

***UNIVERSITY OF MASSACHUSETTS
MEDICAL SCHOOL
OFFICE OF UNDERGRADUATE
MEDICAL EDUCATION***



***MEDICAL STUDENT
SUMMER RESEARCH FELLOWSHIPS***

CATALOGUE

Directors:

Michael Godkin, PhD

Family Medicine and Community Health

2013

Anthony Poteete, PhD

Molecular Genetics and Microbiology

Project Assistant:

Jacqueline Clark

Office of Undergraduate Medical Education

1. Development of a validated risk index aimed at reducing re-admissions following surgery for colorectal cancer

Karim Alavi, MD, MPH

Surgery Department, Division of Colon and Rectal Surgery
67 Belmont Street, Worcester, MA 01605

Colorectal cancer is the 3rd most common cancer in the U.S. with an estimated 143,000 new cases diagnosed annually. Of the \$14 billion spent on CRC in 2010, re-admissions following surgery cost \$300 million in 2010. According to the Medicare Advisory Commission (MedPAC) report to Congress, the majority of these re-admissions are preventable. As of 2013, Medicare will penalize hospitals for re-admissions. Re-admission rates range from 8-25% in colorectal surgery with common causes which include surgical site infections, dehydration, and ileus. Our long-term goal is to reduce readmission rates following colorectal cancer (CRC) surgery by developing and implementing a risk calculator which will be used at the point of care to identify those at highest risk of re-admission. The primary objective of this proposal is to develop and validate a model to predict risk of 30-day readmission following discharge. The central hypothesis is that there are unique clinical, demographic, social and systematic characteristics of patients readmitted within 30 days of surgery for CRC. The rationale for the proposed project is to identify patients at highest risk for readmission prior to discharge and to implement interventions aimed at preventing readmission.

Student's role: The student will be integrally involved in all aspects of the project including research design, data acquisition, and analysis. The student will work closely with the PI as well as lab personnel during this project.

Required skills: Working with excel spreadsheet

Location of research: 67 Belmont- Division of Colon and Rectal Surgery and Surgical Outcomes and Analysis Laboratory (3rd floor, Medical School)

2. Relationship between Pre And Post Event Prescription Drug Use in the Elderly and the Incidence and Outcomes of Surgical Health Shocks

Fred Anderson, PhD; Heena Santry, MD MS
Department of Surgery/Center for Outcomes Research
One Innovation Drive, Suite 110, Worcester, MA 01605-2323 US

The population of Americans aged 65 years and older is projected to increase from 39 million in 2010 to 69 million in 2030. These demographic trends suggest that the elderly will be an increasing proportion of the emergency surgery population in the future. Elderly patients undergoing emergency general surgery (EGS) procedures are at increased risk for both serious morbidity and mortality compared to patients less than 65 years old. Elderly trauma patients are also at higher risk than younger injured patients for mortality. Furthermore, elderly patients are more likely to present with repeated injuries.

Chronic conditions play a role in outcomes for both trauma and non-trauma surgical emergencies (NTSEs). Beyond co-morbidities, however, outpatient medication use may also play a role in both incidence and outcomes for trauma and NTSEs. For example, warfarin use has been associated with adverse outcomes for head injury, gastrointestinal bleeding, and a number of other injuries and NTSEs. Outpatient antibiotic use has been associated with *C difficile* colitis, a condition which increasingly requires emergent colectomy. Based on known effects of statin use on cerebral vasospasm, pre-injury statin use may improve outcomes after head injury. Similarly, outpatient bisphosphonate use may reduce fracture injuries. Given the known benefits of pre-operative aspirin and beta-blocker use for prevention of peri-operative cardiac complications in the elective surgical setting, it is possible that the same benefits may be seen for patients requiring emergency surgery

Our research group is investigating the relationship of elderly Americans' outpatient prescription drug use and the incidence and outcomes of subsequent surgical emergencies. We have obtained 2 years of Medicare data including inpatient and prescription drug (Part D) claims. Current areas of investigation include the relationship of anticoagulants to trauma outcomes, the association of outpatient antibiotics and subsequent *c. diff* infection, and the relationship of bisphosphonate use and adherence in patients suffering from non vertebral fractures. We also have plans to initiate studies examining cardiovascular and diabetic medications and their effect on surgical outcomes in the elderly population.

Student Role:

- Perform a thorough literature search on a specific surgical health shock and participate in the writing of the background and motivation sections of the manuscript on the topic of interest
- Participate in weekly (and additional as needed) methodology/analysis meetings (data analysts to perform actual analysis) on topic of choice
- Participate in summer "Research Introduction" curriculum as part of the Surgical Research Scholars Program
- Assist PI in completing results and discussion portion of the manuscript
- Produce a poster suitable for presentation by end of summer
- Required Skills:
- Ability to work independently and efficiently with instructions from PI
- Comfortable using library resources and Pubmed to perform literature search
- Good written and oral English communication
- Interest in geriatrics and/or surgery
- Completion of CITI training

Location of Research: UMass Department of Surgery, Center for Outcomes Research (University Campus)

3. Treatment of esophageal dysmotility

David R Cave, M.D. PhD.
Department of Medicine/Gastroenterology
55 Lake Ave. N. Worcester. Massachusetts 01655

Esophageal dysmotility is a common problem in older patients. It is a common cause of dysphagia to solids and liquids. The cause is not known. Evaluation by endoscopy and by esophageal manometry is generally unhelpful. Barium studies may demonstrate tertiary contractions. There is no systematic data on how this condition should be treated. However there is anecdotal evidence that esophageal dilation is helpful in terms of controlling symptoms for manometry months after the procedure. The efficacy of this procedure has never been documented.

We propose to perform a two-part study. Firstly, to retrospectively evaluate patients who are known to have this disorder and to who have had esophageal dilation. The dilation is often repeated over time. The interval between dilations and the recurrence of symptoms should provide a measure of effectiveness of the procedure. In parallel with this we plan to initiate a prospective study as we see new patients in the office with this condition. The standard of care for these patients is to have endoscopy, esophageal manometry and a barium swallow. As mentioned above, treatment for this condition is by esophageal dilation. We will then follow these patients longitudinally for recurrence of symptoms and need for repeat dilation. The patients will serve as their own controls. We will develop a diary to provide a weekly assessment of symptoms both before and after dilation.

Student's role: Caitlin's role will be to collect and analyze data. She will have the opportunity of seeing these patients with me, when she is available to help develop her clinical skills. She will be putting the application together for the institutional review board, and if preliminary data looks promising we will seek external funding for the continuation of the project. She is a first-year student and therefore has the opportunity of pursuing this project well beyond the summer of 2013

Required skills: CITI certification, she already has this along with previous clinical research exposure. She will need to become familiar with the electronic IRB application. She already has familiarity with Excel spreadsheets and basic statistics.

Location of research: University campus.

4. Evolution of myosin regulation in muscle

Roger Craig, PhD

Department of Cell and Developmental Biology
School, Basic Sciences wing, S7-210

Our laboratory uses electron microscopy (EM) to analyze the structure of the myosin and actin filaments of muscle. Our goal is to understand these structures in 3D so that we can decipher the molecular basis of contraction and its regulation. We have obtained data on filaments from several key model invertebrate systems (e.g. Woodhead et al., Nature, 436, 1195, 2005: Atomic Model of a Myosin Filament in the Relaxed State). Comparison of different species has provided surprising insights into muscle evolution. A particular feature in common to these species is a self-inhibiting structure in which the two heads of the myosin molecule interact with each other, switching the molecule off, leading to muscle relaxation. Results suggest that this structure is highly conserved, being found so far in arthropods, molluscs, flatworms and mammals (including human), and in skeletal, cardiac and smooth muscles. It must therefore have evolved very early (probably more than 600 million years ago). To further understand the fundamental origins of this structure, we are interested in tracing its phylogeny to the earliest organisms possible. This project has two aspects. In fact it could be two projects for two students with different interests. First we are interested in determining whether this structure is present in the earliest animals that have muscles (Cnidaria = sea anemones, jellyfish). This project would involve obtaining muscle tissue from sea anemones, purifying myosin filaments from the tissue, then examination in the transmission electron microscope by negative staining. An alternative approach would be to purify myosin molecules from the muscle and examine these by EM. These approaches would give complementary answers. This would be an opportunity to learn EM preparative techniques and to obtain experience using a transmission EM. A second project would be more theoretical and literature-based. Our understanding of evolutionary trees is changing rapidly as relationships between groups are now being studied at the molecular level instead of through comparative anatomy. Some of the changes are surprising. We are not an evolutionary laboratory, but need to be up to date in our understanding of current thinking on general evolutionary relationships, and in particular on the evolution of muscle and contractile proteins, as these must underlie our structural observations. This project would involve searching current literature and online resources to build a comprehensive and current evolutionary tree and knowledge base on muscle evolution, upon which we can build our future thinking in the laboratory.

Student's role:

First project – Prepare filaments from anemone, purify, prepare EM grids for observation, carry out EM observations, analyze images computationally. If approach via single molecule method, purify myosin from anemone muscle, prepare molecules for EM observation, analyze images.

Second project – search online for literature concerning evolutionary trees and the evolution of muscle structure (we already have a substantial list of papers). Read relevant papers to build knowledge base. May also involve analysis of relevant sequences in genome databases.

Required skills: First project – Prior wet lab skills would be very valuable. Good manual dexterity. Should be adept at using complex, delicate equipment (EM). Past experience in microscopy and/or biochemistry a plus. Second project – Ability to search, read, absorb and synthesize literature and web data, and to communicate findings in written or tabular form.

Location of research: School, Basic Sciences wing, S7-209

5. Managing High Risk Patients in a Rural Patient Centered Medical Home

Kosta Deligiannidis MD, Christopher Chang MD, Alice Leblanc RN
Department of Family Medicine and Community Health
Barre Family Health Center, 151 Worcester Road, Barre, Ma 01005

The Barre Family Health Center is an NCQA recognized level 3 Patient Center Medical Home (PCMH) family medicine outpatient clinic in a rural community. One of the necessities of being a PCMH is managing the high risk patients in the practice. High risk patients are those who utilize a large amount of medical resources, are at greatest risk of becoming sick, and do not receive the high quality care that they need. Such patients are also quite difficult to care for due to their multiple complex medical, psychological, and social problems. The best approach is using a care team that includes the patient's primary care physician, a behavioral specialist, a nurse, and a clinical care manager.

The goal of this summer project will be to create an efficient process for all members of the care team to participate in together so that these high risk patient receive the high quality care they need. You will work closely with the clinical care manager and the quality improvement leader of the health center to participate in clinical care management and create this process.

Student's role: Work with a clinical care manager to manage our practice high risk patient registry. Specific duties include:

- Provide follow up phone calls and/or home visits on high risk patients after a hospitalization, emergency room visit, or office visit
- Work with patients to create care plans and help them follow through with them
- Actively participate in Patient Centered Medical Home weekly meetings and Patient Advisory Committee meetings
- Actively participate in monthly diabetic group visits
- Create a practice wide work flow to incorporate care planning in routine visits and train staff on how to implement this work flow

Students will also have the opportunity to see patients with a preceptor during a clinical session if they so desire. Student will study existing nursing responsibilities and workflows to identify areas for improving efficiency to create time for nursing staff to routinely use the high risk registry and engage in preventive care

Required skills: Friendly, compassionate interpersonal skills; Ability to communicate effectively with a care team (patient, family, nurses, physicians); Interest in Family Medicine as your specialty preferred

Location of research: Barre, Massachusetts surrounding community

6. NIH/NIMH K23 Study: Neuroimaging and neuroendocrine endophenotypes in postpartum depression

Kristina M. Deligiannidis, M.D.

Departments of Psychiatry and Obstetrics & Gynecology

Center for Psychopharmacologic Research and Treatment, 361 Plantation Street, Worcester, MA

This single-site observational cohort study will prospectively examine perinatal plasma levels of sex hormones and γ -aminobutyric (GABA) in women at High-Risk of developing postpartum depression (PPDHR) as contrasted with Healthy Control Low-Risk (HCLR) women and to evaluate depression, anxiety, functional disability, social support and quality of infant bonding. In the postpartum, women will undergo functional MRI/Magnetic Resonance Spectroscopy (MRS) and resting-state functional connectivity to measure neurochemistry and brain circuitry in both groups. We also collect maternal DNA from both groups for genetics studies and umbilical artery cord blood at delivery for neuroendocrine studies in neonates.

Approximately 900 pregnant women will be screened with a one page questionnaire that assesses risk of PPD during their routine 28 week gestational age prenatal visit at our UMMMC Ob-Gyn clinic. High risk and low risk women who meet criteria will be evaluated prospectively through the 9th week postpartum for depressive symptoms.

Student's role:

The medical student's role, once CITI trained, is hands on with research participants. The medical student will consent and perform depression screening in pregnant women at the Memorial OB clinic (West 4/Levine) and conduct visits on labor/delivery; learn how research psychiatric interviews are conducted which assess not only psychiatric symptoms but obstetric information; evaluate participants longitudinally from late pregnancy to the postpartum; learn about neuroendocrine biomarkers and their significance towards understanding the pathophysiology of perinatal depression; attend neuroimaging sessions at UMMS, obtain collaborative skills with PI and research coordinator involved in the study, perform minimal research database entry to be shared with PI and research coordinator, etc. He/she will be able to learn about clinical trial design, recruitment strategies, research ethics, IRB procedures, etc. as they pertain to the study. There are numerous facets in which to be involved, and the medical student would have a desk adjacent to the research coordinators in our research suite where the PI's office is within the CPRT research group. The medical student would attend all research group meetings so that he/she would have exposure to the other studies ongoing in the CPRT research group. Direct supervision would be by the PI for the entire research fellowship program.

Required skills: Empathic; pays close attention to detail; strong capacity for both independent work and teamwork; dependable; computer adeptness

Location of research: Center for Psychopharmacologic Research and Treatment (CPRT) ; West 4 Obstetrics/Gynecology Clinic at Memorial/Levine; Labor and Delivery Unit at Memorial

7. Molecular Methods for the Diagnosis of Melanoma

April Deng M.D.; Lloyd Hutchinson Ph.D.
Anatomical Pathology, Laboratory of Diagnostic Molecular Oncology
Three Biotech, Room 276, One Innovation Drive, Worcester Ma 01605

Malignant melanoma is the most deadly skin cancer and the incidence is rising dramatically. The prognosis is closely related to the stage of the disease, thus, early diagnosis has summoned importance for patients' survival. However, histopathological diagnosis of melanoma can be very challenging sometime as a variety of benign melanocytic lesions, particularly some pediatric melanocytic neoplasms, such as Spitz nevi and dysplastic melanocytic nevi, share similar morphology with melanoma. A misdiagnosis will have an adverse impact on the patient. Early intervention is important to avoid metastasis, but over diagnosis will result in unnecessary aggressive chemotherapy.

A reliable and accurate assay is needed to distinguish patients with a benign entity from those with true melanoma. The Laboratory of Diagnostic Molecular Oncology has developed clinical molecular assays (Laser Capture, Robotic Nucleic Acid Extraction, Multiplex Ligation-dependent Probe Amplification, PNA-clamp Real Time Quantitative PCR) able to identify DNA mutations and DNA copy# changes. A retrospective pilot study of 400 cancer genes in 20 archived tissue specimens identified a subset of genes with the potential to distinguish benign lesions from malignant melanoma. An molecular signature combining four Fluorescent In Situ Hybridization (FISH) probes and the mutation status of three gene, has been developed.

The study has two goals (1) extend the study to additional archived "melanocytic lesions" including atypical subtypes to determine if this molecular signature can accurately classify low risk versus malignant melanocytic lesions, and (2) extend the analysis of these specimens to Next Generation Sequencing methods validated by the lab. Since, Next Generation Sequencing can provide both mutation status and copy# information of ≥ 50 genes, this approach may streamline testing and/or lead to development of a "better" gene signature. As such the aim of this study remains the creation a new diagnostic test as an adjunct to traditional pathology, that can be used as a "lab-developed" assay for clinical testing.

Student's role

1. Review melanoma lesions with the Dermatopathologist
2. Use a fluorescent microscope and learn to read /count Fluorescent In Situ Hybridization (FISH) slides.
3. Aid in the laser capture microscopy and robotic DNA extraction of specimens
4. With Technologists, aid in performing PCR assays and using a ABI 3700 capillary gel electrophoresis system.
5. Aid in raw data analysis from PCR assays and Next Generation Sequencing data using SoftGenetics Software (e.g. GeneMarker, NextGen).
6. Aid in classification of specimens that are positive/negative for point mutations or chromosomal abnormalities to validate 8 gene signature or identify a better "melanoma signature" from Next Generation Sequencing data set.
7. Aid in the creation/maintenance of a database for statistical analysis of the data.

Required skills: computer literacy

Location of research: Three Biotech, Room 276, One Innovation Drive, Worcester Ma 01605

8. Patients' Perspectives on Foregoing Conventional Cancer Treatment and Using Alternative Medicine

Anand Dhruva, MD

Osher Center for Integrative Medicine, 1545 Divisadero Street, 4th Floor
San Francisco, CA 94115

This project aims to investigate cancer patients' motivations for using alternative medicine – foregoing all or part of the treatment regimen that is recommended by conventional medicine. Patients who forego proven and conventional treatments for cancer may experience increased cancer-related morbidity and mortality. In addition, these patients may be marginalized by the conventional medical system, thereby putting them at risk for worse health outcomes. Very little research has been done to date on this important research question.

In this study, interviews will be conducted with approximately 20 cancer patients who have declined conventional treatment of cancer in favor of alternative treatments. Interviews will be transcribed and coded for major themes, and then, analyzed using thematic analysis. The results of this study will provide preliminary data for a future longitudinal case control study to evaluate experiences and outcomes with alternative medicine for cancer treatment.

Student's role

Assisting with patient recruitment/consent – patients will be referred by their primary care physician or oncologist. Jim will contact the patient, review protocol and consent, and schedule interviews

Conducting interviews with patients – Jim will conduct several of the 1-hour interviews

Analysis and reporting – Jim will work with me and an oncology fellow to code patients' responses and analyze them. I anticipate Jim will have the opportunity to write an one or more abstracts based on this summer work

Required skills: Strong communication skills via e-mail, phone and in-person, as well as a desire to learn are the prerequisites for this summer project. Jim will learn how to complete a thematic analysis of qualitative interviews during the course of this project.

Location of research: Research will be conducted at the medical centers affiliated with the University of California San Francisco

9. REACD Study (Role of Epicardial Adipose in Cardiovascular Disease)

Timothy P. Fitzgibbons, MD, PhD
Department of Medicine, Div of CV Med
55 Lake Avenue North, Dept of Cardiology

Epicardial fat is a visceral fat depot that surrounds the heart. Increased epicardial fat is known to be associated with obesity; whether or not epicardial fat plays a primary role in the development of cardiovascular disease, in particular atherosclerosis, is not known. We have collected samples of epicardial fat from patients with and without coronary disease who have had heart surgery. We then prepared microarrays from epicardial and subcutaneous fat from each patient. We have interesting preliminary results which need to be confirmed with qPCR and *in vitro* experiments. For example, coronary disease is associated with increased expression of omentin/intelectin-1 in epicardial fat. Furthermore, patients without coronary disease have increased expression of orphan nuclear hormone receptors in epicardial fat. We hypothesize that agonists for these receptors may have putative protective effects from cardiovascular disease.

This study, done in conjunction with Dr. Czech and Dr. Tam, will provide great and diverse experience to interested students, and there is already data ready to analyze. There will be significant 1:1 mentoring with Dr. Fitzgibbons throughout the duration of this project.

Student's role: 1) analysis of microarray data, 2) manuscript preparation, 3) possible training in qPCR, western blotting, IHC

Required skills: none

Location of research: Biotech 2

10. Reducing disparities in cancer screening for adult patients with depression in an urban family medicine practice

Mary Flynn MD and Katharine Barnard MD

Department of Family Medicine and Community Health

Address: Plumley Village Health Services, 116 Belmont St #11, Worcester MA 01605

Plumley Village Health Services is a small family medicine practice providing primary care and public health services to the low-income, primarily Hispanic residents of Plumley Village housing and the surrounding neighborhood. In the process of our ongoing Patient Centered Medical Home transformation, we have identified disparate levels of breast and colorectal cancer screening between our depressed and non-depressed adult patients.

We propose a summer student project with the goal of identifying modifiable factors that would improve cancer screening rates in our depressed adult patients. The project would consist of directed readings on underserved populations, adult depression, and qualitative research methods. The student will develop a survey tool to be administered to a sample of our depressed adults in order to identify modifiable barriers to completion of cancer screening. The end product might be a practice improvement to address these barriers and improve patient self-efficacy. Pre- and post-intervention comparison data can be calculated from our patient registry database. Spanish language skills would be an asset but not a requirement.

11. Trauma Screening for Children Evaluated by the Child Protection Program

Heather C. Forkey, M.D

Department: Pediatrics

Rm A2-201 Benedict Bldg, 55 Lake Ave N. Worcester, MA 01655

Evidence continues to grow linking the early experience of trauma to later physical and emotional health. Children who are being evaluated for inflicted injury have likely experienced traumas, but trauma screening has not routinely been part of their medical evaluation. This study would evaluate the feasibility and benefit of including a formal screening for emotional trauma as part of a Child Protection Medical Evaluation.

Student's role: Developing IRB proposal, setting up protocol, administering screening tool to patients

Required skills; Organization, basic statistical skills beneficial

Location of research: University Campus Benedict Bldg, 55 Lake Ave N. Worcester, MA 01655

12. Predictors of functional outcome after surgery for knee and hip arthritis

Patricia D. Franklin MD MBA MPH; Leslie Harrold MD MPH

Clinical and Outcomes Research

Department of Orthopedics and Physical Rehabilitation University of Massachusetts Medical School

This federally funded national research project will evaluate the clinical, patient, and hospital system factors that influence outcome at 6 and 12 months after total joint replacement surgery- the highest volume procedure in the Medicare budget. As US adults age, and greater numbers suffer from knee and hip arthritis, new data are needed to compare effectiveness of varied clinical and surgical approaches to this surgery. This IRB-approved study is in the process of reviewing large numbers of medical records and collecting patient-reported outcomes on hundreds of new patients each month. The student will contribute to the collection, review, and analyses of these key risk factors. Weekly team meetings with statisticians, epidemiologists, surgeons, and rheumatologists are ideal environments to learn the methods of large-scale clinical research. The student can participate in the data review, interpretation, and preparation of a manuscript related to the data.

Student's role:

Chart review, patient interviews, and participate in research team meetings for operations and data analysis of a \$12 million national research study. Learn state of the art comparative effectiveness strategies and assist with the preparation of a manuscript. Literature review and synthesis, and other research-related tasks as required.

Required skills:

Required: Conscientious, detail-oriented, data management skills; entry-level patient interviewing skills; writing skills; Desired, but not necessary: computer analysis skills

Location of research-- UMMS - University campus and UMMHC- Memorial campus

13. Characterization of Mitophagy and Its Role in Human Age-Related Macular Degeneration

James T. Handa, MD

Wilmer Eye Institute, Johns Hopkins School of Medicine, 400 N. Broadway, Smith Building, Room 3015, Baltimore, MD 21287

Age-related macular degeneration (AMD) is the most common cause of blindness in the elderly, with a two-fold increased risk in smokers. The retinal pigmented epithelium (RPE) is composed of specialized cells that maintain photoreceptor integrity by phagocytizing waste and detoxifying reactive oxygen species (ROS). RPE cells rely on a form of autophagy called mitophagy to remove damaged mitochondria. When normal RPE function is compromised, photoreceptors degenerate leading to visual impairment. While oxidative stress is known to play a central role in the pathogenesis of AMD, the role of autophagy and mitophagy is less clear.

Loss-of-function mutations in DJ-1 cause a familial form of Parkinson's disease and plays an important role in mitophagy and mitochondrial redox control. However, very little is known about its role in AMD. In this project, we will determine the cellular distribution of DJ-1 in human samples from patients affected by AMD using immunohistochemistry and biochemistry. Furthermore, we will test the impact of loss of DJ-1 on mitochondrial function using DJ-1 knockout mice. We will induce oxidative stress in mouse eyes by giving intraocular injections of cigarette smoke extract and harvest eyes from DJ-1^{-/-} and DJ-1^{+/+} mice 24 hours later for analysis of reactive oxygen species, mitochondrial function, and mitophagy using immunofluorescence and western blotting. We will test the hypothesis that impaired DJ-1 decreases baseline mitophagy and result in RPE dysfunction after exposure to oxidative stress.

We anticipate these results will provide insight into the protective role of DJ-1 on mitochondria and RPE health after exposure to oxidative stress and during aging.

Student's Role: To design, execute, and analyze experiments to achieve the research goals outlined above. Student will publish results in a peer-reviewed journal and present a poster or talk at a national conference.

Required Skills: Experience with rodent handling, IHC, western blotting, and other pertinent biochemical assays. Experience with statistical analysis of data, making figures with Adobe Photoshop, and writing manuscripts.

Location: Smith Building, Room 3001, Baltimore, MD 21287

14. EPVent 2- A Phase II study of Mechanical Ventilation Directed by Transpulmonary Pressures

Stephen Heard, M.D.

Department: Anesthesiology

UMMS Address: S2-751

This phase II prospective randomized controlled trial of ventilation directed by esophageal pressure measurements will enroll 200 patients with moderate to severe ARDS by the Berlin conference definition in seven academic medical centers in North America. The control group will be ventilated using an alternative high-PEEP strategy with PEEP and FiO₂ set using to an empiric table.

Plasma samples will be obtained at enrollment and days 3 and 7 and assessed for a variety of lung injury biomarkers to better assess the association between our intervention and the inflammation associated with mechanical ventilation and the development of ARDS. Hospital survivors will undergo a brief follow up phone survey to assess survival, functional status (Barthel Index), health-related QOL (Short Form 12), and frailty (VES) twelve months after enrollment.

The study length will be four years with a six month start-up period followed by a planned 30 month enrollment and twelve month follow-up.

Student's role: Learn about the pathophysiology and current treatment of the acute respiratory distress syndrome (ARDS); learn how this intervention is different from standard therapy; identify patients who have developed ARDS; assist in obtaining informed consent; assist in enrolling the patient (including attaching the patient to the study monitoring equipment); ensure the protocol is followed

Required skills: Enthusiasm and punctuality

Location of research: intensive care units at UMass Memorial Medical Center

15. Efficacy of self-study for learning surgical skills: Flexor Tendon Repair

Marci Jones, MD
Orthopedic Surgery and Rehabilitation
Hahnemann Campus, Lincoln Street

Surgical skill simulation is becoming recognized as a more important component of resident training. Proctored simulation labs provide an excellent method of teaching surgical techniques, but they are labor intensive and require a number of residents and faculty present. This is difficult in light of the clinical demands of both the faculty and the residents, as well as the limitations imposed by 80-hour work week. We plan to use a previously published cadaveric model for simulation of flexor tendon repair with a novel self-study design to evaluate the efficacy of self-learning vs. proctored teaching of surgical skills in orthopedic and plastic surgery residents.

Student's role: Assist with study design, preparation of IRB, initial data collection and analysis

Required skills: CITI training, good organization skills, willingness to work flexible hours.

Location of research: Hahnemann Campus, University Campus

16. Inhibition of B lymphocyte kinase (BLK) as a novel treatment for psoriasis

PI: Joonsoo Kang, PhD

Department of Pathology, ASC 1047

Psoriasis is a common chronic skin inflammatory disease affecting more than 100 million people worldwide. Current treatment regimens involve anti-inflammatory agents (e.g. corticosteroids, Enbrel (anti-TNF) and Stelara (anti-IL-23 receptor)). The biologics are particularly effective but they have a major drawback in enhancing susceptibility to infection, especially when administered systemically, and efficacy of the drugs decline over time in most patients suffering from moderate to severe psoriasis. Given the chronic nature of the disease, development of a novel therapeutic with an improved safety profile and precision-guided targeting of disease inducing cell subsets in the skin is a pressing need.

Psoriasis is an autoimmune disease mediated by lymphocytes. Until recently, most studies have attributed aberrantly activated adaptive ab T cells producing IL-17 and IL-22 as the culprits driving the inflammation. However, more recent studies have shown that the central driver of psoriasiform plaque development in mice is the dermal innate lymphocytes. In particular we and others have shown that dermal innate gd T cells producing IL-17 and IL-22 are necessary for the imiquimod (IMQ, Aldara, a TLR7/8 ligand) or inflammatory cytokine (IL-23) induced psoriasis in mice. Using induced mutant mice generated in our lab we showed that mice specifically lacking one subtype of Tgd17 cells are resistant to the induced psoriasis. Critically, published studies have shown that human psoriasis is associated with overt IL-17 production and that gd T cells are the dominant source of the cytokine in the patients' dermis. These results strongly suggest that a blockade of dermal innate lymphocyte function may be an effective therapy against the skin disease.

To selectively inactivate Tgd17 cells in animals requires an accessible target molecule specifically critical for Tgd17 cell function. We found that the dermal Tgd17 cells have a unique signaling requirement. One key molecule in Tgd17 cells necessary for their development is the Src kinase BLK. T cell subsets other than Tgd17 cells do not express BLK, which is predominantly expressed in B cells. Hence, a targeted inhibition of BLK in the skin, where B cells are rare, is predicted to affect only Tgd17 cells. We have also identified two small molecule inhibitors of BLK. Ibrutinib is a BTK (another B cell kinase) inhibitor that has been shown to strongly cross-react to BLK. Another novel BLK-targeted inhibitor is NCGC00262376-01, currently in development at NIH.

Student's Role: Using BLK inhibitors in an in vitro assay of Tgd17 cell function determine whether BLK is required for mature mouse and human Tgd17 cell function and self-renewal.

Required Skill: Cell culture. Experience with mouse models a plus but not required. However, the project may require handling mice.

Location: ASC

17. Antigen-specific anergy in human autoreactive T cells in Type 1 diabetes

Sally C. Kent, Ph.D.

Division of Diabetes

368 Plantation Street, ASC7-2011

A major goal in therapeutics of human T-cell mediated autoimmune diseases is modulation or suppression of autoreactive T cell function in an autoantigen-specific manner (avoiding global immunosuppression). This is an ongoing project where we examine the effect of chemically-coupling peptides or proteins that are the targets of autoreactive human T cells to microparticles and then asking if we can induce anergy or non-responsiveness to that protein/peptide in the T cells in a subsequent stimulation. We will characterize the anergic T cell populations for their surface markers and functionally, in attempts to 'break anergy' (assess how robust the anergy is) *in vitro* assays for both CD4 and CD8 autoreactive T cells.

The larger goal (outside the scope of this summer fellowship) of this assay is to provide appropriate diabetogenic T-cell populations for subsequent *in vivo* transplantation studies and *in vivo* induction of anergy and the basis for mechanistic studies of a clinical trial using microparticles coated with relevant proteins/peptides as inducers of anergy in Type 1 diabetes and multiple sclerosis patients.

Student's role:

The student would work directly with me, my postdoctoral fellow and our research assistant on this project and be involved in discussions of experimental design, execution and analysis.

Required skills:

This is mostly a cell culture project utilizing basic lab skills with analysis by flow cytometry and other techniques like ELISA. As part of the learning process, I would instruct the medical student in these techniques. A knowledge of immunology would be extremely useful.

Location of research:

Diabetes Center of Excellence, ASC7-2011

18. The comparison between Supraclavicular and infraclavicular approach to the brachial plexus block for upper arm dialysis access

Issam Khayata, MD

Department of Anesthesiology

55 Lake Ave, N, Worcester, MA. Second floor dept of anesthesiology

Study Design: Prospective randomized double blind study

Goal of the study: To determine if the Infraclavicular approach of the brachial plexus block is superior to supraclavicular and whether the axillary subcutaneous infiltration is required. The null hypothesis is "infraclavicular approach is more likely to block the T1 & T2 enervation of the upper arm and therefore potentially superior to supraclavicular approach.

Study groups: 4

Supraclavicular block with local anesthetic + axillary subcutaneous infiltration with local anesthetics.

Supraclavicular block with local anesthetic + axillary subcutaneous infiltration with Saline.

Infraclavicular block with local anesthetic + axillary subcutaneous infiltration with local anesthetics.

Infraclavicular block with local anesthetic + axillary subcutaneous infiltration with Saline.

Primary outcome: Incidence and amount of Local anesthetic rescue by surgeons intra-operatively. Incidence of conversion to GA due to inadequate block.

Secondary outcome: Amount of sedation used for the case. Rate of complications.

Power of the study: Number of N in each group. Methods of sensory check before incision. What statistical test to use for comparison : percent Chi-square

Student's role: Collecting demographic DATA perform sensory and motor testing before and after the block. Organize the DATA in a spreadsheet.

Required skills: basic knowledge of anatomy of the brachial plexus, excel DATA management.

Location of research: Surgical admission care unit, second floor, university campus hospital.

19. Confocal Microscopy of human VN1R1 expression

Daniel H. Libraty, M.D.

Associate Professor of Medicine

Department of Medicine, Division of Infectious Diseases

S6-751, University Campus

The student will be trained to use the confocal (fluorescent) microscope. The goal of the project will be to demonstrate cell membrane localization of human VN1R1 (a G-protein coupled receptor) transfected and expressed in an olfactory sensory neuron cell line.

No specific previous training or skills are required.

Location: S6-746 and LRB.

20. Role of Smad7 in GI tumorigenesis

Junhao Mao, PhD

Department of Cancer Biology, University of Massachusetts Medical School
364 Plantation Street, LRB 417, Worcester, MA 01605

Smad7 is an important signaling molecule of the TGF/BMP pathway. Recent large-scale genomic screenings have identified Smad7 as a risk factor for human colon cancer. However, the molecular basis for its involvement in colon cancer tumorigenesis remains poorly understood. Our lab has been using a combination of mouse genetics and cellular approaches to study the. The following aims are proposed for this summer research project.

Aim 1: Examine Smad7 expression in human colon cancer samples and mouse intestinal tumors from the genetically modified mouse models we generated in the laboratory.

Aim 2: Examine whether Smad7 is required for cell survival and proliferation in cultured human colon cancer cell lines.

Student's role: Perform research under the supervision of the PI. Data analysis and presentation.

Required skills: Basic skills in molecular biology and cell biology

Location of research: LRB 470Q

21. Vitamin D Supplementation Treatment in Bipolar Depression

Wendy Marsh, MD
Department of Psychiatry
UMMS Address: Dept of Psychiatry, University of Massachusetts
361 Plantation St
Worcester, MA 01605
Telephone number

Bipolar depression is difficult to treat and nearly all medications either have significant adverse effects or lack rigorous evidence. New effective and tolerable treatment options for bipolar depression would lead to widespread improvement of care. Herein, a study of Vitamin D supplementation for bipolar depression is proposed.

Vitamin D3 is derived from either diet or ultraviolet light on the skin, and is hydroxylated to 25-hydroxy vitamin D (25(OH)D) which is measured in the serum. Low serum (25(OH)D) is common in the Northeast. At UMass the average adult (>21yo) outpatient 25(OH)D level measured insufficient (<30 ng/ml)

Neuroendocrinologically, 25(OH)D is hydroxylated to the neuroactive form calcitriol. Calcitriol has potent endocrine effects via Vitamin D receptors throughout the adult brain. Vitamin D is involved in neurotransmitter synthesis regulation, nerve growth factor enhancement and antioxidant properties.

Calcitriol activates the gene expression of the enzyme tyrosine hydroxylase E, thereby increasing the availability of dopamine, noradrenaline and adrenaline which are well-known in the pathophysiology of mood disorders. Calcitriol enhances nerve growth factor (NGF) and glial derived neurotrophic factor (GDNF) which may also be involved in depression. Finally, vitamin D participates in the brain's defense against oxidative degeneration.

Clinically, cross-sectional studies show associations between low (25(OH)D) and high depressive symptoms. A prospective study has shown that adults with low baseline 25(OH)D experienced increases in depression scores over three to six years compared to those with higher 25(OH)D. Similarly, in patients with bipolar depression, serum 25(OH)D levels have been shown to be low.

Strikingly, there are few studies examining the association between Vitamin D administration and depressive symptoms yet they suggest a dose dependent reduction of depressive symptoms. This proposal is a randomized controlled trial of Vitamin D3 supplementation in adults with bipolar depression.

Hypothesis:

Increased 25(OH)D will result in improved mood stability, primarily reduced depression, in adults with bipolar disorder who are vitamin D insufficient.

Specific Aims:

Primary Prospectively investigate the association between changes in serum 25(OH)D levels and changes in bipolar depression symptoms in persons receiving Vitamin D3 5000 IU daily versus placebo.

Secondary Aims 1) Examine the cross-sectional relationship at study entry between serum 25(OH)D levels and severity of depression and mood elevation symptoms 2) Prospectively assess for change in mood elevation and anxiety associated with changes in 25(OH)D.

Methodology:

Design: Randomized placebo controlled trial of Vitamin D3 for 12wks.

Main Outcome Measure: Change in Montgomery-Åsberg Depression Rating Scale.

Inclusion: Adults >45years old with bipolar disorder, MADRS Score >7 (mild), Vitamin D <30ng/ml.

Exclusion: Systemic diseases, parathyroid disorder, disorders of vitD metabolism, fat digestion disorder, gi surgery, acute psychiatric urgency.

Student's role:

Learn about clinical research in practice and if interested as a career, become an expert on mood disorders and alternative / nutritional treatments. Be proactive executing, facilitating and enhancing the study (recruitment,

subject maintenance, data management, etc). Opportunity for self-directed project, (poster, presentation, case report, review article...).

Become study personnel including completion of CITI training on ethical considerations in engaging in research with human subjects. Thereupon, student may Screen potential subjects on phone, Present study by phone, Learn to administer and then give consents, Learn initial visit procedures with subjects: standardized mood assessments, phlebotomy, randomization procedures, vitamin D physiology, Learn follow up questionnaires: including standardized mood assessments and why they were chosen, Engage and administer questionnaires, Recruit and enroll study participants, phone calls to schedule and confirm appointments, Assess subject's interest in continued involvement, Track subject participation. Student's involvement will also be key to: Help recruit subjects, Help advertise and spread the word about our study, Diagnose and problem solve as it relates to the research project, Handle and protect confidential and sensitive data with integrity, Produce written, tabular and visual materials for research reports and presentations. Assist in the design, execution and evaluation of research projects, including literature reviews, surveys, data integration and analysis. Be trained in administering questionnaires, Prepare research manuscripts and research presentations. Conduct literature reviews.

Opportunity for Self-Directed Project Such as literature review or case report for publication Or presentation Or other based on student's interest

Regular contact with Principle Investigator (PI) addressing broader questions about theory of study, putting the study to practice, clinical research as a career, practice of psychiatry, women's mental health

PI available for didactic discussions related to student's areas of interest.

PI will guide and advise on student's self-directed project

Required skills: Excellent interpersonal skills including: professionalism, empathy, respect for those with mental illness. An organized, initiative taking individual will excel.

Location of research: Outpatient Psychiatry Building (anticipated move to 328 Shrewsbury St Apr13)

22. Event-related potentials in visual processing

Teresa Mitchell, Ph.D.
Dept. of Psychiatry, Shriver Center
200 Trapelo Road
Waltham, MA 02452

This project will examine how novelty and target processing are indexed in human electrophysiology. Electroencephalogram will be recorded from the scalp during active and passive oddball paradigms and components will be analyzed for variations in amplitude, latency, and scalp topography. These data will be used to pilot procedures for use with children who have moderate to severe intellectual disability.

Student's role: To develop stimulus presentation routines, collect data, and perform preliminary analyses on EEG data.

Required skills: facility with statistical packages and some basic programming, experience conducting research with human subjects preferred

Location: Shriver Center, Waltham

23. Development of monoclonal antibodies for therapeutic or diagnostic use

Deborah Molrine, MD

Clinical Affairs, MassBiologics of the University of Massachusetts Medical School
406 Walk Hill Street, Boston MA 02126

Description : MassBiologics is devoted to the discovery, development and clinical translation of monoclonal antibodies with the goal that these scientific discoveries may ultimately benefit patient care. There are several projects ongoing (infectious diseases therapeutics and evaluation of two Mabs as diagnostic biomarkers for preeclampsia) and in different states of discovery and clinical translation . Depending upon the student's interest can insert her/him in one of the projects. The student would be involved in ongoing project meetings, some aspect of hands-on work (eg cloning, ELISA measurements, data compilation), data review sessions. The student would also attend organizational talks and seminars occurring during the summer months.

Student's role: primarily perform laboratory work and assist with data review and analysis

Required skills: none required though prior laboratory experience a plus

Location of research: at MassBiologics, 406 Walk Hill Street, Boston MA 02126

24.

a. Pilot – Gestational Diabetes Mellitus and Adipose Tissue Function (GEDMAT)

b. Validation of Prepregnancy Body Shape in Pregnancy

Tiffany A. Moore Simas, MD, MPH, Med

Department: Obstetrics & Gynecology

UMMS Address: Memorial Campus – 119 Belmont Street, Jaquith Building – Floor 2 – Office JB2.008,
Worcester, MA 01605

(It should be noted that there are 2 studies. The studies are related and both will result in data critical to a grant re-submission. The roles are similar between the two. However, one is more biologic specimen focused and thus involves a labor & delivery operating room component. The other is more physical assessment focused and will be outpatient. The student would be involved in both.)

Affecting 3-8% of gravidas, Gestational Diabetes Mellitus (GDM) is one of the most common pregnancy complications. GDM is an important predictor of future health risk of mothers and their offspring. Mothers with GDM are at long term risk of T2DM (50% in 5 years), metabolic syndrome and CVD, and offspring are at risk of abnormal glucose intolerance, obesity and metabolic syndrome across the life course. Despite pregnancy being associated with weight gain and being an insulin resistant state promoted by diabetogenic placental hormone production, there are multiple other known and unknown contributors to GDM risk. Obesity is the single most powerful risk factor for GDM development; however the association between gestational weight gain (GWG) and GDM is less consistent, raising the question of what factors distinguish non-pathogenic versus pathogenic weight gain in pregnancy. It has been proposed that the expandability of SQ adipose tissue (SQAT) is a critical factor that links weight gain to T2DM risk, and that visceral AT (VAT) macrophage infiltration and inflammation are additional contributors to insulin resistance. In this research project, we will leverage novel techniques established to perform a quantitative study of SQ and VAT stromal and vascular architecture and angiogenic expandability in pregnancy. We will determine the degree of adipocyte hypertrophy, inflammatory state and angiogenic capacity, and compare these features between normal and GDM pregnancies. We hypothesize that insufficient SQAT expandability underlies GDM risk. A prospective cohort of pregnant women (GDM cases and non-diabetic controls) meeting inclusion/exclusion criteria, with plans for a scheduled Cesarean delivery for obstetric indications, will be enrolled. Biological specimens including SQAT, VAT, placenta and maternal serum will be collected at delivery. Regression models that control for potential confounders, including prepregnancy body mass index, gestational weight gain, GDM-treatment modality (i.e., diet, oral hypoglycemic agents and insulin) and pregnancy-induced hypertension, will be used to evaluate each of the study aims. This line of inquiry has the potential to become a landmark study in our understanding of the role of AT in the development of GDM, a condition that significantly increases women's and their children's risk of cardiometabolic sequelae. The mechanistic insights derived from this work will facilitate approaches for screening, monitoring, intervention and even prevention opportunities for mothers and children affected by GDM, especially in high-risk populations.

Student's Role:

1. Prescreen surgical/clinical schedules and charts to identify eligible candidates
2. Assist in contacting attending physicians and getting permission for their patients to be approached for the study
3. Assist in mailing letters to potentially eligible candidates and maintaining contact logs and HIPPA relevant documents
4. Approaching patients to explain study and consenting them into study
5. Administering study-specific surveys and tools
6. Performing study-specific physical assessments including weight measurement, skin-fold thicknesses, waist/hip/arm/thick circumferences, BP measurements, etc
7. Attendance at surgeries for collection of biologic specimens; transport of specimen to Lee lab (Biotech)
8. Chart review for study-specific data
9. Data collection, data entry and data cleaning
10. Maintenance of study stipend logs
11. Other study-related activities

Required skills:

Socially comfortable people-person who is at ease in a clinical environment with multi-disciplinary, inter-professional team members.

Great communication skills – written and verbal.

Meticulous with consistent focus regarding detail.

Ability to follow protocol and navigating medical record systems.

Ability to drive/access to transportation

Location: UMass Memorial Health Care – Memorial Campus (transportation specimens Biotech 2)

25. Treatment of Obesity in Adult Primary Care

Judith K. Ockene, PhD, MEd, MA

Department of Medicine; Division of Preventive & Behavioral Medicine

S7-755

The medical student conducts a literature search to understand the role of the PC physician in helping obese and overweight patients lose weight. She also will interview patients using a Key Informant Interview (KII) that we will develop to help determine what they think primary care physicians can do to help them decrease their weight. The student will implement a qualitative analysis of the KIIs to increase our understanding of what obese/overweight patients need from PC physicians to help them lose weight. This preliminary study will provide important information for developing an R01 to test physician-delivered interventions with obese/overweight patients.

Student's role: Perform literature search; interview participants; analyze qualitative data.

Required skills: Interviewing (communication); analysis of qualitative data will be learned during the fellowship; conducting a KII will be learned during the fellowship.

Location of research: UMMS

26. Long-term prognosis, risk factors and psychological characteristics of stress cardiomyopathy

Elena Salmoirago-Blotcher, MD

Department of Medicine

University of Massachusetts Medical School, 55 Lake Avenue North, S3-855 Worcester, MA 01655

Transient stress cardiomyopathy (TSC) is a condition detected in about 3% of patients admitted for acute coronary syndromes. During the past 20 years this syndrome has attracted the attention of researchers due to its peculiar clinical characteristics, combining a dramatic clinical presentation similar to an ST-elevation myocardial infarction (STEMI) and the almost exclusive involvement of post-menopausal women. TSC has been linked with exposure to emotional stress, high levels of plasma catecholamines, and estrogen deficiency; however, its pathophysiology is still not completely understood and the psychological profile of patients with this condition is still largely unknown. This study is designed to 1) provide preliminary data about the long-term prognosis of TSC; 2) identify possible predisposing factors for the development of TSC. We will identify women consecutively admitted to our institution with a confirmed diagnosis of TSC from January 1, 2002 to December 31, 2012. In order to determine the long-term prognosis of TSC, survival free of cardiovascular events will be compared between 60 TSC female patients and 120 STEMI historical controls. Second, possible risk factors (including psychological characteristics) for the development of TSC will be investigated using a case-control design, where possible predictors of TSC will be compared between 20 female incident cases of TSC and 40 randomly selected incident female STEMI controls.

Student's role: data abstraction; assist with participants recruitment; data analysis

Required skills : none; End-note expertise and analytical skills useful

Location of research: Shaw building

27. Elderly Patients' Perception of Fall Risk and Available Fall Education Material: a Qualitative, Interview Based Study

Heena Santry M.D.

Department of Surgery (Trauma)

55 Lake Avenue North, Worcester, MA 01604

It is estimated that one third of community dwelling Americans over the age of 65 suffer a fall each year. Three quarters of these falls occur at home, often from standing position. These seemingly innocuous events can often lead to devastating injuries.

Falls are the most common cause of traumatic brain injury and fracture in the over 65 age group. While falls are a significant cause of death for all age groups, patients >65 have significantly worse post injury outcomes than their younger counterparts. Fall victims demonstrate an increased mortality risk of 6% per year after the age of 65. Older fall victims also require longer hospital stays fraught with more complications and higher overall costs than younger patients, presumably due to their increased overall fragility^{2, 6}. Mortality rates for elderly fall patients have been estimated at around 10-20% with a near 100% mortality with an injury severity score over 25. Furthermore, 50-75% of surviving fall victims never regain their pre injury functional status and many continue to suffer significant functional decline long after their initial injury.

Despite these grim statistics, it appears that many elderly Americans do not consider fall prevention to be a priority. Elderly patients consistently rate fall risk among one of their lesser health concerns despite the fact that they are much more likely to suffer a fall than a heart attack, stroke, or other health shocks that they do consider important. Accordingly, many elderly patients have resisted traditional methods of fall prevention education. Many patients see fall prevention education as not relevant to them or not particularly important. Finding a better way to educate this population on the real risk of injuries resulting from falls is a health care priority.

The purpose of this project is two-fold. One is to explore the fall experiences of elderly patients in the Worcester area. We will interview patients about their experiences with fall and fall related injuries and the implications these incidents have had on their daily lives. We also will ask the patients about their experiences and perceptions of fall education material to attempt to uncover what the barriers to learning in this population.

To this end we will perform interviews (approximately one hour long) with patients from the trauma clinic as well as geriatric primary care offices. These interviews will be tape recorded, transcribed, and then analyzed with qualitative software for compilation in a manuscript. Once interviews are complete the study may be expanded to include surveys on the same topics. The themes uncovered during this endeavor will be applied to the development of a fall prevention education tool for distribution in the same clinics.

Student Roles:

- Assist with interviews and survey dispersal to the target population.
- Modify the interview script and/or survey questions as needed.
- Utilize software to analyze the content of the interviews.
- Perform a thorough literature search on a relevant topic (perception of fall risk, perception of education materials, etc) and participate in the writing of the background and motivation sections of the manuscript on the topic of interest
- Participate in weekly (and additional as needed) methodology meetings on topic of choice
- Participate in summer "Research Introduction" curriculum as part of the Surgical Research Scholars Program
- Assist PI in completing results and discussion portion of the manuscript
- Produce a poster suitable for presentation by end of summer

Required skills:

- Ability and willingness to interact with patients for one hour interviews.
- Ability to perform literature searches using basic sources (PubMed).
- Experience with interviews and/or surveys is helpful but not required
- Must have excellent interpersonal skills

Location of Research: UMass Department of Surgery, Center for Outcomes Research (University Campus)

28. Defective Daily Thermoregulation in a Mouse Model of Amyotrophic Lateral Sclerosis

William Schwartz, MD
Department of Neurology
S5-745

Our current understanding of the pathogenesis of the familial form of amyotrophic lateral sclerosis (ALS) has been aided by the study of transgenic mice that over-express mutated forms of the human CuZn-superoxide dismutase (*SOD1*) gene. The concept has emerged that mutant *SOD1* in motor neurons determines disease onset but that other non-cell autonomous factors are critical for disease progression; while a role for affected glia has attracted much attention, we have been intrigued by the possibility that a systemic disorder, sp., defective energy metabolism and temperature regulation, may be critically involved in the disease.

We have collected preliminary data in the *SOD1*-G93A transgenic mouse model that demonstrates a significant thermoregulatory defect, with diminished body temperature during the dark (behaviorally active) phase of the light-dark cycle. The defect occurs early in the disease, at the same time that grip strength becomes significantly affected, but well before the onset of neurological signs or altered locomotor activity. Voluntary wheel running normalizes the daily temperature rhythm and possibly slows disease progression.

Our objective in this project is to analyze energy metabolism and temperature regulation in the G93A mouse model. We hypothesize that the dark-phase temperature defect in G93A mice is due to *decreased* heat production from inadequate brown adipose tissue (BAT) thermogenesis and/or *increased* heat loss from excessive thermal conductance.

In **Aim A**, we will quantitatively measure the daily rhythm in metabolic rate, the capacity for nonshivering thermogenesis, and the effect of housing at thermoneutral ambient temperatures. Such studies will provide unique normative data and serve to distinguish pathologies due to reduced heat production from those due to excessive heat loss.

In **Aim B**, we will assess the function of BAT, testing for an afferent defect in its *activation*, an intrinsic deficiency in its *capacity*, and/or the dysregulation of its circadian clock. Such studies are the first step to further dissect the mechanism(s) responsible for a thermoregulatory defect that is restricted to the dark phase.

Understanding the impact of defective metabolism on ALS may improve our understanding of systemic contributions to the disease, pointing the way for therapeutic interventions that could complement those aimed at improving motor neuron survival.

Student's role: The student will work directly with the principal investigator and graduate student (PhD thesis project), from designing and executing experiments to data analysis. The student may be required to travel offsite (Williams College, Williamstown, MA) as some of the experiments may be conducted there. The student will also be expected to become familiar with current literature to better understand the experimental rationale and contribute to data interpretation.

Required skills: Willingness and ability to work with animals (mice) and basic understanding of mammalian anatomy and physiology. General knowledge of laboratory techniques (western blots and QPCR) would be helpful.

Location of research: S5-746, S5-734, S5-724, Animal Facility, (Williams College, see above)

29. The role of employment supervisors in supporting and accommodating workers with chronic medical conditions

William S. Shaw, Ph.D.

Department of Family Medicine and Community Health

Liberty Mutual Research Institute for Safety, 71 Frankland Road, Hopkinton, Massachusetts 01748.

The objective of this qualitative study in occupational health is to extend our knowledge of how supervisors facilitate workers' efforts to manage chronic medical conditions at work and assess whether there are opportunities for supervisor skills training and policy development in this area. This project is the first phase of a larger multi-phased project, which will likely include the development and testing of a supervisor training intervention, including stakeholder feedback from workers, providers, and employers. The results of the qualitative interviews conducted during this first phase will be used to inform a training program to aid supervisors in supporting and accommodating their workers with chronic health problems. To accomplish this first step, we will conduct in-person semi-structured interviews with supervisors at 5 to 6 companies, interviewing 5 to 7 individuals per company – for a total of approximately 35 interviews. Each interview will be audio-recorded and transcribed. We will use a grounded theory approach to analyze the transcribed interviews, using NVivo® qualitative software and coding the interviews for emergent themes and concepts. The results of this study will provide direction and substantively inform the subsequent phases of the overall research project. The project has been fully funded by Liberty Mutual Insurance and has received Institutional Review Board approval from the Harvard School of Public Health.

Student's Role: The Liberty Mutual Research Institute for Safety (LMRIS - located in Hopkinton, MA) is a non-proprietary research center funded by Liberty Mutual Insurance and dedicated to scientific, peer-reviewed research in occupational safety and disability prevention. The student's primary role in this project would be to participate in supervisor interviews and assist in the qualitative analysis of supervisor interview transcripts using the NVivo® software application. This methodology involves review of transcripts for common themes and categories of discussion, and the project team will provide the direction and training necessary to guide the student's work. The project is a joint collaboration between Dr. Shaw (a clinical health psychologist) and Dr. Candace Nelson, a post-doctoral fellow at the Harvard School of Public Health. In addition to the computer-assisted analysis of transcripts, there will be an iterative process involving repeated meetings with the research team to compare observations, agree on common terminology and themes, and discuss discrepancies. This work will ultimately involve the production of a journal manuscript, and the student may elect to participate as a co-author on this future publication to reflect his/her contribution to the study. This summer internship would also involve exposure to and potential involvement with other on-going projects at the Institute in occupational health and wellness. We believe this summer internship would provide an excellent introduction to research issues in occupational health, disability, and chronic medical conditions.

Required skills: The student should have sufficient English language skills to participate in interviews with employment supervisors and analyze verbal transcripts. No prior research experience is necessary. A student with future interests in occupational health or family medicine would be the best fit.

Location of research: Liberty Mutual Research Institute for Safety, 71 Frankland Road, Hopkinton MA

30. Role of microRNAs in liver diseases

Gyongyi Szabo, MD, PhD
Department of Medicine
LRB-208

MicroRNAs (miRNAs) are small, non-coding RNAs that regulate target genes at the transcriptional level. miRNAs play essential roles in liver diseases by regulating processes like inflammation, lipid metabolism, cell proliferation and regeneration. This project will investigate the role of various miRNAs in liver diseases. The utility of circulating miRNAs as biomarkers of liver injury and inflammation will also be studied.

Student's role: Isolation of microRNAs from tissues, serum, plasma and real-time PCT to quantify miRNAs. Other techniques might also be involved.

Required skills: Sufficient ability to hold and use a pipet and enthusiasm for the project.. No specific skills required but previous lab experience is a plus.

Location of research: LRB 2nd floor

31. Role of Hdac3 during Cardiac Development

Chinmay Trivedi, MD PhD
Department of Medicine
368 Plantation St, AS7-1016, Worcester, MA 01605

Description: Congenital and adult heart diseases are the leading causes of mortality in the developed world. The underlying pathology is improper development of cardiomyocytes that leads to the heart defects in 1% of newborn children and loss of diseased cardiomyocytes that leads to heart failure in adults. Unfortunately, heart is one of the least regenerative organs in the body with negligible endogenous capacity to repair or replace affected cardiomyocytes. Ability of pluripotent stem cells and cardiac progenitor cells to progressively and restrictively differentiate into various lineages, like cardiomyocytes, smooth muscle cells and endothelial cells, provides tantalizing promise for exogenous cell-based therapy. However, lack of thorough understanding of the mechanisms governing lineage commitment and differentiation of these progenitor cells to mature cardiomyocytes significantly limits our ability to harness its therapeutic potential. My lab is interested in understanding the roles of chromatin and epigenetic modifications during cardiac development and diseases. Specifically, we study the roles of chromatin modifying enzymes, like histone deacetylase 3 (HDAC3), in cardiac progenitor cells. Using various genetic murine models, we investigate how cardiac progenitor cells differentiate into various lineages to form functional heart in developing embryo. Our recent study shows that Hdac3 acts as a key regulatory switch within bipotent cardiac progenitor cells to promote cardiomyocyte lineage specification. Mice lacking Hdac3 in bipotent cardiac progenitor cells show complete embryonic lethality and severe developmental myocardial defects like hypoplastic ventricles, atrial and ventricular septal defects. In addition, Hdac3 deficient bipotent cardiac progenitor cells precociously and preferentially differentiate towards cardiomyocytes lineage.

Student's Role: We have recently identified an important functional relationship between Hdac3 and T-box transcription factor regulating lineage specification of cardiac progenitor cells. Using various cell and molecular biology / biochemistry related techniques (performed routinely in our lab), student will characterize functional relationship between Hdac3 and T-box gene.

Required Skill: Microsoft office, Prior research experience in cell and molecular biology / biochemistry is desired but not required.

Location of Research: Sherman Center, AS7-1016