

Mentor Name:	Mentor Department	Title of Proposed Project	Hypothesis/Specific Aim
Rami Hallac	Analytical Imaging and Modeling	Automatic Classification of Normal and Cleft Lip Photos using Computer Vision	Hypothesis Compared to manual human segmentation, the CADe system will accurately segment the lip in normal subjects and patients with cleft lip and/or palate to automatically categorize the patients' condition based on shape analysis, removing bias and improving the classification, detection, and efficacy of cleft lip surgery procedures, ultimately improving patient satisfaction.
Tiffany Moon	Anesthesiology & Pain Management	Outcomes of General Anesthesia in Patients with a History of Cocaine Use: A Retrospective Review	Hypothesis: We seek to evaluate the claim that patients who test positive for cocaine metabolites, but do not appear acutely toxic and have a normal ECG and vital signs within the normal range, will not have an increased rate of perioperative complications during elective surgery compared to similar patients with negative urine cocaine screening tests. However, it is possible that patients who are chronic cocaine users may have a higher anesthetic requirement. Specific Aim: The goal of the summer research fellowship will be to enroll 40 patients in a pilot study at Parkland Memorial Hospital. An analysis of the pilot study data will provide critical data on a patient population, which has historically been reluctant to self-report. The information that we obtain will be used to inform the implementation of a greater IRB-approved study by determining the true incidence of this phenomenon at our institution, planning future enrollment through a power analysis, identifying trends in the data, and generating new hypotheses for future research efforts.
Tiffany Moon	Anesthesiology & Pain Management	The Difficult Airway: Incidence and Predictors in Lean vs. Obese Patients in a Large Public Teaching Hospital	Our hypothesis is that BMI alone is a weak predictor for difficult intubation in obese individuals. Other factors such as neck circumference (NC), thyromental distance (TMD), the NC/TMD ratio, presence of OSA, inter incisor distance (IID), upper lip bite test (ULBT) and Mallampati (MP) score may be more predictive of difficult intubation in obese individuals. Specific Aim: To assess the difficulty of intubation using the intubation difficulty scale (IDS), a previously validated tool to assess the difficulty of intubation (Adnet et al., 1997).
Jarett Berry	Cardiology	The Association between Physical Fitness and Longevity	Specific Aim: To characterize the association between exercise training on measures of LV strain. We hypothesize that exercise training will be associated with improvement in left ventricular strain after six months of exercise training.

Subhash Banerjee	Cardiology	Veterans Aortic Aneurysm Cardiovascular Outcome Study	Secondary endpoints: 1. To compare the prevalence of atherothrombotic risk factors; concomitant non-aortic CV disease; PAD, and major adverse CV event rates (MACE) in patients with thoracic or abdominal aortic aneurysms 2. To compare the prevalence of PAD, and major adverse CV event rates (MACE) in patients with patients with aortic aneurysms and those without aortic aneurysm Hypothesis: We hypothesize that given the overlapping risks between aortic aneurysms and coronary artery disease (CAD), especially history of tobacco use and hypertension, in a predominantly male veteran population, the prevalence of atherothrombotic risk factors; concomitant non-aortic CV) disease; PAD, and major adverse CV event rates (MACE) will be similar between patients with aortic root and other thoracic or abdominal aneurysms.
John Abrams	Cell Biology	The Role of Tumor Suppressor p53 in Restraint of Retrotransposon Activity	Hypothesis: Using complementation assays, Abrams lab recently discovered that normal p53 alleles suppress transposons but mutant p53 alleles from cancer patients could not (Wylie et al, 2016).. In addition, unrestrained retrotransposons have been observed in p53 driven human and mouse cancers. This project seeks to advance our understanding of the link between the biology of p53 and the biology of transposons. Specifically, I will test the hypothesis that tumor suppression by p53 is fundamentally coupled to systems that restrain retrotransposon activity.
Marc Diamond	Center for Alzheimer's and Neurodegenerative Diseases	Targeting Distinct Tau Strains with Heparinoids to Determine Binding Specificity and Ultimately Prevent Tau Propagation Between Cells	Hypothesis: Heparinoids will differentially target distinct tau strains.
Ralph Deberardinis	Children's Medical Center Research Institute	Feasibility Study Using Imaging Biomarkers in Lung Cancer	We hypothesize that these tumor cells are using lactate as an alternative fuel source for the TCA cycle. Effective utilization of lactate might enable tumor cells to resist glucose deprivation; in fact, a symbiotic relationship has been proposed between well-perfused and poorly-perfused areas in the tumor, with poorly perfused cells converting glucose to lactate via glycolysis and well-perfused cells oxidizing lactate for energy (5).
Amit Pandya	Dermatology	Validation of the Vitiligo Disease Activity Index	Hypothesis: We hypothesize that the subjective VIDA score correlates poorly with change in vitiligo lesions as measured objectively by investigators over time.
Amit Pandya	Dermatology	Determination of the levels of CXCL 9 and	Hypothesis We hypothesize that chemokine levels decrease in

		10 in the interstitial fluid of the skin of patients with vitiligo undergoing treatment using a novel blistering technique	the skin of patients with vitiligo with treatment.
Melissa Mauskar	Dermatology	Predictors of Mortality in Patients With Systemic Calciphylaxis and End Stage Renal Disease	We hope to look at clinical data to determine if there are any predictors that would indicate the usefulness of early intervention or different management protocols for patients with end stage renal disease who develop systemic calciphylaxis. Our hypothesis is that these patients have a higher mortality rate.
Donald Glass	Dermatology	Evaluation of the Safety, Efficacy, and Indications for Use of Pentoxifylline as a Post-Surgical Keloid Treatment Option	Hypothesis: The use of pentoxifylline in post-surgical keloid treatment will be beneficial in decreasing keloid recurrence and will be well-tolerated by patients. Specific Aims: This study will evaluate the safety and efficacy of oral pentoxifylline in the treatment of keloids through evaluation of the following factors: 1) The number of patients given pentoxifylline at or around the time of surgery 2) The number of patients who discontinued the medication, and if so, what was the reason 3) The recurrence rate at 6 months post-surgery for patients who tolerated pentoxifylline, compared to keloid recurrence rates cited in the literature and for post-surgical patients seen in clinic who did not use or tolerate pentoxifylline 4) The criteria used to select patients put on pentoxifylline versus those who were not, such as history of recurrence, previous surgery, number of lesions, location of lesions, and pain or pruritus
Amit Pandya	Dermatology	Immunological profile of inflammatory cells in the skin of patients with vitiligo undergoing treatment	We hypothesize that CD8+ and CD4+ T cells diminish over time in the skin of patients with vitiligo with treatment while Treg cells increase.
Kimberly Reynolds	Green Center for Systems Biology, Biophysics	Evolution of High Efficiency Allosteric Switches	HYPOTHESIS The engineered DHFR/LOV2 fusions were constructed without any optimization, and showed modest regulation (2-fold change in enzyme activity) in response to light. We now ask how the sector architecture influences optimization of these switches. We hypothesize that the sector architecture provides a pre-wired evolutionary path for the gain of allosteric regulation. Accordingly, short paths of point mutations should allow for the optimization of allosteric regulation displayed by sector-connected DHFR/LOV2 mutants while non-sector connected mutants should remain resistant to allosteric communication despite further mutation. AIMS 1. Measure the effect of each mutation on regulation using a high throughput in

			<p>vivo screen. To do this, I will transform each library into an E. coli knock-out strain missing DHFR (ER2566 <math>\Delta</math>folA <math>\Delta</math>thyA), grow them in selective media under lit and dark conditions, and conduct a time course experiment in which samples are removed from the mixed culture and the relative frequencies of each mutant allele in the population are quantified using next-generation sequencing. 2. Identify mutant alleles that alter growth rates in lit versus dark conditions, quantify their activity through enzyme kinetic measurements, map these mutant alleles on to the DHFR structure, and statistically compare these positions to the allosteric network defined by the sector. 3. Solve high resolution crystal structures of the mutants displaying the greatest magnitude in allosteric regulation to better understand what structural changes underlie the changes in function.</p>
Jeffrey Zigman	Hypothalamic Research	Investigating the Role of Ghrelin in Prader-Willi Syndrome	<p>The overall goal of this Summer Project is to directly test a model predicting novel roles of ghrelin in PWS. In contrast to the prevailing view that ghrelin is detrimental in PWS, we now propose that ghrelin elevation in PWS is protective, preventing premature death in children with PWS while also helping to preserve GH secretion and muscle function, limit depression and anxiety, and ensure survival in adults with PWS. We hypothesize that the elevated ghrelin in PWS is protective, defending against exaggerated degrees of GH deficiency, hypotonia, and hypoglycemia - ultimately preventing death of PWS neonates. To directly test this hypothesis, we will determine if crossing Snord116del mice to ghrelin-KO mice reproduces the striking phenotype obtained using Snord116del/GHSR-null mice. Also, we will determine if administering ghrelin rescues or improves the outcome of PWS mice on the ghrelin-deficient or on ghrelin-replete backgrounds, respectively.</p>
Ian Neeland	Internal Medicine	Impact of Visceral Adiposity on Glycerol Metabolism in Gluconeogenesis among Non-Diabetic Obese Adults	<p>The first hypothesis is that participants with higher visceral fat content by MRI will have a greater relative contribution of unlabeled glycerol to glucose compared with age, sex, and body mass index (BMI)-matched participants with lower visceral fat. The second hypothesis is that participants in the fasting-refed state will have a greater relative contribution of adipose tissue derived glycerol (measured by <math>^{13}\text{C}</math> nuclear magnetic resonance spectroscopy analysis) to hepatic gluconeogenesis compared with participants in the fasting state.</p>

<p>Ricarda La Hoz David Greenberg</p>	<p>Internal Medicine</p>	<p>Epidemiology of Blood-Borne Infections in Solid Organ Transplant Recipients</p>	<p>Hypothesis The incidence of blood stream infections is higher amongst transplant recipients than in the general population. We predict that the most common microorganisms associated with blood stream infections amongst solid organ transplant recipients to be: Coagulase negative Staphylococci, Staphylococcus aureus, Enterococcus species, Escherichia coli, Klebsiella species and Candida species. Transplant recipients will have a higher prevalence of multi-drug resistant organisms than the general population. Specific Aims 1. Describe the epidemiology of blood stream infections in solid and stem cell transplant recipients. a. Identify the most common organisms responsible for blood stream infections in all solid organ transplant recipients and by organ type (lung, heart, liver, and kidney). b. Identify the most common organisms responsible for blood stream infections in stem cell transplant recipients both autologous and stem cell transplant recipients. c. Describe the prevalence of multi-drug resistant organisms as a cause of blood stream infections.</p>
<p>Amit Singal</p>	<p>Internal Medicine</p>	<p>Accuracy of Ultrasound as Screening Modality for Detecting Hepatocellular Carcinoma in Patients with Cirrhosis</p>	<p>Specific aims/ Hypothesis: To identify patient characteristics associated with sensitivity of ultrasound for early-stage detection of hepatocellular carcinoma. We hypothesize patient factors including body mass index, presence of ascites, and degree of liver dysfunction/nodularity are associated with lower ultrasound sensitivity for detecting HCC nodules.</p>
<p>David Gerber</p>	<p>Internal Medicine</p>	<p>Clinical trial design and conduct to optimize accrual and quality</p>	<p>Aim 1. This research project will use a dataset of publically available NCI-sponsored lung cancer clinical trial protocols (N=73) and protocol summaries on the clinicaltrials.gov website to determine predictors and trends in the total number of eligibility criteria and pharmacy-related eligibility criteria (CYP3A4 metabolism, QTc prolongation). Protocols will be characterized according to activation year, principal treatment modality, disease histology and stage, trial phase, and total enrollment number. The association between trial characteristics and eligibility criteria will be assessed by Chi-Square analysis. Aim 2. Working with primary mentor Dr. Gerber and collaborator Dr. Simon Lee, Ms. Garcia will (1) conduct a relevant literature search focusing on interactions between clinical research teams and clinic staff, (2) review transcripts from previously conducted focus groups with clinical research and clinic staff, and (3) develop surveys and questionnaires to be</p>

			administered to staff, providers, and patients. These instruments will be designed to determine perceptions of roles and responsibilities and opportunities to enhance the function of this multi-team system.
Anne Satterthwaite	Internal Medicine - Division of Rheumatology	Role of Foxo3 in B Cell Tolerance	Hypothesis: Foxo3 promotes deletion of immature B cells that remain auto-reactive after receptor editing. Specific Aim 1: Define the mechanism by which Foxo3 mediates immature B cell apoptosis and determine the consequences of this for the elimination of auto-reactive B cells. Specific Aim 2: Determine whether a Foxo3-deficiency results in increased receptor editing due to a longer editing window and assess the consequences for B cell auto-reactivity.
Chris Chen	Orthopedics	Tentative Title: Efficacy of intra-articular administration of EPO and BMP2 from HA microscaffolds on autologous MSC recruitment, local inflammatory responses in synovial space, and cartilage regeneration.	HYPOTHESIS: The intra-articular administration of EPO and BMP2 from HA microscaffolds will enhance autologous MSC recruitment, reduce localized inflammatory responses in the synovial space and promote cartilage regeneration. SPECIFIC AIM: To test the ability of intra-articular injection of EPO-HA and BMP2-HA microscaffolds in preventing the development of PTOA in rabbits.
William M. Lee	Internal Medicine-Hepatology	Histological Findings in the Two Subtypes of Hepatitis B-Related Acute Liver Failure	Hypothesis: We hypothesize that patients with acute HBV-acute liver failure will demonstrate, on liver tissue staining, qualitative and/or quantitative differences in HBcAg expression and/or HBsAg expression, as well as morphological differences on H&E stain from those with chronic HBV-ALF. Specific Aims: By determining that there are antigenic and/or morphological differences between the subtypes of HBV-ALF and specifying what they are, we expand our knowledge of the difference between acute and chronic HBV as it relates to acute liver failure. This is useful for establishing potential therapeutic targets that may modify the course of the disease or allow for stratification of risk within each category.
David Greenberg	Internal Medicine, Microbiology	Development of Novel Gene-Silencing Therapeutics for Pseudomonas aeruginosa Biofilms	Hypothesis: PPMOs targeting the quorum sensing protein lasR when co-incubated with traditional antibiotics will provide synergistic effects in both the prevention and/or breakdown of P. aeruginosa biofilm. Specific Aims: 1) Utilize the LasR PPMO with traditional antibiotics in a strain collection of P. aeruginosa and measure the ability to prevent biofilm formation in both antibiotic-sensitive and antibiotic-resistant strains. 2) Utilize the LasR PPMO with traditional antibiotics in a strain collection of P. aeruginosa and measure the breakdown of pre-formed biofilms

			in both antibiotic-sensitive and antibiotic-resistant strains.
David Greenberg	Internal Medicine, Microbiology	Development of Novel Gene-Silencing Therapeutics for <i>Acinetobacter</i> <i>baumannii</i> Biofilms	We hypothesize that PPMOs targeting the attachment protein CsuE when co-incubated with traditional antibiotics will provide synergistic effects in both the prevention and/or breakdown of <i>A. baumannii</i> biofilm.
Dharam Kumbhani	Cardiology	Assessing the quality of treatment in the use of vascular intervention in patients with PVD complicated by foot ulcer	Specific Aim: To create and analyze a unique database consisting of patient data from Parkland patients from the ASC Foot Wound Clinic (including limited demographic data, history of diagnostic and prognostic care regarding vascular assessment and intervention, data on hemoglobin A1C, comorbidities, and outcomes) of approximately 600 patients over a 6-month time period to assess different outcomes and the quality and inclusion of vascular intervention in patients presenting with foot ulcers.
Peter Douglas	Molecular Biology	Mediating Neuronal Protection against Traumatic Injury through Mitochondrial Metabolism	The aims of this research project are threefold. First, we will assess whether application of cco-1 RNAi knockdown treatments reverse the short-term effects of trauma, which will be measured by paralysis duration, ERK1/2 phosphorylation levels, levels of oxidative damage and respiration rates obtained via a SeaHorse efflux analyzer. Second, we will determine if the cco-1 RNAi treatment can prevent the long-term consequences of early adulthood blunt force trauma by measuring the degree of neurodegeneration in worm food-sensing neurons and the accumulation of toxic protein aggregates such as neuronal polyglutamine expansion proteins such as Q67, muscle-expressed amyloid beta (linked to Alzheimer's disease), and the ALS linked gene, TDP-43. Third, we will determine the precise spatiotemporal requirements for cco-1 RNAi treatment administration.
Rueyling Lin	Molecular Biology	Role of the endogenous siRNA pathway in mRNA clearance and cellular reprogramming.	The aim of this project is to begin testing the hypothesis that the endo-siRNA pathway has an important function during the reprogramming of mammalian cells by generating the blank slate for the new developmental program. Specifically, we will test the role of endo-siRNA in well-developed reprogramming protocols by using either ectopic expression or knockdown of endo-siRNA pathway components. Our hypothesis predicts that enhancing the endo-siRNA pathway should improve reprogramming (measured as efficiency and/or time required), and conversely, inactivating the pathway should negatively

			reprogramming.
Joachim Herz	Molecular Genetics	Inducible Mouse Model for Amyloid Precursor Protein	<p>Hypothesis: By creating a mouse model that allows inducible overexpression of endogenous APP in a timely, regulated, and reversible manner we are able to circumvent several flaws of current AD mouse models. Our transgenic mouse will be crossed with wild type and different available APP-knockin mice allowing us to study the effect of inducible up and down regulation of endogenous wild type and human APP. Specific Aims: Our model makes use of a transcription factor fusion protein that is designed to specifically bind to the mouse endogenous APP promoter. A transgenic mouse line, which expresses such a transcription factor in an inducible manner, can be used to study the physiological function of mouse wild type APP, which is currently not very well understood. Gene overexpression studies and subsequent reversion to normal levels will give important insight in protein function in vivo. The future mouse model will be suited to study synapse formation and function. Furthermore, breeding this transgenic mouse line with available human APP knockin mice will reveal further insights into the pathogenesis of AD under more physiological conditions than current AD mouse models allow. In our mouse model we circumvent the problem of lacking untranslated regions (UTRs) in the APP mRNA transcript, such important regulatory elements are disregarded in current APP overexpression models. Since the subcellular localization of mRNA and transcriptional regulation will be unaffected in our model it reflects the pathogenesis in the human brain more precisely than current models. In summary, this mouse model allows us to study the effect of reversible overexpression of endogenous whole lengths APP to discover APP function in health and disease.</p>
Juan Pascual	Neurology & Neurotherapeutic	Analysis of the glucose transporter type I deficiency registry	<p>The purpose of the Glucose Transporter Type 1 Deficiency (G1D) Registry is to expand the knowledge of the natural course of G1D, improve clinical care, and provide direction for future research. The G1D Registry has been created and funded by the Department of Neurology and Neurotherapeutics at UT Southwestern Medical Center under the guidance of Dr. Juan Pascual. Patients and families directly enter their data in the registry by answering a series of questions. The registry contains information about diagnosis, symptoms, medical and family</p>



			history, treatments and medications, laboratory and imaging tests, and the history of patient's medical care. It is expected that addressing certain questions may ultimately result in a significant change in the standard of care.
Craig Powell	Neurology & Neurotherapeutics	Insulin-Like Growth Factor 1 (IGF-1) therapy in restoring hippocampal neurons in a Gulf War Illness model	Objective/Hypothesis We hypothesize that the delayed-onset decrease in synapse number can be reversed with drugs already in clinical use or clinical trials. The neurotrophic factor IGF-1, FDA approved for use even in children, stimulates synaptic spine and synapse formation during development, during normal aging, and when administered in preclinical studies of human neurological disorders. This project will evaluate the effectiveness of IGF-1 therapy in restoring normal synapse structure and function in our GWI mouse model using extracellular 'field' electrophysiology, neuron reconstruction techniques, and immunohistochemistry (IHC).
Shilpa Chitnis	Neurology & Neurotherapeutics	Patient Perceptions and Knowledge of Parkinson Disease and Treatment	The purpose of this study is to survey patients about their knowledge of PD and available therapeutic options. The results from this survey will be useful to identify possible deficiencies in patient education and help develop a targeted patient education protocol, with the ultimate goal of improving outcomes and providing reasonable quality of life for PD patients depending on the stage of their disease.
Munro Cullum	Neuropsychiatry	Age of Diagnosis of Mild Cognitive Impairment by Race: The Effect of Traumatic Brain Injury History and Apolipoprotein ε4	Hypothesis: It is predicted that the interaction between Apo-E4 and a history of TBI will be associated with a significantly earlier age of MCI diagnosis in Caucasians and not in African American nor Hispanic individuals.
Jerry Niederkorn	Ophthalmology	Mechanisms Leading to Reduced Liver Metastasis in Mice with Defective FasL (CD95L)	Experiment 1 Hypothesis: Although gld/gld mice have non-functional FasL, they may have other anomalies that affect homing of blood-borne melanoma cells to the liver. Rationale: Homing of blood-borne melanoma cells to the liver correlates with metastasis. Design: Homing of radiolabeled B16LS9 melanoma cells to the liver will be assessed in WT and gld/gld mice. Outcome if hypothesis is correct: Liver homing will be higher in WT mice. Experiment 2 Hypothesis: FasL-FasR interaction may promote tumor metastasis through increased liver secretion of c-met. Rationale: C-met is the major chemokine in the liver that is associated with liver metastasis in human UM patients. Design: Livers from WT and gld mice harboring liver metastases will be analyzed by western blot and ELISA to determine c-met protein levels. Liver supernatants from

			<p>WT and gld mice will also be analyzed for differences in tumor cell chemotactic responses in vitro. Outcome if hypothesis is correct: WT mouse livers will have greater c-met levels and will produce greater tumor cell chemotactic responses. Experiment 3 Hypothesis: Absence of functional FasL may enhance liver NK cell cytotoxicity. Rationale: Studies have reported that FasR can dampen immune responses by transmitting signals into FasL-bearing NK cells, via a mechanism known as 'reverse signaling.' Design: Liver NK cell cytotoxicity will be assessed in WT and gld mice. Outcome if hypothesis is correct: gld mice will have higher NK cytolytic activity than WT mice. Experiment 4 Hypothesis: In addition to defective FasL, gld mice may have an anomalous higher production of interferon-gamma (IFN-) or perforin. Rationale: IFN- and perforin are important mediators for the anti-tumor effects of NK cells. Design: IFN- and perforin levels will be measured by ELISAs in the livers removed from tumor-bearing gld and WT mice. Outcome if hypothesis is correct: IFN- or perforin levels will be higher in gld mice. Experiment 5 Hypothesis: FasL-FasR interactions may promote angiogenesis through increased VEGF synthesis in the liver. Rationale: Angiogenesis mediated by VEGF is an important step in the establishment of liver metastases.</p>
Karanjit Kooner	Ophthalmology	Redefining Glaucoma Damage	<p>Hypothesis: NFL analysis will provide more sensitive, reliable and early evidence of optic nerve damage than the current VF tests. Specific aims: 1. to determine if NFL analysis agrees with the current definitions of VF defects by the Hodapp-Parrish-Anderson criteria. 2. Does the thickness of lamina cribrosa correlate with CCT or family history of glaucoma?</p>
Ronald Mancini	Ophthalmology	Examining correlations between preoperative basal and squamous cell carcinoma lesions of the eyelid and postoperative repairs	<p>HYPOTHESIS 1. Our first hypothesis is that preoperative appearance of the lesion is a poor predictor of final lesion/defect size. We expect that the visible tumor on the eyelid will ultimately reveal to be much larger under the surface, requiring more surgical intervention than initially anticipated. 2. Our second hypothesis is that squamous cell carcinoma, a more aggressive tumor than basal cell carcinoma, will likely result in a larger postoperative defect. 3. Basal and squamous cell carcinoma have a predilection for the lower eyelid over the upper eyelid due to more sun exposure on the lower eyelid surface. We hypothesize to find a similar correlation with the population in our study. III. SPECIFIC AIMS By looking at</p>

			preoperative photographs and initial clinical examination of the patients in our study, we will determine whether or not and to what degree we were able to predict the defect size following surgical removal of the lesion. We will also determine whether the type of cancer, basal vs squamous cell carcinoma, has an effect on the ultimate defect size and our ability to predict defect size from initial examination. Lastly, we will determine whether or not our population fits with prior reported studies that show skin cancers have a propensity for the lower eyelid as opposed to the upper eyelid.
David Birch	Ophthalmology	Evaluating Possible Mechanisms of Age Related Macular Degeneration with Reticular Pseudodrusen	Hypothesis: RPD acts as a diffusional block that physically limits the exchange of retinol between RPE and photoreceptors. Specific aims: (1) To determine the extent and progression of rod sensitivity loss in intermediate AMD with RPD (2) To relate the extent of rod and cone sensitivity loss to en face fdOCT structural measures.
W. Matthew Petroll	Ophthalmology	Modulation of Corneal Wound Healing following Photorefractive Keratectomy	Hypothesis: We hypothesize that topical application of Quercetin will reduce corneal fibrosis and haze following photorefractive keratectomy surgery in the rabbit. Specific Aims: To test this hypothesis, we will assess the effects of Quercetin on keratocyte backscattering, alignment, morphology and connectivity in vivo following a keratectomy injury (photorefractive keratectomy, PRK) which produces a fibrotic response on top of the injured stroma. Corneas will be evaluated using the Heidelberg Retina Tomograph Rostock Cornea Module (HRT-RCM) clinical confocal microscope, and these findings will be correlated with en bloc 3-D confocal fluorescence and second harmonic generation (SHG) imaging.
Danielle Robertson	Ophthalmology	Impact of insulin, IGF-1, and hyperglycemia on autophagy in the corneal epithelium and wound healing	Hypothesis: That hyperglycemia-induced alterations in autophagy plays a pivotal role in the development of corneal epithelial complications and impaired wound healing in diabetes. Specific Aims: We will test this hypothesis in the following two specific aims: 1. (a) We will examine the role of insulin in mediating autophagy in the corneal epithelium. (b) We will then test the effects of hyperglycemia on autophagy in the corneal epithelium. 2. We will compare the level of autophagy in normal versus diabetic corneal epithelial cells obtained by primary culture of human donor eye bank corneas.
John Hulleman	Ophthalmology	Development of a primary retinal cell culture model to identify the cause(s) of	We hypothesize that hRPE cells can be used to generate a primary RPE model that recapitulates the formation of sub-RPE

		the rare macular dystrophy, Malattia Leventinese	protein deposits reminiscent of ML/AMD. Specific Aims. 1.) To establish an hfRPE which develops sub-RPE protein deposits. 2.) To test a number of genetic and pharmacologic manipulations in this cell culture model to determine their effect on rescuing protein deposit formation.
Ronald Mancini	Ophthalmology	Risk factors contributing to pathophysiology of primary acquired nasolacrimal duct obstruction	We hypothesize risk factors exist that may contribute to the pathophysiology of PANDO, such as use of glaucoma medications, environmental factors (i.e. cosmetic use), gender, medical co-morbidities, and metabolic disturbances particularly involving Na <sup>+</sup> , K <sup>+</sup> , Cl <sup>-</sup> , Ca <sup>++</sup> which may be associated with stone formation sometimes noted in PANDO. We will aim to identify potential risk factors that lead to PANDO by looking for any possible statistically significant correlation between factors and disease.
Danielle Robertson	Ophthalmology	Pseudomonas aeruginosa Type VI secretion system on neutrophil actin polymerization	Specific Aim: To assess the ability of P. aeruginosa to evade the innate immune system by comparing the potential for wild type (PA01) and H2-T6SS mutant (PA01ΔclpV2) to induce actin polymerization in human neutrophils and inhibit further phagocytosis in vitro. Hypothesis: A Type VI secretion system is utilized by Pseudomonas aeruginosa to interfere with neutrophil actin cytoskeleton, thus hindering its phagocytic capabilities.
Paula Hernandez Valdez	Orthopaedic Surgery	Molecular and Morphological Responses to Severe Burn Injury in Rat Achilles Tendon and Intervertebral Disks	Hypothesis: The Achilles tendon will be affected by systemic expression of pro-inflammatory cytokines altering its remodeling balance. Also, NP cells in the IVDs will be altered both morphologically and in protein expression. Specific Aims: Aim1: To study gene and protein expression of pro-inflammatory cytokines, Collagen I, Collagen III and MMPs in Achilles tendon after skin burn as well as to characterize changes in fiber alignment. Aim 2: To study protein expression in NP cells from IVDs, comparing areas immediately below the site of burn injury with those that are more distant. We will also compare the equivalent discs of non-burned control rats and observe for morphological changes in NP cells after burning.
Michael Khazzam	Orthopaedic Surgery	Effectiveness of Corticosteroid vs. Ketorolac Shoulder Injections: A Prospective Double-Blinded Randomized Trial	The goal of this study is to test the efficacy of intraarticular injections of Ketorolac vs. Corticosteroid on rotator cuff shoulder pathologies, specifically rotator cuff tears and tendonitis. We hypothesize that subacromial injections of Ketorolac will be more effective than corticosteroid injections in pain relief treatment for shoulder pathologies.

Mohammed Khaleel	Orthopaedic Surgery	Sleep Disturbance in Patients with Operative Spine Pathology	Hypothesis: Spine pathology has a negative impact on sleep quality, and surgical treatment will increase the quality of sleep in patients with operative spine pathology.
Michael Huo	Orthopaedic Surgery	Retrospective Database for Total Knee Arthroplasty (TKA)	Specific Aim: To collect clinical and radiographic data in consecutive patients who have undergone primary and revision TKAs at UT Southwestern Medical Center and its affiliates and Parkland Health and Hospital System.
Harry Kim	Orthopaedics	Proximal femoral growth modulation using percutaneous trans-physeal screw placement	Specific aim. We will determine the effects of an eccentrically placed trans-physeal screw on inducing a varus or valgus angulation of the proximal femur in a large growing animal model. Hypothesis. We hypothesize that a medially or laterally placed proximal femoral trans-physeal screw will serve as a growth tether and produce a varus or valgus angulation of the proximal femur, respectively.
Michael Khazzam	Orthopedic Surgery	Effectiveness of Corticosteroid vs. Ketorolac Shoulder Injections: A Prospective Double-Blinded Randomized Trial	Specific Aim: I will be assisting Dr. Michael Khazzam in a prospective, randomized double-blinded study that aims to compare the effectiveness of ketorolac or corticosteroid injections in individuals who have acquired shoulder pathologies including atraumatic full thickness rotator cuff tears and rotator cuff tendinitis. The hypothesis states shoulder injections with Ketorolac will be more effective than corticosteroid injections.
Paula Hernandez	Orthopedics	The role of HtrA1 in the morphologic changes of chondrocyte morphology seen in Osteoarthritis.	Hypothesis: chondrocyte phenotypic regulation is disrupted by overexpression of HtrA1, leading to changes observed in OA. Specific Aims: Aim 1: to compare OA samples with control in (i) HtrA1 expression using qPCR and Western blot, (ii) HtrA1 association with cytoskeleton using co-immunoprecipitation and immunofluorescence, and (iii) analysis of cell morphology parameters such as cell circularity, perimeter, and attachments in order to study changes in phenotype. Aim 2: To compare control chondrocytes versus OA chondrocytes response to Cytochalasin D treatment, using cell morphology parameters. Low doses of Cytochalasin D will cause cytoskeletal disruption, particularly in actin filaments.
Kenneth Lee	Otolaryngology	Improving Patient Hearing Outcomes by Minimizing Insertion Trauma with a Shape Memory Polymer Cochlear Implant Array	Hypothesis: Novel self-coiling electrode arrays made of shape memory polymer allow for atraumatic implantation of cochlear implants, minimizing loss of residual hearing and maximizing hearing outcomes in cochlear implant patients.
Ron Mitchell	Otolaryngology	Polysomnographic variation and Adenotonsillectomy outcomes in the	Hypothesis: Among children with Down syndrome, obesity, age and ethnicity unfavorably predicts outcomes of T&A in children

		pediatric population with Down syndrome	Specific Aims: The specific aims of this project are to correlate demographics and especially weight with the outcomes of T&A in children with Down syndrome and OSA. The goal is identify predictors of resolution of OSA in children with Down syndrome based on demographics, clinical and polysomnographic parameters.
Ron Mitchell	Otolaryngology Head and Neck Surgery	Outcomes of T&A in overweight and obese pediatric patients with obstructive sleep apnea	We hypothesize that T&A will result in improvement or resolution of OSA in overweight and obese patients but the response will not be uniform. We also hypothesize that some predictors of outcome would include age, BMI z-score (specifically weight increase) and ethnicity.
Ron Mitchell	Otolaryngology, Pediatrics	Correlates to Weight Gain in Children with Obstructive Sleep Apnea following Tonsillectomy	Many pediatric cases of obstructive sleep apnea (OSA) occur due to tonsillitis, which may be treated with a routine tonsillectomy. However, many children relapse into OSA after tonsillectomy despite temporary relief of symptoms. One possible cause of this may be due to the association between tonsillectomies and post-operative weight gain, as observed by Lewis et. al. in 'Weight gain after adenotonsillectomy: a case control study' (2015). In obese patients, excessive accumulation of adipose tissue around the neck can lead to airway obstruction, thus resulting in OSA. The goal of this project will be to perform a retrospective multivariate analysis using demographic and other patient data (from the Children's Health EPIC patient records) to identify factors relating to weight gain following a tonsillectomy.
James Malter	Pathology	Identifying recombinant PIN1 proteins at specific phospho-serine sites and establishing if sensitive to B-amyloid	Pin1 is a cis-trans peptidyl isomerase with specificity for serine-proline or threonine-proline peptide bonds, Pin1 targets include APP, tau, 4EBP1 and a variety of other signaling proteins involved in neuronal function and homeostasis, leading to the hypothesis that Pin1 is involved in AD pathology. Pin1 is lost early in AD evolution possibly via oxidation and accelerated clearance. When bound to APP or tau, Pin1 accelerates non-amyloidogenic processing via an alpha-secretase pathway and helps maintain tau in a non-phosphorylated state. Whether or how Pin1 enzymatic activity is acutely or chronically affected by B-amyloid, the likely causal agent in AD, is unknown. Recently, we have identified a new role for Pin1 in the maintenance of dendritic spines. In the absence of Pin1, spines are reduced in number and complexity. Of note, spines are lost during evolving AD that may account for the prominent memory losses and behavioral changes seen early in the disease. Therefore, it was

			hypothesized that Pin1 loss/inhibition was responsible for the reduction in spines seen in neurons treated with/exposed to B-amyloid.
Mohammad Tarique Hussain	Pediatric Cardiology	Clinical Outcomes and Utility of Cardiac Catheterization Prior to Fontan Completion in the Current Era	Hypothesis and specific aims: Our goal is to conduct a retrospective, observational study in which we examine the outcomes of the patients at Children's Medical Center eligible for the Glenn procedure to determine under what circumstances patients proceeded and underwent the Glenn; what circumstances patients were recommended for and received heart transplantation and what circumstances resulted in no further therapeutic options being available to them. We hypothesize that patients are not excluded from the Fontan procedure based on hemodynamic data that was not otherwise found in a history or echocardiogram.
Hannah Piper	Pediatric Surgery	Evaluation of urinary sodium, dietary sodium intake, and somatic growth in children with short bowel syndrome	Hypothesis Children with short bowel syndrome who are receiving sufficient dietary sodium to maintain a urine sodium concentration $\geq 60$ meq/L will have better weight gain and linear growth compared to children with urine sodium $< 60$ meq/L receiving similar kcal/kg. Specific Aims 1. To correlate urine sodium concentration (mmol/L) in children with SBS with average daily weight gain (g/kg/d), linear growth, and daily sodium intake (mEq/kg/d) 2. To develop a guideline for monitoring urinary sodium concentration and dietary sodium supplementation to achieve sufficient somatic growth
Faisal Qureshi	Pediatric Surgery	A review of the treatment of splenic cysts at Children's Medical Center	Hypothesis: We hypothesize that the treatment of splenic cysts with aspiration and sclerotherapy will have fewer complications and a lower failure rate than other treatment modalities.
Joseph Murphy	Pediatric Surgery	IVC Tumor Thrombus- Identification, Management and Consequences	Our hypothesis is those patients with IVC tumor thrombi do worse than those IVC patients are without thrombi. Specific Aims: The aim of this study is to identify children with inferior vena cava (IVC) tumor thrombi, describe their surgical experience and detail their long-term oncologic and physiologic outcomes.
Linda Baker	Pediatric Urology	Novel Surgical Technique for Drainage of Obstructed Uterovaginal Duplication	HYPOTHESIS: Percutaneous obstructed hemivagina access (POHVA) leads to minimally invasive identification and safe entry to the difficult OH compared to blind dissection and successfully identifies the difficult OH in over 50% of cases SPECIFIC AIMS: 1. Report the novel technique of percutaneous obstructed hemivagina access, POHVA. 2. Find success rate of POHVA in

			identification of and safe entry to the difficult OH in all past cases. 3. Determine complications if any that arose secondary to the POHVA technique
Christy Turer	Pediatrics	Automating Clinical Decision Support to Improve Pediatric Hypertension Identification and Management: An Evaluation of Diagnostic Sensitivity, Computational Efficiency, and Cost of Three Proposed Methods	We hypothesize that the third (Cache) method will be the most sensitive for diagnosing pediatric hypertension, followed by use of SDEs, and finally, the substitution of point-of-care height and age measures for missing or inaccurate historical values (COCB).
Darryl Miles	Pediatrics	A Study of Optic Nerve Sheath Diameter to Predict Intracranial Hypertension in Pediatric Brain Injured Patients	Specific Aims: Aim 1: Compile a standardized normative data set of ONSDs in children ranging from infancy to 18 years. Impact: This normative data can be used by future pediatric physicians across the country to inform them whether their patient has normal levels of pressure or not. This could prevent unnecessary surgical procedures and CT scans. Aim2: Determine the sensitivity and specificity of the ONSD procedure to predict pathological changes in ICP in pediatric patients. Impact: If proven, this procedure could detect elevated ICP non-invasively and help physicians monitor pressure levels in their patients once admitted to the PICU without invasive monitoring. This technique could then be used on a wide range of pediatric patients with acute neurologic injury. Hypothesis: We hypothesize that an ultrasound based-measurement ONSD of > 4.5mm in children will correlate with an ICP of greater than 20mmHg with invasive monitoring methods.
May Lau	Pediatrics	Unique Factors of Dating Violence in Asian American Adolescents	Hypothesis: 1. Asian-American adolescents will have dating violence rates equivalent to other races. 2. Unique factors will be identified that explain the equivalent dating violence rates in Asian-Americans Specific aims: The specific aims of this study is: 1. To examine rates of dating violence among Asian Americans adolescents and young adults 2. To identify sociodemographic, academic, violence-related, drug-related, and mental health factors that are associated with dating violence in Asian American adolescents
James Collins	Pharmacology	Analysis of neoblast gene expression and function in Schistosoma flatworms	We hypothesize that neoblast-driven tegument renewal is essential to protect the schistosome from the host's immune system. Specific aims: To test our main hypothesis, we require an in-depth understanding of the molecular events that coordinate the differentiation of neoblasts in to tegumental cells. Therefore, we will clone cDNAs for 20-30 stem cell



			associated genes and perform double fluorescent in situ hybridization experiments with known neoblast markers to confirm these genes are expressed in stem cells.
Elisabeth Martinez	Pharmacology	The effects of Jumonji histone lysine demethylases on the P. falciparum life cycle	I hypothesize that Jumonji histone lysine demethylases play a critical role in regulating gene transcription in P. falciparum and thus mediating parasite virulence, and that disruption of this regulatory mechanism will disrupt its virulence. Specific Aims <ul style="list-style-type: none"> <li>• To determine how the red blood cell stages of P. falciparum are affected by histone demethylase inhibitors. More specifically, I aim to characterize JIB-04-treated blood stage parasites to determine: 1. when morphological changes become apparent, 2. whether the blood cell stage of the parasite impacts the ability of demethylase inhibitors to impede life cycle progression 3. how quickly demethylase inhibitors kill the parasite</li> <li>• To identify changes in gene expression mediated by JIB-04</li> </ul>
Joyce Repa	Physiology	Evaluating therapies for Niemann-Pick type C disease	We hypothesize that LXR agonists and/or a new therapy, triglycerol acetate, may improve hearing function and lung disease in NPC. Specific Aim 1. Determine whether LXR activity impacts hearing. a) Perform Auditory Brainstem Response (ABR) tests in wildtype, Lxralpha-/-, Lxrbeta-/-, and Lxralpha/beta-/- mice. b) Perform ABR testing of Npc1+/+ and Npc1-/- mice treated with the LXR agonist T0901317. Specific Aim 2. Characterize the pulmonary dysfunction in NPC disease, and evaluate the impact of therapies (T0901317, cyclodextrin, and triglycerol-acetate) on lung phenotypes in the Npc1-/- mouse. a) Perform MS-MSALL lipidomics analyses on lung tissues from treated Npc1+/+ and Npc1-/- mice. b) Use quantitative real-time PCR to measure the expression of genes relevant to pulmonary cell types and function (e.g. surfactants), inflammation, and lipid metabolism using lung tissues from these mice.
Christopher Derderian	Pediatric Plastic and Craniofacial Surgery	Determining the craniofacial landmarks important in assessing head shape: A study using eye tracking technology	We hypothesize that there are important reference points in the head and face that individuals compare against thresholds of normal and abnormal and use to make the social determination of deformity. We further hypothesize that these reference points, and the process of evaluation, are conserved between individuals. Specific Aims <ol style="list-style-type: none"> <li>1. Assess the eye movements used in normal head shape evaluation to determine the overall process of evaluation of normal head shape.</li> <li>2. Determine how eye movements deviate from the process of normal head shape</li> </ol>

			evaluation in the evaluation of abnormal head shape.
Bardia Amirlak	Plastic Surgery	Retrospective study to measure efficacy of onabotulinumtoxin A in the context of chronic migraine headaches.	We predict that accurate injection of onabotulinumtoxin A into carefully studied anatomical sites are effective in reducing disease burden. In this study, a retrospective review of patients for headache characteristics will be conducted to measure pre and post treatment changes. Such characteristics include frequency, duration, and severity.
Nicholas Haddock	Plastic Surgery	Co-surgeons in Breast Reconstructive Microsurgery: What Do They Bring to The Table in an Academic Institution?	Hypothesis: The addition of a Co-surgeon we believe will reduce operative time, average patient LOS, and some post-operative complications. We believe that the co-surgery model is associated with increased operative efficiency for Bilateral DIEP Breast Reconstruction.
Jeffrey Kenkel	Plastic Surgery	Clinical Assessment of the Performance of Combination 1470nm/2940nm Laser Therapy for Improved Facial Skin Texture, Tone, and Reduction of Skin Pore Size	Ideally, non-surgical skin rejuvenation will move towards laser treatments that achieve the results of ablative therapies without the unfavorable recovery times and risks. In our summer project, we will initially define what youthful skin looks like using non-invasive techniques such as high resolution photography, 3-dimensional photography, UV light evaluation, high-resolution ultrasound (HRUS), elasticity measurements, and various polarized lights. Specifically, 3D-photography will be used to evaluate improvements in skin tone, texture, and pore size. UV light evaluation will be used to assess improvements in actinic sun damage. HRUS will be used to measure increases in collagen thickness. We will then investigate skin ultrastructure evaluating collagen, elastin, and glycosaminoglycans using electron and confocal microscopy. In addition, we will consider the gene expression using RNA sequencing and Mass spectroscopy.
Sumeet Teota Nicholas Haddock	Plastic Surgery	The 2 staged implant based reconstruction with anatomic textured implants in Nipple-sparing mastectomy	We hypothesize that strict adherence to protocol for textured implants is necessary to optimize patient outcome. Furthermore certain techniques of manipulation of expander size may reduce the complication rate and result in higher patient satisfaction.
Sumeet Teotia	Plastic Surgery	Challenges in radiation of patients with breast cancer, Quantitative Analysis in outcomes of seven-hundred consecutive autologous breast reconstructions at UTSW	Hypothesis: Refinements in multiple-free flap breast reconstructions produce better aesthetic outcomes and patient satisfaction in post-radiation, post-mastectomy, patients.
Carol North	Psychiatry	Secondary Analysis SUNCODA Study Data on Homeless Service Use	Scientific aims and hypotheses Aim 1. To examine the SUNCODA model, exploring the relationships among predisposing, enabling, and need factors, service use, and cost of

services associated with drug abuse and other health conditions, and how these factors and service use are associated with changes in status over time in a drug abusing homeless population. These 'change in status' variables included drug use, housing, consequences of drug use, and HIV risk behaviors. Aim 1 pertains to the SUNCODA model's ability to predict service use and subsequent status changes. These status changes include achievement of stable housing, changes in substance use patterns and their consequences, changes in psychiatric status, changes in HIV risk behaviors, and changes in other behaviors associated with homelessness and substance use disorders and their consequences (e.g., employment, entitlement use, child custody status). The dataset collected for the SUNCODA project provides a rich source of material for investigation of the relative direct costs of service use and their relation to status changes. Analyses related to specific components of the SUNCODA model are prediction of housing outcomes from drug abuse status and treatment utilized. Analysis of data for the SUNCODA homeless model on which the data from this project are structured permits combining attributes of structural analysis (path analytic) models with repeated measures to examine components of the model simultaneously. These analyses are ongoing and will provide years of productive analysis and publication of findings from the SUNCODA databases. Aim 2. To examine the association of drug abuse and the course of homelessness by comparing drug abusing and non-drug abusing homeless individuals over time in terms of status change associated with service use within the SUNCODA homeless model. Hypothesis 1: Drug abusing homeless individuals will not only be more likely to use drug-related services, these individuals will also be more likely to use a variety of services more extensively than will their non-drug abusing counterparts, including alcohol treatment and other psychiatric, medical, and social services. Hypothesis 2: Controlling for the extent and types of services used, drug abusing individuals will have worse consequences than their non-drug abusing counterparts. Service use and extent of use will be less predictive of status changes (e.g., exiting homelessness) in drug abusing homeless individuals than in the non-drug abusing homeless comparison population.

Sherwood Brown	Psychiatry	Relationship Between Depression and Bone Density in the Dallas Heart Study.	Hypothesis: Current depressive symptom severity will be inversely related to BMD Specific Aims: Primary Aim: Determine whether current depressive symptom severity is inversely related to BMD in participants in the DHS. Secondary Aims: 1) Explore racial and ethnic differences in the relationship between current depressive symptom severity and BMD. 2) Determine whether antidepressant use influences the relationship between depressive symptoms and BMD.
Xuejun Gu	Radiation Oncology	Automatic Segmentation for Brain Tumors in Stereotactic Radiosurgery Applications	Specific Aims: The goal of this project is to develop an auto-segmentation clinical tool that can help alleviate the workload of manual contouring during SRS planning, provide good base contours for physicians to refine, and reduce inter-observer contouring variability.
Kevin Albuquerque	Radiation Oncology	Hematologic Toxicity in Intact Cervical Cancer Patients who have Undergone Intensity-Modulated Radiation Therapy with and without Bone Marrow Sparing	Specific Aims Aim 1: Compare the HT occurrence rate between patients irradiated by normal-IMRT, BMS-IMRT and 3D-CRT in an indigent patient population. Aim 2: Determine the predictors of HT in cervical cancer patients receiving IMRT. Aim 3: Report outcomes of patients receiving IMRT for intact cervical cancer. Hypothesis We hypothesize that BMS-IMRT patients will have the least risk of HT while 3D-CRT patients will have the highest risk for HT, because BMS-IMRT will irradiate as little of the bone marrow as possible whereas the 3D-CRT patients will receive the greatest amount of irradiation to the pelvic bone marrow. We hypothesize that the outcome of patients receiving IMRT for intact cervical cancer will not be as favorable as those receiving 3D-CRT, because while IMRT is very effective in defining the borders of the tumor, the tumor could move during treatment, leading to ineffective irradiation of the tumor since the boundaries have changed.
Ivan Pedrosa	Radiology	Identifying histologic and genetic factors explaining correlation between magnetic resonance imaging phenotypes and papillary renal cell carcinoma prognosis	Hypothesis: Because it has been shown that imaging phenotypes are better predictors for assessing prognosis of papillary RCCs, the hypothesis under study is that there are specific MRI imaging phenotypes that correlate with specific histological findings indicative of papillary RCCs, such as the presence of infiltration of the adjacent renal parenchyma and/or perirenal fat at histopathology. A recent study has also elucidated a collection of genetic mutations that correlate with diagnosis of pRCC. Another hypothesis to be investigated in this project is whether there are specific molecular and genetic features that can be identified and correlated with the MR imaging phenotypes and their

			prognostic predictions. By identifying these histological and genetic features and explaining if they correlate with MR imaging phenotypes, we can better understand and explain why MRI phenotypes may be accurate and effective indicators of papillary RCC prognosis.
Daniel Costa	Radiology	A novel model-independent DWI interpretation method for the diagnosis of prostate cancer	Hypothesis The model-independent DWI ratio image (low b value divided by high b value) is noninferior to that of the current gold standard of ADC for diagnosis of prostate cancer. Specific Aims In order to support the use of the b-value ratio as a method for evaluation of prostate cancer, the investigation must compare the accuracy of Gleason scoring between using the b-value ratio and ADC measurement.
Ralph Mason	Radiology	Evaluating photoacoustic tomography (PAT) in breast tumor oxygenation	Hypothesis Photoacoustic tomography will reveal heterogeneity in tumor oxygenation with respect to respiratory challenges. Specific aims Assess ability of photoacoustic tomography to detect changes in breast tumor oxygenation
David Boothman	Simmons Comprehensive Cancer Center, Pharmacology, Radiation Oncology	Role of MTH1 in potentiating b-lapachone tumor selective death in pancreatic ductal adenocarcinomas	Hypothesis: We believe that inhibition of proteins participating in base excision repair (BER), specifically MTH1, will enhance b-lapachone efficacy and improve patient outcomes with pancreatic ductal adenocarcinomas by allowing us to use lower doses of b-lapachone and thereby reduce patient toxicity in the form of methemoglobinemia. This project will focus on the mechanism of action of MTH1 potentiating b-lapachone using PDA cell line cultures. Specific Aims: Inhibiting BER specific proteins, mainly MTH1, and allowing for prolonged apyrimidinic/apurinic (AP) site half-life which will further potentiate PARP1 hyperactivation and tumor cell death. Since MTH1 is involved in preventing the incorporation of DNA damaging molecules, we expect to see increased DNA damage, subsequent hyperactivation of PARP1, and eventual cell death by knocking down MTH1 activity. Specific Aim 1: To explore the in vitro effect of MTH1 inhibition on b-lapachone efficacy in PDA tumors using NQO1+ vs NQO1- MiaPaca2 cell lines. Other PDA cell lines with varied NQO1 levels will also be explored. Specific Aim 2: To elucidate the mechanism of action of MTH1 inhibition to increase the potency of b-lapachone in NQO1+ PDA cells in vitro. Aim1: MTH1 expression will be knocked down in the NQO1+ vs NQO1- MiaPaca2 pancreatic tumor cell line using three different methods: transient siRNA, stable shRNA, and MTH1 inhibitor. Knock down will then be confirmed using

			<p>Western blotting or Real-Time PCR expression analyses. Cell survival assays, including DNA and colony forming assessments will then be performed to ascertain the effects that knock down of MTH1 will have on -lapachone activity. Other PDA cells (12 total cell lines) will then be tested. I expect NQO1+, MTH1- cells will have the greatest loss of overall survival, with no alterations in cell cycle statuses as noted previously. Aim 2: Cell death potentiated by MTH1 inhibition in combination with sub-lethal doses b-lapachone should be accompanied by increased DNA damage. Using nontoxic doses of b-lapachone, I will test for expected losses in glycolysis and TCA cycle metabolism. Additionally, I will monitor for a rise in 8-oxo-dGTP incorporation, increased DNA damage (by comet and <math>\gamma</math>H2AX/53BP1 foci formation assays), and elevated levels of PAR formation.</p>
Steven Wolf	Surgery	Combination therapeutic strategy of muscle function improvement	<p>Hypothesis: A growth response in the skeletal muscle cells with functional improvement through the use of mesenchymal stem cells and UBM, characterized through systemic morphological changes including lipogenesis, fibrosis, muscle fiber structure, and angiogenesis.</p>
Patricio M. Polanco	Surgery	Failure to Rescue after Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy to Treat Peritoneal Carcinomatosis	<p>We aim to define the relationship between surgeon and hospital operative volumes of CRS/HIPEC and FTR after this procedure using the National Inpatient Sample (NIS) dataset. We also aim to identify patients' risk factors and comorbidities associated with FTR following CRS/HIPEC using the National Surgical Quality Improvement Program database (NSQIP). NIS and NSQIP are two large national datasets. We hypothesize that morbidity and mortality following CRS/HIPEC are associated with individual surgeons' and institutional patient volumes. We also hypothesize that FTR is predictable in patients presenting with specific risk factors and co-morbidities undergoing CRS/HIPEC.</p>
Steven Wolf	Surgery	The role of myokine musclin in muscle atrophy after burn	<p>The aim of the study is to investigate the role of musclin in muscle atrophy in response to severe injury. The hypothesis of the study is that musclin is necessary for muscle homeostasis, muscle atrophy following muscle atrophy is at least partly through musclin signaling. The specific aims of study are to 1) to detect musclin level in response to burn; 2) to identify the musclin in regulating mitochondrial impairment in muscle after burn; 3) to investigate the effect of muscle disuse, exercise and insulin in musclin expressions.</p>

Steven Wolf	Surgery	Cholecystitis and the Microbiome of the Gall Bladder	HYPOTHESIS: The microbiota composition in severe acute cholecystitis will be complex and the severity grades of cholecystitis will have significant differences in their microbiota profiles. SPECIFIC AIM: Determine the microbiome profile of the gall bladder in acute cholecystitis.
Steven wolf	Surgery	Changes in Weight During Acute Hospitalisation in the Severely Burned: Modern Clinical Practice and Potential Pitfalls	Our general hypothesis is that weight loss is common in the severely burned and follows a predictable pattern.
Adam Alder	Surgery	A Review of Interval Appendectomy	We aim to use a matched case-control approach to compare the clinical outcomes of patients with complicated appendicitis who were selected for first-line antibiotic versus first-line appendectomy approaches to management. We hypothesize that a first-line antibiotic approach to complicated acute appendicitis in children will not be associated with an increase in ED visits and CT scans compared to a first-line appendectomy approach.
Sergio Huerta	Surgery	Predictors of morbidity and mortality in patients undergoing cholecystectomy in veteran patients	The main goal of this study is to identify outcomes of veteran patients undergoing cholecystectomies at the VA hospital. We hypothesize that while the number of comorbid conditions in our patient population is increasing, the complication rate and mortality remains the same. Further, this analysis will allow us to identify factors that might prevent adverse outcomes in those that have them.
Steven Wolf	Surgery	Testing inflammatory cytokines and mitochondrial proteins and how they affect mitochondrial dynamics in response to burn	Hypothesis: Burn resulted muscle cell death is depend of IL-6 and TNF-alpha stimulation; intracellular pathway is associated with mitochondrial fission/fusion cycle regulated by Drp1/ Mfn1 signals. For specific aim 1, we are going to repeat burn serum stimulation of normal C2C12 muscle cells, but add an IL-6 and TNF-alpha post burn serum stimulation, so that we may observe the effects on mitochondrial morphology. In additional, we are going to test mitochondrial dynamics in primary murine myoblast. For specific aim 2, we are going to knock out Drp1 and Mfn1 in C2C12 muscle cell lines by using crispr/cas9 and lentiviral transfection in vitro.
Michael Choti	Surgery	The role of the intestinal microbiota in postoperative outcomes following pancreatic cancer surgery	In this study, we will investigate whether there is a correlation between intestinal dysbiosis and post-operative clinical symptoms after pancreatic surgery. To determine this we will use stepwise forward logistic regression analysis of clinical

			characteristics to model the independent predictors for post-operative gastrointestinal symptoms. In this study, we will also characterize the intestinal microbiota in patients that have undergone pancreaticoduodenectomy compared to patients who have undergone distal pancreatectomy.
Roshni Rao	Surgery	Evaluation of the Cedille Incision in Skin-Sparing Total Mastectomy	Purpose: To evaluate whether the Cédille incision for performance of skin sparing mastectomy provides superior results when compared to standard 'tennis racket' incisions.
Joselin Anandam Arti Barnes	Surgery and Infectious Diseases	Investigation of effectiveness of screening for anal cancer among HIV patients in the Parkland patient population	Specific Aims: The following specific aims are defined for this project 1. Estimate the current annual - screening rate achieved (via anal Pap testing) for Parkland HIV patients and determine if that screening rate varies across providers and/or across patient demographic subgroups. 2. Estimate the fraction of patients with positive anal Pap results that have appropriate and timely follow-up for diagnostic confirmation. 3. Estimate the distribution of stage at diagnosis for HIV patients screened via Pap testing and ultimately diagnosed with anal cancer, and compare that stage distribution (after demographic adjustment) to unscreened HIV patients with anal cancer diagnoses. 4. Estimate the effect of life-years of annual anal cancer screening via anal Pap testing, as compared to no anal Pap testing.
Brian Williams	Surgery, Division of Burn/Trauma/Critical Care	Posttraumatic Stress Disorder (PTSD) in the primary caregiver of critically patients in the Surgical/Trauma ICU	Individuals who witness, or learn of, traumatic events happening to a close family member or friend are also at risk of developing PTSD symptoms. This may include family members of trauma patients who are admitted to Intensive Care Units. In this prospective pilot study, we will estimate the prevalence of PTSD in the family member who is the primary caregiver of critically ill patients in the Surgical/Trauma Intensive Care Unit (SICU). This observational pilot study will determine if using a validated PTSD self-report questionnaire for the main caregiver of critically ill SICU patients is feasible and investigate whether there is a notable prevalence of PTSD within this population. With this data, we will expand our investigation to evaluate patterns of PTSD based on socioeconomic status, immigrant status, mechanism of trauma, and need for emergency surgery. The primary goal is to improve outcomes for patients and family members of critically ill patients.
Malcolm MacConmara	Surgical Transplant	'Discarded Donor Organs- Can We Do Better?'	This research project aims to examine the impact of employing surgeons dedicated only to the procurement of these organs and to see if this has led to improved utilization by transplant



			<p>programs in the area, especially at UT Southwestern Medical Center. The specific aims of the project are to: (1) identify the incidence of organ discard and the causative factors in the North Texas DSA, (2) examine the impact of an independent donor surgeon on the rate and patterns of organ discards, and (3) determine in the event of organ reallocation if the independent surgeon model has improved recipient outcomes. The goal of this research is to better understand the events and factors that lead to organs being discarded and specifically to assess if better organization within the organ sharing system might increase the number of organs used.</p>
Kemp Kernstine	Thoracic Surgery	Cost and Clinical Outcomes for Pulmonary Lobectomy: Assessing the Comparative Effectiveness for Open, Video-Assisted, and Robotic Procedures	<p>Our specific aim for this project is to provide a greater understanding of the application of these procedures to achieve optimal cost effective outcomes in pulmonary lobectomy, perhaps offering insight into the level and depth of training required to maximize proficiency. On a larger scale, this study will attempt to better inform both surgeons and institutions of the benefits of particular techniques that impact patient safety, performance, and cost-of-care.</p>
Gary Lemack	Urology	Risk Factors Predicting Complications in the Adult Spina Bifida Patient	<p>Hypothesis: We hypothesize that adult patients with spina bifida presenting with complex prior urologic history are at increased risk of complications long-term. Specific Aims: The aim of this project is to identify modifiable risk factors in this population to predict long-term complications. A secondary aim is to characterize the urologic management, quality of life (QOL) and sexual function in this population to assist in guidelines for their evaluation and management.</p>
Philippe Zimernn	Urology	Collegiality and Transparency: How to inform a colleague about a delayed complication of a mesh implanted device to correct stress urinary incontinence and/or pelvic organ prolapse?	<p>It is our belief that long-term outcome data is crucial for re-evaluation of current surgical practice and we feel surgeons with adverse events may benefit from this feedback.</p>
Philippe Zimmern	Urology	Urinary Antibiotic Concentration In Women Not Responding to Urinary Culture-Guided Antibiotic Therapy	<p>Unresolved infections could be due to a variety of factors such as: -an increase in antibiotic-resistant UPEC, -a different bacteria serotype than the one originally identified, -the development of intracellular bacterial communities (IBC) as proven in the urine sediment of women experiencing acute and recurrent UTI's, -an under-dosing of the administered antibiotic -or a treatment too short. Several mechanisms may be at play to explain this surprising and unexpected course of antibiotic non-</p>

			<p>response despite an appropriately selected urine culture-directed antibiotic selection. Among the plausible explanations for this lack of clinical effectiveness leading to an unresolved UTI is the possibility that the antibiotic dosing is insufficient, resulting in non-bactericidal urinary concentrations. It is not clear if the role of fluid intake and urine dilution could be affecting the efficacy of the antibiotic treatment at the bladder level as well. A creatinine urine value to evaluate the level of urinary concentration and urinary antibiotic concentration will be obtained on a urine sample at the completion of antibiotic treatment to verify resolution of infection and study the antibiotic concentration variability in a large cohort of older women with RUTI.</p>
Philippe Zimmermann	Urology	Bacterial and Phage Survey of Urine from Postmenopausal UTI patients	<p>Study aims/hypothesis We are interested in the following issues: Are bacteria in UTI clonal? While many UTI pathogens have been characterized heretofore, the genetic relatedness of pathogens in the same bladder is not known. If, for instance, a UTI includes multiple UPEC strains, then phage-based antibacterial interventions would need to be informed by this knowledge. Does the presence of prophage in any strain make it less susceptible to lytic bacteriophage? CRISPR and restriction systems are common in phage resistant strains. The movement of CRISPR on prophage is not known, but CRISPR elements do influence the retention of pathogenicity islands, which facilitate phage resistance. The simultaneous presence of active prophage in phage resistant strains will provide opportunities to explore mechanisms of lateral transfer of phage resistance by prophage. Do prophages have recipient strains in the same bladder isolates as their hosts? The presence of susceptible strains will facilitate characterization of prophages, but moreover it may suggest pathways of gene transmission and sharing among like/unlike species. What is the rate of spontaneous induction of urine-derived-prophage-carrier-strains? The ability of phage DNA to be mobilized through transduction is salient to the evolution of long-term and chronic infections in patients. If transduction happens in the bladder, then a resident infection may become more recalcitrant to therapy when lysogenized by a transient and less adapted pathogen that acts as a prophage donor.</p>
Gregory Modrall	Vascular Surgery	Renal atrophy and long-term survival in patients with renal artery stenosis and	<p>Hypothesis. We hypothesize that renal artery stenting is associated with less renal parenchymal atrophy, compared to</p>

		renal stenting	patients with renal artery stenosis and no stenting. We further hypothesize that there will be no difference in long-term renal function or survival between the two groups (stented versus unstented). Specific Aims. The two Specific Aims of the project are to: 1) Compare longitudinal renal volume (over time) in two groups with renal artery stenosis: stented versus unstented groups. 2) Compare changes in renal function over time and long-term survival of two groups with renal artery stenosis: stented versus unstented groups.