

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



**MEDICAL STUDENT  
SUMMER RESEARCH FELLOWSHIPS**

**CATALOGUE  
2009**

**Directors:**

***Michael Godkin, PhD***

Family and Community Medicine

***Anthony Poteete, PhD***

Molecular Genetics and Microbiology

**Program Coordinator:**

***Christine Locke***

Office of Medical Education

# TABLE OF CONTENTS

<b><u>Subject Area</u></b>	<b><u>Project Number</u></b>
<b>Clinical</b>	<b>1 – 9</b>
<b>Laboratory</b>	<b>10 – 21</b>
<b>Social</b>	<b>22 – 34</b>
<b>Clinical/Translational Research Pathway Program Projects</b>	<b>35 - 43</b>

*March 2009*

## **1. Clinical**

**TITLE: Clinical Outcomes Following Solid Organ Transplantation of Prisoners – A Single Center Experience**

**Sonia N. Chimienti, MD - Co-PI**  
**Jennifer S. Daly, MD - Co-PI**  
**Shimul Shah, MD - Co-PI**  
**508-856-3158**

**UMass Medical School**  
**Medicine/Infectious Diseases (SNC and JSD)**  
**Surgery/Transplantation Surgery (SS)**  
**55 Lake Avenue North, S7-715 (Division of Infectious Diseases)**  
**Worcester, MA 01655**

**Description:** UMass Memorial Medical Center is the only transplant center in the region that provides solid organ transplantation to incarcerated persons. The outcomes of transplantation of patients who are incarcerated has not been reported in the literature. It is expected that graft survival and patient survival would be equal to, if not better, than patients who are not incarcerated, based on access to medical care and the standard of care in general that patients in prison in the United States receive. For this project, we will retrospectively review data on all incarcerated patients who have received a liver, kidney or pancreas transplant at UMass Memorial Medical Center. Outcomes will be reported, including graft and patient survival and infectious complications.

**Student's Role:** The student will be mentored with regard to the entire process of retrospective clinical research, from IRB approval, to formulating a data collection method, to developing a research database, to searching medical charts for data, entering data, cleaning up data, data analysis, and preparation of a manuscript. It is expected that this project could be completed, in its entirety, with a manuscript in preparation, during the course of the summer.

**Required Skills:** Interest in clinical research, ability to use Microsoft Excel. Knowledge of Microsoft Access is beneficial but not necessary. Similarly, knowledge of basic biostatistics and epidemiology, and familiarity with statistical analysis is helpful but not necessary. Statistical analysis will be done using either STATA or SPSS. Mentoring will be comprehensive, throughout the project.

**Interview:** Required

**Location:** University Campus

## **2. Clinical**

**TITLE: Impact of ED Care of Acute Heart Failure Patients on Short-term Outcomes**

**Chad E. Darling, MD  
(508) 421-1464**

**UMMC  
Emergency Medicine Lakeside 174  
55 Lake Avenue North  
Worcester, MA 01655**

**Description:** This project is an observational study of the clinical care of Heart Failure (HF) in the Emergency Department (ED). The goal is to investigate how the early ED- based treatment of patients with acute HF (AHF) impacts short term outcomes such as: the need for ICU admission and length of ICU stay, total length of hospitalization (LOS), and associated improvements in symptomatology. The primary hypothesis is that **early (<1 hour) use of vasodilators, in AHF patients, will result in improved short-term outcomes compared to patients treated with vasodilators later in their ED stay or in the hospital.** Data collection will be via prospective enrollment/observation of AHF patient-care in the ED as well as from chart reviews done after the patient is discharged home. It is necessary to collect data from direct observation because ED documentation of key pieces of information such as urine output, timing of medication administration and vital signs may be documented inaccurately or incompletely in the medical record. The chart review component is necessary as it will be the primary method of determining several key outcomes such as Length of Stay (LOS). Short-term symptom improvement will be analyzed as an outcome and will be assessed by a Visual Analog Scale both in the ED and later in the hospital.

**Student's Role:** To begin the student will be taught about the nature of the problem and what has driven the development of this research project. The student will have the opportunity to gain experience in clinical research by directly interacting with patients for enrollment (consent) and by obtaining visual analog scale recordings of symptom severity. They will spend time observing care and observing the timing of key interventions such as medication administration, vital sign changes. They will be taught to perform chart reviews, data entry and if they choose to do so they can learn how the data is analyzed by working with the PI. This project would be well suited to motivated individuals who are looking for a patient oriented research experience. The student will also have the option of participating in the development of a research poster based on data already collected in this area.

**Required skills:** Strong interpersonal and communication skills for staff and patient interactions. Other tasks will be taught

**Interview:** Required

**Location:** University Campus ED

### **3. Clinical**

**TITLE:** Total Joint

Patricia D. Franklin, MD, MBA, MPH  
David Ayers, MD Chair – Orthopedics  
Contact: Janel Milner (508) 856-2202  
[Janel.Milner@umassmed.edu](mailto:Janel.Milner@umassmed.edu)

UMMC  
University Campus  
Orthopedic Surgery  
55 Lake Avenue, North  
Worcester, MA

**Project Description:** The student will assist in NIH funded clinical research designed to (1) measure and (2) improve physical activity and function in adults with knee arthritis who have total knee replacement surgery.

**Student's Role:** Daily work will include survey administration, data management, and participation in a clinical research team comprised of surgeons, nurses, and research professionals. Students will be exposed to ambulatory and surgical patient care in the course of the research.

**Interview:** Required

**Location:** University campus Dept of Orthopedic Surgery

#### **4. Clinical**

**TITLE:** Spine Center

**Patricia D. Franklin, MD, MBA, MPH**  
**Patrick Connolly, MD**  
**Contact: Janel Milner (508) 856-2202**  
**[Janel.Milner@umassmed.edu](mailto:Janel.Milner@umassmed.edu)**

**UMMC**  
**University Campus**  
**Orthopedic Surgery**  
**55 Lake Avenue, North**  
**Worcester, MA**

**Project Description:** The student would participate with prospective and retrospective data collection and entry in the Spine Center. The goal of the project will be to establish a database from which meaningful conclusions can be drawn, specifically towards the efficacy and safety of various implants and bone graft substitutes commonly used by UMass Orthopedic Spine surgeons.

**Student's Role:** The student will work closely with residents and Attendings to develop novel hypotheses and resource the database for critical analysis. The student will also attend weekly Spine department research meetings and have an opportunity to shadow a spine surgeon in clinic as well as in the OR.

**Interview:** Required

**Location:** University campus Dept of Orthopedic Surgery

## **5. Clinical**

**TITLE: Evaluation of Wound Bed and Granulation Tissue Before, During and After Negative Pressure Wound Therapy**

**Ronald A. Ignotz, PhD, Janice F. Lalikos, MD and Raymond M. Dunn, MD**  
**Department of Surgery, Division of Plastic Surgery**  
**Room S4-741, University Campus**  
**55 Lake Ave., North**  
**Worcester, MA 01655**  
**508-334-7692**  
[Ronald.ignotz@umassmed.edu](mailto:Ronald.ignotz@umassmed.edu)

**Description:** Negative Pressure Wound Therapy (NPWT) is being used increasingly to facilitate the closure of both acute and chronic wounds as evidenced by the large volume of literature regarding NPWT. The two principal systems for delivering NPWT are via (1) an open pore foam dressing versus (2) a gauze based dressing. Little direct comparison of the effectiveness of the two systems has been reported though a recent retrospective report suggests similar efficacy of the two approaches (2). Several recent reviews, however, point to the paucity of high quality trials and the difficulty in making definitive statements concerning the efficacy of NPWT (3-5). Complete wound closure via NPWT may not be the clinical goal. In some trauma cases, wounds cannot be closed primarily due to loss of tissue or substantial edema initially. In those cases, NPWT is being used to stabilize the wound and permit growth of granulation tissue in preparation for the application of a tissue flap or skin graft to accomplish wound closure. Likewise, application of NPWT to chronic wounds may have the greatest effect in altering the quality and biochemistry of the wound bed such that it may more successfully accept a graft for secondary closure.

Despite the widespread use of NPWT, little analytic data exists in the literature regarding the cellular or biochemical effects on the wound bed. Very recently, a few reports have begun to examine the effects of negative pressure on a few genes and biochemical markers of wound repair including fibroblast proliferation (6-8). In a study comparing 15 patients receiving topical negative pressure (TNP) and 18 patients receiving a conventional dressing of chronic wounds, Moues, et al. (6) reported that the level of pro-MMP-9 was lower in wound fluid following TNP. Greene, et al. (7) also observed lower levels of MMP-9 as well as MMP-2 in VAC treated wounds of three patients with chronic wounds. They also noted an increase in the micro vessel density and correlated these changes to micro deformation caused by the foam dressing. Lastly, Grimm, et al. (8) reported that HIF-1 $\alpha$  (hypoxia-inducible factor-1 $\alpha$ ) is reduced in concentration following TNP therapy (five patients) of radiation-induced wounds implying that there is a decrease in tissue hypoxia following TNP. The authors suggest the decrease in HIF-1 $\alpha$  may be related to an observed enhanced perfusion of the tissue after TNP however this remains to be demonstrated. Each of these reports have appeared within the past eighteen months and are among the initial attempts to understand the biochemical and cellular mechanisms operative during NPWT.

This proposal describes an approach, in patients, to analyze a number of parameters associated with wound healing and how they may change when subjected to negative pressure wound therapy. A comparison will be made of the two primary dressings, woven gauze and open-pore foam. We will analyze the wound bed granulation tissue histologically and biochemically. Biopsies of the wound bed will be collected and subjected to immunohistochemistry for several extracellular matrix components associated with wound healing. These include Collagen Types 1 and 3, Matrix metalloproteinase, elastase, and KI-67, a cell proliferation marker. In addition, biopsies will be extracted and analyzed via ELISA for a panel of growth factors and cytokines. The quantification of biochemical changes in the wound bed is a necessary prerequisite to establishing the efficacy of Negative Pressure Wound Therapy for wound healing.

#### Literature:

1. Chariker, et al. (1989) Effective management of incisional and cutaneous fistulae with closed suction wound drainage. Contemp. Surg. 34: 59-63.
2. Campbell, et al. (2008) Retrospective clinical evaluation of gauze-based negative pressure wound therapy. Internet Wound J. 5: 280-286.
3. P. Vikatmaa, et al. (2008) Negative Pressure Wound Therapy: a Systematic Review on Effectiveness and Safety. Eur. J. Vasc. Endovasc. Surg. (epub, June 2008).
4. S. Gregor, et al. (2008) Negative Pressure Wound Therapy, A Vacuum of Evidence? Arch Surg. 143: 189-196.
5. D.T. Ubbink, et al. (2008) A systematic review of topical negative pressure therapy for acute and chronic wounds. Br. J. Surg. 95: 685-692.
6. C.M. Moues, et al. (2008) The role of topical negative pressure in wound repair: Expression of biochemical markers in wound fluid during wound healing. Wound Rep. Reg. 16: 488-494.
7. A. Grimm, et al. (2007) Expression of HIF-1 $\alpha$  in irradiated tissue is altered by topical negative-pressure therapy. Strahlenther Onkol. 183: 144-149.
8. A.K. Greene, et al. (2006) Microdeformational Wound Therapy, Effect on angiogenesis and matrix metalloproteinases in chronic wounds of 3 debilitated patients. Ann. Plast. Surg. 56: 418-422.
9. S. Ichioka, et al. (2008) A technique to visualize wound bed microcirculation and the acute effect of negative pressure. Wound Rep Reg. 16: 460-465.
10. S. Jacobs, et al. (2008) Efficacy and mechanisms of vacuum-assisted closure (VAC) therapy in promoting wound healing: a rodent model. J. Plast Reconst Aesthet Surg. (epub)



11. A. McNulty, et al. (2007) Effects of negative pressure wound therapy on fibroblast viability, chemotactic signaling, and proliferation in a provisional wound (fibrin) matrix. Wound Rep Reg 15: 838-846.
12. Thompson, H.G.R. et al. (2006) Epithelial-derived TGF- $\beta$ 2 modulates basal and wound-healing subepithelial matrix homeostasis. Am. J. Physiol. Lung Cell. Mol. Physiol. 291: L1277-L1285.
13. Trebault, A. et al. (2007) Regulation of fibroblast migration by tenascin-C. Biochemical Society Transactions 35: 695-697.

**Student's Role:** The student will participate in all aspects of this research from interacting with patients by obtaining informed consent, assisting in dressing application and taking wound photographs and measurements, processing tissue samples for histology and biochemical analysis. The student will be required to complete the CITI course and exam for certification to participate in research with human subjects prior to the start of the project.

**Interview:** Required.

**Location:** Room S4-752, Plastic Surgery Research Laboratory  
University campus

## **6. Clinical**

### **TITLE: Evaluation of the Reliability of Liver Attenuation Measurements using CT**

**Young H Kim, MD., PhD**  
**508-334-2087**

**UMass Medical School**  
**Department: Radiology**  
**55 Lake Ave. North**  
**Worcester, MA 01655**

**Description:** To our knowledge the reliability of liver attenuation measurement using MDCT with different protocols has not been well studied. With the emergence of obesity as the leading co morbidity in the United States today, noninvasive hepatic fat quantification has become increasingly important. Primary nonalcoholic fatty liver disease is now considered the major hepatic manifestation of the metabolic syndrome. Additionally, preoperative evaluation of hepatic steatosis is critical for liver donor selection.

Although hepatic core biopsy is currently the standard method for accurate quantification and characterization of macrovesicular steatosis, it is invasive and is associated with risk. Unenhanced CT provides a reasonable assessment of hepatic steatosis, with fatty infiltration of the liver manifesting as a decrease in parenchymal attenuation. The degree of attenuation decrease has been related to the degree of fatty infiltration of the liver. However, there are multiple technical limitations of CT scanning including the calibration of different scanners and the establishment of standards to account for inter- as well intra-individual variability in attenuation values. In addition, how patient's body habitus and different parameters such as pitch, slice thickness, scanner design and automated tube current modulation affect attenuation measurement have not been well studied. The cohort under investigation will include adult patients with an incidental solitary pulmonary nodule who had undergone noncontrast chest CT that included the liver and spleen within a period of 6 months. Pulmonary nodule follow-up chest CT studies were chosen as patients would have already had multiple studies within the given time frame, allowing us a reasonable standard reference for the study. A computer database search of subjects who underwent chest CT in the department of Radiology at UMass will be performed. Quantitative measurement of liver and spleen will be conducted for statistical analysis. At the end of the research, we will be able to determine reliability regarding liver attenuation measurement using CT.

**Student's Role:** Analysis of CT scan data. Student will determine if available measurements meet inclusion criteria.

**Required skills** Understanding of gross anatomy of the human body, particularly of the liver. Basic computer skills.

**Interview:** Required

**Location:** Radiology Department, University campus

## **7. Clinical**

### **TITLE: The Impact of Perimenopause on the Clinical Course of Bipolar Disorder**

**Wendy Marsh, MD**  
**(508) 865-7051**

**UMass Medical School**  
**Department of Psychiatry**  
**Room S5-418**  
**55 Lake Avenue, North**  
**Worcester, MA 01655**

**Description: Background:** Mood can vary dramatically in relation to a woman's reproductive phases. Increasing prospective evidence indicates the menopausal transition is a period of susceptibility to depression in women without a history of mood disorder. A systematic evaluation is warranted to improve our understanding of the clinical course of bipolar disorder during the perimenopause.

**Aim:** Prospectively evaluate mood and endocrinological changes during the menopausal transition in women with bipolar disorder

**Hypothesis:** Women in the late perimenopause and women with greater fluctuations of FSH and estradiol will have greater severity of depression.

**Methods:** Women with bipolar disorder I, II, or NOS in the early or late perimenopause or post-menopause will undergo a diagnostic mood assessment, menstrual history and reproductive endocrinological battery at entry. The ChronoRecord Software Program, Tall Tree Software, Inc is a novel concept tool developed and validated for prospective mood and reproductive status monitoring. Daily, subjects will enter mood on a 100pt visual analog scale, sleep, medication, menstruation and hot flushes into the ChronoRecord Program (2-5min/day). Monthly assessments include estradiol and follicle stimulating hormone (FSH) and standardized mood evaluations.

**Other:** Author has other projects in relation to mood and reproductive phases including a large prospective data base on patients treated for bipolar disorder from which projects can be crafted to fit student's interests.

**Student's Role:** Can be tailored to student's interests. Including helping initiate the primary study looking at the impact of perimenopause on bipolar disorder. This role would include learning standardized mood assessments for mania and depression including training in the ChronoRecord Software, initiating data organization and management, interacting with subjects (telephone screen, initial visits, etc). Opportunities for self-directed projects and potential for publication/posters include creating a testable hypothesis based on the large longitudinal bipolar disorder patient data base, or literature reviews under the mood disorder and reproductive endocrinology rubric, or support for background and analysis in a paper on hot flashes and depression.

Students interested in psychiatry will be given time/encouraged to attend grand rounds, and relevant resident education and department talks.

**Required Skills:** Interest in Mood Disorders and Reproductive Endocrinology, facile with literature searches, well organized, good people skills.

**Interview:** Required

**Location:** Med School &/or Psychiatry Outpt Building @ 361 Plantation

## **8. Clinical**

### **TITLE: Acute Effects of Vagus Nerve Stimulation on Appetite Hormones in Adults**

**Sherry Pagoto, PhD Assistant Professor**  
**Telephone 508-856-2092**

**UMass Medical School**  
**Department: Medicine, Division of Preventive and Behavioral Medicine**  
**55 Lake Avenue, North, S7-717**  
**Worcester, MA 01655**

**Description:** Vagus Nerve Stimulation (VNS) is an FDA approved treatment for treatment-resistant epilepsy and depression. Animal research has revealed weight loss and decreased appetite as side effects of VNS. One laboratory study with humans demonstrated that acute VNS was associated with change in food cravings for sweets, such that participants with longer device on-time, higher levels of depression and obesity experienced decreased sweet food cravings during activation.<sup>1</sup> A possible mechanism of the effect of VNS on food craving may be related to research linking the vagus nerve to the action of hormones that influence hunger and satiety. For example, appetite-regulating hormones such as leptin and cholecystokinin (CCK) activate vagus afferent nerves which results in reduced food intake.<sup>2</sup> On the other hand, release of ghrelin, which is mediated by vagal nerve pathways, stimulates hunger and meal initiation.<sup>3</sup> Vagotomy has been shown to reduce plasma leptin, elevate plasma ghrelin,<sup>4</sup> and at least partially block CCK-induced satiety.<sup>5</sup> Electrical stimulation of the vagus nerve has been shown to decrease ghrelin in rats<sup>6</sup> and vagal stimulation via sham feeding has been shown to decrease ghrelin in humans.<sup>7</sup> These studies suggest that VNS might have an appetite-suppressing effect, but this has never been directly explored. Therefore, the purpose of this project is to explore the effects of acute VNS on appetite hormones in adults. We hypothesize that ghrelin will be suppressed and leptin and CCK will be increased following consumption of 400-calorie load during VNS activation compared to inactivation. Secondary outcomes include other gut hormones assessed via the multiplex kit (Millipore Corp), including amylin (active and total), PYY, insulin, PP, GLP-1, and GIP. Participants with depression or epilepsy (N=30) are being recruited for this study, with half of the participants use VNS therapy. Two sessions are being completed that last 4.5 hours and blood measures of leptin, CCK, and ghrelin have been assessed every 30 minutes for a total of 8 time points. Participants using VNS therapy will complete two study sessions with their VNS activated at their usual clinical device settings and two study sessions with their VNS inactivated. Following the initial baseline measure, participants will consume a 400 kcal nutritionally-balanced milkshake (40% carbohydrate, 30% protein, 30% fat). Secondary outcomes will include subjective appetite (hunger, fullness, desire to eat, and prospective food consumption) and occur at 0-, 15-, 30- minutes and then at 30-minute intervals afterwards up to 240 minutes.

**Student's Role:** Student will be responsible for assisting in the analysis of appetite hormone data, literature review, and manuscript preparation for this project.

**Required skills:** Strong computer skills, basic knowledge of stats a plus but not mandatory

**Interview:** Required

**Location of research:** Medical School and Shaw Building

## **9. Clinical**

**TITLE:** Assessment of Olfactory Processing in Parkinson's Disease Patients

**Julie G. Pilitsis MD, PhD**  
(508) 334-0046

**UMass Medical School**  
**Department of Neurosurgery – Surgery**  
**Room S2-850**  
**55 Lake Avenue, North**  
**Worcester, MA 01655**

**Description:** It has become increasingly recognized that olfactory loss occurs during the pre-motor stages of Parkinson's Disease. Our group's recent focused on improving the positive predictive value of olfactory testing, by combining with a battery of psychological tests. Forty-five patients (Hoehn and Yahr stages 1-3, age 68.8  $\pm$  10.4, 24% female) and 44 age-matched controls (age 66.2  $\pm$  7.9, 45% female) were recruited and completed surveys of olfaction (Univ. of Penn. Smell Identification Test, UPSIT), mood (Beck depression inventory), apathy (Apathy Evaluation Scale, AES), and general health (UK Parkinson's Disease Society questionnaire, PDS). We found that general olfaction loss is a highly predictive marker of PD (sensitivity 93%, specificity 92%,  $p < 0.0001$ ). When a staged diagnostic algorithm that combines olfaction and apathy was used, it provided a positive predictive value of 91% (sensitivity 98%, specificity 88%). The second stage of this study involves exploring the mechanism of olfactory loss in a subset of PD and control subjects using functional MRI ( $n=12$ ). The mechanism of olfactory loss is under debate. Specifically, two pathways of olfactory processing have been identified, a direct pathway from the piriform cortex to the orbitofrontal cortex and an indirect pathway that includes the mediodorsal nucleus of the thalamus. Thus, it is unclear whether it is changes in the basal ganglia or in the cortical circuitry or both which leads to olfactory loss. In this phase of the study, subjects will undergo an imaging session in the functional MRI. The subject will be exposed to a series of neutral odors (via an odorometer) and tones (via headphones) according to a pre-determined program. Quantitative measure of activation in precise volumes of interest (VOI) related to the olfactory pathway, under different experimental paradigms will be analyzed and the control and PD groups compared. The goal of the study is to collect preliminary data for NIH funding and is currently funded by a pilot grant from the Worcester Biomedical Research Foundation.

**Student's Role:** Greeting patients and facilitating imaging session with qualified personnel, data analysis, statistics, writing.

**Required Skills:** Familiarity with Excel, word processing, basic data analysis, writing skills

**Interview:** Required

**Location:** University Campus S2-850

## **10. Laboratory**

**TITLE: Treatment of Neurodegenerative Diseases Through Axon Protection**

**Zheng-Zheng Bao, PhD  
(508) 853-6202**

**Program in Neuroscience  
Interdisciplinary Graduate Program  
Department of Medicine and Cell biology  
University of Massachusetts Medical School  
LRB #221  
364 Plantation St.  
Worcester, MA 01605**

**Description:** Neurodegenerative diseases affect nerve cells and their long cables (axons) which transmit signals in the neural circuit. Recent results from animal models and patient studies indicate that degeneration of axons may be a primary feature of some of the neurodegenerative diseases including amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) and glaucoma. Damage in the axon cables precedes symptom onset and nerve cell death. This new paradigm points to new therapeutic strategies for treatment of neurodegenerative diseases, including interference of axon cable self-destruction program and re-growth of damaged axons.

However, axons in the adult central nervous system (CNS) normally do not regenerate. My laboratory has established culture systems for screening molecules that promote survival and regeneration of the adult optic nerve axons. This project will utilize this system to screen small molecule compounds and combination of factors to determine whether they enhance regeneration of axons. The factors identified from the in vitro culture screens will be further tested in a glaucoma mouse model, DBA/2J.

**Student's Role:** prepare neural explant cultures, prepare solutions for compounds and factors to be tested, assay axon regeneration by staining with antibodies specific for regenerated axons, quantification of regeneration.

**Required Skills:** None, will train.

**Interview:** Required

**Location:** LRB second floor, 270F

## **11. Laboratory**

**TITLE: Oral delivery of siRNA to Silence genes in Macrophages**

**Michael P. Czech, Professor and Chair  
508 856-2254**

**University of Massachusetts Medical School  
Program in Molecular Medicine  
373 Plantation Street  
II Biotech, Suite 100  
Worcester, MA 01605**

**Description:** The autoimmune reactions that cause destruction of beta cells and type 1 diabetes are driven by autoreactive T cells in association with innate inflammatory cells (macrophages and dendritic cells). Paradoxically, recent research indicates these latter cells in the immature state also play key roles in establishing immunological tolerance, through presentation of antigens to T cells within a “tolerogenic” context. One of the most promising concepts that has emerged from these studies is that induction of immunological tolerance to beta cell auto-antigens might prevent or even alleviate the disease. Immunological tolerance has many forms and mechanisms, but a major paradigm is the generation of regulatory T cells (T-regs) by tolerogenic macrophages or dendritic cells that suppress the cascade of events leading to auto-reactivity and beta cell apoptosis. These events appear to take place in the local regions of the islets and nearby lymph nodes. Further, the gut-associated lymphatic system represents a key site where induction of immunological tolerance may be critically important. This collaborative research project with Gary Ostroff’s laboratory is based on our discovery that siRNA encapsulated within micron-sized, hollow shells of beta 1,3-D-glucan can be delivered orally to mice to target dendritic cells and macrophages in the gut. This technology advance enables us to integrate two approaches that might promote immunological tolerance to prevent or alleviate type 1 diabetes: 1) tolerize the gut immune system to beta cell antigens through targeted antigen delivery to dendritic cells and macrophages in the gut; 2) orally deliver RNAi to silence genes that control the secretion of proinflammatory cytokines, co-stimulatory receptors or “maturity” factors in dendritic cells and macrophages during the early stages of beta cell antigen presentation to induce T-reg and hypo-responsive T cells. Type 2 diabetes in obesity is also associated with an inflammation phenotype—in this case within adipose tissue. Thus, we have also initiated experiments to target macrophages in obese mouse models of type 2 diabetes with orally delivered siRNA directed against genes that control inflammation. Rotation projects in the Czech laboratory applying oral delivery of encapsulated siRNA to mouse models of both types 1 and 2 diabetes are now available to graduate students.



**Student's Role:** the student will work closely with myself and a postdoctoral fellow to test whether oral delivery of encapsulated siRNA will enhance glucose tolerance in obese mouse models of diabetes.

**Required Skills:** Medical school courses

**Interview:** Required

**Location:** II Biotech, Suite 100

## **12. Laboratory**

**TITLE: Regulation of Transmembrane Signaling in the Heart**

**James Dobson, PhD**

**(508) 856-3775**

**[James.dobson@umassmed.edu](mailto:James.dobson@umassmed.edu)**

**University of Massachusetts Medical School**

**Department of Physiology**

**55 Lake Avenue, North**

**Worcester, MA. 01655**

**Description:** Student would carry out a project involving the determination of how left ventricular function is affected by cardioactive agents in intact and genetically modified mouse hearts .

**Student's Role:** Student would carry out a project involving the determination of how left ventricular function is affected by cardioactive agents in intact and genetically modified mouse hearts .

**Required Skills:** None in particular, but perhaps an interest in small animal surgery.

**Interview:** Required

**Location:** UMass Medical School

### **13. Laboratory**

**TITLE:**       **Regulation of Intracellular Signaling in the Heart**

**James Dobson, PhD**

**(508) 856-3775**

**[James.dobson@umassmed.edu](mailto:James.dobson@umassmed.edu)**

**University of Massachusetts Medical School**

**Department of Physiology**

**55 Lake Avenue, North**

**Worcester, MA. 01655**

**Description:** Student would carry out a project involving the determination of how protein kinases and phosphates are affected by cardioactive agents in normal and genetically modified mouse hearts .

**Student's Role:** Student would carry out a project involving the determination of how protein kinases and phosphates are affected by cardioactive agents in normal and genetically modified mouse hearts .

**Required Skills:** None in particular, but perhaps an interest in cellular biochemistry.

**Interview:**     Required

**Location:**     UMass Medical School

## **14. Laboratory**

**TITLE:       The Mechanical Regulation of Biological Mediators of Cartilage and Joint Destruction in Osteoarthritis**

**Paul Fanning, PhD  
(508) 856-3054  
UMass Medical School  
Department Orthopedics  
55 Lake Avenue, North  
Worcester, MA 01655**

**Description:** Currently in the U.S., musculoskeletal conditions are the leading cause of disability. Joint diseases account for 50% of all chronic conditions in the elderly. Worldwide, OA is only the 6th leading cause of years of life lost to ill health. The burden of musculoskeletal disease, both in terms of human illness and health care costs is projected to widen significantly by the year 2030. The aging of the U.S. population is expected to produce an additional 21 million individuals in the 65-and-over age group, representing a 20% increase over current demographics. Surprisingly, despite the wealth of clinical data on OA, surgical treatment which culminates in total joint replacement, remains the most effective therapy for progressive OA. Relatively little is known about the basic biology of OA especially how mechanical wear, the major hallmark of OA, influences fundamental biological control mechanisms in chondrocytes, the cells that populate cartilage.

Mechanical Models of Arthritis:

- Mechanical Force and Signaling Pathways in Cartilage (using specially-designed *ex vivo* cartilage compression devices)
- Molecular Mechanisms of OA Progression (microsurgical OA-induction of knee OA in mice)

The overall goal of this project is to advance the understanding of the molecular mechanisms of osteoarthritis (OA) progression through the novel finding that mechanical force activates critical cellular-signaling pathways in cartilage. A primary goal proposed here is the analysis of the outcomes of these signaling events on the expression and activities of certain degradative enzymes (matrix metalloproteinases, MMPs) and aggrecanases, which are known to be the major effectors of OA.

**Student's role:** Perform PCR, immunohistochemistry (IHC) on OA cartilage specimens, quantification of cartilage components (assay kits, instrumentation) following various *ex vivo* cartilage loading regimens

**Required skills:** General laboratory, (experience with PCR would be plus but can also be taught)

**Interview:** Required

**Location:** Room: S4-806

## **15. Laboratory**

**TITLE: Zebrafish Models of Motor Neuron Disease**

**Lawrence Hayward, MD, PhD  
(508) 856-4147**

**UMass Medical School  
Department Neurology, S5-717  
55 Lake Avenue, North  
Worcester, MA 01655**

**Description:** My lab is characterizing novel in vivo models relevant to amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease) and related motor neuron diseases. This project will provide the student with familiarity in the design and analysis of neurological disease models using the zebrafish system. We are especially interested to express several newly discovered ALS mutant genes in zebrafish embryos and characterize their consequences. Opportunities for phenotypic analysis of zebrafish embryos and larvae will be tailored to student interest.

**Student's role:** The student will gain practical experience with various techniques tailored to interest, including microinjection of mRNA into zebrafish embryos, fluorescence imaging, electrophysiology, biochemistry, and behavioral motor analysis.

**Required skills:** general molecular biology, interest in in vivo models

**Interview:** Required

**Location:** Room: S5-714

## **16. Laboratory**

**TITLE:       Temporal Regulation of Neurodevelopment**

**Daniel L. Kilpatrick, PhD**

**(508) 856-6274**

**[Daniel.kilpatrick@umassmed.edu](mailto:Daniel.kilpatrick@umassmed.edu)**

**University of Massachusetts Medical School**

**Department of Physiology**

**55 Lake Avenue, North**

**Worcester, MA. 01655**

**Description: Temporal Programming of Neuronal Differentiation and its Linkage to CNS**

**Disorders:** Post-mitotic maturation of neurons occurs in discrete stages, including migration, axon extension, dendritogenesis and formation of functional synaptic connections. Elaboration of these events requires the expression of specific gene subsets in the appropriate sequence and timing. A central and unexplored question is how the precise timing of such developmental events is coordinated within maturing post-mitotic neurons. Alteration of this sequential expression can disrupt neuronal development. In particular, several forms of mental retardation, autism spectrum disorders, schizophrenia, tuberous sclerosis and epilepsy have been linked to transcriptional dys-regulation during development, and in several instances altered timing of neurodevelopment has been observed. We recently identified a broad temporal program regulating gene transcription in developing post-mitotic neurons. In addition, numerous genes previously implicated in multiple neurodevelopmental disorders are apparently regulated by this program.

**1. *Identifying temporal gene targets in neurons.*** These studies are designed to define the temporal transcriptome that controls neuronal differentiation. We are employing lentiviral transduction and knockout mice together with qRT-PCR and microarrays to identify genes that are temporally regulated by this program in post-mitotic neurons.

**2. *Transcriptional regulators of the temporal program.*** We are now defining multiple transcription factors that collaborate in regulating the temporal expression of different gene subsets during post-mitotic neuronal differentiation. These are being functionally tested to determine their impact on temporal gene expression.

**Student's Role:** Hands-on performance of experiments to test the functional importance of transcription factors and mechanisms in the temporal regulation of neuronal differentiation

**Required skills:** Basic understanding of biochemistry and molecular biology. Some prior lab experience is definitely helpful, but not an absolute requirement

**Interview:** Required

**Location:** UMass Medical School, Room S4-139

## **17. Laboratory**

**TITLE:        Role of Inflammation in Diabetes**

**Jason K. Kim, PhD  
(508) 856-6840**

**UMass Medical School  
Department of Molecular Medicine  
5 Biotech, Suite 200  
381 Plantation Street  
Worcester, MA 01605**

**Description: Background:** Our research investigates obesity, diabetes and its complications using elegant metabolic procedures and transgenic mouse models of altered metabolism. Our NIH-funded projects examine the role of inflammation in insulin resistance and cardiovascular diseases. The goal of our research is to understand how obesity causes diabetes and to find its cure.

**Student's Role:** One will be trained in metabolic and biochemical experiments to measure insulin action and glucose metabolism in mice. Transgenic mice will be used to understand how inflammation causes insulin resistance in obesity.

**Required Skills:** One must be comfortable working with mice.

**Interview:** Required

**Location:** 5 Biotech, Suite 225

## **18. Laboratory**

**TITLE: Host Defenses Against Fungal Infections**

**Stuart M. Levitz, MD**

[Stuart.levitz@umassmed.edu](mailto:Stuart.levitz@umassmed.edu)

**(508) 856-1525**

**University of Massachusetts Medical School**

**Department of Medicine and Molecular Genetics & Microbiology**

**364 Plantation Street, LRB 317**

**Worcester, MA 01605**

**Description:** Please see my web page for a description of my lab.

<http://www.umassmed.edu/ivp/faculty/levitz.cfm> I am Happy to talk with students about potential projects depending on their interests.

**Student's Role.** Work under the supervision of a graduate student and/or postdoc on an independent project.

**Required Skills:** None, just an enthusiasm to learn!

**Interview:** Required

**Location:** LRB3



## **19. Laboratory**

**TITLE: Developmental Three-Dimensional Anatomy of the Oral Cavity and Neck**

**Richard S. Pieters M.D., Clinical Associate Professor of Radiation Oncology and Pediatrics  
co-PI: Sheila Stille, D.M.D.**

**(508) 334-6550**

**[Richard.Pieters@umassmemorial.org](mailto:Richard.Pieters@umassmemorial.org)**

**UMMC**

**Levine Cancer Center**

**119 Belmont Street**

**Worcester, MA 01605**

**Description:** The Varian Radiation Therapy Treatment Planning System provides the ability to image anatomy in three dimensions. For this project, the de-identified treatment planning CT scans from a number of children of varied ages who have previously been treated with radiation therapy to the head and neck for various malignancies will be utilized. The normal structures of the oral cavity and neck will be defined on CT slices, generating three-dimensional images of the structures. The result will be an atlas of developmental anatomy of the head and neck for use in instruction in the medical and dental school programs. A poster will be generated to conclude the project.

**Student's Role:** After instruction in the use of the technology, the student ( and perhaps interested dental residents) will draw the volumes on the CT slices of the patients with review of the result by Dr. Pieters & Dr. Stille, and then will generate the poster for presentation. If a publishable paper results, the student will receive co-authorship.

**Required Skills:** Baseline first year knowledge of gross anatomy; some familiarity with computers

**Interview:** Required

**Location:** Radiation Oncology Department

## **20. Laboratory**

**TITLE: Three-Dimensional Anatomy of the Pelvis or Extremities**

**Richard S. Pieters M.D., Clinical Associate Professor of Radiation Oncology and Pediatrics**

**Co-PI: Sheila Stille, D.M.D.**

**(508) 334-6550**

**[Richard.Pieters@umassmemorial.org](mailto:Richard.Pieters@umassmemorial.org)**

**UMMC**

**Levine Cancer Center**

**119 Belmont Street**

**Worcester, MA 01605**

**Description:** The Varian Radiation Therapy Treatment Planning System provides the ability to image anatomy in three dimensions. For this project, the de-identified treatment planning CT scans from a number of patients with pelvic or extremity malignancies who have previously been treated with radiation therapy to the either site will be utilized. The normal structures of the pelvis will be defined on CT slices, generating three-dimensional images of the structures. The result will be an atlas of anatomy of the pelvis or extremity for use in instruction in the medical and graduate nursing school programs. A poster will be generated to conclude the project.

**Student's Role:** After instruction in the use of the technology, the student (and perhaps interested surgical residents) will draw the volumes on the CT slices of the patients with review of the result by Dr. Pieters and then will generate the poster for presentation. If a publishable paper results, the student will receive co-authorship.

**Required Skills:** Baseline first year knowledge of gross anatomy; some familiarity with computers

**Interview:** Required

**Location:** Radiation Oncology Department

## **21. Laboratory**

**TITLE: Molecular Mechanism of Gene Amplification**

**Anthony R. Poteete, PhD**

**(508) 856-3708**

**[Anthony.poteete@umassmed.edu](mailto:Anthony.poteete@umassmed.edu)**

**University of Massachusetts Medical School**

**Department of Molecular Genetics and Microbiology**

**Room S6-119**

**55 Lake Avenue North**

**Worcester, MA 01655**

**Description:** Gene amplification is a well-known and biologically widespread mechanism in which a small portion of an organism's genome is selectively and repeatedly replicated, out of synchrony with the rest of the genome. The result is a cell that has many copies of one or a few genes, but only one or two copies of all the others. The amplified genes are typically expressed at elevated levels, commensurate with their elevated copy numbers. Gene amplification is known to play an important role in three key processes: (1) In the development of many animals, gene amplification is employed transiently to supply the products of particular genes at very high levels when needed. (2) Over-expression through gene amplification is one of the processes by which normal genes become cancer genes in tumorigenesis. (3) Amplification of genes conferring weak resistance to chemotherapeutic agents is a well-known mechanism by which both infectious agents and cancer cells can develop effective drug resistance.

Employing genetic engineering techniques, we constructed a variant strain of the common laboratory bacterium *E.coli*, with a duplication of a weakly functional gene, called *lacIZ33*, in its chromosome. Placed under conditions which demand the function of *lacIZ33*, this strain exhibits a remarkably high frequency of amplification—higher than any chromosomal mutation event we know of in a cell with normal DNA replication and repair functions.

A question emerging from studies of this system is how much of the variation we see in the frequency of amplification is due to events occurring during non-selective growth, and how much is due to events occurring after the imposition of selection.

The experimental approach to this question will involve the development and exploitation of a modified experimental system, in which the cells lack *recA* function, and consequently, cannot amplify. At the end of the period of non-selective growth, the cells will be infected with an engineered bacteriophage which will suddenly restore *recA* function.

**Student's Role:** Working with the principal investigator on all aspects of the research.

**Required Skills:** Keeping good notes

**Interview:** Required

**Location:** UMMS, Room S6-110.

## **22. Social**

**TITLE:       Diabetes Collaborative Project**

**Ronald Adler, MD  
Director for Primary Care Practice Improvement  
(508) 334-2684**

**UMass Medical School  
Department of Family Medicine and Community Health  
Benedict Building, A3-122  
55 Lake Avenue, North  
Worcester, MA 01655**

**Description:** The Diabetes Collaborative Project (started in September 2008) is designed to improve the care delivered to > 2000 patients with diabetes in 6 Primary Care Practices (3 Internal Medicine and 3 Family Medicine). Activities include implementation of the Chronic Care Model, development and management of a registry, provision of planned care and group visits. The Collaborative structure promotes joint learning through interactions across practices. The Project is directed by a multi-disciplinary team which includes Dr. Adler, a QI Project Manager, a Certified Diabetes Educator, a Clinical Pharmacist, a Psychologist, a Data Analyst and a Patient Advisor. More information is available at <http://ournet.ummhc.org/C3/C7/Diabetes%20Collaborative%20Project/default.aspx>

The program includes multiple elements which have been implemented in various ways and to variable extent at the different sites. We are interested in determining the relative merits and value of the different program elements. Research questions include: Which elements correlate with improved performance? and What is the magnitude of these effects? The answers to these questions will have implications for spread of the model to other sites. In addition to performance outcomes, we are also interested in measuring what effects the program may have had on the satisfaction of patients, health care providers and office staff.

**Student's Role:**       We are seeking a student who will assist us in the collection, analysis and interpretation of data to answer these questions. In addition to learning about conducting a simple research project, it is anticipated that the student will learn about evidence-based recommendations for the care of patients with diabetes plus important principles of Quality Improvement and Practice Re-Design.

**Interview:**       Required

**Location:**       The student will work primarily at the University campus, but may be asked to visit some participating practice sites (Worcester, Shrewsbury, Barre).

## **23. Social**

**TITLE:           An Investigation of the Oral Literacy Demands of Physician-Patient Encounters Around Human Papilloma Virus**

**Diane (Dede) Blake, MD  
(508) 856-7507**

**UMass Medical School  
Department of Pediatrics  
Benedict Building, A3-109  
55 Lake Avenue, North  
Worcester, MA 01655**

**Description:** The objectives of this study are to describe the oral health literacy demand of the language used by physicians when talking with adolescents about HPV infection, cervical cancer, HPV vaccination, and to identify the questions that adolescent women have about these topics. In order to accomplish these goals, we will conduct qualitative and quantitative analyses of 150 transcripts from digital audio recordings made during adolescent women's office visits to pediatricians, gynecologists, and primary care providers (family practitioners and internists) where there was discussion about HPV, cervical cancer, or the HPV vaccine. The first set of analyses will be qualitative and exploratory. Content analysis techniques will be used to code each encounter. Quantitative analyses will consist of examining the oral health literacy demand of the physician explanations of HPV infection, cervical cancer, and the HPV vaccine. We will use the conceptual framework developed by Roter et al to accomplish these analyses. Roter's conceptual framework of oral literacy demand includes 1) use of unfamiliar technical terms, 2) general language complexity, and 3) structural characteristics of dialogue. The results of this study will include 1) both qualitative and quantitative data on *how* physicians talk with their patients about HPV, cervical cancer and the HPV vaccine, including the language they use, the medical explanations they provide, and the oral literacy demand of the encounter overall; 2) a description of patients' concerns, questions, and misunderstandings as expressed to the provider; and 3) a statistical analysis of the relationship between the oral literacy demand in the physician-patient encounter and adolescent's satisfaction with the encounter.

**Student's Role:** This will be a great introduction to health literacy, particularly for someone interested in primary care. Dr. Blake will teach the student how to conduct the qualitative and quantitative analyses. The student will be a part of the research team, which will meet once every 1-2 weeks. Meetings with Dr. Blake will occur more frequently and as needed. If interested, the student may also spend time shadowing Dr. Blake in the adolescent clinic.

**Required Skills:**       Computer Literacy

**Interview:**            Required

**Location:**            Benedict Building and Meyers Primary Care (Lake Avenue North; Worcester)

## **24. Social**

**TITLE: Medical Spanish Curriculum Development**

**Michael Chin, MD**  
**Michael.Chin@state.ma.us**  
**617-933-3044**

**UMass Medical School**  
**Department of Family Medicine & Community Health**  
**(Office) Health Insurance Connector Authority**  
**100 City Hall Plaza**  
**Boston, MA 02108**

**Description:** This is an opportunity for a highly motivated medical student to help in the development of an innovative curriculum that will help medical students, residents and attendings to improve their “medical Spanish” language skills. There are already a number of textbooks and courses that attempt to teach medical Spanish, but this project will be innovative for the following reasons: (1) the project’s goal is to develop a library of short patient-physician interviews that are recorded and posted on the internet so that any interested person can download them and listen to them on their computer, iPod, or other audio device. (2) each 15-minute patient-physician interview is followed by 2 to 3 minutes of “medical teaching” points, so that any medical student listening to these interviews is both improving their medical Spanish skills, AND improving their medical knowledge.

**Student’s Role:**

- The student will design research instruments, such as surveys that users of the curriculum will complete before and after using the curriculum in order to measure the curriculum’s effectiveness.
- The student will investigate ways to have this curriculum compliment other Medical Spanish activities that are ongoing at UMMC, which includes the *Medical Interviewing in Spanish* course, and the medical Spanish class for UMass family medicine residents.
- The student is welcome to be involved in every part of this project.

**Required Skills:**

- Spanish proficiency equivalent to at least year of college Spanish (and more is preferred)
- highly motivated and independent (this is especially important because the faculty sponsor works in Boston, and therefore collaboration will be done through e-mail and phone conferencing)
- experience living or working in developing countries is preferable
- computer and webpage design skills (this is very helpful, but is not an absolute prerequisite)

**Interview:** Required

**Location:** Wherever the student is able to record medical interviews in Spanish. This can be in Worcester, but it can occur in other locations with the faculty’s approval.

## **25. Social**

**TITLE:       Nicotine Dependence**

**Joseph DiFranza, MD**  
**(508) 856-5658**  
**[difranzi@ummhc.org](mailto:difranzi@ummhc.org)**

**UMass Medical School**  
**Department of Family Medicine and Community Health**  
**Benedict Building, A3-235**  
**55 Lake Avenue, North**  
**Worcester, MA 01655**

**Description:** Student will be assisting us in collecting case histories by interviewing smokers about their nicotine dependence.

**Student's Role:** Student will be interviewing subjects.

**Required Skills:** Interviewing skills

**Interview:**     Required

**Location of research:** Community locations

## **26. Social**

**TITLE: Community-Based Participatory Research Project for Improving the Process of Cancer Screening**

**Chyke Doubeni, MD, MPH; Assistant Professor  
(508) 334-7772**

**[Chyke.doubeni@umassmed.edu](mailto:Chyke.doubeni@umassmed.edu)**

**UMass Medical School  
Department of Family Medicine and Community Health  
Benedict Building, A3-152  
55 Lake Avenue, North  
Worcester, MA 01655**

**Description:** This is an NCI-funded project to explore the barriers and facilitators to cancer screening in the local Worcester area for those in low-income or socioeconomic groups. The project uses a community-based partnership approach to research and so, includes several community partners as co-investigators. There are 2 key components to the research: 1) obtain data from 2 community health centers on their cancer screening rates; 2) conduct interviews with key informants at the health centers and the medical school to complement data previously gathered from community members. It is envisioned that data collection will commence by May and extend into the summer. **This project does not involve lab experiments.**

**Student's Role:** The student will be involved in planning and implementation of data collection for the project and work with an anthropologist in analyzing the qualitative data. A broad range of experiences related to cancer health disparities research is available.

**Required Skills:** Interest in health equity and prior experience in population-based research preferred but required.

**Interview:** Required

**Location:** UMMHC and Worcester Community



## **27. Social**

**TITLE:** An Investigation of Medical Students' Sense of Role as Future Health Care Professionals

**Judith Savageau, MPH and Michael Godkin, PhD**  
**(508) 856-3917**  
[judith.savageau@umassmed.edu](mailto:judith.savageau@umassmed.edu)

**UMass Medical School**  
**Department of Family Medicine and Community Health**  
**Benedict Building**  
**55 Lake Avenir, North**  
**Worcester, MA 01655**

**Project Description:** The project's goals are to develop and distribute a survey to three cohorts of medical students to gather data regarding:

- a) students' perspectives of the healthcare system
- b) students' expectation to participate in:
  - b1) policy change or development
  - b2) public health projects
- c) students' attitudes towards their respective curricula vis-à-vis public health and public policy.

The project design will draw from existing questionnaires as available. The cohorts of students to be invited to complete the survey include those from the University of Massachusetts Medical School, the University of Pittsburgh Medical School and Tufts University Medical School. Strategies will be developed to promote response rates, including identifying local community members to facilitate delivery and follow-up. Focus groups and/or focused interviews may be used to augment the survey data collection.

**Student's Role:** Develop questionnaire, communicate with representatives from other schools, collect data, identify strategies to analyze data.

### **Required Skills**

A willingness to learn about survey methodology, include design, implementation and analysis. Departmental resources will be available to guide the student through this process.

**Interview:** Required

**Location:** The project will be hosted internally at UMMS with regular communication being maintained with co-investigators at Tufts and the University of Pittsburgh.

## **28. Social**

**TITLE:                    Mobile Safety Street**

**Dr. Mariann Manno, MD**  
**Director Pediatric Emergency Medicine**  
**Department of Pediatrics**  
**Co – Director, UMMHC Injury Prevention Program**

**Dr. Michael Hirsh, MD**  
**Director Pediatric Surgery and Trauma**  
**Department of Surgery**  
**Co – Director, UMMCH Injury Prevention Program**

**Contact Person: Allison Rook Burr**  
**508-334-0629**

**UMass Medical School**  
**Departments of Surgery and Pediatrics**  
**55 Lake Avenue, North**  
**Worcester, MA 01655**

**Description:** Preventable trauma is the leading cause of injury and death in children and young adults in the United States. Mobile Safety Street is a clinically based, community oriented program dedicated to educating children how to recognize and prevent common safety hazards that could lead to injury.

**Student's Role:** Student will be participate in community outreach through the MSS program; and assist with public health data management and analysis; exposure to the pediatric emergency and surgery clinical arenas.

**Required Skills:** Must be able to work both independently and as part of a team. Must exhibit strong initiative and have an interest in preventing childhood injury.

**Interview:**    Required

**Location:**     University Campus, Community at Large

## **29. Social**

**TITLE:        Our Proud Tradition: The History of Psychiatry in Worcester, MA**

**Ellen More, Ph.D; Sheldon Benjamin, MD; Jeffrey Geller, MD**

**Contact info:**

**Ellen S. More, Ph.D.**

**Head, Office of Medical History and Archives**

**And Professor, Department of Psychiatry**

**(508) 856-7633**

**University of Massachusetts Medical School**

**Department of Psychiatry**

**55 Lake Avenue, North**

**Worcester, MA. 01655**

**Description:** In honor of the 100<sup>th</sup> anniversary of the visit to Worcester by Sigmund Freud (his only visit to the U.S.), the City of Worcester, Clark University, and UMass Medical School's Dept. of Psychiatry are hoping to combine efforts to hold a month-long series of events next fall, 2009. The Psychiatry Department is hoping to launch a History of Psychiatry web exhibit on its departmental web site.

**Preferred skills:** some background in web design and an interest in the history of Psychiatry.

**Task:** To work principally with historian Ellen More as well as psychiatrists Sheldon Benjamin and Jeffrey Geller to research and design a web page depicting the role of Worcester and UMassMed in the history of American psychiatry.

**Interview:**    Required

**Location:** Most materials are located here at UMass. although some might also be found at the Worcester Historical Museum or at Worcester State Hospital. The materials would include photographs, artifacts, and printed materials (some from the 19<sup>th</sup> c.).

### **30. Social**

**TITLE:       Facilitating Workplace Self-management Strategies for Workers with Low Back Pain: Development and Testing of a Pilot Group Intervention**

**William Shaw PhD, Instructor  
Dept Of FM+CH  
Telephone 508 497 0253**

**Liberty Mutual Research Institute for Safety  
Center for Disability Research  
71 Frankland Road  
Hopkinton, MA 01748**

**Description:** Persistent or recurrent low back pain (LBP) is a frequent problem among working-age adults in the US, although the majority of affected workers are able to maintain gainful employment and continue full-time work without the need of formal job accommodation or physician-ordered restrictions. However, little is known about the self-management strategies used by workers to overcome workplace problems associated with pain and whether these strategies can be developed or improved among more troubled workers. This proposed 18-month study involves design of a group intervention program intended to reduce disability risk of LBP by strengthening self-management strategies in the workplace and a pilot test of its feasibility and appropriateness.

The primary research question is whether a psycho-educational group intervention based on self-management (SM) principles might be a feasible and acceptable approach to prevent workplace disability among individuals experiencing workplace problems due to recurrent low back pain (LBP). Based on prior work of the research team (Shaw & Huang, 2005), we have adopted a tentative conceptual framework for the study that includes five self-management domains: (1) modifying work to reduce discomfort; (2) developing self-care strategies at work; (3) obtaining supervisor and co-worker support; (4) overcoming stigma and negative thoughts; and (5) making appropriate career and job decisions. Workers who report mastery in these domains may experience a diminished effect of pain and functional impairment on job satisfaction, work productivity, and sickness absence. Further, a psycho-educational group intervention may provide an opportunity to improve and reinforce these SM strategies for dealing with back pain in the workplace. If these strategies can be improved, this may improve self-efficacy for performing job tasks and reduce pain worries. This, in turn, may lead to long-term improvements in job satisfaction, work productivity, and reductions in sickness absence.

The proposed study method involves: (1) a qualitative assessment of workplace self-management strategies using focus groups of workers with back pain, (2) identifying opportunities for intervention; (3) development of a test group intervention program employing SM concepts to overcome workplace problems; and (4) pilot testing of the intervention with an initial group of workers with back pain.

**Student's Role:** The student will have a lead role in developing the information base on various workplace interventions that have been instituted to improve outcomes in low back pain. Several have been described in the peer-reviewed medical literature, and others are in the 'grey' literature through organizational reports, monographs, project summaries, and clinical guidelines. With guidance from the principal investigator, the student will use literature and internet searching, networking, and citation review to locate detailed information on program content, and then assemble the information into a logical framework.

**Required Skills:** Critical reading of scientific literature, information searching skills.

**Interview:** Required can be arranged by contacting Dr Shaw at [William.shaw@lib](mailto:William.shaw@lib)

**Location:** Liberty Mutual Research Institute, Hopkinton MA (some work can be performed at UMMS library)

## **31. Social**

**TITLE: The Akwaaba Free Clinic: Outreach and Patient Registry Development**

**Judith Savageau, MPH and Suzanne Cashman, ScD**

**508-856-9635**

**508-856-2930**

**[Suzanne.cashman@umassmed.edu](mailto:Suzanne.cashman@umassmed.edu)**

**UMMC**

**Department of Family Medicine and Community Health**

**Benedict Building**

**55 Lake Avenir, North**

**Worcester, MA 01655**

**Project Description:** The Akwaaba Free Health Clinic is located at the International Central Gospel Church in Worcester's Vernon Hill neighborhood. With a specific focus on African immigrants, it welcomes anyone who seeks care. Volunteer physicians, nurses, and health professions students staff the clinic, open one night a week. Initial outreach efforts were conducted through select churches and word-of-mouth but as the clinic reaches its one-year anniversary, a larger-scale outreach campaign will aim to reach the large, underserved population of recent immigrants living in Worcester and the surrounding towns. This project will include:

- Enhancing outreach strategies through the wide network of African churches in Worcester.
- Developing and implementing a computerized patient registry/database to improve patient follow-up and an understanding of the clinic's patient population.

**Students' Role:** The student will:

- Work with the current volunteers to immerse him/herself into all aspects of the Akwaaba clinic and function as staff to the clinic one night/week.
- Meet with members of the Board of Advisors to solicit their ideas and draw on their community connections on how the clinic can better meet the needs of the community it has been developed to serve.
- Conduct a literature review of free clinics to search for effective strategies employed in the past to reach similar goals.
- Develop and distribute a flyer about the clinic through Worcester's food pantries
- Construct and implement a patient registry that will provide a database for assessing the clinic's patient population.

**Required Skills:** Organization. Ability to work independently. Knowledgeable about database development. Comfortable learning from and about other cultures. Presentation skills a plus.

**Interview:** Required

**Location:** Akwaaba Free Health Clinic in Worcester and UMMS campus

## **32. Social**

**TITLE:        Understanding Your Diabetes Risks**

**Barry Saver, MD, MPH**

**(508) 856-3458**

**[Barry.saver@umassmed.edu](mailto:Barry.saver@umassmed.edu)**

**UMass Medical School**

**Department of Family Medicine and Community Health**

**Benedict Building, A3-146**

**55 Lake Avenue, North**

**Worcester, MA 01655**

**Description:** We are interviewing patients with diabetes and other cardiovascular risk factors about their understanding of their diabetes-related health risks and reactions to being given quantitative information about their risks of different health outcomes. We are trying to understand how patients with diabetes view their risks, whether getting this kind of information can help motivate behavior change, and in general what motivates healthy behavior change.

**Student's Role:** 1) Participate in qualitative analysis of transcripts of interviews (we will teach qualitative analysis skills, since it is very unlikely any student will know this)

2) if desired and time permits, participate in subject interviews

**Required Skills:** 1) Bilingual Spanish/English a huge plus, though not absolutely required - a number of the interviews/transcripts are in Spanish

2) openness to learning qualitative analysis techniques

**Interview:** Required

**Location:** Benedict Building, and Family Health Center of Worcester for some interviews

### **33. Social**

**TITLE:       Measuring Breastfeeding Self-Efficacy in Diverse Urban Populations:  
Clinical Assessment Tool to Identify Women at Risk for Early  
Breastfeeding Cessation**

**Sara Shields MD, MS, FAAFP Clinical Associate Professor  
Patricia A. Reidy, DNPc, FNP-BC Project Coordinator  
(508) 860-7700**

**Family Health Center of Worcester  
Department of Family Medical and Community Health  
26 Queen Street  
Worcester, MA**

**Description:** Breastfeeding is widely recognized as the optimal feeding method for all infants from birth to age 12 months due to the numerous health benefits of human milk. During the first year of life, breastfed infants have a lower incidence of respiratory, gastrointestinal and urinary tract infections resulting in health cost savings. In 2006, the breastfeeding initiation rate exceeded national breastfeeding goals but only 32% of women were breastfeeding at six months, 36% below the established national goal.

Disparities exist in meeting the established breastfeeding goals. Breastfeeding rates are influenced by race/ethnicity, socioeconomic status, maternal age, and psychological factors. In a study of diverse urban families, 34% of women stopped breastfeeding between four and six weeks citing breastfeeding difficulties, lack of support, insufficient milk and low breastfeeding confidence. While socio-demographic factors cannot be modified, identifying modifiable risk factors enable clinicians to target supportive breastfeeding interventions for women at high risk for early breastfeeding cessation.

Breastfeeding self-efficacy based on Bandura's social cognitive theory is defined as the mother's perceived ability to successfully breastfeed her infant. It predicts whether a person will breastfeed, the amount of effort expended, the level of perseverance until mastery is accomplished, thought patterns and emotional attitude with breastfeeding difficulties. Several studies have examined the correlation with maternal breastfeeding confidence and continued breastfeeding. Women who lack self-confidence at baseline are less apt to be breastfeeding at two weeks postpartum. The breastfeeding self-efficacy scale (BSES-SF) measures maternal breastfeeding confidence. It is predictive of breastfeeding behavior at four and eight weeks when administered within one week after birth. Self-efficacy scores can be modified with targeted breastfeeding interventions thereby preventing early termination of breastfeeding.

The project aims to:

1. Identify the level of breastfeeding confidence for women at one week and one month postpartum using the BSES-SF.
2. Identify women at risk for early breastfeeding cessation with low self-confidence scores and refer them for additional supportive services.



3. Determine the predictive validity of the BSES-SF.
4. Evaluate the efficacy of the BSES instrument as a risk assessment tool in clinical practice with a diverse population.

**Student's Role:** Administer Breastfeeding Self-Efficacy Scale (BSES-SF) to breastfeeding women at one and four weeks postpartum. Assist with data collection and analysis

**Required Skills:** Spanish speaking skills are helpful but not required.  
Computer skills: Excel spread sheet

**Interview:** Required

**Location:** Family Health Center of Worcester  
26 Queen St. Worcester, MA

### **34. Social**

**TITLE:       Improving Prenatal Records/Handouts to Improve Provider Testing and Patient Education Compliance**

**Hugh Silk, MD**  
**(508) 334-8846**  
[silkH@ummhc.org](mailto:silkH@ummhc.org)

**Hahnemann Family Health Center**  
**279 Lincoln St**  
**Worcester, MA. 01605**

**Description:** At Hahnemann Family Health Center, we are looking to revise our prenatal record and patient handouts to improve the care we provide to our prenatal patients. We are a family medicine residency site that provides prenatal care to approximately 100 women per year. We have anecdotally noticed that we are doing a poor job offering our patient 1st trimester genetic screening, cord blood donation options and oral health screens. Our current prenatal records are outdated and need to be improved to promote accuracy and also family centered care. We want to review what others are using to provide ideal care and then incorporate those ideas into our records and handouts. Because we are a residency site, we also have forms for precepting the prenatal records that need to reflect the new changes. We want to be inclusive and solicit ideas from all current providers. We want to assess the current care accurately with a chart review and then assess again after the changes are implemented. We will have to teach all providers about the change through a lunch time educational session.

**Student's Role:**

- 1) To do a chart review of current provider compliance of certain testing and patient education including 1st trimester screening, cord blood donation, oral health review, etc
- 2) Perform a literature search on prenatal care and provider compliance as well as prenatal forms and educational handouts
- 3) Survey Hahnemann providers about what they like and dislike about our prenatal forms/handouts
- 4) Help revise our prenatal forms and handouts
- 5) Help revise our precepting forms for prenatal care
- 6) Implement the new forms with an educational session for all providers
- 7) Set up a system for chart reviews to follow improvement on new forms/handouts
- 8) Record initial data

**Required Skills:** Interest in family centered obstetrical care. Initiative and motivation to work independently with frequent meetings of a faculty member.

**Interview:**     Phone interview accepted

**Location:**     Hahnemann Family Health Center, Hahnemann Campus

### **35. Clinical/Translational Research Pathway Program Projects**

**TITLE: Giving Birth Study**

**Tiffany A. Moore Simas, MD, MPH, MEd,  
Assistant Professor of Ob/Gyn and Pediatrics**

**Additional faculty involved:**

**Janet Hardy, PhD, MPH, MSc, Assistant Professor of Medicine, Ob/Gyn and Pediatrics  
Sharon Jackson, MEd, Study Coordinator  
(508) 334-6590**

**University of Massachusetts Medical School/UMass Memorial Health Care Memorial  
Campus Department of Obstetrics & Gynecology  
119 Belmont Street - Jaquith Room 4053  
Worcester, Massachusetts 01605**

**Description** This is an ongoing study, housed in the Department of Obstetrics and Gynecology, to determine pregnant women's desire for either an elective caesarean section or a vaginal delivery, in Worcester. Additionally, it proposes to identify potential reasons why women express a preference of one over the other. Patients will complete a survey at approximately 20 weeks of pregnancy, between 35-37 weeks of pregnancy, and after delivery - the goal of the serial surveys is to identify potential changes in preferences with advancing pregnancy and after an actual delivery experience. Additional, research questions include whether there are trends based on race/ethnicity, prior mode of delivery, and number of children.

**Student's Role:** Consenting and administering the "Giving Birth" survey to patients at Memorial's Ob-Gyn department and patients of midwives and family practitioners in the community. Making contacts with family practitioners and midwives in the community. Coordinating longitudinal survey data, data analysis/ evaluation as needed, collaboration with the research team, and other duties as assigned.

**Required Skills:** Attention to detail, ability to establish research relationships with providers of obstetric care, maintenance of patient relationships and communications to promote serial surveys over course of pregnancy and postpartum period, evaluation and inquiry of data.

**Location:** Department of Obstetrics and Gynecology, Memorial Campus; community family medicine and midwifery offices/clinics.

### **36. Clinical/Translational Research Pathway Program Projects**

**TITLE: Retrospective Chart Review of Patients receiving Valproic Acid for Retinal or Macular Degenerative Diseases**

**Shalesh Kaushal, MD, PhD Associate Professor and Chairman**  
[Shalesh.Kaushal@umassmemorial.org](mailto:Shalesh.Kaushal@umassmemorial.org)  
**( 508) 334 0687**

**UMMHC**

**Department: Ophthalmology**

**Description:** Retinitis Pigmentosa is a catastrophic disease characterized by progressive loss of visual field (VF) until complete blindness. There is no treatment currently available. My lab has been studying valproic acid (VPA) and has discovered that this small molecule has a variety of biologic properties that make it an ideal therapeutic agent for retinal dystrophies. First, VPA can increase the proper folding of the mutant rhodopsin, which is the primary cause of most cases of RP. Second, VPA can protect cells against the apoptosis (cell death) of photoreceptor cells which is the cause of tunnel vision associated with RP. Additionally, VPA doubles the efficiency at which the retinal pigmented epithelium can pump out fluid and is a potent inhibitor of microglial activation which is involved in the inflammatory response in most retinal disorders.

Finally, our lab and others have shown that VPA turns on bone marrow stem cells which may produce various cytokines for protection but more importantly may fuse with mature cells and reprogram them to become new photoreceptor cells.

For these reasons I decided that VPA was an ideal drug for retinal therapy. I treated several retinal dystrophy patients in my practice in the University of Florida with VPA for about a year.

This pilot data suggests that VPA can cause regression of tunnel vision in RP patients. These are staggering results considering there is no treatment currently available to slow progression, let alone REVERSE the disease. Patient testimonials overwhelmingly support that VPA is changing their quality of life in a short period of time. Jenna will review all of clinical data and assist in writing up these important findings for publication.

**Student's Role:** Review the charts and visual results of patients who I have treated with valproic acid

**Required Skills** Elementary statistical analysis

**Location:** Biotech V

### **37. Clinical/Translational Research Pathway Program Projects**

#### **TITLE: Brain Response Following Intracerebral Injection of a-Gal Glycolipids**

**Richard P. Moser, MD Professor of Surgery and Radiation Oncology  
508-334-3721**

**UMass Medical School  
Surgery; Division of Neurosurgery  
Room S2-856  
55 Lake Avenue, North  
Worcester, MA 01655**

**Description:** The purpose of this project is to demonstrate the safety of a localized intracerebral injection of a-gal glycolipids (ceramide with carbohydrate chains capped by the a-gal epitope [Gala1-3Galb1-4GlcNAc-R]), phospholipids and cholesterol that are extracted from rabbit RBC. We hypothesize that injection of a-gal glycolipids will elicit an intense, rapid and self-limited inflammatory and immune-mediated response that will produce neither neurological deficit nor systemic illness. We further predict that the a-gal glycolipids in micelle formation will produce a more intense local inflammatory and immune reaction compared to the liposomal preparation, which may recruit mesenchymal stem cells into the injury site.

**Primary Objective** *Demonstration of the safety pure micelle and liposomal forms of a-gal glycolipids injected directly into brain parenchyma.*

**Secondary Objectives** *Characterization of the inflammatory and immune-mediated response in*

Anti-Gal is the most abundant natural antibody in humans constituting ~1% of all serum immunoglobulins (1). This antibody interacts specifically with the a-gal epitope (Gala1-3Galb1-4GlcNAc-R or Gala1-3Galb1-3GlcNAc-R) on glycolipids and glycoproteins (2, 3). Anti-Gal is produced throughout life as a result of antigenic stimulation by bacteria of the gastrointestinal tract (4). The a-gal epitope is synthesized by the glycosylation enzyme  $\alpha$ 1,3galactosyltransferase ( $\alpha$ 1,3GT) and expressed in very large amounts on cells of non-primate mammals, prosimians and in New World monkeys (5, 6). The  $\alpha$ 1,3GT gene was inactivated in ancestral Old World primates. Thus humans, apes, and Old World monkeys lack a-gal epitopes and produce high titer anti-Gal antibodies (5, 6). Anti-Gal bind avidly *in vivo* to a-gal epitopes on cells when those are administered into humans or Old World monkeys. Since mice and other nonprimate mammals produce the a-gal epitope as a self carbohydrate antigen, they can not produce the anti-Gal antibody (i.e., they are immunotolerant to the a-gal epitope). The only known nonprimate animal that lacks a-gal epitopes and thus can produce anti-Gal is the  $\alpha$ 1,3galactosyltransferase knockout mouse (referred to as KO mouse). In this mouse the  $\alpha$ 1,3galactosyltransferase gene was disrupted (i.e., knocked out), so the mouse lacks a-gal epitopes (7). The KO mice can produce anti-Gal in titers comparable to those in humans after they are immunized with cell membranes from other species which express a-gal epitopes, e.g. pig kidney cell homogenate (8, 9).

**Student's Role:**

The will assist Dr. Uri Galili in the preparation of the KO mice for injection. He will do the stereotactic injections and monitor the mice throughout the post-operative period. He will be responsible for the imaging of the mice at all time points. He will sacrifice the animals and prepare the brain and other vital organs for histology and immunohistochemistry. He will obtain blood at the time of necropsy and prepare for serology. He will assist in the preparation of the tissue slides. He will characterize and semi-quantitate the inflammatory immune-mediated cellular responses. He will present the data in publication form and prepare an appropriate manuscript.

**Required Skills:** The student has experience in rodent experimentation and monitoring. This will greatly aid him in maximizing his productivity during this short period.

**Location:** Department of Surgery Laboratory on Level A, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01604

### **38. Clinical/Translational Research Pathway Program Projects**

#### **TITLE: Assessment of Routine Intraoperative Horizontal Transmission of Potentially Pathogenic Bacterial Organisms and Associated Morbidity and Mortality**

**Stephen O. Heard, MD**  
**508-856-3266**

**UMass Medical School**  
**Department: Anesthesiology**  
**55 Lake Avenue North**  
**Worcester, MA 01655**

**Description:** The first 2 patients undergoing general anesthesia in each operative suite will be evaluated in a serial manner in order to detect horizontal transmission. For case 1, two sites on the anesthesia machine [(adjustable pressure limiting valve complex and agent dial), figure 1] will be decontaminated and cultured aseptically at baseline (T<sub>01</sub>) and at case completion (T<sub>11</sub>). T<sub>01</sub> cultures will be considered to represent a baseline such that any new organism cultured at case conclusion (T<sub>11</sub>) will be thought to be acquired intraoperatively. For case 2, sterile intravenous stopcock sets will be provided preoperatively and cultured on case completion (T<sub>22</sub>). Horizontal transmission will be confirmed by the presence of identical bacterial isolates (as determined by biotype and pulsed field gel-electrophoresis) at T<sub>22</sub>, T<sub>11</sub> and T<sub>02</sub>, combined with their absence at T<sub>01</sub>. Cultures will be quantified by colonies per surface sampled (CPSS) and qualified by standard laboratory bacterial identification protocols. These results will be compared to cultures taken from the hands of anesthesia providers preoperatively as a means to determine the origin of bacterial organisms. The primary outcome of this study will include the incidence of horizontal transmission. Secondary outcomes will include the species identification and antibiotic susceptibility of isolated organisms, bacterial origin and the 30-day postoperative healthcare-associated infection rate and associated mortality as determined by prospective analysis of all patients enrolled.

**Student's Role:** The student will assist in enrolling patients and taking the required cultures of the OR environment and anesthesia providers. He will assist in data collection and preparing case reports.

**Required Skills:** Previous clinical research. Completion of the IRB research education module exam.

**Location:** UMass Memorial ORs (University campus)

### **39. Clinical/Translational Research Pathway Program Projects**

**TITLE:** Worcester Heart Attack Study

**Robert J. Goldberg, PhD**  
508-856-3991

**UMMC**  
**Department of Medicine**  
**377 Plantation Street, Suite 305**  
**Worcester, MA 01605**

**Description:** Through the current period of federal funding support for the Worcester Heart Attack Study, investigators on this large observational study are examining more than 3 decade long trends (1975–2007) in the incidence rates, in-hospital and long-term survival, and therapeutic approaches used in the management of more than 14,000 greater Worcester (MA) residents hospitalized with acute myocardial infarction at all medical centers in the Worcester metropolitan area (1,2).

1. Goldberg RJ, Spencer FA, Yarzebski J, Lessard D, Gore JM, Alpert JS, Dalen JE. A 25-year perspective into the changing landscape of patients hospitalized with acute myocardial infarction (the Worcester Heart Attack Study). Am J Cardiol 94:1373-1378, 2004.
2. Floyd KC, Yarzebski J, Spencer FA, Lessard D, Dalen JE, Alpert JS, Gore JM, Goldberg RJ. A 30 year perspective (1975-2005) into the changing landscape of patients hospitalized with initial acute myocardial infarction: Worcester Heart Attack Study. Circ Cardiovasc Qual Outcomes 2:88-95, 2009.

**Student's Role:** To assist with the collection and analysis of data from the Worcester Heart Attack Study.

**Required Skills:** Good analytical skills and some clinical experience.

**Location:** Biotech 4, 377 Plantation Street, Worcester, MA 01605



#### **40. Clinical/Translational Research Pathway Program Projects**

**TITLE: Role of *Pygo1* in Human Sebaceous Gland Tumors**

**Stephen Lyle, MD, PhD  
508-856-4774**

**UMMHC  
Department: Cancer Biology  
364 Plantation St., LRB 411  
Worcester, MA**

**Description:** The WNT signaling pathway regulates cell proliferation during development and wound healing. It is also frequently disrupted during tumorigenesis. Dr. Lyle's lab recently began work characterizing a gene involved in the WNT pathway that may be a therapeutic target in cancer therapy. *Pygo1* encodes a nuclear protein that appears to negatively regulate  $\beta$ -catenin, a transcription factor involved in WNT signaling. In a sebaceous tumor sample from a patient, members of Dr. Lyle's research group found that the *pygo1* gene was down-regulated. This modified expression pattern is likely crucial to the tumor's proliferative capacity.

The summer student will help the Lyle laboratory to investigate the role of *pygo1* in the formation of sebaceous tumors. He will work with archival tumor tissue samples and human cells derived from sebaceous tumors and use RT-PCR and immunohistochemical techniques to elucidate the extent that *pygo1* expression is involved in the development of this cancer. If *pygo1* expression patterns are affected in multiple tumor samples, the gene could be a novel candidate for use in cancer therapy.

**Student's Role:** Identifying appropriate patient samples, performance of RT-PCR and IHC on samples, tabulating data, drawing conclusions, assist in writing manuscript.

**Required Skills:** None

**Location:** Lazare Research Building, 470U

## **41. Clinical/Translational Research Pathway Program Projects**

**TITLE: Development of novel AAV vector based gene therapeutics for Canavan Disease**

**Guangping Gao, PhD  
508-856-3563**

**UMMC  
Molecular Genetics and Microbiology/Gene Therapy Center  
Biotech V, suite 250,  
381 Plantation Street  
Worcester, MA**

### **Description:**

Canavan disease (CD) belongs to a group of pathological conditions in brain known as Leukodystrophies. This severe neurodegenerative disorder is characterized by swelling and spongy degeneration of white matter in the brain. The clinical features of the affected children include mental retardation, hypotonia, macrocephaly, head lag, and early death. In the past 2 decades, some most significant progresses in CD research have been made. The first breakthrough made by Matalon and Divry was the identification of CD as an inborn error of N-acetyl L-aspartate (NAA) due to a deficiency in aspartoacylase (ASPA). The second milestone in studying molecular etiology of CD was established by my PhD dissertation research in a group led by Matalon and Kaul. This work resulted in isolation of *ASPA* gene and discovery of *ASPA* gene mutations associated with CD and made genetic screening and development of gene therapeutics for CD possible. The third important achievement in CD research was the creation and identification of animal models for CD. Currently, there is no effective treatment for CD. However, some initial attempts to develop gene therapeutics for CD in the past decade represent a promising approach to tackling this devastating disease. While these pioneering studies on *ASPA* gene replacement therapy did not generate significant breakthrough due to the lack of gene transfer efficiency and ability to target appropriate cell type involved with NAA metabolism in the brain by both non-viral and viral gene delivery vehicles used, some monumental advancement in gene therapy vectorology, primarily based on our recent work, has been accomplished in the past several years. After my early work in molecular genetics of CD, I redirected my career to the field of gene therapy research with the determination to seek a path that would eventually cure CD and other genetic diseases and save the lives of those sick children. The major focus of my research in the past 14 years has been to search for highly efficient and safe gene transfer vectors, which led to the discovery of a novel family of primate Adeno-associated viruses (AAVs) with superb gene transfer capability and safety profiles in many target tissues relevant to gene therapy applications including CNS. In addition, a novel self-complementary vector genome design that was developed by Samulski and Xiao and capable of bypassing the rate limiting step in single stranded AAV transduction has proven to be highly effective. Another significant development in molecular medicine in the recent years is the discovery of RNA interference and its potentials as gene therapeutics through regulating gene expression. University of Massachusetts Medical School is a world leader in discovering and developing miRNA/RNAi based therapeutics. Our combined strengths in AAV mediated miRNA/RNAi delivery put us in a unique position for performing the studies proposed here.

The main objectives of this study proposal are the followings. i). To identify some AAV based highly efficient vectors for neuron and oligodendrocyte gene transfer. NAA metabolism in brain is compartmentalized. NAA is produced in neurons but broken down in oligodendrocytes by ASPA. Thus, oligodendrocytes should be a major target for novel gene therapeutics for CD. ii). To explore the use of miRNA/RNAi technology to regulate NAA synthesis in neurons and metabolism in oligodendrocytes. This may shed some lights on understanding the molecular etiology of CD and developing somatic animal models for CD and novel therapeutic strategy to reduce CNS toxicity of NAA. iii) To construct AAV candidate vectors with capsid and gene therapeutic designs developed from a) and b) for future studies on novel gene replacement and/or interference therapeutics to ameliorate the disease phenotype in the Canavan mouse model. To achieve those goals, we are going to first compare different routes of vector administration including multiple site stereotaxic, single lateral ventricular, and systemic injections in neonatal and adult mice using EGFP expressing AAV9 and AAV rh.10 vectors for spreading of EGFP transduction and targeted cell types. The method of vector delivery that results in the widest spread of reporter gene transduction will then be used to screen an expanded panel of novel AAVs that have shown promises in CNS gene transfer for efficient gene transfer to different cell types with a focus on neurons and oligodendrocytes that are implicated in the pathogenesis of Canavan disease. Meanwhile, micro RNAs or sh RNAs that specifically act on the mRNAs of NAA or ASPA to knock down their expression will be designed and optimized in vitro. Finally, the optimal AAV vectors with different designs of gene therapeutics will be constructed for future preclinical gene therapy studies in the CD mouse model.

Student's role: 1). Literature reviews and summary on the current status of Canavan disease and gene therapy of neurodegenerative diseases.

2). Process, analyze and document brain tissue sections for reporter gene (EGFP) transfer by rAAV vector.

3). Design, cloning and screening of shRNA and microRNA for regulating NAA synthesis and metabolism by in vitro assays.

**Required Skills:** Molecular biology cloning, biochemical assays, Vector NTI DNA or other, software, neurobiology, tissue culture, etc

**Location:** Gao lab, Gene Therapy Center, Biotech. V. 381 Plantation street

## **42. Clinical/Translational Research Pathway Program Projects**

**TITLE:** Total Joint

Patricia D. Franklin, MD, MBA, MPH  
David Ayers, MD Chair – Orthopedics  
Contact: Janel Milner (508) 856-2202  
[Janel.Milner@umassmed.edu](mailto:Janel.Milner@umassmed.edu)

UMMC  
University Campus  
Orthopedic Surgery  
55 Lake Avenue, North  
Worcester, MA

**Project Description:** The student will assist in NIH funded clinical research designed to (1) measure and (2) improve physical activity and function in adults with knee arthritis who have total knee replacement surgery.

**Student's Role:** Daily work will include survey administration, data management, and participation in a clinical research team comprised of surgeons, nurses, and research professionals. Students will be exposed to ambulatory and surgical patient care in the course of the research.

**Interview:** Required

**Location:** University campus Dept of Orthopedic Surgery

### **43. Clinical/Translational Research Pathway Program Projects**

**TITLE: Evaluation of MicroRNA in Liver Disease**

**Gyongyi Szabo, MD, PhD, Professor  
856-5275**

**UMMC  
Department: Medicine  
LRB215  
Worcester, MA**

**Description:** Micro RNAs(miRNA) are a class of small, regulator noncoding RNAs that inhibit gene expression by binding to imperfect complimentary sites within the messenger RNA (mRNA). Micro RNAs were found to be misexpressed in various disease conditions such as cancer. While the functional role of miRNAs is most understood intracellularly in mRNA regulations, miRNAs can also be found in the circulating blood. While little is known about the biological significance of miRNA in the circulation, specific changes in circulating miRNA may be associated with disease states. Little is known about the role of miRNAs in liver diseases. Recent evidence suggests that changes in miRNA122 levels in hepatocytes have an association with the presence of hepatitis C infection. The present project aims to evaluate miRNA expression hepatitis C infection or other chronic liver disease to evaluate if a particular miRNA profile is associated with the disease. Results from this study may help to develop biomarkers in liver diseases.

**Student's Role:**

The student will be required to learn basic laboratory techniques such as miRNA isolation and real-time PCR for miRNA measurement. The student will work with samples from liver patients and will be required to take the CIPI test. Training will be provided by the personnel in the Szabo laboratory and the student will work with a team of scientists and students in the Szabo lab.

**Required Skills:** Completion of 1st year of medical school

**Location:** Szabo research lab (LRB2nd floor)