Edwin Chiu Advisor(s): Iuliana Shapira

Race, age and gender-specific trends in mortality in patients with pancreatic cancer from 2001 to 2013 in US.

Background: As the population in US continues to grow older, the care of geriatric cancer patients has become an important aspect of oncology. A study in the changes in mortality in the geriatric population with pancreatic cancer is interesting as no major therapeutic advances have been achieved in the past few decades. We have analyzed the SEER database which has nationwide representation for race-specific and gender-specific mortality in pancreatic cancer patients over a 13 year period (2001 to 2013).
Methods: Mortality data regarding patients who were diagnosed with pancreatic cancer (any stage) was extracted from the Surveillance, Epidemiology and End Results (SEER) database from 2001 to 2013. The statistical query was limited to ages groups <65 and >65 years, included both the genders and races (classified as White and Black with Hispanic). Statistical difference was considered significant when p value <0.05.
Results: Significant differences in mortality exist between age, gender and race groups of patients with pancreatic cancer. White males >65 years have a worsening trend in mortality compared to white males <65 years. A similar difference in mortality was noted in white women with respect to age. Black male and females in both age groups (< and >65 years) had a declining trend in mortality but continue to have statistically significantly higher mortality compared to white patients of both sexes respectively. However, the rising mortality in white elderly patients has reached levels similar to that of black elderly female patients.
Conclusions: The mortality of both male and female black patients with pancreatic cancer, especially those >65 years has remained stable over the past one decade but remains worse compared to white patients of similar age. Notably, a worsening of mortality was noted in white patients (male > female). The persistent disparity between gender and races warrants further study to decrease the disparities.

Zachary Feuer Advisor(s): Andrew Winer

Digital Rectal Examination Remains a Highly Specific Prostate Cancer Screening Tool When Conducted by Urological Surgery Residents at Multiple Institutions

Prostate cancer (CaP) screening methods remain a controversial topic. Though often debated, standard practice is to use the combination of digital rectal examination (DRE) and prostate-specific antigen (PSA) levels to guide patient selection for prostate biopsy. While many studies have assessed PSA screening techniques, the accuracy of DRE should not be overlooked. This becomes more important as studies begin to question the use of singular PSA measurements as independent predictors of CaP in African American men. In this study, we aim to assess the diagnostic value of DRE by urology residents in a predominately African American population who have been pre-selected to undergo prostate biopsy.

Demographic data including age, ethnicity, pre-biopsy DRE, and biopsy pathology results were collected from the EMR of 1250 men who underwent prostate biopsy at two institutions between 1996 and 2014. The specificity, sensitivity, positive predictive value (PPV), and negative predictive value (NPV) of the DRE were calculated using histopathology results as the gold standard.

Of 1208 African American patients biopsied, the average age of our population was 64.30 years (SDev = 7.32) at the time of biopsy. Of the 207 patients with a positive DRE, 128 were found to have CaP and 79 were found to be without CaP. Of the 1001 patients with a negative DRE, 463 were found to have CaP and 538 were found to be without CaP. This resulted in a DRE specificity of 87.20%, sensitivity of 21.66%, PPV of 61.84% and a NPV of 53.75%.

DRE is a highly specific test in an African American population when conducted by urology residents. This implies that a patient with an abnormal DRE is likely to have a positive result on prostate biopsy, due to a low false-positive rate. This can be especially useful for management decisions in patients where the PSA levels and the decision to biopsy are borderline. As demonstrated by our residents, the utility and value of DRE should not be neglected.

Edith Gould Advisor(s): Elizabeth Helzner

Racial Disparity Found in Prevalence of High-Risk Types of Human Papillomavirus in Central Brooklyn

HPV is the causal agent of cervical cancer. There are 14 types of HPV known to cause cancer. Types 16 and 18 are generally considered to be the two most prevalent types of high-risk HPV and cause around 70% of the cervical cancer in the United States. But it is known that the distribution and prevalence of different HPV types varies across the globe and within societies.

Noting that Black and Hispanic women experience higher rates of HPV-associated cervical cancer than women of other races or ethnicities in the U.S., we sought to estimate the prevalence of high-risk types of HPV at SUNY Downstate in central Brooklyn which serves a majority black and immigrant population. After IRB approval, we analyzed the HPV screening test results from the SUNY Downstate Pathology lab from July 2010 to April 2016. Prevalence for HPV types was estimated using the first non-indeterminate test result for each unique individual in the data set (n=9,356). We found that in the SUNY Downstate sample prevalence of all HPV types was 1.48 higher (95%CI: 1.41, 1.55) than in the largest clinical trial study in the U.S. to date (Athena study, n=46,601) and that the largest difference was seen in the high-risk types of HPV other than types 16 and 18 (prevalence ratio 1.56, 95%CI: 1.47, 1.65). The Athena sample was 83% white and 14% black, whereas the SUNY Downstate sample is over 90% black. The key finding of our study is that, using black women as the referent group we found that white women with high-risk HPV are 1.81 times (95%CI: 1.14, 2.82), more likely to have HPV 16 and or 18 than other high risk types and women of other races and unknown race (n=41) show a ratio more like that of white women than of black women. So the women with the highest risk of cancer have a significantly lower risk of 16-18 types of HPV. Further research is required to see if there is clinical and/or public health implications of these findings.

Lindsay Hill Advisor(s): Youssef Wadghiri

Cerebrovascular Analysis of the Aging Mouse Brain using Magnetic Resonance Angiography

Age has a significant influence on the manifestation of diseases affecting the cerebrovasculature. While pre-clinical mouse models have improved our understanding of such diseases, we believe a longitudinal assessment of cerebrovascular changes in aging wild type (WT) mice would provide insight into the role aging plays in individual brains and serve as a baseline for cerebrovascular disease models. Here we employ 3D in vivo contrast enhanced-magnetic resonance angiography (CE-MRA) to study the cerebrovasculature of aging C57BL/6 WT mice over 2 years.

CE-MRA allows us to enhance and visualize the vascular network largely independent of blood flow for quantification of the cerebrovascular density. House-made gadolinium (Gd)-micelles were injected into female WT mice at 2-4 months, 14-16 months, and 24-26 months prior to MRA acquisition on a 7T micro-MRI. Intensity-based vascular quantification of the angiograms revealed a significant decrease in cerebrovasculature over two years throughout the brain regions with the exception of the hippocampus.

Immunohistochemistry was performed on brain sections from each age group to validate MRA findings using chromogenic staining for CD31, an endothelial cell marker, and VEGFR1, a marker of vascular activation involved in angiogenesis and vessel permeability. CD31+ vessels decreased in the cortex and hippocampus of aged mice, suggesting that hippocampal changes may be below MRA sensitivity. However, the percentage of VEGFR1 co-stained vessels increased with age and may be symptomatic of vascular activation as is seen in ischemia-induced angiogenesis.

Here we detected a decline in cerebrovascular density over two years in aging WT mice. Current histological studies, including by immunofluorescence analyzed with automated quantitative imaging, involve investigating the factors associated with this vascular decline. This work stresses the need to study aged controls before or while examining cerebrovascular disease models.

Ahmed Hozain Advisor(s): Gainosuke Sugiyama

Where You Live Matters: Regional Differences in Outcomes After Percutaneous Cholecystostomy

Introduction: With over 200,000 cases per year, acute cholecystitis is one of the most frequent causes for admission to hospitals and management by general surgeons. Percutaneous cholecystostomy is an increasingly used treatment for patients diagnosed with acute cholecystitis, who are otherwise too ill to undergo cholecystectomy. Given these patientsâ€™ significant comorbidities, a retrospective analysis to determine predictors of mortality was performed using the Nationwide Inpatient Sample (NIS).
Methods: The Nationwide Inpatient Sample (NIS) from 2005 â€“ 2012 was sampled. Inclusion criteria included patients with a diagnosis of acute cholecystitis by ICD 9 code (574.0, 574.00, 574.01, 575.0, 575.12) who underwent percutaneous cholecystostomy (51.01). We excluded patients with a diagnosis of acalculous cholecystitis (575.10), patients age < 18 years, and cases where gender, race, weekend admission, and month of admission data were missing. For each case, we computed the Elixhauser-Van Walraven score for comorbidity status. Multiple imputation was performed for missing data. We then performed multivariable logistic regression analysis with inpatient mortality as the primary outcome variable. Age, gender, race, insurance status, income status, hospital size, hospital type, geographical region, weekend admission, month of admission, and Elixhauser-Van Walraven score were used as risk variables.â€¨
Results: 8,299 patients were included in this study. 785 (9.46%) patients died during the hospital admission. After adjusting for the risk variables, predictors for inpatient mortality included age (OR 1.16 [1.00 â€“ 1.34 95% CI], p = 0.0492), receiving care in an urban non-teaching hospital (OR 1.27 [1.08 â€“ 1.50 95% CI], p = 0.0169), female gender (OR 1.30 [1.12 â€“ 1.52 95% CI], p = 0.0006), and the Elixhauser-Van Walraven score (OR 2.13 [1.93 â€“ 2.36 95% CI], p < 0.0001). There was a decreased risk of death for patients receiving care in the Midwest (OR 0.74 [0.59 â€“ 0.94 9

Nonita Mittal Advisor(s): Kay Beharry

Effect of Bumetanide on Biomarkers of Neuro-Inflammation in Response to Intermittent Hypoxia in the Neonatal Rat Brain

Background: Bumetanide (Bum), a diuretic, is currently being investigated in clinical trials for treatment of brain disorders like neonatal seizures and Autism Spectrum Disorder as supported by strong conceptual basis and evidence from case-reports, animal and human data, despite the recent inability of NEMO trial to establish its efficacy. It has been observed that early postnatal Intermittent Hypoxia (IH) may make Extremely Low Birth Weight (ELBW) neonates more prone to above disorders. This may be attributed partly to increased neuro-inflammation. No animal study has examined the effect of Bum on neuro-inflammatory markers in ELBW neonates in the setting of IH which is a common phenomenon observed in all NICUs in the country.
Aim: To determine the effect of Bum on biomarkers of neuro-inflammation in response to IH in neonatal rat brain.
Methods: Neonatal rats at birth (P0) were randomly assigned to oxygen groups of 1) Hyperoxia (50% O2) 2) IH (50% O2 with brief episodes of 12% O2) or 3) room air (RA) until P14. Within each group, animals were administered either: Bum (0.1 mg/kg IP) on P0, P1 and P2 or equivalent volume saline. Pro-inflammatory (IL-6 and TGF-beta) and anti-inflammatory marker (IL-10) were examined in brain at P14 and P21 using ELISA and Immunofluorescence.
Results: IL-6 was substantially lower with Bum in RA (p<0.05) and higher in IH (p<0.05) in comparison to saline at P14 in Brain homogenates. TGF-beta was significantly lower with Bum in 50% O2 (p<0.05) and IH (p<0.05) in comparison to saline group, and 50% O2 (p<0.01) and IH (p<0.05) in comparison to RA at P14. TGF-beta was significantly lower with Bum in RA (p<0.01) and IH (p<0.01) in comparison to saline group at P21.
Conclusions: Bum significantly reduces TGF-beta in IH in neonates, and may be its potential mechanism of action associated with its neuro-protective/therapeutic effect as evidenced by clinical case-reports. IL-6 and IL-10 may play a role in its neuroprotective effects at RA.

Julie Parato Advisor(s): Sheryl Smith

Adolescent synaptic pruning in CA3 hippocampus is due to É‘4Î²Î´ GABAAR expression

Synaptic pruning during puberty has been observed in various brain regions. This pruning is necessary for normal brain function, while dysregulation of the process is linked to schizophrenia and autism disorders. We have recently shown (Afroz, Parato, et al., 2016) that adolescent synaptic pruning in CA1 hippocampus is due to the emergence of Î±4Î²Î´ GABARs on dendritic spines. These receptors produce a shunting inhibition which impairs activation of NMDA receptors and reduces expression of Kalirin-7 (Kal7). Kal7, a Rho-GEF, is necessary for spine stability (Ma et al., 2011).

We have also found that CA3 hippocampus undergoes pubertal synaptic pruning. CA3 facilitates the encoding and retrieval of associations, particularly of spatial locations in rodents. We studied spine density, as well as Î±4 and Kal7 protein levels, across the pubertal period using Golgi staining and immunofluorescence (IF) in the female mouse. We discovered that GABAR Î±4 expression increases by 53% at puberty in the CA3 hippocampus (p<.05). This likely represents an increase in Î±4Î²Î´ GABARs because whole cell voltage clamp recordings revealed an increased response of pubertal CA3 pyramidal cells to gaboxadol (THIP) at a concentration (100 nM) selective for this receptor (pre-pub, 5.94 Â± 2.8 pA vs. pub, 19.3 Â± 2, P<0.05, n=5/group). Î±4 knock-out prevented the post-pubertal decrease in spine density observed in wild-type (pubertal WT, 1.6 Â± 0.1 sp/Î¼m; post-pubertal WT,1.2 Â± 0.1 sp/Î¼m, post-pubertal Î±4-/-,1.6 Â± 0.1 sp/Î¼m; p<.05). Analysis of spine types, revealed a 48% decrease in mushroom spines (p<.05), an effect prevented by Î±4 knock-out. We also measured a 14% decrease in Kal7 levels from pre-puberty to puberty (p<.05), which would reduce spine stability. This outcome is not seen in the Î±4 -/- CA3 hippocampus (p<.05). Our data indicates that pubertal expression of Î±4Î²Î´ GABARs initiates synaptic pruning in CA3 hippocampus via diminished expression of Kal7.

Matthew Regier Advisor(s): Ivan Hernandez

The Role of Ribosome Biogenesis in Learning and Memory

Protein synthesis is necessary for the cellular mechanisms that are thought to underlie learning and memory. The synthesis of new protein requires messenger RNA (mRNA) for sequence information, as well as ribosomes to translate the RNA sequence and catalyze the peptide addition reaction. Ribosomes are often thought to be passive machines readily available, but growing evidence suggests they have the capability of regulating what mRNA they translate. We have recently found that existing ribosomes are not sufficient for the late phase of forskolin induced long-term potentiation (LTP) in hippocampal slices, new ribosome biogenesis is necessary. This uncovers the interesting possibility that ribosomes and/or new ribosome biogenesis have a regulatory role in the cellular mechanisms underlying memory. For the first time, we show that new ribosome biogenesis is necessary for memory but not learning, and that pharmacological induction of ribosome biogenesis enhances learning and memory.

Jeffrey Varghese Advisor(s): Carl Paulino

Dynamic, Three-Dimension Analysis of Gait Patterns Before and After Adolescent Idiopathic Scoliosis (AIS) Surgery.

Introduction: Surgeons can manipulate the spine in all 3 planes during AIS surgery; however the postoperative dynamic impact on gait patterns is poorly understood. Methods: Patients underwent gait assessment and full spine radiographs. Gait analysis was performed in a 6-DOF motion analysis laboratory, sampling frequency was 100 Hz. 34 reflective markers were placed on each patient, who underwent straight-line walking trials. BL and 1yr FU Demographics, radiographic and gait parameters were compared using parametric and non-parametric tests. Results: 25 patients were included. Mean age 15.1 y/o, 78% female, mean BMI 22.1. Patients had significantly lower curve magnitudes at 1yr FU (UT: 26.7 vs. 18.2, TH: 5.8 vs. 21.1, TL: 45.9 vs. 16.8, LL: 28 vs. 7.3Â°). Surgical corrections of curve vs. hip, and knee+ankle 3 plane range of motions, had significant correlations. Univariate analysis showed patients had increased time of knee flexion in swing (70.4 vs. 71.84), increased mean hip internal/external rotation in the stance phase (4.2 vs. 11.02), and increased hip flexion at heel strike (28.2 vs. 35.2), all p<0.05. Patients had increased ROM of hip internal/external rotation in the horizontal plane (25.7 vs. 36.7Â°), and increased ROM pelvic variation in the frontal plane (6.9 vs. 7.4Â°), p<0.05. Mean plantar flexion/dorsiflexion increased (20.7 vs. 23.4Â°). Patients had increased walking speed (1.07 vs. 1.13, ms), p<0.05. Conclusion: Dynamic changes of the hip, knee, and ankle occurred in all 3 planes after posterior spinal fusion in our cohort. Future efforts will focus on developing a pragmatic approach to predicting these changes.

Diana Yusim Advisor(s): Aimee Afable

Pilot Evaluation of Parents as Teachers and Healers (PATH), a Childhood Obesity Program

Objective: In New York City, over 20% of elementary school aged children are obese, but the burden is greater in populations of color and economically disadvantaged areas of NYC. Parents as Teachers and Healers (PATH) is a 6-week intensive lifestyle modification program designed for parents of obese children (5-12 years of age) at Brookdale Hospital Medical Center. PATH is a novel program of Live Light Live Right (LLLR), a childhood obesity management program serving low-income areas of North Central Brooklyn. The long-term goal of PATH is to improve the body mass index and metabolic profile of children of parents who attend PATH. Given the high rates of childhood obesity in Brooklyn, there is a clear need to evaluate the efficacy of PATH.
Method: Twenty seven parents were recruited between fall 2015 and spring 2017. A pre/post evaluation method was to assess changes in primary outcomes including sweetened beverage consumption, frequency of eating out/ordering in, screen time hours, and adherence to structured exercise program by administering a survey at baseline and post-PATH.
Results: A pre/post survey indicated potential efficacy of PATH with improvements in frequency of sweetened beverage consumption, screen time, and understanding of BMI. Compared in pre (n=27) to post-test (n=25) assessments, the proportion of parents reporting no daily sweetened beverage consumption increased from 11% to 36%; 3+ hours of screen time/weekend declined from 74% to 32%; and understanding of BMI increased from 30% to 95%.
Conclusion: The changes in behaviors, sweetened beverage consumption and sedentary time, are excellent indicators of impact and are key factors responsible for obesity epidemic seen in the New York City. The efficacy of PATH provides evidence for institutionalization of PATH into LLLRâ€™s existing program as well as translation of this program to other low-income urban settings that have high prevalence of childhood obesity.