

# Research Briefs

## CORNELL-ITHACA AND WEILL CORNELL MEDICAL COLLEGE, A SYNERGY FOR ADVANCING THE CUTTING EDGE OF RESEARCH

### Brainstorming Cellular and Molecular Biophysics



**Barbara A. Baird, Chemistry and Chemical Biology, and Frederick R. Maxfield, Biochemistry, WCMC,** codirect the Keck Program in Cellular and Molecular Biophysics of Signal Transduction.



Established with seed funds by the W. M. Keck Foundation, WCMC, continues to fund the program's annual retreat that brings researchers from WCMC and Ithaca and others together to exchange research progress and ideas. David A. Holowka, Chemistry and Chemical Biology, and Anant K. Menon, Biochemistry, WCMC, co-organized the seventh annual retreat held in June 2007 in Ithaca. The theme was Biomembranes, and Scott D. Emr, director of the Weill Institute for Cell and Molecular Biology (ICBM) was the keynote speaker. This well-attended retreat, open to the Cornell community, featured 13 additional speakers, two poster sessions, and informal discussions. The interdisciplinary Keck program and these annual retreats have demonstrated success in facilitating communication and collaboration and will continue to be significant in bringing together researchers

across the two campuses. Current participants seek to expand the program to fund intercampus research activities as in the original Keck program.

### Watching Chemotactic Behavior



**Carl A. Batt, Food Science, and Thomas N. Sato, Cell and Developmental Biology, WCMC,** fabricate cantilevers



that will allow them to explore the reaction of bacteria to chemoattractants. The researchers' aim is to watch the process, in action, and characterize the response in one or more physical parameters. The study of chemotaxis in bacteria will add to the understanding of the way bacteria respond to their environment, which is critical to formation of biofilms and the means through which bacteria cause infection.

Batt also collaborates with Scott C. Blanchard, Physiology, WCMC, on the development of single molecule immobilization strategies that will help Blanchard follow protein translation. The translation of information from DNA to protein is at the core of how all living organisms function. Beyond basic

research, the effort will lead to the discovery of new drugs for the treatment of infections.

Batt works with Francis Barany, Microbiology and Immunology, WCMC, creating new nucleic acid-based sensors for the detection of pathogens. This work is leading to novel approaches for the design of instruments that will serve as diagnostic tools in the study of disease and help ensure the safety of foods.

Batt collaborates with Yao-Tseng Chen, Pathology, WCMC, developing immunotherapeutics for cancer treatment. The Cornell University-Ludwig Institute for Cancer Research Partnership has produced cancer vaccines that are based upon Chen's discoveries and these will go into human Phase I clinical trials in early 2008.

### The Patient Visit



**Franklin D. Becker, Design and Environmental Analysis, working with Nancy Farrell, Weill Physician's Organization, and Richard Thomas, Strategic Initiatives,** completed the initial stage of a study involving six outpatient practices at WCMC. The Ecology of the Patient Visit, in which

they found strong positive relationships between the physical attractiveness of outpatient practices and patients' perceived quality of care, including the reduction of reported anxiety and the quality of interaction with staff. The Center for Health Design is actively disseminating the research findings. Becker and the Weill Physician's Organization are currently in the final stages of a second phase of the research in which patients' and staff's attitudes and behavior following the move to the new Weill Greenberg Center are being examined. The study is designed to enhance the patient's experience.

### A Mycobacterium Tuberculosis Enzyme



**Tadhg P. Begley, Chemistry and Chemical Biology, and Luis E. N. Quadri, Microbiology and Immunology, WCMC,** study



Mycobacterium tuberculosis, the causative agent of tuberculosis. They are focusing on the enzyme MAS, which is involved in the biosynthesis of the lipid layer surrounding the bacterium. MAS is a multifunctional enzyme that assembles the mycocerosic acid component of the Mycobacterium tuberculosis immuno-modulatory

cell-envelop lipids called PDIMs and PGLs. These complex lipids are known effectors of mycobacterial virulence and their biosynthetic pathways are potential targets for the development of new anti-infectives against tuberculosis. Anti-tuberculosis drugs are becoming increasingly ineffective as multidrug resistant *Mycobacterium tuberculosis* strains continue to appear. Drugs that block PGL and PDIM production may find a therapeutic niche in the treatments against drug-resistant tuberculosis. The researchers are conducting mechanistic and structural studies that will lead to a better understanding of MAS functioning. In turn, this knowledge will provide information that will facilitate the rational design of drugs that block PDIM and PGL production.

### A Nanoscale Device to Explore Protein Synthesis



Scott C. Blanchard, *Physiology, WCMC*, in collaboration with Carl Batt, *Food Science*, conducts research on the fabrication of patterned, optically transparent surfaces for fluidic devices.



The research is done at the Cornell NanoScale Science and Technology Facility on the Ithaca campus.

### Brain Derived Neurotropic Factor (BDNF)



B. J. Casey, *Psychiatry, WCMC*, Andrew Clark, *Molecular Biology and Genetics*, and Jason Mezey and Carlos Bustamante, *Bioinformatics and Computational Biology*,



seek to understand the role of polymorphisms in BDNF and its effects on behavior and brain development. A common polymorphism in BDNF produces protein variants that have markedly different effects on neuron growth, both in tissue culture and in mice. This difference also

results in differences in anxiety behaviors. Casey recently recruited Clark, Mezey, and Bustamante to assist with the statistical modeling aspects of this ongoing project.

### Lung-Expressed Genes in Chronic Obstructive Pulmonary Disease



Patricia A. Cassano, *Nutritional Sciences*, and Ronald G. Crystal, *Medicine, WCMC*, established a new

collaboration to study the role of genetics



in chronic obstructive pulmonary disease (COPD). They will conduct a clinical intervention study to examine

the response of gene expression in lung-expressed genes to supplementation with antioxidant vitamins, connecting the interests of both research groups. The collaboration involves research fellow Michael O'Mahoney in Crystal's group, and graduate students Anne Agler and Amy Bentley in Cassano's group. If lung-expressed genes respond to antioxidant intervention, the case for dietary manipulations in either the prevention and the treatment of COPD would be strengthened. The project enhances understanding of causal mechanisms and ultimately may support personalized approaches to prevention and clinical care.

### TG-2 and Breast Cancer



Richard A. Cerione, *Molecular Medicine/Chemistry and Chemical Biology*, and Arthur J. Cooper, *Biochemistry*,

WCMC/Burke Research Institute, study the structure-function of a protein called TG-2 [tissue transglutaminase]. The idea is to find small molecule inhibitors of this family of proteins, transglutaminases. Various metastatic breast cancers over-express TG-2, and the researchers believe that this provides a double-edged sword by making it particularly difficult to kill the cancer cells with chemotherapeutic reagents [TG-2 provides a survival advantage to the cells under such conditions] and by increasing the migration and the ability of the cells to invade tissues. These activities are dependent on TG-2's enzymatic crosslinking activity. Cerione and Cooper are collaborating to screen for small molecule inhibitors that might block the enzymatic activity of TG-2 and thus provide a strategy for making breast cancer cells more susceptible to chemotherapeutic reagents and less able to invade and become metastatic. It also turns out that members of the transglutaminase family have been linked to the death of neuronal cells during neurodegenerative diseases, in particular Alzheimer's.

### Cardiac Electrical Dynamics



David J. Christini, *Medicine, WCMC*, and Robert F. Gilmour Jr., *Biomedical Sciences/Physiology*, study spatiotemporal control of cardiac



electrical dynamics. They are conducting animal experiments and computational modeling

to investigate therapeutic approaches that will prevent the initiation of lethal cardiac arrhythmias. They also have a project, MEMS Sensors for Arrhythmia Detection and Intervention, in which they are designing, fabricating, and testing microfabricated multielectrode arrays capable of recording cardiac electrical activity with high spatial resolution. Data obtained using these electrodes have provided key information regarding the cellular mechanisms responsible for the induction and maintenance of tachycardia and fibrillation.

### Biodegradable Materials for Therapeutic Use



Chih-Chang Chu, *Fiber Science and Apparel Design*, and Roger W. Yurt, *Surgery, WCMC*, collaborate on wound



management of burn victims. The dressings, biodegradable artificial skin that promotes healing in burn victims, are ready for testing on pig models. Yurt's group is preparing the animal study report.

Chu also collaborates with Bo Liu, *Surgery, WCMC*, on active absorbable vascular grafts. A doctoral thesis was completed on their work focusing on the non-viral gene transfer system. The researchers are preparing an NIH proposal based on the data obtained. Chu's work on clinical technology aims to advance and integrate new knowledge of biomaterials technology with the medical profession in order to bring research findings closer to clinical reality.

### The Genetic Basis for Variations in Risk of Diabetes, Obesity, and Other Diseases



Andrew Clark, *Molecular Biology and Genetics*, Daniel R. Alonso, *dean, WCMC-Qatar*, and David P. Hajjar, *executive vice dean, Graduate School, WCMC*,



are formulating a grand project to study the genetic basis for variation in

risk of diabetes, obesity, and other diseases, pending a grant from the Qatar Foundation. A cohort from the population would be genotyped at one million SNPs [single nucleotide polymorphisms], and genetic determinants of disease risk would be found by the method of association mapping.

### The Genetics of Infertility



Paula Cohen, Biomedical Sciences, Peter N. Schlegel, Urology, WCMC, and Darius A. Paduch, Urology, WCMC,



are principal investigators for the new Center for Reproductive Genomics. The center combines basic and clinical research in reproductive sciences on Cornell's Ithaca and WCMC campuses.



The center's focus is genetics of infertility with specific emphasis on meiosis, the cell division that results in recombination of genetic material, and the production of sperm in the male throughout life and eggs in the female fetus, which then develop over 20-plus years. The researchers have submitted a NIH proposal to help fund the center. The goal is to have about 100 faculty from both campuses as members who will explore male and female infertility. Members include Zev Rosenwaks, Center for Reproductive Medicine and Infertility, and John Schimenti, Center for Vertebrate Genomics.

### Bladder Cancer Detection



Harold G. Craighead, Applied and Engineering Physics, and Douglas S. Scherr, Urology, WCMC, study methods for the early diagnosis of bladder cancer. Craighead's lab works on miniaturized devices for analyzing biological materials and collaborates with Scherr, a bladder cancer expert, to study various approaches to the automated sorting of cells in a urine sample to identify cells that are abnormal and indicate the presence of cancer.



Craighead's lab works on miniaturized devices for analyzing biological materials and collaborates with Scherr, a bladder cancer expert, to study various approaches to the automated sorting of cells in a urine sample to identify cells that are abnormal and indicate the presence of cancer.

### Chronic Obstructive Pulmonary Disease (COPD) Risk



Ronald G. Crystal, Medicine, WCMC, Andrew Clark, Molecular Biology and Genetics, and Jason Mezey, Biostatistics and Computational Biology,



analyze expression microarrays and genome-wide single nucleotide polymorphisms in order to identify genetic variants that increase susceptibility to COPD. By sampling cells from the lung,



they have shown dramatic changes in gene expression caused by smoking and by COPD, and the magnitude of these changes varies among individuals. They hope to determine if these data can predict risk of disease as well.

### Mycobacterium Tuberculosis



Matthew DeLisa, Chemical and Biomolecular Engineering, and Dirk Schnappinger, Microbiology and Immunology, WCMC, seek to understand the contribution of a novel secretion system to the pathogenesis of Mycobacterium tuberculosis [Mtb]. They made the startling discovery that this pathway is essential to the viability of pathogenic mycobacteria. Therefore, a long-term goal is to develop novel inhibitors of Mtb by specifically targeting this pathway with small molecule drugs.



They made the startling discovery that this pathway is essential to the viability of pathogenic mycobacteria. Therefore, a long-term goal is to develop novel inhibitors of Mtb by specifically targeting this pathway with small molecule drugs.



DeLisa also works with Lorraine Gudas, Pharmacology, WCMC, on engineering antibodies that work inside of cells [most antibodies work outside of cells] to target factors that control the differentiation process in stem cells. They recently identified their first candidate antibodies, and these are being tested in the Gudas laboratory. With these recent breakthroughs, they are planning to write a joint NIH proposal.

DeLisa has an informal collaboration with Scott C. Blanchard, Physiology, WCMC, which focuses on engineering bacterial ribosomes. DeLisa's laboratory is using a technique known as laboratory evolution to create ribosomes that efficiently synthesize protein therapeutics, while Blanchard's laboratory is developing powerful single-molecule fluorescence techniques for characterizing these novel ribosomes.

### Looking for Targets for Drug Development



Steven E. Ealick, Chemistry and Chemical Biology, and Hao Wu, Biochemistry, WCMC, develop methods for applying synchrotron radiation to challenging protein crystallography problems. State-of-the-art facilities are under development at the Advanced Photon Source and include high intensity x-ray beamlines, microdiffraction, and robotic sample changers.

State-of-the-art facilities are under development at the Advanced Photon Source and include high intensity x-ray beamlines, microdiffraction, and robotic sample changers.

Ealick also collaborates with Anthony A. Sauve, Pharmacology, WCMC, to study the structure, function, and inhibitor design for nicotinamidase, an enzyme target for drug development. Their goal is to use x-ray crystallography and biochemical studies to develop novel antimicrobial agents with potential application to a wide variety of human diseases.

### Developmental Cognitive Neuroscience



Barbara L. Finlay, Psychology, and B. J. Casey, Psychiatry, WCMC, collaborate in the study of developmental cognitive neuroscience. They have resubmitted a training proposal to NIH for a project that will support several research collaborations in progress, incorporating graduate training at WCMC and Ithaca which will promote the growth of others. These include projects in computational approaches to vision with Jonathan D. Victor, Neurology, WCMC, and David J. Field, Psychology; disorders of language and dyslexia, with Bruce D. McCandliss, Psychiatry, WCMC, and Michael H. Goldstein, Psychology; and genetic approaches to learning disorders, with Francis S. Y. Lee, Psychiatry/Pharmacology, WCMC, and Barbara J. Strupp, Nutritional Sciences.



Barbara L. Finlay, Psychology, and B. J. Casey, Psychiatry, WCMC, collaborate in the study of developmental cognitive neuroscience. They have resubmitted a training proposal to NIH for a project that will support several research collaborations in progress, incorporating graduate training at WCMC and Ithaca which will promote the growth of others. These include projects in computational approaches to vision with Jonathan D. Victor, Neurology, WCMC, and David J. Field, Psychology; disorders of language and dyslexia, with Bruce D. McCandliss, Psychiatry, WCMC, and Michael H. Goldstein, Psychology; and genetic approaches to learning disorders, with Francis S. Y. Lee, Psychiatry/Pharmacology, WCMC, and Barbara J. Strupp, Nutritional Sciences.

### ACERT: The National Biomedical Research Center for Advanced ESR Technology



Jack H. Freed, Chemistry and Chemical Biology, and David Eliezer, Biochemistry, WCMC, investigate the structure of alpha-synuclein and of tau when bound to micelles and liposomes.



Jack H. Freed, Chemistry and Chemical Biology, and David Eliezer, Biochemistry, WCMC, investigate the structure of alpha-synuclein and of tau when bound to micelles and liposomes.



Freed collaborates with Olaf S. Andersen, Physiology, WCMC, on lipid-peptide interactions of gramicidin A in model membranes. ACERT is an outgrowth of extensive experience in developing the methods of modern electron spin resonance. Freed's work with these projects, funded by NIH is ongoing.

### Watching Neurons Fire



Ronald M. Harris-Warrick, Neurobiology and Behavior, and David J. Christini, Medicine, WCMC, apply software that Christini developed to let researchers add artificial currents to real neurons and observe the effects on their firing activity. This interaction of neuron with machine will allow them to study the molecular and biophysical mechanisms by which the firing properties of neurons are changed by neuromodulators such as dopamine and serotonin, which play critical roles in human behavior and consciousness.



Ronald M. Harris-Warrick, Neurobiology and Behavior, and David J. Christini, Medicine, WCMC, apply software that Christini developed to let researchers add artificial currents to real neurons and observe the effects on their firing activity. This interaction of neuron with machine will allow them to study the molecular and biophysical mechanisms by which the firing properties of neurons are changed by neuromodulators such as dopamine and serotonin, which play critical roles in human behavior and consciousness.

### The Role of NAD in Regulation of Phospholipid Metabolism in Yeast



**Susan A. Henry, Molecular Biology and Genetics/dean, Agriculture and Life Sciences, and Anthony Sauve, Pharmacology, WCMC,** are collaborating in a study of the role of NAD metabolism in regulation of phospholipid synthesis in yeast. The research seeks to answer fundamental questions about the interrelationship of energy and lipid metabolism in yeast, an important model system often used for metabolic research. Henry's laboratory works on regulation of lipid metabolism in yeast. Sauve's laboratory works on the dynamics of NAD metabolism in eukaryotic organisms and how NAD metabolism affects signaling events mediated by ADP-ribosyltransferases and deacetylases. (NAD is a chemical, nicotinamide adenine dinucleotide.)



Henry's laboratory works on regulation of lipid metabolism in yeast. Sauve's laboratory works on the dynamics of NAD metabolism in eukaryotic organisms and how NAD metabolism affects signaling events mediated by ADP-ribosyltransferases and deacetylases. (NAD is a chemical, nicotinamide adenine dinucleotide.)

### Mechanisms by which the Brain Controls Circulation



**Costantino Iadecola, Neurology, WCMC, and Robin L. Davisson, Biomedical Sciences,** study the mechanisms by which the brain controls blood pressure. Selected brain regions exert a powerful control over peripheral blood vessels and are involved in the normal regulation of arterial pressure and in the development of hypertension. The Division of Neurobiology at WCMC, led by Iadecola, and Davisson's laboratory have joined forces to unravel the cellular and molecular mechanisms of this interaction. This multidisciplinary research effort has important implications for understanding the mechanisms of hypertension,



Selected brain regions exert a powerful control over peripheral blood vessels and are involved in the normal regulation of arterial pressure and in the development of hypertension. The Division of Neurobiology at WCMC, led by Iadecola, and Davisson's laboratory have joined forces to unravel the cellular and molecular mechanisms of this interaction. This multidisciplinary research effort has important implications for understanding the mechanisms of hypertension,

a major risk factor for brain, heart, and kidney diseases.

Iadecola also works with Chris B. Schaffer, Biomedical Sciences, on the regulation of blood flow to the brain. The brain needs a constant supply of blood in order to function and to control its own blood flow. Using complementary imaging and neurophysiological approaches, Schaffer and Iadecola investigate how neurons and glia are able to influence brain vessels to ensure that they deliver a sufficient amount of blood. The elucidation of these vital mechanisms is essential to advance the ability to treat stroke and other vascular diseases of the brain.

### Technology for Wireless Dopamine Monitoring



**Manfred Lindau, Applied and Engineering Physics, and Michael G. Kaplitt, Neurological Surgery, WCMC,** are developing a basic technology for wireless monitoring of dopamine. Impaired dopamine release is the fundamental cause of Parkinson's disease. This technology will enable the researchers to understand the correlation of changes in dopamine release with behavioral symptoms and improve therapeutic strategies.

are developing a basic technology for wireless monitoring of dopamine. Impaired dopamine release is the fundamental cause of Parkinson's disease. This technology will enable the researchers to understand the correlation of changes in dopamine release with behavioral symptoms and improve therapeutic strategies.

### Studying Amyloid Protein Formation in Alzheimer's Disease



**Frederick R. Maxfield, Biochemistry, WCMC, Watt W. Webb, Applied and Engineering Physics, and Gunnar K. Gouras, Neurology, WCMC,** are studying the amyloid protein accumulations that are associated with



Alzheimer's Disease. They use conventional fluorescence microscopy to look at breakdown of amyloid by a cell type in the brain called microglia. Gouras' laboratory studies the formation of amyloid in neurons. Webb's laboratory develops ways to image these processes in the brains of living mice using multiphoton microscopy.

### Lipoprotein Interactions with Macrophages in Atherosclerosis



**Frederick R. Maxfield, Biochemistry, WCMC, Jack H. Freed, and Barbara A. Baird, Chemistry and Chemical Biology,** study the relationship between cholesterol content and biological function of cell membranes. Cholesterol loading of macrophages occurs during the early stages of atherosclerosis. The researchers are using spectroscopy methods developed in Freed's laboratory to quantify the effects of cholesterol loading on the properties of macrophage membranes. Baird's group is providing micro-patterned surfaces, to which lipoproteins are attached, so that the interaction of lipoproteins with macrophages can be imaged with high resolution microscopy techniques.



Cholesterol loading of macrophages occurs during the early stages of atherosclerosis. The researchers are using spectroscopy methods developed in Freed's laboratory to quantify the effects of cholesterol loading on the properties of macrophage membranes. Baird's group is providing micro-patterned surfaces, to which lipoproteins are attached, so that the interaction of lipoproteins with macrophages can be imaged with high resolution microscopy techniques.

### Why Do Patients Enroll (or Not) in Clinical Trials?



**Katherine A. McComas and Geraldine K. Gay, Communication, and John P. Leonard and Andrew J. Dannenberg, Medicine, WCMC,** are studying what factors influence patients' enrollment in clinical trials. The project,



**IMPACT for Improving Methods for Patient Enrollment in Clinical Trials,** aims to increase the knowledge of what motivates people to consider enrolling in clinical trials, as well as what barriers they face. Results from this research will be used to develop data-supported strategies to improve patient recruitment and better serve patients.

### Delaying Brain Damage During a Stroke



**William L. Olbricht, Chemical and Molecular Engineering, Y. Pierre Gobin, Neurological Surgery, WCMC, and Walter Zink, Radiology, WCMC,** design new drug therapies for delaying brain damage during a stroke. They develop neurovascular catheters to use in animal studies for testing neuroprotectants—drugs that delay the onset of brain damage during a stroke—and for looking at the efficacy of new neuroprotectants in these preclinical animal studies. Their microcatheter induces a stroke and delivers a neuroprotectant.



design new drug therapies for delaying brain damage during a stroke. They develop neurovascular catheters to use in animal studies for testing neuroprotectants—drugs that delay the onset of brain damage during a stroke—and for looking at the efficacy of new neuroprotectants in these preclinical animal studies. Their microcatheter induces a stroke and delivers a neuroprotectant.

### Chronic Pain and Resilience in Later Life



**Anthony D. Ong, Karl A. Pillemer, and Elaine Wethington, Human Development, and Risa S. Breckman, and M. Carrington Reid Jr., Medicine, WCMC,** are studying pain in later life. Ong is conducting a daily diary study of chronic pain, social support, and emotions in older adults. The researchers are examining resilience resources, such as social connectedness and positive emotions



are studying pain in later life. Ong is conducting a daily diary study of chronic pain, social support, and emotions in older adults. The researchers are examining resilience resources, such as social connectedness and positive emotions



are studying pain in later life. Ong is conducting a daily diary study of chronic pain, social support, and emotions in older adults. The researchers are examining resilience resources, such as social connectedness and positive emotions

## CORNELL FACULTY WITH JOINT APPOINTMENTS AT CORNELL-ITHACA AND WCMC

**Ruth Collins**  
Molecular Medicine/Biochemistry

**Robin L. Davisson**  
Biomedical Sciences/Cell and Developmental Biology

**Gerald Duhamel**  
Biomedical Sciences/Pathology and Laboratory Medicine

**Uri Keich**  
Computer Science/Tri-institutional Research Program, Physiology and Biophysics

**William Lee Kraus**  
Molecular Biology and Genetics/Pharmacology

**Hening Lin**  
Chemistry and Chemical Biology/Tri-Institutional Program

**Suzanne A. Maher**  
Applied Biomechanics in Orthopaedic Surgery/Biomedical Engineering

**Jon Tryggvi Njardarson**  
Chemistry and Chemical Biology/Tri-Institutional Program

**Karl A. Pillemer**  
Human Development/Gerontology in Medicine

**Anthony P. Reeves**  
Electrical and Computer Engineering/Radiology

**Ram V. Sharma**  
Biomedical Sciences/Cell and Developmental Biology

**David J. Skorton**  
President/Biomedical Engineering/Medicine in Pediatrics

**Francisco Valero-Cuevas**  
Mechanical and Aerospace Engineering/Applied Biomechanics in Orthopaedic Surgery

**Yi Wang**  
Radiology/Biomedical Engineering

**Martin T. Wells**  
Industrial and Labor Relations/Biostatistics and Computational Biology/Clinical Epidemiology and Health Services Research

**Ramin Zabih**  
Computer Science/Radiology



that may aid in the recovery from daily stress for populations of older adults with chronic pain.

### Paramyxoviruses and Parvoviruses Infections



Colin R. Parrish, Baker Institute for Animal Health, and Anne Moscona, Pediatrics, WCMC, research the effects of virus-receptor interaction on paramyxoviruses and parvoviruses infections. They are examining the critical



factors that control virus infection of cells by using new methods to engineer virus proteins and cell receptors to define their functional interactions.

### Postoperative Tissue Adhesions



David A. Putnam, Biomedical Engineering, and Dix P. Poppas, Urology, WCMC, are investigating postoperative tissue sealants. Putnam's lab



is responsible for the design, synthesis, and characterization of a new class of biomaterials.

Poppas' lab is responsible for evaluating the efficacy of the biomaterials in an animal model. The research received funding from the Wallace H. Coulter Foundation.

### Interdisciplinary Geriatric Research Center



M. Carrington Reid Jr., Geriatrics, WCMC, Elaine Wethington, Human Development, and Christopher Murtaugh, Visiting Nurse Service of New York, are collaborators on the New York City Interdisciplinary Geriatric Research Center. Their project mentors young investigators in community-based research designed to improve the health of older people in New York City. With the help of the center investigators, young researchers are developing independent intervention studies to alleviate social isolation, chronic pain, and self-neglect.



### Tuberculosis



David G. Russell, Microbiology and Immunology, Matthew DeLisa, Chemistry and Chemical Engineering; Dirk Schnappinger, Carl F. Nathan, Sabine Ehrh, Microbiology and Immunology, WCMC, and



Frederick R. Maxfield, Biochemistry, WCMC, study tuberculosis. Russell and Ehrh work on tissue response to TB; their project, *The Role of the Granuloma in M. Tuberculosis Infection*,



focuses on the identification and characterization of M. tuberculosis lipidoglycans that regulate the development and maintenance of the granuloma structure. Russell, Schnappinger, and DeLisa work on protein secretion pathways in TB; their project, *Environmental Responses and Cues in Tuberculosis*, aligns the transcriptional profiles of M. tuberculosis with the environmental shifts experienced in the phagosome of the host macrophage and within the airways and lung tissue. Russell is starting a collaboration with Maxfield to look at lipid metabolism in macrophages. This collaboration allows the researchers access to high-throughput screening of small molecule libraries. Their project, *Cell Biology of Mycobacterium Tuberculosis*



**“I think that the issue of having hospitals understand service from the ‘hospitality’ perspective is a very rich area for potential collaboration and synergy.”** - Steven A. Carvell, *Hotel Administration*

*Infection*, focuses on the intracellular survival strategies of M. tuberculosis and how the bacteria exploit the intracellular environment to support its growth.

Other projects include *Development of a Novel Strategy of Adjuvant Discovery*, which defines the early correlates of an effective adjuvant, manipulation of the environment at site of inoculation, and development of a screen for new adjuvants. Another project is a *Zeiss LSM10 Meta Confocal Microscope*, which is an application for a confocal microscope for a BSL2 life imaging facility.

### Mechanical Regulation of Stem Cells



Thomas N. Sato, Cell and Developmental Biology, WCMC, and Cynthia A. Reinhart-King, Biomedical



Engineering, study the mechanical regulation of stem cells. They want to find out how stem cells sense and respond to mechanical stimuli. This work will enable them to develop novel therapeutics to enhance organ regeneration as well as to engineer native tissue-friendly transplantable organs.



Sato also collaborates with Mingming Wu, Mechanical and Aerospace Engineering, on microfluidic dynamics in living fly embryos using Sato's sophisticated high-speed imaging system and Wu's expertise in physical tools to characterize fluid motion. The researchers aim to discover novel physical dynamics in living matter to redefine the elements of life. With Abraham D. Stroock, Chemical and Biomolecular Engineering, Sato studies the regulation of endothelial differentiation from stem cells by microfluidic shear stress. Sato uses his expertise to isolate endothelial stem cells and work with Stroock's group

### A Difficult-to-Treat Brain Tumor



Michael L. Shuler, Biomedical Engineering, Susan C. Pannullo, Neurological Surgery, WCMC, and David A. Putnam, Biomedical Engineering, collaborate on controlled delivery of a mixture of chemotherapeutics to the brain following surgery for a particularly difficult to treat type of tumor. Unlike current methods the researchers believe that they can synthesize drug-eluting fibers that completely fill the irregular shape cavity left after surgery in a way that conforms to the shape of the cavity and ensures effective delivery to all sites surrounding the tumor to prevent regrowth of the tumor.



### Bacterial Flora in Crohn's Disease



Kenneth W. Simpson, Clinical Sciences, and Ellen J. Scherl, Medicine, WCMC, study the bacterial flora in Crohn's disease. Simpson's laboratory



researches host-bacterial interactions in the gastrointestinal tract with emphasis

on the role of the mucosa-associated microflora in gastritis and intestinal inflammation in animals and people. Scherl is director of the Jill Roberts Center for Inflammatory Bowel Diseases, which is dedicated to the research and treatment of IBD, a condition affecting more than one million Americans, that most often results from two specific diseases—ulcerative colitis and Crohn's disease. In their studies of patients with ileum-based Crohn's disease, they discovered that a selective increase in a phylogenetically novel group of *E. coli* correlates with the severity of inflammation. They also found a relative decrease in potentially beneficial Clostridiales bacteria. This novel group of *E. coli* bacteria display pathogen-like behavior in cultured cells and have genes similar to bacteria that cause diseases ranging from salmonellosis to cholera and plague. Researchers have long believed that enteric bacteria play a key role in Crohn's disease, but have not yet identified the mechanism that drives the inflammatory response. Research by the Cornell team provides new insights into the ileal mucosal bacterial flora in health and disease that may inform patient management in the future.

### Protein-Protein Interactions



James P. Sethna, Physics, and Harel Weinstein, Physiology, WCMC, are discussing the modeling of the interactions

between bar-domain proteins and membranes and the role these play in mediating protein-protein interactions. Such long-range interactions may play a complementary role to lipid-raft effects in segregating and coordinating protein complexes on the membrane.

**Infant Feeding Support Strategy for HIV-Affected Infants 6-12 Months Old in Haiti**



Rebecca J. Stoltzfus, Nutritional Sciences, Daniel Fitzgerald, Medicine, WCMC, and Jean W. Pape, Medicine, WCMC/GHESKIO Centres, Haiti, are developing and pilot-testing an infant feeding support strategy



for HIV-affected infants from 6-12 months whose mothers are enrolled in the PTMCT (prevention of mother to child transmission) program of GHESKIO Centres. The study is the first step toward an evidence-based and contextually appropriate Haitian policy for nutritional support of infants affected by HIV. Prevention of malnutrition is essential to infant development and survival, especially for the two million children born to HIV-infected mothers in the developing world each year. NIH funds the project.

**Neural Tube Defects**



Patrick J. Stover, Nutritional Sciences, and M. Elizabeth Ross, Neurology, WCMC, study folate and neural tube defects.

The collaboration focuses on elucidating the relationships among signalling pathways and folate nutrition/metabolism. Neural tube defects are a class of common birth defects.

**Medical Endoscopy**



Watt W. Webb, Applied and Engineering Physics, Frederick R. Maxfield, Biochemistry, and Douglas S. Scherr, Urology, WCMC,



and co-investigators are developing multiphoton microscopy endoscopy as



a tool that can be used during surgical procedures to image tissues with high resolution and high information to

provide real-time content about the nature of the tissue, for example, cancerous or normal. While the researchers are working on the engineering issues involved in the development of the endoscope, the group is starting to look at human tissues—initially from various freshly isolated surgical specimens—in order to develop an atlas of what various normal and pathological tissues look like in multiphoton imaging compared to standard histological H&E stained specimens. Warren R. Zipfel, Biomedical Engineering, recently built a custom multiphoton microscope funded by WCMC that is now in use there. This newly funded project (NIH five-year grant) aims to create significant advances in the functional effectiveness of medical endoscopy for public health care. Other co-investigators include Chris Xu and Harold C. Craighead, Applied and Engineering Physics, and 11 other faculty and surgeons from WCMC and two other faculty from Ithaca.

**Cellular and Molecular Biophysics**



Watt W. Webb, Applied and Engineering Physics, Frederick R. Maxfield, Biochemistry, WCMC, and Barbara Baird, Chemistry and Chemical



Biology, study cellular and molecular biophysics of signal transduction. The research aims to characterize diffusion and equilibrium molecular interactions of lipids and proteins on the cell surface



in order to understand transduction of electrical signals and to decode cell surface receptor actions.

**Affordable Plant-Based Remedies for Human Diseases and Illnesses**



Martin T. Wells, Industrial and Labor Relations/Biostatistics and Computational Biology, and Mary E. Charlson, Center



For Complementary and Integrative Medicine, WCMC, collaborate on a large-scale project on affordable plant-

based remedies for human diseases and illnesses. Along with a large group of researchers, they have submitted a \$110 million proposal to Atlantic Philanthropies and a smaller proposal to the Gates Foundation. Wells has also worked with a dozen WCMC physicians on various small data analysis projects. He has a formal faculty appointment in the WCMC (voted by the WCMC faculty to be a professor of clinical epidemiology and health services research). For the past three summers, he has taught courses in WCMC's epidemiology masters program.

**Proteins Avoiding Death by Chemotherapeutic Agents**



Hao Wu, Biochemistry, WCMC, and Sol M. Gruner, Physics,

explore high pressure cryocooling for obtaining

suitable diffraction-quality crystals for high resolution structural analysis of proteins involved in two biomedically important systems. The first system involves the signaling pathways that underlie programmed cell death, apoptosis. Apoptosis is a highly regulated process that is essential for normal development and homeostasis of multicellular organisms. Apoptosis also plays a critical role in immune regulation, such as during viral infection where it is a central point of interplay between the virus and the host. The second system centers on the activation of the nuclear factor kappa B by the TRAF proteins, which play critical roles in immunity and cancer and are potential therapeutic targets for both inflammation and cancer.

**WCMC FACULTY MEMBERS OF CORNELL-ITHACA'S GRADUATE FIELD OF BIOMEDICAL ENGINEERING**

Adele Boskey  
Hospital for Special Surgery,  
Biochemistry

David J. Christini  
Medicine/Physiology and  
Biophysics

Claudia I. Henschke  
Radiology

Suzanne Maher  
Applied Biomechanics in  
Orthopaedic Surgery

Frederick R. Maxfield  
Biochemistry

Jonathan D. Victor  
Neurology

Bruce T. Volpe  
Neurology

Alan M. Weinstein  
Physiology

Timothy Wright  
Applied Biomechanics  
in Orthopaedic Surgery



Anne Moscona, Microbiology and Immunology/Pediatrics



Claudia Fischbach-Teschl, Biomedical Engineering, and John Boockvar, Neurological Surgery