RUTGERS
New Jersey Medical School

OFFICE OF RESEARCH
NJMS SUMMER STUDENT RESEARCH PROGRAM
2017 REPORT OF ACCOMPLISHMENTS

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Acknowledgements

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- Dr. Robert L. Johnson, M.D., FAAP, The Sharon & Joseph L. Muscarelle Endowed Dean
- Dr. William C. Gause, Senior Associate Dean for Research
- Dr. Deborah L. Lazzarino, Assistant Dean for Research
- Mr. David Roe, CFO & Associate Dean
- RU-NJMS Alumni, RU-NJMS Faculty Organization
- New Jersey Health Foundation, Inc.

for your continuous financial support. Year after year, your financial support gives us the opportunity to assist students financially as they seek to broaden their research skills.

2017

STUDENT ABSTRACTS

REPORT OF ACCOMPLISHMENTS

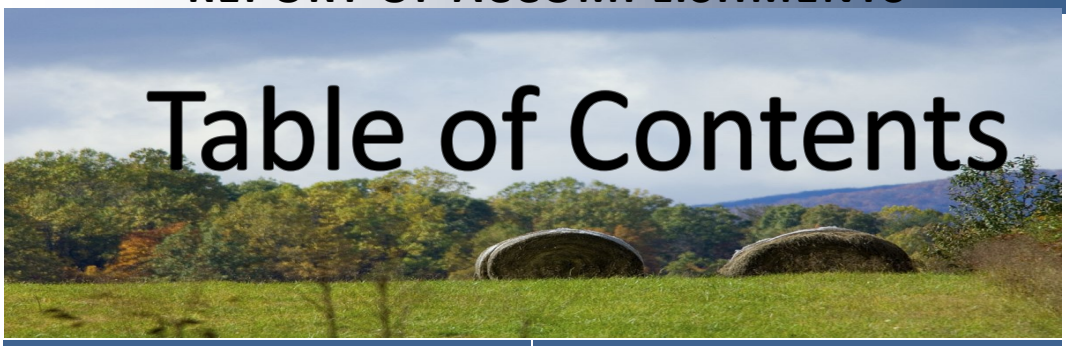

Table of Contents

PREFACE

Since 1968 the New Jersey Medical School First-Second Year Students and Volunteers have participated in this organized research program. This program gives an opportunity for students and volunteers to work alongside an NJMS Faculty Mentor on a specific research project for a period of eight weeks. Over the eight week period the participants are exposed to the dynamic nature of biomedical science. During this time they learn about the methodology and results of laboratory/clinical research; sharpen diagnostic skills, and learn the value and limits of experimental results. This program has been fortunate to have had an array of enthusiastic students seeking to broaden their research knowledge in the treatment of diseases.

This the forty-ninth edition of the Summer Student Research Program Abstracts summarizing research results generated by students, volunteers, and interns working thru this year's program. The Summer Student Research Program continues to provide a significant contribution to the training of our future clinicians and research scientists. It is the continued goal of this program to inspire the next generation of physicians and scientists.

Many thanks and much appreciation to the NJMS Faculty and Researchers who take time from their teaching and administrative responsibilities to mentor over the eight week period. We truly appreciate your continued support and exceptional commitment. It is also with pleasure that we thank the members of the faculty advisory committee for their assistance and commitment in developing the program guidelines, evaluating student abstracts, selection of student participants and participation during the poster symposium. This program could not be successful without your help! Many thanks to your for your kind consideration.

2017 SEMINAR SPEAKERS

2017 KICK-OFF TO THE SSRP SEMINAR

Topic: "360-Degree Approach to Lesions of the Skull Base: A Modernistic Journey to the Center of the Brain"

James K. Liu, MD, FACS, FAANS
Associate Professor of Neurological Surgery
Director of Skull Base and Pituitary Surgery
Co-Director, Endoscopic Skull Base Surgery Program
Director, Surgical Neuro-Oncology and Brain Tumor Center

2017 SSRP POSTER SYMPOSIUM MORNING SEMINAR	*2017 SSRP POSTER SYMPOSIUM AFTERNOON SEMINAR*
Topic: Bringing together theory and practice for right brain rehabilitation"	*Topic: "Navigating the academic research landscape as a clinician-scientist"*
Anna M. Barrett, MD *Director of Stroke Rehabilitation Research* *Kessler Foundation* *Professor, Physical Medicine & Rehabilitation* *Rutgers-New Jersey Medical School*	*Mark H. Einstein, MD, MS, FACS, FACOG* *Professor & Chair* *Department of Obstetrics, Gynecology & Women's Health* *Assistant Dean, Clinical Research Unit* *Rutgers-New Jersey Medical School*

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Mariana De Lorenzo, PhD, Assistant Professor *Department of Cell Biology & Molecular Medicine*	*Jyothi Nagajyothi, PhD, Assistant Professor* *Public Health Research Institute*
J. Christopher Fritton, MD, Assistant Professor *Department of Orthopaedics*	*Yongkyu Park, PhD, Assistant Professor* *Department of Cell Biology & Molecular Medicine*
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Charles Spillert, PhD, Associate Professor *Department of Surgery*	

INTRODUCTION

The Summer Student Research Program provides an eight-week research experience for the New Jersey first-second year medical students, as well as undergraduate students enrolled in our combined BS/M.D. seven-year program. Students are required to participate in research activities in a basic science or clinical laboratory. On many occasions this has been the students first research experience. Participation allows students, interns and volunteers to develop a close working relationship with their mentor.

After completing eight weeks of research in the respective laboratories, students present their research projects at the Summer Student Research Poster Symposium held the last week of July. At the symposium students are interviewed and required to explain the results displayed in their poster presentation. The abstracts assembled is a reflection of the commitment, dedication and enthusiasm of every student who participated in the Summer Student Research Program who presented at the 2017 Poster Symposium.

Congratulations to all the students, interns and volunteers enrolled in the 2017 Summer Student Research Program! Wishing you all the best and may you have continued success in your future endeavors!

Congratulations to Mr. Jacob Ball, MS. Pamela Jumbo-Cuevas, Ms. Chandani Patel, and Mr. Aarsh Shah, the winners of the 2017 Summer Student Research Poster Competition!

PETER ALSHARIF (NJMS 2020)

PROJECT TITLE: **LONGEVITY REGULATION BY A HISTONE DEACETYLASE, RPD3, THROUGH PROTEINS SECRETED FROM THE HEART**

MENTOR: **YONGKYU PARK, PH.D.**

DEPARTMENT: **CELL BIOLOGY AND MOLECULAR MEDICINE**

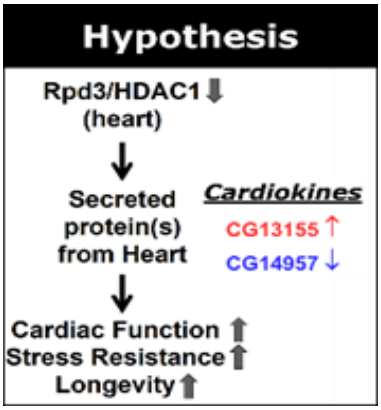
Participation Description:

During this summer project, I took on a number of tasks. These tasks included **1)** Aging fly transfers (used in longevity assays) every 3-4 days with 30-60 genotypes x 1-100 flies. **2)** Virgin fly collections for crosses and experiments (twice each day for most days, on 4-6 genotypes) **3)** RNA purification (3-4* times with multiple genotypes) **4)** cDNA preparation (5-6* times with multiple genotypes) **5)** Real-time quantitative PCR (6-7 experiments) **6)** Drosophila Stock Maintenance (4 days) **7)** Oxidation assays (3-4 experiments). **8)** Alzheimer's Disease Climbing assays (3 times, 4 genotypes each) **9)** Data Entry, analysis, and interpretation (for rtQPCR, Aging assays, oxidation assays, assisted with Climbing assays) **10)** Household tasks (Including preparing fly vials and flasks, etc). I also spent much of my time in the last 3 weeks of the project by helping teach techniques & basic science principles / provide mentoring to a younger member of the lab.

*Approximately

Objective:

Rpd3 is a histone deacetylase found in Drosophila melanogaster homologous to the mammalian Histone Deacetylase 1 (HDAC1). Previous investigations found that RNAi mediated downregulation of Rpd3 in the heart results in increased cardiac function, resistance to oxidative stress, and increased lifespan. In this project, we identify 2 possible downstream effectors of Rpd3, CG13155 and CG14957, that are regulated by Rpd3.



We hypothesize that heart-specific Rpd3/ HDAC1 downregulation enhances stress resistance and lifespan by modulation of secreted protein(s) (cardiokines) in the heart to regulate systemic longevity signaling.

Methods:

We used various assays in this project to establish the how Rpd3 can alter lifespan and downstream effectors.

Aging Assay: 200 flies from each of several genotypes were collected and placed into 10 standard cornmeal medium vials, and kept in a 25°C incubator. The surviving flies were counted, and transferred into new vials every 3-4 days.

RNA Sequencing: In order to identify genes with differential expression under heart-specific Rpd3 downregulation, we screened for levels of coding and noncoding RNAs in two controls (rpd3Ri/+ and +/tinG4,UASG4) and the heart-specific *rpd3* downregulation (rpd3Ri/tinG4, UASG4). We focus on RNAs that likely code for secreted protein.

Quantitative PCR: After converting whole body RNA to cDNA via RT-PCR, this technique is used to amplify the cDNA quantitatively, in order to identify levels of gene expression.

Genotypes Studied: +/G4, rpd3RiS/+, rpd3RiS/G4, rpd3WT/+; rpd3RiS/G4, CG14957/+, CG14957/G4, and CG14957/act -2. (G4: tinG4,UASG4)

Summary:
First, we sought to confirm if Rpd3 Downregulation leads to increased longevity. We find that heart-specific downregulation of Rpd3 leads to an increased lifespan compared to (+/G4) controls (Figure 1). This life-extending effect can be attenuated by re-introducing a wild-type *rpd3* transgene, implying that rpd3RNAi's effect on longevity is due to a specific action on Rpd3 via downregulation.

After confirming that there is an increase in longevity with Rpd3 downregulation, we sought to identify downstream effectors of Rpd3 that may mediate this effect. Using RNA sequencing, we find that Rpd3 downregulation leads to altered expression of various coding RNA's (Figure 2). We focused on genes with over a 2-fold change in gene expression under Rpd3 downregulation, both in young 1 week old flies and old 7 week old flies. Among these, we identify two genes, CG13155 and CG14957, that are upregulated and downregulated respectively in both young and old flies. Interestingly, each of these genes possess an N terminal signal sequence for secretion, likely making them extracellular signaling molecules.

We then performed real-time, quantitative PCR to clarify how Rpd3 downregulation influences the expression of these downstream genes (Figure 3). As wild type flies age, levels of CG13155 and CG14957 decrease and increase respectively. We find that heart-specific Rpd3 downregulation (rpd3Ris/G4, 7w) leads to increased expression of CG13155 and decreased expression of CG14957 in old flies. This represents a return to "younger" levels of CG13155 and CG14957 gene expression, providing a putative mechanism for longevity regulation.

Further, we found that these changes in downstream gene expression of candidate genes, under heart specific downregulation, are restricted to heart tissue (Figure 4). What's more, just as reintroducing transgenic wild-type Rpd3 in the Rpd3 downregulation background can attenuate changes in longevity (Figure 1), it also attenuates these changes in downstream gene expression (Figure 3), implying an Rpd3-specific effect of rpd3RNAi.

Finally, we sought to examine the influence of one candidate gene's effect on longevity (Figure 5). We performed a longevity assay using CG14957 downregulation, both in the heart and in the whole body. We found that Heart-specific downregulation of CG14957 (CG14957RiS/G4) leads to an extended lifespan compared to the control (CG14957RiS/+). Whole-body CG14957 downregulation (CG14957RiS/act-3) leads to no such increase in longevity, indicating a possible heart specific effect of CG14957 on longevity.

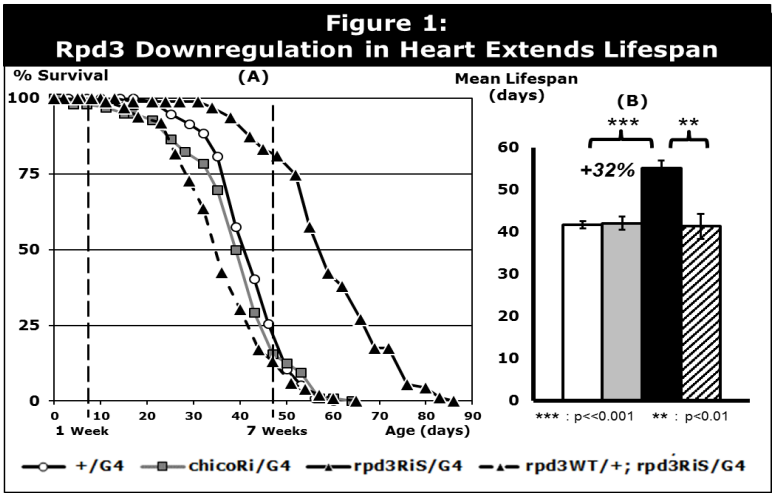


Figure 1: Longevity assay demonstrating that Heart-specific downregulation of Rpd3 leads to an increased lifespan compared to (+/G4) controls. This life-extending effect can be attenuated by re-introducing a wild-type *rpd3* transgene, indicating an Rpd3 specific effect of rpd3RiS.

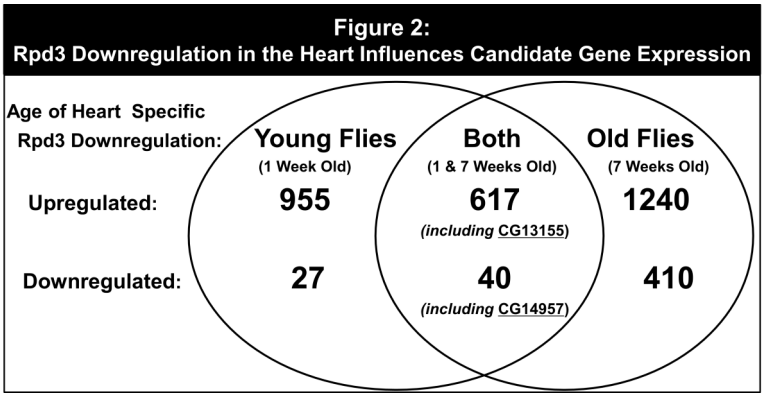


Figure 2. Venn diagram comparing RNA-sequencing results from 1 and 7-week old flies with heart specific Rpd3 downregulation. While the 1 and 7-week old flies have genes that are independently upregulated or downregulated, several genes (including CG13155 and CG14957) are upregulated and downregulated in both 1 and 7 -week old flies respectively.

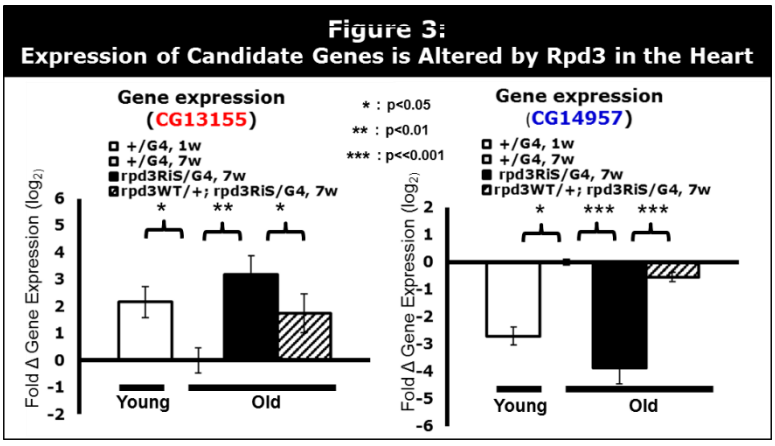


Figure 3. Heart-specific Rpd3 downregulation (rpd3Ris/G4, 7w) leads to increased expression of CG13155 and decreased expression of CG14957 in 7 week old flies, compared to the controls (+/G4, 7w). Driving transgenic wild-type Rpd3 in the Rpd3 downregulation background attenuates these changes in downstream gene expression.

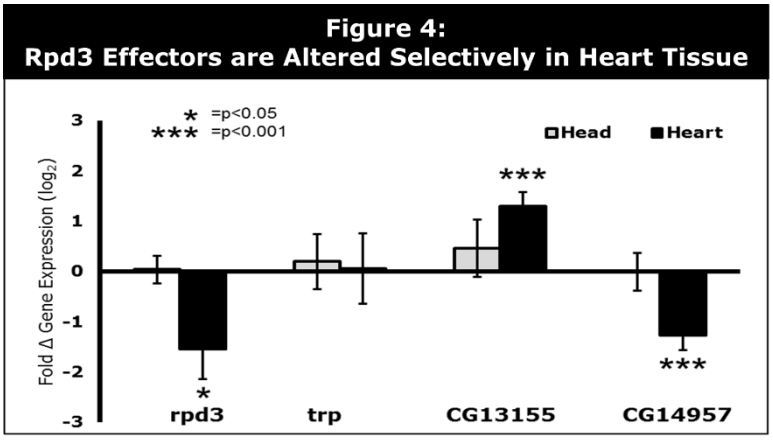


Figure 4: Heart-specific Rpd3 downregulation (rpd3Ris/G4) leads to increased expression of CG13155 and decreased expression of CG14957 in the hearts of 1 week old flies (compared to 1 week old +/G4 controls).

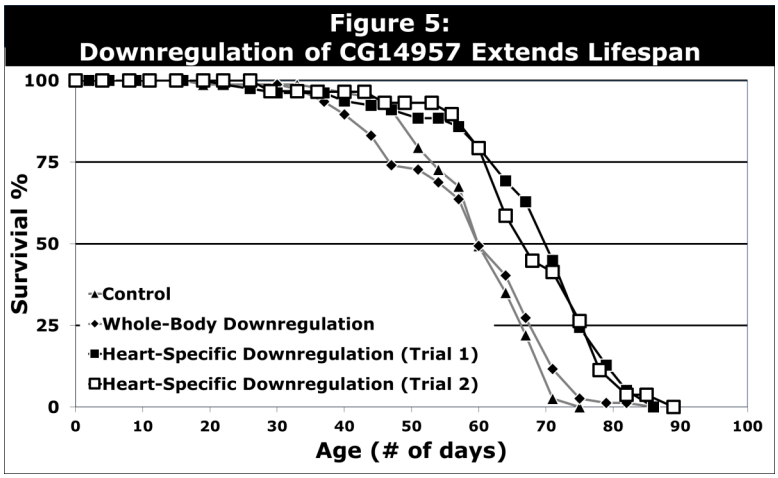


Figure 5: Heart-specific downregulation of CG14957
G4) leads to an extended lifespan compared to the control (CG14957RiS/+) and whole-body CG14957 downregulation (CG14957RiS/act-3).

Conclusion:

In this study, we investigate how Rpd3 downregulation influences the expression of downstream proteins, and the importance of these proteins in longevity. We identify two genes, CG13155 and CG14957 (Fig. 2), with altered expression in both young and old flies secondary to reduced Rpd3 in the heart. Heart-specific Rpd3 downregulation leads to increased CG13155 and decreased CG14957 expression in cardiac tissue (Figs. 3-4). Downregulation of CG14957 directly precipitates the same extended-lifespan phenotype as Rpd3 downregulated flies (Fig. 5). This supports a relationship between the Rpd3 and CG14957 in a longevity signaling pathway. Future studies will ascertain the localization (via secretion) of these downstream proteins (including CG14957), and will elucidate their roles in longevity & stress resistance.

JACOB BALL (NJMS 2020)

PROJECT TITLE: **CORTICAL BONE MECHANICAL AND MICRO-ARCHITECTURAL DIFFERENCES WITH BISPHOSPHONATE**
MENTOR: **J. CHRISTOPHER FRITTON, PH.D.**
DEPARTMENT: **ORTHOPAEDICS**

Participation Description:

For this project, I was responsible for helping to prepare histology as well as analyzing the data. Once sections were stained and cut, I would prepare sections to be mounted onto slides and then I would polish slides. I was also involved in the imaging. Additionally, I was involved in the data analysis by helping to identify microarchitecture. Additionally, I was involved with follow up studies that were using an in vivo model of microdamage

Objective:

The purpose of these studies is to test the hypotheses that (1) long-term bisphosphonate treatment alters mechanical properties of cortical bone; and (2) changes in micro-architecture are consistent with differences in mechanical properties.

Methods:

In an IACUC approved study, adult female beagles (1-2 years old) were divided into 8 equal groups and treated daily with an oral dose of vehicle (VEH, 1mL/kg saline), Alendronate (ALN, 0.1, 0.2 or 1.0 mg/kg), or Risedronate (RIS, 0.05, 0.1, or 0.5 mg/kg) for 1 year prior to sacrifice. 1-6 cortical beams were machined from each beagle rib using a precision saw (Isomet 5000) such that each beam had uniform rectangular cross section (0.5 x 1.5 mm) and length (~12 mm). A total of 250 beams were tested in a saline bath under dynamic mechanical analysis (DMA) followed by fatigue cycling until fracture or a pre-defined number of cycles (2.5×10^5). Beams were centered with the periosteal side in tension and the endosteal side in compression for 3-point bending at specific stress amplitudes (σ) by an electro-mechanical actuator (Bose Testbench). Stress (σ) and strain (ε) were calculated using beam theory. For DMA testing, a 1N load was applied sinusoidally at frequencies ranging from 1 Hz to 10 Hz. Fatigue load was applied sinusoidally at 2 HZ and a stress amplitude of 75MPa until failure. After loading, beams were stained using basic fuchsin, plastic embedded, cut and polished to constant thickness and imaged by light microscopy. Micro-structural features were outlined with interactive pen and tablet display (Wacom Cintiq 21UX) in Photoshop (Adobe) and analyzed in NIH ImageJ.

Summary:

Bisphosphonate treatment dose-dependently decreased the efficiency of energy dissipation in cortical bone. Micro-architectural differences were not observed between treatment groups.

Conclusion:

Higher doses of bisphosphonates decrease the ability of cortical bone to dissipate energy which may help to explain the development of atypical fractures. Changes in cortical bone micro-architecture were not observed in 1 year treated bone which may indicate that changes in mineralization, collagen, or advanced glycation end-products may be contributory to changes in mechanical properties.

SUBHASHINI CHANDRASEKARAN (NJMS 2020)

PROJECT TITLE: **TELEGLAUCOMA: COMPARISON OF DIAGNOSIS AND MANAGEMENT BETWEEN CLINICAL FINDINGS AND TELEPRESENCE**
MENTOR: **ALBERT KHOURI, MD, BERNARD SZIRTH, PH.D.**
DEPARTMENT: **OPTHALMOLOGY**

Participation Description:

During this research, I mainly focused on the telemedicine portion. I would recruit patients from Glaucoma Clinic. Then I would take them to the telemedicine lab and image them on the 4 machines (Auto-tonometer, Auto-refractor, Optical Coherence Tomography and Non-Mydriatic Retinal Camera). After I finish all the data and image capture, I conglomerate the data. The ophthalmologist then reviewed the information from telemedicine and came up with a diagnosis and a therapeutic recommendation. Using Pearson Correlation Coefficient, I compared the two sets of conclusions (from clinic and from telemedicine) to see if there was any association between the data.

Objective:

Telepresence allows for subjects, who normally have limited access to eye care, to get screenings. It was seen in the past that individuals would often fail to come for a full clinical examination. Telepresence allows a health care professional, with any level of experience, to capture the images. Then, remotely, a physician would get access to the screened individuals' data.

The purpose is to test the technical feasibility of developing a system for telepresence in Ophthalmology that will allow a physician to remotely access the patient's data and images. Then they would be able to compare it to traditional physical presence evaluation in glaucoma clinic. This eliminates the need for the subject to come in for an appointment. Teleprescence can be applied to Glaucoma and other vision threatening diseases.

Methods:

Seventy-five subjects, that were established patients at the University Hospital Glaucoma clinic, were enrolled on the same day into the telepresence screening program. Upon consent, the subjects went through several stations (Figure 1), which included personal/family health history, Auto-tonometer, Auto-refractor, and Optical Coherence Tomography (OCT - Optovue, Fremont, CA).

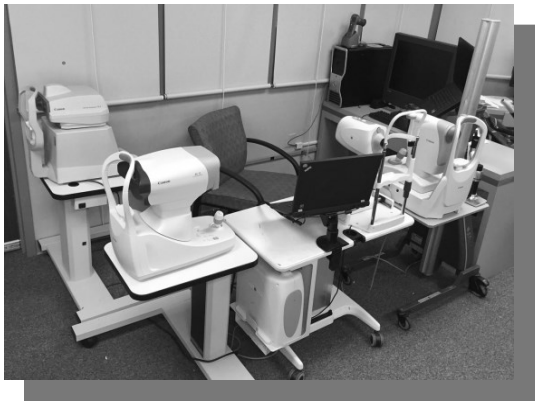


Figure 1: Application of telepresence: Various stations for imaging patients

The OCT (Figure 4) took cross section images of the subject's retina. The optic nerve head cup-to-disc ratio, corneal thickness, angles and level of ganglion cell complex were also collected in the OCT. At the last station, the Non-Mydriatic Retinal Camera (Canon CR2, Tokyo, Japan) (Figure 2 and 3) was used to take color and auto fluorescence images of the retina, and anterior segment images.

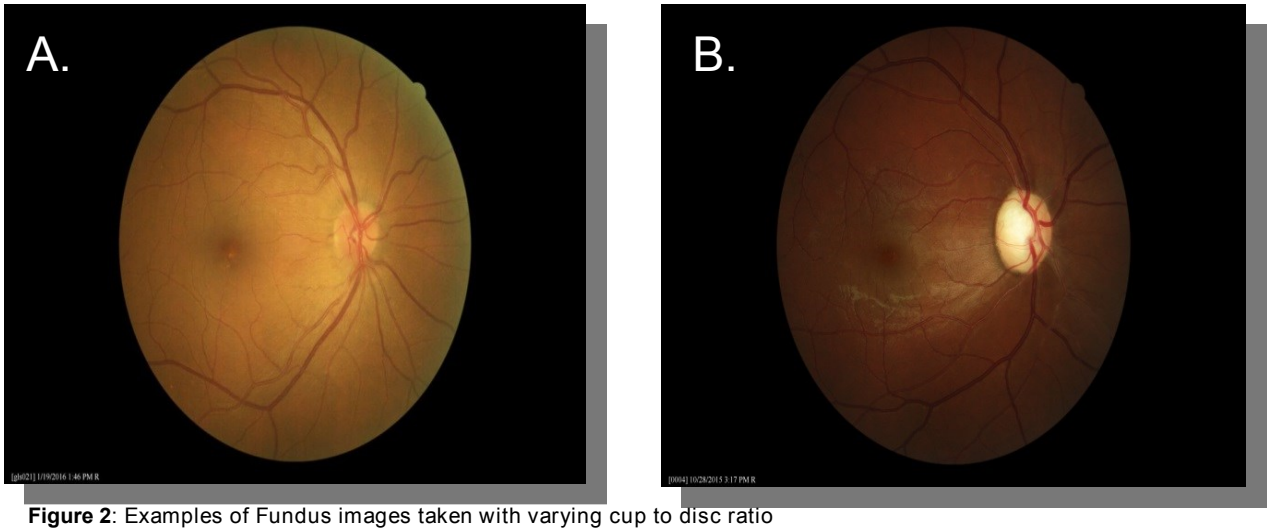


Figure 2: Examples of Fundus images taken with varying cup to disc ratio
A: Cup to disc ratio 0.1 **B**: Cup to disc ratio 0.8.
Note the nerve fiber layer drop off in image B in both superior and inferior arcades

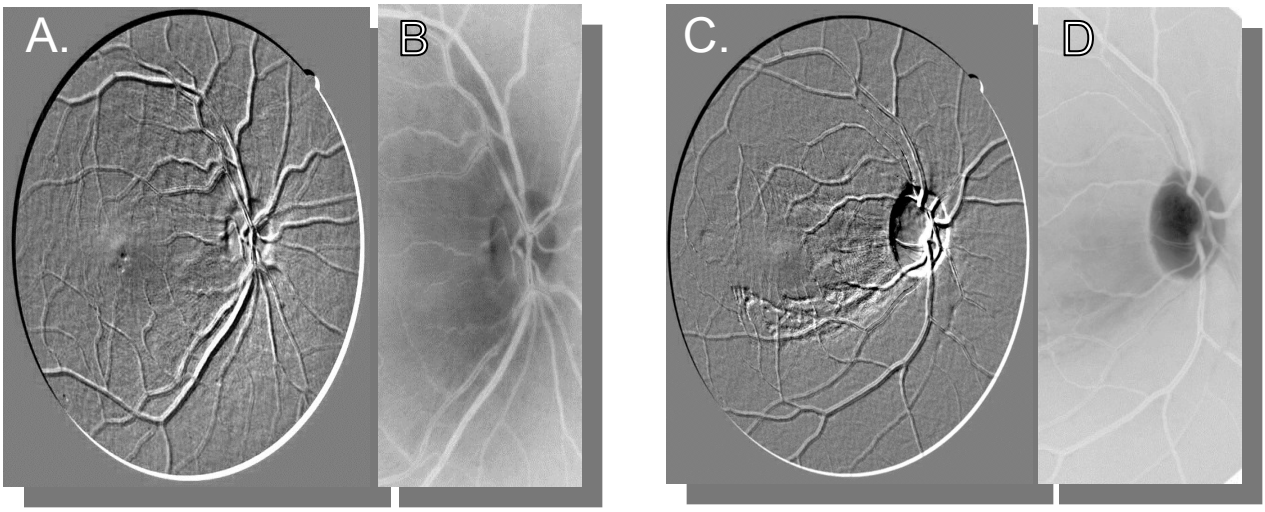


Figure 3: Post processing filters applied to retinal images.
A and **C:** Emboss filter **B** and **D:** Negative filter.
A and B shows smaller C/D ratio and no nerve fiber layer loss.
C and D have a larger C/D ratio and visible nerve fiber layer loss.

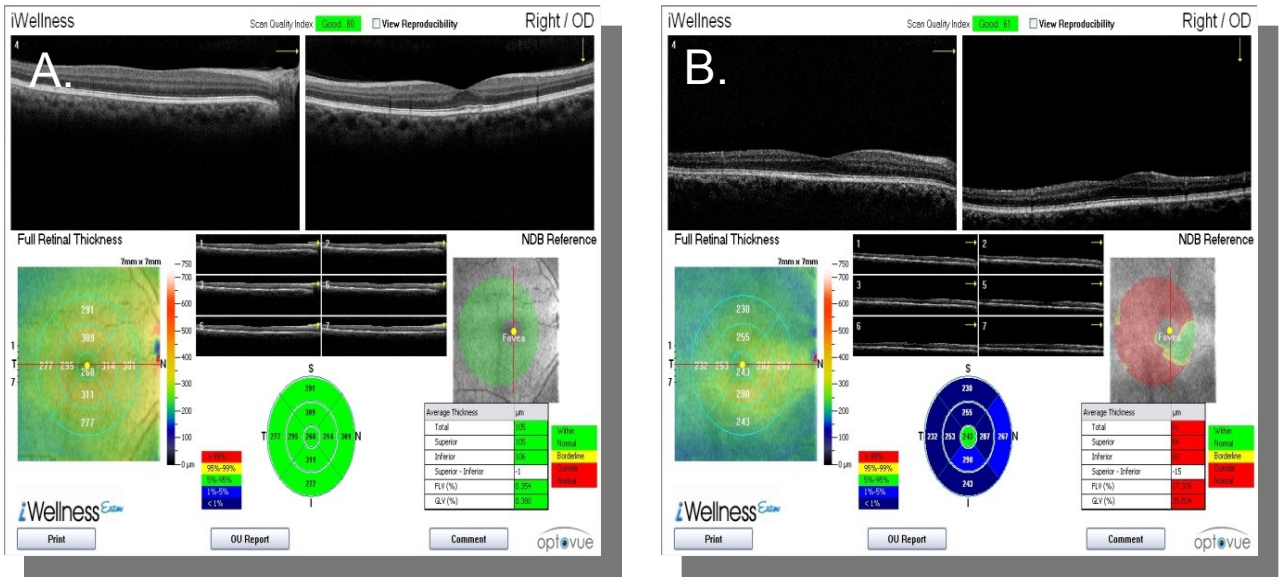


Figure 4: OCT analysis of macula and nerve fiber layer. **A:** Layers of the retina with no nerve fiber layer loss. **B**: Significant nerve fiber layer loss and ganglion cell complex loss

Figure 2 shows two examples of subjects. A has a cup to disc ratio of 0.1. B has a cup to disc ratio of 0.8. In addition, it also shows significant nerve fiber layer loss. The cup to disc ratio and retinal nerve fiber layer loss is more apparent after filters (emboss and negative filter) were applied in Figure 3. Figure 4 is the cross section view of the retina from the OCT analysis. There is

Collected data and images were analyzed by a remote physician who provided diagnostic and therapeutic recommendations. The patient was also examined in Glaucoma clinic. The data collected from telepresence and physical presence were compared (Table 1) for accuracy using Pearson Correlation coefficient. The accuracy of Glaucoma diagnosis and therapeutic recommendations were also compared (Table 2). Limitations on adequate ocular examination or imaging during telepresence were recorded.

Summary:

Seventy–five subjects underwent imaging (mean age of 61 +/- 15 years, 59% females, 52% African American, 38% Hispanic, 6% Indian, and 4% Caucasian). A strong positive Pearson Correlation was seen for intraocular pressure (IOP) of right eye (OD), left eye (OS) (0.78, 0.89), optic nerve cup-to-disc (C/D) ratio OD, OS (0.73, 0.74) and diagnosis (no glaucoma, glaucoma suspect, glaucoma) (0.81). There was a moderate positive Pearson Correlation for treatment plan/return to clinic (RTC) (0.56) with an average shorter RTC in telepresence.

A significant difference was found in providing C/D ratio (higher in clinical exam $p = 0.019$). Telepresence enabled OCT analysis when retinal imaging was precluded by media opacities in 25 patients (29 eyes) and was more likely to elicit a diagnosis not found in the clinic (13 times vs 2 times). However, telepresence was not able to pick up Trabeculectomies and Peripheral Iridectomies as well as clinic exam.

Conclusion:

Telepresence rectifies the issue of individuals having limited access to eye care. With telepresence, the patients can have their ocular data and images analyzed by a trained ophthalmologist remotely. In addition, telepresence can be further used for screening of other vision threatening diseases, such as Age Related Macular Degeneration and Diabetic Retinopathy. It is vital for screening because half of the population with vision threatening diseases is not aware of their condition.

Intraocular Pressure, C/D ratio and diagnosis via telepresence and clinical examination were strongly correlated using Pearson correlation coefficient.

Optical Coherence Tomography provided useful data when retinal imaging was not possible and it was superior in finding diagnosis not seen during clinical evaluation.

Glaucoma diagnosis and treatment plan were feasible through telepresence. Further studies need to be done.

NEIL CHEN AND CARLY RAY (NJMS 2020)

PROJECT TITLE: **PRESENCE OF GASTROINTESTINAL DISORDER IN A COHORT OF ADHD**
MENTOR: **MING XU, PH.D.**
DEPARTMENT: **NEUROLOGY**

Participation Description:

This project was ongoing at the time SSRP began. I coordinated with Carly Ray and Dr. Ming on the gathering of data through interviews with parents and their children. We interviewed patients individually as well as alongside Dr. Ming, totally approximately 40 of the 139 patients in the study. We reviewed all charts to verify diagnosis and medications.

Objective:

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental and neurobehavioral disorder characterized by hyperactivity/impulsivity and or inattentiveness. Despite being one of the most prevalent developmental conditions, affecting approximately 11% of US children ages 4-17, the etiology of the disease remains unclear. Recently, it has been hypothesized that perturbations in host gut microbiome may be a contributing factor to the symptoms of this disorder.

The gut microbiome, consisting of several trillion commensal microbes, plays an active role in maintaining health throughout life, as it continuously "converses" with the central nervous system through hormonal, immune, and neuronal pathways - a system known as the gut-brain axis. These pathways, established through microbiota metabolites, are important to the development of the central nervous system. Consequently, dysbiosis or imbalance of the microbiota may have a negative effect on the most critical moments of cerebral development. Environmental factors which can lead to dysbiosis - maternal diet and infection, maternal and infant stress, and antibiotic use - have been implicated in increased risk of ADHD expression.

The Gastrointestinal Disorder Index (GDI) is a rating tool for quantifying the signs and symptoms of gastrointestinal disturbances. Based off of the Truelove and Witts Severity Index, it contains nine variables related to GI symptoms including constipation, diarrhea, average stool consistency, stool smell, flatulence, abdominal pain, unexplained daytime irritability, night time awakening, and abdominal tenderness. It was used by Schneider et al. to evaluate, in a cohort of children with ASD, the changes in GI disturbances after oral human immunoglobin treatment. Adams et al. used a shortened version of the scale to investigate the severity of GI disturbances in children with autism. In this prospective study, we compared the G.I Severity Disorder Index results of ADHD with controls to ascertain the severity of GI symptoms. We investigated if there were any correlation between GI symptoms and ADHD.

Methods:

Patients were recruited from University Hospital pediatrics and neurology clinics. A total of 68 outpatients with ADHD (51 boys and 17 girls, ages 2-18) and 71 healthy controls (32 boys and 29 girls, ages 2-18) were evaluated with the GDI. ADHD subjects that were recruited were receiving care from University Hospital pediatric neurologists and were diagnosed based on DSM-IV-TR or DSM-V criteria. ADHD subjects were screened for learning disabilities or other neurodevelopmental disorders prior to enrollment. Control subjects were recruited during their wellness visits and were screened for medical and developmental disorders prior to enrollment. Informed consent was obtained from parents/guardians according to the protocol approved by the Institutional Review Board of Rutgers University New Jersey Medical School.

Parents noted whether their children on a 3-part answer scale ranging from 0 for “none/normal” to 2 for “severe/significant” in 6 items regarding constipation, diarrhea, average stool consistency, stool smell, flatulence, and abdominal pain. Demographics (age, sex, BMI) and medication use was collected for all patients.

Summary:
The age and gender, ethnicity of ADHD and controls were comparable. Efforts were made to match the gender and age. Like other ADHD studies, our study included a greater proportion of males consistent with increased male prevalence in ADHD. (Table 1)

	ADHD	Control
Male	51	32
Female	17	39
Mean Age (std)	10.3 (2.97)	9.7 (3.24)
Mean BMI (std)	20.3153 (4.99)	20.3865 (5.27)

Table 1

There was no correlation between total GDI scores with sex, age, and BMI in either groups, with the exception of a weak correlation of total GI scores with sex in the ADHD group (r= .271, p=0.026). In looking at the sub-indexes, the female sex significantly correlated with constipation (r = .320, p=0.008) and abdominal pain (r=.373, p=0.002). No sub-indexes scores were correlated to the male sex.

We found that the mean total GDI (0.38) in patients with ADHD (1.13) was significantly higher than in controls (p=0.001). (G

When specific symptoms of GDI questionnaire was examined, constipation, flatulence, and abdominal pain were found to be significantly different between ADHD and control based on continuity corrected chi square analyses.

No relationship between medication and total GDI scores or demographics was found.

Conclusion:

In this study, we show an association of ADHD with increased GI symptoms; we find that children with ADHD are more likely to present with constipation, flatulence, and abdominal pain. Medical therapy for ADHD did not seem to have an impact on any of the markers of GI disorder.

DANIEL COBAN(NJMS 2020)

PROJECT TITLE: **EFFECTS OF LOCAL VANADIUM ON OSTEOPOROTIC BONE HEALING IN DIABETIC RATS**
MENTOR: **SHELDON LIN, MD**
DEPARTMENT: **ORTHOPAEDICS**

Participation Description:

I am a first-year medical student who has spent the previous year conducting research with Doctor Sheldon Lin in his proof-of-concept lab at Rutgers New Jersey Medical School. Doctor Lin is Chief of Foot Ankle Division and Associate Professor of the Department of Orthopaedics at Rutgers-NJMS. Our interests have focused on the role of insulin and insulin- mimetic agents upon bone healing. My contributions to the team have included maintaining the blood glucose levels of diabetic rats, performing surgical experiments , and assisting with histological staining of bone samples. My experience working in the laboratory has afforded me the opportunity to develop both practical skills in basic science research and a more intimate appreciation for investigating meaningful hypotheses.

Objective:

The objective of this study was to examine the effects of locally delivered Vanadylacet lacetonate (VAC) on bone growth and stability in a B.B. Wistar T1OM-related osteoporoticrat model.

Methods:

A surgical procedure was performed in which experimental groups received a 1.5 mg/kg VAC solution and control groups received a 0.1 ml saline solution injected into the intramedullary canal of each rat's right femur. Animals were sacrificed 8 weeks post-surgery. Age at surgery, percent weight change, and systemic blood glucose measurements were similar between all groups in this study. Micro-computed tomography (Micro-CT) conducted using SkyscanTM software was utilized for a quantitative assessment of percent cortical bone volume (BV/TV) and percent cortical porosity 8 weeks post-surgery.

Summary: VAC-treated femora demonstrated an 11.3% decrease in percent cortical porosity and a 2.4% increase in percent cortical bone volume, relative to controls.

Percent Cortical Bone Volume (BV/TV), Percent Cortical Porosity (Table 1)

Table 1. Micro-CT Analysis at 8 weeks Post-Surgery

	Percent Cortical Porosity	Percent Cortical Bone Volume
Saline Control (n=6)	**1.0399 ± 0.0599**	**0.9912 ± 0.0140**
1.5 mg/kg VAC (n=8)	**0.9342 ± o.0121a**	**1.0151 ± 0.0158 b**

a $p < 0.05$ vs. control

b $p < 0.05$ vs. control

Conclusion:

In conclusion, VAC has potential as a local adjunct treatment for diabetes induced osteoporosis pending appropriate FDA preclinical and clinical trials. Future VAC studiesshould include other experimental models such as post-ovariectomized osteoporotic female

MARK DANILA AND LINDSEY HERNANDEZ (RUTGERS UNIVERSITY 2018, 2019)

PROJECT TITLE: **THE IMPACT OF A NEW BMP2 REGULATORY ALLELE ON BONE CALCIFICATION**
MENTOR: **MELISSA ROGERS, PH.D.**
DEPARTMENT: **MICROBIOLOGY, BIOCHEMISTRY, AND MOLECULAR BIOLOGY**

Participation Description:

This project involves analyzing the impact of a new *Bmp2* regulatory allele on bone calcification via Micro Computed Tomography (MicroCT). The *Bmp2* allele of interest consists of the deletion of an Ultra Conserved Sequence (UCS) that is involved in repressing pathological calcification.

The allele removes the UCS from the 3'UTR on the BMP2 mRNA transcript. MicroCT allows for quantifying the amount of calcification present on bones with both a *Bmp2* genotype (*Bmp2+/+, Bmp2+/ΔUCS, or Bmp2ΔUCS/ΔUCS*), and a Klotho genotype (*Klotho+/+,* or *Klothokl/kl).* Bruker Skyscan 1172 CT Scanner is used for physical image acquisition. Bruker Microphotonics software, CTAn, is an analytical program that allows for image acquisition, reconstruction, and segmentation of the right femur samples. Our responsibility involves developing a task-list in the

CtAn program that comparatively quantifies the calcified densities of each femur. Furthermore, we were responsible for determining the region of interests, pixel sizes, and reconstructive properties. Bone parameters analyzed include: Bone-Volume-to-Tissue-Volume (BV/TV) ratios, Bone/Tissue Mineral Densities (BMD/TMD), and Bone Thicknesses. We hypothesize that *Bmp2* genotype alters bone quality in both healthy mice (*Klotho+/+*) and osteoporotic mice (*Klothokl/kl*).

Objective:

Bone Morphogenetic Protein Signaling in Bone Homeostasis

Bone morphogenetic protein 2 (BMP2, HGNC:1069, GeneID: 650) is a classical morphogen; a molecule that acts at a distance and whose concentration influences cell proliferation, differentiation, and apoptosis. The concentration of BMP2 influences myogenesis, adipogenesis, chondrogenesis, and osteogenesis. BMP signaling and BMP2 is a potent inducer of bone formation that coordinates anabolic and catabolic processes affecting the differentiation and activity of osteoblasts and osteoclasts. Indeed, BMP2 is indispensable for fracture healing. Reduced or absent levels of BMP2 concentration and regulation decrease bone mass and promote fractures similar to osteoporosis.

A New Allele to Test the Influence of BMP2 in Bones

Because the amount, timing, and location of BMP2 synthesis influence pattern formation and organogenesis, the mechanisms that regulate *Bmp2* are crucial. An ultra-conserved sequence (UCS) in the 3' UTR of the BMP2 mRNA mediates post-transcriptional repression. We used homologous recombination and conditional deletion to generate a new allele in which the UCS was deleted from the *Bmp2* 3'UTR *(Bmp2ΔUCS*). Deletion of the UCS was associated withelevated BMP signaling, reduced fitness, and embryonic malformations.

Hypothesis: Elevated BMP signaling associated with deletion of the UCS would alter bone morphology and quality

Aim 1: to compare the morphometric and density parameters of femurs in healthy adult mice with the wildtype *Bmp2* allele *(Bmp2+/+*) or heterozygotes *(Bmp2ΔUCS/+*) or homozygotes *(Bmp2ΔUCS/ ΔUCS*) bearing the UCS deletion allele.

Aim 2: to compare the morphometric and density parameters of femurs in mice with these Bmp2 genotypes that also have a premature aging syndrome associated with reduced bone mineralization (Klotho homozygotes, Klothokl/kl).

Analyzing the Bone and Tissue Mineral Densities via MicroCT

Bruker Skyscan 1172 MicroCT was used to examine morphometric and density measurements within the right femurs of mice ranging from age 47 to 52 days. CTAn is an analytical program that segments trabecular and cortical regions.

Methods:

Necropsy and Excision of Right Femur

The right femur of each sample was extracted and put in 70% ethanol for storage. The left femur is preserved for future studies.

MicroCT Scanning

Each femur scanned was placed into saline solution for approximately 15 minutes before scanning. Once saturated with saline, three femurs were grouped together and scanned in one sitting. Approximately 2000 images were taken along the length of each femur.

Image 3D Reconstruction

The 2D images was reconstructed into 3D images of each femur with Bruker Microphotonics CTAn software. The 2D images displayed a photo of the outer segment. Those 2D images were then reconstructed into cross-sectional images of the femur in the segment being scanned.

Bone Segmentation

Trabecular and cortical segments were separated. The trabecular region was defined at epiphyseal plate. The cortical segment is defined at the mid-region of the bone. The amount of images for trabecular analysis was controlled at 200 images each. The cortical analysis was controlled at 100 images each. The trabecular region was defined by starting analysis 50 images below the epiphyseal plate. The selection of the trabecular region of interests (ROI) varied due to the varying lengths of the bones. Figure 1a, 1b, and 1c all show examples cross- sectional perspectives of the trabecular and cortical segmentation.

Image Data Analysis

Relative bone densities, thicknesses, and bone-volume (BV) to tissue-volume (TV) ratios were calculated using Bruker's Microphotonics CTAn software. Bone mineral density (BMD) signifies trabecular density. Tissue mineral density (TMD) signifies cortical density.

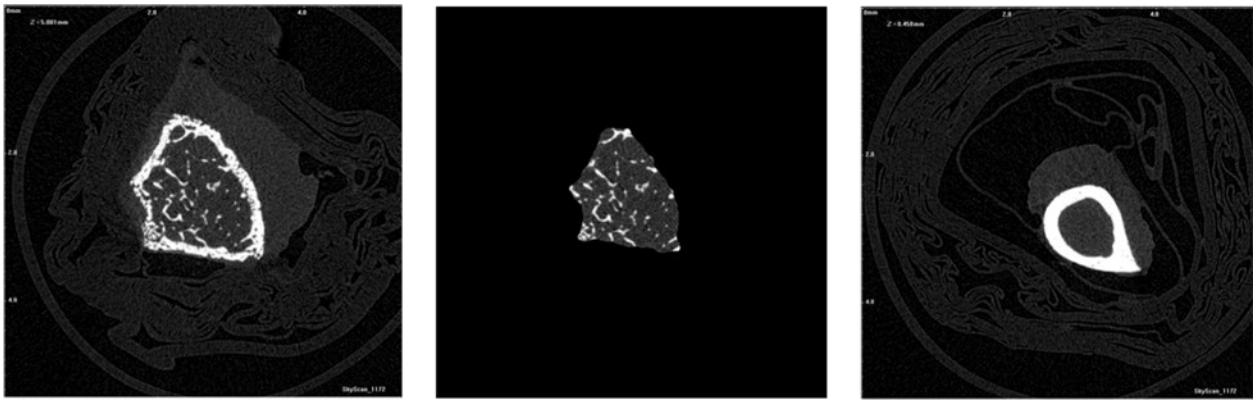


Figure 1a-c: Cross-sectional images of trabecular and cortical segments from a mouse with 2 wildtype Bmp2 alleles (Bmp2+/+) and 2 Klotho mutant alleles (Klothokl/kl). (1a; left) Shows the epiphysis end of the femur where the trabecular segment is defined. (1b; middle) Shows

trabecular region separated from the cortical segment. (1c; right) Shows metaphysis region of the femur where the cortical segment is defined.

Summary of Results:

Legend:

Wt K+ = *Bmp2*$^{+/+}$, *Klotho*$^{+/kl}$

+S K+ = *Bmp2* $^{+/\Delta UCS}$, *Klotho*$^{+/kl}$

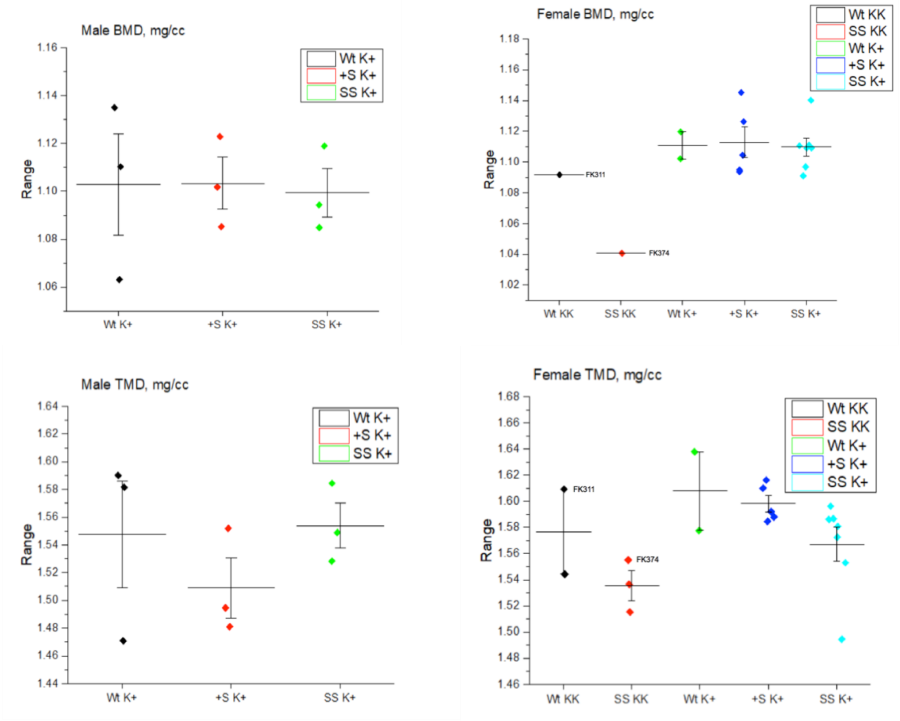


Figure 2a-d: Dot graphs of trabecular bone mineral density (BMD) and cortical tissue mineral density (TMD) values that display the range/spread, means, and standard errors of the mean. The TMD values are higher in females than males (P value = 0.012). The mean TMD for females and males were homozygous for the *Klotho* alleles (*Bmp2*$^{\Delta UCS/\Delta UCS}$).

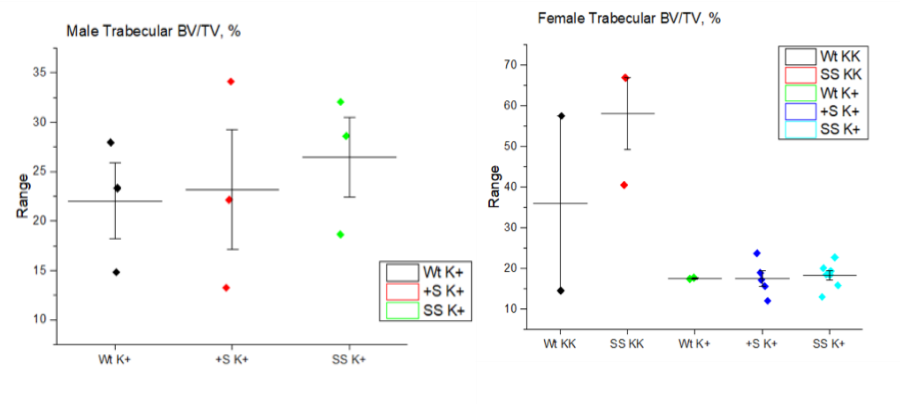


Figure 3a-b: Dot graphs of the trabecular bone - volume-to-tissue-volume ratios (BV/TV,%) that display the

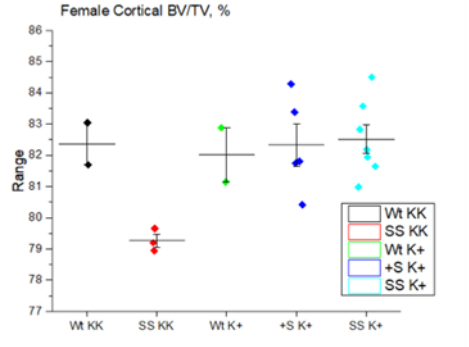


Figure 4: Dot graphs of the cortical bone-volume-to- tissue-volume ratios (BV/TV,%) that display the range/spread, means, and standard

Results and Conclusion:

***Bmp2* Genotype May Alter Bone Quality in Healthy Mice (*Klotho+/kl*)**

Bmp2 genotype did not significantly affect BMD in either sex or TMD in males. Females with 1 or 2 wildtype *Bmp2* alleles (*Bmp2+/+*) tended to have higher TMD relative to mice with the UCS deletion. The mean TMD for *Bmp2+/+, Bmp2+/ΔUCS, and Bmp2ΔUCS/ΔUCS* females respectively were

1.61 mg/cc (n=2), 1.60 mm/cc (n=5), and 1.57 mg/cc (n=7) as shown in Figures 2a-d. Loss of UCS -mediated repression may reduce cortical bone mineralization in female mice, but not male mice.

The *Bmp2* genotype did not obviously affect the trabecular BV/TV% for both males and females heterozygous for the Klotho allele. The male trabecular BV/TV% means for *Bmp2+/+, Bmp2+/ΔUCS, and Bmp2ΔUCS/ΔUCS* genotypes respectively were 22.03 (n=3), 23.17 (n=3), and

26.42 (n=3). The female trabecular BV/TV% means respectively were 17.50 (n=2), 17.45 (n=5), and 18.21 (n=7) as shown in Figures 3a-b.

This data was from young outbred mice in a mixed background. Additional measurements from older mice in other backgrounds are being analyzed.

***Bmp2* Genotype May Alter Bone in Osteoporotic Mice (*KlothoKl/kl*)**

In female mice homozygous for the premature aging *Klotho* mutation (*Klothokl/kl*), mice homozygous for the wildtype *Bmp2* allele (*Bmp2+/+*) had slightly greater TMD relative to mice homozygous for the UCS deletion (*Bmp2ΔUCS/ΔUCS*). The means were 1.577 mg/cc (n=2) and

1.536 mg/cc (n=3), which were not significantly different as shown in Figure 2d.

The cortical BV/TV% means for female *Bmp2+/+* mice and *Bmp2ΔUCS/ΔUCS* mice were 82.37 (n=2) and 79.27 (n=3), respectively as shown in Figure 4. This reduction was statistically significant (P value = 0.012). The reduced mineralization and percentage of trabecular space occupied by bone support the hypothesis that UCS deletion alters bones in osteoporotic mice.

Conclusion:

The data supports the hypothesis that elevated BMP signaling associated with deletion of the UCS would alter bone morphology and quality. It suggests that the *Bmp2* genotype influencing the deletion of the UCS region plays a role in regulating calcification. Specifically, the significant reduction of cortical BV/TV % in females suggests that *Bmp2* genotype may alter bone in osteoporotic mice. Furthermore, there is a trend toward increasing trabecular BV/TV % in male mice. However, the data is not statistically significant.

The variability of the trabecular parameters (BV/TV% and Trabecular Number) between all genotypes were very high for both males and females, which ultimately prevented obtaining significant data. We can repeat the study using the contra-lateral femur. The variability in the pooled data may be due to the variability in strain background and mouse age. Some mice were inbred strain 129 (PCBF) and some were outbred mixtures of 129 and C57Bl/6 (NS) or 129, C57Bl/6, and C3H (FK). Furthermore, selection of the trabecular ROI was partially subjective. Because of the varying bone lengths, we had to make the decision on where to start based on the location and size epiphyseal plate. For example, some ROIs started from 50 images below the epiphyseal plate and others were toward 80 slices. To account for this, we can stratify the data by age and strain and increase the sample size for each genotype.

MATTHEW DELBERT (NJMS 2020)

PROJECT TITLE: **REDEFINING AUTISM UNDER DSM-5 WHO IS BEING MISSED?**
MENTOR: **WATLER ZAHORONDNY, PH.D., JOSEPHINE SHENOUDA, MS**
DEPARTMENT: **PEDIATRICS**

Participation:

My roles in this project were as follows:

Deciding which characteristics of children to analyze, to see if there was a correlation between these characteristics and a missed ASD diagnosis under DSM-5. The variables I chose to examine were sex, race/ethnicity, IQ, level of impairment, age at first Autism evaluation, and total number of evaluations

Completing chi square tests for the analysis, and utilizing logistic regression to adjust for multiple variables.

Interpreting the significance of the data, following analysis of the variables listed above.

Putting everything together into an abstract, and using the abstract as a template to construct the poster using Powerpoint.

*I completed all sections of the poster under the guidance of Walter Zahorodny, PHD, and Josephine Shenoda, MS.

Background:

The prevalence of Autism Spectrum Disorder (ASD) has been rising steadily since the mid-1990's [1, 2]. The most recent edition of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-5), released in 2013, posed a significant revision of the long-utilized definition of Autism represented by DSM-IV-TR[3, 4]. Concerns have been raised that the shift in definition will lead to lower rates of identification and lower levels of care and service to affected individuals. By many considerations, a proportion of individuals who met the diagnostic definition of ASD under DSM-IV-TR criteria may not satisfy the narrower DSM-5 criteria (2, 3). At present, it is not well understood which characteristics are driving a proportion of children to miss the DSM-5 criteria, despite being confirmed under DSM-IV-TR.

Objectives:

To identify the proportion of children with confirmed ASD under the DSM-IV-TR case definition who were disconfirmed under DSM-5, and to describe their basic demographic and functional characteristics. We also analyzed various variables to elucidate their impact on ASD confirmation using the DSM-5 case definition. We hypothesized that there would be no difference in the DSM-5 confirmation rate based on sex or race/ethnicity, and that ASD children with average or above average IQ and those with mild impairments due to ASD would be more likely to be disconfirmed under DSM-5 criteria. Similarly, since more severely impaired children come to attention earlier than others, we hypothesized that children receiving their first evaluation at a later age and those who had fewer professional evaluations, would be disproportionately disconfirmed under DSM-5 criteria

Methods:

Data were collected as part of the New Jersey Autism Study (NJAS), a population-based ASD surveillance investigation carried out in a 4-county metro region. Ascertainment was by an active, multiple-source, Centers for Disease Control and Prevention (CDC)-designed method based on broad review and comprehensive expert analysis of information contained in health and education records. Eligible children were born in 2006 and resided in the study region in 2014. ASD case-determination and detailed scoring was by experienced pediatric development experts following standardized and operationalized DSM-IV-TR and DSM-5-based diagnostic criteria. Data on sex, race, and ethnicity were from the source records and clarified from birth certificates as needed. Cognitive functioning (defined by IQ scores), age of first evaluation, ASD-type and other variables were from the individual case file. Level of impairment due to ASD was rated: Mild, Moderate, and Severe, according to overall assessment by the experts. For this report, statistical analysis was performed using chi-square tests, and logistic regression using IBM SPSS Statistics 24.

Summary:

NJAS surveillance identified 964 eight-year old children with ASD in the study region. Of those, 842 children (87.3%) were confirmed under both DSM-IV-TR and DSM-5 diagnostic criteria and 122 children (12.7%) were disconfirmed under DSM-5 criteria. While there was no significant race or ethnicity-based difference in the likelihood of being disconfirmed under DSM-5, girls with ASD were more likely to be disconfirmed (under DSM-5 criteria) than boys ($p<.014$). Contrary to expectation, higher cognitive functioning was not associated with DSM-5 disconfirmation. Overall, as predicted, most of the subjects failing to satisfy DSM-5 criteria had Mild levels of impairment due to ASD. Interestingly, almost a third (32%) of all disconfirmed under DSM-5 cases showed Moderate or Severe levels of impairment. Adjusting for race/ethnicity and degree of impairment, boys were more likely than girls to be confirmed for ASD under DSM-5 criteria (OR=1.755, 95% CI: 1.126-2.736). Disconfirmed ASD children were also approximately 10 months older at the time of their first professional evaluation than children satisfying both DSM-IV-TR and DSM-5 diagnostic criteria and received fewer professional evaluations by age 8, consistent with less severe impairment.

Conclusion:

This study is the first to report a complete population cohort of surveillance-determined ASD cases according to DSM-IV-TR and DSM-5 criteria in NJ. In our population, 12.7% of ASD cases confirmed under DSM-IV-TR diagnostic criteria did not satisfy the DSM-5 definition of ASD. Previous studies and models have proposed that 19-38% of individuals satisfying DSM-IV-TR criteria may be disconfirmed under the DSM-5 definition[1, 5]. The shift from DSM-IV-TR to DSM-5 ASD diagnostic criteria had a significant impact, but not as dramatic as feared.

Our findings indicate that girls with ASD are more likely to be DSM-5-disconfirmed than boys.

As expected, most of the children disconfirmed under DSM-5 had Mild impairment due to ASD, supporting the claim by some experts that DSM-5 requires more significant symptomatology[1]. Surprisingly, 32% of cases disconfirmed under DSM-5 were moderately or severely impaired by ASD.

Further research is needed to understand the impact of the change in DSM criteria on ASD diagnosis.

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6. http://libguides.brooklyn.cuny.edu/asd/diagnostic_frameworks

JOSEPH DORAN (NJMS 2020)

PROJECT TITLE: **PREVENTION OF RECOMBINANT HUMAN BONE MORPHOGENETIC PROTEIN-2 EXTRUSION RELATED COMPLICATIONS IN LUMBAR INTERBODY FUSION**
MENTOR: **ANTONIOS MAMMIS, MD**
DEPARTMENT: **NEUROLOGICAL SURGERY**

Participation:

My participation in the project started by taking over the project from one of the residents who had already written and submitted a manuscript approximately one year earlier. The manuscript was rejected with revisions, and I was in charge of redesigning the project in accord with the editor feedback. I worked with the PI to plan out the new direction of the study, and I was responsible for gathering patient data so that our sample size was nearly twice as large. Gathering data involved chart reviews, phone calls to patients, and following up with patients in the office. I then took the new data, combined it with the old to generate the new results, and then rewrote the manuscript to reflect the new design of the study and our results. After submitting a draft of the manuscript to Dr. Mammis for final feedback, I identified journals that would be the best fit and proceeded to submit it for publication.

Background:

Recombinant human bone morphogenetic protein-2 (rhBMP-2) is a widely used bone graft substitute in spinal fusion procedures. When initially approved by the Food and Drug Administration, clinical studies demonstrated its safety and efficacy. Recently, numerous studies have reported the complication rates of rhBMP-2 use to be higher than the initial reports. Heterotopic and ectopic bone formation and radiculopathy due to nerve tissue compression or irritation have been reported in lumbar spinal fusion procedures utilizing rhBMP-2, possibly due to rhBMP-2 product extrusion from the interbody cage during cage placement or from BMP-2 dissemination away from the surgical site.

Objective:

Discuss the potential mechanisms of complications related to rhBMP-2 dissemination or sponge extrusion, present a technique to prevent rhBMP-2 sponge extrusion and dissemination during interbody cage placement, and compare outcomes and complication rates using our technique with the standard methods of rhBMP-2 use in spinal fusion.

Methods:

A PEEK cage is packed with a rhBMP-2 soaked absorbable collagen sponge. We then plug the rhBMP-2 sponge within the cage using Actifuse Shape, a moldable bone graft substitute. This technique has been employed in spinal lumbar fusion procedures for 26 patients, all undergoing ALIF. All patients were routinely followed in the outpatient setting and assessed for >50% pain relief, radiographic fusion, graph subsidence or migration, and any additional complications.

Results:

We have not encountered any cases of gross rhBMP-2 sponge extrusion during interbody cage placement. Greater than 50% pain relief was reported in 96% of patients and radiographic fusion was found in 100% of patients. There were two adverse events reported, giving an overall complication rate of 7.69%. The rate of rhBMP-2 associated complications was 3.85%, lower than the average complication rates associated with rhBMP-2 use in ALIF, which are estimated to range from 10% to over 40%.

Conclusions:

The described technique firmly secures a rhBMP-2 sponge within a lumbar interbody cage thus preventing extrusion during cage placement and blocking BMP-2 from dissolving out of the cage and disseminating to local structures. By ensuring adequate containment of rhBMP-2, the described technique reduces the complications associated with local rhBMP-2 spread. In addition, Actifuse works synergistically with rhBMP-2 to achieve fusion, potentially leading to improved outcomes.

SRI PULI and FAM EKLADIOUS (NJMS 2020)

PROJECT TITLE: **TOBACCO PRODUCTS AND ADS IN SOUTH ORANGE AND CLIFTON RETAILERS NEAR SCHOOLS**
MENTOR: **STANLEY WEISS, MD, DANIEL M. ROSENBLUM, MD**
DEPARTMENT: **MEDICINE**

Participation Description:

In preparation for our research project on tobacco retailers in South Orange and Clifton we reviewed the report on audits that were performed in East Orange and Passaic last year as well as the Qualtrics survey utilized in such audits. This allowed us to identify topics of interest which were not included in the original survey which we believed may influence youth smoke initiation (such as content of ads, price discount, product placement, presence of age of sale sign). As the audit information concerned local health officers, we contacted local health officers to gain their input on relevant issues to investigate. We also contacted our collaborators in Passaic who were going to assist with the audits again this year to incorporate their perspective of the design of the supplemental questions. Field research was performed in Newark retailers prior to conducting audits to test the feasibility of our proposed lengthened survey as well as to best pinpoint the most relevant information to be gathered. With this information in hand, we actualized the creation of a new survey tool in Google Forms—this process was overseen and edited for accuracy by Dr. Weiss and Dr. Rosenblum. Our new survey tool incorporated both our newly designed questions as well as all questions from the Qualtrics survey utilized in prior audits. There were 68 total questions in the new survey tool—much time was spent formatting the survey to include multiple skip patterns to streamline the time spent within each store. Field tests were done once again, now utilizing our new survey tool, in West Orange, Metuchen, Newark and Elizabeth so as to better familiarize ourselves with the process. We then began audits in South Orange and Clifton. A list of licensed tobacco retailers in these two cities was provided to us by NJPN but the location of such retailers relative to schools was not well demarcated. To better locate ¼ mile of a school is a point of interest, we measured for distance on Google Maps. We identified 63 stores to be audited in South Orange and Clifton. Along with a high school student, Abhinav Rajasekhar, we conducted 43 out of those audits and the other 20 were conducted by Ashley Lucyk and Ashley Brown at United for Prevention in Passaic County. We began analysis of the data by compiling descriptive statistics and stratified the data by distance to school. For the variables where there seemed to be a suggestive trend, we tested significance with OpenEpi 2x2 tables and with t-tests. We examined the data and summarized the findings. Following the initial analysis, we recognized that it would be interesting to conduct additional audits in stores that were farther than ¼ mile from a school. We concluded our participation in this program by performing 26 audits in the City of Orange; one store was closed; of the remainder, half were within the ¼ mile radius and half were outside that radius.

Objective:

Tobacco smoking is the leading cause of preventable death in the United States1. In New Jersey, 11,800 residents die yearly due to the influence of tobacco. Most smokers (80%) begin smoking before the age of 182. In 2014, 35.1% of New Jersey high school students admitted to having used a tobacco product within their lifetime3. Despite age limits to help prevent youth smoking initiation many youths nevertheless smoke and many have been able to circumvent the law: the New York Department of Health's Youth Tobacco Survey 2008 shows that 1 out of 5 high school smokers purchased cigarettes from a convenience store4.

The Surgeon General reported in 2012 that tobacco advertising at the point-of-sale is associated with youth

tobacco use5. $8.6 billion was spent on point-of-sale advertising in the United States in 20146. Currently, there are no restrictions on point-of-sale advertising. Factors such as product placement, advertisement coloring, and product pricing can affect the initiation of tobacco usage. Indeed, higher levels of product marketing and lower prices offered with promotions were associated with smoking uptake7.

We conducted audits in South Orange (Essex County) and Clifton (Passaic County) to elucidate the presence of point-of-sale advertisements and tobacco products in retailers near schools, which may influence youth smoking initiation. Given the evolving importance of e-cigarettes and hookah in these regions, we studied these as well.

Methods:

Tobacco retailers were audited in many New Jersey cities last year utilizing a tool developed by Qualtrics. Drs. Weiss & Rosenblum's team performed and analyzed audits done in East Orange and the City of Passaic, which documented the presence of tobacco retailers within ¼ mile of an open school and that point-of-sale advertisements were present at many retailers. An expanded, new survey tool was created via Google Forms by us to elicit more pertinent and enhanced local information. This new survey included 68 total questions, with 9 skip patterns to reduce extraneous survey time. New questions inquired about tobacco advertisement specifics (colors and imagery within ads), tobacco product pricing (price range in stores as well as prices of most popular brands), presence of discounts, and product placement within the store. Local health officers, colleagues, and our collaborators contributed to the development of new questions.

Stratified analyses by walking distance (in blocks) from the retailer to the nearest school, were done to give a clearer understanding of differences amongst retailers of varying distances from a school.

The New Jersey Prevention Network **(NJPN)** provided a list of potential tobacco retailers in South Orange (n=11) and in Clifton (n=76). We selected all 11 stores from South Orange and 48 from Clifton for audits (59 total). These stores were chosen either due to their location within ¼ mile of a school (as determined by us by straight-line distance via Google Maps) or (for some stores in Clifton), per the request of our Passaic collaborators, those stores they had audited the prior year. There were an additional 4 stores not on the NJPN list that we identified during our field work that were near these stores and which we visited: 1 in South Orange and 3 in Clifton. Of the total of 63 stores visited for audit, only 59 were open.

Stores were visited in teams of 2-3. Ashley Brown and Ashley Lucyk from United for Prevention in Passaic County performed 20 of the Clifton audits, and we visited all the others (68%). Teams gathered information by observation in store and our observations were entered into our online survey tool. We educated store owners about tobacco age-of-sale information by handing our printed information from NJPN. Members of the team compared their observations after leaving each store to arrive at a consensus for data entry.

Stores were visited in teams of 2-3. Ashley Brown and Ashley Lucyk from United for Prevention in Passaic County performed 20 of the Clifton audits, and we visited all the others (68%). Teams gathered information by observation in store and our observations were entered into our online survey tool. We educated store owners about tobacco age-of-sale information by handing our printed information from NJPN. Members of the team compared their observations after leaving each store to arrive at a consensus for data entry.

Summary:

Of the **59 total stores audited, 49** tobacco retailers were within ¼ mile of a school. All tobacco retailers sold **cigarettes.**

Table 1: Tobacco Products Sold, Ad Presence, Cigarette Pack Pricing

Walking Distance to Nearest School	All Stores	<4 Blocks	4+ Blocks
Total number of stores	**59**	**30**	**29**
Number of stores that sell Cigarettes	59 (100%)	30 (100%)	29 (100%)
Number of stores that sell E-cigarettes	21 (36%)	9 (30%)	12 (41%)
Number of stores that sell Hookah	4 (7%)	3 (10%)	1 (3%)
Numbers of stores with EXT ads	25 (42%)	14 (47%)	11 (38%)
Number of stores with INT ads	25 (42%)	15 (50%)	10 (34%)
Number of stores with EXT Age of Sale sign	24 (41%)	10 (33%)	14 (48%)
Number of stores with INT Age of Sale sign	20 (34%)	11 (37%)	9 (31%)
Average Cheapest Price per Cigarette Pack	$7.64	$7.93	$7.34**
Average Highest Price per Cigarette Pack	$9.18	$9.22	$9.13
Number of stores with Cigarette Packs below $6.00	6 (10%)	4 (13%)	2 (7%)
Number of stores with Cigarette Packs above $10.00	9 (15%)	3 (10%)	6 (21%)
Number of Stores with Smoking Cessation Ads	5 (8%)	2 (7%)	3 (10%)

Table 2: E-Cigarette Pricing (Prices Observed in 18 of the 21 Stores Selling E-Cigs)

Walking Distance to Nearest School	All Stores with E-Cig Pricing	<4 Blocks	4+ Blocks
# of stores with E-cig Pricing	18 (out of 21, 86%)	8 (out of 9, 89%)	10 (out of 12, 83%)
Average Cheapest E-cig Price	$11.78	$9.97*	$13.23
Average Highest E-cig Price	$21.89	$18.22*	$24.82

When the difference between average prices approached statistical significance (see table 4 below), we marked in the tables above those with a lower price closer to schools with an *, and those with a lower price farther from schools with **.

Additional information regarding content and color schemes of present ads as well as placement of cigarette products in relation to counter height was collected; there were no significant differences.

Several attributes were more common in retailers <4 blocks from a school than those 4+ blocks from a school: presence of interior ads, presence of exterior ads, presence of hookah, and presence of cigarette packs below $6.00. The cigarette packs above $10.00 were more common in retailers 4+ blocks from a school. None of these differences reach statistical significance (table 3), but there were trends that suggest further follow-up through additional audits. Some salient findings were:

- Of 49 stores within ¼ mile of a school, **23 (47%) had exterior point-of-sale advertising**, which the Surgeon General in 2012 stated is associated with youth tobacco initiation.
- Both the highest and lowest priced e-cigs are **cheaper at locations <4 blocks from a school**, a trend that approaches statistical significance (table 4).

- Contrary to expectations, the cheapest cigarette packs at retailers <4 blocks from a school were higher than those 4+ blocks from a school (table 4).
- Only four stores (7%) were noted to have sold hookah.

Mid-P version of the Fisher exact test was utilized to assess differences in product availability, product placement, and tobacco ad specifics. We partitioned the 59 stores into those <4 blocks and 4+ blocks from the nearest school as this most closely approximated equal groups.

Table 3: Trends Noted, by Distance to School

Table 3. (N=59)	Risk Ratio (<4blocks/4+ blocks)	1-tailed Mid-P exact p Value
Presence of Interior Ads	1.45	0.12
Presence of Exterior Ads	1.23	0.26
Presence of Hookah	2.90	0.19
Cigarette packs below $6.00	1.93	0.23
Cigarette packs above $10.00	0.48	0.14

Table 4: Mean Price of Products Notably Different with Distance to School

One tailed T-test of mean price by distance <4 vs 4+ blocks from school	p Value
Cheapest E-cigarette (price lower closer to school)	0.0715
Most Expensive E-cigarette (price lower closer to school)	0.0831
Two tailed T-test of mean price by distance <4 vs 4+ blocks from school	**p Value**
Cheapest Cigarette Pack (price lower farther from school)	0.0869

We also analyzed data from inspection reports consolidated by the federal Food and Drug Administration (FDA).[8] Of the **59** stores we audited, there was a record of compliance checks on only **29 (49%)** during the 1.5 year period of Jan2016 – Jun2017. Only **21 (72%)** stores of the 29 had inspections including the assistance of a minor to assess age of sale laws. Violations for tobacco sale to minors occurred in **5 (24%)** of these 21 stores— **4** were given warning letters and **1** was given a civil money penalty due to a repeated violation. Thus, since only **21 (36%)** out of 59 stores were inspected including a minor, enforcement and monitoring are weak. The **5** stores which sold tobacco to minors **underestimate** age-of-sale violations in stores we audited. Note also that **53%** of the 49 stores within 1⁄4 mile of schools were **not** inspected.

Conclusions:

Since the e-cig pricing was lower near schools, there is a concern that this might contribute to e-cig initiation by youth. The unexpected contrasting finding that cigarettes were more expensive close to schools is potentially good news if this were to be sustained in future studies with a larger sample size. The e-cig issue suggests a need to include a focus on e-cigarettes when audits are conducted, even though this issue is not addressed in the Qualtrics survey being employed by other statewide audits.

Much information was gathered about the presence of tobacco products and ads at retailers within ¼ mile of a school. The collection of such data at additional retailers at distances farther than ¼ mile of a school may help to more clearly demonstrate any differences in point-of-sale strategies and tobacco product sale in locations near schools. For this reason, we extended our audits to the City of Orange. Our additional 25 audits, of which 13 were within ¼ mile of a school, were collected after the present analysis.

A limitation in using number of blocks walked to nearest school as the store distance from schools is that blocks vary in size and different auditors may have varying definitions concerning what constitutes a “block” (e.g., where an intersection is a T, making 1 v 2 blocks

arbitrary). An alternative gauge for distance could be walking time as estimated using a GPS application.

As per the NJ Cigarette Tax Act, all licensed tobacco retailers must display a conspicuous age of sale sign at "all points of display and sale of tobacco products." [9] However, only 24 out of 59 (40%) audited stores displayed an exterior age of sale sign and only 20 out of 59 (34%) stores displayed an interior age of sale sign. These data demonstrate that current enforcement of this law is limited. Dedicated funding for enforcement should be considered.

Creating and implementing policies that restrict point-of-sale marketing have the potential to contribute to reduced tobacco use. Policy changes that might be considered include:

- Regulate posting of tobacco ads, especially in tobacco retailers near schools
- Reducing the number of tobacco retailers near schools, and especially not approving new stores to sell tobacco products if they will be near schools.
- The NJ law signed in July 2017, which increased the age from 19 to 21, continues to afford both health officers and law enforcement personnel roles in age-of-sale issues; municipalities should encourage summons and enforcement.

Acknowledgments:

Ashley Brown and Ashley Lucyk from **United For Prevention in Passaic County** provided help in performing audits in Clifton. Elise McGaughran from **Tobacco Free for New Jersey** provided us with educational material to distribute in retailers and provided audit training. Abhinav Rajasekhar helped perform audits and data analysis Dr. Weiss and Dr. Rosenblum provided feedback during survey creation, data analysis, and in write-up.

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MARCUS ELIAS (NJMS 2020)

PROJECT TITLE: **PREDICTING ROUND WINDOW ACCESSIBILITY FOR COCHLEAR IMPLANTATION WITH PREOPERATIVE CT MEASUREMENTS**
MENTOR: **TAPAN PATEL, MD, ROBERT JYUNG, MD**
DEPARTMENT: **OTOLARYNGOLOGY**

Participation Description:

It has been a privilege to work with Dr. Jyung this summer. My involvement regarding this study includes drafting the IRB, working with Image J analysis, and learning SPSS software. I have reviewed CT images of Dr. Jyung's patients, but have yet to peruse the corresponding postoperative notes. I also assisted Dr. Jyung with a another basic science project in which I collected saliva specimen from his patients.

Objective:

Cochlear implantation can provide great quality of life benefits to patients who are deaf or severely hard of hearing. With more than 300,000 devices implanted worldwide to date, the importance of efficiency and safety throughout the procedure cannot be understated. Currently, mastoidectomy with facial recess approach is the most widely used surgical method of cochlear implantation. With this procedure, mastoid air cells of the temporal bone are removed to gain access to the facial recess—a triangular pathway within the temporal bone bounded by the facial nerve (FN) medially, chorda tympani laterally, and fossa incudis superiorly. Through the facial recess, the surgeon can visualize the round window niche (RWN)—a small fossa which protects the round window membrane. Since the round window membrane represents a part of the terminus of the basal turn of the cochlea, it provides an ideal portal to introduce the cochlear implant electrodes. We have noticed that the primary obstacle to clear viewing of the RWN is the degree of posterior sloping of the posterior bony external auditory canal (EAC).

Preoperative CT imaging can provide cochlear implant surgeons with valuable patient-specific information regarding the position of structures within the temporal bone, allowing pre-operative anticipation of surgical difficulty. This study seeks to examine whether measurement of the posterior slope of the posterior bony EAC wall can predict low RWN visibility and hence difficulty of cochlear implantation. Measurement of surgical difficulty in cochlear implantation can be quantified by the number of compensatory maneuvers required to adequately visualize the RWN and carry out successful implantation. The senior author (RWJ) has developed a set of maneuvers of progressively greater complexity to enhance RWN visualization. We hypothesize that measurement of temporal bone anatomic features on preoperative CT images can predict whether additional surgical maneuvers beyond the standard facial recess approach will be required.

Methods:

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CT images will be cropped in the mid-sagittal plane (or there will be establishment of the sagittal/parasagittal plane)

Angles will be measured using the Image J software

1st point will be placed at most lateral point of posterior external auditory canal wall

2nd point will be placed at mid-sagittal plane

3rd point will be placed at most posterior point of mid-sagittal plane

3. Measurements will be interpreted as follows:

Acute angle (<90 degrees) will be interpreted as a posteriorly-directed slant of the external auditory canal wall

No angle (90 degrees) will be interpreted as a direct lateral projection of the external auditory canal wall

Obtuse angle (>90 degrees) will be interpreted an anteriorly-directed slant of the external auditory canal wall

Confounding variables such as facial recess width, aberrant facial nerve position, degree of mastoid pneumatization, low tegmen, and anterior sigmoid sinus positioning will be accounted for with additional CT analysis and measurements.

After compiling the CT analysis, post-operative reports blinded to the prior measures will be analyzed for accessory procedures completed by Dr. Jyung. A holistic view of compensatory procedures will result in a numerical grade by counting the number of surgical maneuvers used in the following order:

Wide skeletization of facial recess

Drilling a trough on the posterior face of external auditory canal wall

Temporary removal of a bone segment from external auditory canal wall

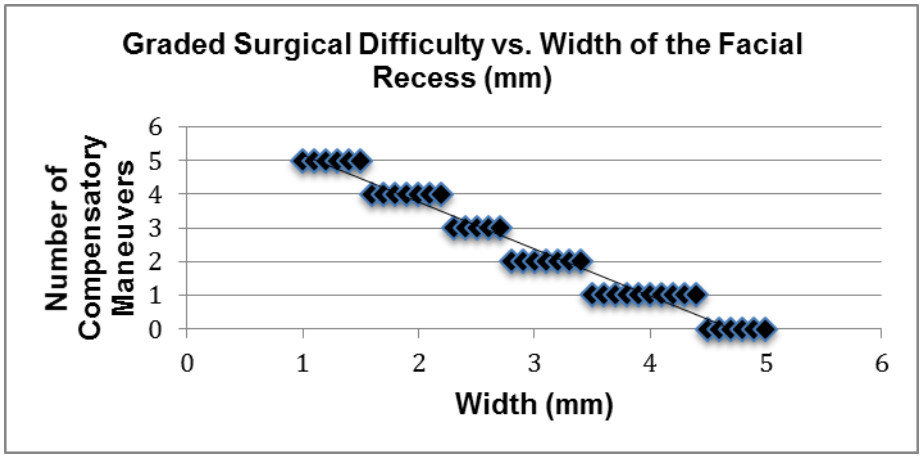
Removal of a bone segment and displacement of external auditory canal skin, fibrous annulus, tympanic membrane

Sacrifice of chorda tympani nerve

SPSS software will be used for data analysis with a P-value < 0.05 considered as significant. Chi-squared and T-tests will be used to analyze differences in surgical difficulty and CT measurements (slope of the posterior bony canal and width of the facial recess).

Summary:

With a goal sample size of n=300, data collection and analysis are yet to be completed. Results are to be determined with the following predictions: 1) cases with wider facial recesses will necessitate fewer compensatory maneuvers [Figure A] and 2) more obtuse angles for the posterior bony canal will also favor less difficult surgeries [Figure B].



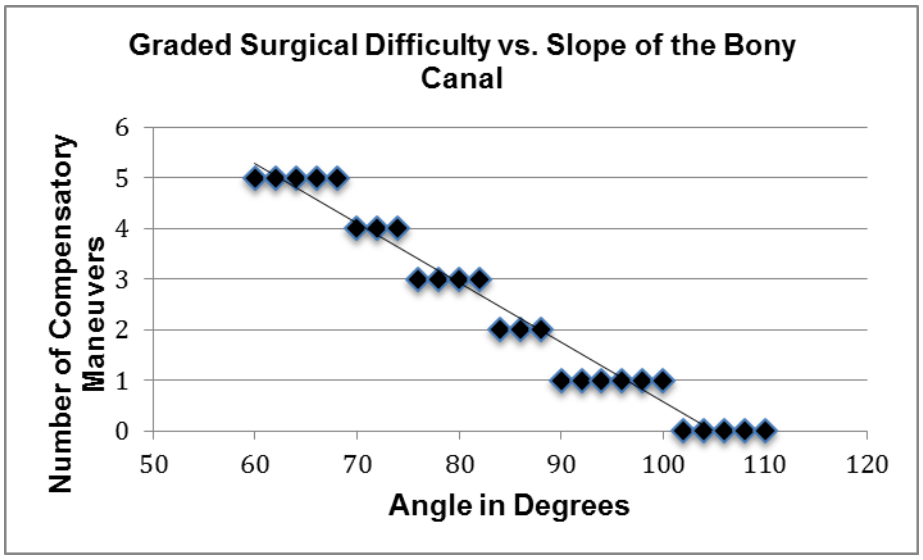


Figure A & B. Hypothesized results

Conclusion:

Consequence and resulting conclusions regarding this study are yet to be determined.

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SHANNON EMILLE (UofA 2019)

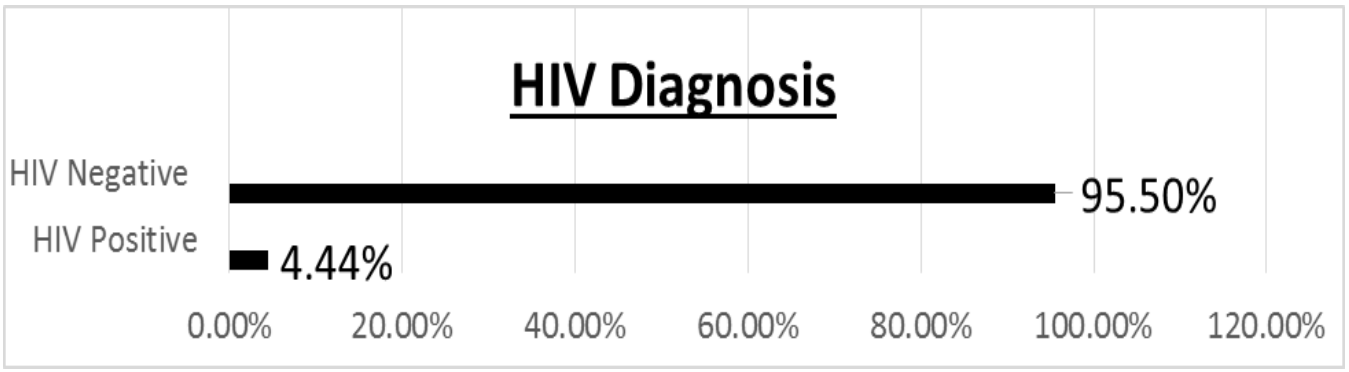
PROJECT TITLE: **HIV PREVALENCE IN A MENTALLY ILL POPULATION IN AN URBAN ACADEMIC MEDICAL CENTER**
MENTOR: **CHERYL KENNEDY, MD**
DEPARTMENT: **PSYCHIATRY**

Participation Description:
My involvement in the HIV Prevalence in A Mentally Ill Population research was hands on. The research conducted was a clinical research that requires obtaining consent and a questionnaire to be completed by each participant. I was involved in distributing the consent forms and aiding the patients with questions they did not understand. From the information collected, I would then enter the collected data from each patient into an excel sheet which contained all the participant's medical records. With approval from the institutional review board, information was collected from 834 patients. Using statistical means, the conclusion was made that 4.4% of mentally ill patients out of 834 participants tested positive for HIV.

Objective: HIV prevalence in a mentally ill population

Methods: With Institutional Review Board (IRB) approval and participants consent, a Patient Satisfaction Questionnaire was administered to 834 adult patients over three years who were about to be discharged from the University Hospital Acute Inpatient Psychiatric Unit. Socio-demographic data such as gender, race, home disposition, legal status, as well as treatment history & HIV were obtained from the medical records. Data were entered in Excel file. Frequency analysis for the socio-demographic variables were done. Mean length of stay (LOS) was also analyzed.

Summary: The purpose of this study is to determine the prevalence of Human Immunodeficiency Virus (HIV) in the mental ill population. According to the Center for Disease Control, there is an increase number of people in the mentally ill population with HIV as opposed to those who are not mentally ill. The mentally community is at an increased risk of contracting HIV due to a number of factors. Those with mental disorders have an increased risk of contracting HIV due to behavioral risk factors like impulse control, sharing of needles for injection drug use (IDU) in the mentally ill increases the risk of transmitting or acquiring HIV. Unprotected sexual encounters (may be common in this population) are another important risk factor.



Conclusion:

HIV prevalence in the mentally ill population is higher than that of those who are not mentally ill. The prevalence of HIV in the mentally ill population in the United States is four times that of the general population. This research project concludes that out of 834 participants in the University Hospital Acute Inpatient Psychiatric Unit, 4.4% have HIV. Effective strategies for HIV prevention are known and hospitalization provides an opportunity to institute education, strengthen medication compliance strategies and make referrals for comprehensive medical care as well as addiction treatment & social support to assist patients in coping more effectively with their risk factors.

MATTHEW FLINT (NJMS 2020)

PROJECT TITLE: **USE OF AN EXPANDABLE TRANSFORAMINAL-LUMBAR INTERBODY CAGE TO SALVAGE AN ANTERIOR-LUMBAR INTERBODY FUSION WITH ANTERIOR ACCESS COMPLICATION**

MENTOR: **ANTIONIOS MAMMIS, MD**

DEPARTMENT: **NEUROSURGERY**

Participation Description:

This project was a case report written about a complication that was incurred during an anterior lumbar interbody fusion procedure and the technique utilized to salvage the procedure despite complication. My role in this paper included a review of literature on lumbar fusion techniques and interbody cages, a review of the patients pre-operative and post-operative information, as well as all writing of the abstract and poster presentation.

Objective:

Anterior lumbar interbody fusion (ALIF) is a recognized technique for the treatment of degenerative diseases of the lumbar spine. Though the direct access ALIF provides to the disk space and spinal column is highly beneficial, it is not without complication. Vascular injury has been noted to occur while retracting the iliac vessels to expose the spinal column. In some cases, mobilization of these vessels may be particularly difficult, leaving a narrower than ideal window of access.

Methods:

We present the case of a 52-year-old female who presented with chronic lumbago who had previously failed medical management and physical therapy. The patient was determined to be a candidate for ALIF. Intraoperative mobilization of the iliac vessels was particularly difficult and only narrow exposure of the lumbar spinal column was achieved. Placement of the ALIF cage was not possible, thus an expandable transforaminal lumbar interbody fusion cage was utilized in its place.

Summary:

The anterior approach to lumbar interbody fusion is known to have complications that include vascular injury, thus a vascular surgeon typically performs the approach to this procedure. While ALIF is performed for the direct access it provides to the spinal column a failure to fully mobilize the iliac vessels negate the possibility of implanting the traditionally large anterior cage. A decision then had to be made whether to abort the procedure or adjust and proceed using a smaller cage. The decision was made to proceed using the expandable transforaminal interbody cage that was developed for a different lumbar interbody fusion approach known as the transforaminal approach. The expandable transforaminal cage was developed to take advantage of the narrower window necessary for the transforaminal approach while providing the large footprint and maximal vertebral endplate contact provided by an anterior approach. While fusion was successful, the patient still developed adjacent segment disease (ASD), a known complication of lumbar interbody fusion that has a widely variable incidence in the literature (2%-30%). Although rates of this complication vary, the literature suggests that a high body mass index (BMI) may be a risk for the development of this condition, as was seen in our patient. Despite the development of ASD, the surgery is viewed as a success as all post-operative imaging indicated successful bony fusion.

Conclusions:

When mobilization of the iliac vessels is unsuccessful it may be impossible to proceed using a standard ALIF cage. The surgeon may need to choose between abortion of the case or utilization of a different sized cage. The expandable TLIF cage can be a viable solution to this problem, as it provides the utility of an ALIF cage through a smaller access window.

PHABINLY GABRIEL (NJMS 2020)

PROJECT TITLE: **EFFICACY OF THE "DOUBLE FLAP" TECHNIQUE IN RECONSTRUCTION OF ANTERIOR SKULL BASE DEFECTS AFTER COMBINED TRANSBASAL AND ENDOSCOPIC ENDONASAL APPROACH**
MENTOR: **JAMES K. LIU, MD**
DEPARTMENT: **NEUROLOGICAL SURGERY**

Participation Description:
My role for this research project has being mainly retrospectively reviewing patient charts, interpretation of the data, and aggregating that into graphs. Ultimately, nine charts were reviewed and qualitative statistical analysis was performed. This research project culminated into a poster and a manuscript.

Methods:

We conducted an institutional review board–approved retrospective chart review on 9 patients who undergone a combined transbasal and endoscopic endonasal approach for large sinonasal malignancies with significant intracranial extension followed by cranial base reconstruction using the double flap technique between 2010 and 2017 at the author's institution. Patient characteristics and outcomes following reconstruction of anterior skull base defect with double flap reconstruction technique, including demographic profile, indication for surgery, method of tumor resection, method of repair, complications, tumor recurrence, and follow-up, were reviewed.

Summary:

Nine patients who underwent a combined transbasal/EEA approach for resection of malignant anterior skull base tumors with significant intracranial extension followed by successful reconstruction of the cranial base using the double flap were identified. Five were men and four were women, with a mean age of 47.6 (range 15—68 years). There was no post-operative cerebrospinal fluid leakage detected, after a mean follow-up of 1.38 years (range, 0. 13–3.4 years). Furthermore, there were no complications of infection, meningitis, epistaxis, mucocele or pneumocephalus. Adjuvant radiation therapy was initiated in only eight of the nine patients after the surgery period without flap necrosis. Tumor recurrence was not observed in any of the patients during the follow-up.

Conclusion:

The double flap technique has proven its efficacy by showing that by providing dual flap support via a combined PCF and NSF during repair of the anterior skull base is beneficial in the prevention of CSF leakages, postradiation flap necrosis, infection, meningitis, tension pneumocephalus, or mucocele created after skull base surgery.

TIMUR GANAPOLSKY (NJMS 2020)

PROJECT TITLE: **EFFICACY OF THE "DOUBLE FLAP" TECHNIQUE IN RECONSTRUCTION OF ANTERIOR SKULL BASE DEFECTS AFTER COMBINED TRANSBASAL AND ENDOSCOPIC ENDONASAL APPROACH**
MENTOR: **LUIS ULLOA, PH.D.**
DEPARTMENT: **SURGERY**

Participation Description:
Dr. Luis Ulloa and I met at least once a day for most week days to plan these experiments together. He gave me constant guidance and ensured I had a clear direction. I was trained by other members of the lab such as Dr. Biju Joseph and Guilherme Shimojo in preparation for conducting all the experiments described in this abstract myself. These techniques include handling mice, preparing solutions of LPS and pentobarbital, performing intraperitoneal and subcutaneous injections, collecting blood and organ samples, isolating serum from blood, preparing lysates from organ samples, performing ELISAs, performing surgical vagotomies and surgical splenectomies, and suturing. I also developed an accurate, modified version of a Bradford assay to quantify total protein in tissue lysates in a manner that suited my needs. After performing the assays, I organized and prepared the data using excel and performed statistical t-tests in the software I used to make the graphs, Graphpad.

Methods:
C57BL6 mice entrained to a 7 am to 7 pm light cycle were used for all experiments. Acute endotoxemia was induced by injecting mice with 10 mg/kg of bacterial LPS in phosphate-buffered saline (PBS). After 90 minutes, blood and organs were collected. This was done to two groups of 3 mice for each experiment, at 8 am for the morning group and 6 pm for the evening group. Serum and tissue lysate TNF was quantified using the Affymetric eBioscience Mouse TNF alpha ELISA Ready-Set-Go! Kit (Ref #: 88-7324-88, Lot #: 4281407). Tissue total protein was measured using a modified Bradford assay and the Biorad Protein Assay Reagent Concentrate (Catalog #: 500-0006). The unilateral cervical vagotomy procedure was initiated by anesthetizing mice with approximately 1.25 mg/kg of pentobarbital in PBS. The right cervical vagus nerve was severed with scissors in each mouse. After surgery, each mouse was injected with 100 µL of 2.26% Baytril enrofloxacin in PBS subcutaneously to reduce the risk of postoperative infection. The splenectomy procedure began with the same method of anesthetization. The spleen was ligated at the splenic artery and then removed through a lateral abdominal incision. Each mouse was provided enrofloxacin subcutaneously after this surgery as well.

Summary:
Mice injected with LPS in the morning had higher levels of serum TNF than mice injected in the evening (Fig. 1a). An analysis of organ TNF levels found that in almost all organs, TNF was higher in the morning (Fig. 1c). To determine the influence of parasympathetic activity fluctuation on this morning/evening difference, a new set of mice were vagotomized. Three days later, morning and evening groups of vagotomized mice were injected with LPS and analysis found higher levels of serum TNF in both groups of mice but with no significant difference between the AM and PM groups (Fig. 1b). As it is known that the vagus nerve primarily acts through modulating spleen macrophages in the parasympathetic inflammatory reflex arc, mice were splenectomized and three days later analyzed for their TNF response to LPS. The AM splenectomized group demonstrated lower levels of TNF in the morning compared to control, but the evening splenectomized mice had much higher TNF than both the morning group and control (Fig. 1d).

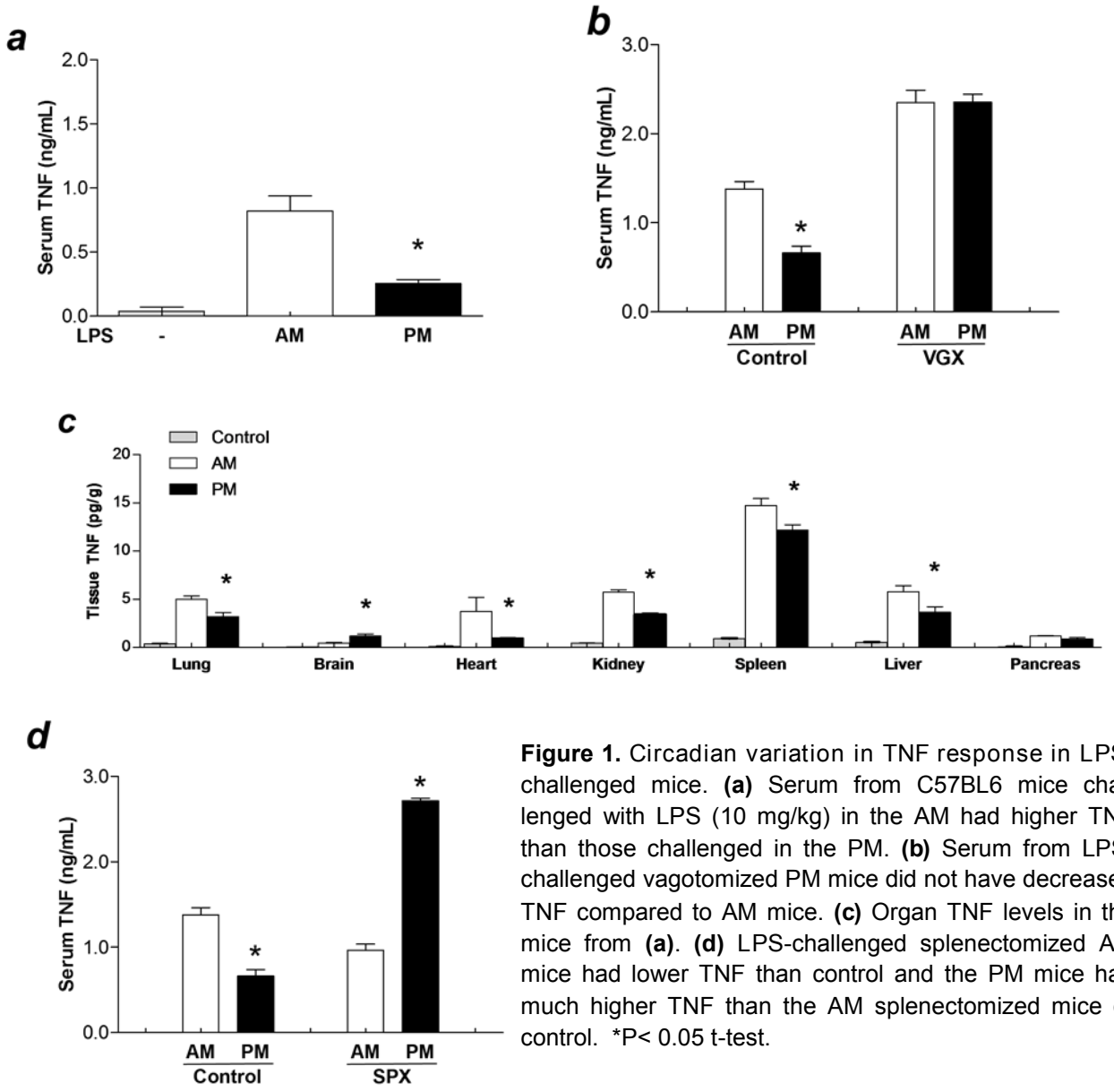


Figure 1. Circadian variation in TNF response in LPS-challenged mice. **(a)** Serum from C57BL6 mice challenged with LPS (10 mg/kg) in the AM had higher TNF than those challenged in the PM. **(b)** Serum from LPS-challenged vagotomized PM mice did not have decreased TNF compared to AM mice. **(c)** Organ TNF levels in the mice from **(a)**. **(d)** LPS-challenged splenectomized AM mice had lower TNF than control and the PM mice had much higher TNF than the AM splenectomized mice or control. *P< 0.05 t-test.

Conclusion:

Our preliminary findings suggest that the inflammatory response to acute endotoxemia is more severe in the morning than in the evening. Vagotomy eliminates the difference in morning and evening TNF responses to LPS, suggesting the vagus nerve mediates the circadian variation in pro-inflammatory response to acute endotoxemia. Splenectomy suppresses TNF production in the morning but increases TNF production in the evening, suggesting the spleen is more important in suppressing TNF production in other organs in the evening. These experiments will be repeated to further ensure the validity of these results. In the future, mice with other surgical manipulations of organs involved in inflammation will be challenged with LPS and analyzed for their TNF responses to further investigate the physiological mechanisms of circadian influences on inflammation.

OWEN GANTZ (NJMS 2020)

PROJECT TITLE: **THE COST OF SURGICAL SITE INFECTIONS IN COLORECTAL SURGERY: A LONGITUDINAL ANALYSIS**
MENTOR: **AZIZ MERCHANT, MD**
DEPARTMENT: **SURGERY**

Participation Description:

Owen Gantz performed a literature review, obtained and processed the data, designed the statistical analysis, and interpreted the results.

Objective:

SSI represent a significant burden on healthcare utilization and a main focus of public health and infection control initiatives. SSI were identified by a single ICD-9 code in the HCUP-NIS database over a 12 year period from 2001-2013 in order to identify trends in length of stay and total cost of admission for patients who developed SSI subsequent to colorectal surgery. On average, patients that developed an infection spent 8.2 more days in the hospital and billed $19,752 more by the time of discharge. These trends were largely constant over time

Surgical site infections (SSI) remain the most commonly occurring type of nosocomial infection in the United States, occurring in 2-5% of all surgical procedures performed. SSI are associated with significant morbidity and mortality and have also been demonstrated to vastly increase utilization1 of healthcare resources, with some studies demonstrating an increased length of stay (LoS) of up to 14 days and up to a $20,000 increase in total cost of care at discharge [1]. Abdominal and GI surgery are known to carry the greatest risk of of SSI, and while rates of SSI have decreased every year, colorectal surgery has historically shown the worst improvement with a 2% decrease in SSI rates between 2015 and 2016 for colon surgery [2]. Given the impact of SSI on healthcare utilization, it is perhaps unsurprising that a dearth of studies have been published examining the cost associated with operative infections. However, many of these studies are fairly limited in scope, covering a limited number of years and geographies. Researchers have noted that even comparisons between studies are difficult as methods used to identify SSI cases may vary vastly between studies citebroex.1 We propose a method using the National Inpatient Sample database to identify trends in length of stay and total cost associated with surgical site infections in colorectal surgery specifically over a 12 year period from 2001 to 2013.

Methods:

Study Data

This analysis used hospital stay data sourced from 2001-2013 in the National Inpatient Sample (NIS), a publicly available dataset available from the Agency for Healthcare Quality and Research (AHQR) Healthcare Cost and Utilization project [3]. The HCUP database is federally sponsored and is designed as a stratified sample of 20% of all discharges from hospitals in the United States. It is the largest inpatient care database in the United States representing a diversity of geographies and hospital types. The large sample size of the HCUP-NIS database allows for the assessment of relatively rare events, such as SSI with sufficient power. Each HCUP record represents a single hospital admission and includes demographic data on the patient admitted, data on that patient's clinical course with respect to diagnosis and procedures performed, and data related to that patient's length of stay and total billed charges.

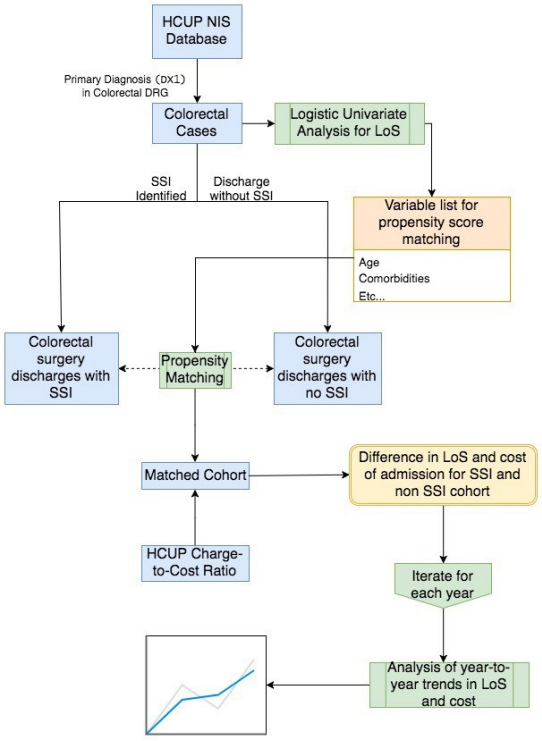


Figure 1. Overview of method

Selection of Colorectal Surgical Cases

This study focused on SSI in colorectal surgery only, due to the comparatively high incidence of SSI in these surgeries. Relevant surgical admissions were selected by using diagnosis related grou (DRG) codes which are published by the Centers for Medicare and Medicaid Services and can be used to group related procedure codes. Codes defined by version 24 of the DRG grouper (DRG24) was available in HCUP data starting in the year 2006. Prior to that, version 18 of the DRG grouper (DRG18) was used to identify colorectal cases. In the conversion from DRG18 to DRG24, the group "major small & large bowel procedures w/ CC" was split further into those with and without "major GI dx" and group 148was depreciated (table 2).

Comorbidity Derivation and Identification of SSI Cases

ICD-9 codes in each admission record were abstracted to identify relevant comorbidities using the Elixhauser Comorbidity Software Tool version 3.7 citeelixhauser. Literature has suggested that blood transfusions may represent a risk factor for SSI, so they were identified from ICD-9 procedure codes in the 99.0X group [5]. Given that the HCUP-NIS database does not provide full medical records for patients, we rely on the specification of the ICD-9 code 998.59 which corresponds specifically to postoperative infection. While this method of identifying SSI is very specific, it does exclude other possible codings of SSI.

Matching and Impact Analysis

Total costs were determined by adjusting the total billed charges for each patient record using a hospital- and year- specific charge-to-cost ratio supplied by the HCUP-NIS database. When hospital-specific ratios were not available, the group-average ratio was applied instead. Group averages were calculated by identifying hospitals in the same geographic region with similar

Table 1. Comparison of mean total cost and length of stay between SSI and matched non-SSI groups. (CAGR = Compound Annual Growth Rate)

Year	Total Cost (2013$)			LoS (days)		
	SSI	No-SSI	Diff	SSI	No SSI	Diff
2001	$29,965.15	$17,293.21	$16,673.56	18.6	11.0	7.6
2002	$33,513.05	$18,858.40	$18,979.53	19.4	10.7	8.7
2003	$35,514.38	$19,059.50	$20,832.31	19.3	10.7	8.5
2004	$36,443.40	$20,099.93	$20,153.65	18.9	10.6	8.3
2005	$38,233.66	$21,871.73	$19,519.43	19.0	10.6	8.3
2006	$39,354.82	$21,906.36	$20,165.88	19.0	10.4	8.6
2007	$41,225.41	$23,742.56	$19,641.79	18.6	10.8	7.8
2008	$44,033.00	$24,373.45	$21,275.64	19.1	10.6	8.5
2009	$42,658.14	$24,214.50	$20,023.92	18.7	10.6	8.0
2010	$45,382.65	$25,670.95	$21,056.04	18.9	10.5	8.5
2011	$44,180.27	$26,081.13	$18,744.97	18.0	10.5	7.5
2012	$47,038.89	$27,210.07	$20,119.26	18.5	10.8	7.7
2013	$46,458.81	$26,874.14	$19,584.67	18.5	10.4	8.1
CAGR	**3.7%**	**3.7%**	**1.4%**	**0.0%**	**-0.5%**	**0.6%**

numbers of beds, teaching/non-teaching status, and urban/rural location. Costs were then inflation-adjusted by converting all nominal costs to 2013 dollars. This was performed by applying a conversion factor based on each year's mean Consumer Price Index [8]. In order to control for the effects of comorbid conditions on SSI which might confound the effect of SSI on total cost and length of stay, we used a propensity score matching technique implemented in the R package MatchIt [6]. This process is designed to simulate post-hoc randomization of patients by first modeling each patient's likelihood of developing an SSI. SSI patients are then matched to non-SSI controls by those scores based on the assumption that had they been "randomized", those two patients would have an equal likelihood of appearing in each group [7]. The logistic model used incorporated all abstracted comorbidities and appears in table 3. Each patient that experienced an SSI was matched to a non-SSI control on the basis of their binary logistic propensity score using a 1:1 nearest-neighbor matching method. Means were then calculated for length of stay and total cost in the SSI and non-SSI group by year.

Results

Impact on LoS and Total Cost

Over the 12-year period that this study examined, patients with SSI billed $19,752 more than did patients without an SSI. These patients also had an average length of stay that was 8.2 days longer than their counterparts who did not experience an SSI. Overall, the cost of treating operative infections in colorectal surgery has kept pace with the increasing cost of colorectal surgery in general at 3.7% annual growth in the period from 2001-2013 (see table 1). Over the same period, the length of stay for SSI patients has remained largely un-changed, with the length of stay associated with colorectal surgery in general decreasing modestly. These results imply that the cost associated with SSI in colorectal surgeries have remained fairly fixed over the past 12 years, and that even with increased infection con-trol budgets in hospitals [10], they have not become any more efficient in treating patients who do develop SSI.

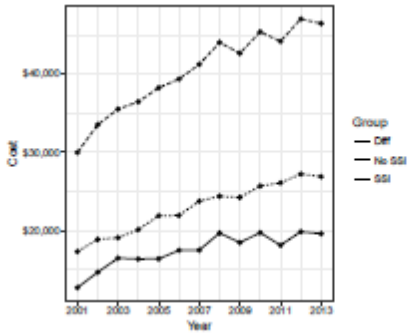


Figure 2. Graph comparing total cost associated colorectal surgery based on presence of SSI. The dotted line indicates the difference b tween the cost of colorectal surgery with associated SSI vs.the cost without.

Discussion

Administrative databases such as the HCUP-NIS database, while providing a large and nationally representative sample have inherent limitations that stem from inconsistent coding and payment incentives that may encourage or discourage the use of certain codes . These faults have been widely explored in the literature and has found to cause over- or under-reporting of a variety of conditions [11]. Presently however, these large administrative claims databases represent the most complete perspective available for national healthcare in the United States. Methods for the identification of SSI in claims data also vary widely. Our method which relied on a single ICD-9 code to identify cases in which SSI occurred is very specific, however other studies have included more codes, many of them reporting higher rates of SSI [12].

Conclusion

The cost of treating SSI in colorectal patients and increased LoS associated with infection have remained largely constant over the period from 2001 to 2013. Further analysis is needed to calculate national incidence of SSI based on this data and determine the national burden of SSI by year.

Appendix

Table 2. DRG codes used in the selection of colorectal cases

DRG Name	DRG18 Code	DRG24 Code	Total Cases
Rectal Resection w/ CC	146	146	48 378
Rectal Resection w/o CC	147	147	21 023
Major small & large bowel procedures w/ CC	148	569 (w/ major GI dx) 570 (w/o major GI dx)	654 621
Major small & large bowel procedures w/o CC	149	149	185 012
Anal & stromal procedures w/ CC	157	157	50 887
Anal & stromal procedures w/o CC	158	158	50 297

Table 3. Binary logistic regression statistics for propensity score matching

Predictor	OR (95% CI)	P-Value (2 tailed)
Age (continuous)	1.000 (0.999,1.001)	0.78702
Elective procedure	0.864 (0.846,0.882)	<0.0001
Female sex	0.846 (0.829,0.863)	<0.0001
Transfusion procedure	1.754 (1.711,1.798)	<0.0001
Comorbid Conditions		
No comorbid conditions	Ref.	
Congestive heart failure	1.103 (1.063,1.145)	<0.0001
Valvular disease	0.717 (0.678,0.759)	<0.0001
Pulmonary circulation disorder	1.425 (1.334,1.522)	<0.0001
Other neurological disease	0.878 (0.833,0.925)	<0.0001
Chronic pulmonary disease	1.068 (1.039,1.097)	<0.0001
Diabetes without chronic complications	0.891 (0.864,0.919)	<0.0001
Hypothyroidism	0.808 (0.776,0.842)	<0.0001
Coagulation deficiency	1.16 (1.106,1.217)	<0.0001
Obesity	1.346 (1.298,1.396)	<0.0001
Weight loss	2.146 (2.086,2.208)	<0.0001
Electrolyte disorders	1.623 (1.587,1.661)	<0.0001
Blood loss anemia	0.683 (0.646,0.723)	<0.0001
Deficiency anemia	0.849 (0.826,0.873)	<0.0001
Psychoses	1.218 (1.145,1.296)	<0.0001
Hypertension	0.783 (0.766,0.801)	<0.0001
Chronic peptic ulcer diseaes	1.018 (0.666,1.555)	0.93445
Rheumatoid arthritis	1.009 (0.939,1.085)	0.79720
Diabetes with chronic complications	0.971 (0.897,1.052)	0.47541
Liver disease	1.027 (0.958,1.101)	0.44872
Lymphoma	0.929 (0.82,1.053)	0.25201
Renal failure	0.972 (0.927,1.018)	0.22973
Depression	1.028 (0.988,1.07)	0.17348
HIV/AIDS	0.843 (0.671,1.06)	0.14318
Alcohol abuse	1.053 (0.987,1.122)	0.11725
Metastatic cancer	1.044 (1.006,1.083)	0.02326
Peripheral vascular disease	0.942 (0.896,0.991)	0.02037
Drug abuse	1.122 (1.028,1.226)	0.01036
Paralysis	0.881 (0.802,0.968)	0.00817
Solid tumor without metastasis	1.153 (1.076,1.235)	0.00005

Acknowledgments

Many thanks to Dr. Sri Nam Pentakota for providing access to the HCUP database and to my faculty mentor Dr. Aziz Merchant, without whom this project would not be possible. Thanks to the Rutgers University Office of Research and Sponsored Programs for sponsoring this summer research project.

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LEA GEORGE (NJMS 2020)

PROJECT TITLE: **RELATION BETWEEN ALCOHOL CONSUMPTION AND OPIOD USE**
MENTOR: **STANLEY H. WEISS, MD, DANIEL ROSENBLUM, PH.D.**
DEPARTMENT: **MEDICINE**

Participation Description:

This summer, I worked with Dr. Weiss and Dr. Rosenblum as well as another SSRP student, Reid Muenzen, as a research assistant on an ongoing study of drug users. As a first step, I completed the human subjects training and thoroughly acquainted myself to the study protocol, to which I was then added. As part of the project, I was encouraged by my preceptor to both critically evaluate the methodological implementation strategies during continual discussion of the data issues and to explore topics of importance. I contributed toward developing a new, more comprehensive questionnaire instrument that will be used at some future juncture and prepared a draft document of the rationale behind the proposed changes for the IRB. I helped explore with some outside investigators potential realms of expansion of studies of drug users, such as testing for metabolomics, which may become a future laboratory endeavor and collaboration, and which has been encouraged by an officer at the National Institution on Drug Abuse.

For the current field study, I was trained to be an interviewer, practiced and observed on multiple occasions, and then received approval to be part of a team of interviewers at collaborating drug treatment programs in our region. I explained to treatment program clients the study design, obtained written consents, and administered in person interviews of the clients. I was trained on editing procedures, and vigorously edited the questionnaires that I administered. The study procedures required that there always be a second reviewer before data entry and thus, I also edited those administered by others. I identified items that needed to be clarified and discussed resolutions of problems with my preceptors. To better understand methadone prescribing practices, I met with the treatment program physician at one of the facilities.

Our preceptor asked us to create our own questions that we would like to analyze based on our experience with the interviews. After completing a thorough literature search on human and non-human data, and discussing with our preceptor, we decided to explore the association between alcohol consumption and opioid use. I recognized which variables needed to be analyzed via SAS and with the help of Dr. Rosenblum output was created, based on these variables for our analysis. Through this experience, I learned about setting up a research project, following an investigation through to writing a manuscript (which I have been encouraged to take a lead on), developing the many integral parts of a study, and understanding the evolution and execution of an interdisciplinary study.

Objective:

The opioid crisis has been growing in the United States, leading to its declaration as a public health epidemic by the President (1, 2). Addictive behavior in heroin and non-heroin opioid users must be studied to tackle this issue. Based upon our own past studies of drug users, which date back to the 1980s, many heroin users use multiple other drugs; among opioid users, tobacco and alcohol are by far the most commonly used non-opioids. Not many human studies have thus far examined the influence chronic alcohol consumption may have on opioid use behavior.

Reasoning from the few relevant studies on rats and mice (3, 4, 5), we hypothesize that heavy, chronic alcohol drinkers within our population of drug users can have an increased tolerance for opioids. Thus, they might need a higher dose or more frequent use of an opioid to feel a sensation of euphoria. Not all substances that produce antinociceptive tolerance produce cross tolerance to multiple opioids. The interaction among various opioids and alcohol are not clear. Thus, it is important to examine heroin and non-heroin opioid users separately. However, rodent studies have shown that alcohol consumption does produce tolerance to both mu-ligands: morphine and (^{3}H) (D-Ala^2, MePhe^4, Gly-ol^5) enkephalin (DAMGO) (5). Methadone is an opioid; the possible relation between a subject's methadone dose, in terms of the dose given, and alcohol use in this population is explored. Clients enrolled in methadone drug treatment programs generally have a history of heroin abuse. In determining methadone dosage, considerations are made with how heroin has been used before starting treatment to determine a dose that may work long-term.

Based upon long-term experience of experts in the field, plus the common knowledge that the mix and potency of street drugs vary continually and erratically, it is acknowledged that self-reports cannot reliably quantify the amount of illicit opioids used. Furthermore, due to the multiplicity of drugs, comprehensive measurement is expensive and is available only thru a handful of special labs. Thus, a standard method to measure illicit opioid use is the frequency of use each week, and is the approach we have taken.

Methods:

After Institutional Review Board approval and an NIH-issued Certificate of Confidentiality were obtained, interviews were begun in July of 2016 and are continuing. Participants were volunteers, recruited from one of three drug treatment facilities in New Jersey at which they were enrolled in at the time of the interview: Spectrum Healthcare Inc. (in Jersey City), The Lennard Clinic Inc. of Newark, and the Lennard Clinic Inc. of Elizabeth. Participants were eligible if they were 18 years or older. All participants consented to partaking in the study. No monetary compensation nor additional medical treatment was provided to those who participated. Data from the 221 participants to date are analyzed below.

Participants were interviewed by trained staff using a survey instrument, which was based on a 1984 cohort study of drug users in New Jersey conducted by S.H. Weiss, MD. There are eight sections in the current questionnaire: demographics, Hepatitis C, past medical history, HIV and AIDS, alcohol, smoking, drug use, and sexual history. Two versions of the questionnaire were administered during this one-year period; the original questionnaire was revised in December of 2016, based on results from the first version and an expanding set of goals. None of the questions analyzed here differed between the two versions. The questionnaire portion of the current interview took about 20 minutes to complete and contact information was collected on each participant in case any follow-up was needed. Interviews conducted through July 18, 2017 were used for the current analysis.

The drug use section asked if subjects were currently taking methadone or buprenorphine/naloxone and the dose they were taking. It also asked about drug use history, including age of first regular use of each drug and how frequently it was used per week.

All analyses were conducted in SAS (Cary, NC). Participants' levels of alcohol use were categorized based on the Dietary Guidelines for Americans (6, 7): see Table 1, which is gender dependent, based on longstanding understandings about differences in metabolism. Body weight also influences the effect of alcohol and its use, but was not incorporated in this analysis. One drink corresponded to intake of 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of hard liquor. These were separately quantified, and then combined into a measure of total drinks per week.

Table 1: Drinking Level Based on Number of Drinks per Week

Drinking Level	Abstain	Light	Moderate	Heavy
Females	$\leq 0.2^a$	0.21 – 3.99	4-7	>7
Males			4-14	>14

a. Less than ~1 drink per month was categorized as abstention.

Summary:

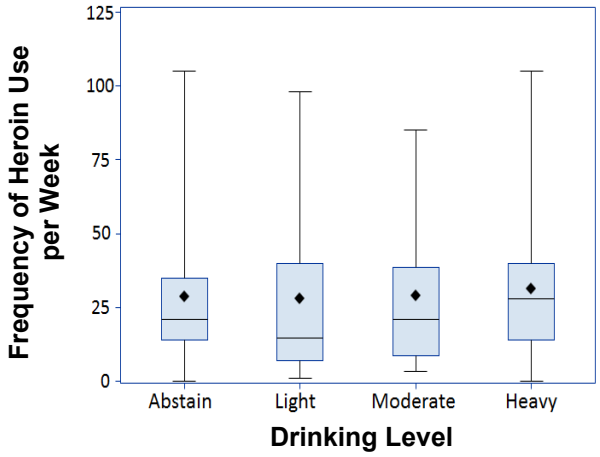
220 of our 221 participants quantified their alcohol use. Of the 220, 54.5% (120) were female. Most subjects were either abstainers or heavy drinkers, with nearly identical proportions as categorized in Table 1 by gender (Table 2). The proportion of light and moderate drinkers varied slightly between men and women – but was not statistically significant (Table 2).

Table 2: Drinking Level Based on Number of Drinks per Week

Drinking Level	Abstain	Light	Moderate	Heavy
Percent of Total (N = 220)	39.1%	14.1%	13.6%	33.2%
Percent of Females (N = 120)	39.2%	17.5%	10.0%	33.3%
Percent of Males (N = 100)	39.0%	10.0% 18.0%		33.0%

Of the 220 participants who quantified their alcohol use, 212 (96.4%) have used **heroin** on a regular basis at some point in their life, as displayed in Figure 1

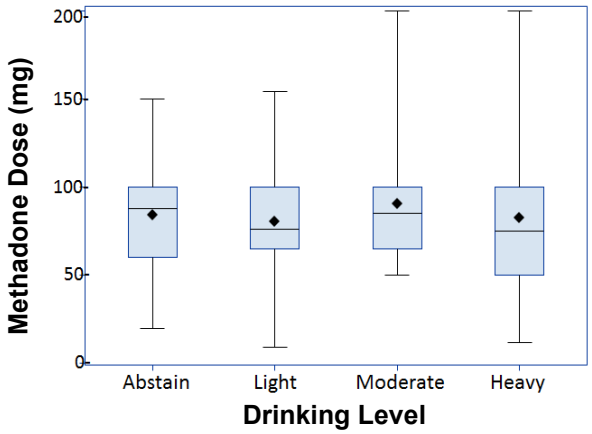
Figure 1: Distribution of Heroin Use (Winsorized Box and Whisker Plots), by Drinking Level (N =212). 2 persons used heroin 350 times/week & one used 280 times/ week; the next highest count was 105. To reduce the influence of outliers, the statistical technique "winsorization" was used: the outlying values of 280 & 350 were replaced by 105, the next highest value. For each drinking level, the responses were displayed in box & whisker plots: the diamond represents mean heroin use; whiskers, minimum and maximum; box, 1st, 2nd, and 3rd quartiles.



Among the non-abstainers (the light, moderate, and heavy drinkers), although the winsorized mean shows an increasing trend, it was not statistically significant (Table 3). The rate of heroin use is significantly higher in heavy versus light drinkers (p = 0.048, one-tailed median test, which compares counts above and below the median).

Of the 220 participants that were able to quantify the alcohol section, 214 were using **methadone** and gave information on their current methadone dose (Figure 3). [Of the 6 who were not included: 2 took buprenorphine/naloxone, 1 took neither buprenorphine/naloxone nor methadone, and 3 were unsure of their methadone dose.]

Figure 3: Distribution of Methadone Dose, by Drinking Level (N = 214) – box and whiskers plots. There were no obvious trends in either the means (Figure 3, to the right) or the median (Table 3, above) in methadone dose among these 4 drinking levels.



Conclusions:

Overall, in both heroin users and non-opioid heroin users, there is a trend toward more frequent opioid use with heavier alcohol use among non-abstainers. The increase in heroin and non-heroin opioid usage in heavier drinkers may not merely reflect an "addictive personality" to consume more, since a similar pattern is not seen with respect to methadone dose. Positive associations between alcohol use and opioid use may be due to a number of factors. In addition to biological effects such as those impacting μ -opioid receptors: e.g., there may be underlying psychological issues that can affect the propensity to consume psychoactive substances. One way of assessing the extent to which such psychological issues may be relevant is to examine the frequency of use of other common drugs, such as tobacco and marijuana. We plan to extend our analyses, using data already collected in our extensive surveys, to examine these substances.

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ANDIRUDH GOYAL (NJMS 2020)

PROJECT TITLE: **ROLE OF FIBROBLAST GROWTH FACTOR 21 (FGF21) AND ITS MODULATORSIN TUMOR GROWTH**
MENTOR: **MARIANNA S. DE LORENZO, PH.D.**
DEPARTMENT: **CELL BIOLOGY AND MOLECULAR MEDICINE**

Participation Description:
The project focused on studying the role of the natural FGF21 molecule in triple negative breast cancer. Much data has suggested the FGF21 marker to be elevated in metabolic states ranging from diabetes to obesity. Additionally, De Lorenzo et al. showed increased levels of FGF21 in RCC as well as mammary tumor cells. Our research focused on identifying the effects of FGF21 on proliferation and growth of the triple negative breast cancer tumor cells. To that end, I performed cell cultures and cell proliferation assays to assess for changes in TNBC cell line growth upon exposure to FGF21. Additionally, I worked to study the role of other potentially anti-neoplastic compounds such as curcumin and resveratrol to see how they may interact with TNBC cell lines, and so I prepared concentrations of those various drugs as well. To get a baseline, I measured how tamoxifen inhibited TNBC cell growth and compared it to the above findings. Dr. De Lorenzo previously performed assays to assess levels of FGF21 in cells and also Kaplan-Meier survivorship curves. Before entering the lab, CRISPR-Cas9 was also being performed and the first step of isolating the ss gRNA via flow cytometry was performed, and the data were collected for that as well.

Objective:
Triple negative breast cancer (TNBC) is vicious disease due to its lack of receptors for estrogen, progesterone and HER2/neu on cancer cells (Hudis et al.2011). Lack of these specific receptors limits the treatment options for TNBC patients. Obesity has been established a strong risk factor for developing postmenopausal breast cancer and furthermore increases the incidence of metastases in breast cancer patients.

The main premise of our project focuses on studying the role of the FGF21 on breast cancer. FGF21 is a metabolic regulator involved in a multitude of roles ranging from insulin sensitivity to fat storage. FGF21 is released mainly from liver cells but has also been shown to be released from adipocytes, skeletal muscle and even pancreatic cells (Beri et al. 2015). The pathology of obesity, along with diabetes and heart disease, has shown increased FGF21 levels. Despite increased levels, FGF21 has been previously suggested to play a myriad of protective effects in an attempt to reset homeostasis in the aforementioned various disease pathologies (Cheng et al. 2016). Recently, Dr. De Lorenzo and her collaborators reported that clear cell renal cell carcinoma patients (Knott et al. 2016) as well as mammary tumor patients have increased levels of circulating FGF21 (Knott et al., AACR 2015). It is still unknown whether the tumor itself or the tumor microenvironment promotes the increased circulating FGF21 secretion. But with this association established along with the link between obesity and breast cancer, we explored the role that FGF21 may play in TNBC tumor initiation and development in the following sets of experiments.

Because of the protective roles FGF21 plays in other metabolic disorders, we hypothesized that exogenous FGF21 administration would ultimately reduce levels of tumor growth and progression. Additionally, because of the link between obesity and TNBC, we chose to also explore the role environmental adipocytes (one of the main producers of FGF21) may play in the progression of tumor cells by exposing tumor cells to adipocyte-conditioned medium. Lastly, we evaluated products in our food which can modulate FGF21 like curcumin and resveratrol found which are known to modulate FGF21 in other systems. These compounds derived from spices and fruits have been suggested to play a beneficial role against inflammation in various pathological states like cancer, Alzheimer's disease and hepatocellular carcinoma (Mishra et al. 2009) and our goal was to study whether these compounds could also induce similar effects on TNBC cell lines.

Methods:

Cell Culture: Media from 4T1 or E0771 cell monolayers were aspirated. 4 mL of PBS was added to rinse any traces of medium in the plate and then aspirated. Another 4 ml of PBS was added with Trypsin-EDTA (10X) to facilitate a disaggregation of the cells. Cells from each plate was then added to a separate tube with 5 ml of growth medium and centrifuged. Upon centrifugation, medium was aspirated and the cellular pellet then was re-suspended in 2 ml of growth medium. A 40 µl of the re-suspended solution was isolated and mixed with a 40 µl of trypan blue dye to aid in visualization. Using the contrast phase microscope and the Neubauer chamber, the number of cells per ml was calculated in each case.

Cell Proliferation Assay. Before the seeding, 4T1/EO771 cell concentrations were calculated. Each 96 well plate either contained 10,000 or 15,000 cells/well. Basal medium, growth medium or 1% FBS were used as controls and were kept consistent throughout the treatment. Dilutions of each of the treatments of tamoxifen, resveratrol, curcumin and FGF21 were prepared using the same control medium. Specific dilutions were obtained from past literature. 1% FGF21 solution was used. All the dilutions and control for one treatment were distributed equally within 1-96 well plate.

Treatments: Concentrations used for Tamoxifen: 0-10 µM. Concentrations for Resveratrol were between 0-20 µM in all experiments. Concentrations for Curcumin were 0-20 µM in all experiments. After 24-48 hours (depending on cell confluence), the medium was removed and then a MTT/PBSsolution (0.5mg/ml) was added. 200 µl of diluted MTT was added per well and the entire plate was subsequently covered and incubated at 37ºC. After 3.5 hours, the MTT reagent was eliminated and 100 µl of DMSO was added to stop the reaction. Absorbance was measured at 560nm by spectrophotometer.

Differentiation of 3T3-L1 Cells into Adipocyte like Cells and Medium: 3.10^3 of 3T3-L1 cell were seeded in a 6 well plate. Cells were grown in DMEM (Dulbecco's Modified Eagle's medium) containing 10% Calf serum until cells were at roughly 70% confluency. Then, DMEM was aspirated and MDI (IBMX, dexamethasone, insulin medium was added to promote adipogenesis. After 72 hours, the MDI was aspirated and pure INS was added. After another 72 hours, the INS was aspirated and the DMEM was reintroduced. Once the adipocytes were differentiated, basal medium was added and incubated overnight to produce the adipose-conditioned medium.

Results and Representative Figures:

Role of Tamoxifen, Curcumin and Resveratrol in Breast Cancer Proliferation: Tamoxifen and Curcumin administration to both breast cancer cell lines curtailed proliferation. However, reduced cell proliferation was no seemingly significant decrease in cell growth when resveratrol was administered to either of the cell lines. Representative figures from each experiment are shown below. **Figure 1 and 2** show data for 4T1 for curcumin and resveratrol respectively.

Effect of Extra-Cellular Matrix Proteins on Cell Proliferation in the Presence of TNBC Inhibitors: Even with the coating of the plates with the extracellular matrix molecules laminin or fibronectin, 4T1 cell proliferation was still significantly reduced in the presence of Tamoxifen or Curcumin. **Figure 3** depicts proliferation on fibronectin plate for 4T1.

Role of Adipocyte-Conditioned Medium (ACM) Environment on Tumor Cell Proliferation: ACM significantly increased 4T1 cell growth but had no impact on E0771 cells. **Figure 4** shows proliferation increased in 4T1 cells in ACM.

Effect of Exogenous FGF21 Administration on Tumor Growth: Surprisingly, rFGF21 had an inhibitory effect on tumor growth in both the EO771 and 4T1 cell lines, suggesting that rFGF21 may play a protective role as an anti-neoplastic agent at least during the initiation phase of tumor. **Figure 5** shows 4T1 cells have reduced proliferation with rFGF21.

Conclusion:

Overall, we showed that curcumin and tamoxifen both successfully decreased the proliferation of both 4T1 TNBC lines as well as EO771 breast cancer cell lines. However, the reseveratrol data although showing a significant reduction in proliferation at higher doses; but it had opposite effects at lower doses. Given the strong past literature suggestion of resveratrol's role as an anti-oxidant and potentially anti-neoplastic agent, it is worth repeating the set of experiments for resveratrol. Our study also further corroborated the significance of a tumor microenvironment, specifically that which is inherent in obesity. When exposed to adipocyte conditioned medium, a significant increase in proliferation of 4T1 cells was observed. Certain growth factors may be released from adipocytes to stimulate this growth and because FGF21 can also be released by adipocytes, this can be further looked into. Interestingly, we demonstrated that it was shown that rFGF21 exogenous administration to 4T1 cells curtailed proliferation. Therefore, there is more support that FGF21 may play more a role as an anti-neoplastic agent beyond just being a biomarker at least at the earlier steps of tumorigenesis. It is worth further investigating the potentially antineoplastic role of FGF21. To that end, we are working to knock-out FGF21 by CRISPR-Cas9 in the E0771 mouse cells. We have currently isolated the sgRNA segments via the use of a vector with GFP and flow cytometry. Subsequently, we used PCR to ensure the appropriate sgRNA sequence was present in each clone. Our long term goal is to specifically identify the consequences of FGF21 knock-out *in vivo* and study the effects on tumor growth and metastases in a more realistic setting.

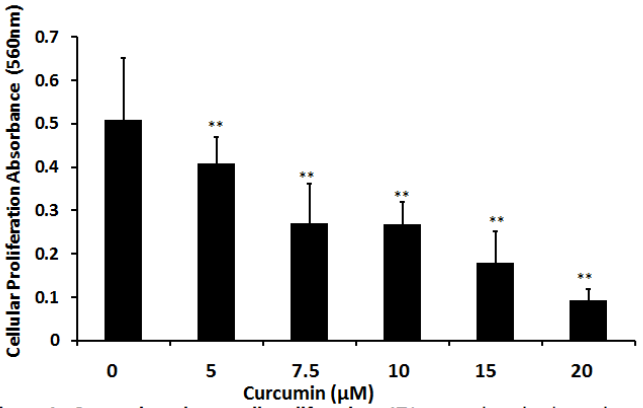

Figure 1: Curcumin reduces cell proliferation. 4T1 unsynchronized growing cultures in growth medium (1% FBS) were grown for 24 hours in the presence of Curcumin (0-20μM). The viability of 4T1 cells was reduced by Curcumin in a dose-dependent manner. ** p < 0.01 vs. 0 μM Curcumin.

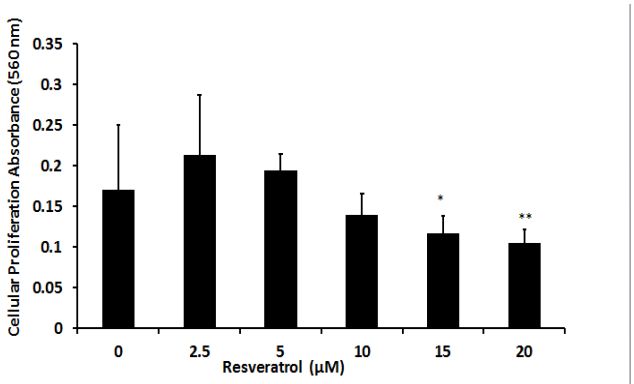

Figure 2: Resveratrol reduces cell proliferation. 4T1 unsynchronized growing cultures in growth media (1% FBS) were grown for 24 hours in the presence of Resveratrol (0-20μM). The viability of 4T1 cells was reduced by Resveratrol at higher concentrations. *p<0.05 and ** p < 0.01 vs. 0 μM Resveratrol.

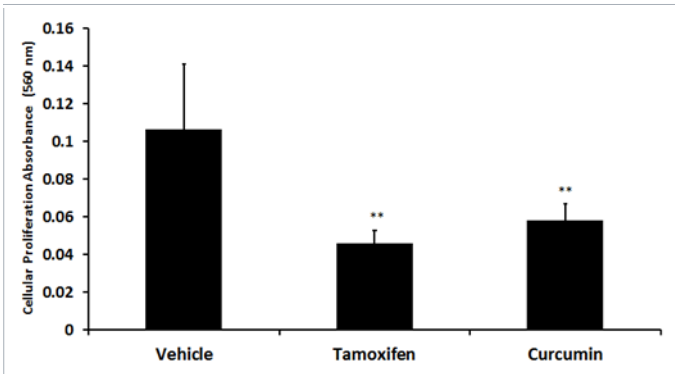

Figure 3: Tamoxifen and Curcumin reduce cell proliferation. 4T1 unsynchronized cells were seeded in laminin-coated wells in basal media for 48 hours in the presence of vehicle, Tamoxifen (4 μM) or Curcumin (4 μM). The viability of 4T1 cells was reduced by Tamoxifen and Curcumin in a dose-dependent manner. ** p < 0.01 vs. vehicle.

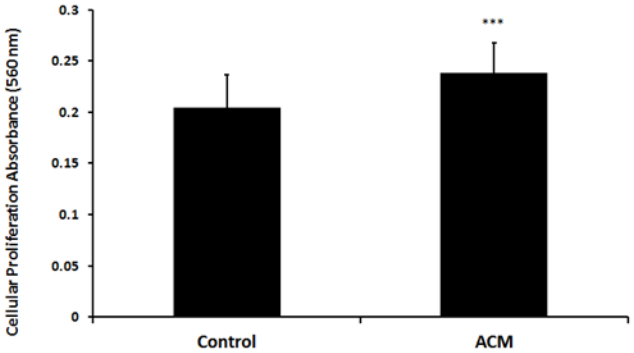

Figure 4: Adipocyte-Conditioned Media (ACM) increases cell proliferation. 4T1 unsynchronized growing cultures were grown for 24 hours in the presence of either adipocyte control media or adipocytes-conditioned media. The viability of 4T1 cells was increased by ACM. *** p < 0.001 vs. control.

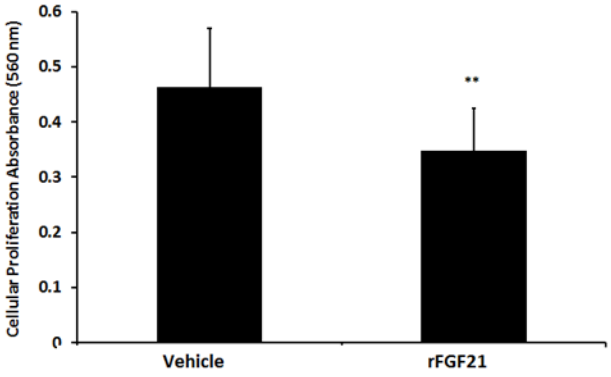

Figure 5: 4T1 Cell Proliferation was Reduced with Treatment of rFGF21. 4T1 unsynchronized growing cultures for 48 hours in medium containing vehicle or recombinant Fibroblast Growth Factor 21 (rFGF21, 10ng/ml). The viability of 4T1 cells was reduced by the rFGF21. ** $p < 0.01$ vs. Vehicle.

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JACK HABERL (NJMS 2020)

PROJECT TITLE: **PREDICTING SHORT-TERM COMPLICATION RISK OF PATIENTS TREATED WITH RADICAL RESECTION OF BONE TUMORS**
MENTOR: **KATHLEEN BEEBE, MD**
DEPARTMENT: **ORTHOPAEDICS**

Participation Description:

In this study, I alone conducted the literature review and led the writing of the abstract, manuscript, and poster. I worked with both Brianna Siracuse (MS3, NJMS) and Joseph Ippolito (PGY1, Orthopaedics Resident, NJMS) to identify risk factors on the State Inpatient Database and analyze the data using SAS and Microsoft Excel.

Objectives:

The American Cancer Society estimates that there will be 3,260 new cases of bone and joint cancer in the Unites States this year. Wide resection is currently the mainstay of treatment for many of these cancers; however, this treatment modality has a high rate of complications and hospital readmissions. Many of the present strategies aimed at reducing hospital costs focus on reducing the number of complications and readmissions. The purpose of this study was to use a large population-based statewide database to evaluate the potential risk factors associated with 30-day readmission following wide resection of bone tumors.

Methods:

Discharge data on 5,644 patients from New York, California, Florida, and Washington who underwent resection to treat either primary or metastatic bone tumors were collected from the State Inpatient Database, a part of the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality (2006-2011). Demographic and clinical characteristics were abstracted. Univariate and multivariate analyses were performed to determine which factors were associated with increased risk for readmission. All analysis was performed using SAS statistical software, version 9.3.

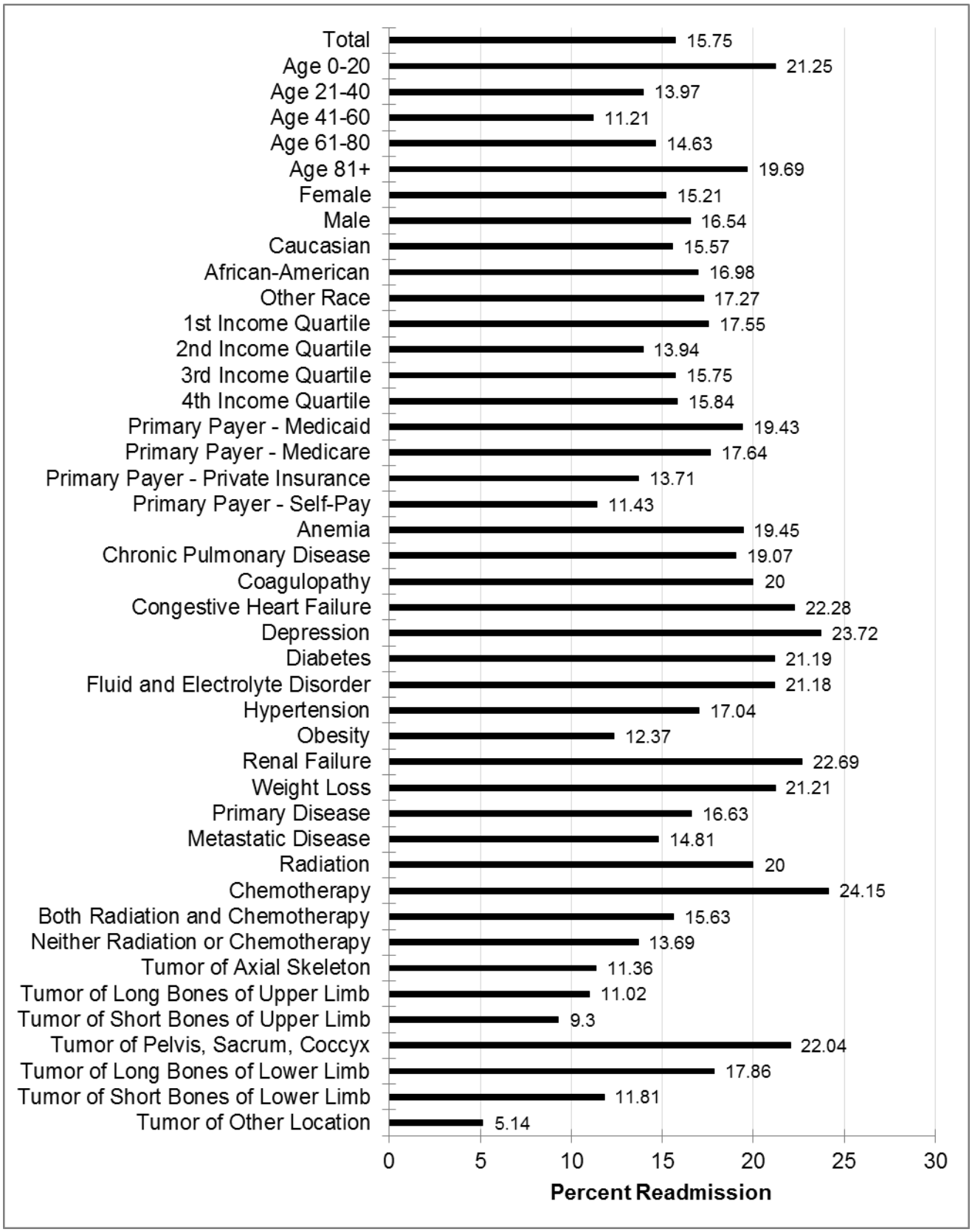
Summary:

The overall 30-day readmission rate for the patients with primary or metastatic bone tumors who underwent wide resection was 15.75%. The following factors were significantly associated with increased 30-day readmission rates: age ≤20 years (odds ratio (OR), 2.04; 95% confidence interval (CI), 1.56-2.68), depression (OR, 1.75; 95% CI, 1.34-2.29), diabetes (OR, 1.48; 95% CI, 1.20-1.82), and fluid and electrolyte disorder (OR, 1.43; 1.17-1.74). Resection of tumors of the pelvis, sacrum, and coccyx had the highest readmissions rates (22.04%) followed by resection of tumors of the long bones of the lower limb (17.86%). Adjuvant treatment with chemotherapy (24.15%) or radiation (20.00%) alone was also associated with higher readmission rates than treatment with both modalities together (15.63%) or when neither treatment modality was employed (13.69%), (p<0.01). Readmission rates were higher in the treatment of primary tumors (16.63%) than in the treatment of metastatic tumors (14.81%), (p<0.01). The top 3 primary causes for readmission were neutropenia (13.3%), post-operative infection (7.44%), and sepsis (3.98%).

Conclusions:

Several risk factors were identified as being associated with an increased risk for readmission following wide resection of bone tumors: age ≤ 20 years, depression, diabetes, fluid and electrolyte disorder, tumor location, treatment type, and primary disease. These factors should be identified in patients preoperatively, and attempts should be made to optimize these patients' conditions before and after surgery in order to reduce the risk of costly complications and readmissions.

Figure 1: Readmission Rates by Demographic and Clinicopathological Characteristics Among Patients with Bone Tumors



PAMELA JUMBO-CUEVA (NJMS 2020)

PROJECT TITLE: **MEASURING THE MAGNITUDE AND VALUE OF SALVAGED ITEMS FROM THE NJMS RECOVER INITIATIVE**
MENTOR: **ZIAD C. SIFRI, MD**
DEPARTMENT: **SURGERY**

Participation Description:

I participated in this project by assisting in the collection and selection of supplies during the months of June and July. I assisted other research staff in sorting items and adding their quantities to the online inventory system. I was also responsible for compiling inventory data between March and June of 2017 and analyzing it to produce the results and conclusions presented in this report. In terms of the future direction of this project, I was in charge of redacting multiple sections of the protocol document that will be submitted for Institutional Review Board (IRB) approval, which will allow us to administer surveys to donation recipients and assess the impact of our donations. I uploaded the surveys that were designed by other research staff to an online survey development software, so that they could be completed by donation recipients abroad upon IRB approval. Finally, I was responsible for contacting other medical recovery organizations to learn about their protocols and compare them to ours.

Objective:

The purpose of this study was to determine the amount, type, and value of medical supplies that could be salvaged from the University Hospital through RECOVER, a medical supply recovery initiative sponsored by the NJMS Center of Global Surgery. Clean and unused medical supplies were recovered from multiple sites at the University Hospital and then organized for donation after meeting World Health Organization (WHO) standards. Donation recipients are hospitals in low and middle income countries (LMICs) that lack access to such supplies and humanitarian surgical non-governmental organizations (NGOs), which rely on donations to provide surgical care in LMICs**.**

Every year, US academic medical centers discard approximately 2 million pounds of usable medical supplies and equipment, estimated to have a US $15 million value [1]. Meanwhile, many hospitals in impoverished communities in LMICs are unable to provide basic medical care due to the lack of necessary medical supplies and equipment, while clean and unused surgical kits, gauze, gloves, and sutures are some of the most abundant supplies discarded from operating rooms in the US [1-2].

Multiple medical supply and equipment recovery programs operate in the US, yet few published studies have assessed the different models used by such organizations. Assessment and publication of our collection protocols and results will hopefully provide further reference for other recovery initiatives in the US. By gathering data throughout our collection and selection process, we also aimed to identify what quantity of the salvaged supplies constituted useful and appropriate donations. Prior literature focuses on the items recovered from operating rooms in US academic institutions, while our approach expanded to other patient care areas.

Methods:

Medical supplies were recovered from 4 locations at the University Hospital. In addition to the main OR, we expanded our study to incorporate other collection sites at the University Hospital, including the surgical intensive care unit, doctor office center OR, and trauma bay. Salvaged supplies that were suitable for donation were selected and stored by volunteers.

Weights before and after selection were recorded and the net weight of usable supplies was obtained. Monetary values were estimated and assigned to each item to create a comprehensive inventory list. Inventory data between March and June of 2017 was analyzed to determine the most common and valuable items from each collection site, as well as their projected yearly yield and value. Finally, we projected the yearly value of donations that could be recovered if all US academic hospitals adopted a similar initiative

Summary:

Over a period of 4 months, we recovered 7,317 individual supplies with an estimated value of US $23,382. Supplies were recovered from the main operating room, surgical intensive care unit, doctor office center OR, and trauma bay at the University Hospital. From the bulk of collected items, a small amount was discarded and most of it was weighed and stored for future donation (Fig. 1). For instance, only 5% of the collected supplies from the SICU and 10% from the Main OR were discarded after selection. The main contributor based on both supply quantity and value was the Main OR (Fig. 2). The top 5 items based on quantity and value were analyzed for each locale (Table 1).

Top 5 Items by Amount Collected						Top 5 Items by Value					
Rank	Item	Amount	Value ($)	Amount/Year	Value/Year ($)	Rank	Item	Amount	Value ($)	Amount/Year	Value/Year ($)
UH Trauma Bay											
1	Saline Flush (10mL)	10	5.4	30	16.29	1	Suture (sterile/unexpired)	8	36.40	24	109.80
2	Suture (sterile/unexpired)	8	36.4	24	109.80	2	ACE bandage	2	12.96	6	39.09
3	Scalpel Blades	5	2.5	15	7.54	3	Betadine bottle (small)	2	10.62	6	32.04
4	Sterile Gloves	5	6.05	15	18.25	4	Betadine prep sponges	4	6.72	12	20.27
5	Betadine prep sponges	4	6.72	12	20.27	5	Sterile Gloves	5	6.05	15	18.25
UH DOC OR											
1	Sterile Gloves	208	251.68	627	759.20	1	Sterile Gloves	208	251.68	627	759.20
2	Suture (open or expired)	180	0	543	0.00	2	Bovie Pencils	12	204.72	36	617.54
3	Sterile Gloves (opened)	51	9.18	154	27.69	3	Gowns, Non-Sterile	23	132.25	69	398.94
4	Betadine prep sticks	26	43.68	78	131.76	4	Betadine prep sticks	26	43.68	78	131.76
5	Gowns, Non-Sterile	23	132.25	69	398.94	5	Betadine prep sponges	23	38.64	69	116.56
UH SICU											
1	Saline ampules	543	325.84	1638	0.00	1	Saline ampules	543	325.80	1638	982.79
2	Oral Care Set	33	1.65	100	4.98	2	Sequential compression devices (SCDs)	3	230.01	9	693.83
3	Silk tape (various sizes)	29	13.34	87	40.24	3	Disposable Stethoscope	4	99.92	12	301.41
4	Syringes (various sizes)	28	8.12	84	24.49	4	Pressure infuser	15	81.45	45	245.70
5	Needles (various gauge)	20	4.2	60	12.67	5	Suture (sterile/unexpired)	14	63.7	42	192.15
UH Main OR											
1	Blue Towels	353	924.86	1065	2789.87	1	Sequential compression devices (SCDs)	126	9660.42	380	29140.94
2	1/4 Sheets	225	337.50	679	1018.08	2	Bovie Pencils	60	1023.6	181	3087.72
3	Drapes	348	646.80	1050	1951.09	3	Blue Towels	353	924.86	1065	2789.87
4	Sterile Gloves (opened)	155	27.90	468	84.16	4	TED Stockings	54	808.92	163	2440.13
5	Sequential compression devices (SCDs)	126	9660.42	380	29140.94	5	Gowns, Non-Sterile	119	684.25	359	2064.06

Table 1: Top 5 items by amount and value for each collection site: UH Main Operating Room, Surgical Intensive Care Unit, Doctor Office Center OR, and Trauma Bay. Estimated annual quantities and values were extrapolated from 03/01/2017-06/30/2017 inventory data.

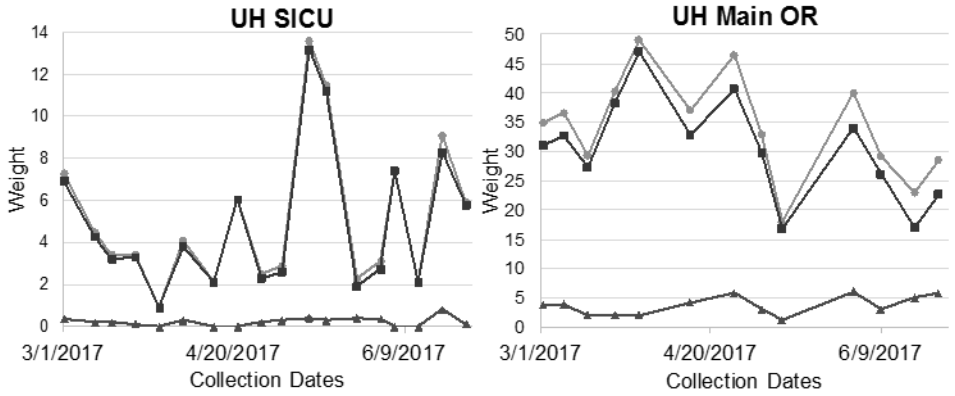


Figure 1: Weight of salvaged materials as a function of time for the UH Surgical Intensive Care Unit (UH SICU) and the UH Main Operating Room (UH Main OR). Data series include Total Weight □ , Trash Weight □ , and Net Weight □ . Obtained from 03/01/2017-06/30/2017 inventory data.

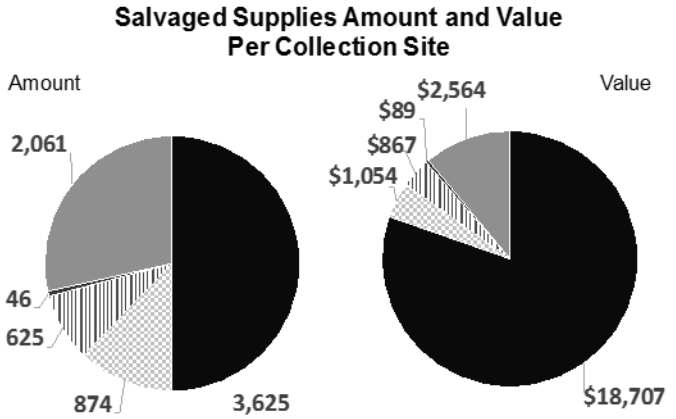


Figure 2: Breakdown of the value and amount of salvaged materials per collection site: UH Main Operating Room , Surgical Intensive Care Unit , Doctor Office Center OR , Trauma Bay , and miscellaneous donations . Obtained from 03/01/2017-06/30/2017 inventory data.

Conclusion:

The amount and the type of medical supplies salvaged from 4 locations at the University Hospital through RECOVER is steady and substantial. It varies significant by location with the Main OR being the biggest contributor. The collection sites at the University Hospital are projected to generate 21,813 items per year which have an estimated value of US $70,231. Collected materials were suitable for donation almost in their entirety, as assessed by the minimal trash weight produced after the selection of items.

By using our institution as a model, we can project the 232 academic hospitals in the US to produce over US $19 million of medical supplies suitable for donation annually. Thus, hospitals in LMICs and surgical humanitarian NGOs could greatly benefit from the widespread institution of supply recovery programs in US academic hospitals.

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KATRICE KARANFILIAN (NJMS 2020)

PROJECT TITLE: **MODIFIED ONE-PIECE EXTENDED TRANSBASAL APPROACH FOR ANTERIOR SKULL BASE LESIONS**
MENTOR: **JAMES LIU, MD**
DEPARTMENT: **NEUROSURGERY**

Participation Description:

This summer I worked on the "Modified One-piece Extended Transbasal Approach" project with Dr. Liu. I first did a literature review to gain a better understanding about the transbasal approach and the variety of modifications of this approach that have been previously proposed. I wrote a letter to the editor in regards to a recent publication which discussed a similar approach to Dr. Liu's, but did not cite his previous works. I went through Dr. Liu's patients and compiled the list of the 44 patients that had been treated with this surgical approach. I then conducted a retrospective review of these patients' charts, including their operative reports, radiographs, and post-operative follow-up notes. After sorting the patient information including categorizing their pathologies and extent of their resections, I wrote a draft of the manuscript. The manuscript describes this surgical approach, evaluates the outcomes of the 44 patients treated with this approach, and analyzes its strengths compared to the other variations of the transbasal approach.

Objective:

The transbasal approach is used in the resection of a variety of intradural and extradural skull base pathologies. It consists of a bifrontal craniotomy using a bicoronal incision. In the standard transbasal approach, the inferior margin of the bone flap is a horizontal line above the supraorbital bar, which can leave bony overhang that impairs visualization of the anterior skull base. While many modifications of this approach have been developed, these techniques center around adding additional osteotomies of the suparobital bar or nasion. In the modified one-piece extended transbasal approach, the anterior frontal sinus is incorporated into the bone flap allowing for the osteotomy to follow the contour of the anterior cranial fossa in the coronal orientation. This enables the bone flap to be removed in one piece, providing excellent visualization of the anterior skull base, while leaving the supraorbital bar intact.

The objective of this project was to describe the surgical procedure of the modified one-piece extended transbasal approach and analyze the outcomes of patients treated with this technique.

Methods:

From 2007 to 2016, 44 patients (26 females, 18 males) with anterior skull base lesion were treated with the modified one-piece extended transbasal approach. This was combined with an endoscopic endonasal approach in 15 patients who had lesions extending into the sinonasal cavity. Two patients had the transbasal approach combined with a pterional approach for pathologies which extended more laterally. 45 total lesions were treated in the 44 patients because one patient had two different pathologies.

A retrospective review of these patient charts and radiographs was performed to determine the type of lesions that can be treated with this approach, the extent of resection, and any complications that arose.

Summary:

The following 45 lesions were treated: 29 anterior skull base meningiomas (including olfactory groove, orbital frontal, parafalcine, parasagittal, planum sphenoidale, sphenoid wing, and tuberculum sellae), four craniopharyngiomas, one esthesioneuroblastoma, one granulomatous lesion, one fibroma, one mucocele, one prolactinoma, one Rathke cleft cyst, one sinonasal teratocarcinosarcoma, one sinonasal undifferentiated carcinoma, two squamous cell carcinomas, one suprasellar juvenile palisading astrocytoma, and one suprasellar metastasis (Table 1).

Gross total tumor removal was achieved in 31/44 patients (70.45%), near-total resection in 8/44 patients (18.18%), and subtotal resection in 5/44 patients (11.36%). Self-retaining and subfrontal retractors were only used in 15 patients.

Complications included two cases of intracranial hypotension requiring blood patching, one case of pressor-induced posterior reversible encephalopathy syndrome, and a bone flap infection. The five patients with the Rathke cleft cyst and craniopharyngiomas. The five patients with craniopharyngiomas and the rathke cleft cyst developed diabetes insipidus. Two of these patients also experienced panhypopituitarism. One patients had delayed hydrocephalous and required placement of a VP shunt. There were no CSF leaks or retraction injuries.

19 patients had radiation therapy or chemotherapy after their surgery. A double-flap technique was used in reconstruction for nine of the patients who were expected to have radiation or chemotherapy post-operatively.

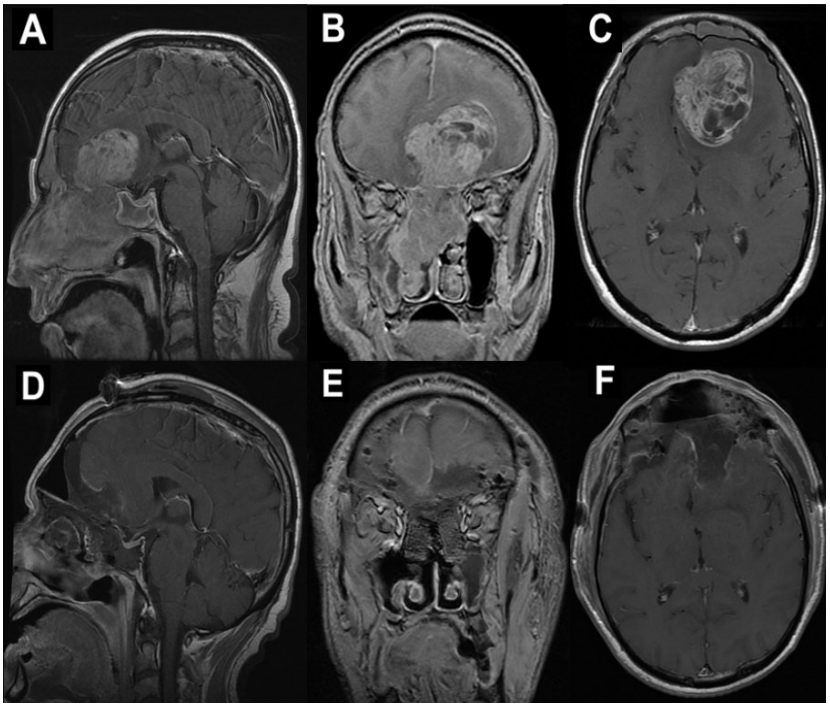


Figure 1. Preoperative (**A**: sagittal; **B**: coronal; **C**: axial views) and postoperative (**D**: sagittal; **E**: coronal; **F**: axial) MRIs of a 63-year-old male patient with sinonasal teratocarcinosarcoma who was treated with a one-piece extended transbasal approach.

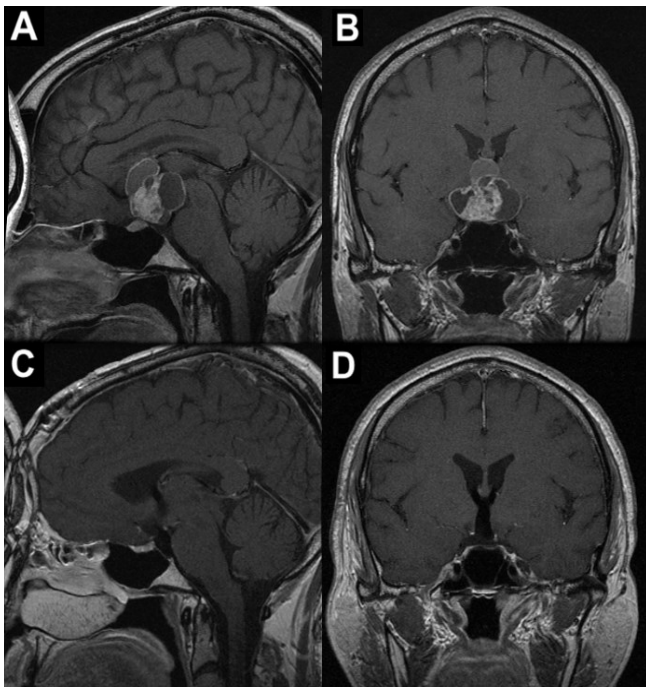


Figure 2. Preoperative (**A**: sagittal, **B**: coronal) and postoperative (**C**: sagittal, **D**: coronal) MRIs of a 50-year-old male patient with a retrochiasmatic craniopharyngioma**.**

	Number of Cases
Anterior Skull base Meningioma	29
Olfactory Groove	18
Orbital Frontal	1
Parafalcine	2
Parasagittal	2
Planum Sphenoidale	1
Sphenoid Wing	2
Tuberculum Sellae	1
Other	2
Craniopharyngioma	4
Ethesioneuroblastoma	1
Granulomatous Lesion	1
Fibroma	1
Mucocele	1
Prolactinoma	1
Rathke Cleft Cyst	1
Sinonasal teratocarcinosarcoma	1
Sinonasal Undifferentiated Carcinoma (SNUC)	1
Squamous Cell Carcinoma	2
Suprasellar Juvenile Palisading Astrocytoma	1
Suprasellar Metastasis	1
Total	45 Lesions (in 44 patients)

Table 1. Distribution of 45 lesions treated with the modified one-piece extended transbasal approach in 44 patients from 2007-2016.

Conclusions:

This study has demonstrated that the modified one-piece extended transbasal approach is a versatile technique that is effective in treating a wide variety of skull base pathologies with excellent resection and minimal complications.

ALVIN MATHEW (NJMS 2020)

PROJECT TITLE: **FURTHER ELUCIDATION OF GM1 GANGLIOSIDE DEFICIENCY IN THE ETIOLOGY OF SPORADIC PARKINSON'S DISEASE (PD)**

MENTOR: **ROBERT LEDEEN, PH.D.**

DEPARTMENT: **PHARMACOLOGY, PHYSIOLOGY & NEUROSCIENCE**

Participation Description:

For the first two weeks of the project, Itrained and worked closely with my mentor to learn all the techniques required to complete the project. This included many skills and assays, such as: RNA extraction, DNase treatment, conversion of RNA to cDNA, and running RT-PCR. For the remainder of the project, Iwas left in charge to run the project rather independently. I performed all scientific procedures with pre-approval and consultation from my mentor and then presented my results. I also used Microsoft Excel to calculate fold change in gene expression using the comparative CT method.

Objective:

Previous studies have shown that a GM1 ganglioside deficiency predisposes individuals to Parkinson's Disease (PD) and that PD patients have a significant systemic deficiency in GM1.A subgroup of PD patients also have a mutation in the glucocerebrosidase (GBA) gene and individuals with GSA mutations also have a higher incidence of PD, usually with more severe phenotypes. This project aimed to take these concepts one step further upstream to investigate if the GM1 deficiency in PD patients is caused by decreased expression of the genes responsible for its production as well as to investigate the possible role of GBA mutations in the process. The ultimate goal is to understand the etiology of sporadic PD and its variants and implement a new therapy based on that understanding.

Methods:

A total of 8 peripheral blood mononuclear cells (PBMC) samples were assayed: 3 PD patients, 3 age-matched controls, and 2 PD-GBA patients. RNA was extracted, converted to cDNA, and used to run RT-PCR to measure gene expression in 4 genes which contribute to the

biosynthetic pathway of GM1: ST3GAL2, ST3GAL5, B4GALNT1 , and 83GALT4 (Figure 1). A 5th gene, GAPDH, was assayed as an endogenous control. Cycle Threshold (CT) values from raw data were normalized to GAPDH to obtain 6CT values. Gene expression was then estimated by the comparative CT method to determine fold change in gene expression.

Summary:

Expression of all genes were equivalent between the 3 groups except for one gene, B4GALNT1, which showed decreased expression in PD and PD-GBA patients. Expression of the B4GALNT1 gene had a 0.26 fold change in PD patients as compared to controls. Expression of the B4GALNT1 gene had a 0.00063 fold change in PD-GBA patients as compared to controls, indicating even more reduction in gene expression than in regular PD patients. In fact , expression of that gene by PD-GBA patients was always below the threshold of detection.

Conclusion:
The data suggests that decreased expression of the B4GALNT1 gene specifically is what causes a GM1 deficiency. The other 3 genes showed no real difference between PD and controls. While regular PD patients show a moderate decrease in expression of B4GALNT1, PD-GBA patients show severe reduction in expression of that gene. This finding supports previous TLC analyses that revealed GM1 and GD1a are reduced in PD patients as compared to controls and are even more reduced in PD-GBA patients (Figure 5). Therefore, GBA mutations, by some unknown mechanism, enhance the reduction in expression of B4GALNT1 and therefore cause enhanced decrease in GM1, beyond that experienced by regular PD patients

EMILY MOORE (NJMS 2020)

PROJECT TITLE: **DELIRIUM AND SPATIAL NEGLECT AMONG STROKE SURVIVORS DURING IN PATIENT REHABILITAITION**

MENTOR: **OLGA BOUKRINA, PH.D., A.M. BARRETT, MD**

DEPARTMENT: **PHYSICAL MEDICINE AND REHABILITATION, KESSLER FOUNDATION**

Participation Description:

Before beginning my project, I consulted with Dr. Boukrina and Dr. Barrett to plan a retrospective study examining delirium and spatial neglect in stroke survivors in the inpatient rehabilitation setting. I reviewed the admission charts of 628 stroke patients admitted to Kessler Institute for Rehabilitation in West Orange, NJ. Oluwadamilola Thomas documented stroke side, presence of delirium search term(s), and presence of aphasia search term(s) for all patients, and I corrected errors in this documentation. I documented the presence or absence of alcohol use disorder, antibiotic use, antipsychotic use, dementia, depression, hearing loss, infection, polypharmacy, surgery, and vision loss for all delirious patients; and the presence of antibiotic use, antipsychotic use, and polypharmacy for all non-delirious patients. I removed patients based on several exclusion criteria, including bilateral stroke and unspecified stroke side. I documented whether each chart mentioned the presence or absence of spatial neglect. Following chart review, I conducted statistical analyses using SPSS software, including chi squared tests and logistic regression. Finally, I created a poster for the Summer Student Research Program symposium and wrote an abstract based on my project. Throughout the summer, I also had the opportunity to work with Dominique Bryant and Rama Bikkina to administer the Confusion Assessment Method (CAM) and Behavioral Inattention Test (BIT) to patients of Dr. Radhika Bapineedu; attend rounds with Dr. Barrett; attend behavioral rounds led by Dr. Maha Yousef; learn about the KF-NAP and prism adaptation therapy; and review relevant literature on spatial neglect and delirium.

Introduction:

Delirium is an acute state of disturbed attention and cognition.[1] Clinical diagnosis of delirium requires acute onset mental status change, inattention, and disorganized thinking and/or altered level of consciousness.[2] Disorientation, psychomotor problems, and other symptoms of delirium indicate increased severity.[2] Spatial neglect is the failure to report, respond to, or orient to contralesional stimuli following a brain injury when such failure cannot be attributed to other underlying deficits or disorders and is associated with functional disability.[3,4] A patient with spatial neglect suffers from diminished perception and mental representation of the side of space opposite a brain injury as well as premotor dysfunction manifested as impaired direction of action, particularly on the side of the body opposite the brain lesion.[4]

Despite the availability of clinical assessments for delirium, such as the Confusion Assessment Method (CAM), and spatial neglect, such as the Behavioral Inattention Test (BIT) and Kessler Foundation Neglect Assessment Process (KF-NAP), both conditions remain underdiagnosed.[2,5,6,7,8] Improved identification is critical since delirium and spatial neglect complicate stroke recovery. Delirium worsens mortality and functional abilities while costing the healthcare system billions of dollars.[1] Spatial neglect necessitates specialized post-stroke care and stresses caregivers responsible for these patients.[3] Both conditions keep patients hospitalized longer.[1,3] Without consistent delirium and neglect screening of stroke survivors, these hidden disorders will continue to negatively affect functional outcomes after stroke.

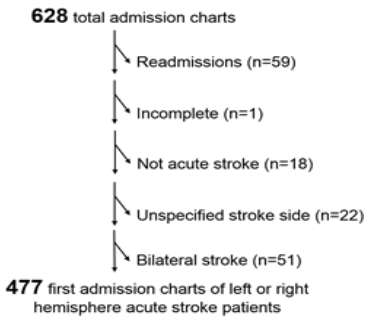
Delirium affects up to half of right brain stroke patients; about half of right stroke patients also experience spatial neglect.[1] Delirium and spatial neglect cause many of the same symptoms, including inattention, impaired memory, perceptual disturbances, and disorganized thinking.[1] Given the striking similarities between delirium and spatial neglect, it has been proposed that the disturbance of right brain-dominant cortical and subcortical attention and arousal pathways causes delirium and spatial neglect to co-occur after right stroke.[1] One of these pathways is the Ascending Reticular Activating System (ARAS), a series of nuclei beginning in the brainstem that travel up to the cerebral cortex.[1] Sensory deprivation created by spatial neglect could also facilitate the onset of delirium.[1]

Objectives:

1. To determine if delirium and spatial neglect are more common following right than left brain stroke, we investigated the incidence of delirium and spatial neglect among stroke survivors undergoing inpatient rehabilitation
2. To determine if delirium and spatial neglect co-occur, we investigated the incidence of both conditions among stroke survivors undergoing inpatient rehabilitation
3. To determine if medication use predicts the presence of delirium, we examined polypharmacy, antibiotic use, and antipsychotic use among stroke survivors undergoing inpatient rehabilitation

Methods:

Participants



We examined admission charts of 628 stroke patients (259 males, 218 females) admitted to Kessler Institute for Rehabilitation (KIR) in West Orange, NJ, between 3/4/2015 and 3/28/2016. The mean age was 66.94 years (SD=14.28, range 17-97). For patients with multiple admissions to KIR between the above dates, only the earliest chart was considered in the final data analysis. Complete exclusion criteria are outlined here.

Figure 1. Flow chart of medical records reviewed and included in final data analysis

Procedures

Searching electronic medical records (EMRs) for key terms associated with delirium may locate patients who suffer from this condition.[9] We adopted this method to check electronic medical records of stroke patients for indications of aphasia, delirium, and spatial neglect. Aphasia is a communication disorder whose impact on speech and comprehension may mimic symptoms of delirium. Therefore, charts indicating both delirium and aphasia were not marked as positive for delirium. Stroke side, polypharmacy, antibiotic use, and antipsychotic use were also noted during chart review. Complete search criteria are provided below.

CONDITION	CRITERIA
Aphasia	"Aphasi-", "communic-"
Delirium	Mental status change, change in mental status, altered mental status, disoriented, reoriented, unresponsive, agitation, agitated, confused, confusion, delirium, delirious, sitter, one-to-one, restraints, haloperidol, Haldol, antipsychotic, attention problem, impaired attention, inattentive, inattentions, disorganized, disorganized thinking, dazed, uncooperative; the "Mental Status" section of the chart was also examined for other language consistent with delirium
Spatial neglect	"Neglect"
Polypharmacy	Taking at least four medications upon admission to KIR
Antibiotic use	History of antibiotic use, taking/placed on antibiotic(s) upon admission to KIR
Antipsychotic use	History of antipsychotic use, taking/placed on antipsychotic(s) upon admission to KIR

Table 1. Criteria used to determine the presence of aphasia, delirium, spatial neglect, polypharmacy, antibiotic use, and antipsychotic use

Data Analysis

Objective 1. To assess the association between stroke side and delirium status, a chi squared test was performed using SPSS software.

Objective 2. To assess the association between delirium and neglect, a chi squared test was performed using SPSS software.

Objective 3. To assess whether polypharmacy, antipsychotic use, and antibiotic use can predict delirium status, a logistic regression was performed using SPSS software.

Summary:
Objective 1. The incidence of delirium was significantly higher following right hemisphere stroke. X^2 (1) = 6.572, p = .010. The incidence of spatial neglect was also significantly higher following right hemisphere stroke. X^2 (1) = 22.723, p = .000.

Objective 2. The incidence of spatial neglect was not significantly higher among delirious patients. X^2 (1) = 1.075, p = .300.

Objective 3. More than 95% of the patients were taking at least four medications upon admission, so polypharmacy was not studied in the final analysis. Neither antipsychotic (p = 0.310) nor antibiotic use (p = 0.805) significantly predicted the presence of delirium.

Conclusion:
The frequency of post-stroke delirium (27.3%) was consistent with recent reviews (10-27%); however, the nature of retrospective chart review may overestimate rate of delirium.[10] For example, 9.09% of patients with delirium had dementia. Chart terms reflecting dementia may overlap with those reflecting delirium. The incidence of delirium in right brain stroke survivors (33%) was consistent with previous work showing that delirium may develop in as many as half of right brain stroke patients.[1] The comparison of the incidence of delirium among right (33%) and left (22.5%) brain stroke survivors was consistent with previous studies showing that delirium is more common after right brain stroke.[1] The comparison of the incidence of spatial neglect among right (15.3%) and left (3.1%) brain stroke survivors was consistent with previous work showing that spatial neglect is more common after right brain stroke.[3]

Only 69 (14.47%) admission charts included in our analysis mentioned spatial neglect, which is unsurprising since past work has shown spatial neglect to be underreported by clinicians.[11] This could explain the unexpectedly low frequency of spatial neglect among right hemisphere stroke survivors (15.3%), which differs from previous work stating that the frequency of spatial neglect among right brain stroke survivors is closer to half.[1] This might also explain why the incidence of spatial neglect was not significantly higher among delirious patients compared to non-delirious patients. Notably, of the 69 charts mentioning neglect, 41 indicated presence of neglect and 28 indicated absence of neglect. Of the 41 charts indicating presence of neglect, 14 contained evidence of delirium. All 14 charts positive for neglect and delirium were from right brain stroke patients, supporting the hypothesis that disruption of right-brain dominant cortical and sub-cortical networks responsible for spatial attention and arousal leads to the co-occurrence of the two conditions.[1]

Due to limited number of charts mentioning neglect, we cannot rule out the idea that spatial neglect contributes to the onset of delirium. The actual incidence of spatial neglect among right brain stroke survivors is likely higher than the one we obtained. Delirium among the right brain stroke patients in our sample may have stemmed from undocumented and/or unrecognized spatial neglect. Our results highlight the need for improved assessment and documentation of spatial neglect and delirium among stroke patients.

Consistent with previous work highlighting polypharmacy as a delirium risk factor in older patients in hospitals, most delirious patients were taking four or more medications upon admission.[12] This was true for non-delirious patients as well. Future studies should obtain the average number of admission medications taken by stroke patients and redefine polypharmacy based on the average. Given that delirium status was not predicted by antibiotic or antipsychotic use, number of admission medications may matter more than type when it comes to predicting delirium status.

To further test the hypothesis that right brain cortical and subcortical networks damaged during right stroke lead to co-occurrence of delirium and spatial neglect, future work should include a prospective study of delirium and spatial neglect in stroke patients in the inpatient rehabilitation setting. This should include routine, repeated clinical testing for delirium and spatial neglect in every patient admitted to an inpatient rehabilitation facility following stroke.

Acknowledgements/Disclosures

We would like to thank Oluwadamilola Thomas for her initial medical record review; Dr. Radhika Bapineedu, Dr. Maha Younes, Dominique Bryant, and Rama Bikkina for clinical collaboration; the Stroke Rehabilitation Research team at Kessler Foundation; and the NJMS Office of Research/Summer Student Research Program. No disclosures apply. This work was funded by Rutgers New Jersey Medical School and Kessler Foundation.

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REID MUENZEN (NJMS 2020)

PROJECT TITLE: **IS METHADONE DOSE ASSOCIATED WITH SUCCESS IN METHADONE MAINTENANCE**
MENTOR: **STANLEY H. WEISS, MD, DANIEL ROSENBLUM, PH.D.**
DEPARTMENT: **MEDICINE**

Participation Description:
This summer, I worked with Dr. Weiss and Dr. Rosenblum as the research study coordinator for their study that focused on drug users. I worked alongside another SSRP student, Lea George, and performed many similar tasks as she did. As a first step, I completed the human subjects training and thoroughly acquainted myself to the study protocol, to which I was then added. As part of the project, I was encouraged by my preceptor to both critically evaluate the methodological implementation strategies during continual discussion of the data issues and explore topics of importance. I contributed toward developing a new, more comprehensive questionnaire instrument that will be used at some future juncture and prepared a draft document of the rationale behind proposed changes for the IRB.

For the current field study, I was trained to be an interviewer, practiced, and observed on multiple occasions, and then gained approval to be part of a team of interviewers at collaborating drug treatment programs in our region. I administered in person and explained to treatment program clients the study design, obtained written consents, and interviewed the clients. I was trained on editing procedures, and vigorously edited the questionnaires that I administered. The study procedures required that there always be a second reviewer before data entry and thus, I also edited those administered by others. I identified items that needed to be clarified and discussed resolutions of problems with my preceptors. As the study coordinator for the summer, I was responsible for supervising other medical, graduate, as well as undergraduate students in delegating work. In total, I made 17 trips to the facilities and performed 16 interviews. In the end, the team I supervised performed 47 interviews and contacted over 150 individuals in advertising the study.

Then after working in the field for 6+ weeks, our preceptor asked us to create our own questions that we would like to analyze based off experiences in interviewing. Afterwards, I turned to the primary literature to better focus my ideas. To better understand methadone prescribing practices, I met with the treatment program physician at one of the facilities. After deciding on a single topic, I pursued it and spent the remaining weeks working on the analysis of data. To do so, I identified which variables and in what ways they should be examined to help Dr. Rosenblum write programs in SAS that provided me with data output for analyses. After analysis was complete, I completed the poster.

Objective:
Methadone hydrochloride, a synthetic μ-opioid-receptor agonist, is used in the treatment of opioid addiction and is given as a daily medication.[1] By blocking the euphoric effect of shorter acting opioids such as heroin, methadone removes the so-called “narcotic-hunger.”

- Methadone dose is inversely correlated with illicit opioid use.[2]
- A 1998 consensus report by the NIH stated that although abstinence may be obtained with 60 mg/day, many need a higher dose.[3]
- In two studies, >50 mg/day and 60-100 mg/day doses were better than lower doses in preventing illicit opioid use.[4,5]
- A ≥100 mg/day dose had even lower rates of illicit opioid use than doses of <100 mg/day.[6]

If a higher daily maintenance dose of methadone more effectively blocks the euphoric effects of heroin, we propose that methadone dose is positively correlated with both length of time in treatment and phase status. Those that remain in MMT are able to abstain from illicit opioids with a dose that allows them to avoid relapse. On the other hand, those that do relapse must subsequently have their dose increased by the clinic physician to prevent any further relapse.

Methods:

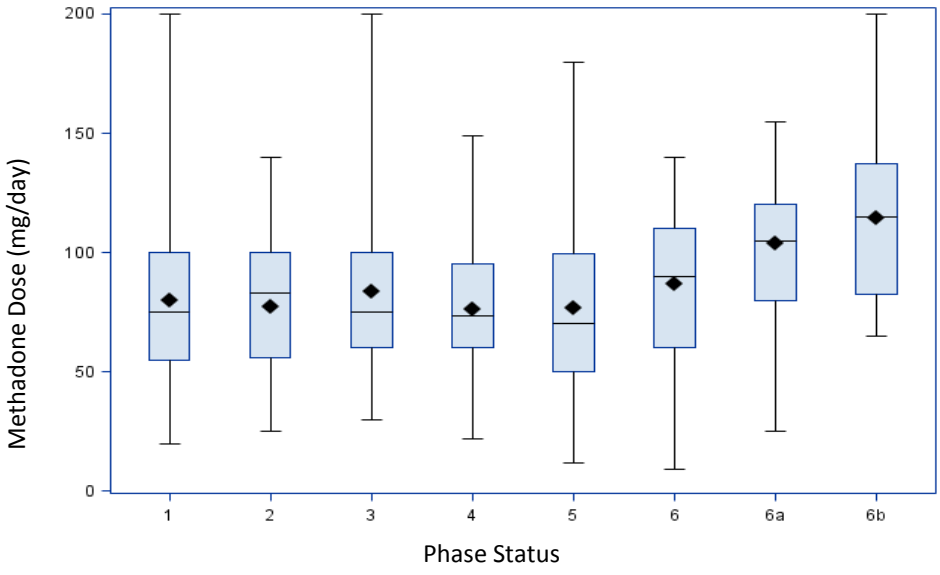
Between July 2016 and July 2017 (study ongoing), participants 18+ in age were recruited from 3 outpatient opioid treatment facilities in our area. Participation was voluntary and no medical treatment or monetary compensation was provided. The study was IRB approved. Data is protected by a Certificate of Confidentiality from the National Institute of Drug Abuse. Signed consent was obtained. Subjects' phase was ascertained by asking their frequency of visits for medication and how many take-home-bottles they received, and sometimes supplemented by treatment program records. A trained research staff member administered the questionnaire in a private, one-on-one setting at each center. To assess whether a patient still used illicit opioids in treatment, the date of enrollment in treatment was compared with the subjects' self-reported date of last heroin or other illicit opioid use.

Summary:

Of the 221 subjects interviewed, methadone dose was analyzed for 214 subjects. (The 7 not included were: 2 taking buprenorphine/naloxone, 3 did not know their dose, 1 refused to answer, and 1 reported not taking either buprenorphine/naloxone or methadone.) The mean dose for females was 82.838 mg/day (N=117); males 85.072 (N=97). Analyzed by race and ethnicity, the mean dose for African Americans was 76.816 mg/day (N=98), Hispanics 88.356 (N=59), Caucasians 92.556 (N=54), and other 68.333 (N=3).

With a longer time in treatment, or advancing phase, methadone dose does not necessarily increase. It was relatively constant for phases 1 through 5, as displayed in Figure 1; for statistical comparison, phases 1 through 5 were grouped. Starting with phase 6, methadone dose increases with phase. The difference between dose in phase 6 and phases 1 through 5 does not reach statistical significance, while mean doses in both phases 6a and 6b are significantly higher than in phases 1 through 5 (see table 2).

Figure 1: Methadone dose and phase of treatment (Diamond represents mean; whiskers, max and min doses; box 1st, 2nd, and 3rd quartiles, N=214)



Although the methadone dose often progressively changes during treatment, for our analysis we used the reported dose at the time of interview. The drug treatment physician, in consultation with the drug treatment counselor, is responsible for individually adjusting a patient's dosage.

In MMT, phases of treatment are designated 1, 1a, 2, 3, 4, 5, 6, 6a, and 6b.[7] The higher the phase, the more take-home-bottles the subject is given for self-medication. At phase 1, a client is required to come in for supervised medication each day the clinic is open. Those who abstain from illicit opioids can gradually progress to 6b after 3 years (see table 1).

Table 1: Phase designation as per NJAC 10_161B Licensure of Substance Abuse Outpatient Facilities[7]

Phase	1	2	3	4	5	6	6a	6b
Months illicit drug free	< 3	3-6	6-9	9-12	12-18	18-24	24-36	36+

If a higher daily maintenance dose of methadone more effectively blocks the euphoric effects of heroin, we propose that methadone dose is positively correlated with both length of time in treatment and phase status. Those that remain in MMT are able to abstain from illicit opioids with a dose that allows them to avoid relapse. On the other hand, those that do relapse must subsequently have their dose increased by the clinic physician to prevent any further relapse.

Methods:

Between July 2016 and July 2017 (study ongoing), participants 18+ in age were recruited from 3 outpatient opioid treatment facilities in our area. Participation was voluntary and no medical treatment or monetary compensation was provided. The study was IRB approved. Data is protected by a Certificate of Confidentiality from the National Institute of Drug Abuse. Signed consent was obtained. Subjects' phase was ascertained by asking their frequency of visits for medication and how many take-home-bottles they received, and sometimes supplemented by treatment program records. A trained research staff member administered the questionnaire in a private, one-on-one setting at each center. To assess whether a patient still used illicit opioids in treatment, the date of enrollment in treatment was compared with the subjects' self-reported date of last heroin or other illicit opioid use.

Summary:

Of the 221 subjects interviewed, methadone dose was analyzed for 214 subjects. (The 7 not included were: 2 taking buprenorphine/naloxone, 3 did not know their dose, 1 refused to answer, and 1 reported not taking either buprenorphine/naloxone or methadone.) The mean dose for females was 82.838 mg/day (N=117); males 85.072 (N=97). Analyzed by race and ethnicity, the mean dose for African Americans was 76.816 mg/day (N=98), Hispanics 88.356 (N=59), Caucasians 92.556 (N=54), and other 68.333 (N=3).

With a longer time in treatment, or advancing phase, methadone dose does not necessarily increase. It was relatively constant for phases 1 through 5, as displayed in Figure 1; for statistical comparison, phases 1 through 5 were grouped. Starting with phase 6, methadone dose increases with phase. The difference between dose in phase 6 and phases 1 through 5 does not reach statistical significance, while mean doses in both phases 6a and 6b are significantly higher than in phases 1 through 5 (see table 2).

Figure 1: Methadone dose and phase of treatment (Diamond represents mean; whiskers, max and min doses; box 1st, 2nd, and 3rd quartiles, N=214)

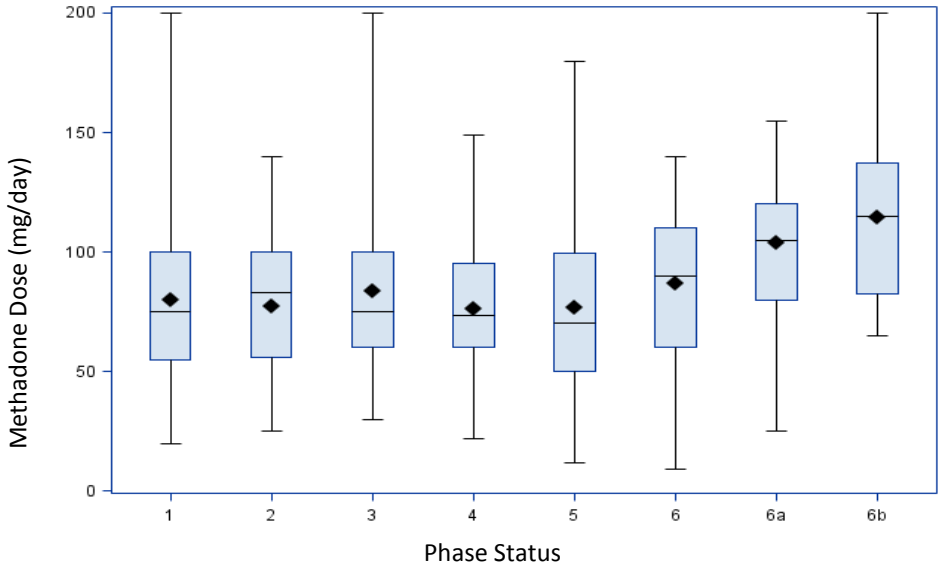
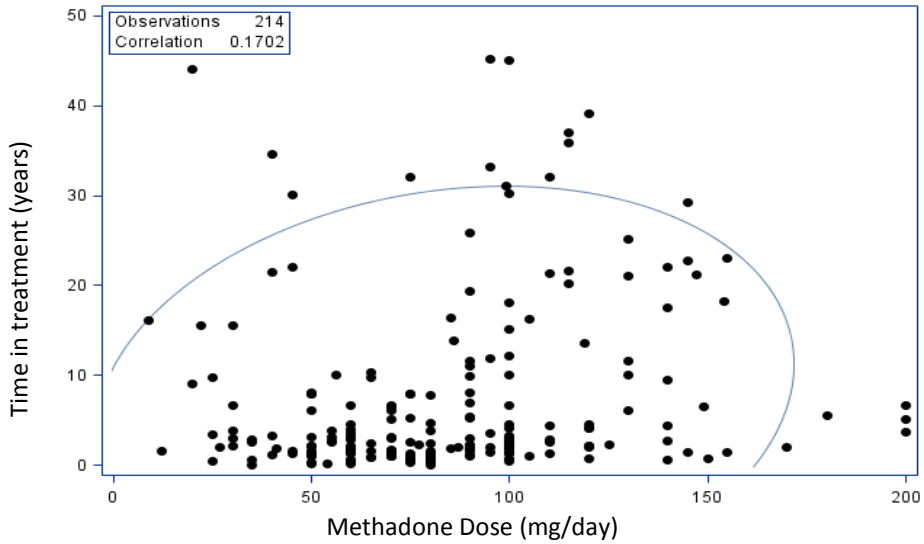


Table 2: A comparison of mean methadone dose received by subjects in phases 1 through 5 (N=149), to phase 6 (N=39), 6a (N=14), and 6b (N=12)

Phase(s)	1-5	6	6a	6b
Mean Methadone Dose (mg/day)	78.825	86.615	103.600	114.200
Standard Deviation	34.431	32.769	36.679	38.129
p value: Student's t-test, comparison to grouped phases 1-5 (two tailed) [bold: p<0.05]		0.206	**0.011**	**0.001**

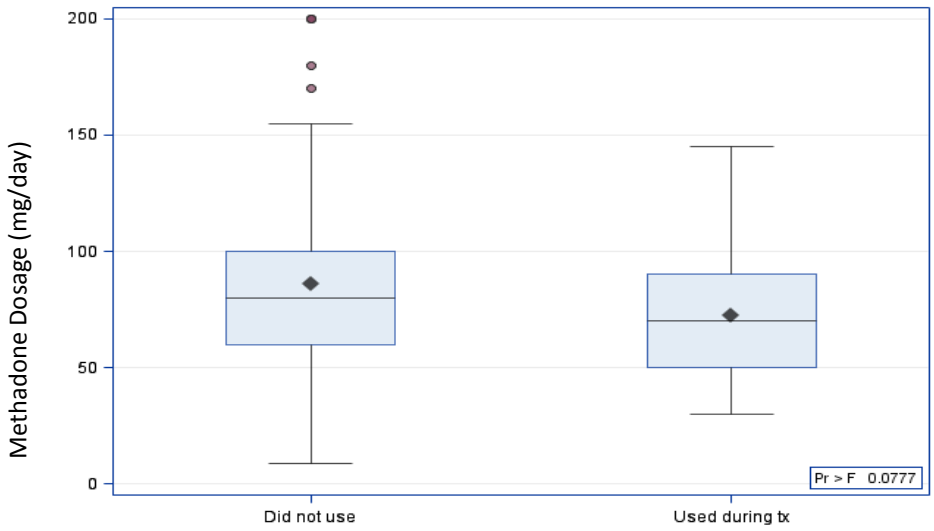
Next, the relationship between the time in treatment and current methadone maintenance dose was explored, as seen in Figure 2. A statistically significant, positive correlation with an R-value of 0.1702 was found (p=0.0126), but there was considerable variation. Length in treatment did correlate, albeit weakly, with methadone dose.

Figure 2: Scatterplot showing the relationship between time in treatment and methadone dose (r=0.1702, p=0.0126; N=214)



When self-reported date of enrollment in treatment was compared with self-reported date of last heroin or other illicit opioid use, 187 subjects were found to not have used in the past 2 months, whereas 25 had. There were 2 who had used within the past 2 months, but before their treatment enrollment date, and were thus not included in the following analysis. Those that had abstained received a mean dose of 85.77 mg/day, compared to those that used during the prior 2 months who received a mean dose of 72.40 mg/day (p=0.048, Student's t-test, two tailed). In summary, those who have been successful in MMT, defined as abstaining from illicit opiate use while in treatment for at least the prior 2 months were receiving statistically higher daily doses of methadone – as seen in Figure 3.

Figure 3: Comparison of methadone dosage among abstainers and those who used illicit opioids during the prior two months while enrolled in treatment (N=212)



Conclusions:

Those who had recently relapsed and used illicit opioids tended to be receiving a lower daily methadone dose.

- Our observations showing, that those receiving a higher methadone dose tended to have been in treatment longer, is consistent with a therapeutic strategy to give a higher methadone dose to prevent relapse (see figure 2).
- Higher doses of methadone may be more effective at inhibiting the craving for heroin than lower doses, as those who abstain in treatment are receiving doses that are statistically higher than those who relapse into illicit opioid use (see figure 3).

Methadone for the treatment of opioid addiction is not a short-term strategy.

- High doses are still needed for treatment beyond two years (see figure 2).
- Methadone maintenance treatment should be thought of in the context of treatment for a chronic disease – for many, it remains necessary for life.

These findings are consistent with both previously published data and the approach espoused by our local drug treatment program physicians. A limitation of this study is the cross-sectional study design, which limits the ability to make causal inferences.

Acknowledgements:
First, thank you to Lea George, who assisted in all aspects of this abstract. In addition, the following students assisted with innumerable aspects of the study this summer: Sri Puli, Fam Ekladious, Mark Fahmy, Jash Patel, Sudeep Peddireddi, Meehir Shah, Joseph Lomuti, Adam Kurland, and Richard Wolferz. Additional thanks are conveyed to the staff and patients at The Lennard Clinic in both Elizabeth and Newark, NJ as well as Spectrum HealthCare in Jersey City, NJ.

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ALEXIS NICHEPORUCK (NJMS 2020)

PROJECT TITLE: **MANAGEMENT OF METASTATIC DISEASE TO THE HUMERUS WITH CEMENTED OSTEOSYNTHESIS VERSUS ENDOPROSTHETIC REPLACEMENT**

MENTOR: **JOSEPH A. IPPOLITO, MD, VALDIS LELKES, MD, PETER G. GIBSON, MD MICHAEL DORAN, BS, KATHLEEN BEEBE, MD, FRANCIS R. PATTERSON, MD JOSEPH BENEVENIA, MD**

DEPARTMENT: **SURGERY**

Participation Description:
Since this was a retrospective study, most of my work in this project involved analyzing radiographs and CT scans using PACS. I measured the length and width of tumor lesions and the percentage of cortex involved, and noted the anatomical area of the lesion. I used all of that information to calculate the Mirel's criteria for pathological fracture risk for each patient.

Background
Metastatic lesions to the humerus can be associated with a variety of pathologies, fracture types, and lesion sizes. Traditionally, these lesions have been managed with either osteosynthesis or endoprosthetic replacement. The purpose of this study was to retrospectively report on outcomes of patients managed with each method of treatment and ask the following questions: (1) Do complication risks differ following metastatic lesions with endoprosthetic reconstruction versus cemented osteosynthesis? (2) Do functional outcomes differ between methods of reconstruction? (3) Does tumor volume impact outcomes?

Patients and Methods:
We retrospectively reviewed the records of 229 consecutive patients from our musculoskeletal oncology center surgically treated for metastatic disease from 2001-2016. Forty-four patients were treated for metastatic disease of the humerus. Diagnoses included Renal Cell Carcinoma (15), Multiple Myeloma (8), breast (7), lung (6), cervical (3), colon (2), skin (1), prostate (1), and thyroid (1) cancer to the humerus. There were 23 males and 21 females with a mean age of 61±13 (range, 27-90). A total of 31 patients underwent endoprosthetic reconstructions, while 13 patients underwent osteosynthesis with cementation. In cases where a metastatic lesion was abutting an articular surface or led to segmental destruction, resection with endoprosthetic replacement was performed. In patients without segmental destruction or articular surface involvement, osteosynthesis with cementation was performed. The following characteristics were analyzed between groups: tumor location, tumor volume and circumferential involvement of bone utilizing AP and lateral radiographs, MSTS functional outcome scores, and complications. Complications were classified by failure mode types 1-5: Soft tissue failure (type 1), aseptic loosening (type 2), structural failure (type 3), infection (type 4), and tumor progression (type 5)[1]. Minimum follow-up was two years unless death preceded study period

Results:
At latest follow-up, 36 patients are dead of disease and 8 are alive with disease. Mean follow-up was 22 months (range, 1-100 months). Patients alive with disease were followed at a mean of 42 months (range, 5-82 months). The majority of lesions (24) were at the humeral shaft, with 14 lesions proximally and 8 distally. Overall rate of complications was 9%. Complication types were as follows: Type 1 (1); type 2 (1); type 3 (2); and type 4 (1).
Across all anatomic locations, patients treated by osteosynthesis (n=13) with greater than two-thirds circumferential involvement of bone (n=4) were at increased risk for mechanical failure (2/4 vs. 0/9; p=0.021). At the humeral shaft, patients treated with osteosynthesis (n=6) versus intercalary endoprosthesis (n=17) were at increased risk for mechanical failure (2/6 vs. 0/17; p=0.013). At the distal humerus, complication risk was comparable between osteosynthesis (n=2) versus distal humeral replacement with total elbow (n=7) (0/2 vs. 2/7; p=0.391). No complications occurred at the proximal humerus in patients with osteosynthesis (n=5) or hemi-arthroplasty (n=7).

Overall, mean MSTS scores were comparable between patients with endoprosthetic reconstruction versus osteosynthesis (24.6±0.7 vs. 24.3±1.0; p=0.822); scores were also similar at the proximal humerus (23.4±1.3 vs. 23.5±1.9; p=0.975), humeral shaft (25.4±0.9 vs. 24.8±1.3; p=0.712), and distal humerus (23.6±1.8 vs. 24.5±3.5; p=0.810). Mean tumor volume was 21.9±14.8 cm^3. Higher tumor volume was associated with lower MSTS Scores, (r= -0.448; p=0.007).

Conclusions:
When pathologic pattern permits, cemented osteosynthesis allows for stabilization of pathologic bone, while minimizing risk of soft-tissue detachment, with mean MSTS scores of 81%. In patients with segmental defects or articular surface involvement, cemented endoprosthetic replacement provides similar outcomes with mean MSTS scores of 82%. Patients with humeral shaft lesions managed with osteosynthesis versus endoprosthesis were at increased risk of mechanical failure. Increased tumor volume was associated with lower MSTS scores. Further studies are warranted on the association between tumor volume and method of reconstruction in patients with metastatic disease to the humerus.

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AESHA PATEL (NJMS 2020)

PROJECT TITLE: **INTIMATE PARTNER VIOLENCE VICTIMS AND ASSOCIATED COMORBIDITIES**
MENTOR: **PING-HSIN CHEN, PH.D.**
DEPARTMENT: **FAMILY MEDICINE**

Participation Description:

I screened patients at the 2 clinics mentioned and scored the survey responses. If a victim was identified, I would notify the social worker and ask the victim if they wanted to participate in any of the 4 possible programs. I constantly updated the results from the screenings and conducted detailed chart reviews on the victims. I analyzed the information from their charts as well as the screening results. I interpreted the results and determined what conclusions to draw from them.

Objective:

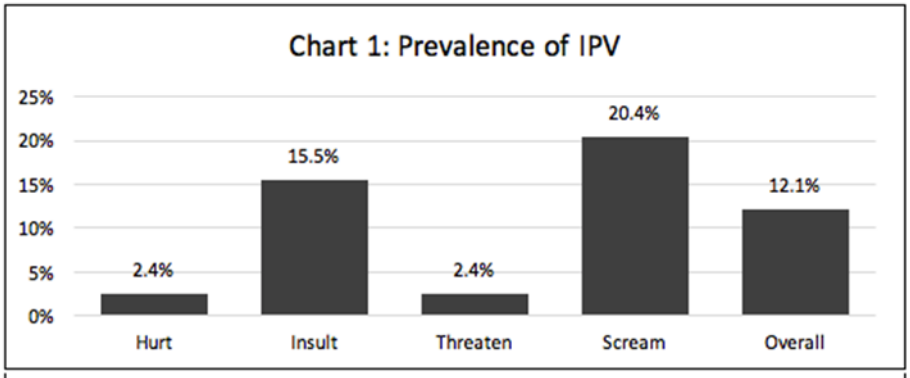
Intimate Partner violence (IPV) is a term used to describe physical, sexual, or psychological harm by a current or previous intimate partner or spouse. More than 12 million individuals are affected by IPV annually[1]. About 1 in 3 women (35.6%) and 1 in 4 men (28.5%) having experienced IPV in their lifetime, with women suffering more severe forms of IPV[2]. IPV is associated with immediate adverse health effects such as injury or death, as well as many long term health consequences such as PTSD and depression. Universal screening and case findings helps identify victims in clinical settings and provide them with necessary and life-saving interventions[3]. According to the U. S. Preventative Services Task Force, there is adequate evidence that effective interventions like screening can reduce violence, abuse, and physical or mental harms for women of reproductive age and recommends regular screenings for this population[4]. The objective of this study was to assess the prevalence of domestic violence in the Newark area and provide intervention to victims as well as to understand the health risks associated with domestic violence by looking at specific comorbidities.

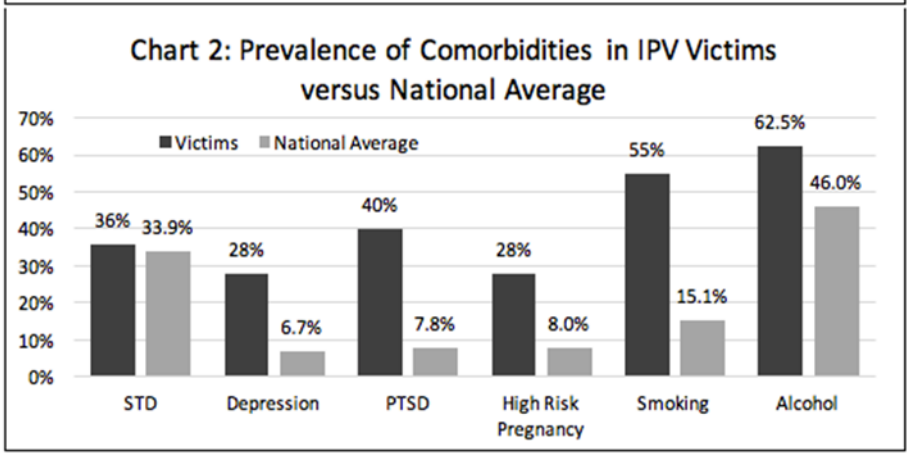
Methods:

Female patients of reproductive age were screened for IPV using the 4-item HITS questionnaire in the University Hospital OB/GYN Clinic (n=205) and Pediatric Clinic (n=1). Patients who were positive (≥6) were referred for immediate intervention with a social worker and provided information on available services at NJMS including individual counseling, support groups, parent education program, and children's empowerment program. Chart reviews were done on victims to assess for health problems, pregnancy complications, and other high risk conditions. The prevalence of these variables were compared to national averages of females of reproductive age according to the Center for Disease Control and National Health Institute.

Summary:

A total of 206 patients were screened using HITS questionnaire. Screening results indicated that 12.1% were positive for domestic violence (n=25). Specifically, 2.4% of women were physically hurt, 15.5% were insulted, 2.4% were threatened, and 20.4% were screamed at (Chart 1). Of the 12.1% that were victims, the average age was 29.8 and 43% were high school graduates. Forty-eight percent of the victims were African American, 40% were Hispanic, 8% were white, and 4% were other. Majority of victims were single (80%) and unemployed (80%). Thirty-six percent of the victims had an STD, 28% had depression, 40% had PTSD, 28% had a high-risk pregnancy, 55% were smoking, and 62.5% drank alcohol. These percentages were compared to national averages where 33.9% of the U.S. population has a STD, 6.7% has depression, 7.8% has PTSD, 8% has a high-risk pregnancy, 15.1% smoke, and 46% drank alcohol (Chart 2)[5-9]





Conclusion:

The results demonstrate that IPV is common in the greater Newark area. While only about 1 in 8 women were victims of IPV as defined clinically, about 1 in 5 women were victims of verbal abuse, a minor form of IPV. Previous studies have shown that only about 25% of women of reproductive age get screened for domestic violence and a majority of individuals do not disclose their IPV victimization to medical professionals[4]. These findings indicate that IPV rates might be significantly higher than currently thought to be. Compared to the general populations, IPV victims were 3-5 times more likely to have depression, PTSD, high risk pregnancies, and smoke[5-9]. They were also slightly more likely to have an STD and drink alcohol[6,9]. These findings show that there are significant health risks associated with IPV victims besides traumatic injuries from the violence. Overall, due to the prevalence of IPV and high risk of associated comorbidities in females of reproductive age, it is important to screen this population regularly and help victims get the needed intervention to combat such comorbidities.

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CARLY RAY (NJMS 2020)

PROJECT TITLE: **EVALUATION OF DYSTONIA AND DYSTONIC POSTURING IN A COHORT OF CHILDREN WITH ASD**
MENTOR: **SUE MING, MD, PH.D.**
DEPARTMENT: **NEUROSCIENCES**

Participation Description:

Myself and fellow medical student Neil Chen (2020) were responsible for developing an experimental outline for this study, based off Dr. Sue Ming's suspicion that dystonia may be present amongst some of her patients with ASD. I constructed an informational letter to distribute to any parent interested in the study, explaining the aims of the study and outlining what we would like them to record. All 7 videotapes recorded during office visits were recorded by myself and/or Neil Chen. I mailed encrypted USB's to 4 parents to obtain video footage of their children and was in charge of ensuring their return. I analyzed 20 video recordings both independently and along with Dr. Sue Ming (6 office video, 7 home video, 7 VEEG). I reviewed medical records of all 8 subjects in which dystonia was positively identified and collected demographic information, HPI, information on comorbid illness and medication regimen, which I later used to assemble Table 3 in the above abstract. Myself and Neil Chen explained and collected informed consents from the parents/guardians of all subjects involved in the study.

Objective:

Autism spectrum disorder (ASD) is a neurodevelopmental disorder clinically characterized by impaired social interactions and communications coupled with repetitive and restricted behavioral patterns. Motor mannerisms are an integral component of the disorder, falling under the second diagnostic criteria for autism in the DSM-V; "restricted, repetitive patterns of behavior, interests, or activities." Children with ASD are often found to display head tilting or shaking, tongue movements, hand or finger flapping, and complex whole body movements. These movements are a common therapeutic focus in the treatment of ASD.

While it is well recognized that children with autism exhibit abnormal movements, careful classification and categorization of these movements has been limited, as they are incredibly varied. Classically, these movements have been grouped into a broad category known as "motor stereotypies," rhythmic or repetitive acts or postures with no obvious purpose. To date, there is no clear understanding of the pathogenesis of the stereotypies though many models have been put forward. The predominant models hypothesize that movements are reinforced by subsequent social interactions or act as modulations to an under/over stimulating environment (hence the common use of the term "self stimulatory movements"). An alternative approach considers stereotypies as a motor disorder - the movements an involuntary result of a dysfunctional motor control system involving the basal ganglia and dopaminergic pathways. Interestingly, imaging studies performed by Hollander et al and Langen et al reported increased basal ganglia volume, specifically increases of the caudate and putamen, amongst children with ASD. These volume abnormalities have been linked with the presence and severity of repetitive behaviors.

To our knowledge, what has not been well described is the presence of dystonia and/or dystonic posturing in children with autism. Dystonia is a neurologic movement disorder characterized by sustained or intermittent simultaneous agonist-antagonist muscle contraction, resulting in abnormal twisting and posturing. Basal ganglia abnormalities have been well established in this disorder. Given possible basal ganglial dysfunction in both ASD and dystonia, we question whether there may be miscategorized dystonic movements in those with autism. We found only two studies which reported dystonia amongst children with ASD. In a 1978 study by Damasio and Maurer, dystonic posturing of the feet, hands and fingers was observed in a group of children with autism. The authors propose a neurological model for ASD which included dysfunction of the neostriatum. In a study by Goldman et al, brief episodes of sustained dystonic posturing was identified in the upper and lower limbs of one ASD subject.[3] Beyond these studies, there is little to no mention of dystonia amongst patients with ASD.

As a preliminary investigation, we have used video-analysis to determine whether or not any of the motor mannerisms exhibited by cohort of children with autism may in fact be categorized as dystonia or dystonic posturing. Positive identification of dystonia may shed light on the physiological basis of motor mannerisms in autism, the role of the basal ganglia in development of the autism as well as new avenues for therapeutic intervention.

Methods:

To determine whether dystonia or dystonic posturing is present in a subset of children with autism, we analyzed 20 videotapes of children age 3 to 30 diagnosed with ASD. 6 video recordings were collected by the child's parent/guardian and mailed to research team via encrypted USB. 7 videos were recorded by an IRB approved research assistant during patient office visit. 7 video were obtained from the patients' video EEG recording. Videotapes were analyzed by Dr. Xue Ming and her research team. Subjects were recruited from the Rutgers New Jersey Medical School Department of Neurology in Newark, NJ. All subjects were under the care of pediatric neurologist Xue Ming. Diagnoses were made by the Diagnostic and Statistical Manual of Mental Disorders, Fourth and Fifth Editions (DSM-IV, DSM-V). IRB approved consent for videotaping and analysis was obtained from parents/guardians. This study was approved by the Institutional Review Board of Rutgers University New Jersey Medical School.

Summary:

20 subjects were enrolled in this study. Dystonic movements and /or posturing were positively identified in 7 low and 1 high functioning autism subjects. All subjects were male with a mean age of 18.5 (Table 1). All movements were spontaneous with no after effect and of brief duration. Body sites of movements/ posturing included hands, face, eyes, neck and arm.

Table 1: Demographics of ASD Subjects

	Number
Subjects (n)	20
Age (years)	18.5
M/F	20:0
ASD Diagnosis	AD: 19 Asperger's: 1
Medications	19

Table 2: Types of movements

	n (subjects)	Body Site	Description
Dystonic movements	4	Hands/ fingers (2) Face (2) Eyes (3)	Spoon deformity Facial grimace Staring out of corner of eyes
Dystonic posturing	5	Hands/ fingers (4) Neck (1) Arm (1)	Spoon deformity Neck twisting

Qualitative description of video clips:

Subject 1: Subject shows a single episode of dystonic movement; contraction of fingers of either left or right hand. Subject also exhibited non-dystonic, repetitive movements such as arm flapping and rapid finger movements.

Subject 2: Subject shows several episode of sustained dystonic posturing of the left hand during the video recording. Subject also showed facial tics including eye blinking.

Subject 3: Subject shows several dystonic movements including facial twisting and ocular deviation.

Subject 4: Subject showed several episodes of dystonic posturing of the right hand. Subject exhibited continuous writhing movements as well as audible teeth grinding and vocalizations. This subject has Down's syndrome and autism.

Subject 5: Subject showed both dystonic movements and postures including facial twisting, cervical deviation and ocular deviation.

Subject 6: Subject showed a single episode of simultaneous ocular deviation and dystonic stretching/ opening of the mouth. Subjects right hand was in a contracted position for the majority of the videotape. Subject also exhibited other movement such as several episodes of rapid head jerk.

Subject 7: Subjects left arm was in a sustained dystonic posture above his head while lying in bed.

Subject 8: Subject showed several episodes of dystonic movement of his fingers.

Table 3: Characteristics of ASD Subjects

	Age	Gender	Ethnicity	Diagnosis	Comorbidity	Medications
Subject 1	23	M	Hispanic	Autism- Lo fn	Seizure disorder Sleep problem	Depakote Clonidine Seroquel Xanax
Subject 2	21	M	African American	Autism- Lo fn	Sleep apnea Aggression	Abilify Risperidone
Subject 3	21	M	Hispanic	Autism- Lo fn	Anxiety OSA	None
Subject 4	15	M	African American	Autism- Lo fn	Down Syndrome OSA	Propranolol Clonidine
Subject 5	5	M	Hispanic	Autism- Lo fn	Microcephaly Global Developmental Delay Sensorineural Hearing Loss Seizure	Oxcarbazepine
Subject 6	29	M	Caucasian	Autism- Lo fn	Mood disorder Obsessive Compulsive	Abilify
Subject 7	23	M	Hispanic	Autism- Lo fn	Epilepsy Developmental Delay	Lamictal Trileptal Zonegran Clonidine
Subject 8	11	M	African American	Asperger's	Anxiety Obsessive Compulsive	Herbal GABA

Conclusion:

Dystonia was identified in this cohort of children with ASD. All movements and posturing had qualities consistent with simultaneous agonist antagonist muscle contraction. The dystonia was brief and atypical of classic dystonia; movements and postures were typically non-sustained and of low intensity. The movements of highest intensity were exhibited by subject 5 and included facial grimacing, cervical and ocular deviation. The dystonia varied in terms of frequency and was typically intermixed with other movements such as tics or simple repetitive motions, which is perhaps why they eluded previous detection.

While cortical pathways have long been implicated in the pathogenesis of ASD, the role of the basal ganglia has come under investigation. Our findings support this notion of a potential basal ganglial dysfunction in ASD and suggest that this is a worthwhile avenue for future research. Basal ganglia abnormalities are well established in dystonia as well as various other movement disorders such as Parkinson's and Huntington's disease. Hyperkinetic disorders like dystonia have been linked with atypically low levels of inhibitory basal ganglial signals. Rodent models serve as the basis for these claims, often citing lesions of the globus pallidus as a trigger for resultant dystonia. Identification of dystonia in this cohort of patients with ASD suggests a potential basal ganglial dysfunction in these children, a conclusion which has been previously reported following research into their repetitive and stereotyped behaviors (RSB). Morphometric studies using MRI have described abnormalities in basal ganglial volume amongst children with ASD. In a 2005 study by Hollander et al, right caudate volume was increased in (#) subjects with DSM IV diagnosed ASD as compared with 17 neurotypical controls. This increased persisted following correction for total brain volume.[v] The caudate nucleus was also reported as enlarged amongst children, adolescents and young adults with autism ad Asperger syndrome as compared with healthy controls in these age groups in a 2007 study by Langen et al.[iv] In addition to perturbations in motor function, basal ganglia dysfunction has been implicated in OCD and impulsivity – common co-morbidities of the disorder.

Our findings have clinical relevance to avenues of treatment. The current standard of care for the treatment of motor stereotypies in children with ASD includes antipsychotics such as Risperidone and Seroquel, which target D3 and D4 receptors of the cingular gyri. These drugs are non-selective and act at D1 and D2 receptors as well, resulting in potential side effects of dyskinesia and dystonia. In patients in whom dystonia is both positively identified and is a source of discomfort or a disturbance due to frequency, administration of these antipsychotics may be of little benefit and may even exacerbate the movements. In these situations, use of D1- D2 selective therapeutics may be of most help.

There were some limitations to our current study, the most significant being medication effect. Of the 8 subjects analyzed, 3 were on a medication regimen which included antipsychotics with dystonia as a potential side effect. Medications included Seroquel (Subject 1- 100mg), Abilify (Subject 2- 5mg, Subject 6- 20 mg) and Risperidone (Subject 2- 0.125 mg). Interestingly subject 5, the patient who exhibited the most intense dystonia, was not on any of the aforementioned antipsychotics. An additional limitation of our study was the absence of a standardized video recording protocol. To study the prevalence of dystonia in ASD, a standardized protocol is required. Of the 8 subjects in which dystonia was positively identified, 5 videos were obtained during office visits, 2 videos were obtained at the subjects' homes and 2 VEEG's were obtained. Of the 12 subjects in which dystonia was not identified 2 videos were obtained at office visits, 4 videos were obtained from subjects' home and 6 VEEG's were obtained. Based on this data we conclude that analysis of video obtained in a standardized environment such as a clinical office may be most useful. The optimum length of video recordings needs to be determined. Finally, our sample size was small as this was a preliminary investigation.

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JASMINE SHAFEI (RUTGERS UNIVERSITY 2019)

PROJECT TITLE: **GENOTYPIC VERIFICATION OF OREXIN-CRE MICE**
MENTOR: **VANESSA ROUTH, PH.D.**
DEPARTMENT: **NEUROSCIENCE, PHARMACOLOGY, & PHYSIOLOGY**

Participation Description:

Objective:
The overall goal of this project is to genotypically identify Orexin-Cre mice from Orexin-Wild Type mice. Genotypic verification of Orexin-Cre positive mice contributes to the Routh lab's research in terms of classifying which mice are useful for specific cellular testing mechanisms and different experimental studies and procedures. The overarching goal of the Routh lab's project is to investigate the glucose sensing mechanism of Perifornical Hypothalamic orexin neurons to prevent hypoglycemia unawareness in Type 1 diabetes mellitus.

Methods:
Through the initial DNA Extraction process, DNA from mouse tail samples was extracted and purified. To a microcentrifuge tube containing a sample of mouse tail approximately 0.4-0.6 cm in length,180 µL of Buffer ATL were added, along with 20 µL of proteinase K. The contents were mixed thoroughly by vortexing, and then were incubated at 56^{O}C until the sample was completely lysed. The tissue was vortexed occasionally during lysis and after removal from incubation for 15 seconds. 200 µL Buffer AL were added, and then 200 µL ethanol were added, and the mixture was vortexed after each addition. Mixture was pipetted into a DN'easy spin column placed in a 2 mL collection tube, 500 µL Buffer AW1 were added, and then mixture was centrifuged at 8,000 rpm for 1 minute. After discarding remaining flow-through and collection tube, and replacing 2 mL collection tube, 500 µL of Buffer AW2 were added, and mixture was centrifuged at 14,000 rpm for 3 minutes. Remaining flow-through and collection tube were discarded again, and 2 mL collection tube was replaced. 200 µL of Buffer AE were added to mixture by pipetting, and mixture was centrifuged again at 8,000 rpm for 1 minute. Mixture was transferred to new microcentrifuge tube and extracted DNA was read in the Nanodrop to determine adequacy of concentration and quality.

Samples then underwent the Polymerase Chain Reaction, where sequences of the extracted DNA were amplified. Keeping all reagents and samples on ice, the following volumes were added to the individual PCR tubes before they were placed into the Bio-Rad Thermal Cycler:

- diH2O: 5.8 µL
- 2x REDTaq: 10 µL
- Cre F Primer: 0.6 µL
- Cre R Primer: 0.6 µL
- DNA: 3 µL

* (-ve) tube received 8.8 µL of diH2O and no DNA.

Primers for Orexin-Cre Mice:
Cre_F: 5' GGGATTGCTTATAACACCCTGTTACG 3'
Cre_R: 5' TATTCGGATCATCAGCTACACCAGAG 3'
Common Primer Tube: 6 µL of each Cre F and Cre R, and then add 1.2 µL increments of CPT.

Samples were then run in a gel electrophoresis setup, where DNA was separated and visualized by molecular size and charge. To an Erlenmeyer Flask, 0.5 grams of agarose and 50 mL of 1x TAE buffer were added, then dissolved by heating in microwave for 1.5 minutes, until solution turned clear. Flask was cooled under running cool water, and then 6 µL of ethidium bromide were added to solution. Gel was poured into gel plate apparatus, gel comb was inserted, and gel was

left to set for 30 mins. 1x TAE Buffer was then poured into apparatus, filling wells and covering gel. 2 µL of DNA Ladder were added into the first well, the second well was left blank, and the following wells held 10 µL of either (-ve) or CRE samples. Voltage was set to 150 V, and time was set to 30 mins. After casting and running gel, gel tray was placed into FluorChem Machine to read gel. With filter set to 2, gel bands were visualized under transillumination UV light.

Summary: NanoDrop results indicated successful DNA Extraction technique, as samples had DNA concentrations ranging from 38.8-71.44 µg/µL, which indicated that DNA from mice tails had been adequately washed and eluted during the DNA extraction stage of the genotypic verification of Orexin-Cre mice. The ratio of absorbances at 260 and 280 also stood to support the purity of the DNA, mostly ranging from the desired amounts of 1.8 to 2.1. This suggested that there were little to no chemical or other contaminants within the process, allowing for the continuation of the next procedural step in the genotypic identification of Orexin-Cre, the Polymerase Chain Reaction.

Figure 1. NanoDrop results reveal DNA concentrations ranging from 38.8 ng/uL-71.44 ng/uL, and A-260/A-280 values ranging from 1.73-1.96, suggesting that DNA was sufficiently pure and concentrated.

Sample ID	Date	Time	ng/uL	A260	A280	260/280	260/230
210	7/13/2017	12:37 PM	50.82	1.016	0.54	1.88	0.96
211	7/13/2017	12:41 PM	38.8	0.776	0.449	1.73	1.23
212	7/13/2017	12:43 PM	67.18	1.344	0.737	1.82	1.16
213	7/13/2107	12:45 PM	46.5	0.93	0.475	1.96	1.11
214	7/13/2017	12:48 PM	71.44	1.429	0.763	1.87	1.43
215	7/13/2017	12:50 PM	51.75	1.035	0.563	1.84	0.93
216	7/13/2017	12:51 PM	51.21	1.024	0.531	1.93	1.02
217	7/13/2017	12:53 PM	59.29	1.186	0.626	1.9	1.01
218	7/13/2017	12:54 PM	48.81	0.976	0.527	1.85	0.86

Amplification of the desired DNA sequences was achieved during the Polymerase Chain Reaction, a mechanism that occurs by thermal cycling. The first peak describes an increase in temperature, up to 94 degrees Celsius, denaturing the double-stranded DNA helix into two single strands of DNA. The next decline in temperature down to 60 degrees Celsius, or cooling, anneals the primers onto the DNA strands. The final increase in temperature up to 72 degrees Celsius represents the elongation of the DNA sequences by DNA Polymerase, synthesizing new strands complementary to the template, and thereby amplifying the DNA sequence after 34 cycles.

Figure 2. PCR reaction is a mechanism of thermal cycling, involving denaturation, annealing, and elongation of DNA.

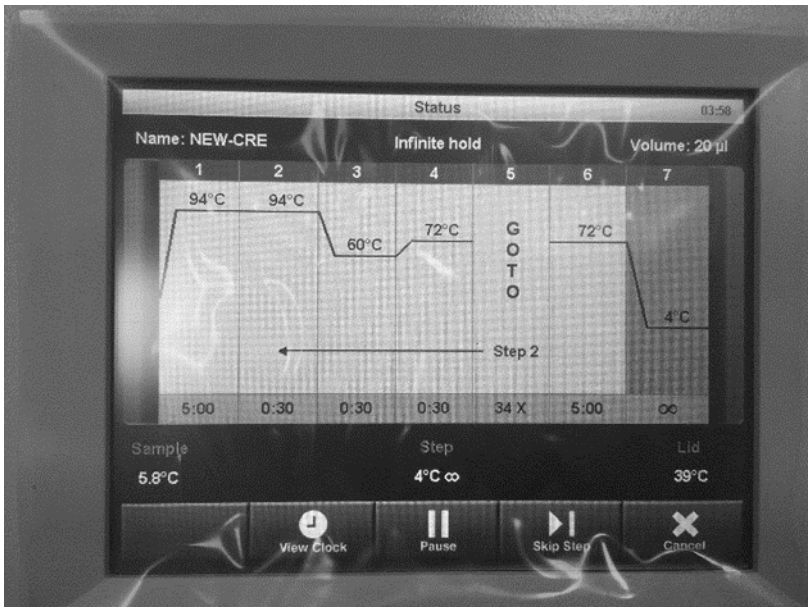
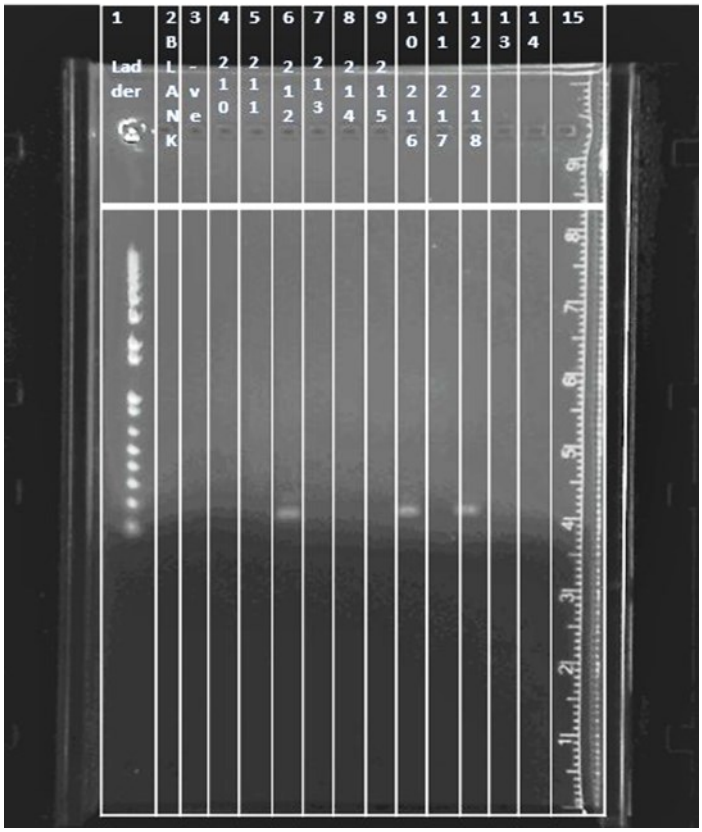


Figure 3. Visualization of DNA molecule bands via Gel Electrophoresis and FluorChem Machine



Conclusion: With the DNA Ladder used as a reference in the first lane, it was observed that DNA samples of Orexin-Cre mice (212, 216, and 218) displayed bands at around 250 bp, while those mice that were not Orexin-Cre showed no bands in their respective lanes. For those lanes with no bands, the Cre primer was unable to bind to the DNA, and the ethidium bromide as a result left no fluorescence under UV light, as the DNA could not be amplified in the previous PCR reaction. Identifying Orexin-Cre mice by their bands under the UV light contributes to the research of the Routh lab, as it helps identify which mice serve which certain functions throughout the different experimental procedures that are carried out.

AAKASH SHAH (NJMS 2020)

PROJECT TITLE: **LEUKEMIA INHIBITORY FACTOR (LIF) REDUCES INJURY AND AIDS NEURO LOGIC RECOVERY AFTER CLOSED HEAD INJURY**

MENTOR: **STEVEN LEVINSON, PH.D**

DEPARTMENT: **PHARMACOLOGY, PHYSIOLOGY, AND NEUROSCIENCES, NEUROLOGICAL SURGERY**

Participation Description:

The Levison Lab has been working on LIF for some time now. They previously wrote a paper on haplodeficient LIF mice and showed that mice require LIF to recover from traumatic brain injury (TBI). Then, the lab moved forward and tried to see if intranasally administered LIF could help enhance recovery by neuroprotection and neuroregeneration. This is when I came to the lab. I performed surgeries on three groups of mice (each group containing about 10 mice). I and another person in the lab, then dosed the groups of mice after surgery for a week. We then sacrificed and perfused them. We then froze the brain tissue. We then sectioned the brain tissue and did some immunohistochemistry. I have probably done surgery on about 30 mice. I have perfused them all, and frozen all of the tissue. We haven't finished cutting all the brains nor have we finished staining the tissue. Most of the experiments had been previously planned but they had been done about a year ago. Therefore, I helped re-plan some of the experiments to make them more optimal. The mice surgeries involved slicing the scalp and giving the mice mild concussions with an anvil apparatus. We cut the brains using a cryotome machine. I have performed cresyl violet, flurojade, and Olig-2/CC1 stains.

Objective:

Leukemia inhibitory factor (LIF) is paramount for recovery from traumatic brain injury (TBI). The goal of this study was to establish whether intranasal administration of LIF, at various time points post TBI, will reduce brain injury, enhance regeneration, and improve functional recovery in juvenile mice.

Methods:

To assess whether intranasally administered LIF gained access to the brain and induced signaling, mice were administered 10 µL of a 2 µg/mL LIF solution, dissolved in water, or 10 µL of H2O, which was applied as 2 µl drops alternately to each nostril, every 2 minutes over 10 minutes. Mice were euthanized 30 minutes after intranasal administration. Immunofluorescence was performed for phosphorylated Stat3 (pSTAT3). To produce brain injuries, juvenile CD1 or C57Bl/6 (~postnatal day 18) mice received blunt, closed head injuries (CHI). CHI was produced using a controlled cortical impactor (5mm rounded tip, 4 m/s velocity, 150 ms dwell time, 1.0 mm depth) under isoflurane anesthesia. The mice were divided into three groups: Sham, vehicle, and LIF. Sham operated animals received only a scalp incision. Vehicle and LIF mice received CHIs; their operations were identical on the day of the surgery. Intranasal LIF administration was divided into two groups: acute and delayed. For the acute group, LIF or H2O was administered 4 hours after the surgery and every 12 hours for the next three days. For the delayed group, LIF or H2O was administered every 12 hours for three consecutive days starting three days after the day of the surgery. Administration of LIF and H2O for the acute and delayed groups followed the protocol stated above**.** On the final day of LIF administration, 50 mg/kg of BrdU was intraperitoneally injected. Three days after injection of BrdU, the mice underwent several behavioral tests and were subsequently euthanized by intracardiac perfusion with 3% paraformaldehyde.

Summary:

Intranasal LIF significantly increased the number of pSTAT3 positive cells in the subventricular zone (SVZ), neocortex, and olfactory bulb compared to intranasal H_2O. In the delayed CHI group, the mice that were administered LIF had significantly less neurodegeneration in the corpus callosum when compared to the vehicle group (as detected using Fluoro-Jade Stain). The delayed group also demonstrated a significant increase in mature oligodendrocytes in the white matter of LIF treated mice when compared to vehicle treated mice.

Additionally, the mice in the delayed group that received intranasal LIF had significantly more proliferating cells in the SVZ (as assessed by BrdU) when compared to the mice that were intranasally administered H2O. Behavioral analysis showed a trend for motor function improvement after acute and delayed LIF administration. Discordantly, analysis of cresyl violet stained sections demonstrated a trend for greater injury after acute LIF administration and less injury after delayed LIF administration; however, neither the behavioral nor the cresyl violet results were statistically significant due to the relatively small number of subjects analyzed.

Conclusion:

These data demonstrate that intranasal LIF penetrates deep into the brain, after intranasal administration, where it activates the canonical Jak-STAT pathway. Our data also support the conclusion that delayed LIF administration is both neuroprotective and neuroregenerative; however, some of our analyses were underpowered; therefore, additional studies are required.

AARSH SHAH (TCNJ 2019) CHANDANI PATEL (NJIT 2019)

PROJECT TITLE: **EFFECT OF RPD3 DOWNREGULATION ON ALZHEIMER'S DISEASE AND LONGEVITY**
MENTOR: **YONKYU PARK, PH.D.**
DEPARTMENT: **CELL BIOLOGY AND MOLECULAR MEDICINE**

Participation Description:

Our role in this research project was to carry out the climbing assay, aging assay, and continue data collection from beginning to when we ended. Although minimal, we were tasked to aid in collected samples of flies as well for future studies as well as our own studies at the start of the project. Furthermore, we carried out the climbing assay every 3-5 days and the aging assay every 3-5 days as well. After each assay was completed, we were to input the data in the excel sheet for data collection and data interpretation. We were able to use the data collected and transfer it into viable graphs for proper conclusions.

Objective:

The purpose of this project is to investigate if the downregulation of histone deacetylase, rpd3, in the brain extends lifespan with reducing neurodegeneration of those flies with Alzheimer's Disease characteristics. Alzheimer's Disease (AD) is a neurodegenerative disorder leading to amnesia, cognitive impairment and senile dementia. From the previous experiments, it was demonstrated that accumulation of amyloid-β (Aβ) peptides in brain is the primary event in the sequential progression of AD. Expression of Aβ42 in brain leads to formation of diffused amyloid deposits, age-dependent learning defects, and extensive neurodegeneration. Currently, we are investigating the impact of brain-specific Rpd3 downregulation on flies with AD. UAS-elavGal4 system is used for expression of Aβ peptide in the fly brain which gives rise to clear amyloid deposits, age dependent locomotor defects and neurodegeneration. Gal4 is a yeast transcriptional activator and its target is Upstream Activating Sequence (UAS). The binding of Gal4 to UAS activates gene transcription of downstream genes. Elav is a promoter of neuron-specific protein that leads to rpd3Ri (RNA interference) expression in brain.

Amyloid-β peptide inducement is observed using the climbing assay technique in the Alzheimer's Disease (AD) flies along with aging assays. Downregulation of histone deacetylase, Rpd3, in *Drosophila melanogaster* increases longevity and possibly impedes accumulation of amyloid-β peptides in the brain. The UAS-elavGal4 system was used along with Rpd3 downregulation in the experimental flies. RNA interference mediated downregulation of *rpd3* in this project results in increased neurological function amongst AD flies with induced neurodegeneration. We hypothesize that the downregulation of Rpd3 in the brain extends lifespan while reducing neurodegeneration caused by the peptide, Aβ42, and Alzheimer's Disease.

Methods :

There were three major methods that were used throughout the duration of this study, the fly cross, aging assay, and the climbing assay.

Fly Cross

Given two parent genotypes, the progeny genotype was determined. For each set of genotypes, the number of surviving flies was counted and indication of Alzheimer's Disease in the brain was examined.

Aging Assay

Flies from each genotype were collected and placed accordingly into standard cornmeal medium vials, and kept in a 25°C incubator. The surviving flies were counted, and transferred into new vials every 3-4 days. There were twenty flies placed into each vial, with a total of one hundred flies prepared for each of the three genotypes, at the start of the project.

Climbing Assay

After the aging flies were transferred into new vials, the flies were used for climbing assay. Each vial was tapped for about two seconds and the number of flies that climbed in the vial were counted for next 30 seconds in intervals of ten seconds.

Summary of Results

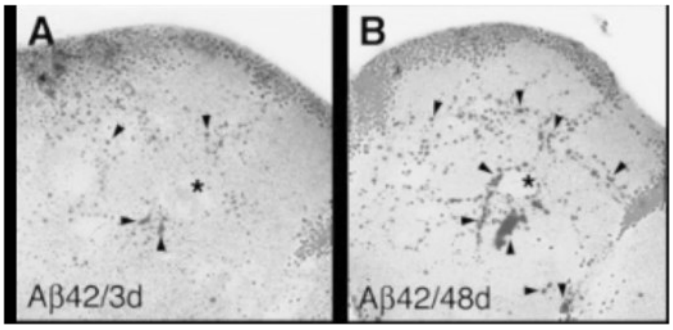


Figure 1. Detection of Aβ deposits (arrowhead) in fly brain over given time span (reference 1)

Whole-mount immunohistochemical staining was performed to determine whether expressed and accumulated Aβ peptides form Aβ deposits in fly brain. 48 day old Aβ42 flies showed Aβ deposits which are indicated by arrowheads in figure 2B. Both the number and size of deposits were increased during aging (reference 1).

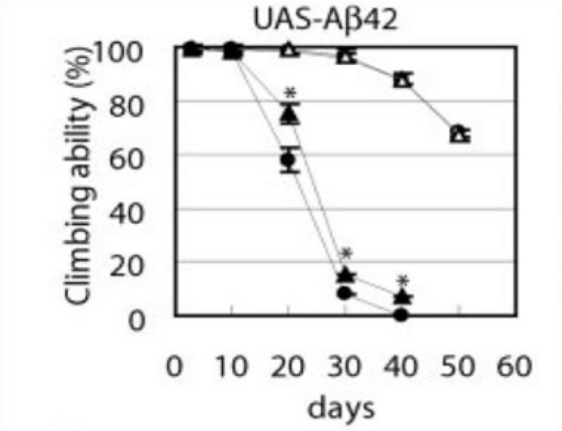


Figure 3. Comparative progressive climbing disability of Aβ42 flies during aging due to neurodegeneration (reference 1).

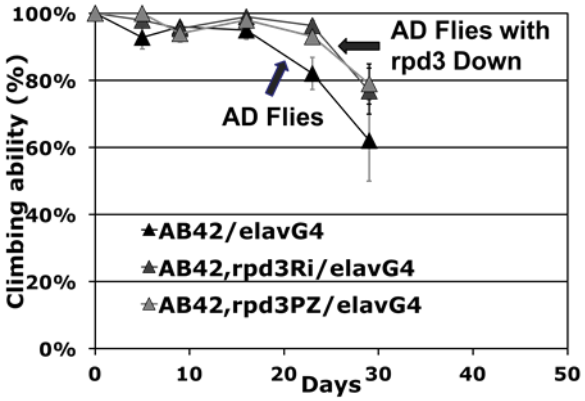


Figure 4. The climbing disability in Aβ42 flies is rescued by Rpd3 downregulation(rpd3Ri:RNA Interference;rpd3PZ(rpd3 deletion mutant) in the Brain.

The results of climbing assay are depicted by figure 5. Aβ42/elavG4 are the flies with Alzheimer's disease which was induced using elav-Gal4 system. Aβ42, rpd3Ri/elavG4 are the Alzheimer's flies with rpd3 downregulation only in the brain and Aβ42,rpd3Pz/elavG4 are the Alzheimer's flies with full body downregulation which makes roughly as half as much rpd3 because it has the nonsense mutation in one of the copies of rpd3. The results of climbing assay so far indicated that Alzheimer's flies with some form of rpd3 downregulation tend to have lower climbing disability and thus less neuronal loss caused by Aβ42 compared to Alzheimer's flies with no rpd3 downregulation. No significant difference was observed between flies with rpd3 downregulation only in the brain and flies with rpd3 downregulation in the entire body.

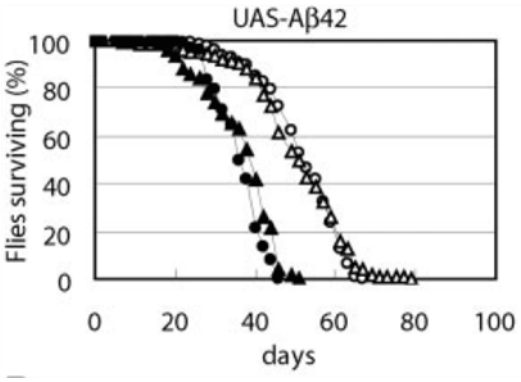


Figure 5. Comparative survival rate of Aβ42 flies in previous studies of longevity in flies with Alzheimer's Disease (reference 1).

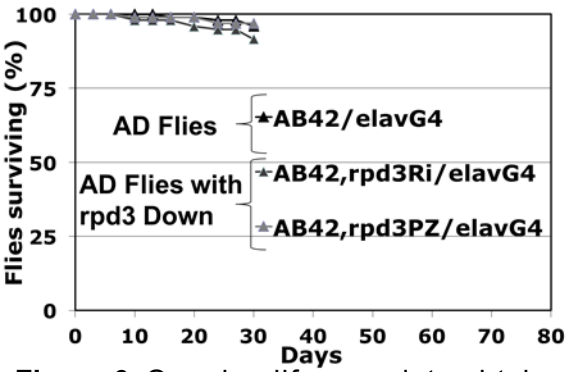


Figure 6. Ongoing lifespan data obtained from current Alzheimer's fly aging assay research.

Figure 7 shows the results of aging assay that was conducted. No significant results have been observed so far. We are expecting that Alzheimer's flies with rpd3 downregulation will have a longer lifespan compared to Alzheimer's flies with no rpd3 downregulation. Figure 6 indicates results of aging assay conducted in reference 1. The flies with Alzheimer's Disease have a shorter lifespan compared to the control flies.

Conclusion:

The purpose of this project is to investigate if Rpd3 downregulation in the brain extends lifespan with reducing neurodegeneration of AD flies. Interestingly, the climbing disability in Aβ42 flies was rescued by Rpd3 downregulation in the brain (**Fig. 4**). From the results of climbing assay, we interpret that Rpd3 downregulation in Aβ42 flies leads to reduce neurodegeneration in the brain which occurs from the Aβ42 accumulation (**Figs. 1**). In our previous study, the aging data indicated that flies with Rpd3 downregulation have longer lifespan than flies without Rpd3 downregulation. We may expect that Rpd3 downregulation in the brain will rescue shortened lifespan of Aβ42 flies (**Figs. 5-6**). Future research using dissections along with anatomical studies and mass spectrometric analysis are being conducted to investigate more about longevity in the AD flies through Rpd3 downregulation.

EMAAD SIDDIQUI (NJMS 2020)

PROJECT TITLE: **IMAGE ANALYSIS OF EPITHELIAL MIGRATION OF THE TYMPANIC MEMBRANE**
MENTOR: **ROBERT JYUNG, MD**
DEPARTMENT: **OTOLARYNGOLOGY**

Participation Description:

My participation as a the lead student in charge was to take the images from Dr. Jyung's clinical practice and develop my own method of analyzing the ear drums. This included testing many different features and plugins with the image analysis software, ImageJ, until we found a procedure that effectively analyzed the epithelial ridges and could be reproduced with other images. Throughout the process I had read many different articles and journals that were related to not only clinical otology, but also general force mechanics and image analysis. I had also personally reached out to Ron DeSpain, an image analysis expert who is now heavily involved in developing a program for this type of analysis. I am also currently working on preparing the manuscript for this research.

Objective:

mpaired epithelial migration may play a role in pathological conditions such as cholesteatomas. We hypothesize that computerized analysis of endoscopic images demonstrating impaired epithelial migration can be quantified using image analysis software. Quantification of these ridges may be useful for revealing the underlying force vectors of the epithelial migration. This same analysis may be useful for discriminating between ears with normal versus impaired epithelial migration.

Methods:

High definition endoscopic photographs of the tympanic membrane and ear canal were taken by Dr. Jyung in his practice as a routine measure. These pictures did not contain any personal identifiers and therefore were used for analysis and presentation. The images were selected if they contained any visible wrinkle formation on the tympanic membrane. The NIH's open-source image analysis program Image J was used as the primary tool for image analysis. The image was 3D rotated to adjust for the depth of the retraction pocket. The images were all filtered using the "convolve" feature inside Image J to highlight the wrinkles of the ear drum. A multi-step filter and processing macro was used to create ellipses that capture the epithelial ridges on the ear drum. The measure tools in Image J were used to draw mean force vector based on forces perpendicular to the short axis of the ellipses. The data that describes the long and short axis of the ellipsis were extracted from Image J. The plot profile of the epithelial ridges were found and the graph of the peaks correlating to the ridges was extracted

Summary:

The convolution feature highlights the epithelial ridges against the background noise from the rest of the tympanic membrane. The 3D rotation helps account for the distortion of the epithelial ridges from the retraction pocket, since it is 3D structure that must be analyzed on a 2D plane. The epithelial ridges are captured in ellipses after image processing and therefore represent an important feature on the tympanic membrane when the retraction pocket forms. The ellipses have short axis, which perpendicular lines can be drawn to form force vectors. The average force vector can be determined from each individual force vector, and points in a direction that is expected based on previous ink-dot studies of epithelial cell migration. The plot profile demonstrates the consistency and patterns of the epithelial ridges that form on the membrane.

Conclusion:
Many changes associated with disease processes are often hard to find with observation with the eye or endoscope. Image analysis using software like ImageJ unlocks a huge potential for a better understanding of common pathological conditions such as a cholesteatoma of the ear. Using image analysis, the epithelial ridges formed on the tympanic membrane were highlighted and isolated against the tympanic membrane. Further processing allowed us to capture the images in ellipses and from vectors that point toward the direction of epithelial migration. There are some limitations to our procedure, the biggest being the actual process of taking the image. The lighting and angles must be standardized since they affect the way the ridges are shown.

The procedure developed in this project can be used to compare normal and pathological ear drums by applying the same filters and plugins to determine if any general force vectors exist. This procedure can be used on any pathological process that involves the formation of epithelial ridges on a surface. Future considerations for this project include obtaining quantifiable data from the force vectors and plot profiles, as well as developing an artificial intelligence program that effectively differentiates between normal and pathological ear drums.

NICOLE A. SILVA (NJMS 2020)

PROJECT TITLE: TRANSBASAL VS. ENDOSCOPIC ENDONASAL VS. COMBINED APPROACHES FOR OLFACTORY GROOCE MENINGIOMAS: A SINGLE SURGEON'S EXPERIENCE

MENTOR: JAMES K. LIU, MD

DEPARTMENT: NEUROLOGICAL SURGERY

Participation Description:

My participation on the research consisted of a multitude of requirements. I worked alongside the surgeon collecting and discussing patient data, case by case. I worked with the EPIC hospital software for patient data as well as PACs software in order to read and analyze MRIs. I contacted patients to learn about their olfaction experiences pre and post surgery.

Finally, I worked along side Dr. Liu and a third year student to create and update his OGM database. Personally, I took a free online Stanford course to really learn medical statistics well, and thus performed statistical tests on our data from SPSS software. I interpreted, analyzed data and wrote an entire manuscript, about 3000 words which will be submitted either to Neurosurgery Journal or Neurosurgical Focus Journal. This abstract is a summary of my work this summer. Thank you for the opportunity!

Objective:

Olfactory groove meningiomas (OGM), arising from skull base arachnoid cells of the lamina cribosa and the frontoethmoidal suture, account for 4.5 – 18% of all intracranial meningiomas. These neoplasms are intimate to the olfactory nerves and tend to infiltration the cribiform plate, surrounding bone and vasculature. The ideal intervention is gross total resection (GTR) with removal of invaded dura and bone, but even after surgery, recurrence rates can be as high as 30%. There is increasing interest in the use of endoscopic endonasal approach (EEA) to remove tumors of the anterior skull base. However, the role of EEA for skull base meningiomas remains controversial. Here, we review the surgical results for olfactory groove meningiomas (OGMs) from a single surgeon (J.K.L) using open transbasal approach, EEA, and a combination of both. We analyze the factors involved in approach selection.

Methods:

We retrospectively reviewed 28 OGM cases from a prospective database. Diagnosis of OGM was based on clinical presentation, neurological examination, neuroimaging, and pathological confirmation. Patients medical charts were further reviewed and post-operative complications, discharge date, 30-day readmission and mortality were extracted. Three groups were created based on surgical approach taken: transbasal (Group 1, 15 cases), EEA (Group 2, 5 cases) and the combined approach (Group 3, 8 cases), which was a transbasal combined with EEA technique.

Summary:

Twenty-eight consecutive treatments were treated for OGM between the July 2007 and March 2016 by a single surgeon (J.K.L.). Their ages were between 15 and 83, with a mean age of 50.96 years (±13.62), and a clear female predominance in the patient pool (19 female; 9 male) (Table 1). The most common clinical presentations included vision loss (25%), headaches (21.43%), seizure or seizure-like activity (14.28%), personality changes (14.28%), and altered mental status (AMS) (10.71%). All combined transbasal-EEA approach patient cases presented with recurrent tumors and associated symptoms.

Eighteen patients (64.3%) presented with primary tumors, whereas 10 (35.7%) presented with recurrent ones. The combined group had largest mean tumor volume (101.148 cm3, ±71.24 cm3), while the transbasal group had the highest incidence of cerebral edema (73.33%, *P*=<0.001) and lowest incidence of a cortical cuff (33.33%, *P*=0.019). The pure EEA group had the smallest mean tumor volume (33.3 cm3, ±18.98 cm3), all with a cortical cuff, without optic nerve or vascular involvement. The combined transbasal-EEA group all had recurrent tumors that invaded the sinonasal cavity with the highest incidence of vascular

(37.5%, *P*=0.08) and optic nerve involvement (62.5%, *P*<0.011). Gross-total resection was achieved in 100% of EEA, 76.9% of transbasal, and 62.5% of combined cases. CSF leak rate was 0% in the transbasal and combined groups, while there were two leaks in the EEA group (40%). 30-day readmission occurred in 13.3% of transbasal cases, 40% of EEA cases, and 25% of combined approach cases. mRS score was a mean of 0.79 after transbasal, 2 after EEA, and 2.4 after combined approach (*P*=0.0604). Length of hospital stay (LOS) was a mean of 6.6 days (± 3.52 days) for transbasal cases, 4.2 days (± 3.11 days) for EEA cases, and 5.25 days (± 2.38 days) for combined transbasal-EEA cases (*P*=.309). LOS was also dependent on tumor size and patient comorbidities. There was no 30-day mortality. Follow up was a mean of 14.5 months (± 16.59 months). Comprehensive information is provided in **Tables 1** and **2**.

An open craniotomy continues to be proven to be the more successful approach for OGMs that are larger, specifically greater than 40 mm. Tumor size is repeated discussed in the literature to be a decisive variable in chosen surgical approach, favoring an open craniotomy for tumors greater than 40 mm to achieve GTR and reduce chance of recurrence. A "sweet-spot" tumor diameter has been described in the literature to be about 30-40 mm for GTR of OGMs with the EEA approach. Our single-surgeon experience contributes similar finding GTR was achieved with all EEA, with only one tumor exceeding the 40 mm "sweet spot" by 4.2 mm. All other tumors larger than 44.2 mm were approached through the transbasal technique or combined transbasal-EEA technique.

In our experience, we cautiously reserve EEA for case where this approach would be the most safe, effective, and cosmetically appealing for the patient. The presence of a cortical cuff is indicative of EEA consideration. Although Khan et al. found no significance of cortical cuff in treating EEA, we felt that cortical cuff provided a protective layer to proceed with EEA. Neurovascular involvement as well as optic and olfactory nerves attachment of tumor weighed heavily on favoring a transbasal approach. Although an "eyebrow" incision or supraorbital approach is used by several surgeons, the senior author feels that viewing angle is oblique even with expansive drilling of orbital roofs. This may be compensated using an angled endoscope for viewing. Finally, although there is good control on the ipsilateral side, the contralateral side is left vulnerable. We feel that a wide exposure through the one-piece transbasal approach is not a morbid procedure if the surgeon is cautious and skilled with handling surrounding nerves and vasculature.

OGMs grow slowly over time before becoming large enough to unilaterally or bilaterally compress the olfactory nerves and subsequently cause anosmia, phantosmia, dysosmia, dysgeusia and ageusia. The connection between the olfactory nerves to the taste tracts of the brain explain symptoms that include both taste and smell in patients with primarily large OGMs. Smell is a multivariate component of a patient's quality of life as it impacts social and cultural experiences. Youseff et al. describes smell as an important part of the limbic system, in which anosmia can cause psychological impairments. Thus, functional outcome of smell should be a pertinent consideration for the patient when deciding surgical approach. Because of rapid access after resection of the cribiform plate to the intranasal regions and the olfactory bulb and nerves, EEA manipulation of the anatomical region will destroy both olfactory nerves.

Olfaction was preserved in none of the EEA cases and combined cases, as the EEA approach inevitably destroys the olfactory nerves when entering through the sinonasal cavity to the cribiform plate. Only eleven patients had detailed information regarding their olfaction. After surgery a spectrum of olfaction sensitivity was reported by several patients. For example, a patient who reportedly had strong sense of smell before surgery, intraoperatively, had the olfactory nerves spared by the surgeon. In follow-up, she reported a loss of smell of certain flora scents, but enhanced smell of chemicals. In total, from the existing data, 36.3% of patients who underwent transbasal approach retained olfaction or experienced dysosmia. The remaining lost smell due to tumor infiltration and removal. Comprehensive description of the olfaction often patients is further explained in **Table 3**.

A noteworthy case from our cohort demonstrates the preservation of olfaction through a transbasal approach. A 48-year-old male presented with seizures to which further imaging revealed a lesion that was later confirmed to be OGM. His smell was intact before surgery and his tumor diameter was only 23 mm. This case, usually, would be a EEA candidate, yet the patient still had the sense of smell. As a result, the surgeon decided on the possibly of retaining smell through a transbasal approach and was successful. In follow up, the patient reports no change in his olfaction. Overall, the sense of smell is still intact pre-operatively in a number of patients with OGM and thus, should be taken into account when choosing the appropriate surgical approach. The transbasal approach allows for GTR, and a lower Simpson grade resection, while offering possible preservation of olfaction if the surgeon is extremely skilled and cautious.

Conclusion:

When addressing OGM, maintaining an armory of surgical tactics is paramount. In our practice, the transbasal approach remains the workhorse for removing larger, complex tumors in patients with pre-existing anosmia. The role of EEA appears to be limited to smaller, appropriately selected tumors. EEA also plays an important adjunctive role in sinonasal inspection and skull base reconstruction when combined with transbasal approaches in recurrent OGMs invading the sinonasal cavity. Careful patient selection and individualized case analysis dictates optimal approach for best functional outcome and recovery.

Table 1: Cohort and Tumor Characteristic of 28 patients with OGM

	Transbasal (n=15)	*P* value	EEA (n=5)	*P* value	Combined (n=8)	*P value*
Age (range)	52.13 (34-66)	-	51.07 (28-58)	-	52.88 (15-83)	-
Gender						
Male	5		1		3	
Female	10		4		5	
Tumor Volume, cm3 (range)	92.02 (4.35-300.06)		33.33 (15.69-60.77)		101.05 (30.59-260.60)	
Cerebral Edema, no.	11	<0.001*	3	0.70	2	0.17
Cortical Cuff	5	0.019*	5	-	7	<0.001*
Vascular Involvement	10	<0.001*	0	-	3	0.08
ON Involvement	7	0.004*	0	-	5	0.011*

Table 2: Functional Outcomes and Recovery by Group				
	Transbasal (n=15)	**EEA (n=5)**	**Combined (n=8)**	***P* value**
GTR	12	5	5	0.271
S1	8	5	4	-
S2	2	0	1	-
NTR	3	0	3	-
CSF leak	0	1	1	-
Length of Stay (SD)	6.6 (+/- 3.52)	4 (+/- 3.11)	5.25 (+/-2.38)	0.309
30-Day Readmission	2	2	2	-
Complications	0	2	2	-
mRS	0.786	2	2.4	0.0604
anosmia (n=7)	2	5	8	-
dyosmia (n=7)	2	0	0	-
olfaction preservation (n=7)	4	-	-	-

Table 3: Outcomes of Olfaction in 10 Transbasal Patients			
Patient	**Pre-Operative Olfaction**	**Post-Operative Olfaction**	**Intraoperative Report**
1	smell	anosmia	-
2	-	-	olfactory nerves preservation
3	smell	dysosmia	olfactory nerves preservation
4	dysosmia		-
5	smell	dysosmia	-
6	-	-	olfactory nerves destruction by tumor
7	anosmia	-	-
8	smell	dysosmia	-
9	smell	smell	olfactory nerves preservation
10	smell	smell	olfactory nerves preservation
11	-	-	olfactory nerves destruction by tumor

AMY SONG (TCNJ 2020, NJMS 2023)

PROJECT TITLE: **CIS-REGULATION OF BMP2 EXPRESSION IN LUNGS**
MENTOR: **MELISSA ROGERS, PH.D.**
DEPARTMENT: **MICROBIOLOGY, BIOCHEMISTRY AND MOLECULAR GENETICS**

Participation Description:

As a summer student intern, I learned how to design the experimental layout, schedule experiments, and perform the experiment itself. As part of the experiment, I learned how to grind tissues snap-frozen as well as those kept in RNAlater. I also learned how to prepare RIPA lysates after the sonication of frozen tissue powder. I learned how to perform a Bradford colorimetric assay and prepare Laemmli lysates. I was also involved in running gels in SDS-PAGE and the entire western blotting process, which involved immunoblotting and ECL/Fluorochem imaging. I also learned how to analyze results using the Alphaview quantification software. Using the software, I was able to quantify amounts of the desired protein and normalize protein quantities to a loading control. Over the course of my internship, I participated in four assays, which consisted of a total of approximately sixty samples.

Objective:

To understand the role of the ultra-conserved sequence (UCS) in regulating bone- morphogenetic protein 2 (BMP2) expression to potentially aid in the development of novel cancer therapies for lungs cancers.

Methods:

We had two available alleles, one of which was a wildtype allele with the UCS intactand a ΔUCS allele with the UCS deletion. Mouse lung lysates were prepared through dissection, perfusion, tissue grinding, and sonication. Phosphorylated SMAD (pSmad) and total SMAD (tSmad) levels were detected using western blotting.

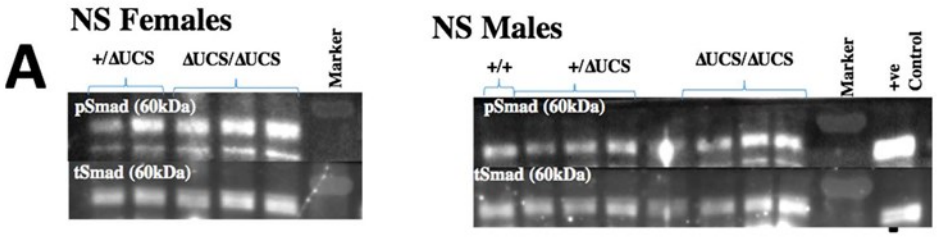
Summary:

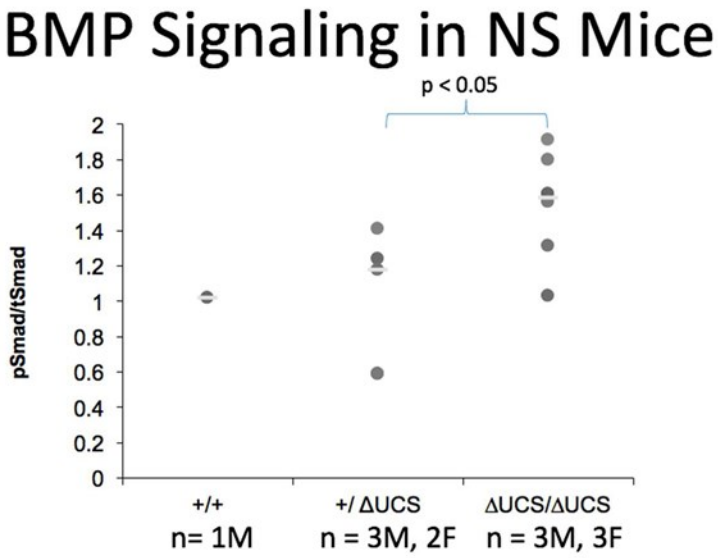
Outbred mouse strains showed a trend of increased BMP signaling in homozygousΔUCS mouse lungs relative to heterozygous (+/ΔUCS) or wildtype (+/+) mice. In contrast, the inbred mouse strain showed a trend of decreased BMP signaling in homozygous ΔUCS mouse lungs relative to heterozygous (+/ΔUCS) or wildtype (+/+) mice.

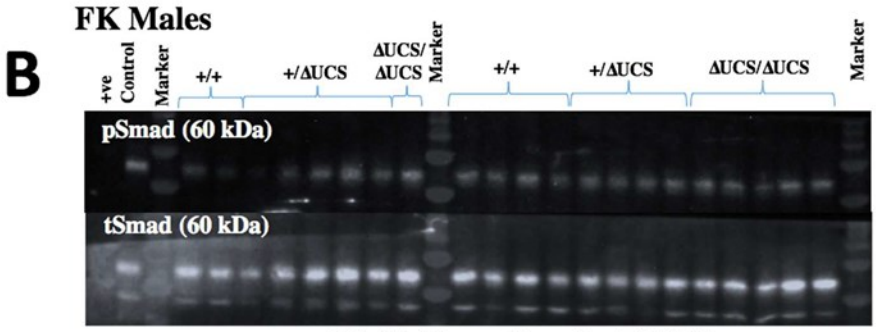
Conclusion:

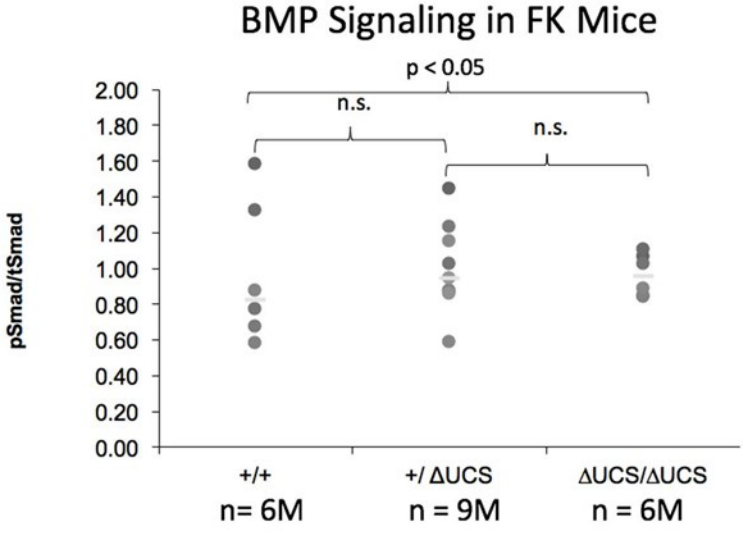
We hypothesized that BMP signaling differs in the lungs of homozygous ΔUCS mice relative to heterozygous (+/ΔUCS) or wildtype (+/+) mice. As both outbred and inbred mouse strains showed differing BMP signaling levels in the homozygous ΔUCS mice relative to the other genotypes, the hypothesis was supported.

Figures:


A
NS Females
+/ΔUCS
ΔUCS/ΔUCS
Marker
pSmad (60kDa)
tSmad (60kDa)
NS Males
+/+
+/ΔUCS
ΔUCS/ΔUCS
Marker
+ve Control
pSmad (60kDa)
tSmad (60kDa)


BMP Signaling in NS Mice
p < 0.05
pSmad/tSmad
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
+/+
+/ ΔUCS
ΔUCS/ΔUCS
n= 1M
n = 3M, 2F
n = 3M, 3F


B
FK Males
+ve Control
Marker
+/+
+/ΔUCS
ΔUCS/ ΔUCS
Marker
+/+
+/ΔUCS
ΔUCS/ΔUCS
Marker
pSmad (60 kDa)
tSmad (60 kDa)


BMP Signaling in FK Mice
p < 0.05
n.s.
n.s.
pSmad/tSmad
2.00
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
+/+
+/ ΔUCS
ΔUCS/ΔUCS
n= 6M
n = 9M
n = 6M

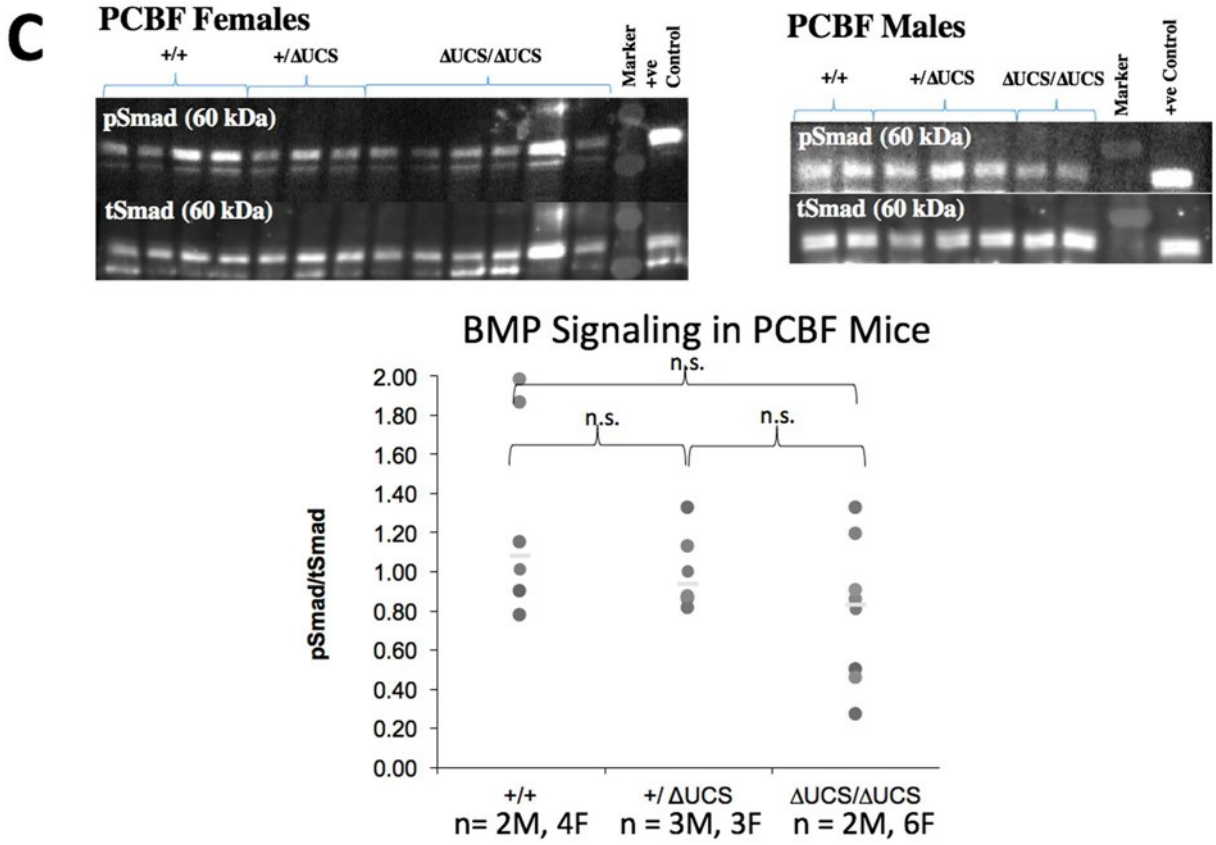


Fig 1. Relative BMP signaling in mice with a wildtype (+/+), heterozygote (+/ ΔUCS), or homozygote (ΔUCS/ ΔUCS) genotype bearing the UCS deletion allele. BMP signaling was assessed by measuring pSmad and tSmad levels using western blotting. Scatterplots show amounts of pSmad normalized to tSmad. A) BMP signaling in males and females of NS outbred strain (aged 450-550 days, strains C57Bl/6 and 129). B) BMP signaling in males of FK outbred stain (aged 40-50 days, strains C57Bl/6, 129, and C3H). pSmad levels were assessed 3 times. A representative gel is shown. C) BMP signaling in males and females of PCBF inbred strain (aged 250-300 days, strain 129).

MAX WARD (NJMS 2020)

PROJECT TITLE: **TRANSCALLOSAL INTERFORNICEAL APPROACH TO THE THIRD VENTRICLE: THE ROAD LESS TRAVELED**
MENTOR: **JAMES K. LIU, MD**
DEPARTMENT: **NEUROLOGICAL SURGERY**

Participation Description:

With Dr. Liu I have spent the summary analyzing outcomes in the transcallosal interforniceal approach to the third ventricle. My work for this summer included an extensive literature review for manuscripts pertaining to this surgical approach, review of Dr. Liu's case history for patients who underwent this approach, I created figures for the manuscript and poster, and I performed a retrospective chart review to assess their outcomes. I was assisted in figure creation, chart review, and writing by Naveed Kamal and given guidance, data clarification, and directional clarification by Dr. Liu. We have begun writing a manuscript for this project.

this project.

Objective:

To retrospectively investigate patient outcomes associated with the transcallosal interforniceal approach to the third ventricle and to provide useful technical nuances in the procedure.

Methods:

Chart Review
We performed a retrospective chart review of patients who underwent transcallosal interforniceal surgery for third ventricular tumors since 2011. All patients were confirmed as having third ventricular tumors by MRI (Figures 1 and 2).

Surgical Technique

After exposing the corpus callosum within the interhemispheric fissure, a small 2-cm callosotomy is made at the midline. This is dissected down until it is possible to visualize the ependyma of the lateral ventricle. A right-sided entrance to the lateral ventricle is confirmed by identification of the septum, thalamostriate vein, and choroid plexus. A septostomy is created at the most superior margin of the septum pellucidum where it meets the corpus callosum. This allows entry into the left ventricle, which is followed by identification of the left choroid plexus along the ventricular floor.

The microscope is then aimed in an anterior to posterior direction until it is possible to visualize the posterior aspect of the corpus callosum. After identifying the leaflets of the septum pellucidum and visualizing both fornices, the fornices are gently spread using a microbayonet spread technique. The lateral position provides beneficial gravity assistance during forniceal spread. This allows visualization and entrance into the tela choroidea. It is then possible to visualize both internal cerebral veins and the arachnoid forming the roof of the posterior third ventricle, dissection of which allows entrance into the third ventricle (Figure 3).

Summary:

Patient Information
Fourteen patients underwent transcallosal interforniceal resection of third ventricular tumors, two patients underwent re-operation for tumor recurrence for a total of 16 cases. There were 8 males and 6 females, the average age at surgery was 35.75 years. Average post-operative stay was 11.3 days and average follow-up was 6.5 months. Clinical presentation included headache, nausea/vomiting, visual disturbances, altered mental status, vertigo, lower extremity weakness, and two patients were asymptomatic at diagnosis (Table 1). Pre-operative hydrocephalus was present in eleven cases.

Pathology and Surgical Outcome
Postoperative diagnosis included eight colloid cysts, two WHO grade II astrocytomas (one recurrent), two WHO grade III astrocytomas (one recurrent), one papillary tumor of the pineal region, one central neurocytoma, one ependymoma, and one glioneuronal tumor. Tumors were present in all three regions of the third ventricle. Gross total resection was confirmed in ten patients, near-total (99%) resection in one patient, and subtotal resection in 5 patients. Nine patients were scored as 0 (no neurologic symptoms) on the modified rankin scale, four patients were scored as 1 (some neurologic symptoms but no disability), and one patient was scored as a 3 (moderate disability).

Postoperative Complications
Post-operative morbidity was limited to one patient with transient supplementary motor syndrome, one patient with transient supplementary motor syndrome and short0term memory loss, and one patient with panhypopituitarism and a postoperative DVT which lead to a pulmonary embolus. There were no postoperative morbidities for colloid cyst patients. Within this study there was only a 6.25% incidence of short term memory loss compared to 36% within the literature.

Conclusion:

The transcallosal interforniceal approach can be utilized for the resection of tumors anywhere within the third ventricle. When preformed properly, we believe this approach does not significantly increase the risk of memory deficit when compared to other approaches.

Table 1: Clinical Presentation of Patients

Clinical Presentation	No. of Cases with Symptom
Headaches	9
Nausea/Vomiting	5
Visual/Ocular Disturbances	4
Altered mental Status	2
Vertigo	2
Asymptomatic	2
Lower Extremity Weakness	1

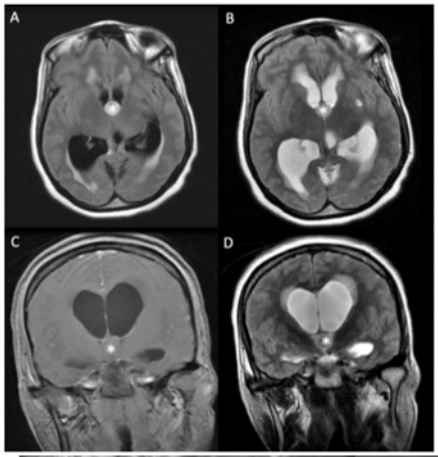
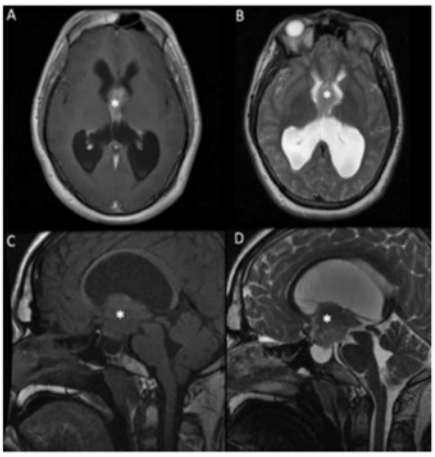


Figure 1 (Left): A colloid cyst (star) in the third ventricle seen in T1 weighted axial MRI (A), T2 weighted axial MRI (B), T1 weighted coronal MRI (C), T2 weighted coronal MRI (D). There is associated hydrocephalus with increase in size of the lateral ventricles.

Figure 2 (Right): A neurocytoma (star) in the third ventricle seen in T1 weighted axial MRI (A), T2 weighted axial MRI (B), T1 weighted saggital MRI (C), T2 weighted saggital MRI (D). There is associated hydrocephalus with increase in size of the lateral ventricles.



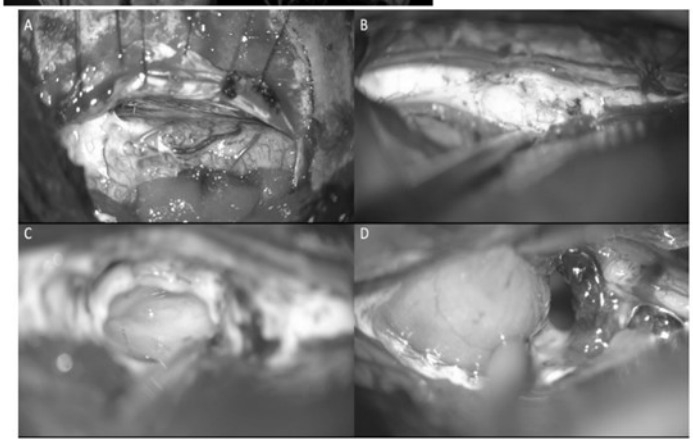


Figure 3 (Left): Transcallosal interforniceal approach for the resection of a third ventricular colloid cyst. The dura is incised and retracted adjacent to the midline (A). Subsequently, careful microsurgical dissection is applied in order to expose the corpus callosum, taking care not to injure the callosomarginal and pericallosal arteries (B). The corpus callosum is incised and the fornices are spread to obtain visualization into the third ventricle (C) following which the cyst is removed from the third ventricle (D).

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PAVLY YOUSSEF (NJMS 2020)

PROJECT TITLE: **NJMS DOMESTIC VIOLENCE INTERVENTION PROGRAM IN NEWARK PUBLIC SCHOOLS**
MENTOR: **PING-HSIN CHEN, PH.D**
DEPARTMENT: **FAMILY MEDICINE**

Participation Description:

The NJMS DV Program took the initiative to prevent domestic violence cases and lessen its effects. Along with Dr. Chen, my peers and I addressed the issue of domestic violence in Newark public schools and discussed methods to decrease the prevalence of the violence. I was involved in the planning for each session along with my peers. For instance, I participated in preparing the PowerPoint slides for the discussion part of each session. In addition, I was involved in coming up with an activity for each session that incorporates the topic of the discussion into an engaging and enjoyable activity. I was also involved in collecting the data from the surveys conducted during multiple sessions of the program, as well as in the analysis and interpretation of the data. Through engaging presentations, our program allowed students to become educated on the topic and learn ways to prevent them from becoming a perpetuator of violence.

Objective:

Children may be exposed to various forms of abuse in their homes, which include but is not limited to verbal, physical, and emotional abuse. In the year of 2012, there were around 65,000 domestic violence cases reported by the state of New Jersey (NCADV 2015). Of these cases, 29% involved children. Around 10% to 20% American children experience adult domestic violence in their homes each year (Edleson 2006). Considerable evidence has shown that domestic violence makes a negative impact on the health of survivors and witnesses. Children who are exposed to violence are affected mentally and have a greater risk of becoming victims or perpetrators of domestic violence (Moyer 2013). Exposure to adult domestic violence tends to lead to depression, low self-esteem, and substance abuse in adulthood (Illinois Department of Human Services 2000). Children who live in homes where violence between adults is a regular occurrence are nine times more likely to intervene. Some children isolate or distract themselves from violent situations that occur in their homes (Edleson 2006). Public attention to domestic violence and its impact on children has become significant. Research and programs like this program have been imposed to curb the rise of domestic violence and to aid the children who experience it. Taking into consideration the traumatizing mental and psychological effects of exposure to domestic violence at a young age (Chen et al., 2013), the project aimed to empower children of the community with the information they need to cope with and avoid different forms of violence.

Methods:

The domestic violence prevention program was designed for third graders at 2 Newark elementary schools. The duration of the program was 12 weeks (12 sessions) starting in April 2017. Our team visited 5 third grade classrooms at the 2 schools for 30-45 minutes each week. Each session included a presentation and a short activity coinciding with the topic at hand. Topics and activities were carefully constructed around domestic violence awareness and its effects, including diet, exercise, coping with stress, safety planning, culture, diversity, and career exploration. After each session, our group met and reviewed how well the children understood the topic. The team then prepared the presentation and activity for the upcoming week. We administered a needs and risk assessment and program evaluation during the 12 sessions. Data from these assessments were analyzed to describe the prevalence of different forms of violence exposure among children as well as evaluate their knowledge and perceptions of the topics addressed in the program.

Summary:

Figure 1 depicts the percentage of children who are exposed to different forms of violence. Thirty percent of children have seen physical violence between adults. More than one third (35.7%) of the children said they have heard adults talk down someone. The majority (54.8%) said they had heard an adult curse and scream at someone. Furthermore, 44.9% of the children have been exposed to different forms of violence on the media such as scenes depicting murder scene of murder, theft, animals fighting or eating each other, or torturing.

Table 1 shows the percentage of students choosing correct answers to post test questions. Almost all of students (>92.5%) answered correctly to questions about vital topics discussed in the program including dealing with stress, violence, bullying, and other types of stresses.

Figure 2 depicts the children's feedback towards the. The vast majority have been well informed about all the crucial topics that were presented to them, such as coping with stress, adopting a healthy lifestyle, dealing with bullying and preventing it, and staying safe whenever they experience domestic violence between adults (ranging from 79.4% to 92.4%). Also, most of the of the students (91.1%) believe that other students will benefit from this program in the future. However, only 56.7% of the students stated that the presentations were easy to understand.

Figure 1. Percentage of children of third grade exposed to different forms of violence.

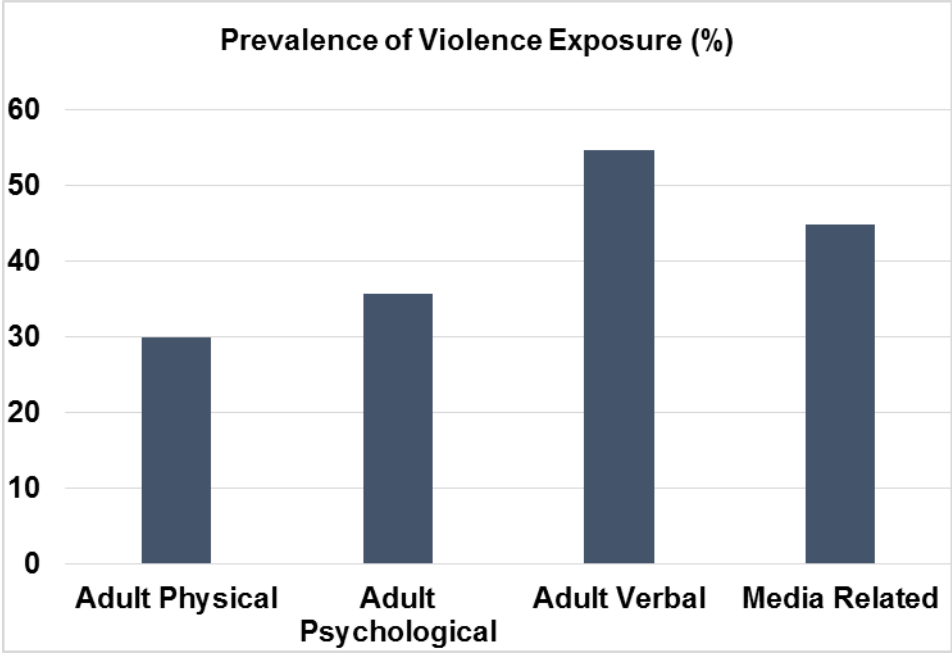
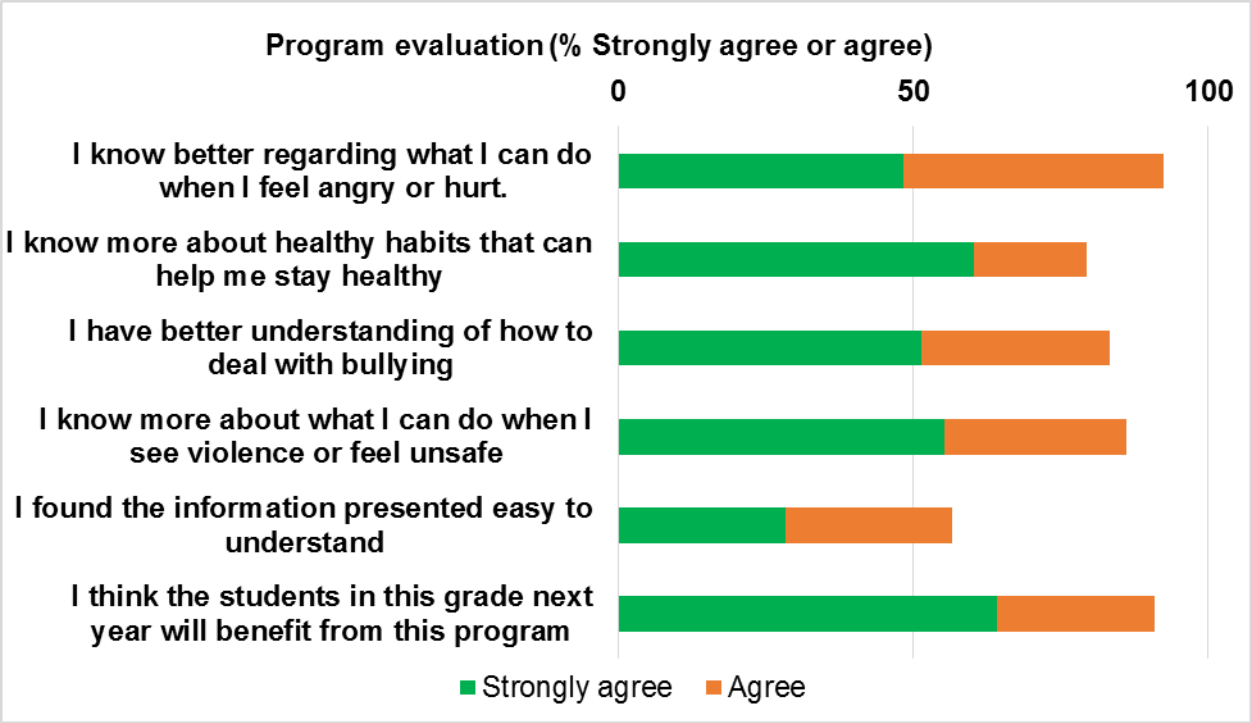


Table 1. Percentage of students choosing correct answers to post test questions

Percentage of students choosing correct answers at post test	
Q: What can you do when you feel angry or hurt? A: Exercise, listen to music or do something else that calms you.	100.0
Q: What can you do to stay healthy (physically and mentally)? A: Eat nutritious food like fresh fruits and vegetables.	92.7
Q: Jim says mean things to John that make him feel bad. What should John do? A: Talk about his feelings with a trusted adult.	95.6

Figure 2. Exit survey conducted at the end of the program to have the children's feedback in order to evaluate the success of the program in fulfilling its objectives.



Conclusion:

Violence is very prevalent and is experienced by a significant number of the community's children. Children are constantly exposed to adults fighting, talking down others, and cursing and screaming at others. The media contributes greatly to our children exposure to violence through scenes of murder, theft, torturing, and others. Overall, the program was successful by engaging students with interactive presentations and fun activities. The program has empowered the children of the community with information and instructions to assist them in preventing domestic violence and also to prevent them from becoming the perpetuators of violence. Through this program, children may cope positively if exposed to different forms of violence. Future work should continue to provide more children with tools to guard them against violence. Students' feedback should be incorporated into future works through modifying curriculum and teaching strategies. In light of the outcomes of the program, it seems necessary for programs to focus on teaching children of the community on violence prevention and its related consequences.

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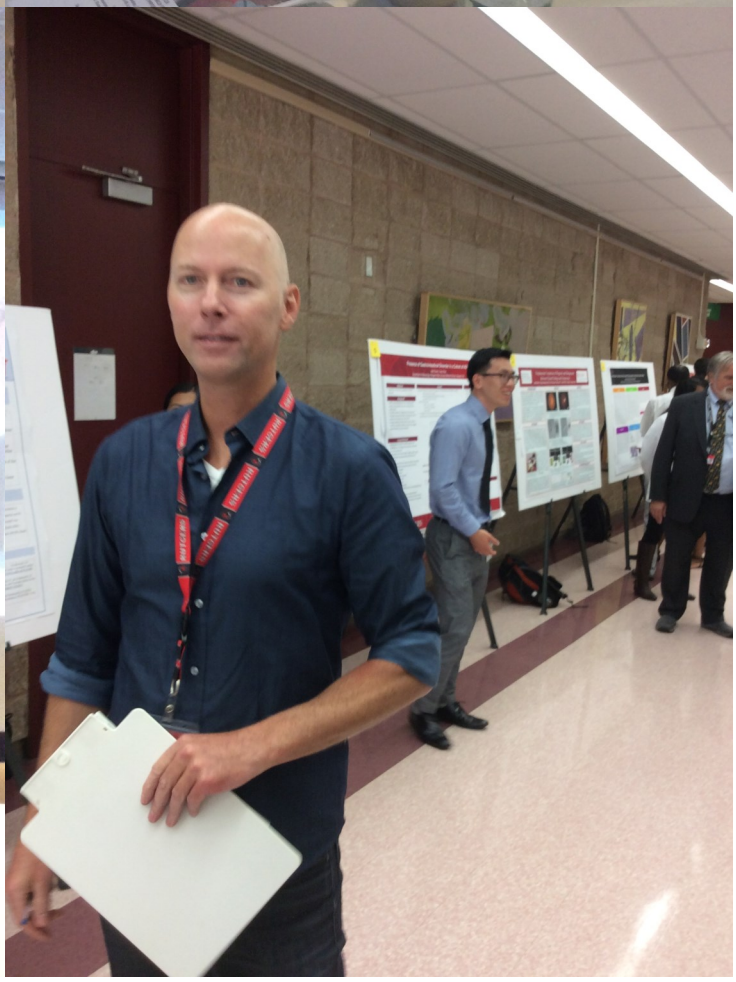

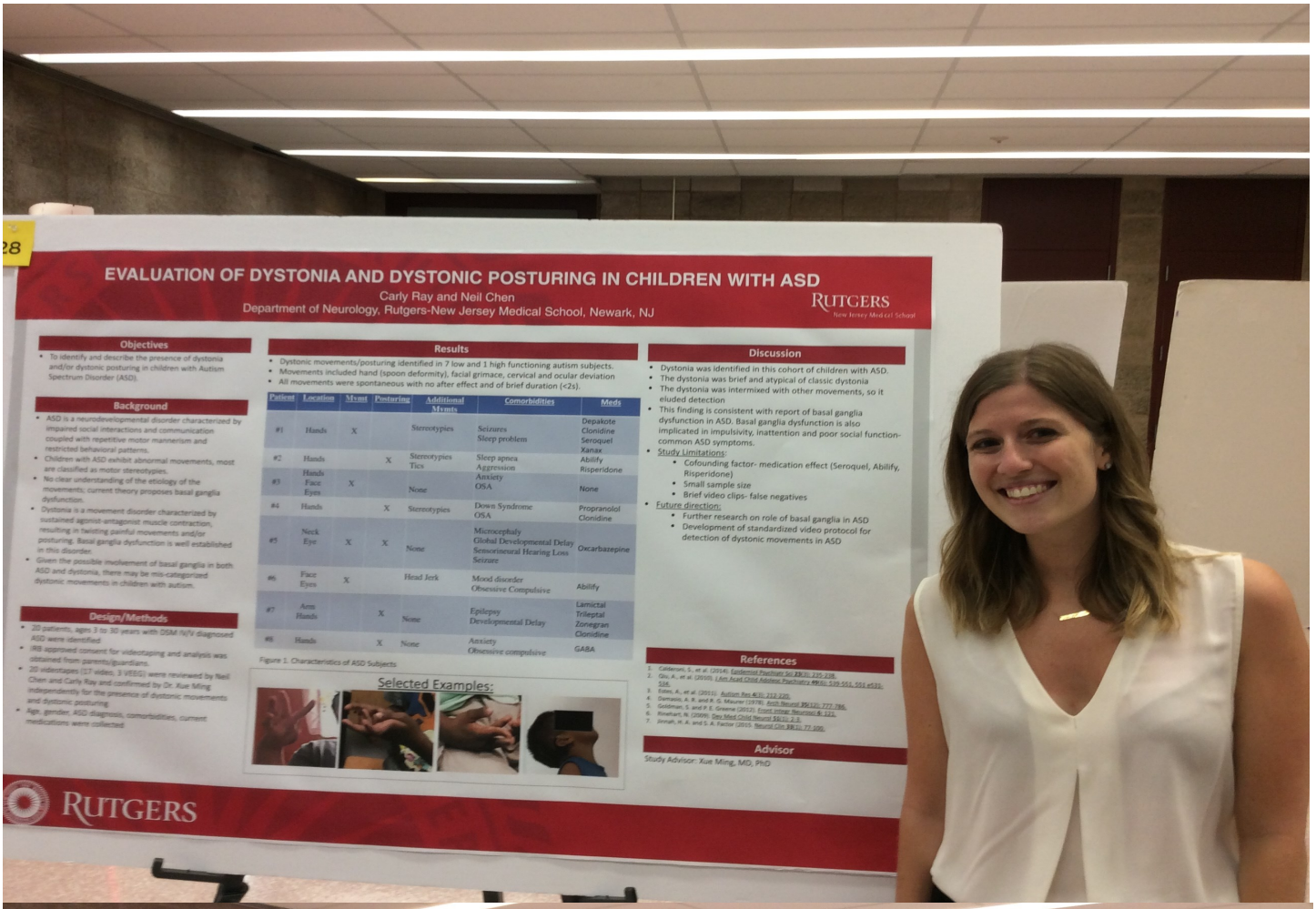
28
EVALUATION OF DYSTONIA AND DYSTONIC POSTURING IN CHILDREN WITH ASD
Carly Ray and Neil Chen
Department of Neurology, Rutgers-New Jersey Medical School, Newark, NJ
RUTGERS
New Jersey Medical School
Objectives
To identify and describe the presence of dystonia and/or dystonic posturing in children with Autism Spectrum Disorder (ASD).
Background
ASD is a neurodevelopmental disorder characterized by impaired social interactions and communication coupled with repetitive motor mannerism and restricted behavioral patterns.
Children with ASD exhibit abnormal movements, most are classified as motor stereotypies.
No clear understanding of the etiology of the movements; current theory proposes basal ganglia dysfunction.
Dystonia is a movement disorder characterized by sustained agonist-antagonist muscle contraction, resulting in twisting painful movements and/or posturing. Basal ganglia dysfunction is well established in this disorder.
Given the possible involvement of basal ganglia in both ASD and dystonia, there may be mis-categorized dystonic movements in children with autism.
Design/Methods
20 patients, ages 3 to 30 years with DSM IV/V diagnosed ASD were identified.
IRB approved consent for videotaping and analysis was obtained from parents/guardians.
20 videotapes (17 video, 3 VEEG) were reviewed by Neil Chen and Carly Ray and confirmed by Dr. Xue Ming independently for the presence of dystonic movements and dystonic posturing.
Age, gender, ASD diagnosis, comorbidities, current medications were collected.
Results
Dystonic movements/posturing identified in 7 low and 1 high functioning autism subjects.
Movements included hand (spoon deformity), facial grimace, cervical and ocular deviation
All movements were spontaneous with no after effect and of brief duration (<2s).
Patient | Location | Mvmt | Posturing | Additional Mvmts | Comorbidities | Meds
#1 | Hands | X | | Stereotypies | Seizures, Sleep problem | Depakote, Clonidine, Seroquel, Xanax
#2 | Hands | | X | Stereotypies, Tics | Sleep apnea, Aggression | Abilify, Risperidone
#3 | Hands, Face, Eyes | X | | None | Anxiety, OSA | None
#4 | Hands | | X | Stereotypies | Down Syndrome, OSA | Propranolol, Clonidine
#5 | Neck, Eye | X | X | None | Microcephaly, Global Developmental Delay, Sensorineural Hearing Loss, Seizure | Oxcarbazepine
#6 | Face, Eyes | X | | Head Jerk | Mood disorder, Obsessive Compulsive | Abilify
#7 | Arm, Hands | | X | None | Epilepsy, Developmental Delay | Lamictal, Trileptal, Zonegran, Clonidine
#8 | Hands | | X | None | Anxiety, Obsessive compulsive | GABA
Figure 1. Characteristics of ASD Subjects
Selected Examples:
Discussion
Dystonia was identified in this cohort of children with ASD.
The dystonia was brief and atypical of classic dystonia
The dystonia was intermixed with other movements, so it eluded detection
This finding is consistent with report of basal ganglia dysfunction in ASD. Basal ganglia dysfunction is also implicated in impulsivity, inattention and poor social function- common ASD symptoms.
Study Limitations:
Cofounding factor- medication effect (Seroquel, Abilify, Risperidone)
Small sample size
Brief video clips- false negatives
Future direction:
Further research on role of basal ganglia in ASD
Development of standardized video protocol for detection of dystonic movements in ASD
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Advisor
Study Advisor: Xue Ming, MD, PhD
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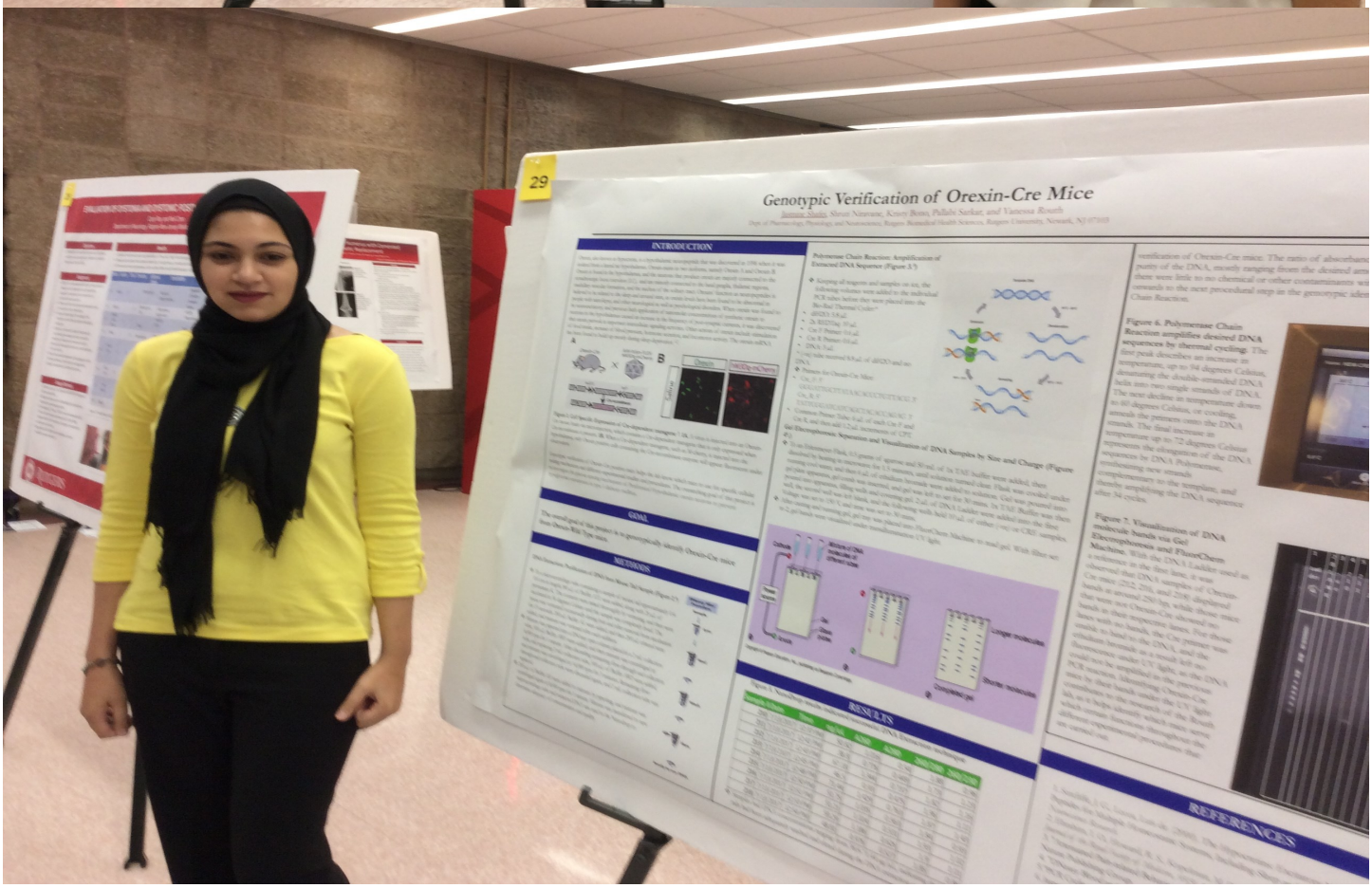
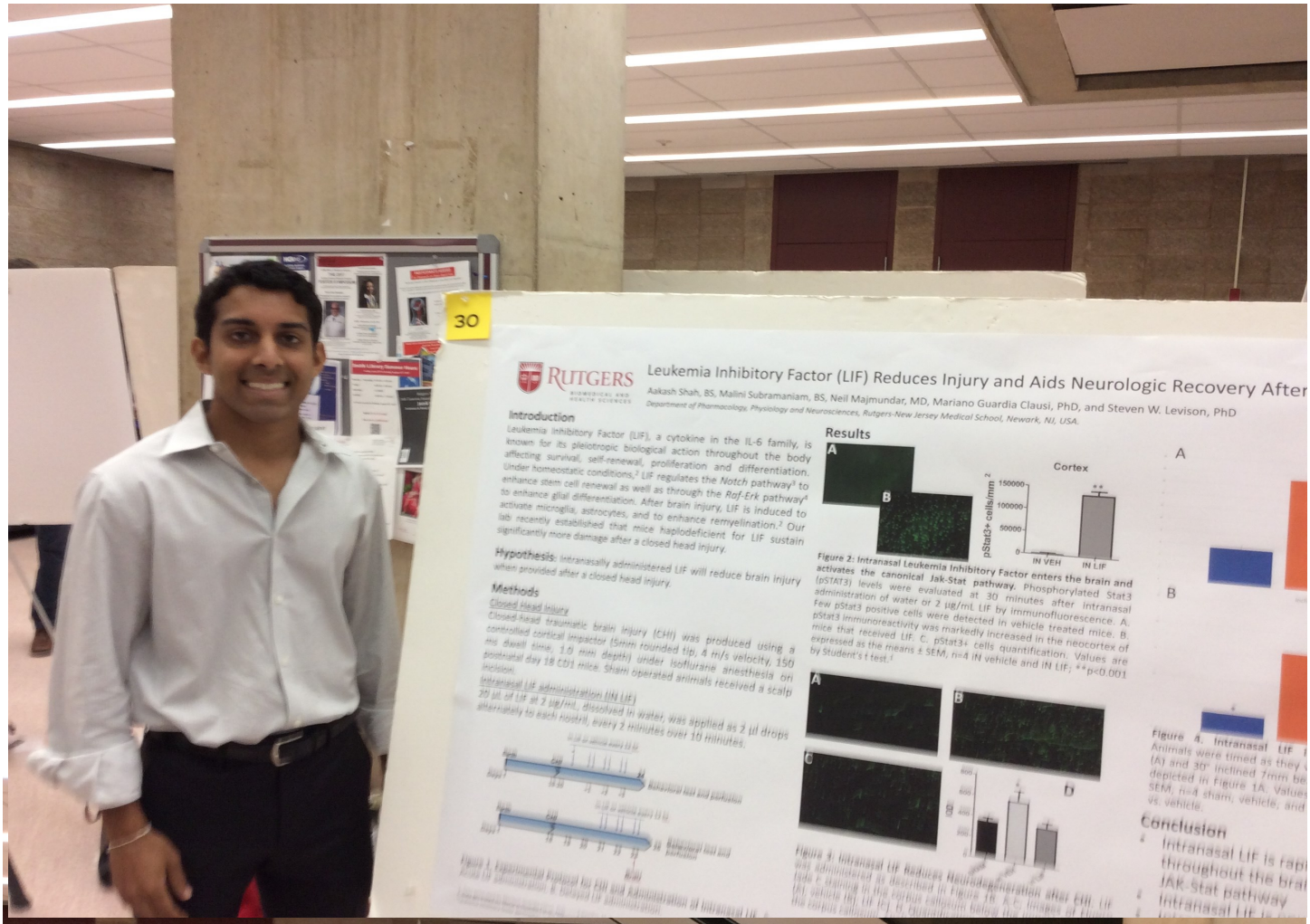

29
Genotypic Verification of Orexin-Cre Mice
INTRODUCTION
GOAL
METHODS
RESULTS
REFERENCES


30
RUTGERS
Leukemia Inhibitory Factor (LIF) Reduces Injury and Aids Neurologic Recovery After
Aakash Shah, BS, Mallini Subramaniam, BS, Neil Majmundar, MD, Mariano Guardia Clausi, PhD, and Steven W. Levison, PhD
Department of Pharmacology, Physiology and Neurosciences, Rutgers-New Jersey Medical School, Newark, NJ, USA.
Introduction
Leukemia Inhibitory Factor (LIF), a cytokine in the IL-6 family, is known for its pleiotropic biological action throughout the body affecting survival, self-renewal, proliferation and differentiation. Under homeostatic conditions,[2] LIF regulates the Notch pathway[3] to enhance stem cell renewal as well as through the Rof-Erk pathway[4] to enhance glial differentiation. After brain injury, LIF is induced to activate microglia, astrocytes, and to enhance remyelination.[2] Our lab recently established that mice haplodeficient for LIF sustain significantly more damage after a closed head injury.
Hypothesis: Intranasally administered LIF will reduce brain injury when provided after a closed head injury.
Methods
Closed Head Injury
Closed-head traumatic brain injury (CHI) was produced using a controlled cortical impactor (5mm rounded tip, 4 m/s velocity, 150 ms dwell time, 1.0 mm depth) under isoflurane anesthesia on postnatal day 18 CD1 mice. Sham operated animals received a scalp incision.
Intranasal LIF administration (IN LIF)
20 µl of LIF at 2 µg/mL, dissolved in water, was applied as 2 µl drops alternately to each nostril, every 2 minutes over 10 minutes.
Results
Cortex
pStat3+ cells/mm²
150000
100000
50000
0
IN VEH
IN LIF
**
Figure 2: Intranasal Leukemia Inhibitory Factor enters the brain and activates the canonical Jak-Stat pathway. Phosphorylated Stat3 (pSTAT3) levels were evaluated at 30 minutes after intranasal administration of water or 2 µg/mL LIF by immunofluorescence. A. Few pStat3 positive cells were detected in vehicle treated mice. B. pStat3 immunoreactivity was markedly increased in the neocortex of mice that received LIF. C. pStat3+ cells quantification. Values are expressed as the means ± SEM, n=4 IN vehicle and IN LIF; **p<0.001 by Student's t test.
Conclusion
Intranasal LIF is rap
throughout the brai
JAK-Stat pathway
Intranasal LIF i
31
Effect of Rpd3 Downregulation on Alzheimer's Disease and Longevity
Chandani Patel, Aarsh Shah, Peter Alsharif, Karan Randhawa, Amelia Lake, and Yongkyu Park
Department of Cell Biology and Molecular Medicine, Rutgers-New Jersey Medical School, Newark, New Jersey, USA
RUTGERS
New Jersey Medical School
Abstract
Amyloid-β peptide inducement is observed using the climbing assay technique in the Alzheimer's Disease (AD) flies along with aging assays. Downregulation of histone deacetylase, Rpd3, in Drosophila melanogaster increases longevity and possibly impedes accumulation of amyloid-β peptides in the brain. The UAS-elavGal4 fly stem was used along with Rpd3 downregulation in the experimental flies. RNA interference mediated downregulation of rpd3 in this project results in increased neurological function amongst AD flies with induced neurodegeneration. The aging assay has been conducting in hopes of finding what occurs as the flies aged, but has not been conducted long enough to see significant difference. The experiment will continue to find a significant data using the Rpd3 regulator for gene expression specifically in the brain.
Introduction
Alzheimer's Disease (AD) is a neurodegenerative disorder leading to amnesia, cognitive impairment and senile dementia. From the previous experiments, it was demonstrated that accumulation of amyloid-β (Aβ) peptides in brain is the primary event in the sequential progression of AD. Expression of Aβ42 in brain leads to formation of diffused amyloid deposits, age-dependent learning defects, and extensive neurodegeneration. Currently, we are investigating the impact of brain-specific Rpd3 downregulation on flies with AD. UAS-elavGal4 system is used for expression of Aβ peptide in the fly brain which gives rise to clear amyloid deposits, age dependent locomotor defects and neurodegeneration. Gal4 is a yeast transcriptional activator and its target is Upstream Activating Sequence (UAS). The binding of Gal4 to UAS activates gene transcription of downstream genes. Elav is a promoter of neuron-specific protein that leads to rpd3R (RNA interference) expression in brain.
Control (A)
UAS
Aβ42
elav
Gal4
Experimental (B)
rpd3R
Figure 1. Transgenes used for: (A) Overexpression of Aβ42 gene (AD Gene). (B) Overexpression of Aβ42 with Rpd3 downregulation with rpd3R.
Hypothesis
We hypothesize that Rpd3 downregulation in the brain extends lifespan with reducing neurodegeneration caused by Aβ42 and Alzheimer's Disease.
Methods
Fly Cross
Given two parent genotypes, the progeny genotype was determined. For each set of genotypes, the number of surviving flies was counted and indication of Alzheimer's Disease in the brain was examined.
Aging Assay
Flies from each genotype were collected and placed accordingly into standard cornmeal medium vials, and kept in a 25°C incubator. The surviving flies were counted, and transferred into new vials every 3-4 days. There were twenty flies placed into each vial, with a total of one hundred flies prepared for each of the three genotypes, at the start of the project.
Climbing Assay
After the aging flies were transferred into new vials, the flies were used for climbing assay. Each vial was tapped for about two seconds and the number of flies that climbed in the vial were counted for next 30 seconds in intervals of ten seconds.
Results
A
B
Aβ42/3d
Aβ42/48d
Figure 2. Detection of Aβ deposits (arrowhead) in fly brain over given time span (reference 1).
A
Kc
Ca
PB
CA
A: Aβ/3d
Figure 3. Late onset progressive neurodegeneration and progressive neuronal loss (arrowhead) occurred in Aβ42 Kenyon cell region (reference 1).
Results (cont.)
UAS-Aβ42
Control
AD Flies
Climbing ability (%)
days
Figure 4. Comparative progressive climbing disability of Aβ42 flies during aging due to neurodegeneration (reference 1).
Aβ42 flies recovered by Rpd3 downregulation
AD Flies with rpd3 Down
AD Flies
Aβ42/elavGA
Aβ42,rpd3R/elavGA
Aβ42,rpd3PT/elavGA
Figure 5. The climbing disability in Aβ42 flies is rescued by Rpd3 downregulation (rpd3R: RNA interference, rpd3PT: rpd3 deletion mutant) in the brain.
UAS-Aβ42
Control
AD Flies
Survival rate (%)
Figure 6. Comparative survival rate of Aβ42 flies in previous studies of longevity in flies with Alzheimer's Disease (reference 1).
Results (cont.)
Lifespan of Aβ42 flies with Rpd3 downregulation
AD Flies
AD Flies with rpd3 Down
Aβ42/elavGA
Aβ42,rpd3R/elavGA
Aβ42,rpd3PT/elavGA
Flies surviving (%)
Days
Figure 7. Ongoing lifespan data obtained from current Alzheimer's fly aging assay research.
Conclusion
The purpose of this project is to investigate if Rpd3 downregulation in the brain extends lifespan with reducing neurodegeneration of AD flies. Interestingly, the climbing disability in Aβ42 flies was rescued by Rpd3 downregulation in the brain (Fig. 5). From the results of climbing assay, we interpret that Rpd3 downregulation in Aβ42 flies leads to reduce neurodegeneration in the brain which occurs from the Aβ42 accumulation (Figs. 1-3). In our previous study (reference 3), the aging data indicated that flies with Rpd3 downregulation have longer lifespan than flies without Rpd3 downregulation. We may expect that Rpd3 downregulation in the brain will rescue shortened lifespan of Aβ42 flies (Figs. 5-7). Future research using dissections along with anatomical studies and mass spectrometric analysis are being conducted to investigate more about longevity in the AD flies through Rpd3 downregulation.
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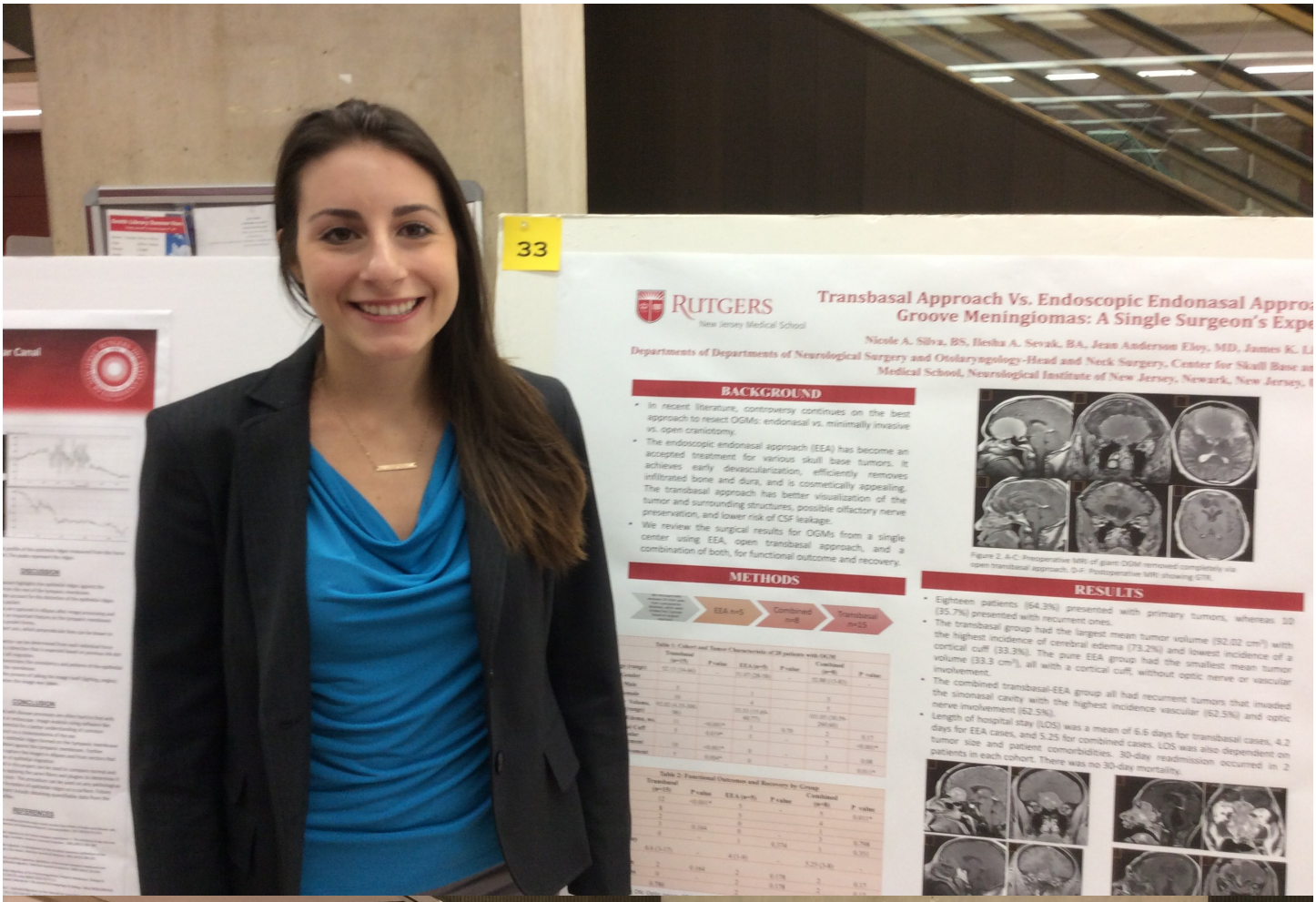
33
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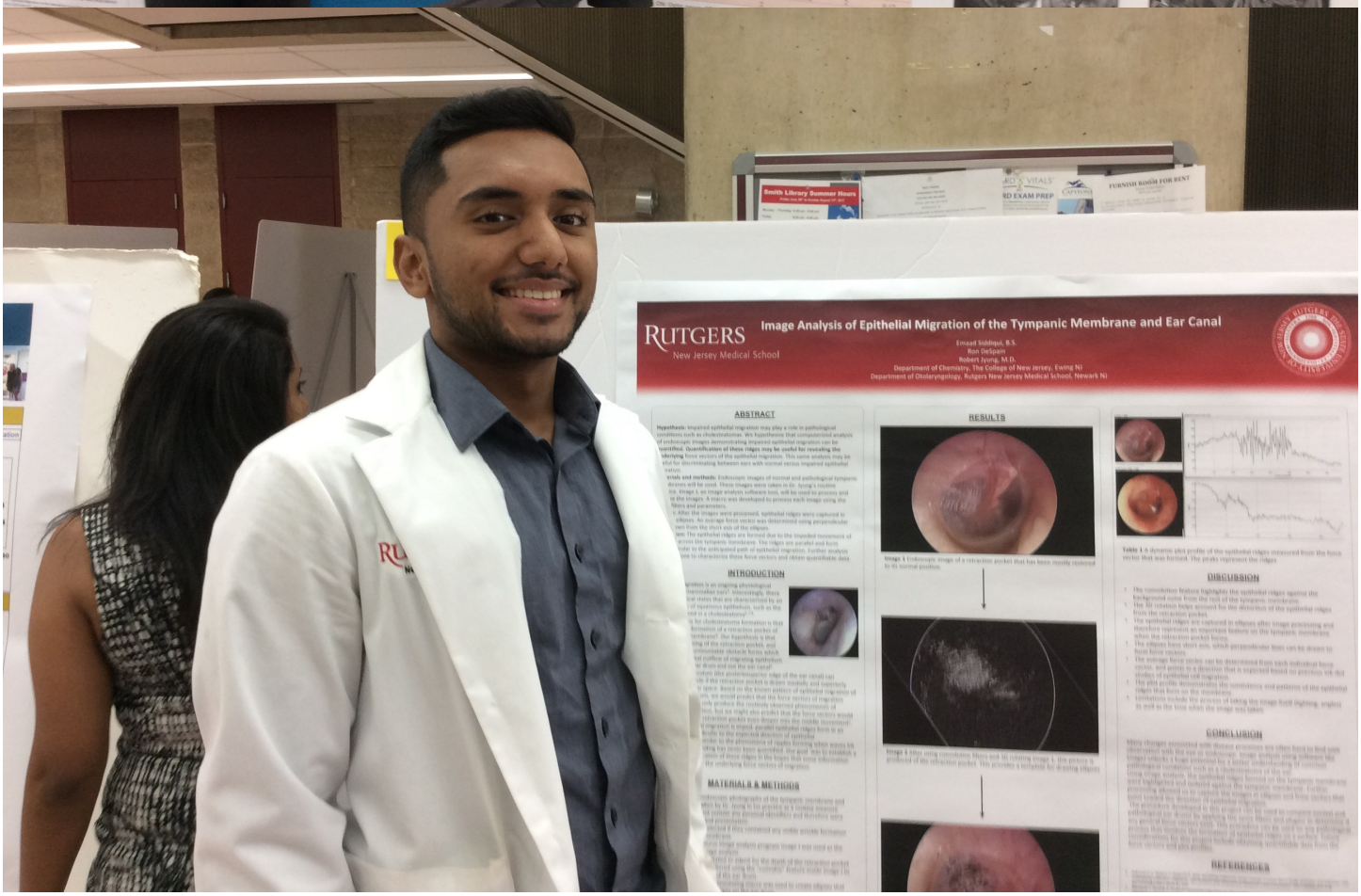
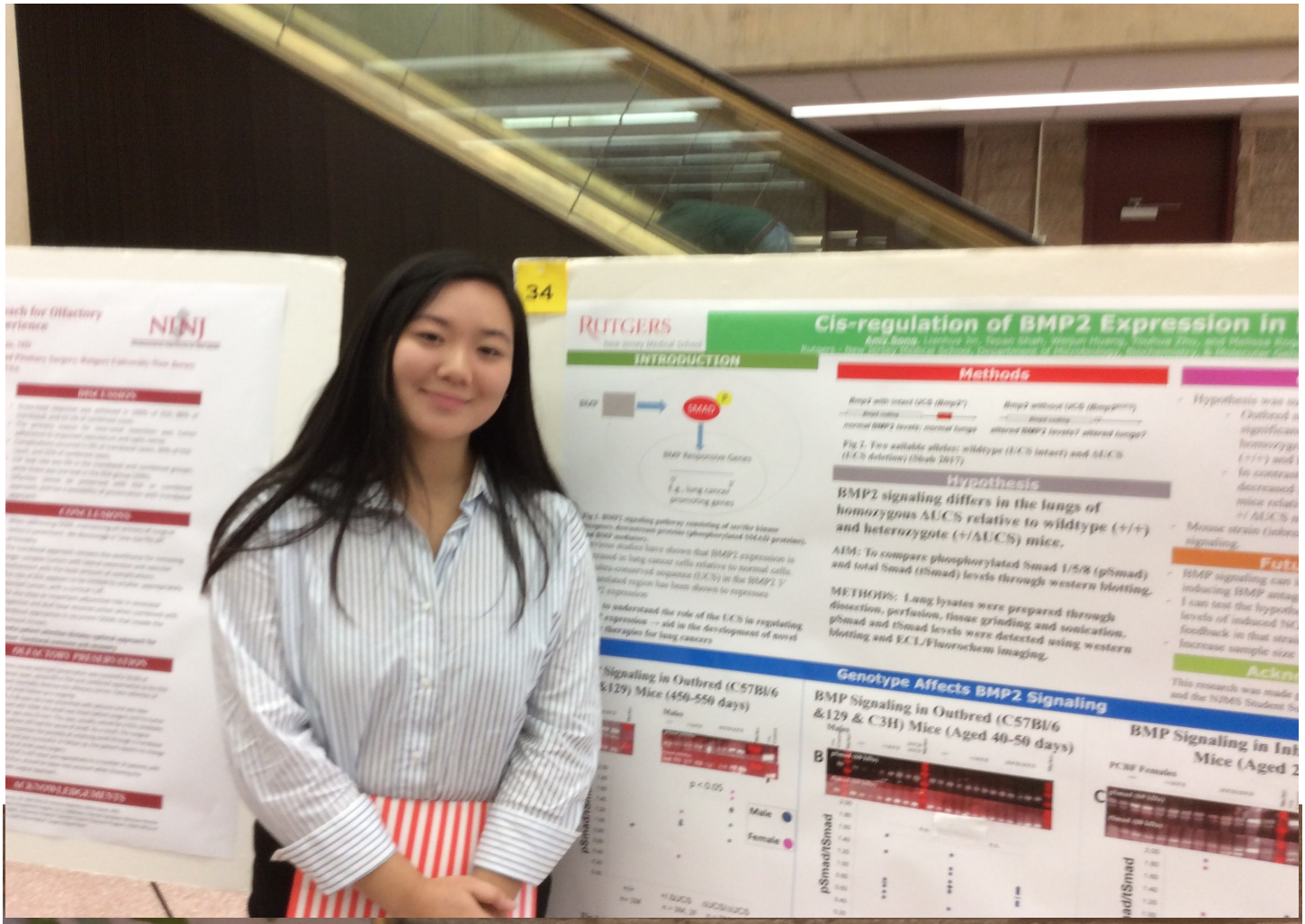
New Jersey Medical School
Transbasal Approach Vs. Endoscopic Endonasal Approa
Groove Meningiomas: A Single Surgeon's Expe
BACKGROUND
METHODS
RESULTS


RUTGERS
New Jersey Medical School
Image Analysis of Epithelial Migration of the Tympanic Membrane and Ear Canal
ABSTRACT
INTRODUCTION
MATERIALS & METHODS
RESULTS
DISCUSSION
CONCLUSION
REFERENCES


34
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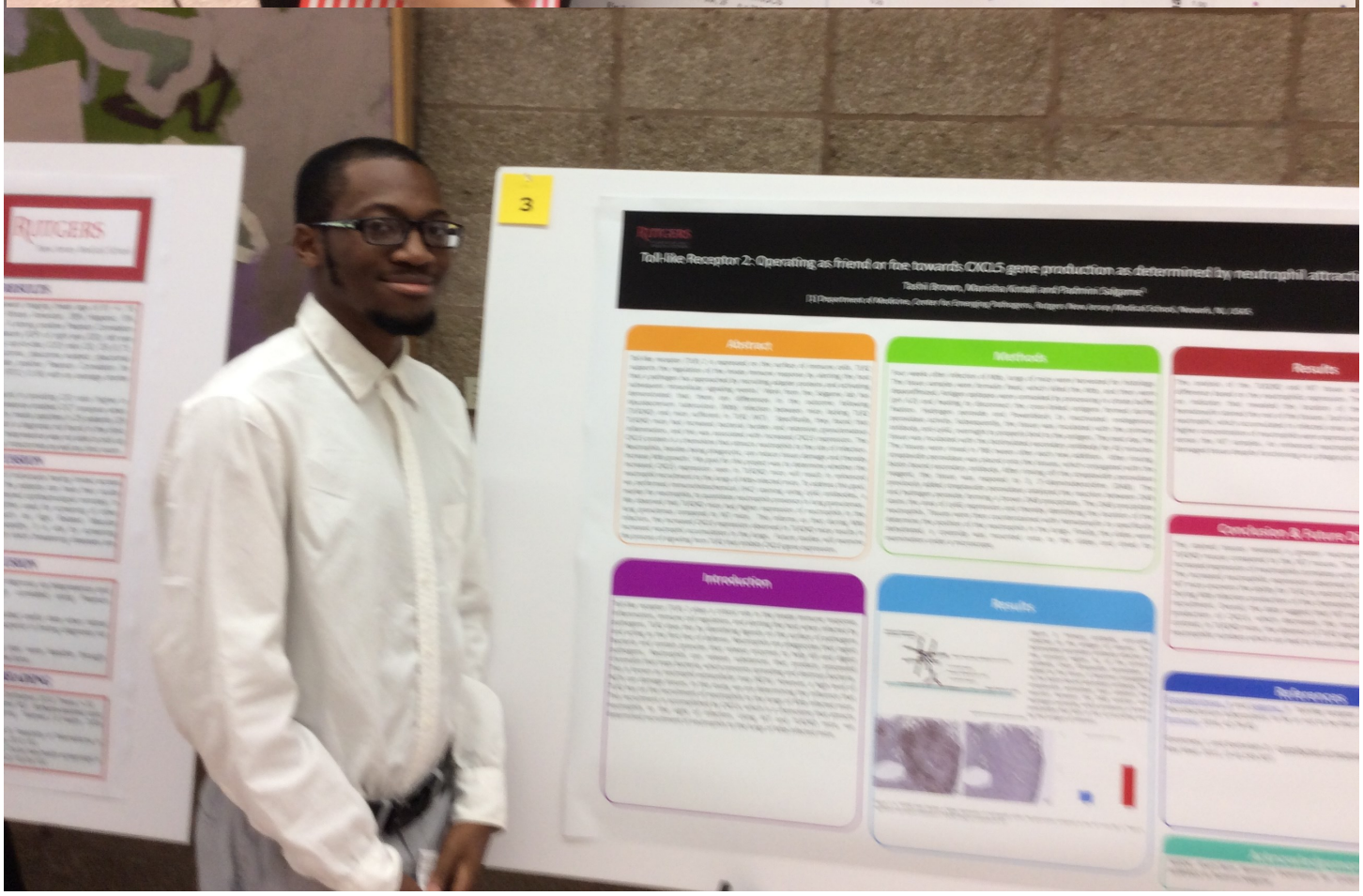
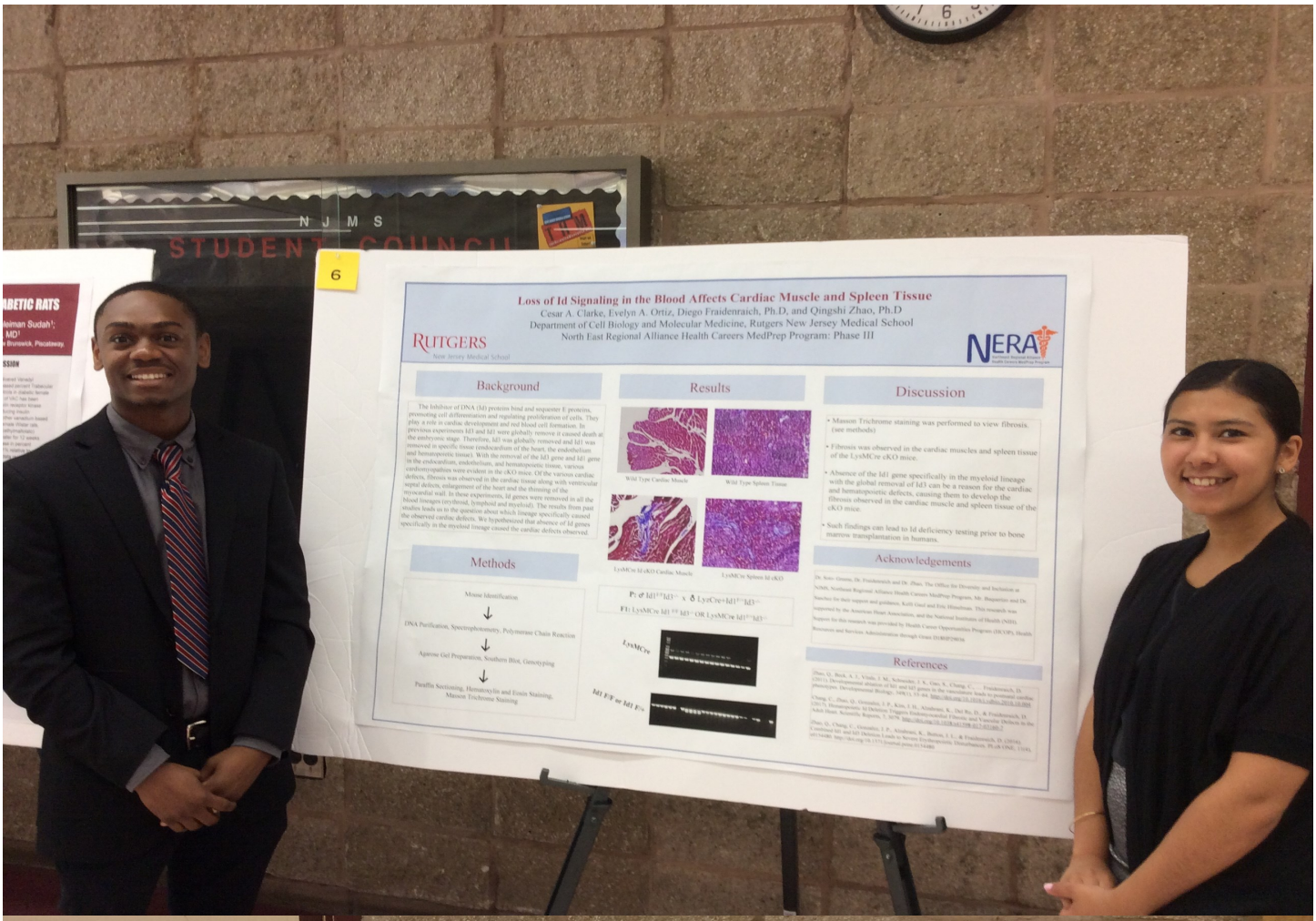
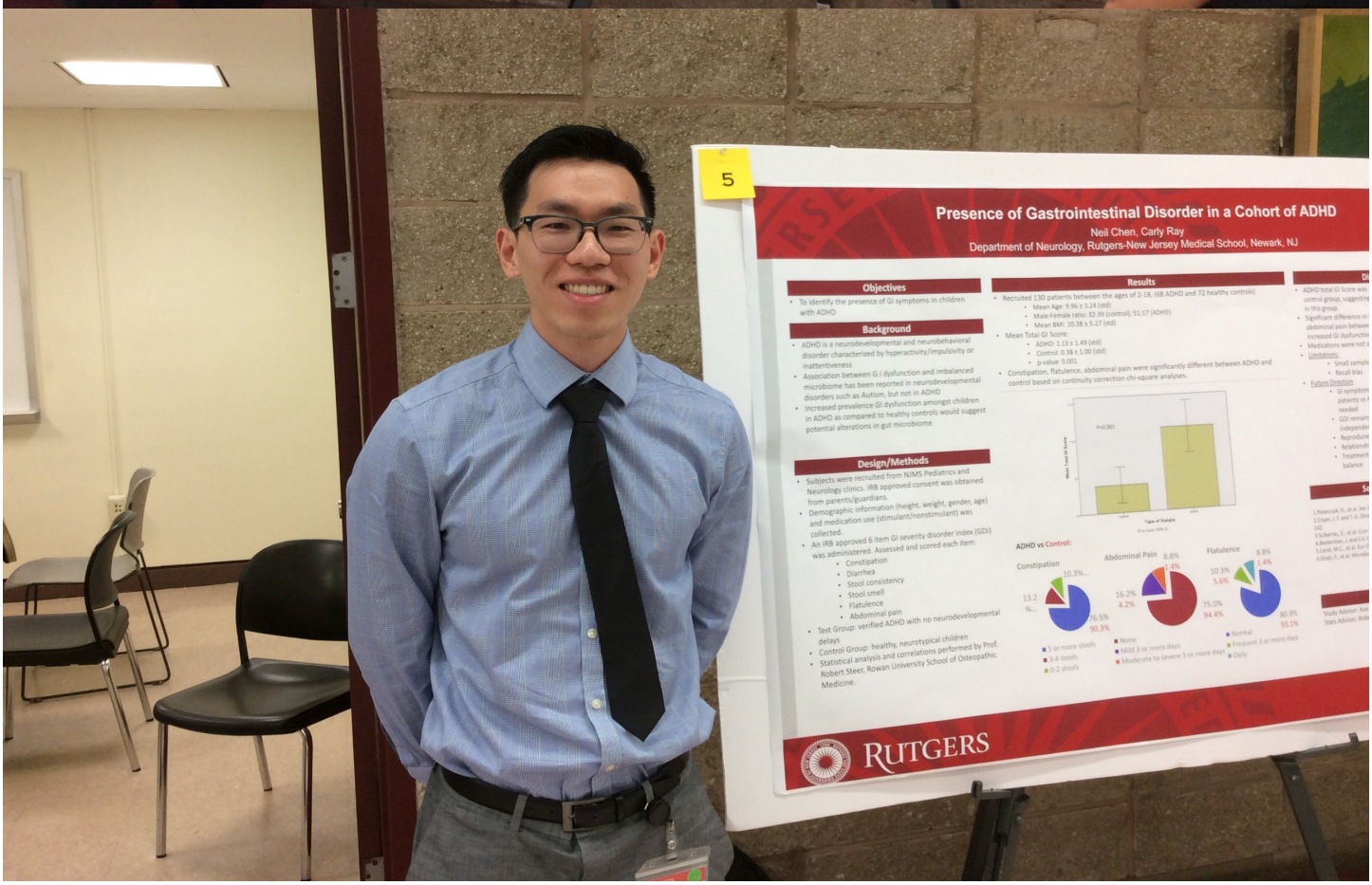
Cis-regulation of BMP2 Expression in
INTRODUCTION
Methods
Hypothesis
BMP2 signaling differs in the lungs of homozygous ΔUCS relative to wildtype (+/+) and heterozygote (+/ΔUCS) mice.
AIM: To compare phosphorylated Smad 1/5/8 (pSmad) and total Smad (tSmad) levels through western blotting.
METHODS: Lung lysates were prepared through dissection, perfusion, tissue grinding and sonication. pSmad and tSmad levels were detected using western blotting and ECL/Fluorochem imaging.
Genotype Affects BMP2 Signaling
BMP Signaling in Outbred (C57Bl/6 &129 & C3H) Mice (Aged 40-50 days)
Male
Female


3
RUTGERS
Abstract
Methods
Introduction
Results


6
Loss of Id Signaling in the Blood Affects Cardiac Muscle and Spleen Tissue
Cesar A. Clarke, Evelyn A. Ortiz, Diego Fraidenraich, Ph.D, and Qingshi Zhao, Ph.D
Department of Cell Biology and Molecular Medicine, Rutgers New Jersey Medical School
North East Regional Alliance Health Careers MedPrep Program: Phase III
RUTGERS
NERA
Background
Results
Discussion
Methods
Acknowledgements
References


5
Presence of Gastrointestinal Disorder in a Cohort of ADHD
Neil Chen, Carly Ray
Department of Neurology, Rutgers-New Jersey Medical School, Newark, NJ
Objectives
Background
Design/Methods
Results
RUTGERS


e and Spleen Tissue
Qingshi Zhao, Ph.D
Jersey Medical School
ram: Phase III
NERA
Discussion
• Masson Trichrome staining was performed to view fibrosis. (see methods)
• Fibrosis was observed in the cardiac muscles and spleen tissue of the LysMCre cKO mice.
• Absence of the Id1 gene specifically in the myeloid lineage with the global removal of Id3 can be a reason for the cardiac and hematopoietic defects, causing them to develop the fibrosis observed in the cardiac muscle and spleen tissue of the cKO mice.
• Such findings can lead to Id deficiency testing prior to bone marrow transplantation in humans.
Acknowledgements
References
5
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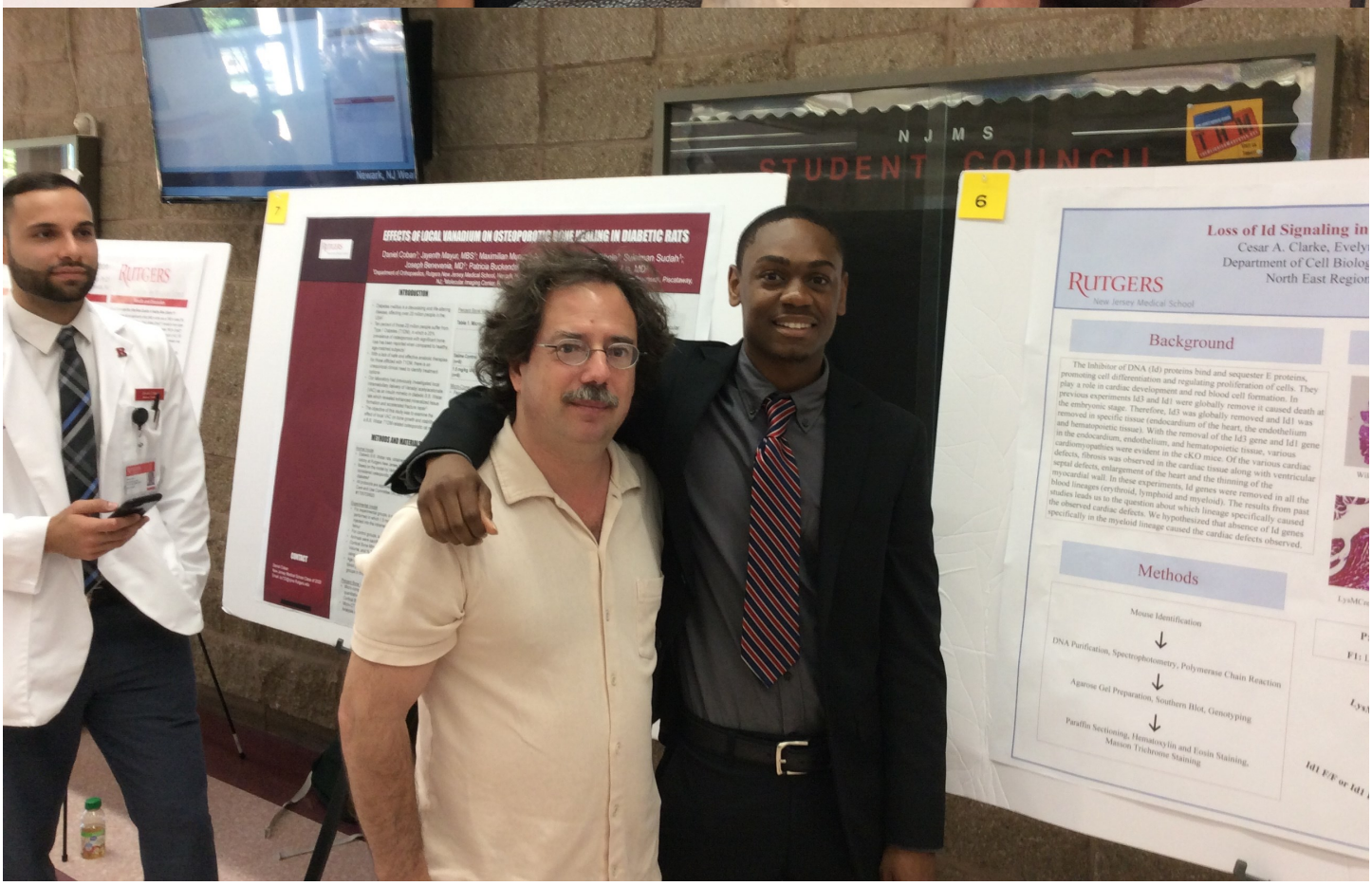
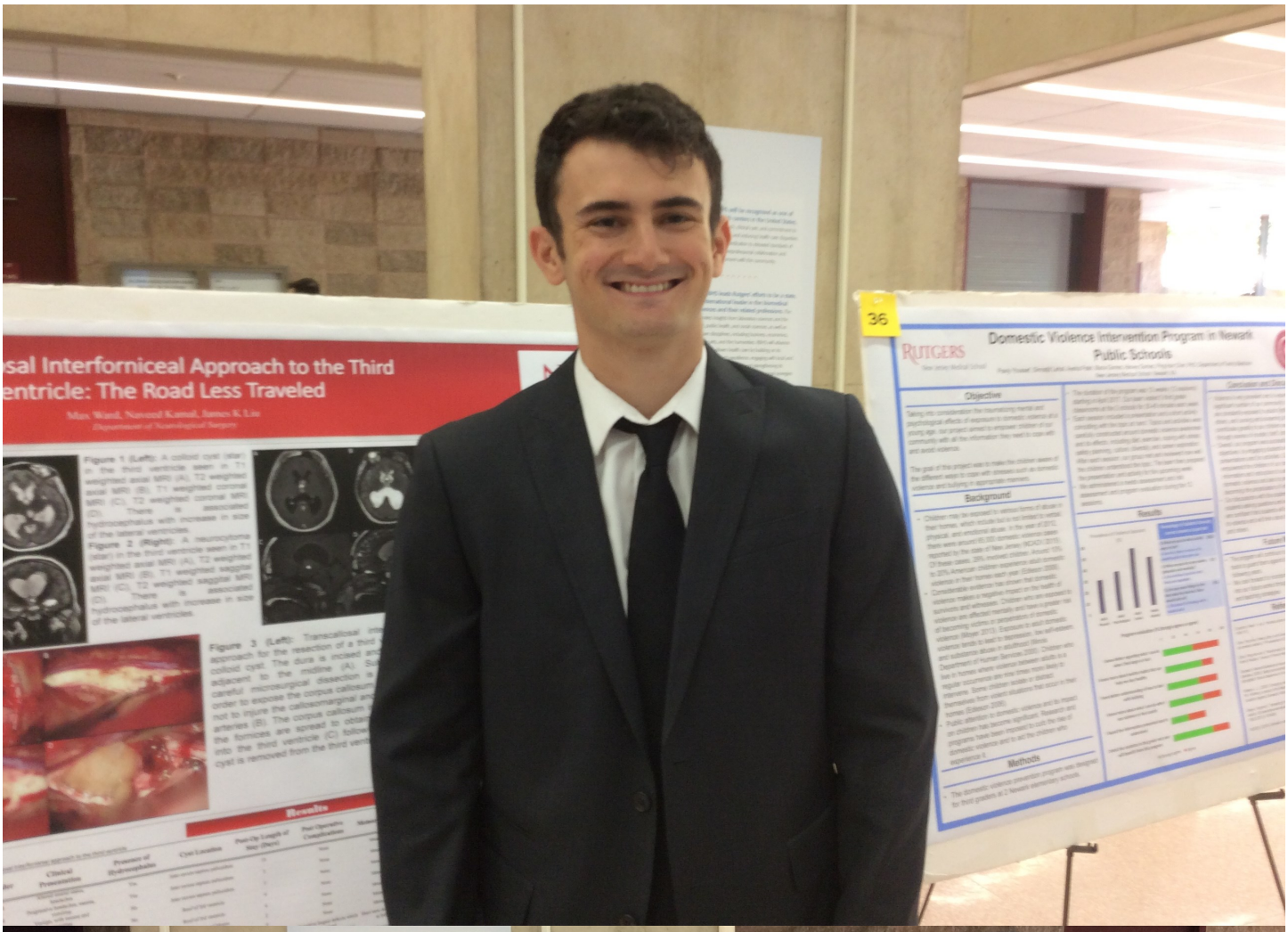
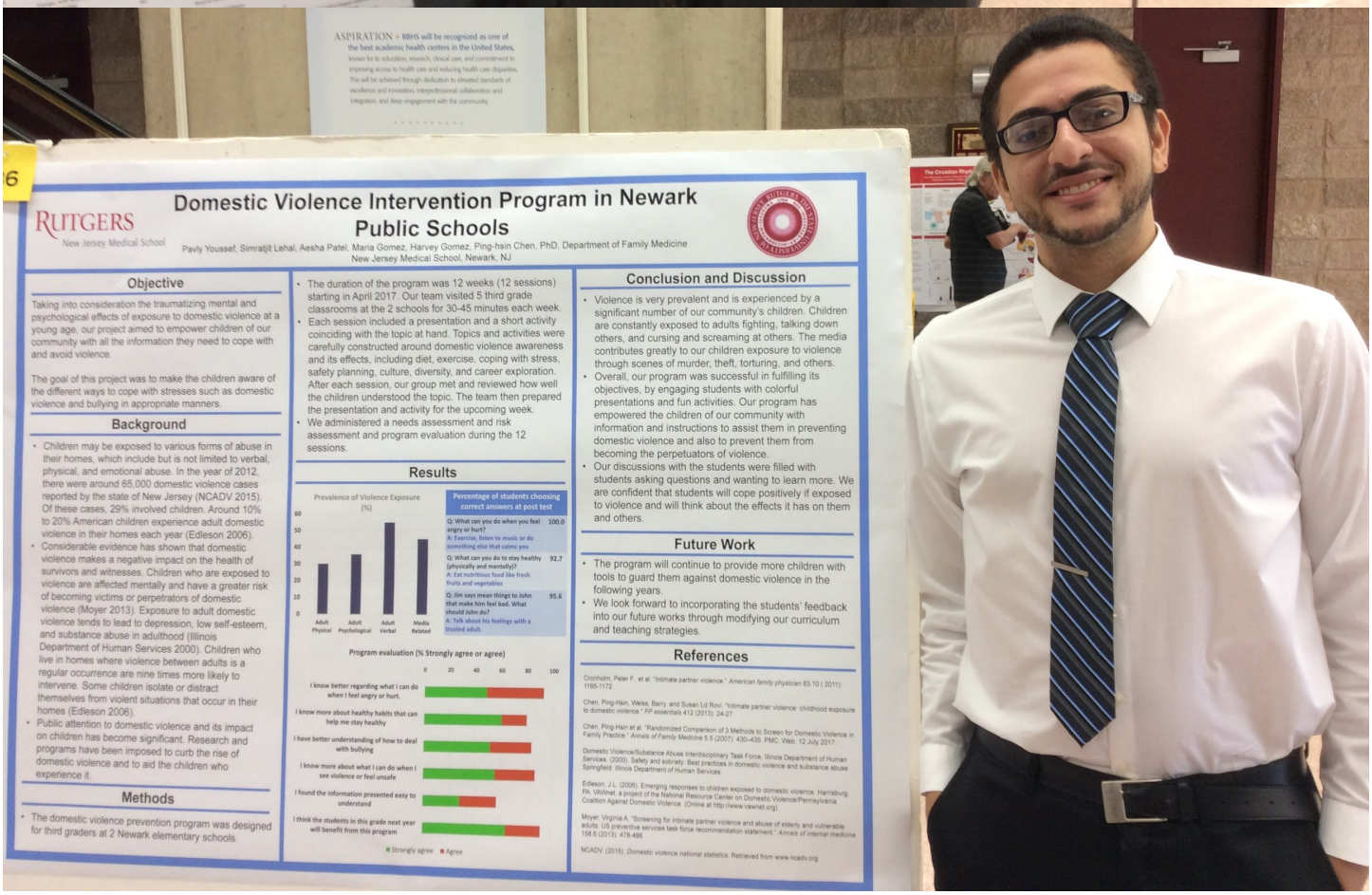

N J M S
STUDENT COUNCIL
7
EFFECTS OF LOCAL VANADIUM ON OSTEOPOROTIC
DIABETIC RATS
6
Loss of Id Signaling in
Cesar A. Clarke, Evely
Department of Cell Biolog
North East Region
RUTGERS
New Jersey Medical School
Background
The inhibitor of DNA (Id) proteins bind and sequester E proteins, promoting cell differentiation and regulating proliferation of cells. They play a role in cardiac development and red blood cell formation. In previous experiments Id3 and Id1 were globally remove it caused death at the embryonic stage. Therefore, Id3 was globally removed and Id1 was removed in specific tissue (endocardium of the heart, the endothelium and hematopoietic tissue). With the removal of the Id3 gene and Id1 gene in the endocardium, endothelium, and hematopoietic tissue, various cardiomyopathies were evident in the cKO mice. Of the various cardiac defects, fibrosis was observed in the cardiac tissue along with ventricular septal defects, enlargement of the heart and the thinning of the myocardial wall. In these experiments, Id genes were removed in all the blood lineages (erythroid, lymphoid and myeloid). The results from past studies leads us to the question about which lineage specifically caused the observed cardiac defects. We hypothesized that absence of Id genes specifically in the myeloid lineage caused the cardiac defects observed.
Methods
Mouse Identification
DNA Purification, Spectrophotometry, Polymerase Chain Reaction
Agarose Gel Preparation, Southern Blot, Genotyping
Paraffin Sectioning, Hematoxylin and Eosin Staining, Masson Trichrome Staining


sal Interforniceal Approach to the Third
entricle: The Road Less Traveled
Max Ward, Naveed Kamal, James K. Liu
Domestic Violence Intervention Program in Newark Public Schools
RUTGERS
Objective
Background
Results
Methods


ASPIRATION
RBHS will be recognized as one of the best academic health centers in the United States,
Domestic Violence Intervention Program in Newark Public Schools
RUTGERS
New Jersey Medical School
Pavly Youssef, Simratjit Lehal, Aesha Patel, Maria Gomez, Harvey Gomez, Ping-hsin Chen, PhD, Department of Family Medicine
New Jersey Medical School, Newark, NJ
Objective
Taking into consideration the traumatizing mental and psychological effects of exposure to domestic violence at a young age, our project aimed to empower children of our community with all the information they need to cope with and avoid violence.
The goal of this project was to make the children aware of the different ways to cope with stresses such as domestic violence and bullying in appropriate manners.
Background
Children may be exposed to various forms of abuse in their homes, which include but is not limited to verbal, physical, and emotional abuse. In the year of 2012, there were around 65,000 domestic violence cases reported by the state of New Jersey (NCADV 2015). Of these cases, 29% involved children. Around 10% to 20% American children experience adult domestic violence in their homes each year (Edleson 2006).
Considerable evidence has shown that domestic violence makes a negative impact on the health of survivors and witnesses. Children who are exposed to violence are affected mentally and have a greater risk of becoming victims or perpetrators of domestic violence (Moyer 2013). Exposure to adult domestic violence tends to lead to depression, low self-esteem, and substance abuse in adulthood (Illinois Department of Human Services 2000). Children who live in homes where violence between adults is a regular occurrence are nine times more likely to intervene. Some children isolate or distract themselves from violent situations that occur in their homes (Edleson 2006).
Public attention to domestic violence and its impact on children has become significant. Research and programs have been imposed to curb the rise of domestic violence and to aid the children who experience it.
Methods
The domestic violence prevention program was designed for third graders at 2 Newark elementary schools.
The duration of the program was 12 weeks (12 sessions) starting in April 2017. Our team visited 5 third grade classrooms at the 2 schools for 30-45 minutes each week.
Each session included a presentation and a short activity coinciding with the topic at hand. Topics and activities were carefully constructed around domestic violence awareness and its effects, including diet, exercise, coping with stress, safety planning, culture, diversity, and career exploration. After each session, our group met and reviewed how well the children understood the topic. The team then prepared the presentation and activity for the upcoming week.
We administered a needs assessment and risk assessment and program evaluation during the 12 sessions.
Results
Prevalence of Violence Exposure (%)
Adult Physical
Adult Psychological
Adult Verbal
Media Related
Percentage of students choosing correct answers at post test
Q: What can you do when you feel angry or hurt? 100.0
A: Exercise, listen to music or do something else that calms you
Q: What can you do to stay healthy (physically and mentally)? 92.7
A: Eat nutritious food like fresh fruits and vegetables
Q: Jim says mean things to John that make him feel bad. What should John do? 95.6
A: Talk about his feelings with a trusted adult.
Program evaluation (% Strongly agree or agree)
I know better regarding what I can do when I feel angry or hurt.
I know more about healthy habits that can help me stay healthy
I have better understanding of how to deal with bullying
I know more about what I can do when I see violence or feel unsafe
I found the information presented easy to understand
I think the students in this grade next year will benefit from this program
Strongly agree
Agree
Conclusion and Discussion
Violence is very prevalent and is experienced by a significant number of our community's children. Children are constantly exposed to adults fighting, talking down others, and cursing and screaming at others. The media contributes greatly to our children exposure to violence through scenes of murder, theft, torturing, and others.
Overall, our program was successful in fulfilling its objectives, by engaging students with colorful presentations and fun activities. Our program has empowered the children of our community with information and instructions to assist them in preventing domestic violence and also to prevent them from becoming the perpetuators of violence.
Our discussions with the students were filled with students asking questions and wanting to learn more. We are confident that students will cope positively if exposed to violence and will think about the effects it has on them and others.
Future Work
The program will continue to provide more children with tools to guard them against domestic violence in the following years.
We look forward to incorporating the students' feedback into our future works through modifying our curriculum and teaching strategies.
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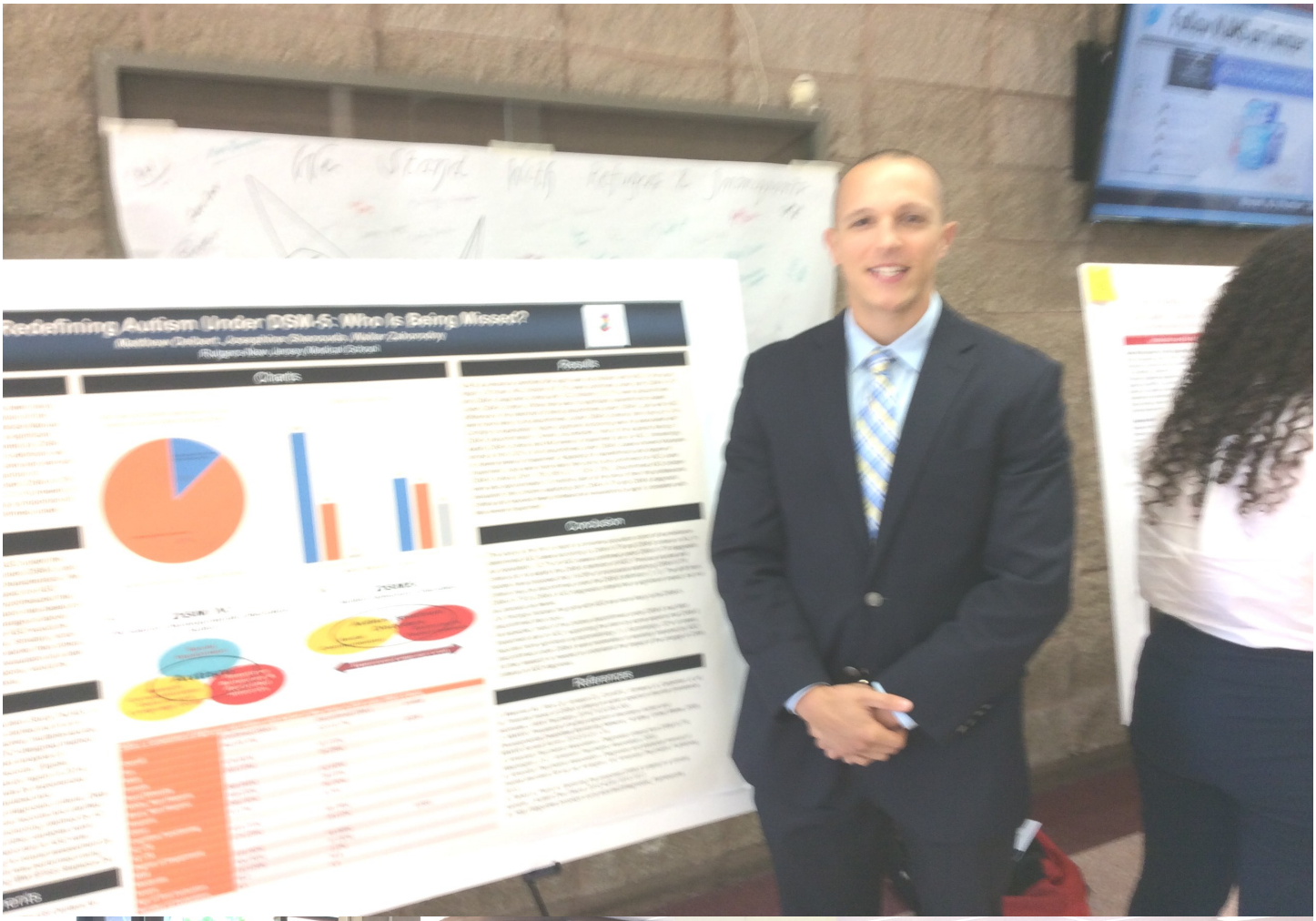
Redefining Autism Under DSM-5: Who is Being Missed?
Methods
Results
Conclusion
References


HIV PREVALENCE IN A MENTALLY ILL POPULATION IN AN URBAN ACADEMIC MEDICAL CENTER
Shannon Emile, Cheryl Kennedy, MD, Chiadikaobi Okeorji, MD
UNIVERSITY HOSPITAL
Newark, New Jersey
Methods
With Institutional Review Board (IRB) approval and participants consent, a Patient Satisfaction Questionnaire was administered to 834 adult patients over three years who were about to be discharged from the University Hospital Acute Inpatient Psychiatric Unit. Socio-demographic data such as gender, race, home disposition, legal status, as well as treatment history & HIV were obtained from the medical records. Data were entered in Excel file. Frequency analysis for the socio-demographic variables were done. Mean length of stay (LOS) was also analyzed.
Variables
Patient demographics (age, gender, race)
Length of Stay
Legal Status
Gender
Race
Disposition
Psychiatric Diagnosis
Medical History, including HIV status, Hospital Medications
Results
There were 834 participants men (57%) and women (42%). The average length of stay in the In-Patient Psychiatric Unit at University Hospital was 10 days. The race distribution showed that 68% were Black/ African American and 19% White. 84% of patients were domiciled while 14% were homeless. 51% of patients were admitted voluntarily to the In-Patient Psychiatric Unit at University Hospital and 47% were involuntarily committed. 4.44% (37) of the 834 patients tested positive for HIV at the rate of 4436 per 100,000 persons.
Gender
Female 42%
Male 58%
Female
Male
HIV Diagnosis
Results
Race
Conclusion
HIV prevalence in the mentally ill population is higher than that of those who are not mentally ill. This study showed that HIV percentage in our sample population at 4.44%, is similar to the result of other studies previously done. The prevalence of HIV in the mentally ill in the United States is four times that of the general population.[2] Effective strategies for HIV prevention are known and hospitalization provides an opportunity to institute education, strengthen medication compliance strategies and make referrals for comprehensive medical care as well as addiction treatment & social support to assist patients in coping more effectively with their risk factors.
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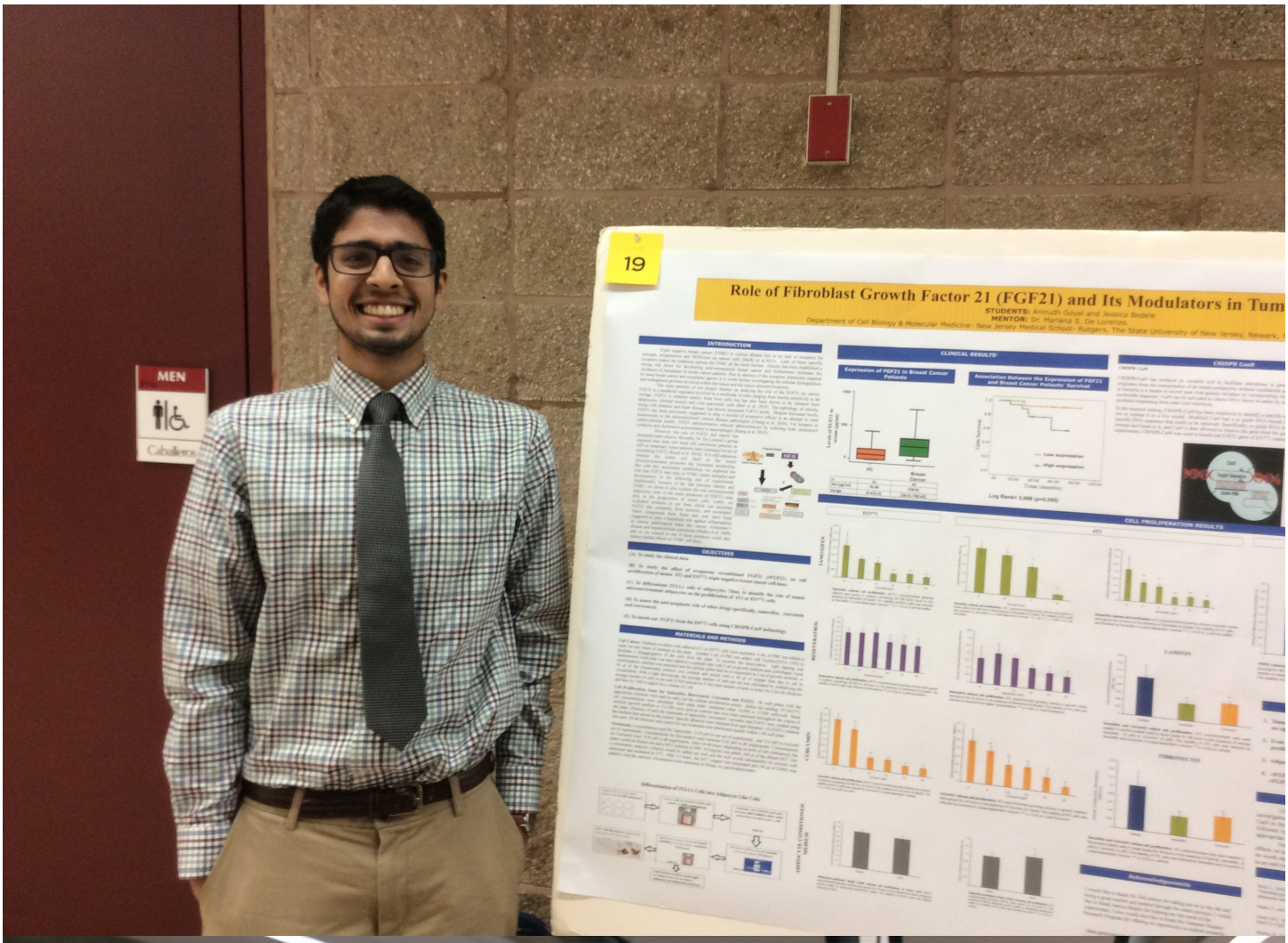
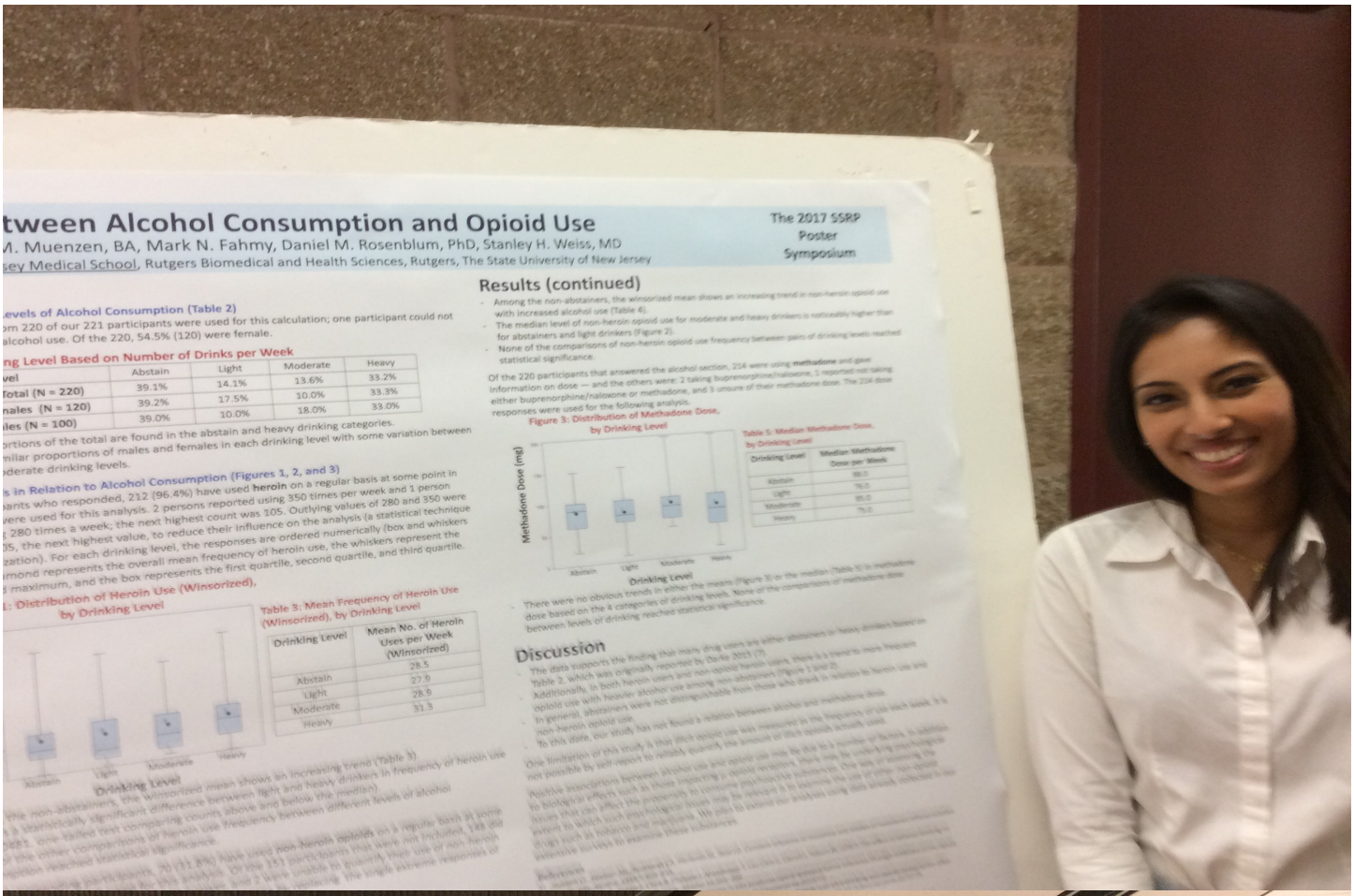
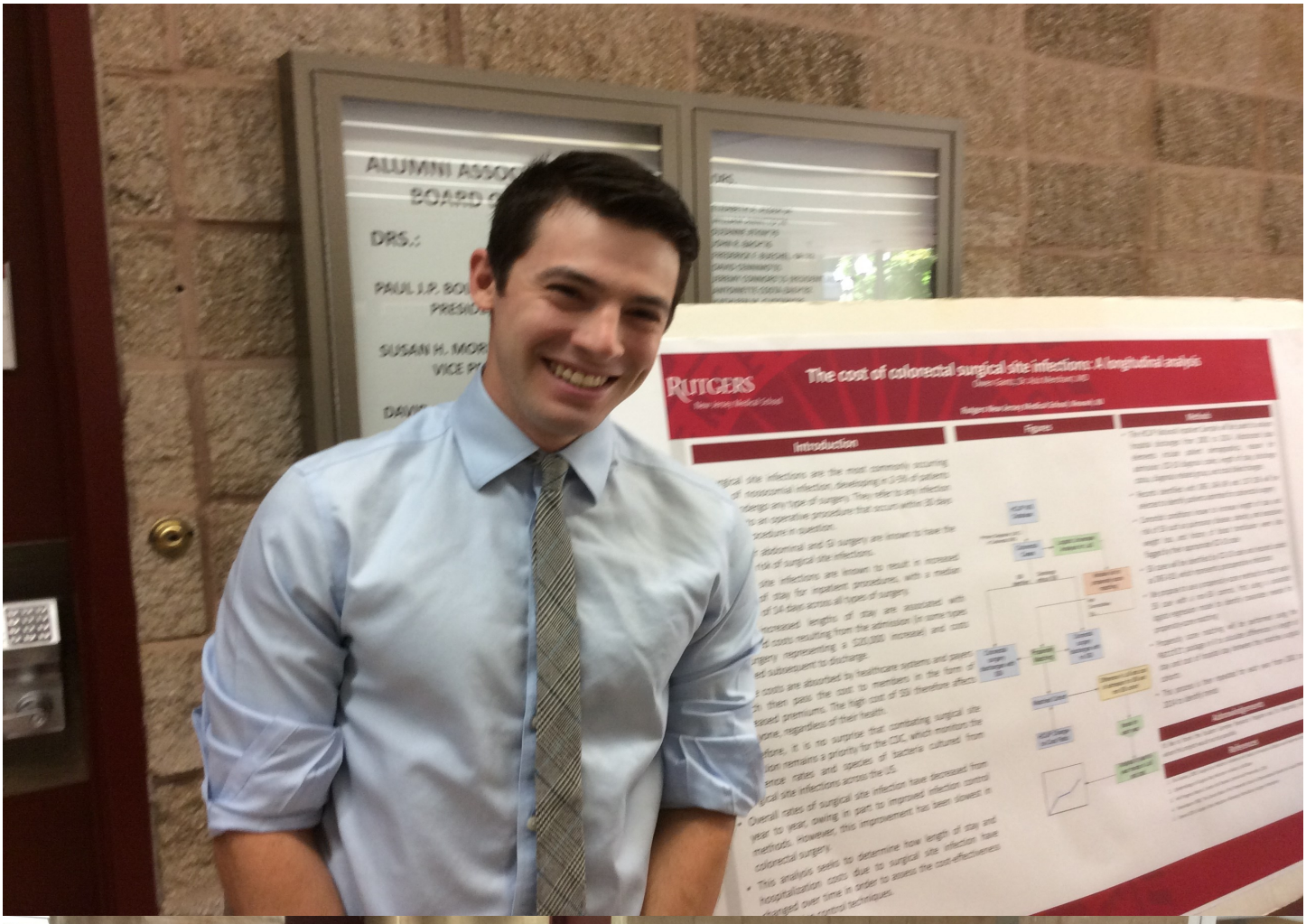
3. KESSLER, R. C., ANGERMEYER, M., ANTHONY, J. C., DE GRAAF, R., DEMYTTENAERE, K., GASQUET, I., ... FOR THE WHO WORLD MENTAL HEALTH SURVEY CONSORTIUM, T. B. (2007). Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization's World Mental Health Survey Initiative. World Psychiatry, 6(3), 168–176.
Acknowledgements
I would like to acknowledge the support from Department of Psychiatry and University Hospital Inpatient Psychiatric Unite staff. Also, I would like to acknowledge Dr. Cheryl Kennedy, Dr. Chiadikaobi Okeorji, and Dr. Vandana Dodia and Humberto Baquendo for allowing me to partake in this research project. Support for this research was provided by Health Career Opportunities Program (HCOP), Health Resources and Administration through Grant D18HP29038.
EXIT
Accessibility for Cochlear Implantations with Preoperative CT Measurements
Marcus Elias, BS, Tapan Patel, MD, Robert Jyung, MD
Department of Otolaryngology, Rutgers New Jersey Medical School, Newark NJ


The Circadian Rhythm of Sepsis
RUTGERS
B502
Technology Assistance Center
ITeNMS


MEN
19
Role of Fibroblast Growth Factor 21 (FGF21) and Its Modulators in Tum
INTRODUCTION
CLINICAL RESULTS
OBJECTIVES
MATERIALS AND METHODS
CELL PROLIFERATION RESULTS


tween Alcohol Consumption and Opioid Use
M. Muenzen, BA, Mark N. Fahmy, Daniel M. Rosenblum, PhD, Stanley H. Weiss, MD
sey Medical School, Rutgers Biomedical and Health Sciences, Rutgers, The State University of New Jersey
The 2017 SSRP Poster Symposium
evels of Alcohol Consumption (Table 2)
ng Level Based on Number of Drinks per Week
Results (continued)
Discussion
Drinking Level


20
Predicting Short-Term Complication Risks of Patients
Bone Tumors
RUTGERS
New Jersey Medical School
Jack K. Haberl, Brianna L. Siracuse, Joseph A. Ippo
Rutgers New Jersey Medical School, Departme
Background
Methods
Results
Procedure Terminology
Pre-Op
Limb Salvage
Amputation
Univariate and Mult
Factors Affecting R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The cost of colorectal surgical site infections: A longitudinal analysis
Introduction


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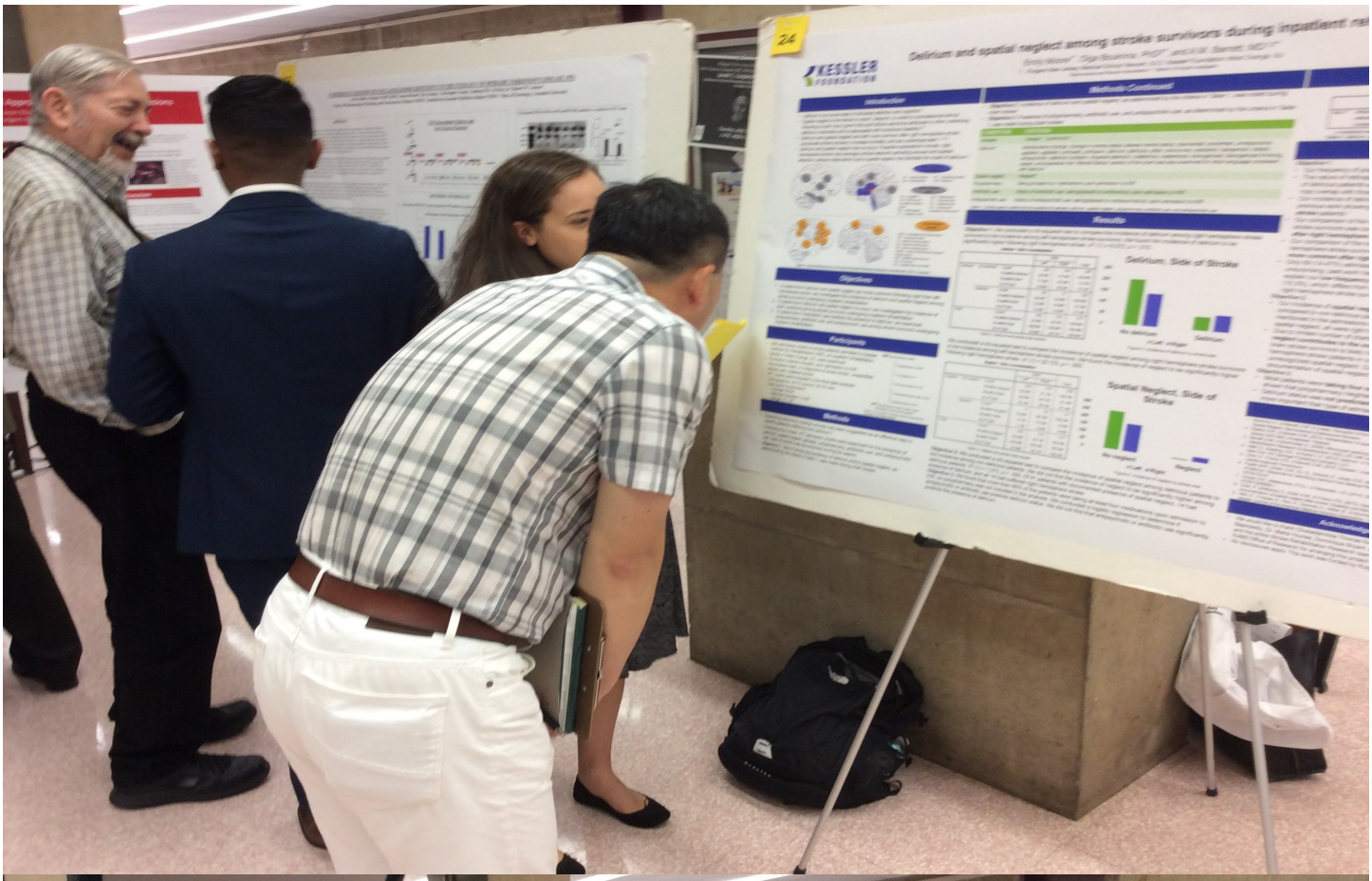
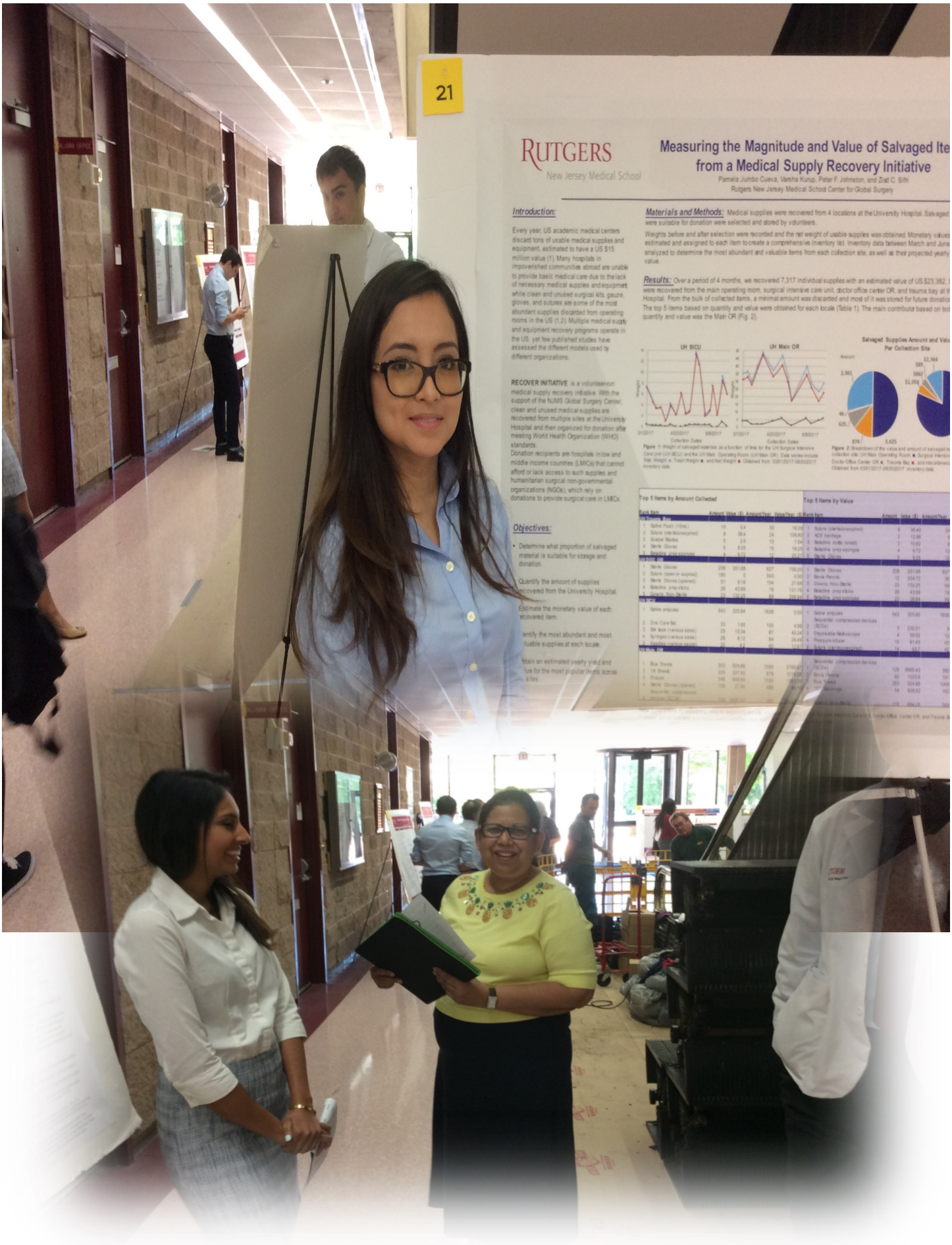
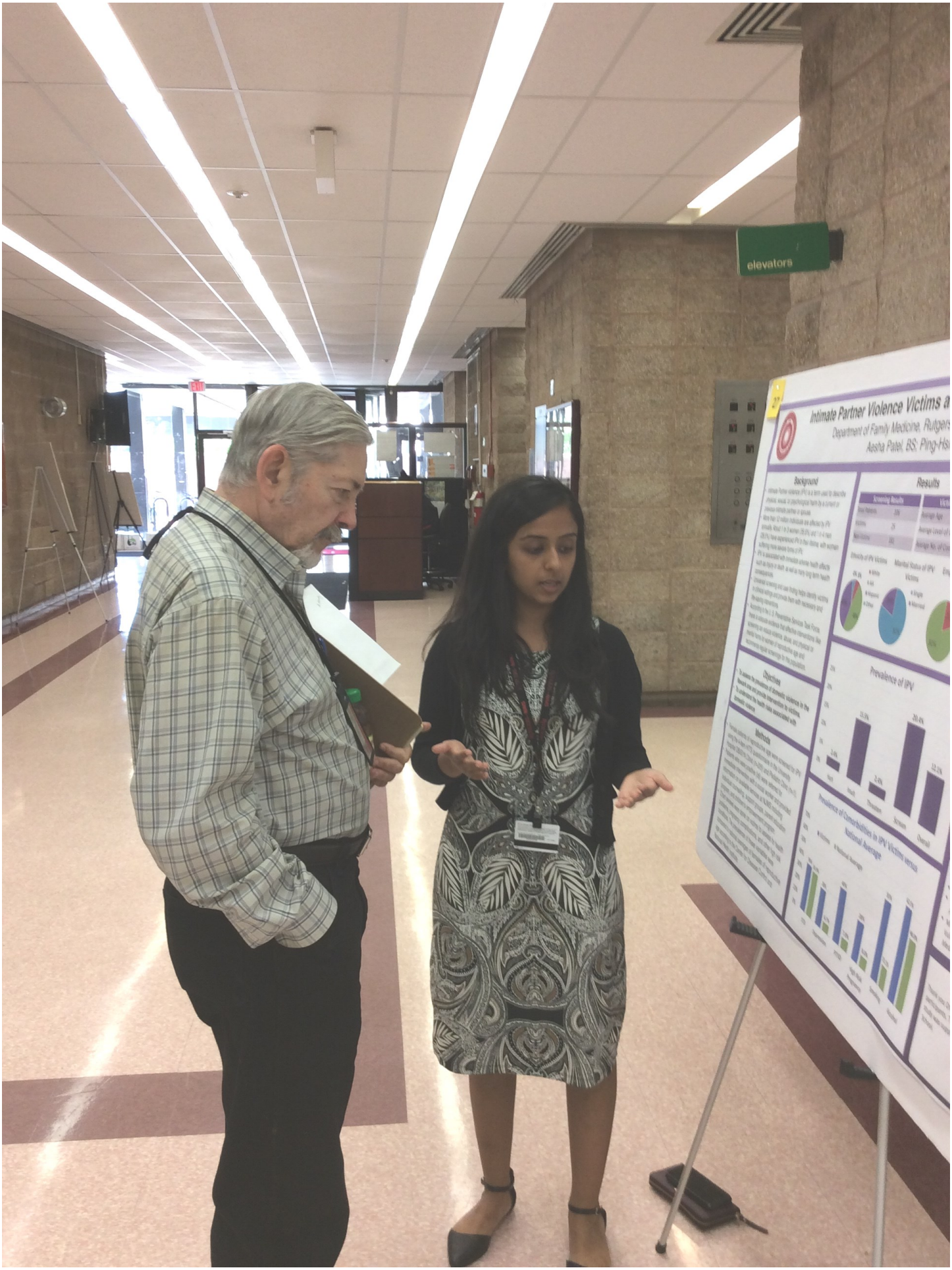
Management of M
Osteosynth


24
KESSLER FOUNDATION
Delirium and spatial neglect among stroke survivors during inpatient
Introduction
Methods Continued
Results
Objectives
Participants
Methods
Delirium, Side of Stroke
Spatial Neglect, Side of Stroke


24
KESSLER FOUNDATION
Objectives
Participants
Methods


21
RUTGERS
New Jersey Medical School
Measuring the Magnitude and Value of Salvaged Ite
from a Medical Supply Recovery Initiative
Pamela Jumbo Cueva, Varsha Kurup, Peter F. Johnston, and Ziad C. Sifri
Rutgers New Jersey Medical School Center for Global Surgery
Introduction:
Every year, US academic medical centers discard tons of usable medical supplies and equipment, estimated to have a US $15 million value (1). Many hospitals in impoverished communities abroad are unable to provide basic medical care due to the lack of necessary medical supplies and equipment while clean and unused surgical kits, gauze, gloves, and sutures are some of the most abundant supplies discarded from operating rooms in the US (1,2). Multiple medical supply and equipment recovery programs operate in the US, yet few published studies have assessed the different models used by different organizations.
RECOVER INITIATIVE is a volunteer-run medical supply recovery initiative. With the support of the NJMS Global Surgery Center, clean and unused medical supplies are recovered from multiple sites at the University Hospital and then organized for donation after meeting World Health Organization (WHO) standards.
Donation recipients are hospitals in low and middle income countries (LMICs) that cannot afford or lack access to such supplies and humanitarian surgical non-governmental organizations (NGOs), which rely on donations to provide surgical care in LMICs.
Objectives:
Materials and Methods:
Results:
UH SICU
UH Main OR
Salvaged Supplies Amount and Valu
Per Collection Site
Top 5 Items by Amount Collected
Top 5 Items by Value


elevators
Intimate Partner Violence Victims a
Background
Results
Prevalence of IPV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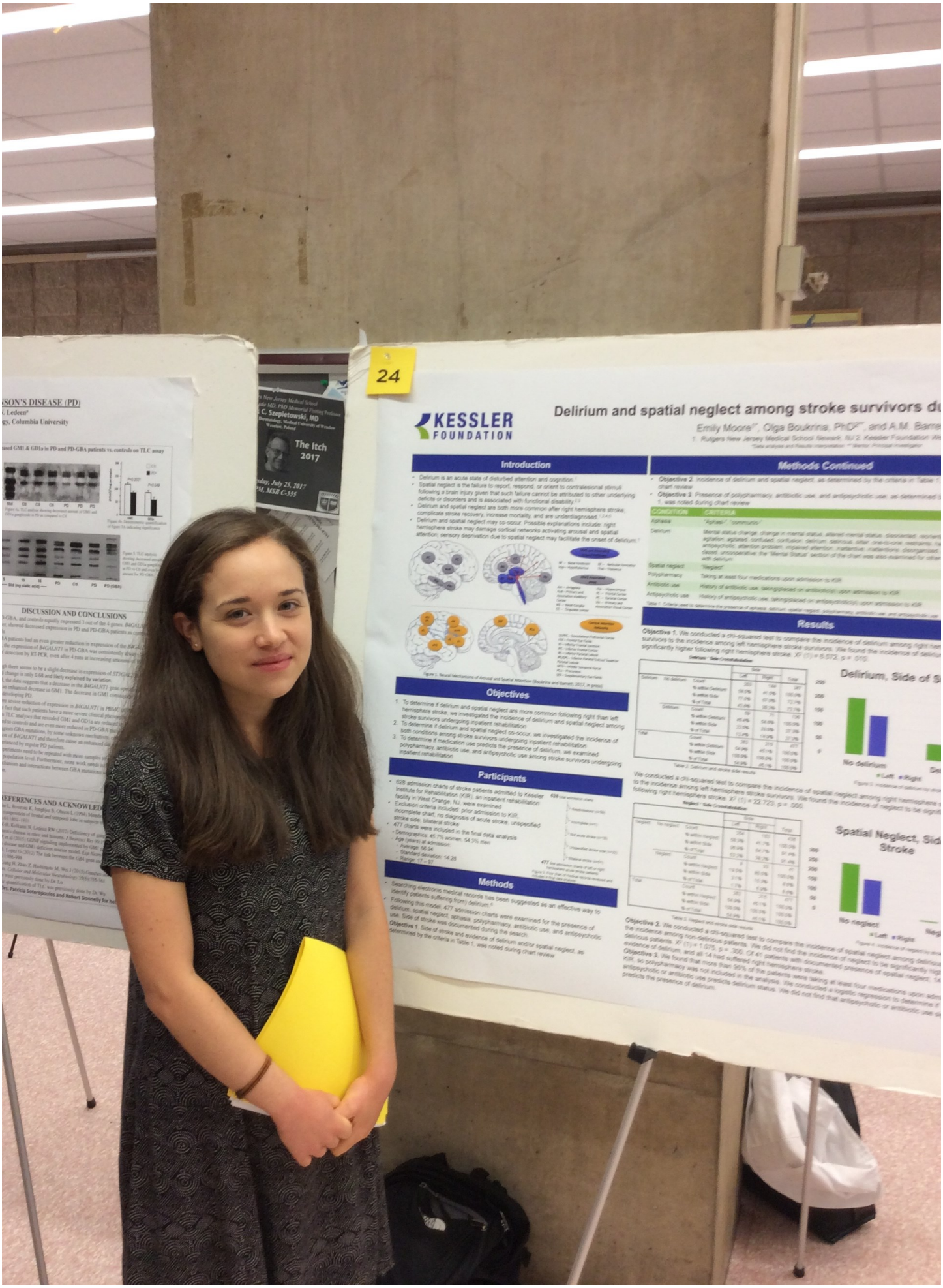
Bank of America


24
KESSLER FOUNDATION
Delirium and spatial neglect among stroke survivors d
Introduction
Objectives
Participants
Methods
Methods Continued
Results
Delirium, Side of
Spatial Neglect, Sid
Stroke
No delirium
No neglect
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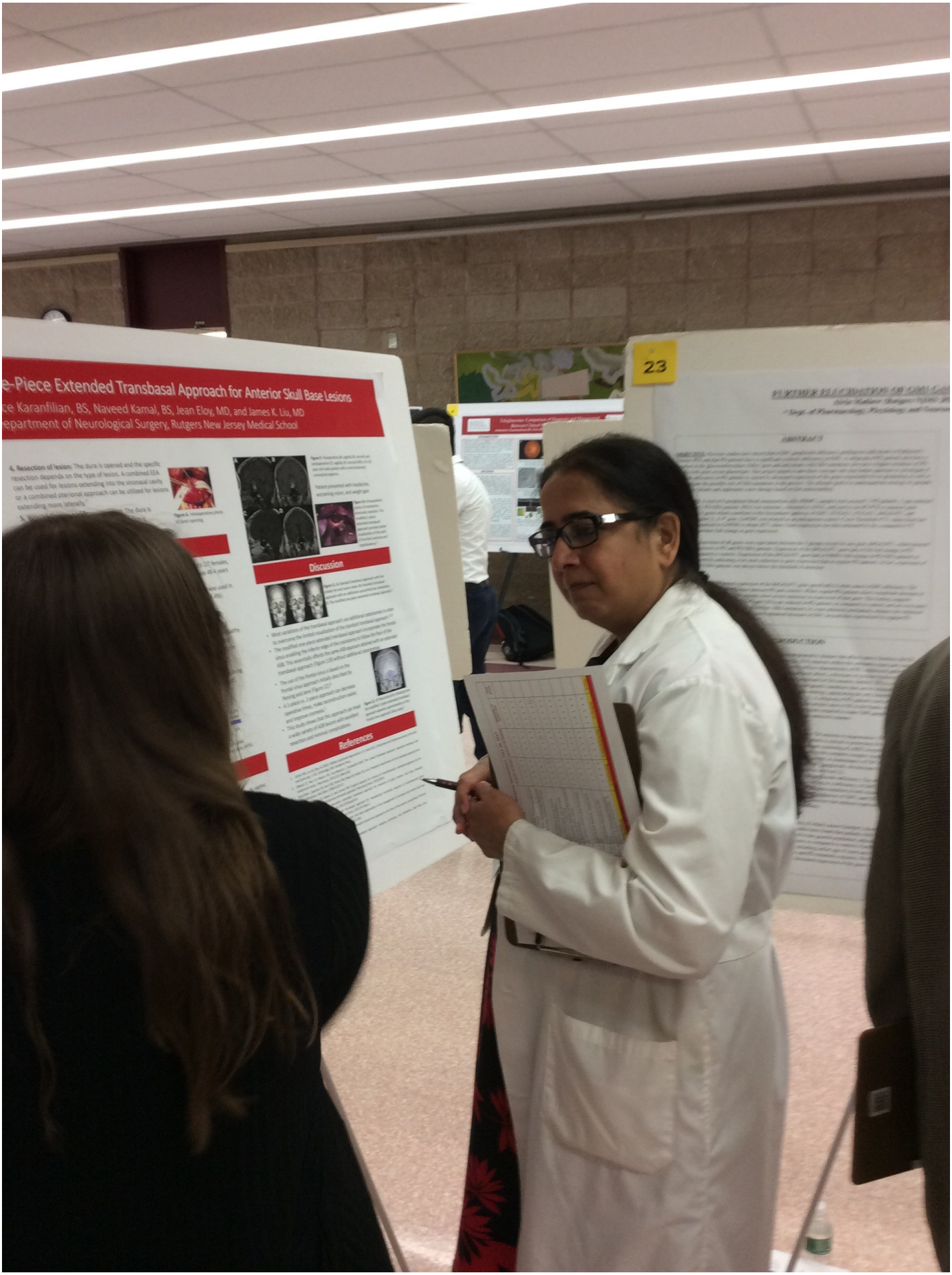
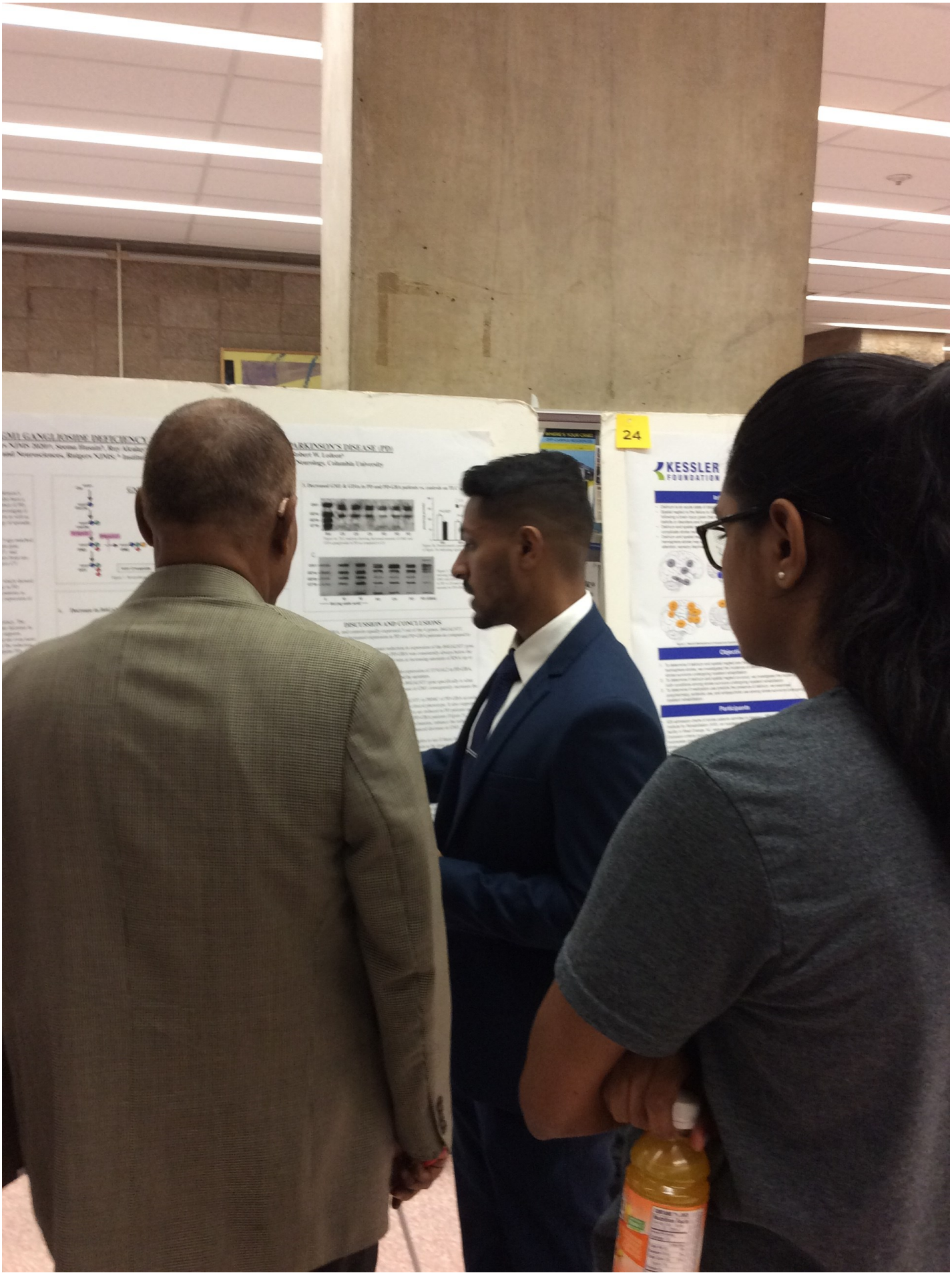

e-Piece Extended Transbasal Approach for Anterior Skull Base Lesions
ce Karanfilian, BS, Naveed Kamal, BS, Jean Eloy, MD, and James K. Liu, MD
epartment of Neurological Surgery, Rutgers New Jersey Medical School
4. Resection of lesion: The dura is opened and the specific resection depends on the type of lesion. A combined EEA can be used for lesions extending into the sinonasal cavity, or a combined pterional approach can be utilized for lesions extending more laterally.
Discussion
References
23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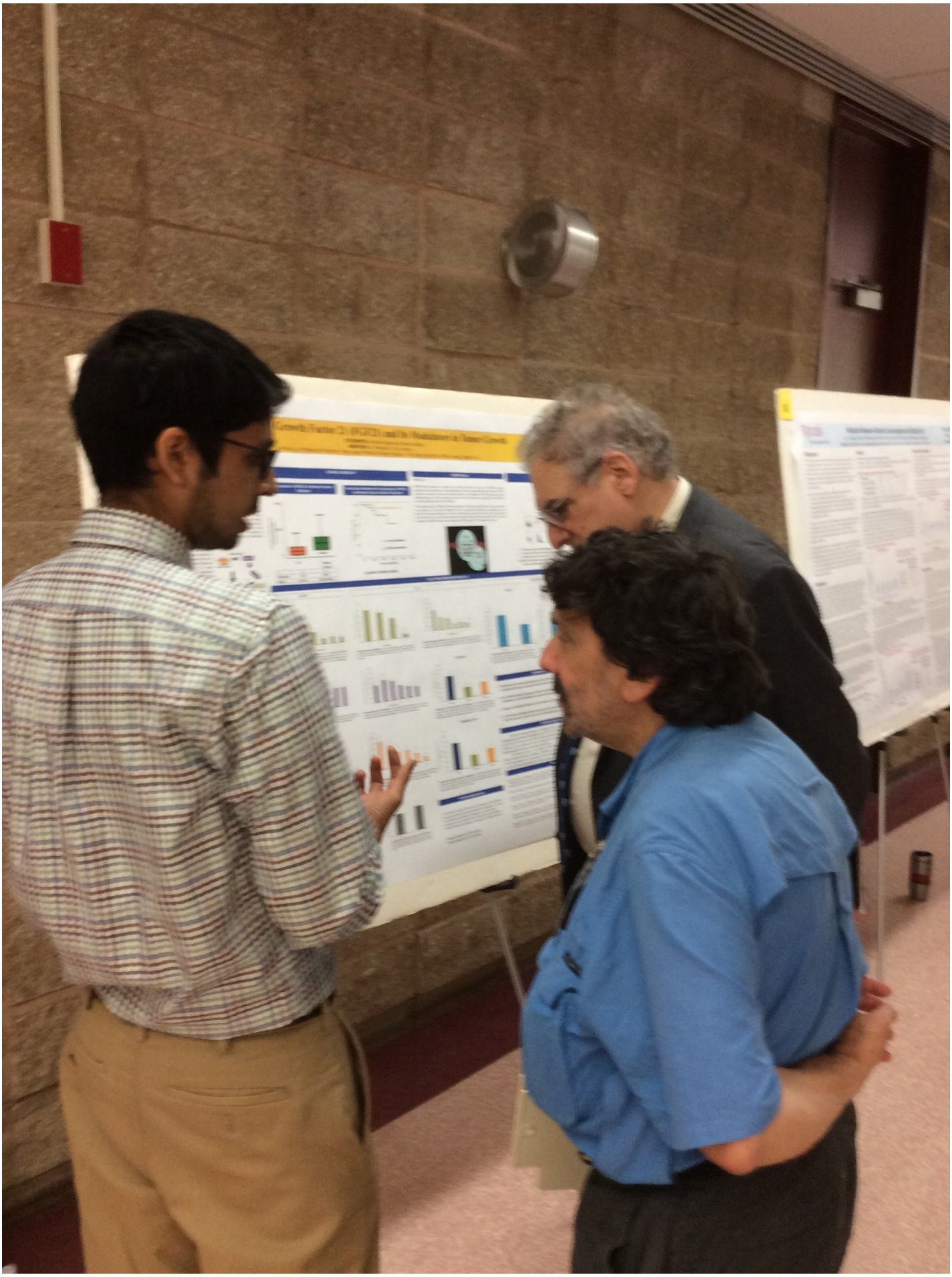
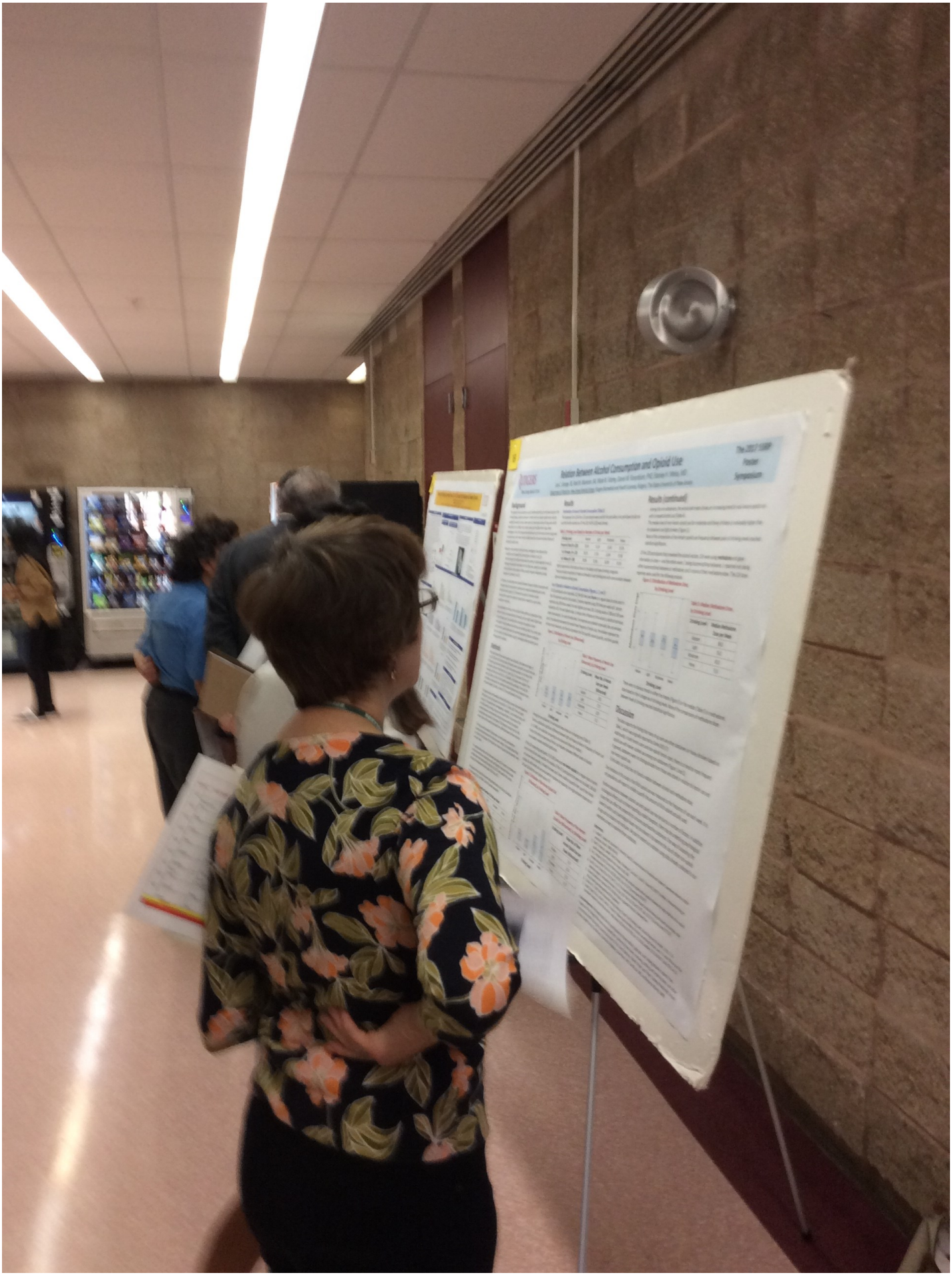
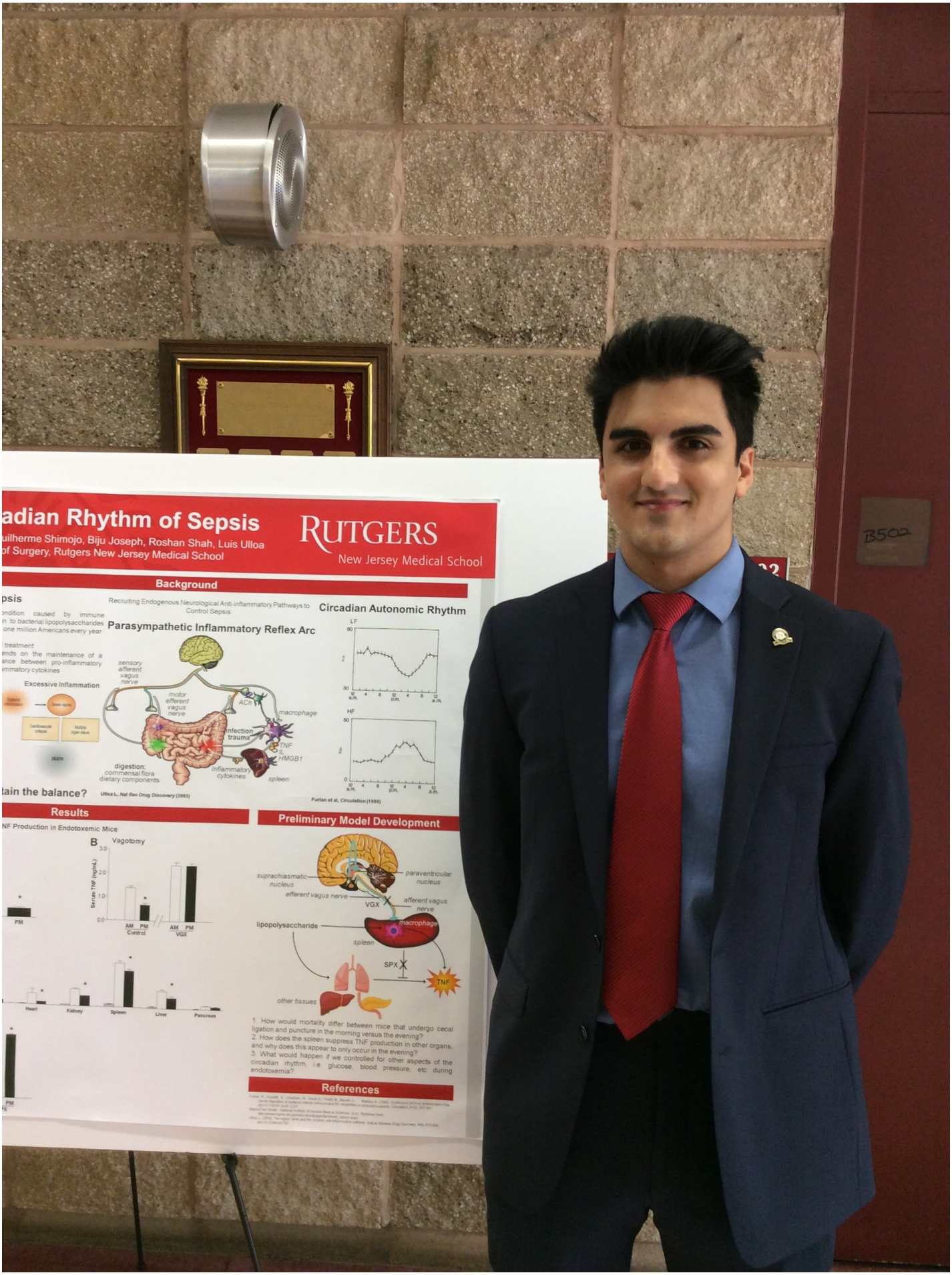
KESSLER
FOUNDATION




Relation Between Alcohol Consumption and Opioid Use


adian Rhythm of Sepsis
uilherme Shimojo, Biju Joseph, Roshan Shah, Luis Ulloa
of Surgery, Rutgers New Jersey Medical School
RUTGERS
New Jersey Medical School
Background
psis
ondition caused by immune
n to bacterial lipopolysaccharides
one million Americans every year
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mmatory cytokines
Excessive Inflammation
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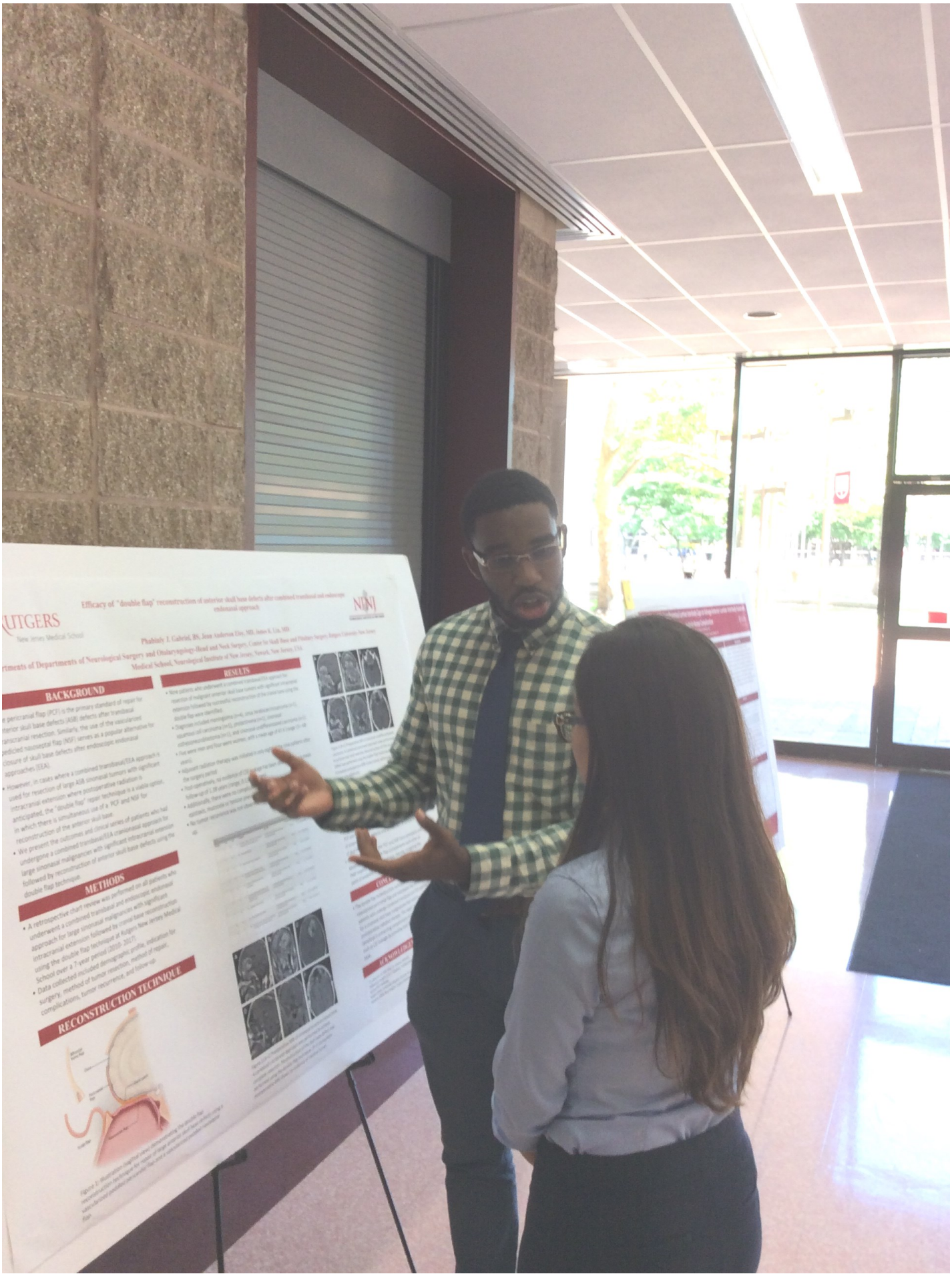
Recruiting Endogenous Neurological Anti-inflammatory Pathways to Control Sepsis.
Parasympathetic Inflammatory Reflex Arc
sensory afferent vagus nerve
motor efferent vagus nerve
ACh
macrophage
infection trauma
TNF
IL
HMGB1
digestion: commensal flora dietary components
Inflammatory cytokines
spleen
Ulloa L, Nat Rev Drug Discovery (2005)
Circadian Autonomic Rhythm
LF
HF
Furlan et al, Circulation (1990)
Results
NF Production in Endotoxemic Mice
Vagotomy
Serum TNF (ng/mL)
AM PM
Control
VGX
Heart
Kidney
Spleen
Liver
Pancreas
Preliminary Model Development
suprachiasmatic nucleus
paraventricular nucleus
efferent vagus nerve
VGX
afferent vagus nerve
lipopolysaccharide
macrophage
spleen
SPX
TNF
other tissues
1. How would mortality differ between mice that undergo cecal ligation and puncture in the morning versus the evening?
2. How does the spleen suppress TNF production in other organs, and why does this appear to only occur in the evening?
3. What would happen if we controlled for other aspects of the circadian rhythm, i.e. glucose, blood pressure, etc during endotoxemia?
References


Efficacy of "double flap" reconstruction of anterior skull base defects after combined transfacial and endoscopic endonasal approach
RUTGERS
New Jersey Medical School
Phabiola J. Gabriel, BS, Jean Anderson Eloy, MD, James K. Liu, MD
Medical School, Neurological Institute of New Jersey, Newark, New Jersey, USA
BACKGROUND
METHODS
RESULTS
RECONSTRUCTION TECHNIQUE


EXIT
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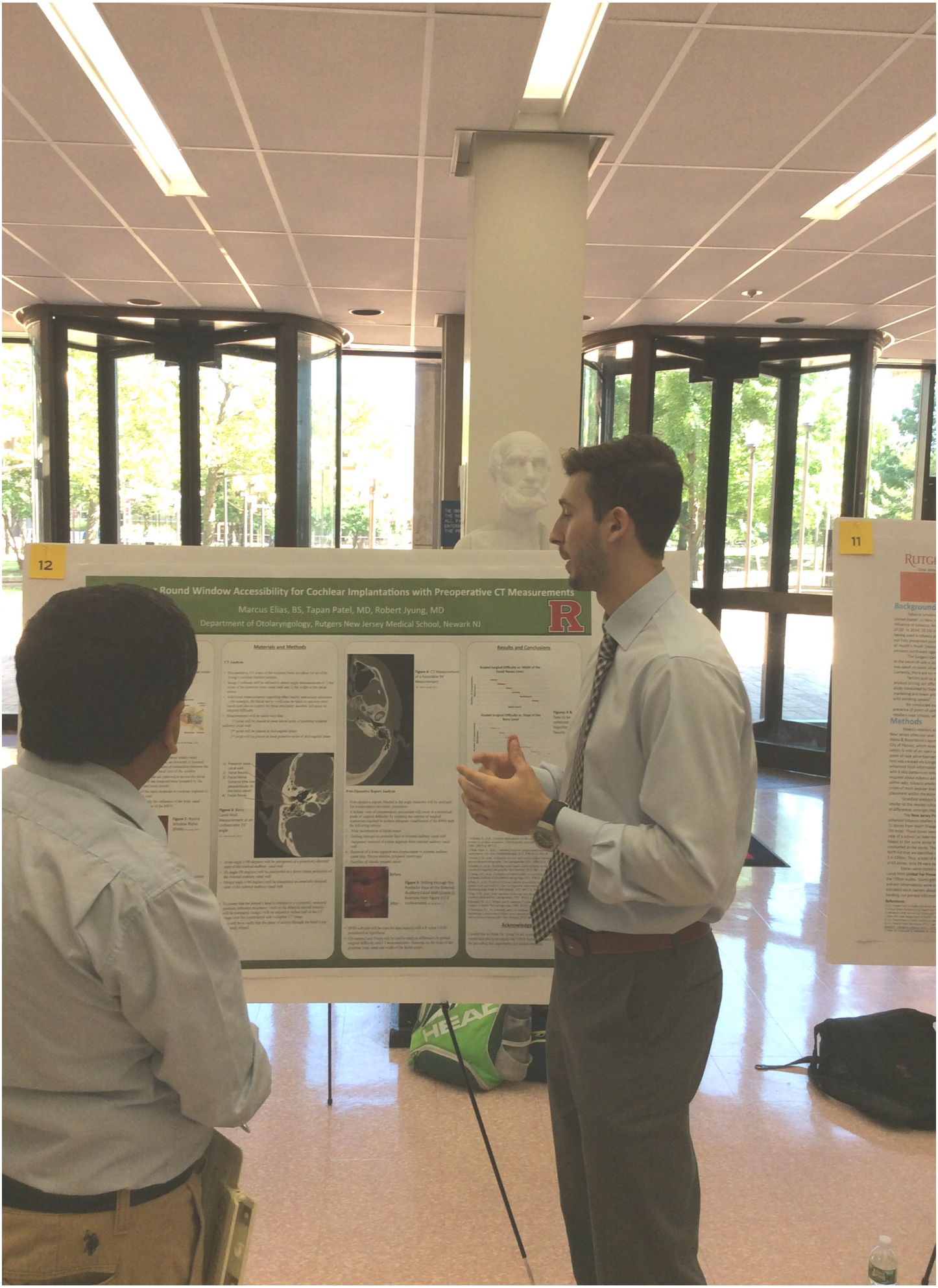
12
Round Window Accessibility for Cochlear Implantations with Preoperative CT Measurements
Marcus Elias, BS, Tapan Patel, MD, Robert Jyung, MD
Department of Otolaryngology, Rutgers New Jersey Medical School, Newark NJ
Materials and Methods
Results and Conclusions
11
Background
Methods


UNITY
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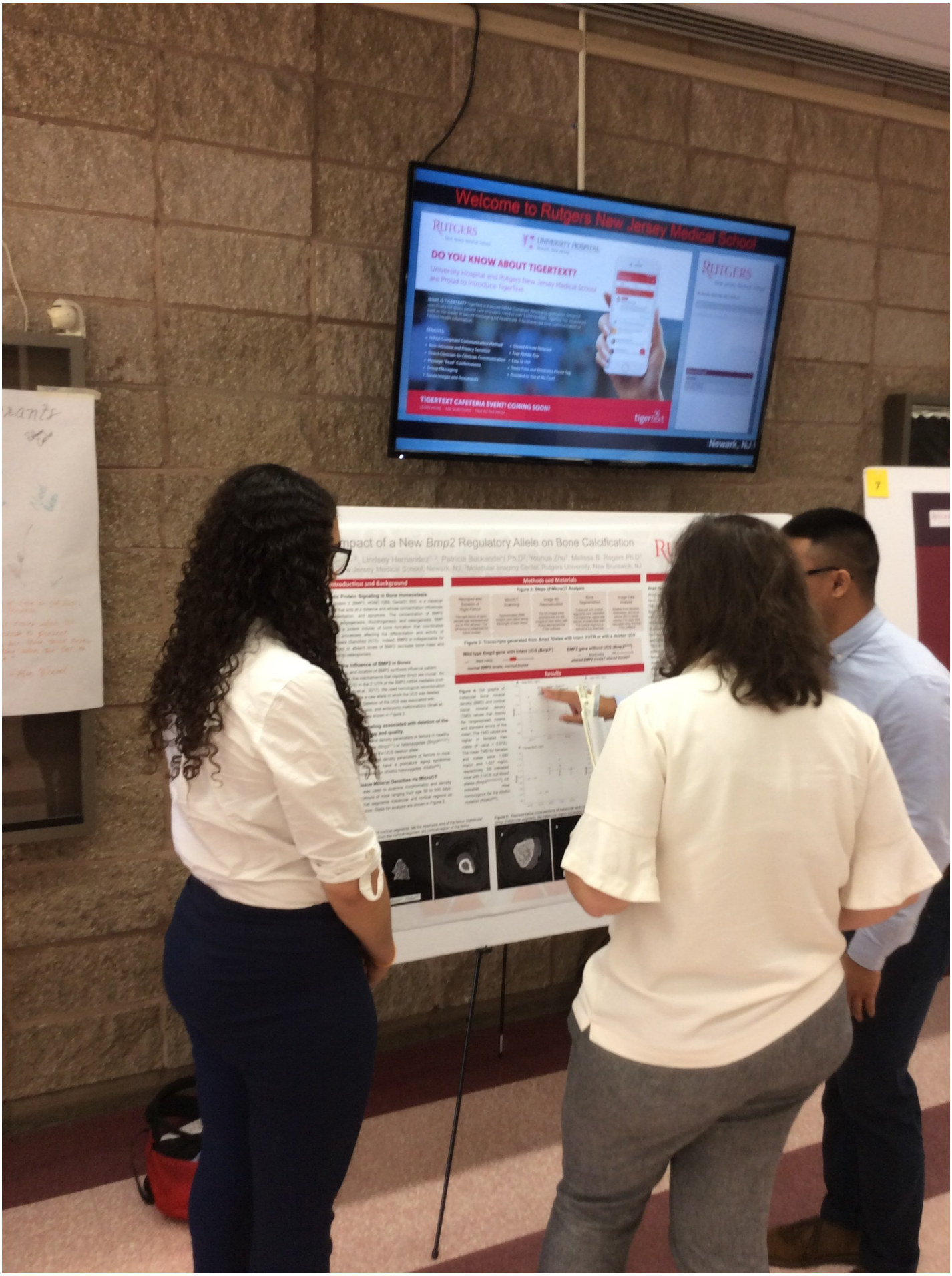
FAIR
9
RUTGERS
Redefining Autism Under
Missed?
Background
Charts
Objectives
DSM IV:
Methods
Acknowledgments


Welcome to Rutgers New Jersey Medical School
RUTGERS
UNIVERSITY HOSPITAL
DO YOU KNOW ABOUT TIGERTEXT?
TIGERTEXT CAFETERIA EVENT! COMING SOON!
Newark, NJ
mpact of a New Bmp2 Regulatory Allele on Bone Calcification
Introduction and Background
Methods and Materials
Results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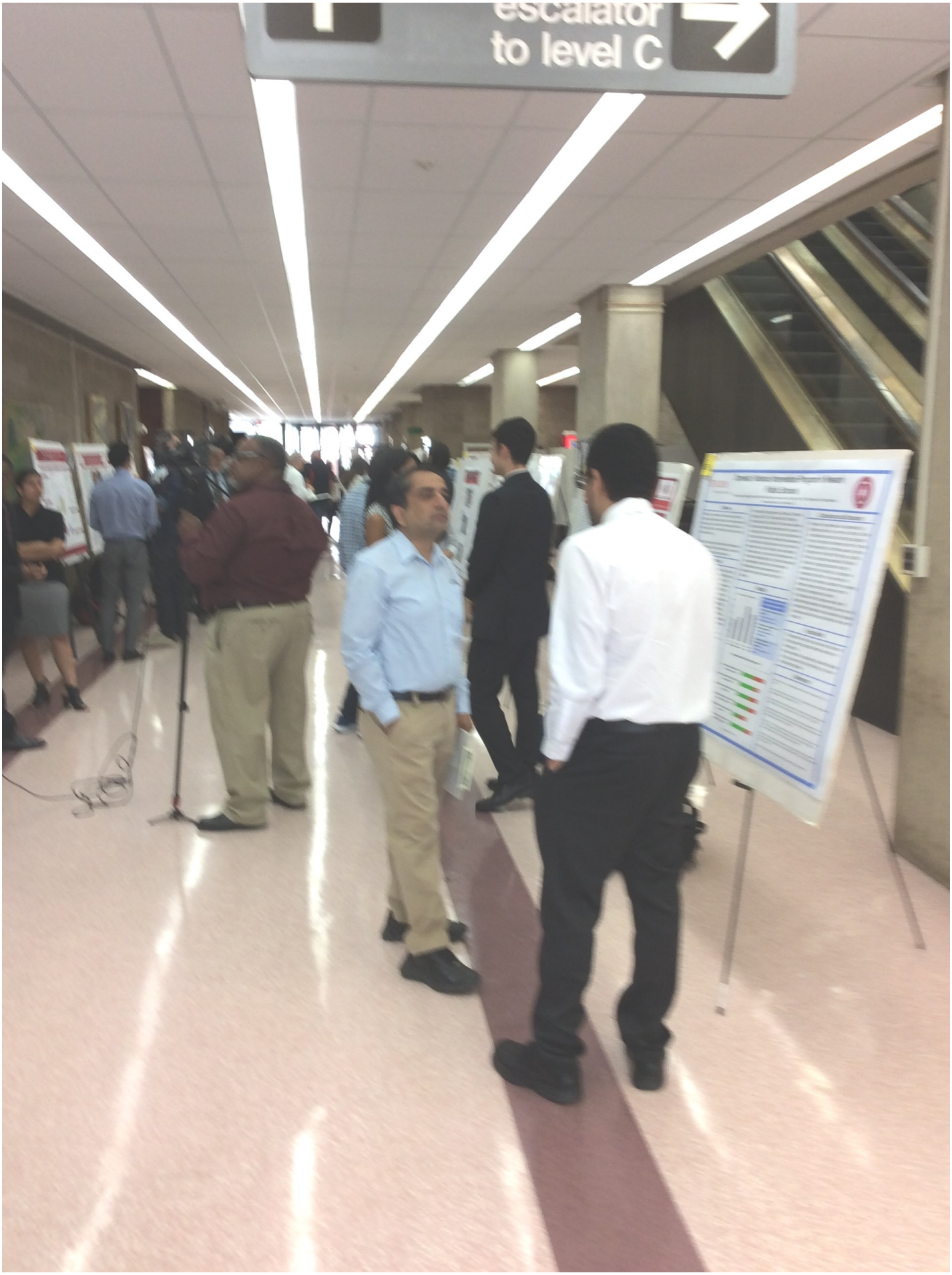
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esence of Gastrointestinal Disorder in a Cohort of ADHD
Neil Chen, Carly Ray
Department of Neurology, Rutgers-New Jersey Medical School, Newark, NJ
Results
Discussion
Telegluaucoma: Comparison of Diagnosis and Management Between Clinical Findings and Telegluaucoma
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Genotypic Verification of Orexin-Cre Mice
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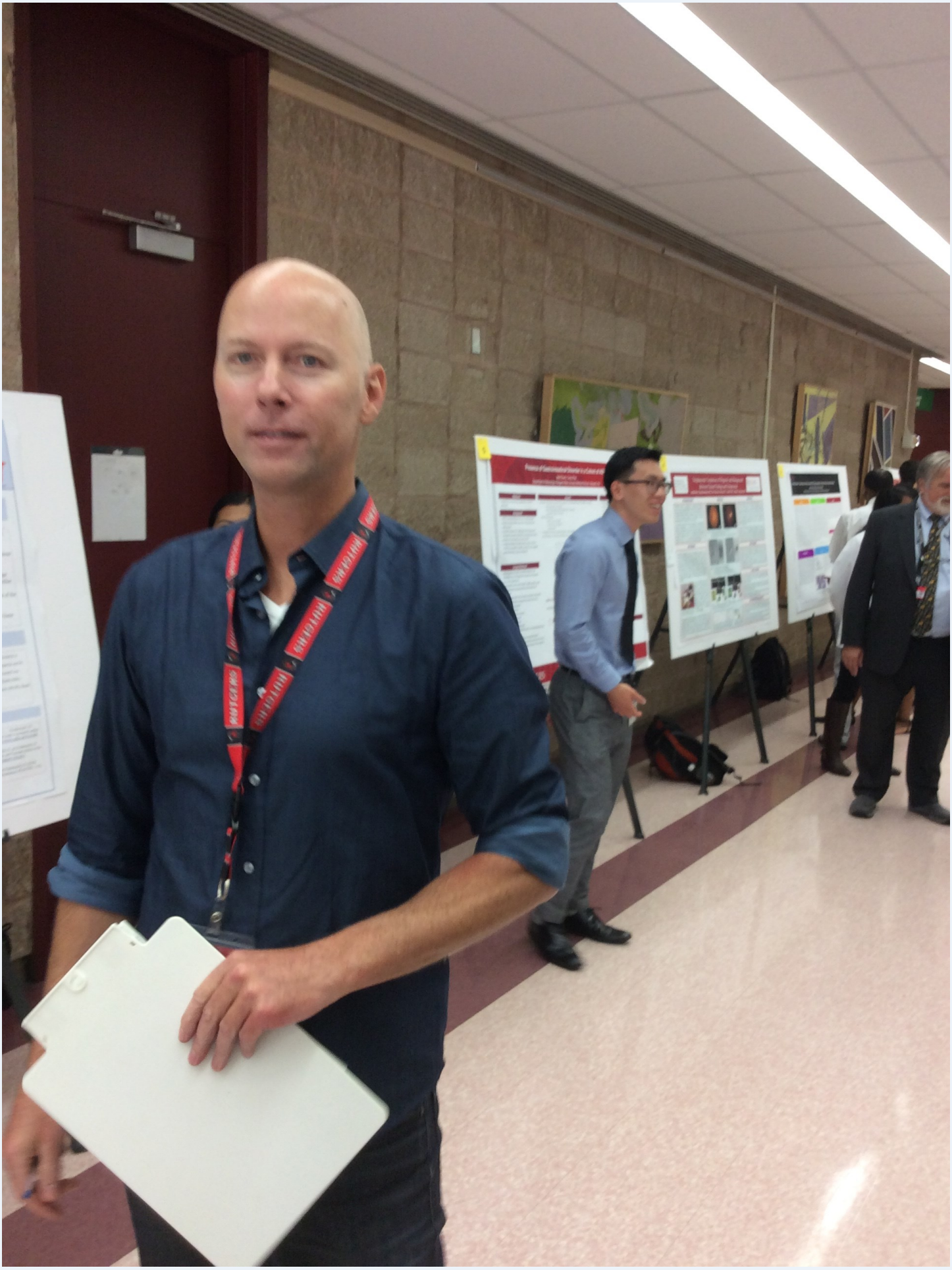


29
plaza
escalator
to level C