1. Establishing a High-throughput Drug Screen For Soil-transmitted Helminths

PI: Raffi Aroian, Professor; Molecular Medicine

Description:
Soil-transmitted helminths like hookworms and whipworms are major contributors to disease globally and major factors in impoverishment in the developing world. We are developing high-throughput screens to be able to find much needed drugs to treat these parasites. Successful applicant will work with parasites in tissue culture wells and experiment with various imaging techniques to see if we can develop a high-throughput means to find drugs that target these parasites as a prelude to clinical development.

Student's role:
Test various imaging techniques to find ones that allow for high-throughput screening of parasites in multi-well format.

Required Skills:
Enthusiasm. Basic lab techniques (pipetting) and good hands.

Location of research:
Biotech 2, Suite 219
Collaboration with Harvard and other labs at UMass Medical School

2. Improving care by utilization of prehabilitation for hip and knee joint replacement

PI: Jennifer Baima, MD / David Ayers, MD; Orthopedics and Rehabilitation

Interview required – submit CV with current contact information for an in-person interview

Description:
Reducing length of stay in post-acute care after joint replacement is an important goal in the current model of accountable care. The best way to do this without sacrificing quality care is likely to reduce comorbidities and postoperative complications. Prehabilitation is the use of rehabilitation prior to an intervention, such as surgery, to improve outcomes after the intervention. Prehabilitation has been shown to improve postoperative functional outcome in patients undergoing knee or hip joint replacement. Preoperative physical therapy has been shown to reduce utilization of post-acute care services.[i] Barriers to preoperative physical therapy, such as the cost of copays and parking and time off work, may prevent patients from achieving these benefits. An appropriate universal exercise program, demonstrated by a student health care provider, may be an effective option to reduce post-acute care utilization in joint replacement.

Student's role:
Learn and demonstrate prehabilitation exercises appropriate for hip or knee joint replacement surgery. Consent patients to participate in this program (with referral from treating orthopedic surgeon.) Call patients to see if they are doing the exercises in the two to four weeks prior to joint replacement surgery and if they have any questions related to these exercises. Document the presence of and/or length of stay in rehabilitation or skilled nursing facility after joint replacement. Record this data and compare to the established utilization of post-acute care for the prior two months. Present this comparison in poster format at the end of the project.

Required Skills:
Interest in exercise as medicine and musculoskeletal medicine. Basic interpersonal skills and musculoskeletal anatomy knowledge. CITI training completed for IRB. Knowledge of basic media in making and posting video would be helpful, but not necessary.

Location of research:
Arthritis and Joint Center
Memorial Campus – 119 Belmont Street

3. Role of miRNA-132 and extracellular vesicles in liver fibrosis

PI: Shashi Bala, Instructor; Medicine

submit CV with current contact information for an in-person interview

Description:
miRNAs are small regulatory RNAs and deregulated in liver disease. Extracellular vesicles (EVs) are small vesicles shed from almost all type of cells. Both circulating EVs and miRNAs have promising potentials for biomarker discovery and treatment monitoring. Liver fibrosis is characterized by excessive scarring caused by various chronic inflammatory processes. In this project, we will determine the role of miR-132 and extracellular vesicles in liver fibrosis.

Student's role:
RNA extraction, real time PCR, protein extraction, western blot, apoptosis assay, exosome isolation and characterization and other routine lab protocol.

Required Skills:
N/A

Location of research:
Lazare Research Building - LRB270N

4. Screening Strategies for Lynch Syndrome

PI: Leslie Bradford, MD, Assistant Professor of Obstetrics and Gynecology

Description:
Lynch Syndrome is a heritable cancer susceptibility syndrome caused by genetic defects in mismatch repair (MMR) genes. It accounts for 2-3% of cases of colon cancer and 2.3% of cases of endometrial cancer. Women with mutations in MLH1 or MSH2 have a 48% incidence of colon cancer and a 62% risk of endometrial cancer. Thus, a woman with Lynch Syndrome has a much higher lifetime risk of developing endometrial cancer rather than colon cancer. In addition, over half of women who are ultimately diagnosed with a synchronous and/or metachronous colonic and gynecologic malignancy are diagnosed with a gynecologic cancer first.

Historically, non-colonic colon cancers have not been the focus of Lynch Syndrome research. Currently, physicians use the Amsterdam criteria or Bethesda guidelines, but the validity of these tests is mainly limited to the colon cancer population and has been difficult to implement for the gynecologic cancer population. Thus, the recommendation of testing based on family and personal history is inadequate for women presenting with an extracolonic, Lynch-associated cancer.

For patients with newly diagnosed colon cancer, testing for MMR with immunohistochemistry (IHC) and PCR amplification for genotyping to identify microsatellite instability (MSI) is performed as primary triage. This then determines which patients require genetic counseling and potentially further analysis with full sequencing. This has been shown to be highly effective in colon cancer. Although not as accurate as MSI, recent data suggests that IHC for the MMR proteins may be the best tool for primary triage for Lynch Syndrome in women with endometrial cancer. It has also been shown to be a more cost effective screening tool than MSI testing.

This project will investigate the feasibility of implementing a large scale screening program based on the current disease in the proband instead of family and personal history. All women less than 60-years-old with newly diagnosed endometrial cancer will have IHC for defects in mismatch repair genes performed on their tumors, with subsequent directed genetic testing based on the primary triage with IHC.

Student's role:
The student will be involved in all aspects of this project and will have exposure to the clinical, bench science, and biostatistical aspects of the project. The student will spend time in the clinic and the operating room with me (~ 2 days per week). The remainder of the time will be divided so as to allow the student to work with our multidisciplinary team of investigators. This will include attending Tumor Board conferences, shadowing our genetic counselors, spending time in the Pathology lab to understand and perform the IHC and PCR testing on tumor samples, and attending meetings with our biostatistician. Some time will be devoted to data entry and manuscript writing.

Required Skills:
N/A

Location of research:
Levine Ambulatory Center – Memorial Hospital

5. Improved Selection of Antigen Specific Human Hybridomas

PI: Lisa Cavacini, PhD, Associate Professor of Medicine

Interview required – submit CV with current contact information for a phone interview

Description:
Several monoclonal antibody (mAb) products have been approved for clinical use. While some of these products are fully human antibody proteins, there are a number that are not and an anti-drug response can frequently limit the use of this antibody as well as others. It is generally believed that going forward, only fully human mAb will be approved for clinical use. My laboratory has developed human mAbs for a number of years and since joining MassBiologics, we have been working on improving our platform for generating human monoclonal antibodies to address unmet medical needs. One way to generate an antibody producing cell lines is fusion of antibody producing B cells with an immortalized human B cell line, resulting in hybridomas. While we have generally found this to be more efficient that cloning antibody genes from B cells, there is room for improvement of efficiency and potentially high-throughput analysis. We have found that in addition to secreting antibody, our human hybridomas also express antibody on the cell surface. Membrane expression of immunoglobulin is driven by co-expression of CD79a and CD79b. We propose that membrane expression of antibody can be used to select for antigen reactive hybridomas shortly after fusion. The advantage to this is that there will be a significant reduction in the number of cells that must be cultured, fed and screened which will increase our ability to handle multiple fusions at a time. Given that a particular antibody response is only 0.01-1% of an antibody repertoire, selection for antigen reactive hybridomas shortly after fusion will allow a substantial reduction in the number of plates required and increase capacity. There are two aims to this study: Aim 1 is to identify if CD79a and CD79b are normally expressed in our fusion partner cell line. If they are not or one is missing, the fusion partner cells will be transfected with an expression plasmid for the missing protein(s) and a stable cell line isolated. Aim 2 will determine the time post fusion where membrane expression of antibody can be observed. This will be accomplished by staining hybridoma cells every 1-2 days post fusion by flow cytometry for expression of human IgG. This study represents an important contribution to our human hybridoma platform which will greatly facilitate our ability to develop human mAb products that will significantly improve public health.

Student's role:
The student will participate in the design of the studies, carry-out the experiments including cell culture, flow cytometry, cell transfection and hybridoma generation. Training will be provided for the particular laboratory skills required. The student will participate in laboratory and departmental group meetings on a weekly basis.

Required Skills:
It would be helpful to have had experience handling common laboratory equipment such as pipets, pipet aids and some knowledge of aseptic technique. This is not absolutely required but will facilitate the work.

Location of research:
The laboratory is located at MassBiologics of the UMMS. We are located in the Mattapan section of Boston. Public transportation is available as is on-site parking.

6. Molecular Methods for the Diagnosis of Borderline Melancytic Neoplasms

PI: Kristine Cornejo MD, Assistant Professor; Lloyd Hutchinson PhD, Assistant Professor; April Deng, MD Professor - Anatomical Pathology, Laboratory of Diagnostic Molecular Oncology

Interview required – submit CV with current contact information for an informal in-person interview

Description:
Malignant melanoma comprises <2% of all skin cancer cases, but the majority of skin cancer related deaths (80%). Despite efforts emphasizing earlier detection, death rates continue to rise. The histopathological diagnosis of melanoma can be very challenging at times, as a variety of benign melanocytic lesions, particularly Spitz tumors and dysplastic nevi, share similar morphology with melanoma. A misdiagnosis will have an adverse impact on the patient as early intervention may help to avoid metastasis, but over diagnosis will result in unnecessary therapy.

The current gold standard for melanoma diagnosis is histopathology, although a subset of melanocytic neoplasms are difficult to unequivocally categorize as benign or malignant, and are termed atypical or borderline melanocytic neoplasms. Melanomas have been found to contain numerous chromosomal copy number alterations and their own signature of gene mutations in comparison to benign nevi.

Our Laboratory of Diagnostic Molecular Oncology at UMass has developed clinical molecular assays (Laser Capture, Robotic Nucleic Acid Extraction, Multiplex Ligation-dependent Probe Amplification, PNA-clamp Real Time Quantitative PCR, Next Generation Sequencing) able to identify DNA mutations and DNA copy# changes. A retrospective pilot study identified a molecular profile by analyzing a subset of genes for mutation and copy # changes using Fluorescent in situ hybridization (FISH) and Next Generation Sequencing to distinguish benign nevi from malignant melanoma.

The study has two goals: (1) extend the study to additional archived "atypical or borderline melanocytic neoplasms" to determine if this molecular signature can accurately classify them into benign or malignant categories, and (2) correlate the molecular profile with outcome data.

Student's role:
1. Review atypical or borderline melanocytic neoplasms with the Dermatopathologist.
2. Aid in the laser capture microscopy and robotic DNA extraction of specimens.
3. Aid in performing and/or analyzing FISH testing and Next Generation Sequencing.
4. Aid in classification of specimens that are positive/negative for point mutations or chromosomal abnormalities to determine whether they are benign or malignant.
5. Review medical records for outcome data.
6. Aid in the creation/maintenance of a database for statistical analysis of the data

Required Skills:
Computer literacy

Location of research:
Biotech 3, Room 276

7. Synthesis of Laughing Gas

PI: Manisha S. Desai, MD; Anesthesiology

Interview required – submit CV with current contact information for an in-person interview

Description:
Background: Analgesic properties of nitrous oxide (N2O) were known to Humphy Davy as early as the late 18th century. However, it was not until Horace Wells observed its anesthetic properties in 1844 that it began to be used in dentistry. Itinerant showmen used to demonstrate its hilarious properties, and thus it was called 'laughing gas.' The synthesis of nitrous oxide also results in the production of toxic oxides of nitrogen. We wish to examine the methods by which nitrous oxide has been synthesized, identified, purified, and its toxic by-products identified and removed.

Methods: Materials in the public domain will be consulted for this project. These will include textbooks, review articles, research articles, and original descriptions by pioneers.

Expected results: We expect to find a fair amount speculation in the early decades before nitrous oxide's chemical structure was identified, and later methods to avoid toxic oxides to accumulate during synthesis. We will compare earlier methods of obtaining pure nitrous oxide versus modern synthetic techniques.

Expected conclusions: We expect to be amazed by the ingenuity exhibited by early chemists, not only in their ability to synthesize gases, but also how they could identify them. We also expect to be impressed with their ability to know pure from impure mixtures, and whether the gas they had synthesized had been diluted by room air.

Student's role:
Under my direct supervision, become familiar with background information from review articles, textbooks of anesthesia history. Then find suitable additional resources from the basic article references, textbooks of chemistry and analytical chemistry and primary source references. There after, analyze the information and create a power point presentation and a manuscript for submission for publication.

Required Skills:
Interest in history, chemistry, good writing skills, good internet search skills, willingness to work hard to finish the project, write the manuscript and be prepared to present at our annual national meeting in 2015

Location of research:
UMass, anywhere with internet facility

8. **Historical Examination of the Hippocratic Oath**

PI: Manisha S. Desai, MD; Anesthesiology

Interview required – submit CV with current contact information for an in-person interview

Description:
The father of Western Medicine, Hippocrates lived in ancient Greece, and was the founder of the Hippocratic School. Although none of his personal writings survive, what is considered the Hippocratic Corpus most likely originated over decades, or centuries, through the work of guardians of this school. We wish to examine the original intent of the Hippocratic Oath, as judged by their writings and appropriateness to those times. We then examine its use in current US Medical Schools, and how appropriate its rules might be in modern medical practice.

Methods: After studying the main points of the Hippocratic Corpus, and understanding the tenets of those beliefs, we plan on surveying practices of all US Medical Schools – whether the schools practice any sort of graduation or other ceremonial ritual where medical students take the Hippocratic Oath. Next we examine how appropriate each of his tenets is to modern medical practice.

Expected Results: We expect only a minority of medical schools to administering the Hippocratic Oath to graduating medical students.

Conclusions: Some values change over time, while others remain timeless. We provide reasons why the value of some of his tenets is no longer applicable in modern medicine.

Student's role:
Under my direct supervision, become familiar with background information from review articles, textbooks of medical history. Then find suitable additional resources from the basic article references, textbooks of medical history and writings of the Hippocratic School and primary source references. There after, analyze the information and create a power point presentation and a manuscript for submission for publication.

Required Skills:
Interest in history of medicine, good writing skills, good internet search skills, willingness to work hard to finish the project, write the manuscript and be prepared to present at our annual national meeting in 2015.

Location of research:
UMass, anywhere with internet facility

9. **Lung mechanics and Control of Breathing in the Pompe Murine model**

PI: Mai K. ElMallah, MD MS; Assistant Professor; Pediatric Pulmonary and Gene Therapy Center

Interview required – submit CV with current contact information for an in-person interview

Description:
Pompe Disease is a genetic disease that affects the muscles and central nervous system (CNS). The only FDA approved therapy is enzyme replacement therapy (ERT) but this therapy does not cure the muscle and CNS problems that these children encounter. Children with this disease have a weak diaphragm and upper airway dysfunction and often need a tracheostomy tube. Despite ERT, they often become dependent on a ventilator for breathing. The upper airway problems include a large, weak tongue which results in obstructive sleep apnea, difficulty controlling secretions, difficulty feeding, problems with speech, and aspiration. These problems occur because the tongue and the CNS area controlling the tongue is affected. No treatment currently exists for the upper airway pathology of Pompe Disease. This research will help us better understand the mechanisms of CNS pathology involved in this disease and the role of gene therapy in treating the CNS and muscular component of the upper airway problems.·

Student's role:
The student will be responsible for leading a side project of this research. He/she will mainly be involved in learning and conducting pulmonary function tests in mice including whole body plethysmography and lung resistance and compliance. They will be involved in collecting and analyzing data and will be first author on a poster.

Required Skills:
Will need to work with animals but no prior skills needed

Location of research:
Albert Sherman Building

10. Exenatide Weekly Injection as an Adjunctive Treatment in Patients with Schizophrenia

PI: Xiaoduo Fan, MD, MPH, MS; Associate Professor of Psychiatry; Director, Psychotic Disorders Clinic and Research Program

Interview required – submit CV with current contact information for an in-person meeting

Description:
The Psychotic Disorders Research Program at the University of Massachusetts Medical School (UMMS), Department of Psychiatry, aims to elucidate the etiology of each facet of the triple jeopardy (devastating mental illness, medical co-morbidity, and substance use), and possibly shared pathophysiological pathways and mechanisms among these three conditions. The goal of our research is to develop innovative intervention strategies combining pharmacological and psychosocial approaches to treat schizophrenia symptoms, medical co-morbidity and substance use, and ultimately to improve the quality of life in this patient population

The medical student will be involved in the exenatide study which is described below:

Extensive evidence in recent years has suggested that exenatide, a glucagon-like peptide-1 (GLP-1) analogue that crosses blood-brain barrier, exerts significant anti-inflammatory, neurotrophic, and neuro-protection effects. These promising findings raise several critical questions regarding the potential therapeutic role of exenatide in schizophrenia and the underlying mechanism.
This is a 24-week, randomized, double-blind, placebo-controlled trial of exenatide weekly injection (2mg per dose) as an adjunctive therapy in 70 schizophrenia subjects to examine exenatide's effects on negative symptoms and cognition.

Primary aim: Examine the efficacy of exenatide weekly injection in improving negative symptoms as measured by the Scale for the Assessment of Negative Symptoms (SANS) total score.
Secondary aims: Examine the efficacy of exenatide in improving cognition as measured by the MATRICS Consensus Cognitive Battery (MCCB) composite score.

If interested, the medical student can also be involved in any one of our ongoing clinical trials. To learn more about our program and other ongoing research studies please visit our website http://umassmed.edu/psychiatry/psychotic-disorders-research-program/

Student's role:
Research Assistant

Required Skills:
N/A

Location of research:
Biotech 1 and CHL

11. "Should Infants with Down Syndrome Be Screened More Frequently for Thyroid Dysfunction?"

PI: Penny Feldman, MD; Assistant Professor of Pediatrics

Interview required – submit CV with current contact information and a 3-4 line statement of interest

Description:
Thyroid hormone is critical for brain development in all infants. Infants with Down syndrome have an increased incidence of congenital hypothyroidism. Currently, the American Academy of Pediatrics recommends screening infants with Down syndrome for thyroid dysfunction at birth and at 6 and 12 months of age. This study will determine whether these recommendations are adequate or whether infants with Down syndrome need to be screened more frequently or at different time points for thyroid dysfunction.

Student's role:
Recruit study subjects, collect data, coordinate study visits

Required Skills:
CITI Certification

Location of research:
UMASS Memorial Children's Medical Center – University Campus

12. HOTFAT Study

PI: Tim Fitzgibbons, MD, PhD; Assistant Professor of Medicine – Cardiovascular Division

Description:
We are studying the histological and molecular features of human peri-aortic fat before and after the exposure to the cold during cardiopulmonary bypass. Our hypothesis is that this exposure will activate a program of brown adipose specific genes. Students will have almost daily interaction with the PI and other study participants.

Student's role:
Student's will participate in two translational research projects aimed to investigate the role of perivascular and epicardial fat human cardiovascular disease. Students will consent patients, collect biopsies, perform experiments (as experience permits) and analyze the data.

Required Skills:
Professionalism, motivation, enthusiasm

Location of research:
Main Hospital building and Biotech 2

13. Cytoxotic, autoreactive CD8 T cells from the periphery and from spleen and pancreatic islets from human subjects with Type 1 diabetes

PI: Sally C. Kent, PhD; Assistant Professor of Medicine; Diabetes Center of Excellence

Interview required – submit CV with current contact information for an in-person or phone interview

Description:
Autoreactive CD8+ T cells infiltrating the Islets of Langerhans in the pancreas is thought to be a major cause of the destruction of the insulin-producing islets cells leading to a clinical diagnosis of type 1 diabetes (T1D). Our current understanding of the detailed function of these potentially pathogenic T cells is incomplete human donors and especially from the site of cell destructions, the islets.We currently have access to spleen, pancreatic lymph node and islets isolated from multiple tissue donors with T1D. We have developed assays to culture out autoreactive T cells from these tissues and to use HLA-A2-multimer reagents loaded with autoreactive peptides to specifically isolate autoreactive CD8+ T cells.

For this summer research project, we will isolated autoreactive CD8+ T cells from these tissues by single cell sorting with HLA-A2 multimers, flow cytometry and cell culture techniques to determine their functional properties. This is a unique examination of autoreactive CD8+ T cells derived from the source of pathology in human T1D.

Student's role:
The student would work directly with Dr. Jenny Babon, a seasoned postdoctoral fellow in the lab and 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 including analyses of cell sorting/flow cytometry, and cytotoxic T lymphocyte killing assays. As part of the learning process, Dr. Babon and I would instruct the medical student in these techniques. Knowledge of immunology would be extremely useful, but not essential.

Location of research:
ASC7-2012

14. Investigation of Emergency Department Use by Clients of the MA Department of Developmental Disabilities

PI: Emily Lauer, MPH; Center for Developmental Disabilities Evaluation and Research (CDDER), Eunice Kennedy Shriver Center

Interview required – submit CV with current contact information and a 3-4 line statement of interest for an in-person interview

Description:
People with Intellectual and Developmental Disability (I/DD) often have complex care needs and challenges with communication of their medical needs. Their use of emergency services tends to differ from the general population, and their experiences in the Emergency Room can be more stressful and risky than other populations. Understanding how to prevent unnecessary Emergency Room visits specifically for this population of people is important in order to improve their care experiences and minimize care costs. Concerns regarding the frequency and quality of emergency department encounters of their clients prompted the MA Department of Developmental Services (DDS) to analyze on Emergency Room utilization and experiences; similarly, the U.S. health system has focused extensively on identifying and reducing preventable emergency visits. While previous national work has identified strategies to enhance community-based care for vulnerable opulations, the needs of these populations can vary greatly. In this project we will create a model to understand preventable and avoidable Emergency Room visits specifically in the I/DD population. Using clinical and multi-disciplinary input, a framework will be formulated along with a crosswalk of relevant ICD codes with descriptions of conditions/symptoms. In addition, a pilot test of the framework will be conducted with de-identified DDS incident data and aggregate claims data, allowing refinement of the model for avoidable ER use. The output is expected to provide informed targets for strategic improvements in service delivery and health policy for people with I/DD and it is expected that the findings will be a useful benchmark for other states as ER use patterns have not previously been studied in a population with ID of this scope and size.

Student's role:
The student will participate as part of a multidisciplinary team working on this project. At this time, it is expected that we will be working to finalize the proposed model and beginning its application to datasets. The student will have exposure to how this type of classification is developed through available literature and multidisciplinary perspectives, as well as to data analysis. The role of the student will be matched with their skills. At minimum they will be involved in reading and synthesizing evidence from the literature, the decision process for model construction, the documentation of the model and team-based discussion of considerations for application to the data.

Required Skills:
None, scalable

Location of research:
Eunice Kennedy Shriver Center, 465 Medford Street, Suite 500, Charlestown, MA 02129

15. A screen for small molecules in zebrafish to stimulate lymphatic growth

PI: Nathan D. Lawson, PhD, Professor

Interview required – submit CV with current contact information for an in-person interview

Description:
The lymphatic system is a network of blind-ended vessels that plays an essential role in fluid homeostasis, lipid absorption and transit of lymphoid cells. A number of congenital diseases (e.g. Milroy disease) result in lymphatic hypoplasia leading to severe lymphedema. Likewise, loss of lymphatic vessels and lymph nodes in the setting of breast cancer resection can lead to profound lymphedema. Thus, promoting lymphatic vessel formation in these cases is highly beneficial. Fortunately, it is possible to study the signals required for lymphatic development in model organisms. We have used the zebrafish as a model to study blood vascular and lymphatic vessel development. Using transparent zebrafish embryos expressing fluorescent proteins specifically in lymphatic endothelial cells, it is possible to directly visualize lymphatic growth as it occurs *in vivo*. Moreover, we have generated zebrafish bearing mutations in homologs of human genes (*flt4* and *vegfc*) known to be causative for congenital lymphedema. Consistently, zebrafish *flt4* and *vegfc* mutant embryos display defects in lymphatic development and subsequent lymphedema. Additional benefits of the zebrafish embryo are their small size and rapid external development. These benefits make it possible to treat zebrafish embryos with small molecules to screen for their potential effects on various developmental processes, including lymphatic development.

In this project, we will use *flt4* mutant zebrafish embryos, which fail to form a lymphatic system, to screen for small molecules that rescue this phenotype. *Flt4*-mutant zebrafish embryos bearing a lymphatic endothelial-specific red fluorescent transgene will be treated with a panel of small molecules and then observed for rescue of lymphatic growth, which can be easily observed using a fluorescence dissection microscope. Given the high degree of conservation between zebrafish and humans, any potential small molecule hit in this screen has the potential to be a lead in alleviating lymphedema due to hypoplastic lymphatic growth in humans.

Student's role:
The student will be involved in all aspects of performing the small molecule screen, under the supervision of a post-doc and the PI. This will include breeding of zebrafish carrying the *flt4* mutation, handling of zebrafish embryos, and treatment with small molecules. The student will also perform preliminary screening for lymphatic growth. Given the ease with which it is possible to handle zebrafish embryos and visualize lymphatic structures in transgenic zebrafish, these types of small molecule screens have proven ideal projects for students in other labs.

Required Skills:
This project requires handling of small liquid volumes using pipets and pipetman. Thus, previous experience in using pipets would be beneficial. Also, generally good observational skills are essential. Previous experience with microscopy would be helpful.

Location of research:
Lazare Research Building, LRB670P

16. Residency Training in Opioid Dependence Therapy & Opioid Prescribing in Residency Practice

PI: James Ledwith MD; Dept of Family Medicine and Community Health; Residency Director, UMass Fitchburg Family Medicine Residency

Description:
The residency program provides family medicine residents immersion in opioid dependence therapy with the goal of promoting implementation of this therapy in future practice. The program seeks to evaluate the outcomes of this training by surveying graduates of the program about their practices. A secondary phase of the project will explore issues of opioid prescribing in the residency practice, with investigation of the Massachusetts Prescription Monitoring Program files of patients under therapy and tracking for diversion of medications prescribed by practice physicians.

Student's role:
The student will assist in distribution and follow up of surveys with the program faculty, collation results, and drafting of a summary of findings. The student will examine the MA-PMP database for additional controlled drug prescriptions from other providers. The student will review prescription patterns and data about diverted prescriptions for evidence of whether this data influences prescribing habits.

Required Skills:
N/A

Location of research:
UMass Fitchburg Family Medicine Residency, 326 Nichols Road, Fitchburg, MA 01420

17. Community Variations in and Neighborhood Impacts on Health and Health Behaviors

PI: Wenjun Li, PhD; Preventative Medicine, Department of Medicine

Interview required – submit CV with current contact information and a 3-4 line statement of interest for an interview

Description:
This project analyzes community socioeconomic and built environmental influences on lifestyle, health behaviors and health outcomes. We use state of the-art statistical modeling and geographic information system (GIS) to analyze the extent and causes of variations in prevalence of healthy and unhealthy lifestyle factors, access to care and associated variations in health care utilizations and costs. The results may inform public health policy and practice. Outcomes of interest include but are not limited to healthy eating, active living, utilitarian/recreational walking, smoking, adult/childhood obesity, diabetes, hypertension, elderly falls and fall injuries. We are analyzing existing data and preparing manuscripts for publication.

Student's role:
Literature review, assisting with basic statistical analysis and manuscript preparation; possible field data collection on human subjects

Required Skills:
Good professional writing, basic understanding of biostatistics and epidemiology, strong interest in community health and neighborhood environment and lifestyle research

Location of research:
Medical School Building

18. Isolation of broadly neutralizing antibodies to dengue viruses

PI: Daniel Libraty, M.D. Associate Professor of Medicine

Description:
Dengue is a common tropical infectious disease caused by any of 4 serotypes of the mosquito-borne dengue viruses. A goal in developing an effective dengue vaccine is to generate broadly neutralizing antibodies. We plan to pool dengue-immune sera collected from mothers in the Philippines and attempt to isolate a polyclonal mixture of broadly neutralizing antibodies using affinity chromatography. The anti-dengue virus neutralizing capacity of the antibodies will be examined *in vitro* and in a mouse model.

Student's role:
Laboratory bench-work; possible mouse experiments

Required Skills:
Prior laboratory experience preferred but not required

Location of research:
S6-746

19. Type 2 diabetes impairs mesenchymal stem cells' function

PI: Louis Messina, MD; Professor and Chief

Description:
Mesenchymal stem cells (MSCs) were originally discovered in the 1950s. These cells were named MSCs as they could be induced to differentiate into adipocytes, chondrocytes and osteocytes-cells which all comprise the mesenchyme. Studies indicate that MSCs may also be induced to transdifferentiate into cells of the endoderm and the ectoderm. Therefore, many current clinical trials are exploring autologous MSC therapies in chronic conditions such as heart failure, retinopathy therapy, bone regeneration, pulmonary diseases, wound healing, respiratory diseases, myocardial infarction, musculoskeletal injury, neurodegenerative diseases and osteonecrosis. With the potential to treat a wide range of disease, autologous MSC therapies are at the forefront of stem cell therapies.

Peripheral arterial occlusive disease (PAD) affects more than 200 million people worldwide. Numerous preclinical studies show that autologous MSC transplantation improves limb function, reduces the incidence of autoamputation, and attenuates muscle atrophy in limb ischemia models, indicating that autologous MSC transplantation may lead to promising therapies for PAD patients.

Type 2 diabetes (T2D) has been identified as the most independent potent risk factor for PAD. Type 2 diabetic patients display an astonishingly reduced capacity for postischemic neovascularization, highlighting the need for innovative therapeutic approaches for PAD in these patients. Our previous study indicates that T2D attenuates the transdifferentiation of MSCs towards endothelial cells, suggesting that T2D limits the potential of autologous MSC therapy for PAD. Furthermore, the effects of T2D on MSC transdifferentiation towards other vascular cells remain unknown. Therefore, the mechanistic studies of MSCs from a diabetic background are essential for developing efficient clinical therapies for PAD in T2D patients.

We hypothesize that T2D limits the transdifferentiation capacity of MSCs towards endothelial cells, smooth muscle cells and pericytes, resulting in the impaired therapeutic potential of autologous MSC transplantation for PAD patients with T2D.

Aim 1: To compare the differentiation capacity of MSCs from T2D and wild type mice towards vascular cells.
Aim 2: To identify genes responsible for the impaired transdifferentiation of MSCs towards vascular cells in T2D mice.

Clinical relevance: The importance of PAD in T2D patients is several-fold higher than in the general population. Considering that between 120 and 140 million people suffer from diabetes mellitus worldwide and that diabetic patients are at high risk of developing PAD, the implications of the problem are enormous. Therefore, there is urgent demand for effective revascularization strategies in these patients. Our study will help improve autologous MSCs therapy for T2D patients with PAD.

Student's role:
By the end of this project, the student will be able to culture and differentiate bone marrow MSCs. He/She will also perform RNA extraction and qPCR to look at the expression of differentiation markers.

Required Skills:
N/A

Location of research:
Albert Sherman Center AS7-2003, 2004

20. 1. Pilot – Gestational Diabetes Mellitus and Adipose Tissue Function (GEDMAT)
2. Collection of Biologic Specimens

(It should be noted that the primary study is GEDMAT. However if time allows, the student will be involved in collection of biologic specimens that are specific to L&D (e.g. placenta, umbilical cords and cord blood). These specimens help support research activities in numerous basic science labs both at UMass and WPI).

PI: Tiffany A. Moore Simas, MD, MPH, Med; Director, Ob/Gyn Research Division; Associate Director, Ob/Gyn Residency Program; Associate Professor of Ob/Gyn & Pediatrics

Description:
GEDMAT Description:

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

Student's role:

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

Required Skills:

1. Socially comfortable people-person who is at ease in a clinical environment with multi-disciplinary, inter-professional team members.
2. Great communication skills – written and verbal.
3. Meticulous with consistent focus regarding detail.
4. Ability to follow protocol and navigating medical record systems.
5. Ability to drive/access to transportation
6. CITI certification

Location of research:

UMass Memorial Health Care – Memorial Campus
(transport of specimens to and lab meetings in Biotech 2)

21. A Virus Like-particle-based EBV prophylactic and therapeutic vaccine

PI: Javier Ogembo; Medicine

Description:
Invasive cervical cancer (ICC), an AIDS-defining malignancy, is the leading cause of cancer mortality among women in sub-Saharan Africa (SSA), where approximately 99,000 new cases and 57,400 deaths occurred in 2012. The disproportionately high burden of ICC in SSA is due to lack of cost-effective screening programs for early detection and treatment of precancerous lesions and a high burden of HIV/AIDS, an important permissive cofactor in human papillomavirus (HPV) infection and ICC. Although highly active antiretroviral therapy (HAART) has reduced the incidence of other AIDS-defining malignancies such as Kaposi's sarcoma and non-Hodgkin's lymphoma, the incidence of ICC is thought to have remained essentially unchanged. Several meta-analyses confirmed the five most prevalent human papillomavirus (HPV) strains in women with and without cervical neoplastic diseases are HPV16, 18, 31, 52, and 58. HPV16/18 are the predominant oncogenic genotypes, causing approximately 70% of global cervical cancer cases. The vast majority of the women studied were from Europe, North America, Asia, and most recently Latin America and the Caribbean. Despite the high burden of cervical cancer morbidity and mortality in African women, a robust meta-analysis of HPV genotype prevalence and distribution, particularly among HIV positive women is lacking.

Student's role:
HPV genotyping, review of literature, data extraction for meta-analysis and manuscript writing

Required Skills:
Background in lab work and statistics will be helpful

Location of research:
Lazare Research Building

22. A Virus Like-particle-based EBV vaccine

PI: Javier Ogembo; Medicine

Description:
Every year, Epstein-Barr virus (EBV) infection is estimated to be responsible for over 200,000 cancer cases globally. However, this may be a huge underestimation due to lack of cancer diagnostic tools and the absence of a population-based national cancer registry in most low-income countries where EBV+ malignancies are highly prevalent among children and people living with human immunodeficiency virus. To date, despite varied attempts to generate an EBV vaccine based on viral glycoprotein (gp)350/220, late membrane proteins (LMP1-2), and EBV nuclear antigen 1 (EBNA1), a broadly effective vaccine against EBV has not been licensed. To our knowledge, no vaccine candidate combining EBV multiple glycoproteins (gps) mediating viral entry and tumor-associated antigens has been developed and tested in a clinical trial.

Efforts to develop EBV vaccines are limited due to the oncogenic potential of the EBV genome and lack of animal models to test potential vaccine candidates. Antibodies provide a first line of defense against virus infection. Several lines of evidence indicate that neutralizing antibodies directed to EBV envelope gps are present in humans, may prevent neonatal infection, and are readily generated in response to immunization of humans and other animals. However, in small Phase I/II clinical trials, vaccination with either vector constructs expressing gp350/220 or with the purified recombinant gp350/220 protein did not prevent infection although the incidence of acute infectious mononucleosis was reduced in young adults. While these observations indicate that immunity to gp350/220 can limit infection, the variable success of using a single immunogen (gp350/220) as a vaccine candidate calls for new alternative approaches combining multiple EBV proteins. Recombinant EBVΔgp350/220 has been shown to infect both primary B cells and epithelial cells *in vitro*. Unfortunately, recombinant defective viruses currently proposed as vaccine candidates for EBV raise serious safety concerns. Like other herpesviruses, EBV uses multiprotein complexes to initiate host cell infection. The recent success of human papilloma virus-like particle (VLP)-based vaccines utilizing two envelope gps raises the possibility that similar strategy could prove effective in developing EBV vaccine expressing multiple gps.

Despite strong evidence indicating that antibodies to gH/gL are capable of neutralizing EBV infection, to our knowledge, no vaccine candidate has exploited the use of these proteins against EBV infection. We now provide evidence that virus tumor-associated antigens such as EBNA1 (consistently recognized by CD4+ T cells) or LMP2 (primarily targeted by CD8+ T cells), can be packaged inside VLPs decorated with gH/gL or gp350/220 on the surface of the particle. In our preliminary study, serum from BALB/c mice immunized with four doses of EBVgp350/220 VLPs (alone) did not completely neutralize EBV infection *in vitro*. Thus, there is a need to explore the use of other EBV envelope gps involved in virus entry or to devise strategies that prime immune system to target EBV+ cells *in vivo*. *We hypothesize that incorporating a functionally inactive fusion protein containing the C-terminal portion of immunodominant EBNA1, but lacking the Gly-Ala rich domain known to impair presentation of cis-linked sequences, LMP2, gH/gL into a single or multiple VLPs will stimulate robust humoral and cellular responses against EBV and its associated diseases*. Our long term goal is to generate EBV-gH/gL:EBNA1-LMP2 VLPs that can be used independently or together with EBVgp350/220 VLPs to prevent EBV infection and its associated diseases.

Student's role:
Generation and characterization of VLPs for testing in mice

Required Skills:
Previous benchwork will be helpful

Location of research:
Lazare Research Building

23. Quality Improvement Project

PI: Rachel Vuolo, MD; Internal Medicine – Pediatrics

Interview required – submit CV with current contact information for an in-person interview

Description:
Student may choose from a list of important health topics that require attention in every primary care office and help design a quality improvement project in that area. Projects may address efficiency, prevention of medical error, adherence to primary care practice guidelines, patient satisfaction or other quality goals. Potential health topics include but are not limited to health care proxy counseling and documentation in the geriatric population, alcohol abuse diagnosis and counseling, or pediatric diagnosis of and referral for obesity. Student will achieve LEAN white belt and yellow belt training and certification during the project period. Student will take part in the design of the QI project as well as help implement and assess each PDSA cycle.

Student's role:
Pending funding, student may spend part- or full-time here for the designated eight weeks. If full-time he or she may do an additional QI project, start to develop an office website with links to reliable patient educational resources, and obtain additional clinical experience in a busy Med-Peds primary care practice.

Required Skills:
N/A

Location of research:
Marlborough Primary Care, 640 Bolton Street, Marlborough, MA

24. Evidence-Based Medicine in a Public Payer Setting: Medical Necessity Guideline Development

PI: Christina G.D. Baah MD, MPH, Assistant Professor and Umbereen S. Nehal, MD, MPH

Description:
The office of Clinical Affairs provides clinical expertise to MassHealth, the Medicaid program in Massachusetts that covers one in four Massachusetts residents. Student will participate in a revision and writing of new MassHealth Medical Necessity Guidelines which are the cornerstone of evidence-based care that drives utilization management.

These guidelines are developed through a multi-step process including literature review, expert review, and peer review. These guidelines are updated periodically; updates require a review of current evidence, review of recent literature, an "environmental scan" of other payers' guidelines and other Medicaid program guidelines.

Student's role:
Student will work with the PIs to complete the review of current and available evidence, develop tables, and develop guideline content.

Required skills:
Basic internet and literature searching skills necessary

Location of research:
Office of Clinical Affairs, 100 Hancock Street, 7th floor, Quincy, MA 02171

25. Home Exercise Program for Patients Diagnosed with High Grade Astrocytoma

PI: Jennifer Baima, MD / Zehra Omer; Orthopedics and Rehabilitation

Interview required – submit CV with current contact information for an in-person interview

Description:
With the recent advancements in brain cancer treatment, the survival of adults with brain cancer is markedly improved. Patients in this population who undergo inpatient rehabilitation therapy in the acute post-surgical period have favorable functional outcomes and length of hospital stay comparable to patients undergoing rehabilitation for stroke. [ii]

Subacute post-surgical period is the time when impact of the tumor, surgery and adjuvant therapies such as radiation, chemotherapy and other medical therapy are acutely apparent. In this period, brain tumor patients present with varying deficits that include muscle weakness, fatigue, ataxia, gait and balance problems. Many of these deficits significantly alter patients' quality of life and functional abilities; thus, they may greatly benefit from continued rehabilitative intervention in the subacute period after surgery. However, many patients do not undergo rehabilitation due to preference or only having minor deficits that are still functionally impairing in this period. Studies have shown that patient preferences for exercise therapy increase in this period and that most patients prefer to exercise at home or at an outpatient supervised setting rather than at a hospital based setting. [iii]

The goal of this project is to evaluate the feasibility of a novel home exercise regimen and its efficacy in improving functional status and quality of life in the six months following high grade.

Student's role:
- Learn and demonstrate the novel home exercise program developed for patients with brain tumor surgery
- Identify patients eligible for the research study
- Consent patients to participate in the research study
- Train patients in the study on how to perform the exercises in the home exercise regimen
- Conduct monthly study visits with the subjects at the UMass Cancer Center (alternating phone and clinic visits) to collect data on their progress (functional status, balance, fatigue, mood, quality of life)
- Work with other study staff and statistician on analyzing the data and interpreting the results
- Prepare a poster presentation of research experience and results
- Depending on the student's performance and level of interest, this summer research opportunity has the potential to be extended into a longer term project.

Required Skills:
- No required clinical skills
- Student will be expected to have completed CITI training
- Interpersonal skills, enthusiasm for clinical research and willingness to learn is highly appreciated.
- Possible areas of interest include
    - Exercise as medicine
    - Physical Medicine and Rehabilitation
    - Neuro-oncology
    - Cancer Rehabilitation

Location of research:
UMass Memorial Health Care
Ambulatory Care Center (55 Lake Avenue, Worcester, MA 01655)

[i] Snow, Richard, et al. "Associations Between Preoperative Physical Therapy and Post-Acute Care Utilization Patterns and Cost in Total Joint Replacement." *The Journal of Bone & Joint Surgery* 96.19 (2014): e165.

[ii] Geler-Kulcu, D., Gulsen, G., Buyukbaba, E., & Ozkan, D. (2009). Functional recovery of patients with brain tumor or acute stroke after rehabilitation: a comparative study. *J Clin Neurosci*, 16 (1): 74-8.

[iii] Jones, L., Guill, B., Keir, S., Carter, K., Friedman, H., Bigner, D., & Reardon, D. (2007). Exercise interest and preferences among patients diagnosed with primary brain cancer. *Support Care Cancer*, 15 (1): 47-55.