UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL OFFICE OF UNDERGRADUATE MEDICAL EDUCATION

MEDICAL STUDENT SUMMER RESEARCH FELLOWSHIPS

CATALOGUE 2012

Directors:
Michael Godkin, PhD
Family Medicine and Community Health

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Molecular Genetics and Microbiology

Administrative Assistant
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Office of Undergraduate Medical Education

Contents

Note: Some projects are pre-matched. See the signup sheet for availability and funding status.

Project # 1

Title: Barriers to Delivery of Standard of Care Colorectal Cancer Treatment

Karim Alavi, MD, MPH
Program Director, Colon and Rectal Surgery Fellowship
(508)334-1392

UMASS Memorial Medical Center
Department of Surgery, Division of Colon and Rectal Surgery
67 Belmont Street
Worcester, MA 01605

Description: Despite an overall decline in the incidence and mortality of colorectal cancer (CRC), disparities in CRC treatment and outcomes continue to exist in low socioeconomic status (SES) patients. Not only are they less likely to receive guideline appropriate adjuvant therapy but they are more likely to die of same stage CRC. This difference is less likely due to more aggressive tumor biology and more likely related to inadequate treatment. Limited access to cancer specialists, co-morbid conditions, race/ethnicity, and age have consistently been linked to less use of effective therapies. However, even after accounting for these differences, under-use of treatment among lower SES patients persists. **Lack of awareness of treatment options, mistrust of the system/physician, cultural biases, and/or poor communication of treatment risks and outcomes may provide possible explanations**. This persistent gap in outcomes suggests that traditional methods of conveying risk enhance anxiety and may not translate well to vulnerable populations.

Storytelling, a method of narrative communication, may offer a unique opportunity to promote evidence-based choices in a culturally appropriate context. The narrative method for conveying risk has been shown to promote health behavior change and CRC prevention in Latinos. Yet little is known about narrative communication and its impact on promoting compliance with treatment recommendations for CRC. As surgeons, we play a pivotal role in the decision-making process, shepherding patients along the colorectal cancer treatment pathway. It is the initial surgeon-patient interaction which is essential in engendering a level of trust that enhances participation in treatment recommendations.

We will be proposing a research plan for a K award to the National Cancer Institute aimed at better defining the source for disparate care in the treatment of CRC. As part of the initial stages prior to submitting the application, we are in the process of obtaining preliminary data aimed at determining the impact of SES (as defined by income, education level, occupation) on standard of care CRC

Student's Role: The students' responsibilities would include the following: 1) use of an already established/populated CRC database (~ 400 patients) to analyze associations between low SES and CRC outcomes, 2) continue to populate the CRC database simultaneously, and 3) to help write and critically review an abstract for submission and the preliminary data section of grant. The student will learn valuable skills including data collection, developing a hypothesis, critically analyzing data, and scientific writing.

Interview: Required

Location: UMASS Memorial Medical Center

Project # 2

Title: Multi-Modal Approach to Acute Pain in the Peri-Operative Period

Arnel Almeda, MD, Russell Flatto, MD and Anthony Schwagerl, MD, PhD
Assistant Professors of Anesthesiology at UMASS Medical School
(508) 231-6431

UMASS Memorial Medical Center
Department of Anesthesiology
119 Belmont Street
Worcester, MA 01605

Description: We have recently started an Acute Pain Service in January 2011, here at UMASS Memorial that has been recognized by the Joint Commission as well as UMMMC as one of the "5 Best Practices". The Acute Pain Service first started with Orthopedics and their "Joint Replacement Service" to provide a multi-modal approach to treat their pain before, during and after their hip or knee operation. Since starting this service, we have accumulated an enormous amount of clinical data in the charts that needs to be acquired and tabulated in a database format. This would involve some time with Medical Records looking at what kind of regional technique was used, what medicines was given pre, intra and post-operatively. Additional time would be spent analyzing the data, putting it into a chart format and preparing it for some type of publication. The goal of this project is to show quantitatively how much success we had with our multi-modal approach in reducing the amount of opioids needed post-operatively and qualitatively in regards to patient comfort. We also need someone to act as a liaison between the Anesthesia staff and patient regarding our new project "Regional Success Survey". This would involve seeing the patient after surgery, inquiring about their regional technique and tabulating how much medicine they required during their hospital stay. The medical student who participates in this summer project would be working with three Attending Anesthesiologists who currently rotate on a daily basis with the Acute Pain Service. By the end of this rotation, the student will have an excellent knowledge base of some familiar regional techniques as well as common opioids used in the peri-operative setting. This project would be an excellent fit for someone interested in Orthopedic Surgery and/or Anesthesiology and who would like a greater breath and depth of both fields before his/her clinical rotations start.

Student's Role: To obtain, chart and analyze clinical data obtained over the past year in preparation for future publication either within the department or with a scientific journal.

Required Skills: Focused: fluent, clear, concise oral and written work. Ability to communicate effectively with support staff, nurses and physicians. Excellent follow through on assignments.

Interview: Required

Location: UMASS Memorial Medical Center, Dept of Anesthesiology

Project # 3

Title: Perinatal Depression and the Impact of Stress during Pregnancy on Mother and Infant (UMMS Center for Clinical & Translational Science, NIH-CTSA Pilot Project Program Grant)

Kristina M. Deligiannidis, MD
(508) 334-7262

UMass Medical School
Center for Psychopharmacologic Research and Treatment
Department of Psychiatry and Obstetrics & Gynecology
361 Plantation St
Worcester, MA 01605

Description: This single-site observational cohort study will prospectively examine the antenatal and postpartum plasma levels of cortisol, sex hormones and γ–aminobutyric (GABA) in women at High-Risk of developing postpartum depression (PPDHR) as contrasted with Healthy Control Low-Risk (HCLR) women and to evaluate depression, anxiety, functional disability, social support and quality of infant bonding. We will examine basal (unstressed) hypothalamic-pituitary-adrenal (HPA) neuroendocrine functioning as measured by repeated plasma cortisol, sex hormone and GABA measurements in late pregnancy and in the postpartum in two cohorts of community women: PPDHR women with depressive symptoms and HCLR women without symptoms. Standardized mood and psychosocial assessments will be completed throughout late pregnancy and in the early postpartum. We will also examine dynamic (stressed) HPA neuroendocrine functioning with a psychosocial stress test (Trier Social Stress Test) in third trimester women and evaluate its association with the development of postpartum depression (PPD). This stress test will involve repeated salivary cortisol measurements and serial blood draws. Exploratory aims of the study include collecting maternal DNA from both cohorts for genetics studies, and umbilical artery cord blood at delivery for future neuroendocrine functioning studies in neonates born to both cohorts of women.

Approximately 350 pregnant women will be screened with a one page questionnaire that assesses risk of PPD during their routine 28 week gestational age prenatal visit at our UMMMC West 4 Ob-Gyn clinic. High risk and low risk women who meet criteria will undergo a stress test and be evaluated prospectively through the 10th week postpartum for depressive symptoms.

Student's Role: The medical student's role, once CITI trained, can be extensive and hands on with research subjects. The medical student could be involved in consenting subjects, performing depression screening in prenatal subjects at the Memorial OB clinic (West 4) and conducting visits on labor/delivery; can learn how research psychiatric interviews are conducted which assess not only psychiatric symptoms but obstetrical data; follow subjects longitudinally from late pregnancy to the postpartum; learn about neuroendocrine biomarkers and their significance towards understanding the pathophysiology of major depression during pregnancy; obtain collaborative skills with PI and research coordinator involved in the study, perform minimal research database entry to be shared with PI and research coordinator, etc. He/she will help administer the psychological stress test (i.e. subject gives an unprepared speech and performs math calculations) with repeated endocrine measures. He/she will be able to learn about clinical trial design, recruitment strategies, research ethics, IRB procedures, etc. as they pertain to the study. There are numerous facets in which to be involved, and the medical student would have a desk adjacent to the research coordinators in our research suite where the PI's office is within the CPRT research group. The medical student would attend all research group meetings so that he/she would have exposure to the other studies ongoing in the CPRT research group. Direct supervision would be by the PI for the entire research fellowship program. There is also an IRB-approved neuroimaging study in postpartum women, which the student could gain experience from as well, if interested.

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

Interview: Required

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

Project # 4

Title: Sperm Chemoattraction Mechanisms

Harvey Florman, PhD
(508) 856-1675

University of Massachusetts Medical School
Department of Cell Biology
Room S7-304
55 Lake Avenue North
Worcester, MA 01655

Description: In order for fertilization to occur sperm must locate the mammalian egg in the upper segment of the oviduct (Fallopian tube). This targeting process involves sperm response to local chemoattractants. We discovered that Pkdrej, a member of the polycystin-1 family, plays a role in sperm migration to the egg and may be part of a chemoattractant receptor complex. Chemotaxis assays will be carried out on sperm from wild-type and Pkdrej mutant males in order to test this hypothesis.

Student's Role: The student will be trained to perform chemotaxis assays.

Required Skills: The student should have some basic lab skills, such as preparing media. All other skills can be acquired during the term of this project.

Interview: Required

Location: Medical School Building (S7-304)

Project # 5

Title: Gene Therapy of Inherited Neurodegenerative Disease, Canavan Disease

Guangping Gao, PhD
(508) 856-3563

University of Massachusetts Medical School
Gene Therapy Center
Biotech V, Suite 250
381 Plantation Street
Worcester, MA 01605

Description: Canavan disease (CD) is a rare and fatal childhood leukodystrophy caused by autosomal recessive mutations in the aspartoacylase gene (ASPA) (as established by this PI's graduate work). ASPA deficiency in Canavan patients leads to elevated N-Acetyl-Aspartic Acid (NAA) and spongy degeneration of white matter (WM) throughout the CNS, producing severe psychomotor retardation and early death. The pathophysiology of CD is not well understood yet. Currently, there is no effective treatment available for CD. Recombinant adeno-associated virus (rAAV) - based ASPA gene therapy is a promising strategy for treating CD. An earlier clinical study to directly inject AAV2 into brain parenchyma generated no clinical improvement in the patients, likely due to inadequate transduction efficiency of rAAV2, and limitations of localized intraparenchymal vector delivery. However, recent studies by us and others suggest that several novel primate rAAVs are highly efficient in transducing the CNS by either crossing the blood-brain-barrier (BBB) after intravenous (IV) injection or widely spreading in the brain parenchyma following intracerebroventricular (ICV) delivery. Moreover, an ASPA-/- mouse model created by Matalon et al. mimics the neuropathology and clinical manifestation seen in the patients with congenital and infantile forms of CD. These advances provide us a unique opportunity for a preclinical proof-of-concept study to address the unmet challenge in CD gene therapy. Single IV injections of novel rAAVASPA in the postnatal CD mice at P1, P7, or P14 corrected metabolic defects, mitigated motor malfunctions, neuropathology, retinopathy and nephropathy, and rescued the lethal phenotype (<4wks of life span v.s. > 6 months). Hence, we hypothesize that we can develop effective and sustained rAAV gene therapeutics that will correct the metabolic defect, alleviate the disease phenotype, and prolong survival of CD mice without causing a significant toxicity. In this project, we will take several novel approaches to test this hypothesis: a). novel AAV capsids (AAV9, rh.8 or rh.10) capable of crossing the BBB after IV injection and/or distributing widely after ICV delivery for efficient CNS transduction, b). novel self-complementary (SC) genome design to further enhance ASPA transduction, c). novel routes of administration (ROA) (e.g. IV and/or ICV) for efficient CNS gene transfer, d). novel miRNA-regulated and/or CNS-specific promoter-directed codon-optimized transgene cassettes for tissue-specific ASPA expression

Student's Role: rAAV-mediated systemic gene delivery to the CNS of Canavna mice via different routes of administration. Follow the study animals by biochemical, neurological, developmental parameters to assess therapeutic efficacy and safety profiles.

Required Skills: Strong background and technical skills in molecular biology, neurobiology, virology, cell culture and experimental animals.

Interview: Required

Location: Gene Therapy Center, Biotech V

Project # 6

Title: AAV Vector-mediated Long Term Overexpression and Knock Down of miR-122 to Study its Role(s) in Tumorigenesis of Hepatocarcinoma

Guangping Gao, PhD
(508) 856-3563

University of Massachusetts Medical School
Gene Therapy Center
Biotech V, Suite 250
381 Plantation Street
Worcester, MA 01605

Description: miR-122 is the most abundant miRNA in the liver. It plays important roles in liver biology and pathology. Using recombinant Adeno-associated virus vector, we have recently developed a novel technology to efficiently and stably over express and/or knock down of endogenous miRNA in adult mammals (Nature Methods, in press). In a proof-of concept study, we utilized this technology to explore the potential roles of miR-122 in the development and treatment of HCC. Our preliminary data suggested a strong correlation between the abundance of miR-122 transcripts and HCC. Extensive long term studies are in the process to further characterize the role(s) of miR-122 in tumorigenesis.

Student's Role: Perform animal necropcies to examine gross pathology as well as histopathology of liver and other major tissues. Perform molecular analyses to evaluate respected miRNAs, target mRNAs, vector genomes and proteins to study the role(s) of miR-122 in the development and treatment of HCC.

Required Skills: Strong background and technical skills in molecular biology, neurobiology, virology, cell culture and experimental animals.

Interview: Required

Location: Gene Therapy Center, Biotech V

Project # 7

Title: Interaction Between Vancomycin and Methicillin Resistance in *Staphylococcus aureus*

Jon Goguen, PhD
(508) 856-22490

University of Massachusetts Medical School
Department of Molecular Genetics and Microbiology
Room S6-210
55 Lake Avenue North
Worcester, MA 01655

Description: We have recently discovered a phenomenon of substantial clinical interest. An strain of methicillin-sensititive Stapyhlococcus aureus (MSSA) gave rise to a methicillin resistant clone (MRSA) within a patient during antibiotic therapy. While both MSSA and MRSA are common, this is the first instance in which MRSA was clearly derived from MSSA within an individual patient. Usually, MRSA arises from acquisition of new segment of DNA (the SCCmec cassette) containing the gene mecA, responsible for methicillin resistance. This requires the presence of other bacteria to serve as donor of the cassette. In this patient, the original MSSA isolate carried the SSCmec cassette, but the mecA gene was interrupted by the presence of an insertion sequence, a type of transposable element. The strain converted to MRSA via precise excision of this element. Strains of this nature are problematic, because they test sensitive for methicillin in the clinical lab, but will rapidly convert to resistant if the patient is treated with methicillin. In addition, we have evidence that MRSA strains increase their resistance to the alternative antibiotic vancomycin when MecA is inactivated. Vancomycin is the most important antibiotic used to treat MRSA, and our data suggest that treatment with vancomycin may select for inactivation of MecA by transposable. This implies a vicious cycle in which exposure to vancomycin increases the frequency of apparently methicillin-sensitive strains that are untreatable with methicillin because they rapidly convert to resistance.

Student's Role: A student choosing to work on this project would contribute to determining the frequency of such strains in the hospital environment, determining the most effective way to detect them, and determining if and how exposure to vancomycin increases their frequency.

Required Skills: Useful contributions could be made by a student with brief training in microbiological techniques that we can provide. A student with, or willing to learn, more advance skills in molecular genetics (e.g. PCR, strain construction) could contribute more fully.

Interview: Required

Location: UMMS Room S6-209

Project # 8

Title: Injury Prevention Studies

Michael P. Hirsh, MD, FACS, FAAP
(774) 443-2189

UMMHC
55 Lake Avenue, North
Worcester, MA 01655

Description: The IP Center or UMMHC is dedicated to the active prevention of injury to patients of all ages. Our group is studying the impact of a number of different interventions on vulnerable populations, including school aged children, pregnant teens, Teen drivers and geriatric patient groups. We use the summer months to collate the data we accrue during the school year, test new interventions and collect data to submit as abstracts to various injury prevention meetings upcoming in the fall.

Student's Role: The Student would help in all the above activities, including developing databases and doing statistical analyses of the data. Potential students should be aware that community outreach is a significant piece of our program and they may be asked to attend an event on a weekend or evening.

Required Skills: Familiarity with Excel is preferred. Knowledge of some basic Epidemiology and statistical analysis techniques is recommended.

Interview: Required

Location: Office based at the University hospital, but field work may also be required.

Project # 9

Title: Characterization of New Patients Presenting to the Hand Clinic

Marci Jones, MD
(508) 334-5183

UMMC
Department of Orthopedic Surgery
Hahnemann Campus
281 Lincoln Street
Worcester, MA 01605

Project Description: This study will utilize the newly implemented Hand Outcomes Registry to characterize new patients presenting to the Hand Clinic in terms physical and mental health composite scores. There is increasing literature supporting the association of upper extremity pain and dysfunction with psychosocial factors, including depression, pain anxiety and catastrophizing behavior. We plan to evaluate any trends in the physical and mental health composite scores of patients presenting to the hand clinic and determine if there is a relation to upper extremity diagnosis.

Student's Role: Assist with design and implementation of study. This will include assistance with data collection and entry, general data analysis and preparation of abstracts/manuscripts resulting from this research. There is the opportunity to extend participation in the research project beyond the summer.

Required skills: Must have passed CITI exam. Understanding of and appreciation for precision in data collection and good organization skills needed. Familiarity with Excel and basic data analysis is helpful but not required

Interview: Required

Location: Hahnemann Campus
University Campus Access Building

Project # 10

Title: Induction of Anergy in Human Autoreactive T Cells in Type 1 Diabetes

Sally Kent, PhD
Assistant Professor of Medicine, Division of Diabetes
508-856-2044

University of Massachusetts Medical Center
381 Plantation Street
Biotech 5, Suite 226
Worcester, MA 01605

Description: A major goal in therapeutics of human T-cell mediated autoimmune diseases is modulation or suppression of autoreactive T cell function. Here, we are examining the effect of chemically-coupling peptides or proteins that are the targets of autoreactive human T cells to antigen-presenting cells and then asking if we can induce anergy or non-responsiveness to that protein/peptide in the T cells in a subsequent stimulation. This project will involve the generation and characterization of both CD4 and CD8 T cell lines and clones that recognize immune targeted proteins/peptides from immune targets of the islet cells. We will optimize in vitro anergy assays for both CD4 and CD8 autoreactive T cells and determine which functional outcomes provide the most relevant data concerning the fate of autoreactive T cell function. The larger goal (outside the scope of this summer fellowship) of this assay is to provide appropriate diabetogenic T-cell populations for the subsequent in vivo transplantation studies and in vivo induction of anergy and the basis for mechanistic studies of a clinical trial using microparticles coated with relevant proteins/peptides as inducers of anergy in Type 1 diabetes and multiple sclerosis patients.

Student's Role: The student would work directly with me on this project and be involved in discussions of experimental design, execution and analysis.

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

Interview: Required

Location: 381 Plantation St
Biotech 5, Suite 226

Project # 11

Title: Induction of Cytokine Secretion from Human Autoreactive B Cells from Type 1 Diabetic Subjects

Sally Kent, PhD
Assistant Professor of Medicine, Division of Diabetes
508-856-2044

University of Massachusetts Medical Center
381 Plantation Street
Biotech 5, Suite 226
Worcester, MA 01605

Description: In NOD mice, B-cells accumulate in pancreatic islets during the autoimmune response as a precursor to the onset of Type 1 diabetes (T1D) and are necessary for disease initiation. The recent clinical trials in T1D with rituxin highlight the importance of B cells in the autoimmune response in T1D, but we know little about how they function in the autoimmune response. In human subjects with T1D, B cell studies have been mostly limited to serum antibodies as diagnostic markers and rare immunohistochemical studies of tissue samples with B cells infiltrating the islets. However, B cells contribute to the initiation and amplification of immunological responses as antigen-presenting cells, cells with co-stimulatory properties, and as secretors of effector cytokines. The functional nature of autoreactive B cells in the autoimmune response has not been addressed. We propose that autoreactive B cells from T1D subjects will have a more pro-inflammatory profile as compared to those from healthy subjects. Here, we will utilize cell culture techniques for examining autoreactive B cells from the peripheral blood, spleen and pancreatic draining lymph nodes from subjects with T1D with varying disease durations and from controls for cytokine effector functions after stimulation. This will entail examining methods of B cell stimulation will antigen and with polyclonal stimulations and determining the frequency and functional of autoreactive B cells from these groups of subjects. This study is part of a larger examination of autoreactive B cells from T1D subjects in order to understand B cell function in diseases and in therapies targeting B cells in autoimmune diseases.

Student's Role: The student would work directly with me on this project and be involved in discussions of experimental design, execution and analysis.

Required Skills: This is mostly a cell culture project utilizing basic lab skills with analysis by flow cytometry, potentially cell sorting (FACS) and other techniques like ELISA. Some PCR will be performed. As part of the learning process, I would instruct the medical student in these techniques. A knowledge of immunology would be extremely useful.

Interview: Required

Location: 381 Plantation St
Biotech 5, Suite 226

Project # 12

Title: Characterization of the DKK3b:βTrCP β-catenin Inhibitory Complex in Human Prostate Cancer Cells.

Jack Leonard, PhD
508-856-6687

Microbiology and Physiological Systems
University of Massachusetts Medical School
Department of Microbiology and Physiological Systems
Office: S4-428; lab: S6-319
55 Lake Avenue North
Worcester, MA 01655

Description: Prostate cancer is the second most common cancer in men. Current treatment options include surgery, radiation and/or hormone withdrawal therapy; methods that effectively treat early stage tumors. Unfortunately, prostate cancer often progresses and no longer responds to conventional treatments. The etiology of the disease is poorly understood, but shows a typical life history—genetic and/or chromosomal instability leading to polyploidy/aneuploidy, unrestrained cell proliferation and ultimately high-grade tumor formation. A treatment strategy currently being tested in the clinic is based on administration of Dickkopf 3 (DKK3, a member of the Dkk family of Wnt antagonists) to block tumor growth and enhances apoptosis by an ER-stress induced mechanism. We have discovered a paradigm shifting approach based on recent works in our laboratory. We found that the DKK3 molecule currently in clinical trials (termed DKK3a) exerts an indirect, non-specific effect, *not a direct effect on Wnt signaling*. **In contrast**, **we have discovered a previously unrecognized role for a novel DKK3 gene product termed DKK3b that directly blocks the Wnt signaling pathway, arrests cell proliferation and induces apoptosis of prostate tumor cells.** The summer project will define the specific protein domains of DKK3b used to assemble the β-catenin inhibitory complex in the prostate cancer cell.

Student's Role: Prepare domain construct, evaluate protein:protein interactions and test these in cancer cells

Interview: Required

Location: S6-319

Project # 13

Title: The Impact of Perimenopause on the Clinical Course of Bipolar Disorder

Wendy Marsh MD MS
(508) 859 5071

UMass Medical School
Department of Psychiatry
361 Plantation St
Office B12
Worcester, MA 01605

Description: The menopausal transition is a time of increased risk of depression in women with or without a history of depression. In women with bipolar disorder, times of rapid hormonal decline like the postpartum period are associated with severe, often depressed, mood episodes. Yet, despite the late perimenopause being a time of rapid decline in reproductive hormones, the risk of depression during the menopausal transition has not been studied in women with bipolar disorder. The objective of this K12 funded study is to prospectively assess the impact of perimenopause on mood episodes in women with bipolar disorder. Sixty women with treated bipolar disorder, twenty in each early perimenopause, late perimenopause and postmenopause, will prospectively record mood and menopausal symptoms daily for 4 months. Monthly they will complete standardized mood assessments, and estradiol and follicular stimulating hormone (FSH) plasma levels will be assayed. Mood severity will be compared between early, late, and post menopausal stage and hormonal status. High rates of depression, especially in the late menopausal transition and during times of greatest increase in FSH are hypothesized. Findings will inform future studies and will contribute concretely to the preparation of future independent investigator funding proposals. Lessons learned from affective dysregulation and reproductive neuroscience will help better address women's mental health during menopause, including the relationships between perimenopausal phase, hormonal status, and depressive symptoms on the course of bipolar disorder.

Student's Role: Become CITI trained on ethical considerations in engaging in research with human subjects

Subject Contacts

- Screen potential subjects on phone
- Present study by phone
- Learn to administer and then give consents
- Learn initial visit procedures with subjects
- Learn follow up questionnaires: including standardized mood assessments and why they were chosen
- Engage and administer questionnaires
- Recruit and enroll study participants
- Phone calls to schedule and confirm appointments
- Assess subject's interest in continued involvement
- Track subject participation

Study Involvement

Help recruit subjects
Help advertise and place advertisements and spread the word about our study
Diagnose and problem solve as it relates to the research project
Handle and protect confidential and sensitive data with integrity
Produce written, tabular and visual materials for research reports and presentations.
Assist in the design, execution and evaluation of research projects, including literature reviews, surveys, data integration and analysis.
Be trained in administering questionnaires
Prepare research manuscripts and research presentations
Conduct literature reviews

Opportunity for Self-Directed Project

Such as literature review for publication
Or presentation
Or other based on student's interest

Regular contact with Principle Investigator (PI)

For PI to answer broader questions about
theory of study,
putting the study to practice
clinical research as a career
practice of psychiatry,
women's mental health
PI available for didactic discussions related to student's areas of interest.
PI guide and advise on self-directed project

Required Skills: Excellent interpersonal skills including professionalism, empathy, and respect for those with mental illness. Organized, takes initiative, works independently.

Interview: Required

Location: 361 Plantation St
Worcester, MA 01605

Project # 14

Title: Face Processing in Young Children With and Without Autism Spectrum Disorders

Teresa Mitchell, PhD
(781) 642-0253
teresa.mitchell@umassmed.edu

University of Massachusetts Medical School
Eunice Kennedy Shriver Center
200 Trapelo Road
Waltham, MA 02452

Project Description: This project investigates behavioral, eye tracking, and electrophysiological characteristics of basic face processing in children with mental ages of 8 to 12 years. Performance of typically developing children will be compared to those with mild to moderate intellectual disability and either an autism spectrum disorder or Down syndrome. The larger aim of the study is to examine whether there is diagnostic specificity in face processing deficits in young children with intellectual disability. While it is known that children with autism who are high functioning have a unique profile of strengths and weaknesses in face processing, it is unknown whether children on the autism spectrum who also have intellectual disability will show a similar pattern and whether that pattern will be specific to the diagnosis of autism. Participants perform a series of behavioral tasks that parametrically increase in difficulty to examine patterns of discriminability. Then participants complete an eye tracking tasks that examines how gaze across faces varies with task demands. Finally, an electrophysiological paradigm examines whether a typical unique signature of face processing is observed in children with atypical development. Relationships between performance on the three measurement domains will be explored to further understand the behavioral consequences of eye gaze and neurophysiology

Student's Role: The student will be involved in data collection, data analysis, recruitment, and data presentation.

Required Skills: Comfort with young children, experience with data spreadsheets, attention to detail.

Interview: Required

Location: E. K. Shriver Center
Waltham, MA

Project # 15

Title: Clinician Variations in Early Outcome Prediction in Patients with Moderate-severe Traumatic Brain Injury

Susanne Muehlschlegel, MD, MPH
508-856-4684

University of Massachusetts Medical School
Departments of Neurology, Anesthesia/Critical Care and Surgery
55 Lake Ave North, S-5
Worcester, MA 01655

Description: Traumatic brain injury (TBI) is a major public health problem in the U.S. and worldwide. Each year, approximately 1.7 million people sustain a TBI in the U.S., with 275,000 hospitalizations and 52,000 deaths attributed to TBI. TBI may afflict us all, but young adults are particularly at risk. Moderate-severe TBI, defined by a decreased level of consciousness (Glasgow coma scale ≤ 8 for severe, and 9-12 for moderate), comprises the majority of hospitalizations and deaths due to TBI, and 90% of all TBI related medical costs. In the acute hospitalization phase, families of affected patients yearn for accurate early outcome prediction of functional long-term outcome, in order to make informed decisions about the aggressiveness of care and future planning. Medical providers are asked to prognosticate on a daily basis, but this can be quite difficult due to the lack of a comprehensive outcome prediction tool in TBI. The only known predictors of outcome in moderate-severe TBI stem from the IMPACT study group (International Mission for Prognosis and Analysis of Clinical Trials in TBI), which have identified admission pupillary reactivity, initial head CT findings, first motor examination, laboratory values and presence of hypoxia and hypotension on presentation to be predictive of outcome. These predictors, however, explain only about 1/3 of the variability in outcome after moderate-severe TBI, leaving families and clinicians to guess rather than predict with a certain degree of accuracy patients outcomes in the early phase of TBI. The goal of this research project is to assess the variations in outcome prediction by physicians from different specialties (Neurocritical Care, general surgical critical care, Neurologists, Neurosurgeons and trauma surgeons). In addition, we would like to assess whether and how these physicians take intensive care unit (ICU) complications (i.e. sepsis, pneumonia, renal failure etc.) into account when predicting outcome to families in the ICU. In order to assess these variations, we will design an online survey which will be emailed to members of national subspecialty societies: Neurocritical Care Society, American Academy of Neurology, Society of Critical Care Medicine and American Association of Neurological Surgeons. We plan to design the survey now, and email it out before the start of the summer student, so that responses are available and ready to be compiled and analyzed by June.

Student's Role:

- Compile responses from a national survey previously sent out to members of national subspecialty societies: Neurocritical Care Society, American Academy of Neurology, Society of Critical Care Medicine and American Association of Neurological Surgeons and
- analyze that data.
- Survey UMMS faculty members in the departments of Neurology, Neurosurgery, Trauma Surgery, and Surgical Critical Care.
- Student will learn about study design, background research, basic statistical analysis of clinical studies, how to put results into context.
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- Student is expected to present the results locally to the immediate research group, Neurology Grand Rounds (with assistance by the PI).
- We aim to prepare the results in abstract form for a poster presentation at a national meeting. Student will learn about abstract writing and submission
- Ideally, a manuscript will result from this project. Student will learn about manuscript writing and submission

Required Skills: Diligence, advanced computer knowledge with advanced skills in WORD, EXCEL, POWER POINT, if possible (but not necessary) Survey Monkey, RedCAP.

Interview: Required

Location: University Campus UMMS, online, and in the Trauma- and Neurointensive care unit at UMASS (Lakeside 2)

Project # 16

Title: Targeted Antimicrobial Delivery to Combat Drug-resistance

Gary Ostroff, PhD
(508) 856-1930

University of Massachusetts Medical School
Program in Molecular Medicine
373 Plantation St
Biotech 2, Suite 113
Worcester, MA 01605

Description: The growing problem of drug-resistance requires new approaches in developing antimicrobials. Our hypothesis is that the targeted delivery of antimicrobials to phagocytic cells will aid in the killing and clearance of pathogens able to subvert the functions of these innate immune cells. Targeted delivery will allow for attaining supra-effective antibiotic levels at the site of infection and allow the utilization of effective antibiotic classes that have poor solubility, pharmacokinetic/clearance or toxicity issues to fight drug-resistance. We utilize glucan particles (GPs), which are phagocytosed by innate immune cells in a receptor-dependent fashion to deliver antibiotics into these phagocytic cells. Ongoing work has shown that targeted GP antibiotic delivery enhances bacterial killing in macrophages 2-5 log orders compared to free antibiotic.

Student's Role: Prepare and characterize GP antibiotic formulations and perform in vitro macrophage – microbial killing assays. Potential for working with collaborator testing GP antibiotic formulations in vivo

Required Skills: Sterile technique, microbial culture, tissue culture

Interview: Required

Location: 373 Plantation St., Biotech 2, Suite 113

Project # 17

Title: Interaction of Homologous Recombination and DNA Replication Systems

Anthony R. Poteete, PhD
(508) 856-3708

University of Massachusetts Medical School
Department of Molecular Genetics and Microbiology
Room S6-119
55 Lake Avenue North
Worcester, MA 01655

Description: Homologous genetic recombination is a universal life process. It is nature's most accurate way to repair double strand breaks in DNA.

The Red system of the bacteriophage λ is one of the simplest and most intensively studied homologous recombination systems, and serves as a model for the vastly more complex Rad52 system of humans. The main pathway of Red-mediated recombination operates on DNA which is undergoing replication. To probe interactions between Red and the replication system, we have isolated Escherichia coli mutants which are altered in these interactions. The project for this summer is to map, sequence, and measure the recombination-related phenotypes of these mutants.

Student's Role: Working with the PI on all aspects of the research.

Required Skills: Keeping good notes

Interview: Required

Location: UMMS Room S6-120.

Project # 18

Title: What Factors are Associated with High Dose Opioid Utilization in the Management of Acute Work-related Low Back Pain?

Glenn Pransky, MD
(508) 497-0234

UMMS
Department of Family Medicine and Community Health
Liberty Mutual Research Institute
71 Frankland Road
Hopkinton MA 01748

Description: Low back pain (LBP) is one of the most common reasons for working-age adults to visit a primary care physician.[1] Fortunately, most patients with acute, uncomplicated LBP recover quickly, regardless of what medication or treatment they receive. Evidence-based treatment guidelines suggest a "trial" of opioids in appropriately selected patients, with reassessment conducted for patients who fail to respond to the treatment to provide control of severe, disabling pain in order to improve activity tolerance.[2] Despite these recommendations, there has been an increasing trend towards use of opioids to treat acute LBP, which has been associated with misuse, accumulation of unused prescriptions, abuse, overdose, and accidental death.[3-10] A study by LMRIS researchers of early opioid use found that workers with acute, disabling LBP who receive early opioid prescriptions are at higher risk for prolonged disability, higher medical costs, and surgery; even after controlling for a number of severity indicators. In addition, the outcomes were found to be dose-related.[11] Although these findings are recognized in workers compensation (WC) population data,[12-14] there has been no investigation in detail of individual cases to understand why some patients receive high, inappropriate doses of opioids for acute LBP. This project will address this gap, through detailed review of WC claims files for selected cases with early, high-dose opioid prescribing for uncomplicated acute LBP. The student will actively participate in all phases of the research – planning the case selection and review process, designing and executing the review, compiling results and preparing a scientific report. This is an excellent opportunity to work closely with well-established health services researchers and to develop useful research skills.

Student's Role: Planning the case selection and review process, designing and executing the review, compiling results and preparing a scientific report.

Required Skills: Basic clinical knowledge, systematic approach to problems, chart review

Interview: Required

Location: Liberty Mutual Research Institute for Safety
Center for Disability Research
Hopkinton, MA

Project # 19

Title: Regulation of DNA Replication Kinetics

Nick Rhind, PhD
(508) 856-8316

University of Massachusetts Medical School
Department of Biochemistry and Molecular Pharmacology
LRB 940
Worcester, MA 01655

Description: DNA replication is organized so that certain regions of the genome replicate earlier than others. This replication timing pattern correlates with transcription, chromatin structure and genome evolution. We study the mechanisms that regulate replication timing and have discovered that heterochromatin inhibits the activation of loaded replication complexes. This project is to measure genome-wide replication kinetics by deep sequencing in yeast heterochromatin mutants and compare these profiles to our replication-complex mapping datasets.

Student's Role: Prepare and sample synchronous yeast cultures. Prepare deep sequencing libraries. Analyze data.

Required Skills: Basic molecular biology

Interview: Required

Location: LRB 940E

Project # 20

Title: Is Post-Traumatic Stress Disorder a Missing Link inChronic Medical Conditions?

Tina Runyan, PhD, ABPP
508-334-8856

University of Massachusetts Medical School
Dept of Family Medicine and Community Health
A-377 Benedict Building University Campus
or
Hahnemann Family Health Center
279 Lincoln Street
Worcester, MA

Description: The proposed research aims to explore associations between chronic medical conditions, including chronic pain, and several physiological health parameters among patients with symptoms of PTSD. For the past year, Hahnemann Family Health Center has used a 4-item PTSD screen, which is embedded in a larger behavioral health screening tool that includes other measures. The screening instrument is routinely given to patients with Type II diabetes every six months as well as to all patients during annual physical exams and at the discretion of the PCP during acute care or continuity medical visits. Scores on these screening measures are entered into a flow sheet in the electronic medical record (Allscripts).

The specific aim of this research project is to utilize retrospective electronic record review methodology to assess the hypothesized associations among body mass index, blood pressure, lipid values and glucose intolerance indicators (as available) in primary care patients (adults age 18 over) with and without PTSD symptoms and chronic medical conditions.

A secondary aim is to conduct four focus groups to ascertain barriers to recruitment and innovative ideas for the implementation of a group based primary care intervention for patients with co-morbid PTSD and chronic medical conditions. Two focus groups will be with 4-6 primary care providers each and two focus groups will be with prospective patients that are invited to participate by their PCP. The patient focus groups will be with 4-8 patients per group. A standard set of questions will be developed for each type of focus group and the group will be audio taped.

Student's Role: One or more of the following depending on student's skills and interests:

- Review relevant literature
- Help with data extraction from Allscripts
- Help with data analysis plan and interpretation
- Plan and conduct focus groups

Required Skills: Literature review and synthesis skills; Writing ability; Data analysis and interpretation skills (will be supported in this activity); Ability to plan for and conduct focus groups

Interview: Required

Location: Benedict Building, University Campus;
Hahnemann Family Health Center

Project # 21

Title: Investigation of the Novel Role of MicroRNA-155 in CCl4-induced Liver Inflammation and Fibrosis

Gyongyi Szabo, MD, PhD
(508) 856-5275

University of Massachusetts Medical School
Department of Medicine
LRB 208
364 Plantation Street
Worcester, MA 01605

Description: Liver fibrosis results from continuous damage (inflammation) to the liver. Chronic viral hepatitis, alcohol abuse, metabolic diseases, autoimmune diseases, and cholestatic liver diseases are the common causes of liver fibrosis. Various signaling molecules have been shown to play a role in this process; however, the role of microRNA is largely unknown. MicroRNA (miRNAs) have emerged as a class of single-stranded non-coding RNAs of 19-24 nucleotides that control gene expression at the post-transcriptional levels. Various innate immune responses are fine tuned by miRNA-155, miR-125b and miR-146a where these miRNAs regulate multiple genes. MiR-155 is a master regulator of inflammation and exerts a positive effect on TNF alpha via enhancing its translation. Our preliminary results indicate the induction of miR-155 in mice administered with CCl4. Since sustained inflammation leads to fibrosis or cancer and miRNA-155 is a major regulator of inflammation, here we sought to elucidate the novel role of miRNA-155 in CCl4-induced inflammation and fibrosis.

Student's Role: Measure micro-RNA levels

Required Skills: PCR

Interview: Required

Location: LRB

Project # 22

Title: Childhood and Adolescent Obesity Prevention Through Community Education Programs of the Whiteriver Indian Health Service

Faculty advisors:
At UMMS: Mick Godkin PhD; at Whiteriver IHS: Marc Traeger MD

Marc Traeger, MD
Preventive Health Officer
Whiteriver Indian Health Service
PO Box 860
200 West Hospital Drive
Whiteriver, AZ 85941

Description: The intent of this project is to develop an effective community childhood and adolescent obesity prevention program on the Whiteriver Reservation using methods that have been used successfully by other public health organizations. The initiative is to be implemented by the reservation's Preventive Health Office in partnership with other departments within the Indian Health Service as well as with other local community health organizations. The first phase of the project will consist of collecting current statistics about obesity on the reservation and to do a study to determine major causes and contributors to obesity that may be targeted by educational programs in either the clinical or community setting. In addition, a review of existing public health programs targeting children or adolescent obesity will be made to establish possible strategies for the launching of Whiteriver's initiative. In the second phase, the results of this review with be considered in the framework of the needs and available resources at Whiteriver and a plan will be developed to implement an obesity prevention program on the reservation. The plan will target major factors that are determined to be major contributors to obesity and will be developed with sensitivity to the social and cultural environment of its target population. Potential aspects of the program include offering brief nutrition counseling to patients before or after scheduled doctors' appointments, creating visual displays advocating for simple lifestyle changes, or other community related projects. Finally, this plan will be implemented and monitored for its community reception and effectiveness.

Student's Role: Student will begin with completing a literature survey of established obesity prevention programs used by public health organizations to determine what types of tools and strategies have been the most effective and may be relevant to the initiative. Student will be in charge of developing and maintaining a database of existing data relating to obesity rates on the Whiteriver Reservation. Finally, student will work with Dr. Traeger and staff from other departments at the Heath Service to develop and implement an obesity prevention initiative.

Required Skills: Quantitative Analysis, Patient surveying and counseling. Cultural Literacy.

Location: Whiteriver Indian Health Service, Whiteriver, AZ

Project # 23

Title: Role of Hdac3 During Cardiac Development

Chinmay Trivedi, MD, PhD
(508-856-6947)

University of Massachusetts Medical School
Cardiovascular Medicine
Department of Medicine
381 Plantation Street
Biotech V, Suite 250
Worcester, MA 01605

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

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

Required Skills: Microsoft Office. Prior research experience in cell and molecular biology/ biochemistry is desired but not required.

Interview: Required

Location: Biotech V, Suite 250

Project # 24

Title: Function of Ciliary Disease Proteins

George Whitman, PhD
(508) 856-1033

University of Massachusetts Medical School
Department of Cell Biology
55 Lake Avenue, North
Worcester, MA 01655

Description: Cilia are present throughout the body and have essential roles in reproduction, development, fluid movement, sensory perception, and cell signaling. In humans, defects in cilia cause diseases collectively referred to as ciliopathies. Cilia emanate from a microtubule-based structure called the basal body. The basal body is comprised of triplet microtubules that transition into doublet microtubules within the transition zone (TZ) at the base of each cilium. The TZ is thought to function like a gate that allows or facilitates the entry of specific proteins destined for the ciliary shaft, while preventing the entry of non-ciliary components. Although only some of the proteins that localize to the TZ have been identified, defects in all of the TZ proteins identified thus far result in ciliopathies, highlighting the important role for this specific region of the cilium. The goal of this project is to identify novel TZ proteins, determine their specific function within the TZ, and elucidate why defects in these proteins result in ciliary disease.

Student's Role: Chlamydomonas is the best model organism for studies of the cilium. The student will analyze a Chlamydomonas mutant with defective CC2D2A, a TZ protein involved in COACH, Meckel and Joubert syndromes (OMIM: 612013). In addition, the student will generate novel Chlamydomonas mutants using insertional mutagenesis, identify the disrupted genes, and characterize the function of the identified gene products.

Required Skills: The student will be trained in all required techniques, but the student is expected to proceed with increasing independence as new skills develop over the course of the project period. A knowledge of basic laboratory techniques and previous experience in a research laboratory will expedite the student's progress.

Interview: Required

Location: S7-100

ADDITIONAL PROJECT # 25

Title: Developing a Pathophysiologically Based Nicotine Dependence Measure

Joseph DiFranza, MD
(774) 442-5658

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

Description: The summer student would be involved with the development of a new pathophysiologically based nicotine dependence measure. In doing this they would receive experience in study design and primary data collection via subject recruitment, survey administration, data management, and some basic psychometrics. In order to work in a clinical setting with human subjects, students will have to complete the CITI human subjects certification if they are not already certified. In addition the student will gain exposure to the process of measure development from conceptual phase through the initial stages of instrument refinement. Work will be primarily done in Worcester on the University Campus under the supervision of Dr. DiFranza or his research coordinator.

Student's Role: Developing and administering a working questionnaire in an adult population. Students will also receive experience in primary data collection, subject recruitment, human subjects training, data management, clinical research design, and basic psychometrics.

Required skills: Good interpersonal skills, basic proficiency in Microsoft office (specifically Excel), must have or receive Human Subjects Certification which can be done at the start of the internship, knowledge of any statistical software (SPSS, STATA, or SAS) would be helpful but not

Interview: Required

Location: University Campus

ADDITIONAL PROJECT # 26

Title: Integrating Medical Humanities into the Curriculum

David Hatem MD
(774) 442-5972

University of Massachusetts Medical School
Department of General Medicine and Primary Care
Benedict Building, A3-140
Worcester, MA 01655

Description: Motivated, humanistic students enter medical school, yet on graduation evidence suggests that they are more cynical, less patient-centered, and suffer significant rates of depression, anxiety and burnout. While there is research that seeks to describe or explain this, there is less designed to reverse this trend. Efforts in the medical humanities have often focused on electives for select groups of students that exist in parallel with the curriculum, but not necessarily integrated into the curriculum.

As UMass unveils its new Learner-centered Integrated Curriculum (LInC), there is an opportunity to more clearly integrate Medical Humanities in a way that reinforces and compliments the scientific focus of medical school so that UMass will produce well-rounded and more humanistic students, capable of learning the intricacies of medicine, while also keeping focused on the central reality that the practice of medicine is an applied science involving patients with significant needs beyond knowledge about their disease.

For this summer research project, our aim is to build on last year's project that took first steps in developing an integrated medical humanities curriculum. One key outcome of last year's project was an annotated bibliography of readings, listed by topic that is now housed in the Faculty Resources section of the Office of Undergraduate Medical Education web site. Efforts in developing this bibliography focused on the principle that if medical humanities are to be successfully integrated, material must be

1. Short
2. Immediately relevant including the depiction of both values aspired to and challenges faced in situations encountered
3. Have applications for those with varied experience with medical humanities

The aim of this summer's project would be to refine the bibliography and apply it to the current curriculum. We would aim to do this for 4 years of the curriculum, with the initial focus on the first 2 years, and the secondary focus on the clinical years.:

Project

1. Review curriculum and courses specifically with attention to opportunities to integrate medical humanities material
    a. Consider applications in various Courses
    b. Meet with selected course directors to enhance buy-in
2. Collaboratively plan with project PI a 4 year curriculum
    a. Meet with local experts in Medical Humanities to solicit ideas
    b. Review UMass and other resources (NYU data base, various medical humanities course sites) for medical humanities readings used throughout medical education
    c. Generate supplementary bibliography with applications to core clinical clerkships to consider generating this by clerkship.

3. Implement additional curriculum in fall of 2012 and spring of 2013 (an addition to works added to curriculum in fall 2011 and spring 2012.)
4. Develop an Evaluation plan for curriculum implemented
    a. Incorporate into course evaluation
    b. Develop plan to check effect of integration into curriculum

Student's Role and Pre-requisites:

1. Primary “data” collection of medical humanities resources, both internal and outside UMass
2. Will work collaboratively with PI to supplement current resources
3. Will work collaboratively with PI to meet with course directors
4. Will develop a summary document detailing resources and make this available to course directors

Required Skills:

1. Knowledge of medical humanities and resources
2. Interest in medical humanities
3. Ability to work with diverse group of people to implement project
4. Ability to work independently
5. Weekly meetings with PI/Co-PI

Interview: Required

Location: Benedict Building/Library