean performance of low income children was significantly below the normative mean of 100 on the PPVT and PLS, yet the groups' performance approximated a normal distribution. In this study, we compare their findings to the performance of a group of middle income children ( $n = 149$ ) from Nashville, TN. The middle income children performed significantly above the normative mean. Implications for practice are considered.

**3) Phonological Awareness Development: Kindergarten Children's Segmentation and Representation of Consonant Blends**

Krystal Werfel—Department of Hearing & Speech Sciences

This study explored kindergarten children's phonological awareness by examining the segmentation and representation of initial (e.g., *skate*) and final (e.g., *jump*) consonant blends. In the course of development of phonological awareness, segmentation of blends is a distinct achievement from segmentation of singleton consonants. This aspect of phonological awareness is an understudied area. Children completed a 26 word developmental spelling measure three times in kindergarten (6 week intervals). Responses were analyzed for logical representation of speech sounds to describe developmental change and differential accuracy across blend types. Results indicated that kindergarten children demonstrate an emerging ability to segment consonant blends and that children are differentially successful at segmentation based on properties of the phonemes that comprise blends. Blend segmentation was positively correlated with word reading. Implications for practice will be discussed.

**4) (Strategies of) Spatial Disorientation in Mark Z. Danielewski's House of Leaves**  
Lucas Faugere—Department of French & Italian

Sometimes, we stumble upon a text that defies clear categorization, instant elucidation, or even sound spatialization. Indeed, when first confronted with *House of Leaves*, the reader—and moreover, the scholar—experiences acute disorientation. Danielewski takes us into a labyrinth that constantly challenges our traditional conceptions of “literature.” The novelty of this 21st century take on the novel lies in Danielewski’s play on spaces: those of the page, the story, the structure, the genre, of dream and reality. Exploring them, we look for directions in each page—as the characters do. They struggle with this overwhelming house that is larger on the inside than on the outside, as we try to adapt to the ever-changing layout, genre, narrative voice.

Relying on a rigorous close-reading to open the door to literary theory, philosophy, Ästhetics..., we can make sense of Danielewski’s purposeful strategies of disorientation. Seemingly random and/or arbitrary, *House of Leaves*’s heterogeneity, ubiquity and equivocality are in fact carefully crafted to create meaning—a system that stems from modern and “post-modern” problematizations of actual and literary spaces. Finally, this ambiguous luxuriance is encapsulated in one book, a “house” that hosts “leaves.” Yet this groundbreaking novel calls for an articulation of finite and infinite spaces, reasserting skillfully the potentiality of literature, which leads the willing and perceptive reader beyond any apparent boundary to discover along the way new territories, renewed mindscapes. *House of Leaves* might be the first masterpiece of our “digital age,” consciously, playfully, pleasurable taking into account today’s transformations of society, technology, literature.

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## **Macroeconomics**

**1) Everyday Low Prices and Temporary Price Reductions**  
P.J. Glandon and Matthew Jaremski—Department of Economics

This project theoretically and empirically evaluates the response of incumbent retailers to the entry of a competitor with a lower cost technology. We adapt a model from the marketing literature to show that the

entry of a low cost competitor can cause firms with loyal customers to increase the frequency of price promotions in order to preserve market share. We test this prediction using promotion data from the University of Chicago's Dominick's Database. The evidence suggests that the Dominicks Fine Foods grocery chain responds to the presence of a Wal-Mart Supercenter by increasing the frequency of promotions in certain product categories. This result suggests that the incremental diffusion of Walmart Supercenters is partially responsible for the increase in the frequency of sales that occurred during the 1990's (Nakamura and Steinsson QJE 2008).

**2) So Far Away?: Distance vs. Firm Risk in Determining Banknote Exchange Rates**

Matthew Jaremski—Department of Economics

**3) Real effects of the New England Monetary Experiment**

Caleb Stroup—Department of Economics

Was the monetization of New England successful? We provide econometric tests of the link between paper money emissions and economic activity in colonial New England. Contrary to previous analysis which has focused on nominal effects, our analysis suggests monetization may have stimulated real economic activity in the medium to long run.

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### **Microeconomic Theory**

**1) Redundant disclosure of product information**

Roger Crawford—Department of Economics

Voluntary versus mandatory disclosure of a firm's private information about a product has for years been of interest to economists. It can easily, howsoever anecdotally, be verified that even under mandatory full disclosure of such information, firms may include additional and even redundant product information on packaging, etc. The goal of this project is to construct a model using heterogeneous consumer preferences to analyze such redundant disclosure, and investigate the effects of mandatory versus voluntary disclosure in the context of social welfare.

**2) Enhancing transportation security against terrorist attacks**

Sunghoon Hong—Department of Economics

We study a model of strategic interaction between a terrorist organization and a security agency in a transportation network carrying passengers and freight between locations. By carrying explosives to a target location through the transportation network, a terrorist organization can damage the target and disrupt the operation of the network. While the terrorist organization gains utility from damaging the target and from disrupting the operation, carrying explosives to the target through the network is costly. A security agency is informed of the terrorist attack. By shutting down some routes in the transportation network, the agency can protect the target. However, the agency can continue the operation of the network as usual, since the shutdown of routes disrupts the usual operation of the network. The agency loses utility from the target's damage and from the network's disrupted operation. In this model we first find an optimal policy for the security agency. We then characterize the subgame perfect equilibria of the model. We also introduce algorithms to find a maximum flow and a minimum cut in a transportation network.

**3) A Characterization of Pairwise Nash Stable Networks**

Valeska Groenert—Department of Economics

**Abstract:** I show that the set of pairwise Nash stable (PNS) networks is equivalent to the set of networks arising from pure strategy Nash equilibria of a modified version of Myerson's linking game. Thus a PNS network does not exist if and only if a pure strategy Nash equilibrium of the modified linking game does not exist. Because the modified linking game is finite, it always has a mixed strategy Nash equilibrium. Therefore, even though a PNS might not exist, an equilibrium of the underlying network formation game always exists. The outcome of this equilibrium is a probability distribution over networks.

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## **Preparing tomorrow's teachers for today's students**

1) Second Language Acquisition Theory and Teacher Preparation for English Language Learners  
Mikel Cole—Department of Teaching and Learning

English language learners (ELLs) are the fastest-growing population of students in public schools in the United States (McKeon, 2005), and these students are not confined to English-as-a-Second Language (ESL) or bilingual classrooms; in fact, they are increasingly prevalent in mainstream classrooms, with some estimates suggesting that more than 60% of mainstream classrooms contain at least one ELL (American Federation of Teachers, 2008). Despite the increasing need for all teachers to be trained to teach these students, most teachers are woefully unprepared. This paper reviews second language acquisition theory and empirical research from three orientations in order to provide a background of some of the language-related issues involved in educating ELLs. Then, a prominent paper by Wong-Fillmore and Snow (2000) “What teachers need to know about language” is reviewed in light of this research background. Finally, some recommendations for additional things that all teachers of ELLs should know are provided.

2) Mobility & Reading Achievement: A Multi-level Analysis  
Kelly Puzio—Department of Teaching & Learning

Students in the United States change schools frequently. Although students often change schools upon graduation or promotion, some students shift from one school to another for reasons other than promotion. The activity of students making non-promotional school changes has been defined as student mobility (Rumberger et al., 1999). While there are many different causes and reasons for changing schools, data sources indicate that poverty, Black, and Hispanic students are much more likely to change school than their White and non-Poverty peers. In addition, there is strong evidence to suggest that student mobility matters. It affects student psychologically, socially, and academically. Students who change schools are more likely to engage in anti-social and disruptive behavior (Holland, Kaplan, & Davis, 1974; Pribesh & Downey, 1999; Rumberger et al., 1999; Elleckson & McGuigan, 2000), have lower standardized test scores (NAEP 2002; Blane, 1985; Lee & Smith, 1999), and are less likely to graduate from high school (Haveman & Wolf, 1994; Rumberger & Larson, 1998). Notably, however, most of the mobility research has focused on the mobile individual rather than the mobility levels in schools. This study will use hierarchical linear modeling (HLM) to examine the relationship between school-level mobility, standardized reading test results, and individual background characteristics.

3) Professional Development: When Preparation is Not Enough  
Christopher Keyes—Department of Teaching and Learning

A growing gap exists between teachers and their students. As the students in schools in the United States come from more multicultural backgrounds, their teachers are still predominantly White, middle-class females. The difference between the teachers’ cultures and that of the students can create a cultural and understanding gap which impacts the learning and success of the students (Milner, 2006). Many schools of education are attempting to address the gap by offering classes in multicultural education; yet, such attempts are often too short and singular to truly help teachers grow in their understandings. Thus, multicultural education should be part of teachers’ professional development experiences after they enter in the classroom as well. In this presentation, I will review several theories of how effective professional development is designed. I will then look at the various designs of teacher professional development which address the issues surrounding multiculturalism and diversity. I also will address the effectiveness of the many forms that professional development takes. Milner, H. R. (2006). Preservice teachers’ learning about cultural and racial diversity: Implications for urban education. *Urban Education* 41(4), 343-375.

4) The Place for Narrative: Literacy Instruction for African American students  
Emily Bigelow—Department of Teaching & Learning

A central component of Critical Race Theory is the use of storytelling as a tool for deeper understanding. Stories allow for exposure, analysis and challenging of beliefs held central to educators. One key characteristic of African American Language is that of narrative or storytelling. The practice of narrative in the African American community can be traced to the fugitive slaves who used narrative to identify themselves as a specific group. Over time, the use of narrative has become a key characteristic of everyday language in the African

American community. While many educators have moved to valuing home languages as a resource, most schools still expect academic language in written and oral work. Even though the majority of P-12 students are urban students representing a variety of languages and cultures, the white, middle class language characteristics are still valued over other forms of language in the schools. This paper looks at current practices using narrative as an instructional strategy in the literacy classroom. This analysis includes more traditional uses of narrative such as oral and written narrative practices as well as multimedia practices such as digital storytelling. In addition, ways that researchers can gain access to African American students experiences through the use of narrative as a tool are analyzed. Both classroom practice and research using narrative are critiqued and suggestions for both classroom practice and research are provided.

### 5) Beyond the Digital Divide: Reviewing the Intersections of New Literacies and Issues of Diversity Nathan Phillips—Department of Teaching and Learning

This presentation considers the intersection of two educational topics that, to this point, have not been widely considered in connection to one another—“new literacies research and issues of diversity. In considering them together, the presentation attempts to centrally position discussions about the role that changes in technology connected with changes in the diversity of the school population will play for the future of teachers in the U.S.

The importance of moving this topic from the margins to the center of educational discourse is underscored by two realities: 1) what Don Tapscott (1998) has called the rise of the Net Generation—that is, the fact that young people today “grow up digital” (Tapscott, 1998) and that fluency in the literacies associated with digital technologies are vital for “economic success and societal well-being” (Tapscott, 1998, p. 11); and 2) the need for a multicultural education that will, as articulated by Banks (1998), “help all students, including White mainstream students, to develop the knowledge, skills, and attitudes they will need to survive and function effectively in [an increasingly diverse] future U.S. society” (p. 23). If students are to be prepared in and for a world that is both digital and increasingly multicultural—according to the U.S. Census Bureau (2008), by 2050 more than half of the U.S. population will be people of color—then there are perhaps no more important issues for educators in the near- and distant-future to understand than diversity and new literacies.

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### Radical Agrarianisms

#### 1) Convivial Communities: An Agrarian Alternative to Violent Empire Timothy Eberhart—Department of Religion

This paper will explore the theological and ecclesial linkages to an agrarian focus on food and eating as the principle site of resistance against a global political economy that feeds upon the exploitation of the poor and degradation of the earth. My claim will be that the agrarian tradition offers critiques of the violent imperial economy governing contemporary existence, along with tangible social and economic alternatives, that are naturally aligned with the „holistic“ perspective of the holiness and communitarian strands of the Christian church. My aim is to provide a prospectus – a looking forward to – the basic features of an Agrarian political economy. In doing so, I hope to simultaneously clarify what I understand to be the primary criticisms agrarianism has leveled against modern industrial capitalism – namely, that it is intrinsically marked by *violence*, in the perpetual „tearing asunder“ of that which properly belongs together, and inherently prone to *domination*, in the imperial expansion of corporocratic control. In its place, Agrarianism proffers the possibility of a political economy rooted in the nurturance of socio-ecological relations of *conviviality* within locally-sufficient, decentralized, egalitarian communities.

## 2) Notes Toward a Radical Agrarianism

Charles Sentell—Department of Philosophy

Strictly speaking, to speak of “radical agrarianism” is to be redundant. Agrarianism is already about roots: roots of the plants that sustain the stalk that is the common physical and social bond of food. As a necessity for human life, food stands at a unique junction between the social and the natural worlds. As a mode of radical inquiry, agrarianism pursues the roots of social relations hidden within global and local markets by raising again and again the necessary questions arising between the production of food and the consumption of life, between the freedom of production and the slavery of consumption.

In outlining the aesthetics and politics of radical agrarianism, I address the inextricably linked objections that agrarianism is a romantic or nostalgic mode of analysis, and that agrarianism is synonymous with a type of neo-Luddite criticism, out of touch with the technological demands of the present. This paper focuses on conceptions of the past operative within agrarian thinking, and how these affect an agrarian comportment to technology. That is, how does agrarianism as a political and environmental ethic use the concepts of past, present, and future in the service of contemporary social problems, particularly in the areas of technological development and application? What does an agrarian philosophy of technology look like, and how does it relate to an agrarian philosophy of history? What is the relation of agrarianism to radical democratic theory, and how do conceptions of history and technology function in agrarian visions of democratic life?

## 3) Farming the Future: Agrarianism, Utopia, and the Challenges Ahead

John Morrell—Department of English

If agrarianism’s proper attitude toward the past is one of ruefulness, its mode of relating to the future should be utopian. In pursuing this argument, I distinguish between the pejorative senses of the term, in which utopian is taken to mean impractical or coercive, and the reconstructive sense of the term, in which utopianism is understood as a dialectical project of imagining and enacting a better world. Agrarianism, as a uniquely pragmatic utopian project, highlights a fundamental tension in utopian thought between envisioning the future as a *revolutionary* break from the present and a envisioning it as a *radical* (rooted) transformation of the present.

This paper looks forward to consider some of the specific challenges and opportunities in response to which the utopian project of agrarianism might productively take shape. Most provocatively, the global community faces a shrinking time frame within which it might respond effectively to the challenge of global climate change, and agrarianism is well-positioned to contribute to a workable vision of sustainable future. In my discussion, I gesture towards two other related challenges, which, in my view, agrarianism has not sufficiently theorized. With its traditional focus on the local and the rural, agrarianism has stood largely in opposition to the forces of globalization and urbanization. It is unrealistic, and indeed undesirable, to take such a stance. Agrarians must offer reconstructive visions of urban life, and they must be willing to theorize migration and mobility, particularly in the context of a warming world.

## 4) Fractal hegemony: ethnoecological model for hunter-gatherers of the rain forest

Gerson Levi-Mendes—Department of Anthropology

How do hunter-gatherers keep their control over environment and what are the strategies they use to keep socio-economical organization under stability? Through the history of ethnography several models were built on energy exchange, behavioral ecological models and several ecological-like frames of references to explain this superficial stability. However, few anthropologists advanced from an emic perspective to understand how man-nature stability advances in history in these societies, a factor that limits theoretically how anthropology has been explaining hunter-gatherers societies. Fractal hegemony is a new concept elaborated by the author in order to conciliate natural factors with the hegemony these populations have on nature using their emic perspectives on hegemony and ethnogeography applied in a historical perspective.

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## **Structural Biology**

### **1) Structure and Functional Analysis of the U-Box Domain of E4B reveals Unique Monomeric Assembly** Kyle Nordquist—Department of Biochemistry

We have determined the solution structure of the U-box domain of the mus musculus E3 ligase E4B (E4BU). Unlike previously determined U-box structures, E4BU retains a monomeric assembly. Slight deviances in the sequence alignment of E4BU with other U-box containing proteins reveal the basis for the monomeric organization. Increased steric hindrance and decreased hydrophobic packing result in the single molecule arrangement. To investigate the functional characteristics of E4BU, NMR chemical shift perturbation experiments were used to analyze E2-U-box binding. The interaction interface between E4BU and the E2 conjugating enzyme, UbcH5c has been mapped and structurally modeled. To further assess the functional role of E4BU, *in vitro* ubiquitination assays were carried out with a variety of E2 enzymes. These assays reveal distinct E2 partners of E4BU as well as reinforce previous hypotheses that different E2s catalyse different ubiquitination events.

### **2) Structural Insights into RPA Architecture and Function from Heteronuclear NMR Spectroscopy** Chris Brosey—Department of Biochemistry

DNA replication, damage response, and repair are fundamental biochemical processes necessary for cellular survival. Replication Protein A (RPA), the primary single-stranded DNA-binding protein in eukaryotes, plays a critical role in organizing and protecting DNA during these processing events. While a high level of structural detail is available for individual domains of RPA, there has to date been little insight into the protein's global architecture and how this structure facilitates DNA processing. NMR spectroscopy on intact 116-kDa RPA and a number of multi-domain constructs provides striking evidence of a highly dynamic interdomain structure. Studies of the DNA-bound state of RPA by NMR demonstrate specific remodeling of the protein's DNA-binding domains (DBDs) upon interaction with ssDNA. Together, these results provide a foundation for developing a systematic structural understanding of the remodeling of RPA quaternary structure, consistent with its proposed role in orchestrating the assembly and disassembly of multi-protein DNA processing complexes.

### **3) CryoEM guided de novo Protein Fold Elucidation** Steffen Lindert—Department of Chemistry and Physical Biology

Using cryo-electron microscopy (cryoEM) numerous sub-nanometer resolution density maps of large macromolecular assemblies have been reported recently. Although generally no atomic detail is resolved in these density maps, at 7 Å resolution  $\alpha$ -helices are observed as density rods. Here we present the development of a computational protein structure prediction algorithm that incorporates the experimental cryoEM data as restraints. The placement of helices is restricted to regions where density rods are observed in the cryoEM density map. The Monte Carlo based protein folding algorithm is further driven by knowledge based energy functions.

The method has been benchmarked with ten highly  $\alpha$ -helical proteins of known structure. The chosen proteins range in size from 250 to 350 residues. Starting with knowledge of the true secondary structure for these ten proteins, the method can identify the correct topology within the top scoring 10 models. With more realistic secondary structure prediction information, the correct topology is found within the top scoring 5 models for seven of the ten proteins.

The algorithm has been applied to human adenovirus protein IIIa. This protein, for which there is no high resolution structure, is predicted to be highly  $\alpha$ -helical. It is resolved in a 6.9 Å resolution cryoEM adenovirus structure as a bundle of ~13  $\alpha$ -helical density rods.

### **4) Move it, move it: The 1.85 Å crystal structure and mechanism of a phosphopentomutase** from *Bacillus cereus* Timothy Panosian—Department of Pharmacology

Phosphopentomutases (PPMs) catalyze a crucial reaction in the nucleoside salvage pathway, the interconversion of ribose-5-phosphate with ribose-1-phosphate. Since PPMs can be expressed at high levels

and are easily purified, they are attractive tools for biotechnology applications that require sugar-1-phosphates, which are challenging to produce *in situ*. To further understand the enzymatic mechanism and identify the substrate binding motif, the x-ray crystal structures of apo and ribose-5-phosphate bound PPM were determined at 1.85 Å and 2.0 Å resolution, respectively. The structure of PPM reveals two distinct domains joined by a flexible linker. The active site is at the interface of the two domains; it contains two Mn<sup>2+</sup> ions and a single phosphorylated threonine residue, T85. Mutation of T85 to alanine abolishes enzyme activity. In the substrate bound structure a possible covalent intermediate was observed with ribose bound to the phosphate of phosphorylated T85 at the 1-carbon. Thus, PPM may proceed through a multi step mechanism where ribose-5-phosphate phosphorylates T85, and the resulting ribose is rotated to orient the 1'-OH to be phosphorylated by T85. Elucidating the molecular mechanism of PPM and the determinants of substrate specificity are important steps toward the use of PPM in future biotechnological applications.

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### **Target Cell Selection and Replication Mechanisms of Mammalian Reoviruses**

1) Molecular determinants of reovirus binding to cell-surface sialic acid

Johnna Allen—Department of Microbiology and Immunology

Reoviruses are nonenveloped dsRNA viruses that display serotype-specific patterns of cell tropism and disease within the central nervous system (CNS) of infected mice. Distinct patterns of CNS disease caused by the different reovirus serotypes are genetically linked to the viral S1 gene, which encodes attachment protein σ1, a filamentous trimer with head-and-tail morphology. While all reovirus serotypes use junctional adhesion molecule-A as a receptor, they differ in utilization of carbohydrate coreceptors, suggesting that carbohydrate binding by σ1 is a determinant of reovirus tropism and pathology in the CNS. Type 3 (T3) σ1 binds sialic acid (SA), whereas other strains do not. Previous studies using recombinant σ1 proteins indicate that sequences in T3 σ1 responsible for SA binding cluster in the tail domain. To define sequence determinants of carbohydrate engagement by T3 σ1, we engineered viruses containing point mutations in this putative SA-binding domain of reovirus strain T3D. Viruses singly substituted at amino acid positions 198, 202, and 204, and a triple-mutant virus, were tested for SA-binding using hemagglutination assays and growth assays with murine erythroleukemia (MEL) cells, in which SA engagement is required for reovirus infection. In comparison to wild-type, each mutant exhibited diminished capacity to agglutinate erythrocytes and inefficient growth in MEL cells. These results suggest that residues 198, 202, and 204 function in SA engagement by T3D σ1. Identification of sequences in σ1 that bind carbohydrate will enhance an understanding of ligand-receptor interactions and direct experiments to determine the function of carbohydrate binding in reovirus neuropathogenesis.

2) Identification of reovirus cell-tropism determinants in replication protein μ2

Laura Ooms—Department of Pathology

Mammalian reoviruses are nonenveloped particles containing 10 double-stranded RNA gene segments. Viral genome replication is thought to occur within nonmembrane-bound cytoplasmic inclusions. Reovirus core protein μ2 is a multifunctional mediator of viral replication that is indispensable for completion of the infectious cycle. The μ2 protein likely functions as a subunit of the reovirus RNA-dependent RNA polymerase, and μ2 also serves as an integral component of viral inclusions. However, the roles of individual μ2 functional domains and structural motifs in viral replication have not been defined. To elucidate μ2 functional mechanisms in the reovirus life cycle, we have identified sequences in μ2 that regulate efficiency of viral replication in Madin-Darby canine kidney (MDCK) cells, in which yields of strain T1L greatly exceed those of strain T3D. We used reverse genetics to introduce T1L μ2 into an otherwise T3D genetic background and found that yields of the resultant monoreassortant virus were equivalent to those of T1L. Replication assays using a panel of recombinant virus strains containing T1L x T3D chimeric μ2 proteins revealed a sequence region

between amino acid residues 209 and 390 required for efficient growth of T1L. Substitution of Leu<sup>347</sup> in T3D μ2 with the corresponding Phe residue present at this position in T1L μ2 was sufficient to raise T3D yields to the level of T1L. However, a Phe<sup>347</sup> → Leu substitution in the μ2 protein of T1L did not significantly reduce viral yields relative to the parental strain. Similarly, replacement of the T3D μ2 protein with wild-type T1L μ2 did not result in diminished viral yields, whereas simultaneous introduction of the T3D μ2 and λ3 proteins into the T1L background reduced viral replication to the level of T3D. Viral yields of T1L and T3D were unaffected by

exchange of only their  $\lambda_3$  proteins. These results indicate that the Phe/Leu polymorphism at amino acid position 347 of  $\mu_2$  is an essential determinant of viral replication efficiency in MDCK cells and suggest that a structural or functional interaction between  $\mu_2$  and  $\lambda_3$  regulates reovirus tropism for certain cell types.

**3) Identification of Cellular Proteins that bind Mammalian Reovirus RNA: A Role for Editing Enzymes?**  
Charles Martinez III—Department of Pathology

The ability of viruses to parasitize cellular metabolic machinery in favor of viral genome expression and amplification is responsible for the myriad of pathologies triggered in infected cells. Mammalian reoviruses are double-stranded RNA (dsRNA) viruses and serve as a model for the globally important human pathogen, rotavirus, and the economically significant livestock pathogen bluetongue virus. Viruses with RNA genomes demonstrate a sophisticated interplay of transcription, translation, and replication involving genomic and anti-genomic strands. Reovirus RNAs, despite being short and lacking 3' poly(A) tails, are translated with remarkable efficiency in infected cells. Viral gene expression and genome amplification are thus complex processes requiring multiple integrated control mechanisms likely aided by cellular RNA-binding proteins. To date, host-cell-derived RNA regulatory proteins have not been identified for animal dsRNA viruses. The purpose of this research was to identify cellular proteins that bind a region of conserved sequence in the non-translated region (NTR) of reovirus RNA. Using multi-dimensional protein identification technology mass spectrometry (MudPIT MS) we have identified many cellular proteins that bind a conserved region of viral RNA. Ontology analysis categorized our peptide hits into many diverse classes of RNA biology including mRNA processing and regulatory factors, basal and accessory components of the translational apparatus, and a number of interferon-inducible RNA-binding proteins. One of the latter is the dsRNA-binding protein Adenosine Deaminase Acting on RNA-1 (ADAR1), which has been implicated in the replication of several DNA and RNA viruses. However, the role of ADAR1 in dsRNA virus replication is unknown. We found that ADAR1 expression is increased in reovirus-infected murine L929 fibroblast cells and that reovirus in ADAR1 null murine embryonic fibroblasts is significantly reduced in comparison to that in wildtype cells. Transient transfection of an ADAR1 encoding plasmid results in the near-complete restoration of viral titer in ADAR1 null cells. From these experiments, we find that cellular proteins bind to conserved sequences in the 3'-terminal region of reovirus RNA. Native functions of cellular proteins that bind reovirus RNA include RNA processing, transport and localization, and transcriptional and translational control. Reovirus infection of murine L-cell fibroblasts induces expression of the RNA-editing enzyme, ADAR1, which is required for efficient reovirus replication in cultured MEFs. These results suggest that ADAR1 is an essential cellular determinant of viral replication efficiency.

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**The Dynamic Host-Pathogen Interaction: How Host & Infectious Agent Respond to Each Other**

**1) Long-range distal elements within the Ifng locus**  
Patrick Collins—Department of Microbiology and Immunology

Transgenic mice carrying an 8.6 kb Ifng transgene do not recapitulate Th1/Th2 selectivity, but mice carrying a transgene with the surrounding 190 kb of non-coding sequences do. It is unknown why Ifng requires 190 kb of regulatory sequences and space. To understand distal regulation of Ifng, we constructed transgenic mice carrying ~40 kb deletions within the 190 kb transgene. We identified two large regions which regulate Ifng expression. We then created small, 1 kb, deletions to identify specific regulatory elements. We identify two 1 kb regions at -30 kb and at -77 kb which are necessary for IFN-g transcription and repress IFN-g transcription, respectively. Our results demonstrate that multiple long-range distal regulatory elements cooperate to drive the proper temporal and quantitative expression of a single gene.

**2) Staphylococcus aureus heme oxygenases are differentially regulated during infection**  
Michelle Reniere—Department of Microbiology & Immunology

The bacterial pathogen *Staphylococcus aureus* is responsible for significant human morbidity and mortality. The ability of *S. aureus* to cause disease is absolutely dependent on the acquisition of iron from the host. During infection, the most abundant iron source to invading staphylococci is in the form of the porphyrin heme, most of which is bound by hemoglobin in circulating erythrocytes. Following secretion of staphylococcal

hemolysins, which lyse red blood cells, the released hemoglobin is bound by *S. aureus* and the heme cofactor is internalized via the iron-regulated surface determinant system (Isd). The Isd system is composed of nine proteins that act in concert to remove heme from host hemoglobin for transport into the cytoplasm. Upon entry into the staphylococcal cytoplasm, iron is liberated from heme by IsdG and IsdI, two structurally identical heme oxygenases whose contribution to the host-pathogen interaction has not been previously evaluated. We have found that IsdG and IsdI are each required for heme-iron utilization, suggesting that these enzymes have distinct functions during infection. A potential mechanistic explanation for these in vivo observations has been uncovered by experiments into the regulatory mechanisms controlling IsdG and IsdI expression. These studies have revealed that expression of staphylococcal proteins involved in nutrient acquisition is affected by the local microenvironment at the site of infection. Moreover, we have found that both heme oxygenases are critical for full *S. aureus* virulence. Current experiments are focused on determining the mechanism responsible for this unique regulatory strategy.

3) Sodium chloride induces increased antibiotic resistance in *Acinetobacter baumannii*  
Indriati Hood—Department of Microbiology and Immunology

*Acinetobacter baumannii* has recently emerged as an important cause of nosocomial infections. While extensive antimicrobial resistance has been described clinically, the molecular determinants mediating resistance and the mechanisms involved in regulation of these determinants are poorly defined. We sought to identify environmental signals encountered in the hospital setting or within the human host, which alter the resistance phenotype of *A. baumannii*. In this regard, we have identified NaCl as an important environmental signal that modulates antibiotic resistance in *A. baumannii*. *A. baumannii* cultured in NaCl concentrations ranging from 50mM-300mM show increased resistance to aminoglycosides, quinolones and colistin. Inhibition of transcription abolished the observed NaCl-induced resistance demonstrating that this response is transcriptionally-dependent. The global transcriptional response to NaCl was determined by microarray analyses suggesting a role for efflux in mediating resistance to antibiotics. Specifically, 14 transporters with putative roles in antibiotic efflux were significantly up-regulated in response to NaCl. To identify genes responsible for this phenomenon, a transposon insertion library was generated and screened for mutants that failed to show increased resistance to antibiotics in response to NaCl. To date this screen has identified several candidates including genes with predicted roles in transcriptional regulation, oxidative stress and membrane structure/stability. Taken together, these data demonstrate an adaptive response to NaCl resulting in resistance to antibiotics of distinct classes. Future work will be focused on using mutants identified in the transposon screen to define the molecular mechanisms governing NaCl-induced antibiotic resistance in *A. baumannii*.

4) PD-1 is highly expressed on dominant CTL clonotypes over time and during varying levels of antigen exposure  
Joseph Conrad—Department of Microbiology and Immunology

HIV-specific T-cell responses play a critical role in the control of HIV replication. In the absence of anti retroviral therapy, HIV infection causes progressive immune dysfunction. Recent work identified PD-1 as a surface marker for functionally impaired T-cells. We performed in depth studies of PD-1 expression on T-cell clonotypes within HIV-specific CTL populations to determine whether the dominance of circulating T-cell clones was related to their level of PD-1 expression.

HIV-specific populations are often comprised of multiple TCR V-beta clonotypes. Within epitope-specific CTL populations, dominant circulating clonotypes have a higher percentage of PD-1+ cells ( $p<0.0001$ ) and dominant populations express higher levels of PD-1 ( $p=0.0005$ ) than sub-dominant clonotypes. Dominant clonotypes maintain position in the clonotypic hierarchy over time and, despite fluctuations in PD-1 expression, express PD-1 to relatively higher levels than sub-dominant clonotypes. Dominant clonotypes retain their prominence within the repertoire and continue to express more PD-1 even after initiation of ART and subsequent reduction in viral load.

Within a population of epitope-specific T-cells, dominant circulating clonotypes have a phenotype consistent with exhaustion despite their ability to produce cytokines and proliferate upon activation with peptide antigen. Our studies highlight potential mechanisms at work in the development and maintenance of antiviral T-cell responses. Understanding factors which define the capacity of HIV-specific T-cells to respond to antigen will be

critical to the qualitative evaluation of vaccine induced immune responses and may help in the development of immunomodulatory therapies to reverse HIV-induced immune dysfunction.

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### **The Metabolic Syndrome**

1) Characterization of *Gulo* knockout mice on Vitamins C & E double deficient diet  
Marquicia Pierce—Department of Molecular Physiology & Biophysics

Vitamins C and E help prevent the oxidation of intercellular compounds. Previous *in vitro* research has demonstrated that these molecules can act synergistically. *In vivo* studies by Hill et al. (2003) described a progressive paralytic phenotype in guinea pigs on a double-deficient diet for vitamins C and E. These animals showed high concentrations of F2-isoprostane which is indicative of increased lipid peroxidation in the central nervous system. It is our hypothesis that this phenotype is caused by oxidative injury to the neurons. To test this, we aim to develop a similar model in mice. Mice that are deficient of the gulono- $\gamma$ -lactone oxidase (*gulo*) gene are not able to synthesize vitamin C and depend on dietary supplementation for survival. By manipulating the diet of *Gulo* -/- mice, we can control the amount of vitamins C and E intake and thus, tissue concentrations in the animals. Our studies characterize mice placed on the double-deficient diet for 2-6 months based on behavioral analysis and tissue specific nutrient levels. Quantification of oxidant stress markers will be assessed.

2) Leptin-Mediated Macrophage Chemotaxis into Adipose Tissue  
Dario Gutierrez—Department of Molecular Physiology and Biophysics

The role of adipose tissue as a site of energy storage is well understood; however, its involvement in systemic inflammation and insulin resistance has not been thoroughly studied. Adipose tissue macrophage (ATM) numbers increase in obesity, augmenting the secretion of proinflammatory cytokines from adipose tissue (AT), and leading to the development of insulin resistance. Leptin is a hormone predominantly secreted by white adipose tissue (WAT), and its circulating serum levels correlate directly with AT mass. Previous studies from our laboratory have shown that leptin stimulates THP-1 monocyte migration at concentrations ranging from 0.001-100 ng/ml with its maximum effect at 1 ng/ml. However, its role *in vivo* as well as the migratory intracellular signaling pathways activated downstream of the leptin receptor (ObRb) are poorly understood. In this project we investigated the signaling pathways activated in J774 macrophages upon leptin treatment, and their ability to support chemotaxis *in vitro*. Western blot experiments show that there is a 47 % increase in ERK1/2 phosphorylation, 5 minutes post-treatment with 100 ng/ml of leptin. This closely resembled the increases in phosphorylation seen with C5a, an established macrophage chemoattractant. Furthermore, pharmacological inhibition of this pathway led to the disruption of leptin-induced monocyte chemotaxis. In addition, time-lapse microscopy micropipette protrusion assays with J774 macrophages show that leptin induced cell polarization and formation of membrane protrusions within 5 minutes of gradient generation, suggesting that leptin is stimulating actin cytoskeletal rearrangements. Altogether, these results suggest that leptin acts as a monocyte/macrophage chemoattractant *in vitro* and that the ERK1/2 pathway may be the main orchestrator of this process. Future studies will investigate the regulation of small Rho GTPases as well as the *in vivo* role of leptin in macrophage recruitment into AT.

3) Macrophage Inflammatory Protein-1 $\alpha$  Has a More Significant Role in Diet Induced Obesity in Hyperlipidemic LDLR-/- Mice than in Normolipidemic Mice  
Bonnie Surmi—Department of Molecular Physiology & Biophysics

Expression of the chemokine macrophage inflammatory protein-1 $\alpha$  (MIP-1 $\alpha$ ) is significantly elevated in human atherosclerotic plaques and in white adipose tissue (WAT) from obese humans and mice. We hypothesized that MIP-1 $\alpha$  is important for macrophage recruitment to the aorta and WAT in diet induced obese mice. To test MIP-1 $\alpha$ 's role in lesion formation, bone marrow from MIP-1 $\alpha$ -/- or MIP-1 $\alpha$ +/+ mice was transplanted into LDLR-/- mice. After 4 weeks mice were started on Western diet (WD). Six weeks later, male and female recipients of MIP-1 $\alpha$ -/- marrow had significantly decreased plasma lipids relative to mice with MIP-1 $\alpha$ +/+ marrow. Only female mice continued to have reduced plasma lipids ( $P<0.005$ ) after 12 weeks on WD. Male MIP-1 $\alpha$ -/- recipients had a 56% reduction in total fat mass at 6 and 12 weeks ( $P<0.01$ ), and their plasma fasting insulin and leptin levels were significantly reduced. Mean atherosclerotic lesion area was lower in MIP-1 $\alpha$ -/- recipients at 12 weeks ( $P<0.05$ , males;  $P=0.22$ , females). To test the role of MIP-1 $\alpha$  in macrophage recruitment

to WAT, MIP-1 $\alpha$ +/+, MIP-1 $\alpha$ +/-, and MIP-1 $\alpha$ -/- mice were fed WD for 16 weeks. Surprisingly, the MIP-1 $\alpha$ -/- mice had a very similar metabolic phenotype to MIP-1 $\alpha$ +/+ and MIP-1 $\alpha$ +/-' littermates. Male MIP-1 $\alpha$ -/- mice had a mild reduction in perigonadal fat, and MIP-1 $\alpha$ +/-' and MIP-1 $\alpha$ -/- male mice had elevated fasting glucose and decreased plasma NEFAs, but no other significant changes were observed. In conclusion, our data suggest that MIP-1 $\alpha$  is not important for macrophage recruitment to WAT but that in hyperlipidemic mice MIP-1 $\alpha$  influences lipoprotein metabolism, atherosclerosis, and WAT expansion.

#### 4) Assessment of Energy Expenditure and Substrate Utilization in Obese and Normal Weight Patients with Heart Failure

Joshua Squiers—Department of Nursing Science

The Neurohormonal Model of heart failure (HF) posits that a variety of short-term and long-term compensatory systems provide adequate systemic perfusion at the cost of continued disease progression. While many of the deleterious effects of long-term activation have been documented, the net metabolic result has yet to be described. It is reasonable to hypothesize that long-term up-regulation of these compensatory systems may increase energy expenditure (EE) and alter substrate utilization (SU). Further complicating the situation, a variety of cohort studies concluded that obese patients with HF have improved survival over normal weight patients with HF. What is unknown is the mechanism responsible for this apparent survival benefit, and how it varies between obese and normal weight patients. While several studies have described EE in patients with HF, none have measured EE and SU over an entire 24 hour period. Identification of the EE and SU patterns may add to our understanding of the metabolic changes associated with HF. This study will assess the feasibility of using indirect, whole chamber calorimetry in measuring energy balance, and to provide an initial description of differences in EE and SU between normal weight and obese patients with HF. Currently, whole room indirect calorimetry is viewed as the gold standard for these systemic level metabolic measurements. While this system has been used to assess metabolic function in a number of clinical populations, its value in HF research remains unexplored. Data from this study will be used to guide hypothesis generation in future research.

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### Translational Biology: From Bench to Bedside

#### 1) Formation and Metabolism of 15-deoxy-D<sup>12,14</sup>-prostaglandin J<sub>2</sub> (15-d-PGJ<sub>2</sub>) in Vivo

Klarissa Hardy—Department of Pharmacology

15-Deoxy-delta-12,14-prostaglandin J<sub>2</sub> (15-d-PGJ<sub>2</sub>) is a unique cyclopentenone eicosanoid generated from the dehydration of cyclooxygenase (COX)-derived prostaglandin D<sub>2</sub> (PGD<sub>2</sub>). This compound possesses two highly reactive a,b-unsaturated carbonyl moieties that can readily adduct thiol-containing biomolecules such as glutathione and cysteine residues on proteins via Michael addition. Due to its reactivity, 15-d-PGJ<sub>2</sub> is thought to exert potent biological activity and mediate a wide variety of cellular responses. Among its diverse functions, 15-d-PGJ<sub>2</sub> is postulated as an important mediator of inflammatory and apoptotic processes and is believed to be an endogenous ligand for the peroxisome proliferator-activated receptor-g (PPAR-g). However, despite the large number of publications ascribing bioactivity to this molecule, the extent to which 15-d-PGJ<sub>2</sub> is formed in vivo and the mechanisms that regulate its formation are unknown. Previously we have reported the formation of PGD<sub>2</sub> and PGJ<sub>2</sub>-like compounds, termed D<sub>2</sub>- and J<sub>2</sub>-isoprostanes (IsoPs), produced in vitro and in vivo by the free-radical catalyzed peroxidation of arachidonic acid (AA). Based on these findings, we investigated whether 15-d-PGJ<sub>2</sub> can also form via the nonenzymatic peroxidation of AA. We now report the generation of 15-d-PGJ<sub>2</sub> in vitro and in vivo via the nonenzymatic peroxidation of AA. In rats treated with CCl<sub>4</sub> to induce lipid peroxidation, levels of 15-d-PGJ<sub>2</sub> formed esterified in phospholipids derived from liver increased 12-fold (6.4 + 1.1 ng/g of liver) compared to levels in untreated rats (0.55 + 0.21 ng/g of liver). These studies have, for the first time, demonstrated the formation of 15-d-PGJ<sub>2</sub> in vivo via a second pathway independent of COX.

#### 2) *Caenorhabditis elegans* as a model to study mechanisms of methylmercury toxicity

Kirsten Helmcke—Department of Pharmacology

Methylmercury (MeHg) is a toxicant having detrimental effects on the mammalian nervous system, but the mechanisms of toxicity are unknown. Humans are exposed to MeHg in seafood and the toxicant is able to traverse the blood-brain and placental barriers, making it harmful to the nervous system, particularly that of

the developing fetus. *Caenorhabditis elegans* is an organism amenable to use in toxicological research. Therefore, *C. elegans* was used as a model to discern pathways involved in MeHg developmental neurotoxicity. Previous results indicated that although MeHg was lethal to *C. elegans*, surviving animals show no defects in locomotion, birthrate or neuronal morphology. However, MeHg accumulated in treated animals in a dose and time-dependent manner (after 15 hour treatment L4 worms treated at 0.1 and 0.4 mM MeHg had 20- and 150-fold increases in MeHg content, respectively) and induced a dose-dependent delay in development and pharyngeal pumping rate (after 15 hour exposure of L4 worms, at 0.1 and 0.4 mM MeHg, pumping rate was reduced 27% and 70%, respectively) indicating an effect of MeHg on the pharyngeal nervous system. Following initial MeHg insult, worms were less sensitive to subsequent MeHg exposure, shifting the lethality dose response curves of MeHg rightward with increasing initial MeHg exposure. These results indicate that exposure to non-lethal concentrations of MeHg induces factors in *C. elegans* that protect it from additional insults and candidates are being studied to assess involvement in this process.

### 3) BMP signaling regulates eNOS expression and function in the murine pulmonary vasculature Jonathan Lowery—Department of Cell & Developmental Biology

Endothelial nitric oxide synthase (eNOS) plays a major role in maintaining low vascular resistance in the pulmonary circulation. Previously, mice deficient for eNOS have been shown to develop pulmonary hypertension (PH) in response to chronic hypoxia. In this study, we implicate a role for Bone Morphogenetic Protein (BMP) signaling in the regulation of eNOS expression and function in the pulmonary arterial circulation. Mice with heterozygous hypomorphic mutation in the BMP type II receptor (*Bmpr2*<sup>Flx2/+</sup>) develop exacerbated PH and attenuated induction of pulmonary eNOS in response to chronic hypoxia. Ex vivo analysis of intra-pulmonary arteries (IPAs) revealed that *Bmpr2*<sup>Flx2/+</sup> mice exhibit enhanced vasoconstriction combined with severe defects in nitric oxide-dependent vasodilation. This functional relationship is supported in vitro in that BMP ligands up-regulate expression of eNOS in IPAs and cultured endothelial cells (ECs) (5- and 7-fold, respectively), leading to an approximate 2-fold increase in basal eNOS activity and activated phosphorylation status. BMP-mediated regulation of eNOS is diminished in *Bmpr2*<sup>Flx2/+</sup> mutant IPAs and ECs. The importance of BMP-Bmpr2-eNOS signaling is underscored in that the majority of patients with Familial Pulmonary Arterial Hypertension inherit heterozygous mutations in BMPR2. As such, our findings suggest a mechanism by which mutation in BMPR2 might lead to dysfunctional BMP-mediated regulation of eNOS, thereby causing defects in pulmonary vascular reactivity and PH.

### 4) Foxd3 Regulates Neural Crest Multipotency and Self-Renewal Nathan Mundell—Department of Pharmacology

The neural crest (NC) is a specialized group of progenitor cells that arise from the developing spinal cord. At the onset of migration, NC is a heterogeneous pool of multipotent and fate-restricted progenitors that follow regionally defined pathways to sites of differentiation, giving rise to a variety of adult cell types including neurons, glia, melanocytes, smooth muscle, and cartilage. The forkhead transcription factor Foxd3 is required for self-renewal and maintenance of a multipotent state in two other progenitor cell types: embryonic stem cells (ES cells) and trophoblast stem cells. Foxd3 is also one of the earliest molecular markers of the NC. NC-specific deletion of Foxd3 in the mouse embryo results in severe defects in NC derivatives including craniofacial and pharyngeal arch defects, and complete loss of the enteric nervous system. We show that the progenitor pool is depleted and much of the premigratory and early migrating NC is lost by apoptosis in a rostral to caudal progression in mutant embryos. Lineage labeling analysis of Foxd3 mutant embryos demonstrated that vagal NC progenitors failed to migrate into the foregut, and were greatly reduced in the outflow tract of the heart. Surprisingly, this reduced amount of cardiac NC is able to mediate cardiovascular remodeling, but does not contribute to parasympathetic innervation of the heart. In vitro analysis of differentiation in clonally-derived NC indicated that Foxd3 mutant NC have an increased percentage of smooth muscle restricted progenitors and reduced potency to differentiate into multiple lineages. Serial neurosphere culture experiments suggest that mutant NC do not maintain progenitor self-renewal. These results demonstrate a global role for Foxd3 in NC maintenance along the anterior-posterior axis, and establish the requirement of Foxd3 in multipotent NC stem cell subpopulations.

5) Parametric Variation with the Reference Region Model for Dynamic Contrast Enhanced MRI (DCE-MRI)  
Mary Loveless—Department of Biomedical Engineering

DCE-MRI models the kinetics of an injected contrast agent (CA) to map perfusion within a particular region of interest (ROI). To drive the model, the CA concentration in the blood plasma ( $C_p$ ) is required. Methods of obtaining an accurate  $C_p$  can be difficult but reference region (RR) models allow characterization of an ROI without obtaining  $C_p$  based on a reference tissue,  $C_{t,RR}$ . Recently, these models have been modified to be more physiologically accurate. However, *a priori* knowledge of the RR parameters is required. We assess the accuracy of the RR model in determining ROI parameters given an error range for assigned RR parameters. First, a  $C_p$  curve was simulated and applied to construct a  $C_{t,RR}$ . In constructing the RR curve, we varied  $K^{trans}$ ,  $v_e$ , and  $v_p$  over a physiologically relevant range. The true RR parameters were fixed at values appropriate for muscle. To investigate how fluctuations in the estimated  $C_p$  affect ROI measurements, a  $C_{t,ROI}$  was simulated with the true  $C_p$  and fixed ROI tissue parameters. The estimated  $C_p$  and  $C_{t,RR}$  were then used to estimate parameters in the ROI, and errors in  $K^{trans}$ ,  $v_e$ , and  $v_p$ , were assessed. Preliminary data identify  $v_{e,RR}$  as the most stable parameter, reflecting accurate  $C_{p,RR}$ . Error in  $K_{trans,RR}$  and  $v_{p,RR}$  dominate error in the estimated  $C_{p,RR}$ , yielding increased error propagation into the ROI parameters. Experimental studies are underway to assess to measure the  $C_p$  from the left ventricle in mice while comparing it to an estimated  $C_{p,RR}$  obtained from reference tissue.

6) Functional characterization of an intronic epilepsy mutation in the GABRG2 gene.  
Mengnan Tian—Department of Pharmacology

We explored the basis for dysfunction of GABA receptor currents produced by an autosomal dominant intronic mutation in the human GABA<sub>A</sub> receptor  $\gamma 2$  subunit associated with the epilepsy syndrome, childhood absence epilepsy and febrile seizures (Kananura et al., Arch Neurol., 59:1137, 2002). In the GABRG2 (IVS6+2T→G) mutation the second nucleic acid in the intron 6 splice donor site is mutated from T to G, which could result in abnormal intron splicing. This is the first intronic mutation identified in a GABA<sub>A</sub> receptor gene, but no evaluation of the functional consequence of this splice donor site mutation has been reported. We hypothesized that the mutant mRNA might contain a premature translation-termination codon (PTC) that could degrade mutant mRNA by non-sense mediated decay (NMD), thereby producing epilepsy due to haploinsufficiency. To explore the splicing of wild type and mutant GABAR mRNAs, we first designed a minigene construct that included the full length intron 5 and a short form of intron 6 in the GABRG2 cDNA sequence. Both introns in the minigene were completely spliced out from wild type transcripts, while a noncanonical cryptic splice donor site was activated during mutant minigene mRNA splicing, resulting in retention of part of intron 6 and a frame shift in exon 7 that produced a PTC in the mutant mature mRNA. This result suggested that the mutation would activate NMD. However, this result must be confirmed in the full GABRG2 gene to determine if it is physiologically relevant. Thus, we designed a BAC recombineering experiment to characterize the consequence of this mutation on GABA<sub>A</sub> receptor expression. BAC constructs containing the wild type GABRG2 or mutant GABRG2(IVS6+2T→G) genes were expressed in mammalian cells to compare their mRNA splicing pattern, and to determine if the mutation affects GABA<sub>A</sub> receptor  $\gamma 2$  subunit mRNA and protein level in both homozygous and heterozygous expression conditions. These studies will further clarify the molecular etiology of idiopathic generalized epilepsies, and pave the way for further *in vivo* studies. Supported by NIH 1 R01 NS051590 to RLM and Epilepsy Foundation Predoctoral Research Training Fellowship to MT.

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### Tumorigenesis and Cancer Therapy

1) AKT activation in HNSCC predicts survival and correlates with HPV status  
Xinyuan Lu—Department of Cancer Biology

25% of unselected head and neck squamous cell carcinomas (HNSCC) and 50% of oropharyngeal HNSCC are caused by human papilloma virus (HPV) infection. It has been shown HPV-associated HNSCC respond better to therapy and those patients with HPV-associated HNSCC have improved survival. Molecular mechanisms correlating with improved response and survival in HPV-positive HNSCC are still unknown. We explored the phosphotidylinositol-3 kinase (PI3K) / AKT pathway in HPV-positive and HPV-negative HNSCC. The pathway was examined in forty primary HNSCC (20 HPV+, 20 HPV-) using various techniques including immunoblotting, fluorescent in situ hybridization, reverse transcription real time PCR, and direct sequencing

for mutational analyses. Our quantitative immunoblot data revealed that phospho-AKT was increased in HPV-negative tumors relative to HPV-positive HNSCC. Similar results were observed using the phospho-AKT:total AKT ratio. High phospho-AKT levels correlated with worse survival and with HPV-negative tumor status. Low phospho-AKT levels and HPV-positive status correlated with one another and with improved survival. AKT kinase is implicated in many aspects of tumorigenesis. The major activator of AKT is PI3K. Interestingly, we observed low-level amplification of the gene encoding the catalytic subunit of PI3K, PIK3CA gene, and modestly higher expression of p110 $\pm$  in HPV-positive samples. Additionally, all mutations of PIK3CA within this cohort were seen in HPV-positive HNSCC. These data suggesting that AKT activation may be a molecular marker of poor outcome in HNSCC. Additionally, PIK3CA expression and/or mutation are not responsible for AKT activation in HPV-negative HNSCC suggesting that alternative mechanisms of AKT activation are utilized in HPV-negative tumors.

## 2) JAK3 Mutations May Be Tumor Progression Events in Adult T-cell Leukemia/Lymphoma Natalina Elliott—Department of Cancer Biology

Adult T-cell Leukemia/Lymphoma (ATLL) is caused by infection from a complex retrovirus, Human T-Lymphotropic virus type-1 (HTLV-1), that expresses viral oncproteins such as Tax. Although Tax is necessary for T-cell transformation, ATLL only ensues in 5% of carriers and after a long latency of 30 years, implying that additional host mutations are necessary for ATLL induction. Upon infection with HTLV-1, T-cells have up-regulated IL-2 autocrine signaling which is lost with tumor progression. We hypothesized that gain of function in the IL-2 signaling pathway may account for IL-2-independence and constitutive Stat5 activity that has been observed in advanced ATLL. Recently, activating mutations were described in the JAK3 tyrosine kinase in cases of acute megakaryocytic leukemia. Since JAK3 is immediately downstream of the IL-2 receptor, we thought similar mutations may be detected in ATLL. In 4 out of 10 patients studied, we found two mutations in the FERM domain of JAK3. Our preliminary data suggests that these FERM domain mutations create a more active JAK3 tyrosine kinase and suggest an autoregulatory role for the FERM domain in kinase regulation.

## 3) The role of Bid in the ATR-mediated DNA damage signaling pathways Yang Liu—Department of Cell and developmental biology

Bid is a proapoptotic Bcl-2 family protein that plays dual roles in the DNA damage as well as cell death signaling pathways. Following genotoxic stress, Bid is accumulated in the nucleus to be phosphorylated by PI-3-like kinase ATM/ATR. Bid knockout cells show an intra-S phase checkpoint defect upon DNA damage and Bid-deficient mice spontaneously develop chronic myelomonocytic leukemia. However, the function of Bid in the DNA damage pathway is unclear. In our study, we demonstrate that Bid mediates the ATR-directed DNA damage response to replicative stress. Following replicative stress, Bid-deficient cells demonstrate diminished Chk1 phosphorylation, reduced recovery of DNA synthesis, and reduced accumulation of ATR/ATRIP on chromatin and at DNA damage foci. In addition, Bid directly interacts with ATRIP following DNA damage, and this association is required for normal ATR-directed Chk1 and Rad17 phosphorylation. These results establish a direct role for the BH3-only Bcl-2 family member, Bid, acting at the level of the damage sensor complex to amplify the ATR-directed cellular response to replicative DNA damage.

## 4) Development of a Lymphedema Symptom Checklist in Head and Neck Cancer Patients Jie Deng—School of Nursing

**Background:** Head and neck cancer patients may develop secondary lymphedema externally (e.g., submental area) and internally (e.g., laryngeal, pharyngeal, and oral cavity). It not only influences patients' most visible areas of their body (e.g., face and neck), but also influences basic functions, such as speech, breathing, swallowing, and neck range of motion. Currently, there is no instrument available to assess secondary lymphedema-related symptoms in head and neck cancer patients. The purpose of this study was to develop a symptom checklist for head and neck cancer patients with secondary lymphedema. **Methods:** The study developed the symptom checklist-Head & Neck (SC-HN) through the following two phases. During phase one, the expert panel and 18 head and neck cancer patients with secondary lymphedema reviewed the initial item pool developed by the researcher via literature review. The initial item pool was revised into an initial symptom checklist according to the expert panel's suggestions and the patients' symptomatic experiences. During phase two, 18 additional head and neck cancer patients with secondary lymphedema completed the

initial symptom checklist. Results: Through the two phases, the final symptom checklist for head and neck cancer patients with secondary lymphedema was constructed. Conclusion: Preliminary results show that the SC-HN addressed the symptoms of external and internal lymphedema in head and neck cancer patients. The content validity and face validity of the SC-HN was supported by the expert panel during developing the SC-HN. Further psychometric testing is needed.

## **GSRS 2009 Participant Abstracts: Poster presentations (alphabetical order by participant)**

1) The Wnt modulator sFRP2 enhances mesenchymal stem cell wound repair  
Maria Paula Alfaro—Department of Pathology

Cell-based therapies using multipotent mesenchymal stem cells (MSCs) for organ regeneration are being pursued for cardiac disease, orthopedic injuries and biomaterial fabrication. The molecular pathways that regulate MSC-mediated regeneration or enhance their therapeutic efficacy are, however, poorly understood. In an attempt to elucidate a way to strengthen the regenerative potential of MSCs, preliminary studies were performed comparing MSCs isolated from wildtype and regenerative mouse strains. The MRL/MpJ mouse has been described as a “super healer” mouse that is able to repair soft tissue with minimal scarring. MSCs were isolated from the MRL/MpJ mouse (MRL-MSCs) and from C57/Bl6 mice (WT-MSCs) and their differing qualities assessed. Compared to WT-MSCs, MRL-MSCs demonstrated increased proliferation in vitro. We used a Poly-vinyl alcohol (PVA) sponge model of repair stimulation to assess their capacity to generate wound repair tissue. We observed that the MRL-MSCs demonstrated increased in vivo engraftment, experimental granulation tissue reconstitution, and tissue vascularity. The MRL-MSCs also reduced infarct size and improved cardiac function as compared to WT-MSCs in a murine myocardial infarct model. Genomic and functional analyses indicated a downregulation of the canonical Wnt pathway in MRL-MSCs characterized specifically by upregulation of secreted frizzled related proteins (sFRPs). In vitro proliferation studies confirmed that recombinant sFRP2 mediated enhanced proliferation of both mouse and human MSCs. Based on these observations, we hypothesized that sFRP2 served an important role in MSC-mediated repair and regeneration. We generated WT-MSCs overexpressing sFRP2 (sFRP2-MSCs) by retroviral transduction to test this hypothesis. sFRP2-MSCs maintained their ability for multilineage differentiation in vitro and proliferated faster than the vector only control MSCs (GFP-MSCs). When implanted in vivo in the PVA sponge model, the sFRP2-MSCs recapitulated the MRL phenotype by mediating greater, more vascularized granulation tissue. Moreover, peri-infarct intramyocardial injection of sFRP2-MSCs resulted in reduced infarct size, favorable remodeling and better preserved left ventricular function following myocardial injury in mice. These findings implicate sFRP2 as a key molecule for the biogenesis of a superior regenerative phenotype in MSCs.

2) In vitro and in vivo studies of cPLA<sub>2</sub> involvement in VEGF mediated retinal neovascularization  
Josh Barnett—Department of Pharmacology

Cytosolic Phospholipase A<sub>2</sub> (cPLA<sub>2</sub>) promotes VEGF induction through catalyzing the hydrolysis of phospholipids directly releasing arachidonic acid, the precursor of prostaglandins. In order to better understand the role of cPLA<sub>2</sub> in retinal VEGF regulation, the temporal distribution and level of retinal cPLA<sub>2</sub> involvement was examined using in vitro and in vivo models. Primary retinal Müller cells were isolated from 14 day old Long Evans rat pups and exposed to hypoxia for 24 hours after treatment with the cPLA<sub>2</sub> inhibitor, cPLA<sub>2</sub> protein and mRNA were then collected from the cells and used in western blots and microarray analysis. Growth medium from the cells was also collected and assessed for VEGF levels. Sprague-Dawley rat litters were exposed to alternating 50% and 10% oxygen atmospheres from birth through P14. Upon removal from the exposure chamber, some rats received an intraocular injection of a cPLA<sub>2</sub> inhibitor (Cayman Chemical). These animals were sacrificed 6 days later, and their retinas were ADPase-stained and evaluated for neovascularization (NV) and avascular area. Other animals were sacrificed at 1, 3 and 6 days post oxygen exposure, and retinal cPLA<sub>2</sub> levels were measured by western blot analysis. Primary retinal Müller cells exposed to hypoxia for 24 hours exhibited a 3-fold increase in VEGF secretion, while only a 1.1-fold increase was observed in samples treated with a cPLA<sub>2</sub> inhibitor. Additionally, these cells demonstrated a 3- to 5-fold induction of phosphorylated cPLA<sub>2</sub> protein levels. A 3.2-fold increase in phosphorylated retinal cPLA<sub>2</sub> protein was observed in oxygen exposed animals compared to room air raised controls at 1 day post oxygen exposure. The evaluation of the retinas from animals treated with an intraocular injection of a cPLA<sub>2</sub> inhibitor revealed a 30% ( $p < 0.05$ ) decrease in NV and a 26% ( $p < 0.05$ ) decrease in avascular area compared to control retinas. Increased cPLA<sub>2</sub> mRNA and protein levels were associated with increased VEGF levels and both increased retinal NV and avascular area, which where both significantly decreased with the inhibition of cPLA<sub>2</sub>. Continued research into the induction of VEGF through arachidonic acid derivatives may identify additional and novel therapeutic targets.

### 3) Determination of Functionalization Efficiency of Gold Nanoparticles Charleson Bell—Department of Biomedical Engineering

Bionanotechnology is a field quickly gaining popularity amongst scientists looking to specifically target cancer and pathogens for diagnostics and treatment. When coated with thiol-polyethylene glycol, following a place exchange reaction with stabilizing citrate molecules, gold nanoparticles are both biocompatible and therapeutically bioefficient. However, in order to characterize the therapeutic capacity of such ligand coated particles, the number of ligands bound must be quantified. Herein, we enumerate the therapeutic capacity or functionalization efficiency<sup>TM</sup> of place-exchanged functionalized gold nanoparticles ranging in diameters from 5-250 nm using thermogravimetric analysis.

### 4) Role of RGS2 in myeloid cells and tumor vascularization Kimberly Boelte—Department of Cancer Biology

Tumor growth is known to be intimately linked with stromal interactions, such as immune response. Over the past few decades, myeloid derived suppressor cells (MDSCs) have been implicated in dampening immune response to tumors. MDSCs are immature cells of the myeloid lineage, accumulate in tumor bearing mice, and are found in peripheral blood of cancer patients. MDSCs are capable of attenuating immune response and increasing vascularization in tumors. We have found that Regulator of G protein signaling-2 (Rgs2) mRNA is increased in tumor-derived MDSCs compared to control MDSCs. Tumor growth in Rgs2<sup>-/-</sup> mice is retarded, and the tumors exhibit significantly less vascular density. We observe no difference in proliferation of the tumor cells, but see more apoptosis in the null mice. Interestingly, tumors in null mice exhibit greater leukocyte infiltration, shown by immunofluorescent staining for CD45 and Gr-1, and flow cytometry for Gr-1+CD11b+ cells. When examining other markers on wild type and Rgs2<sup>-/-</sup> MDSCs under tumor conditions, we found that Rgs2<sup>-/-</sup> MDSCs express less Sca-1, but more c-Kit and CD34, suggesting a role for Rgs2 in differentiation. Stimulation of HL-60 cells to differentiate by DMSO, and 32D cells by G-CSF, led to increasing levels of Rgs2 mRNA, and ex vivo studies with bone marrow stem cells from Rgs2<sup>-/-</sup> mice indicate a delay in myeloid differentiation. Additionally, Rgs2<sup>-/-</sup> MDSCs in tumors produce less angiogenic and tumor-promoting cytokines than wild type MDSCs. Our data indicate that Rgs2 affects vascularization of tumor tissue and tumor progression by affecting MDSC function and differentiation.

### 5) Effect of Dyslipidemia on Natural Killer T Cell Activation Nicole Braun—Department of Pathology

Natural killer T (NKT) cells are a specialized subset of immune regulatory cells that recognize glycolipid antigens and are thought to be pro-atherogenic under hyperlipidemic conditions. Interestingly, we observed that hyperlipidemic apoE<sup>-/-</sup> mice have decreased NKT cell-mediated cytokine production in response to  $\alpha$ -galactosylceramide ( $\alpha$ -GalCer), a prototypic NKT cell glycolipid antigen. These data suggest changes in circulating lipids can affect normal NKT cell functions; however the mechanism(s) for this effect remains unclear. In the current study, we hypothesized that chronic hyperlipidemia leads to an unresponsive NKT phenotype. To test this hypothesis, we compared surface expression of the inhibitory marker PD-1 on NKT cells isolated from C57Bl/6 and apoE<sup>-/-</sup> mice. Interestingly, apoE<sup>-/-</sup> NKT cells had significantly increased PD-1 expression in both the spleen and liver. Additionally, in response to i.p. injected  $\alpha$ -GalCer, apoE<sup>-/-</sup> mice showed significantly decreased splenic NKT cell expansion at 3 days post-injection; a profile associated with NKT cell anergy due to chronic stimulation. Because antigen presenting cells (APCs), especially dendritic cells (DCs), can induce or inhibit NKT cell activation, we tested the ability of C57Bl/6 and apoE<sup>-/-</sup> splenic DCs and bone marrow-derived DCs (BMDCs) to present  $\alpha$ -GalCer to an NKT cell hybridoma in vitro. NKT cell hybridoma-mediated IL-2 secretion in culture supernatants was reduced in the presence of apoE<sup>-/-</sup> splenic DCs. However, BMDCs from apoE<sup>-/-</sup> and C57Bl/6 mice equally induced IL-2 secretion in response to  $\alpha$ -GalCer. Taken together, these data suggest that chronic hyperlipidemia induces an NKT cell phenotype that is unresponsive to further stimulation by exogenous glycolipid.

**6) Discovery of a highly M<sub>5</sub>-preferring muscarinic acetylcholine receptor allosteric potentiator**  
Thomas Bridges—Department of Pharmacology

Activation of muscarinic acetylcholine receptor subtype-1 (M<sub>1</sub>) has been investigated preclinically as a potential strategy for treatment of Alzheimer's disease (AD). Selective targeting of subtype-5 (M<sub>5</sub>) may also be therapeutically relevant to AD due to its role in regulation of cerebral vascular tone and certain cognitive functions as suggested by studies with M<sub>5</sub>-KO mice. Historically, high homology of the orthosteric acetylcholine-binding site across the five muscarinic receptor subtypes has made discovery and development of highly subtype-selective or preferring compounds challenging, and non-selective activation of M<sub>2</sub> and M<sub>3</sub> has contributed to failure of muscarinic agonists in clinical trials. To date, no ligands exhibiting high M<sub>5</sub>-preference or selectivity have been reported. Recently, functional cell-based high throughput screening was used to identify a number of novel muscarinic potentiators, including VU0119498, which enhanced acetylcholine (ACh) potency at M<sub>1</sub>, M<sub>3</sub>, and M<sub>5</sub> via an allosteric interaction. An iterative analog library approach was used to chemically optimize VU0119498 for increased M<sub>5</sub> activity, which identified VU0238429 as the first highly M<sub>5</sub>-preferring small molecule. In calcium mobilization assays, VU0238429 displayed an EC<sub>50</sub> of approximately 1 μM for potentiation of acetylcholine at M<sub>5</sub> and an EC<sub>50</sub> of >30 μM for potentiation at M<sub>1</sub> and M<sub>3</sub>, with no effect at Gq15 co-transfected M<sub>2</sub> or M<sub>4</sub> receptors. In similar cell-based assays, a fixed 30 μM concentration of VU0238429 induced an approximately 14-fold leftward shift of a full Ach concentration-response curve at M<sub>5</sub>. This novel allosteric potentiator represents the first highly M<sub>5</sub>-preferring small molecule ever reported and may serve as a useful pharmacological tool for probing the therapeutic potential of M<sub>5</sub> activation within the context of AD and cerebrovascular dementia.

**7) Regulation of cell adhesion and motility: a novel function of arrestin proteins**  
Whitney Cleghorn—Department of Pharmacology

Arrestins regulate G protein-coupled receptors and other signaling proteins. Over 100 arrestin interaction partners have been identified, implicating arrestins in various signaling pathways and cellular functions. The interactions of many proteins (e.g., Src, JNK3, ERK<sup>1/2</sup>, Mdm2, etc.) with receptor-bound arrestin localize these molecules to receptor-rich membranes. Our recent finding that arrestins bind microtubules and recruit signaling proteins to the cytoskeleton prompted us to investigate whether arrestins affect cell adhesion, motility, and morphology. Here we show that the overexpression of arrestin<sub>2</sub> and arrestin<sub>3</sub> differentially regulates cell adhesion. Arrestin<sub>3</sub> causes a significant reduction in cell adhesion to extracellular matrix protein fibronectin, whereas arrestin<sub>2</sub> does not affect it. We also found that overexpression of arrestin<sub>2</sub> and arrestin<sub>3</sub> dramatically decreases migration, with arrestin<sub>2</sub> showing the greatest reduction. Rhodamin-phalloidin staining revealed that arrestin<sub>2</sub> and arrestin<sub>3</sub> induce strikingly different changes in cell morphology. In addition overexpression of arrestin<sub>3</sub>, but not arrestin<sub>2</sub>, decreases the amount of active Focal Adhesion Kinase (FAK) in these cells, implicating arrestin<sub>3</sub> in the regulation of focal adhesion complex signaling. Thus, the two non-visual arrestins differentially regulate cell adhesion, spreading and migration. This is a novel biological role for arrestin proteins.

**8) Engineering a Nanoporous Carbon Adsorbent for Separation of Light Gases from Air**  
Amanda Furtado—Department of Chemical and Biomolecular Engineering

Incorporation of metals into ordered mesoporous carbons is used to separate and purify gaseous and liquid mixtures. This work focuses on incorporating metals, specifically zinc and copper, into microporous carbon silica composite (CSC) materials to act as catalysts for the separation of light gases from air. These novel materials are specifically engineered for use as adsorbents in gas masks and industrial filters. Copper and zinc have successfully been incorporated into CSC materials in two distinct phases of the material, the MCM-41 silica phase and the carbon phase. These novel materials have been characterized by XRD, ICP-MS, adsorption isotherms, and TGA. Breakthrough times of ammonia and sulfur dioxide have also been calculated for these adsorbents. The characterization techniques have shown that the metals are successfully incorporated into both the carbon and silica phases of the composite materials and the metals do not disrupt the hexagonal mesoporous silica structure. Preliminary breakthrough results show that the impregnation of the carbon phase leads to longer breakthrough times than impregnation of metals in the silica phase, and that the zinc impregnated samples have longer breakthrough times than the corresponding copper-impregnated samples.

9) The Role of NKT Cells in the Pathogenesis of Obesity and Type 2 Diabetes  
Curtis Gabriel—Department of Microbiology and Immunology

The dangers of overnutrition have become apparent in the United States where, according to the Centers for Disease Control and Prevention, nearly 33% of adults can be classified as obese or overweight and the incidence of type 2 diabetes mellitus (T2DM) is rapidly rising. Many obesity-related comorbidities, including T2DM, appear to be associated with chronic inflammatory processes. The mechanistic relationship between obesity and inflammation involves a complex network of cells and signaling molecules from both the immune system and the metabolic system. This project focuses on the relationship between Natural Killer T (NKT) cells and the development of insulin resistance in the context of obesity.

We have shown that: 1) NKT cells isolated from mice fed lard-containing diets have a hypo-proliferative and pro-inflammatory phenotype, 2) Mice lacking NKT cells are protected against obesity comorbidities including insulin resistance and non-alcoholic steatohepatitis, and 3) Chronic treatment with alpha-GalCer, a potent activator of NKT cells, exacerbates diet-induced insulin resistance in mice.

10) Rewiring the murine hepatitis virus replicase polyprotein to function with a single papain-like protease  
Mark Gadlage—Department of Microbiology and Immunology

The coronavirus positive-strand RNA genome encodes a replicase polyprotein that is processed into 16 mature nonstructural proteins (nsps) by virus-encoded proteases. For murine hepatitis virus (MHV), the first three cleavage sites (CS1, CS2, and CS3) of the replicase polyprotein are processed by two papain-like proteases, PLP1 and PLP2. SARS-CoV encodes only one PLP, PLpro, that mediates cleavage of the first three CSs. MHV PLP2 and SARS-CoV PLpro are similar in that both proteases cleave immediately after L-X-G-G amino acid motifs. The functional and evolutionary basis for these similarities and differences in MHV and SARS-CoV PLP-mediated processing are not known. Specifically, it is not known if proximal CS amino acid sequences are necessary and sufficient to determine protease specificity. To examine MHV PLP/CS interactions and to test whether MHV could serve as a model for analysis of SARS-CoV PLP-mediated processing, we rewired MHV ORF1a to express the minimal PLP2 cleavage site sequence (L-K-G-G) in place of PLP1 processing sites CS1 (CS1(3)) and CS2 (CS2(3)), either in the context of catalytically active or inactive PLP1. Viable viruses were recovered with CS1(3) and CS2(3) mutations in both active and inactivated PLP1 backgrounds. Recombinant mutant viruses containing CS1(3) demonstrated no detectable processing at the substituted cleavage site. Recombinant mutant viruses containing CS2(3) exhibited processing in both the active and inactive PLP1 backgrounds, demonstrating cleavage at substituted CS2(3) by PLP2. These results indicate that the L-X-G-G recognition site may be sufficient to alter PLP specificity at CS2, but that additional determinants may be required for processing at CS1. The results also provide a model to study the evolutionary relationships of conserved or divergent functions between nsps 1-3 of MHV and SARS-CoV.

11) Cortical regulation of medium spiny neuron dendritic spine loss in a parkinsonian rat model  
Bonnie Garcia—Department of Pharmacology

Striatal medium spiny neurons (MSNs) receive a dopaminergic input from the substantia nigra (SN), which synapses onto the neck of the MSN dendritic spine, and an excitatory glutamatergic input from the cortex onto the spine head. Striatal dopamine (DA) loss, as occurs in Parkinsonâ€™s Disease (PD), results in dystrophic changes in MSN dendrites, including a decreased density of dendritic spines. We hypothesize that the decrease in MSN spine density that occurs in response to DA denervation is the result of overactive glutamatergic drive onto the spine head. We recently reported that in organotypic co-cultures consisting of cortex, striatum, and ventral mesencephalon, cortical ablation at the time of MPP+ treatment prevented dopamine depletion induced spine loss. We have confirmed this phenomenon *in vivo*, noting that lesions of the motor cortex in animals with 6-OHDA lesions of the substantia nigra dopamine cells prevented the spine loss seen in animals with intact corticostriatal projections. We then sought to determine if cortical denervation performed after MSN spine loss was present would reverse the spine loss. Adult male rats received unilateral ibotenic acid cortical lesions of the M1 motor cortex four weeks after 6-OHDA lesions were made. Four weeks after the lesion, a time during which spine loss becomes well established, animals were sacrificed and the striatum subjected to Golgi impregnation. Lesions disrupting the corticostriatal projection significantly attenuated the established DA depletion-induced loss of spines, compared to animals with striatal DA denervation and an intact cortex. This attenuation was seen in the M1 recipient zone of the striatum, but not in an adjacent striatal

territory that does not receive cortical afferents from the site of the lesion. The partial reversal appears to be attributable to sprouting of corticostriatal neurons from the contralateral hemisphere to partially reinnervate the striatum. These data indicate that cortical ablation both prevents and reverses the MSN dendritic spine loss associated with Parkinsonâ€™s Disease.

12) YAP signaling plays a role in TGF-beta activation of epithelial plasticity  
Lin Ge—Department of Urologic Surgery

Yes Associated Protein (YAP), the homologue of Yorkie in *drosophila*, plays an important role in development. YAP has attracted recent attention because overexpression in non-tumorigenic cells can both prevent cells from apoptosis and promote proliferation, mimicking the behavior of cancer cells. Human prostate cancer is reported to over express YAP. Like many other epithelia cancers, prostate cancer, cells that express proteins associated with epithelial to mesenchymal transdifferentiation (EMT) is a poor prognosis factor. As TGF- $\beta$  signaling is a well described mediator of EMT, we hypothesized that YAP is important in TGF- $\beta$ -mediated EMT in prostate cancer progression. TGF- $\beta$  signaling induces EMT in a human prostate cancer cell line, DU145. Confocal microscopy revealed TGF- $\beta$  mediates nuclear translocation of YAP from the cytoplasm. Further, the knockdown of YAP by siRNA inhibited TGF- $\beta$  mediated EMT. These studies indicate a novel role of YAP in TGF- $\beta$  signaling. Further, since YAP is considered a sensor of cell-interactions, this finding further fine tunes our understanding of TGF- $\beta$ -mediated EMT, a mechanism for cancer cell motility and possible metastasis. For the future study, we would conduct the similar experiment in other cancer cell lines sensitive to TGF- $\beta$  EMT progression.

13) New iNKT cell phospholipid reactivity revealed after release from negative selection by inhibiting N  
Laura Gordy—Department of Microbiology and Immunology

Positive and negative selection events shape the development of a functional, MHC-restricted and self-tolerant T cell repertoire. Invariant natural killer T (iNKT) cells are a unique subset of CD1d-restricted, self-reactive T cells that express an invariant T cell receptor (TCR)  $\alpha\beta$ -chain paired with a limited set of  $\gamma\delta$ -chains. Current evidence indicates that positive selection of iNKT cells by a self glycolipid shapes the TCR repertoire. However, unlike conventional T cells, negative selection is not thought to play a major role in shaping the iNKT cellsâ€™ restricted repertoire. We generated a transgenic mouse model in which thymic negative selection events are suppressed within thymocytes, and assessed the effect on the iNKT cell receptor repertoire and specificity. Our results identify subtle changes in TCR  $\gamma\delta$  expression upon blockade of negative selection within iNKT cells. Furthermore, in vitro stimulation assays with purified and synthetic lipids revealed iNKT cells with altered specificity for certain endogenous and exogenous lipid antigens. Thus, these findings provide direct evidence indicating that negative selection shapes the lipid specificity of iNKT cells. The removal of highly reactive iNKT TCR may play an important role in preventing iNKT cell-induced autoimmune responses and extreme, detrimental anti-microbial responses. Our data support a model in which positive selection broadly shapes the iNKT cell TCR repertoire and negative selection fine tunes the TCR repertoire and its specificity.

14) Light Scattering by White-Emitting CdSe Nanocrystals and Traditional YAG:Ce<sup>3+</sup> Phosphor Particles  
Jonathan Gosnell—Department of Materials Science

In order for solid state lighting technology to become a mainstream technology, one of the major challenges to overcome is increasing the efficiency of these devices while maintaining a proper color balance. A significant source of efficiency loss in commercial phosphor-based white light-emitting diodes (LEDs) is light scattering off large, micron-sized phosphor particles. The use of recently reported single-size CdSe white-light nanocrystals in place of traditional phosphors, such as YAG:Ce<sup>3+</sup>, could lead to lower scattering losses and higher device efficiencies as a result of the extremely small CdSe core diameter of approximately 1.5 nm. This work theoretically and experimentally investigates the absorption, scattering, and extinction coefficients and cross sections of CdSe white-light nanocrystals in comparison to YAG:Ce<sup>3+</sup> phosphor particles. Calculations were performed based on the Rayleigh approximation and Mie theory of scattering. Experiments were carried out using thin films of encapsulated nanocrystals. By measuring the absorbance and thickness of the films, in addition to the concentration of the nanocrystals, extinction coefficients and cross sections were determined using the Beer-Lambert law. A reasonable agreement was obtained between theoretical and experimental data

showing that the size of the particle has a significant impact on the extinction, absorption, and scattering properties of thin films. The considerably reduced scattering from the nanocrystals compared to traditional phosphors, along with their inherent high quality white light emission, makes them a promising candidate for future solid state lighting applications.

15) Injectable, Biodegradable, Porous Polyurethane Scaffolds for Tissue Regeneration  
Andrea Hafeman—Department of Chemical Engineering

Numerous synthetic and biological scaffolds show promise for tissue regeneration, but few are injectable, which could facilitate minimally invasive surgical procedures and allow customization. We have developed porous, injectable polyurethane scaffolds that support cellular infiltration, new tissue formation, and degrade to non-cytotoxic products. Their elastomeric, resilient mechanical properties may promote thorough contact with wound boundaries. These biodegradable, tunable PUR materials demonstrate potential as a template for both skin and bone regeneration. Scaffolds were synthesized by syringe-mixing of LTI-PEG prepolymer and polyester polyol-based hardener. Hyaluronic acid (HA) was added to absorb excess moisture in the wound area. Mechanical properties were ascertained by dynamic mechanical analysis. The scaffolds were applied into excisional dermal wounds and femoral plug defects, both in male Sprague-Dawley rats. Dermal histology showed rapid material biodegradation resulting with mononuclear cell infiltration in early granulation tissue by day 4. Collagen deposition and new tissue organization proceeded by day 11 with material remnants engulfed by giant cells. Mature granulation tissue was visible by day 18, accompanied by evidence of folliculogenesis in the neoepidermis, which might suggest regeneration and limited scarring. Bone histology shows the porous PUR structure and thorough adhesion of the material to the surrounding bone, as well as immediate infiltration of blood into the scaffold pores. MicroCT images at 2, 4, & 6 weeks show new bone formation and scaffold degradation. In addition to providing a template for tissue regeneration, biologicals (growth factors, antibiotics, and drugs) also may be incorporated in the scaffolds to enhance healing.

16) Triadin deletion Alters Calcium Sparks in Murine Cardiomyocytes  
Fredrick Hilliard—Department of Biomedical Engineering and Department of Clinical Pharmacology

Gene-targeted deletion of the sarcoplasmic reticulum (SR) protein triadin (Trdn<sup>-/-</sup>) causes a 50% reduction in ryanodine receptor (RyR2) Ca<sup>2+</sup> release channels, cardiac calsequestrin and t-tubule SR junctions in mouse heart muscle. Here we report on the Ca<sup>2+</sup> spark properties of Trdn<sup>-/-</sup> cardiomyocytes. Isolated ventricular myocytes from Trdn<sup>-/-</sup> mice (N=5) and wild-type littermates (Trdn<sup>+/+</sup>, N=8) were loaded with the Ca-sensitive fluorescent indicator Fluo4-AM and Ca<sup>2+</sup> sparks were measured by confocal microscopy in line scan mode. As illustrated in the figure, triadin deletion caused a dramatic reduction in spark amplitude ( $\Delta(F/F_0)$ ), spark width (FWHM) and spark upstroke velocity ( $\Delta(F/F_0)/\Delta t_{max}$ ), whereas spark frequency was modestly increased:  $\Delta(F/F_0)$ : Trdn<sup>-/-</sup>  $0.43 \pm 0.01$ , n=893; Trdn<sup>+/+</sup>  $0.61 \pm 0.02$ , n=745, p<7.27E-22; FWHM(μm): Trdn<sup>-/-</sup>  $2.64 \pm 0.03$ , n=893, Trdn<sup>+/+</sup>  $2.90 \pm 0.03$ , n=745, p<1.77E-09,  $\Delta(F/F_0)/\Delta t_{max}(\Delta(F/F_0)/s)$ : Trdn<sup>-/-</sup>  $31.67 \pm 0.90$ , n=891, Trdn<sup>+/+</sup>  $58.35 \pm 1.62$ , n=741, p<3.49E-48 and spark frequency(sparks/100μm/s): Trdn<sup>-/-</sup>  $0.92 \pm 0.08$ , n=255 myocytes, Trdn<sup>+/+</sup>  $0.71 \pm 0.06$ , n=321 myocytes, p<0.03. The changes in spark properties occurred in absence of significant changes in SR Ca<sup>2+</sup> content measured by rapid caffeine application. These data suggest that loss of triadin has a drastic effect on spark properties, possibly by altering the number of RyR2 and/or the RyR2 cluster size.

17) G-protein mediated regulation of  $I_{Ca}$  and catecholamine release in adrenal chromaffin cells  
Mark Jewell—Department of Pharmacology

G-protein coupled receptors play important roles in controlling neurotransmitter and hormone release. In chromaffin cells ATP, DAMGO, and PGE<sub>2</sub> activate P2Y purinergic, μ-opioid and EP receptors respectively to produce G $\beta\gamma$  mediated inhibition of voltage-gated Ca<sup>2+</sup> channel currents ( $I_{Ca}$ ).  $I_{Ca}$  and exocytosis (monitored with membrane capacitance) stimulated with a relatively short step depolarization are reduced in parallel. However, we recently showed that in addition to causing voltage-dependent inhibition of  $I_{Ca}$ , G $\beta\gamma$  also reduced the inactivation of recombinant N-type  $I_{Ca}$  during sustained 5Hz trains of action potential-like waveforms (APW). Thus, after ~8s of stimulation, Ca<sup>2+</sup> entry triggered by each APW was identical in the absence or presence of ATP (McDavid & Currie, J Neurosci 2006: 26, 13373-83). To investigate this we stimulated adrenal chromaffin cells with sustained trains of APW and monitored  $I_{Ca}$  and secretion with carbon fiber

amperometry. Under control conditions there was little inactivation of  $I_{Ca}$  during trains of APW applied at 0.5Hz or 1Hz for 5 mins. When the train was repeated in the presence of ATP the amplitude of  $I_{Ca}$  was reduced by ~40-50% and again there was no decline in current amplitude with time. Consequently, there was significantly less Ca<sup>2+</sup> entry during the train and the number of amperometric spikes elicited by the train was significantly reduced. In contrast, under control conditions a 5Hz or 15Hz APW train lasting 90s produced rapid inactivation (~50%) of  $I_{Ca}$  in the first 5-10s followed by a stable plateau for the remaining 80s of stimulation. The initial amplitude of  $I_{Ca}$  was reduced (~40%) by ATP but so was the inactivation during the first 10s. The stable plateau amplitude of  $I_{Ca}$  that was reached after the first 10s was identical to that in control conditions. Washout of ATP returned the amplitude and kinetics of  $I_{Ca}$  to control levels. The total number of amperometric spikes was not reduced by ATP in cells stimulated at 5Hz or 15Hz. At 5Hz stimulation there was a small decrease in the number of spikes elicited during the first 10s of stimulation but this was not seen at 15Hz. In another approach we stimulated cells by sustained (5min) bath application of 60mM KCl. Cells exposed to ATP showed no significant decrease in the number of amperometric spikes. In contrast, application of DAMGO significantly reduced the number of spikes. Our data suggest that G $\beta\gamma$ -mediated modulation of calcium channels is ineffective at reducing secretion during prolonged trains of APW at frequencies >5Hz.  $\mu$ -opioid receptors might act by an additional pathway(s) to reduce secretion independently from modulation of calcium entry.

18) Characterization and antiparkinsonian effects of novel positive allosteric modulators of mGluR4  
Kari Johnson—Department of Pharmacology

Activation of metabotropic glutamate receptor subtype 4 (mGluR4) has recently been implicated as a therapeutic strategy for treating Parkinsonâ€™s disease (PD). Unfortunately, highly selective and efficacious pharmacological tools to study the therapeutic potential of mGluR4 activation have been difficult to develop. Due to the high level of conservation of the glutamate-binding site among the mGluR subtypes, developing subtype-selective orthosteric agonists has not been feasible. However, positive allosteric modulators (PAMs) may have more potential for subtype selectivity because they act on less conserved regions of the receptor. To date, only one commonly used mGluR4 PAM, (-)-PHCCC, has been reported. Unfortunately, poor potency and physical properties of this compound have limited its use as a tool for evaluating the physiological roles and therapeutic potential of mGluR4. In addition, attempts to modify the structure of (-)-PHCCC in order to improve its pharmacological and physical properties have been unsuccessful. In order to identify novel selective PAMs of mGluR4, we performed a high-throughput screen. Here we report the identification and characterization of a novel class of PAMs of mGluR4. Structure-activity relationship analysis revealed a range of potencies and efficacies as well as stereochemistry preferences. Importantly, active compounds in this structural class are selective among all tested mGluRs. Excitingly, intracerebroventricular (icv) administration of the best compound in this series reverses akinetic deficits in preclinical models of Parkinsonâ€™s disease. We anticipate that these compounds will be useful tools for evaluating the physiological roles of mGluR4 in the CNS, as well as novel therapeutic indications for mGluR4 PAMs.

19) Updating objects in visual short-term memory  
Philip Ko—Department of Psychology

The purpose of this study was to examine whether the process of updating information in visual short-term memory (VSTM) is object-based. We investigated whether modifying the memory of one feature of an object would automatically promote refreshing the memory of all its other features. The results showed that the facilitative effect of updating was specific to the updated feature of an object, and did not spread to its non-updated features. This feature-selective effect suggests that updating VSTM is not object-based (Experiment 1), even though storage was object-based (Experiment 2). Control experiments ruled out strategy (Experiment 3) and stimulus-related (Experiment 4) accounts. Feature-selective updating may indicate that the mechanism used to modify the contents of memory may have a different basis than that used to encode or store information in memory.

**20) IDPicker 2.0: Improved Protein Assembly with High Discrimination Peptide Identification Filtering**  
Zeqiang Ma—Department of Biomedical Informatics

Tandem mass spectrometry-based shotgun proteomics has become a widespread technology for analyzing complex protein mixtures. A number of database searching algorithms have been developed to assign peptide sequences to tandem mass spectra. Assembling the peptide identifications to proteins, however, is a challenging issue because many peptides are shared by multiple proteins. IDPicker is an open-source protein assembly tool that derives a minimum protein list from peptide identifications filtered to a specified False Discovery Rate. Here we update IDPicker to increase confident peptide identifications by combining multiple scores produced by database search tools. By segregating peptide identifications on both charge state and the number of tryptic termini in validation, IDPicker yields more confident identifications for protein assembly. The new version achieves higher accuracy by requiring additional novel peptides in the parsimony process, especially when searching against multiple-species databases. IDPicker has been tuned for incorporation in many identification workflows by the addition of a graphical user interface and the ability to read identifications from the pepXML format. These advances position IDPicker for high peptide discrimination, reliable protein assembly, and highly-scalable proteomics studies.

**21) Gene expression correlates of spontaneous physical activity and BMI in the motor cortex and striatum**  
Amanda Mitchell—Department of Neuroscience

A growing body of evidence suggests that physical activity is neuroprotective, slowing the progression of many neurodegenerative conditions, including Parkinsonâ€™s disease, Alzheimerâ€™s disease, and Huntingtonâ€™s disorder. Numerous studies also associate the modern sedentary lifestyle with increased risks for obesity, cardiovascular diseases, type 2 diabetes, cancer, and depression. Rodent models have been used to assess which genetic pathways contribute to neuroprotection and a sedentary lifestyle. We are using a Rhesus monkey (*M. mulatta*) model to explore gene expression correlates of spontaneous activity, forced exercise, and forced exercise following a 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) lesion mimicking Parkinsonâ€™s disease. In this study gene expression correlates of spontaneous physical activity and body mass index (BMI) in the motor cortex and striatum of 14 spontaneously active and sedentary Rhesus monkeys were investigated using transcriptome profiling by DNA microarrays and qPCR. The different gene signatures in the motor cortex and striatum suggest that spontaneous activity and BMI trigger distinct physiological processes across brain areas, which may be mediated via the Akt signaling pathway.

**22) Fabrication and Optical Applications of Nanostructured Vanadium Dioxide**  
**Joyeeta Nag**, Davon W. Ferrara, Eugene U. Donev, Jae Y. Suh, Leonard C. Feldman, Richard F. Haglund, Jr. Department of Physics and Vanderbilt Institute of Nanoscale Science and Engineering, Vanderbilt University and Andrew E. Payzant and Karren L. More, CNMS and SHaRE Facilities, Oak Ridge National Laboratory

Vanadium dioxide (VO<sub>2</sub>) is a functional oxide that exhibits a metal-insulator transition near 67 degree C, accompanied by huge changes in its electrical resistivity and near-infrared transmission. This characteristic makes vanadium dioxide a â€œsmart materialâ€, suitable for a wide variety of applications including optical switching, limiting, thermal energy management, solar cells and smart window coatings, and many others. Vanadium dioxide is also of great interest in condensed-matter physics because it is a classic strongly correlated electron system. In this poster, we discuss the fabrication of vanadium dioxide thin films and nanoparticles by pulsed laser deposition, with special emphasis on epitaxial film growth on sapphire substrates. Using the metal-insulator transition of vanadium dioxide we also demonstrate a plasmonic switch, i.e., the modification of the plasmonic response of gold nanoparticles covered with a thin film of vanadium dioxide. Another interesting optical phenomenon – extra-ordinary transmission of light through subwavelength hole arrays in vanadium dioxide – will also be presented.

**23) Does Understanding of Social Cues Affect Toddlersâ€™ Ability to Learn From People on Video?**  
Kate O'Doherty—Department: Psychology

We examined toddlersâ€™ word learning in four contexts: live addressed- adult spoke directly to the child; live onlooker – adult spoke to another adult as child looked on; video addressed - adult on pre-recorded video spoke directly to camera; video onlooker- adult spoke to another adult on pre-recorded video. Based on

previous research, we expected toddlers in live contexts to learn a new word whereas toddlers in video addressed would not. We believe toddlers have difficulty learning from people on video because social expectations (e.g., contingent interaction) are missing. In video onlooker expected social cues are in place between adults (just not directed at the child), thus we hypothesized that children would learn from watching two adults on television. Results indicate that participants ( $N=75$ , mean =29.5 mos.) learned from observing an adult address another person, whether the two were present or on video. Toddlers did not learn from a speaker (present or on video) who directly addressed them but did not contingently interact with them. We suspected children in the live addressed context expected to interact with the speaker (e.g., handle the object being labeled) and were frustrated. We ran a modified live addressed in which the adult handed the child the labeled object and those children learned. We think these toddlers learned because social expectations were met, not because they handled the toy (children did not handle the toy in onlooker conditions and yet learned.)

24) Speech recognition and subjective ratings with wireless speech transmission via hearing aids  
Erin Picou—Department of Hearing & Speech Sciences

The efficacy of wireless transmission as a potential solution for problematic telephone listening was investigated with people who wear hearing aids. Participants were 20 adults fitted with receiver-in-the-canal hearing aids, using either non-occluding or occluding eartips. Speech recognition scores and subjective ratings were tested in a noisy environment with six wireless speech transmission conditions and one acoustic telephone condition. In the wireless conditions, speech was transmitted to both ears simultaneously (diotic speech) or to only one ear (monotic speech). Diotic speech transmission allowed for significantly better speech recognition than monotic wireless transmission. Diotic and monotic wireless conditions resulted in significantly better speech recognition than the acoustic telephone condition for participants fitted with occluding domes only. Pattern of results for subjective measures was similar to speech recognition measures. The benefits of this technology may be limited to hearing aid fittings that have limited venting.

25) Bone Marrow Derived Cells Incorporate in the Prostate During Regrowth Following Castration  
Veronica Placencio—Department of Cancer Biology

It is necessary to understand mechanisms of androgen independent prostate cancer development and progression. We hypothesized that enhanced chemokine signaling results in the recruitment of immune cells to the prostate microenvironment from the bone marrow. We developed a chimeric mouse model with GFP-labeled bone marrow to allow us to identify bone marrow cells recruited to the prostate. We studied how bone marrow derived cells (BMDCs) contributed to an androgen refractory response, specifically prostate regrowth. Host mice were castrated or left intact as a control. Chimeric mice were generated by introducing GFP-labeled fetal liver cells. After the bone marrow was reconstituted with the GFP-labeled cells we gave exogenous testosterone to the chimeric mice. The non-castrated and castrated control mice had a low number of BMDCs recruited to the prostate. However, three and seven days following testosterone-induced regrowth of the prostate resulted in a dramatic increase in BMDC recruitment. Immunohistochemistry staining for F4/80 suggested some of these BMDCs were macrophage. However, four weeks after induced prostate re-growth, a number of GFP-labeled BMDCs appeared to be incorporated in the epithelial compartment of the prostate. Double immunofluorescence staining illustrated that a subset of BMDCs also expressed p63, a basal cell marker in the prostate. The transient recruitment and eventual incorporation of BMDCs was coincident with prostate regrowth to suggest a new cell population associated with androgen refractory prostate cancer growth.

26) Immune Defenses of *Xenopus laevis* Against a Fungus Linked to Global Amphibian Declines  
Jeremy Ramsey—Department of Microbiology & Immunology

Many amphibian species have suffered unprecedented population declines in the last four decades. Patterns of declines suggest one or more emerging pathogens that are spreading globally, including a skin-invasive chytrid fungus, *Batrachochytrium dendrobatidis*, linked to declines in Australia, Central America, the western U.S., Europe, and Africa. Little is known about amphibian innate and adaptive immune defenses against this skin pathogen. Here we show that antimicrobial peptides secreted onto the skin of *Xenopus laevis* are able to inhibit *B. dendrobatidis* growth in vitro, protecting frogs from *B. dendrobatidis* colonization. We examined relative amounts of antimicrobial peptides secreted by *X. laevis* under resting conditions, after activity simulating a predator attack, and after norepinephrine stimulation of granular gland discharge. These

amounts were within the concentrations required to inhibit *B. dendrobatidis* growth in vitro. The amount of time necessary to recover peptides to initial levels after secretion was also studied. In *X. laevis*, a species resistant to *B. dendrobatidis*, peptide depletion and/or X-irradiation increased susceptibility to *B. dendrobatidis* after exposure as shown by an increased percentage of individuals infected, higher fungal loads in the skin, and decreases in weight. Immunization of *X. laevis* against *B. dendrobatidis* resulted in a strong IgM and IgY antibody response in vivo. Exposure of a susceptible species, *Bufo boreas*, after immunization resulted in high mortality demonstrating that the resulting systemic response was not protective. However, if *B. boreas* were able to stay dry after exposure, mortality was reduced, suggesting the development of an adaptive immune response.

**27) Structure of DNA glycosylase AlkD reveals a new architecture for locating and excising alkylpurines**  
Emily Rubinson—Department of Chemical and Physical Biology (CPB)

DNA glycosylases safeguard the genome by locating and excising chemically modified bases from DNA. AlkD is a recently discovered bacterial DNA glycosylase specific for positively charged alkylpurine nucleobases 3-methyladenine and 7-methylguanine. The crystal structure of *Bacillus cereus* AlkD revealed that the protein is composed exclusively of helical HEAT-like repeats, which form a solenoid perfectly shaped to accommodate an undistorted DNA duplex on the concave surface. Structural analysis of the variant HEAT repeats in AlkD provides a rationale for how this protein scaffolding motif has been modified to bind DNA. Comparison of AlkD to existing DNA glycosylase structures, along with mutational studies of 7mG excision and DNA binding activities, provides important insight into the requirements for alkylation repair within DNA. We suggest that AlkD utilizes a novel strategy to manipulate DNA in its search for alkylpurine bases.

**28) Toward a General Active Cannula Model**  
Caleb Rucker—Department of Mechanical Engineering

Active cannulas are meso-scale continuum robots, enabling dexterity in diameters from hundreds of microns to tens of centimeters. Constructed from telescoping, concentric, precurved, superelastic tubes, they exhibit "Coetenatacle-like" dexterity with a form factor similar to a needle, making them well-suited for applications in minimally invasive surgery. Such applications are facilitated by an accurate kinematic model. The accuracy of prior models has been limited by the assumption of infinite torsional rigidity beyond initial straight transmissions. This poster presents a model which considers both bending and torsion, describing the total elastic energy stored in two curved concentric tubes. We determine the shape of the active cannula that minimizes the stored energy via variational calculus. Experiments demonstrate that this framework can be used predict the shape of a 3-link active cannula more accurately than previous models, reducing tip error by 72% over a bending-only model, and 35% over a model that includes only transmisional torsion. An implication of our work is that the general shape of an active cannula is not piecewise constant curvature (as basic assumptions of previous models have implied), but rather a general shape which under certain conditions closely approximates piecewise constant curvature.

**29) Visual attention in deaf, unilaterally hearing-impaired and hearing adults**  
Hollea Ryan—Department of Hearing and Speech Sciences

It is well known that early deficits in one sensory system can influence changes in another sensory system. The Eriksen Flanker Task was used to measure the visual attention abilities of normal hearing (NH), unilaterally hearing-impaired (UHL), and Deaf adults. Participants viewed a centrally-located target letter flanked by same (compatible) or different (incompatible) letters on a computer monitor. The letters N and H served as both targets and flankers. Flankers were spaced at varying degrees of eccentricity from the target. Participants quickly pressed a button to indicate if the target was H or N and reaction times were recorded. Typically, reaction times are longer in incompatible conditions and when incompatible flankers have a small degree of separation from the target. This lengthening of the reaction times because of flankers influence is known as the flanker compatibility effect. Both the UHL and Deaf groups demonstrated a flanker compatibility effect at farther eccentricities than did the NH group. These results will be discussed in terms of possible contributing experimental factors.

30) Type III Transforming Growth Factor- $\beta^2$  Receptor regulates proliferation and apoptosis in epicardial c  
Nora Sanchez—Department of Pharmacology

Epicardial cells transform into the myocardium and form coronary vessels. The Type III Transforming Growth Factor- $\beta^2$  Receptor (Tgfbr3) is required for coronary vessel development. Tgfbr3 $^{-/-}$  embryos have an irregular epicardium, few coronary vessels, and die at E14.5. To explore TGF $\beta^2$ R3 signaling we made immortalized epicardial cell lines from E11.5 embryos. Tgfbr3 $^{+/+}$ ,  $^{+/-}$ , and  $^{-/-}$  cells form a tight epithelium. TGF $\beta^2$ 1 or TGF $\beta^2$ 2 (250 pM) caused transformation and induced the smooth muscle marker, SM22 $\alpha$ . Circular wounds were made in cell monolayers and the percent wound closure calculated. Tgfbr3 $^{+/+}$  and  $^{+/-}$  cells closed the wound by 48h. Tgfbr3 $^{-/-}$  cells required 72h ( $p<0.05$ ). Tgfbr3 $^{+/+}$  and  $^{+/-}$  cells gave similar proliferation rates when measured by BrdU, peaking at 48h (33.1% and 33.93%) and returning to basal levels (19.9% and 20.85%) by 72h. Tgfbr3 $^{-/-}$  cells sustained a basal proliferation rate 13% lower at 48h ( $p=0.001$ ). As a second measure of proliferation, we used the in vivo reduction of MTS tetrazolium. Tgfbr3 $^{-/-}$  cells had a rate of proliferation 2-fold lower at 48h and 2.6 fold lower at 72h ( $p<0.05$ ). Apoptosis was determined by Apo-One Caspase 3/7 Homogenous assay. The apoptosis rate in Tgfbr3 $^{-/-}$  cells was 1.8, 3.3 and 5.9- fold higher than Tgfbr3 $^{+/+}$  cells at 24, 48, 72h, respectively ( $p<0.05$ ). In summary, TGF $\beta^2$ R3 is not required for transformation in epicardial cells, but does regulate proliferation and apoptosis.

31) Multi-Resolution Comparison of Single-Shot EPI, 3DFFE, and PRESTO for fMRI at 7T  
John Sexton—Department of Biomedical Engineering

Single-shot Echo-Planar Imaging (EPI) is the sequence most commonly used for fMRI experiments. At high field, magnetic field inhomogeneities cause spins to become out of phase quickly, and distortion and signal dropout become severe. Consequently, single-shot EPI fMRI suffers technical limitations at high field. Here we consider two alternatives to EPI for high field fMRI: 3D Fast Field Echo (FFE), a multi-shot EPI sequence, and 3D PRESTO (Principles of Echo-Shifting with a Train of Observations), a 3D sequence that uses echo-shifting to achieve efficient T<sub>2</sub>\* weighting.

Seven healthy adult subjects were scanned on a Philips Achieva 7T scanner with a 16 channel SENSE receive-only head coil with an outer quadrature transmit coil at four different resolutions. Subjects were presented with a flashing checkerboard wedge (8Hz) which occupied 30 degrees of the left visual field. Subjects were instructed to ignore the wedge and to press a button with their right index finger when a small dot appeared in the center of their visual field.

While the activation maps produced by both EPI and 3DFFE/PRESTO were similar, single-shot EPI produced larger numbers of activated voxels and more highly significant activations than 3DFFE in our high-resolution, limited field-of-view ( $\approx 1.75\text{mm}^3$ ) fMRI trials. The opposite was true for low resolution, full-brain fMRI. These results demonstrate that 3DFFE and PRESTO are strong candidates for high field fMRI applications at a variety of resolutions, and that in some cases these sequences appear more sensitive to fMRI activation than single-shot EPI.

32) Effects of Sensitivity Encoding and Physiological Noise on Temporal Signal Stability and fMRI at 7T  
John Sexton—Department of Biomedical Engineering

High field MRI scanners show increased signal-to-noise ratio (SNR) of MR images and increased contrast from blood oxygen level dependent (BOLD) effects in functional MRI (fMRI) relative to lower field scanners. However, increasing Bo also increases magnetic field inhomogeneities, signal dropout, image distortion, and physiological noise effects in single-shot echo-planar fMRI. Parallel imaging techniques such as Sensitivity Encoding (SENSE) can reduce these effects, but also incur SNR penalties. Here we examine the effects of parallel imaging on a) the relative contributions of physiological noise to the total noise of an fMRI time series, b) fMRI sensitivity, and c) the temporal signal-to-noise ratio (TSNR) of the time series at 7T.

Ten healthy volunteers were scanned on a Philips Achieva 7T scanner with a 16 channel SENSE receive-only head coil with an outer quadrature transmit coil. Subjects were presented with a flashing checkerboard (8Hz) [on 24s, off 24s] in four blocks. Each run was 192 seconds. Acquisition parameters: single-shot echo planar imaging at  $1\times 1\times 2\text{mm}^3$ ; TR = 2s; TE = 25ms; FOV = 192mm<sup>2</sup>; Slices = 9; Images per run = 96; Partial Fourier factor H = 0.6; R = 1 through 8.

Our results show that the relative contributions of respiratory noise decrease significantly as R increases. This suggests that it may be possible to reduce or eliminate the contributions of physiological noise to fMRI

data by acquiring a time series with a sufficiently high reduction factor. Parallel imaging coils with more elements may yield significant benefits for high field EPI fMRI.

33) MDs on the move: The ecological and psycho-political validity of the African medical brain drain  
Benjamin Siankam—Department of Human and Organizational Development

While the problem of the African medical brain drain is increasingly reported in the literature, few studies have provided migrants an opportunity to tell their stories, or have explored the process of migration at different stages. To broaden our understanding of skilled migration in sub-Saharan Africa (SSA), this study will observe different groups of physicians and medical students at three distinct stages of the migration process: pre-migration; immigration; and return migration. A heterogeneous sample including African physicians currently living and working in the USA and Canada, African medical students enrolled in medical schools in their home countries, and African physicians formerly living and working overseas will be interviewed. Aspirations, expectations, experiences, patterns, adaptive and disruptive migratory processes will be explored through in-depth interviews. Participants will be recruited from five countries representing four geographical regions of the subcontinent: Central (Cameroon), East (Ethiopia), Southern (South Africa), and West Africa (Ghana and Senegal). This study is currently in its initial stage and will be implemented in fulfilment of my dissertation requirement. It is anticipated that findings from this study will increase our understanding of some of the underlying dynamics and processes of skilled migration in SSA, inform migration policy, and help devise strategies that can insulate vulnerable communities from the worst effects of brain drain.

34) Quantitative or Qualitative Differences with DIMCAT, Applied to Differences in Successful Intelligence  
Stijn Smeets—Department of Psychology and Human Development

In this paper we used the Dimension vs. Category Framework (DIMCAT; De Boeck, Wilson, & Acton, 2005) to investigate whether there are qualitative or quantitative differences in successful intelligence (Sternberg, 1993), that can be interpreted as referring to giftedness. In DIMCAT, qualitative and quantitative differences are defined as follows. If one latent dimension suffices to describe the heterogeneity within categories, then we have qualitative differences when the latent dimension differs for members of different categories. Dimensions are anchored in indicators, and they differ from one another if the discriminations or locations of the indicators are different. We have quantitative differences if the latent dimension is the same for members of different categories (indicators have the same locations and discriminations) and the distribution of one category is located at a lower level than is the distribution of the other category on the same dimension. We applied this model to scores of 2712 finish students (aged 12 or 13) on the Sternberg Triarchic Ability Test (STAT; Sternberg, 1993), a test for successful intelligence. We found a small group that on average scored higher and differed qualitatively on creative-numeric items from the majority group. We found unambiguous differences in the discriminations of these items, that were systematically higher in the small group. This means that members of this group use another skill to solve these items. The higher discriminations and the larger variance show that not every member of the smaller group uses this skill equally effectively.

35) Separation and Reproducibility of Touch Activations in Areas 3b and 1 within the Primary Somatosensory  
Elizabeth Ann Stringer—Department of Neuroscience

The primary somatosensory (S1) cortex is the principal neural region for processing touch sensation, comprising four distinct cytoarchitectural regions each responsive to different stimuli. Nonhuman primate studies have shown topological organization of areas 3b and 1. Human imaging studies have lacked the spatial specificity to distinguish these functional and anatomical subdivisions within S1. The advent of ultra-high field fMRI (7T) provides greater sensitivity and increases spatial resolution, resulting in finer scale activity maps than at lower fields. Here, we test the feasibility of 7T fMRI to visualize somatotopy and functional activations along the cytoarchitectural subdivisions within S1.

**Methods:** Healthy human subjects were studied using a 7T Philips Achieva scanner. High spatial resolution functional images (1x1x2mm<sup>3</sup>) covering S1, S2, insula, and thalamus were acquired using GE-EPI. Innocuous tactile (2Hz air puffs) stimuli were delivered to the glabrous skin of alternating fingers in a 24s on/off design.

**Results:** Repeated trials within single subjects showed reproducible topological activations within areas 3b and 1 of S1. The mean digit separation between adjacent digits in areas 3b and 1 are 7.40mm and 5.28mm, respectively.

**Conclusion:** High-resolution EPI-BOLD fMRI at 7T can resolve fine-scale digit maps in areas 3b and 1 of the primary somatosensory cortex (S1) in individual subjects, reproducible across multiple runs. Our data showing larger digit separation in area 3b than in area 1 support nonhuman primate studies that have shown area 3b has a larger digit representation, also known as the cortical magnification factor, than area 1.

### 36) Getting a "Feel" for Dynamic Systems

Jenna Toennies—Department of Mechanical Engineering

Even with a good understanding of fundamental electromechanical theories, concepts associated with dynamic systems are difficult for engineering students to grasp when they lack physical interaction with a real system. In response to this, we revamped the laboratory associated with the System Dynamics class to enable students to construct, analyze, calibrate, program, and physically interact with a robotic haptic device called a haptic paddle. A haptic paddle, which can simulate a variety of dynamic systems, provides force feedback enabling students to feel forces generated by interactions in virtual reality environments on a computer screen. Although this project-based laboratory has successfully been implemented at other universities, student learning was difficult to assess due to open-ended questions and small class sizes. We have enhanced these studies by performing a rigorous assessment of student learning for 65 students in in-class lectures, labs, and in-lab instruction. To do this, we developed 25 conceptual multiple choice questions (5 questions per laboratory), that relate to the specific key concepts students should learn from the haptic paddle laboratories. The 25 questions were administered at the beginning of the semester to assess students' initial understanding, and the 5 relevant questions were administered at different times throughout the laboratory to measure the effectiveness of each learning component independently. A score increase from before lab to after lab suggests that each one was successful in teaching its conceptual learning objectives. This study will further quantify the effectiveness of haptic paddle laboratories and will be useful in revising subsequent labs.

### 37) Superhydrophobic films: Biomimicing water repellency

Juan Tuberquia—Department of Chemical and Biomolecular Engineering

Superhydrophobic, or self cleaning, films are surfaces that do not “like” to be wet by water. These surfaces are inspired in the wetting properties of biological structures, especially plant leaves such as those of the Lotus (*Nelumbo nucifera*), and insects wings such as those of the cicada (*Cicada orni*). In this study we develop a new surface polymerization strategy that yields a surface with the appropriate combination of roughness and low surface energy materials that makes superhydrophobic behavior possible. Superhydrophobic surfaces present potential applications for MEMS/NEMS, oil/water separations, anti-sticking, and cleaning applications.

Polymethylene films were synthesized over gold surfaces through a surface initiated polyhomologation. These surfaces have advancing water contact angles of  $167^{\circ}$  with a low water roll-off angle and a hysteresis of  $2^{\circ}$ ; all which demonstrate the characteristics of a superhydrophobic surface. This novel polymerization strategy only requires the immersion of the sample in different solutions, which represents an appreciable advantage when compared to other nanotechnologic fabrication methods of these surfaces including casting, sputtering, etching, photolithography, and deposition methods.

### 38) Cervical Cancer Detection with Raman Spectroscopy

Elizabeth Vargis—Department of Biomedical Engineering

Cervical cancer is the second most common malignancy among women worldwide with over 490,000 cases diagnosed and 274,000 deaths each year. When cervical cancers are detected early, they are highly curable. In fact, early detection of cervical pre-cancers using Pap smears and coloscopies has played a central role in reducing the mortality associated with this disease in the US over the last 50 years. However, this trend is not observed in countries such as Zambia where the mortality and prevalence rate of invasive cervical cancer is the second highest in the world. An automated diagnostic method with sufficient sensitivity and specificity that could allow for a “See and Treat” protocol would significantly improve the management of the cervical cancer in developing countries. We have developed an instrument that can acquire Raman spectra from the cervix, as well as a sophisticated algorithm to classify tissue as normal (benign or inflammatory), squamous metaplasia, low-grade dysplasia, and high-grade dysplasia. Our results show that high-grade spectra classified correctly 95% of the time and low-grade spectra classified correctly 74% of the time with a sensitivity of 98% and a

specificity of 96%. This tool will greatly impact areas where professional care is difficult to achieve. Currently, our focus is to obtain data from a more diverse population at Nashville General Hospital to ensure our design is applicable for all patients.

39) The lupus susceptibility locus Sle3 is not sufficient to accelerate atherosclerosis in LDLr<sup>-/-</sup> mice  
Nekeithia Wade—Department of Pathology

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by the presence of autoantibodies. Patients with SLE have an increased risk for developing premature cardiovascular disease. It is thought that immune dysregulation plays a role in the acceleration of atherosclerosis in SLE. However, the link between the two diseases has not been studied extensively. Understanding the mechanisms of SLE-accelerated atherosclerosis is critical for the development of effective therapeutics to treat both cardiovascular disease and SLE.

Our laboratory previously demonstrated that radiation chimeras of SLE-susceptible B6.Sle1.2.3 and low density lipoprotein receptor (LDLr)<sup>-/-</sup> mice have augmented atherosclerosis, which is associated with increased T cell burden and activation in the lesion. Because we observed a significant increase in T cell infiltration in the lesions of LDLr.Sle1.2.3 mice, we examined if the single lupus susceptibility locus Sle3, which is associated with T cell dysregulation, was sufficient to accelerate atherosclerosis.

We transferred B6.Sle3 or C57Bl/6-derived bone marrow cells into irradiated LDLr<sup>-/-</sup> mice. Sixteen weeks after transplantation, the mice were placed on a Western-type diet for 8 weeks. Our analyses revealed that transfer of the Sle3 bone marrow to LDLr<sup>-/-</sup> mice is sufficient to affect serum cholesterol and exacerbate humoral immune responses that are frequently associated with atherosclerosis. However, in our model, this does not result in enhanced atherosclerosis. We conclude that T cell dysregulation alone cannot accelerate atherosclerosis and that Sle3 in combination with other lupus susceptibility loci may be necessary to mediate changes in atherosclerosis development.

40) ATF4 regulates chondrocyte proliferation and differentiation during limb development by activating *Indian Hedgehog* transcription.

**Weiguang Wang**, Na Lian, Lingzhen Li, Florent Elefteriou and Xiangli Yang—Department of Pharmacology

Indian hedgehog (*Ihh*) is an indispensable regulator controlling the coordination of chondrogenesis and osteogenesis. Surprisingly, our understanding of the regulation of *Ihh* expression is limited. Here we show that ATF4, a leucine zipper-containing transcription factor in the CREB family, is expressed in chondrocytes and acts as a major transcriptional regulator of *Ihh*. *Atf4*-deficient (*Atf4*<sup>-/-</sup>) mice displayed dwarfism and their growth plate is characterized by decreased chondrocyte proliferation and expansion of hypertrophic chondrocyte zone. These structural abnormalities are accompanied by a marked decrease in expression of *Ihh*. Ectopic expression of ATF4 in chondrocytes increases endogenous expression of *Ihh* mRNA. Furthermore, ATF4 directly binds to the *Ihh* promoter and activates its transcription. Most importantly, reactivation of *Ihh*-signaling by purmorphamine in *Atf4*<sup>-/-</sup> limb cultures corrects the *Atf4*<sup>-/-</sup> chondrocyte proliferation and short limb phenotype. Together, this study identifies that ATF4 as a novel transcriptional regulator of chondrogenesis, which paces the growth of long bones by controlling growth plate chondrocyte proliferation and differentiation.

41) Mtgr1 is a tumor modifier in inflammatory carcinogenesis in the colon  
Caitlyn Whitten—Department of Cancer Biology

MTGR1 (Myeloid Translocation Gene, Related-1) is a member of a gene family originally identified as targets of chromosomal translocation in acute myeloid leukemia (AML). Recent work from our laboratory has shown that MTGR1 plays a role in intestinal differentiation, wound healing, and inflammation and that this, in part, occurs via MTG-mediated repression of TCF4. Given the role of MTG family members in hematopoietic malignancy, the ability of MTGR1 to modulate WNT signaling, and the fact that loss of MTGR1 results in sensitization to gut injury, we hypothesized that MTGR1 may influence tumorigenesis arising in an inflammatory background. The AOM/DSS model is a robust model for interrogating modifiers of intestinal carcinogenesis. 19 C57bl6 Mtgr1<sup>-/-</sup> and 22 WT mice were injected with 12 mg/kg AOM followed 5 days later with the first of four cycles of 4 days of 3% DSS ad lib, with each cycle separated by 16 days of recovery and animals sacrificed 1 month after the last cycle of DSS treatment. Two hours prior to sacrifice 16.5 ug/kg of BrdU was injected IP. At

necropsy colons were isolated and tumor burden, size and distribution scored. IHC for BrdU, beta-catenin, COX-2, and CD3 was performed. RNA was isolated and expression array analysis performed using the Affymetrix Mouse Gene 1.0 platform. Mtgr1<sup>-/-</sup> mice were protected from tumorigenesis with decreased tumor number (1.7 vs 7.5 polyps per colon, p<0.001), decreased multiplicity, and reduced surface area per lesion (27 vs 82 mm<sup>2</sup>, p=0.01). Mtgr1<sup>-/-</sup> tumors had similar proliferation, but significantly higher intra-tumoral apoptosis rates when compared to WT tumors, potentially explaining the difference in size and number (32 vs 13 TUNEL (+) cells/HPF, p<0.001). Panther analysis of mRNA expression array data from Mtgr1<sup>-/-</sup> vs WT tumor samples revealed significant upregulation of inflammatory networks and a decrease in WNT signaling networks in the Mtgr1<sup>-/-</sup> tumors (p<0.001). In support of these observations, beta-catenin IHC showed decreased nuclear beta-catenin and CD3+ IHC revealed increased T-cell infiltrate in Mtgr1<sup>-/-</sup> tumors (49.4 vs 13.6 CD3+ cells/hpf, p<0.001). MTGR1-specific TaqMan analysis of Origene TissueScan Cancer surveys revealed a trend towards increased expression in breast, colon, prostate and lung carcinoma. Surveying of matched colorectal cancer and normal tissue revealed heterogeneity in expression with 68% of samples showing increased Mtgr1 expression. These studies provide the first evidence that MTGR1 may function as a tumor promoter in intestinal carcinogenesis.

## **GSRS Participants indexed by Department and Departmental Participation 2009**

(% = # departmental participants/total # students enrolled in dept., Fall 2008), \*Poster presentation

### **School of Arts & Sciences**

#### Anthropology—6.7%

Gerson Levi-Mendes  
Mike Tidwell

#### Chemistry—1.8%

Steven Combs  
Sten Heinze

#### Economics—27.7%

Heng Chen  
Roger Crawford  
Yariv Fadlon  
Rosa Ferrer  
P.J. Glandon  
Valeska Groenert  
Zhengfeng Guo  
Sunghoon Hong  
Matthew Jaremski  
Suman Seth  
Katharine L. Shester  
Omolola Soumonni  
Caleb Stroup

#### English—7.7%

Amanda Hagood  
John Morrell  
Derrick Spires

#### French—20%

Rachel Early  
Lucas Faugere

#### History—3.9%

Selena Sanderfer  
Kevin Vanzant

#### Philosophy—4.4%

James Grady  
Charles Sentell

#### Physics & Astronomy—9.6%

Alicia Aarnio  
Katie Chynoweth  
Thompson Le Blanc  
Joyeeta Nag\*  
Timothy Pennycook  
Sonali Shukla  
William Teets

#### Psychology—5.6%

Phillip Ko\*  
Kate O'Doherty\*

### **Biomedical Sciences**

#### Biochemistry—4.8%

Chris Brosey  
Kyle Nordquist

#### Biomedical Informatics—4.8%

Zeqiang Ma\*

#### Cancer Biology—10%

Kimberly Boelte\*  
Natalina Elliott  
Xinyuan Lu  
Veronica Placencio\*  
Caitlyn Whitten\*

#### Cell and Developmental Biology—3%

Yang Liu  
Jonathan Lowery

#### Chemical and Physical Biology—12%

Gordon Lemmon  
Steffen Lindert  
Emily Rubinson\*

#### Hearing and Speech Sciences—25%

Kathryn Guillot  
Erin Picou\*  
Hollea Ryan\*  
Krystal Werfel

#### Microbiology and Immunology—23.7%

Johnna Allen  
Patrick Collins  
Joseph Conrad  
Indriati Hood  
Curtis Gabriel\*  
Mark Gadlage\*  
Laura Gordy\*  
Jeremy Ramsey\*  
Michelle Reniere

#### Molecular Physiology & Biophysics—8.1%

Dario Gutierrez  
Marquicia Pierce  
Bonni Surmi

#### Neuroscience—3.2%

Elizabeth Ann Stringer\*  
Amanda Mitchell\*

#### Nursing Science—14.3%

Jie Deng  
Jonathan Squiers

#### Pathology—23.8%

Maria Paula Alfaro\*  
Nicole Braun\*  
Charles Martinez III  
Laura Ooms  
Nekeithia Wade\*

#### Pharmacology—25.5%

Josh Barnett\*  
Thomas Bridges\*  
Molly Brown\*  
Whitney Cleghorn\*  
Bonnie Garcia\*  
Klarissa Hardy  
Kirsten Helmcke  
Mark Jewell\*  
Kari Johnson\*  
Nathan Mundell  
Timothy Panosian  
Nora Sanchez\*  
Mengnan Tian  
Weiguang Wang\*

#### Urologic Surgery

Lin Ge\*

### **Divinity School, Graduate Department of Religion—8%**

Timothy Eberhart  
Kate Lassiter  
Tamara Lewis  
Claire McKeever  
Chris Paris  
Brandon Simonson  
Linzie Treadway  
Natalie Wigg-Stevenson

### **Peabody College**

#### Teaching and Learning

Emily Bigelow  
Mikel Cole  
Christopher Keyes  
Nathan Phillips  
Kelly Puzio

#### Psychology & Human Dev.—1.8%

Stijn Smeets\*

### **School of Engineering**

#### Biomedical Engineering—10.2%

Charleson Bell\*  
Fredrick Hilliard\*  
Mary Loveless  
John Sexton\*  
Elizabeth Vargis\*

#### Chem. & Biomolecular Eng.—17.9%

Amanda Furtado\*  
Andrea Hafeman\*  
Jian Liu  
Benjamin Schmidt  
Juan Tuberquia\*

#### Mechanical Engineering—5.9%

Nicholas Roberts  
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