



PATHOLOGY RESEARCH DAY

MAY 11, 2018 • NORMAN C. NELSON STUDENT UNION

2018 Theme:
Advancing Research Through Collaboration



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"Alone we can do so little; together we can do so much"

- Helen Keller

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About the cover: Collaboration is key to the immune system, whose diverse cell types work together to recognize, attack and remove invaders. Here, T-cells (green) are attacking a cancer cell (blue).

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Associate Vice Chancellor for Research, UMMC

Junming Wang, PhD

Professor of Pathology
Director of Research Pathology, UMMC

About the cover: Collaboration is key to the immune system, whose diverse cell types work together to recognize, attack and remove invaders. Here, T-cells (green) are attacking a cancer cell (blue).

AGENDA

MAY 11 • 8:00 AM - 2:00 PM

8:00 REGISTRATION, POSTER VIEWING AND
CONTINENTAL BREAKFAST

8:30 WELCOME AND ANNOUNCEMENTS
James Neill, MD - Associate Professor of Pathology
Director of Anatomical Pathology, UMMC

WORKSHOP I: "BUILDING SYNERGY"

Moderator: **Christian R. Gomez, PhD** - Associate Professor of
Pathology and Radiation Oncology, UMMC

8:35 INTRODUCTION TO WORKSHOP
Christian R. Gomez, PhD

8:40 THE UNIQUE ROLE OF PATHOLOGY IN THE ERA OF
PRECISION MEDICINE
Richard Summers, MD - Associate Vice Chancellor for
Research, UMMC

9:00 GRANTMANSHIP FOR OUTSTANDING
COLLABORATIVE RESEARCH
Merry Lindsey, PhD - Professor of Physiology and
Biophysics, and Medicine
Director, Mississippi Center for Heart Research, UMMC

9:20 WORKING WITH IRB TO MOVE YOUR PROJECT FORWARD
Ike I. Eriator, MD - Professor of Anesthesiology and Pain
Management; Director, Pain Fellowship Program
Chair, IRB1 Committee, UMMC

9:40 GENERAL DISCUSSION

9:45 POSTER VIEWING WITH COFFEE AND SNACKS

WORKSHOP II: "ART OF COLLABORATION"

Moderator: **Israh Akhtar, MD** - Professor of Pathology;
Director of Cytopathology Fellowship Program, UMMC

10:15 INTRODUCTION TO WORKSHOP
Israh Akhtar, MD

10:20 QUALITY IMPROVEMENT RESEARCH
Stephen Raab, MD - Professor of Pathology
Director of Quality Assessment, UMMC

10:40 LNCRNAs IN NEURAL CELL BIOLOGY AND ALCOHOL-
INDUCED NEURODEGENERATION
Junming Wang, PhD - Professor of Pathology
Director of Research Pathology, UMMC

11:00 MOLECULAR PATHOLOGY OF VISION
Federico Gonzalez-Fernandez, MD, PhD - Professor of
Ophthalmology and Pathology, UMMC
Associate Chief of Staff for Research & Development,
G.V. (Sonny) Montgomery Veterans Affairs Medical Center

11:20 DEVELOPING NEW THERAPIES FOR RENAL DISEASE
Gene L. Bidwell, PhD - Associate Professor of Neurology,
UMMC
Alejandro Chade, MD, FAHA - Professor and Associate
Director, Physiology Graduate Program, Department of
Physiology and Biophysics, UMMC

11:40 GENERAL DISCUSSION

11:45 POSTER VIEWING AND BREAK WITH FINGER FOOD

WORKSHOP III: "CORNERSTONES OF PARTNERSHIP"

Moderator: **Federico Gonzalez-Fernandez, MD, PhD** - Professor
of Ophthalmology and Pathology, UMMC
Associate Chief of Staff for Research & Development, G.V.
(Sonny) Montgomery Veterans Affairs Medical Center

12:15 INTRODUCTION TO WORKSHOP
Federico Gonzalez-Fernandez, MD, PhD

12:20 UMMC BIOBANK: A NICHE FOR COLLABORATIVE
RESEARCH
Jesus Monico, PhD, MPH - Assistant Professor of
Pathology and Otolaryngology and Communicative Sciences
Executive Director, UMMC Biobank; Director, Histology
Research Lab, UMMC

12:40 DAY-TO-DAY COLLABORATIVE RESEARCH IN OUR
MEDICAL CENTER
Ingrid Espinoza, PhD, CCRP - Associate Professor of
Preventive Medicine, John D. Bower School of Population
Health, UMMC

1:00 PROTECTING YOUR INVENTIONS, WHY AND HOW
James K. Petell, PhD, USPTO - Registered Patent Agent
Director, Innovation Development and Licensing Office,
UMMC

1:20 GENERAL DISCUSSION

1:25 POSTER VIEWING AND BREAK WITH DESSERT

1:45 AWARD PRESENTATIONS AND CONCLUDING REMARKS
James Neill, MD - Associate Professor of Pathology
Director of Anatomical Pathology, UMMC

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POSTER ABSTRACTS

1. RETROSPECTIVE STUDY OF RACIAL AND GENDER DIFFERENCES ON HEPATOCELLULAR CARCINOMA.

Akram Shalaby, Jaswinder Kaur, Lakshmi Ramachandran Nair, Charu Subramony, Xinchun Zhou.

Department of Pathology, University of Mississippi Medical Center, Jackson, MS.

Background: Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver. HCC is now the second most common cause of cancer-related death worldwide. In the US, there has been an 80% increase in the annual incidence of HCC during the past two decades.

Objective: This study is aimed to investigate racial and gender disparities of HCC at Mississippi region in incidence and clinical manifestations.

Methods: At the University of Mississippi Medical Center we conducted a retrospective study on 142 HCC patients admitted to our institution from 2001 to 2017. We investigated the racial disparities between African American (AA, $n=70$) and Caucasian American (CA, $n=72$) as well as gender disparities (Males = 103 and Females = 39).

Results: We noticed a similar incidence of HCC in AA and CA populations and a higher incidence in males than females (2-4: 1), which is consistent with the published national data. We also observed an earlier age of onset, higher levels of plasma lipids, and higher values of Liver function tests in AA compared to CA patients. Viral hepatitis B & C rates were similar in AA and CA (60.7% and 59.3%, respectively), but they were higher in male (63.3%) than female (48.5%) patients. More AA patients (80%) smoked than CA (72%). However, smoking rates were quite similar in male and female patients (82.6% and 83.8%, respectively).

Conclusions: Our results suggest that AA Patients with HCC have an earlier onset, higher plasma lipid levels and worse liver function tests compared to CA patients. We also concluded that racial disparity among patients with HCC in our population was more prominent than gender disparity. Our data also suggest that viral infections and smoking could be potential risk factors for HCC.

2. IMPAIRED RECOVERY FROM NOISE-INDUCED HEARING LOSS IN A TYPE 2 DIABETES ANIMAL MODEL T2DN.

Alberto A. Arteaga¹, David S. Sandlin^{2,3}, Laura Lee Beneke⁴, Kathleen T. Yee⁵, Douglas E. Vetter⁵, Fan Fan⁶, Richard J. Roman⁶, Wu Zhou^{1,5,7}, Hong Zhu^{1,5}.

¹Department of Otolaryngology and Communicative Sciences, ²Program in Neuroscience, ³M.D./Ph.D. Program, ⁴M.D. Program, ⁵Neurobiology and Anatomical Sciences, ⁶Department of Pharmacology, ⁷Neurology, University of Mississippi Medical Center, Jackson, MS, USA.

Background: Diabetes and noise-induced hearing loss (NIHL) are two common conditions in the US population. Approximately 29.1 million Americans, 9.3% of the population, have diabetes (CDC 2014), and approximately ten million people in the U.S. have a noise-related hearing loss. Recent comprehensive report (Agrawal et al. 2009) indicates that diabetes is a risk factor for hearing loss in US adults. There were several clinical studies investigated the interaction between diabetes and NIHL, but conflicting findings have been reported (Ishii et al. 1992; Hodgson et al., 1987).

Objective: In the present study, we examined the susceptibility and recovery to NIHL of T2DN, a new diabetic rat model that mimics the human Type 2 diabetes mellitus. This normotensive model develops spontaneous diabetes with progressive diabetic nephropathy similar to humans.

Methods: Five 9-month-old T2DN rats and 3 age-matched Wistar control rats were involved the study. The animals were unrestrained within a subdivided cage suspended in a rotatory floor directly below the horn of a calibrated speaker in a reverberant chamber. An octave band of noise (8-16 kHz) at 103 dB SPL was continuously delivered for 2 hours. Under ketamine and xylazine anesthesia, auditory brainstem responses (ABR) were measured at 5.6, 8, 11.3, 22.6, 32 and 45.25 kHz, at 3 different time points: pre-noise, 24 hours and 7 days following the noise exposure. ABR thresholds were defined as the lowest intensity at which tone bursts generated a well-defined and reproducible wave I.

Results: T2DN and Wistar rats' ABR thresholds were significantly increased 24 hours after noise exposure at 11.3, 22.6, 32 and 45.25 kHz ($p < 0.05$). After 7 days following noise exposure, Wistar rats' thresholds returned to pre-noise levels in all frequencies except for 45.25 kHz ($p < 0.05$). T2DN rats' thresholds remained significantly elevated at 11.3, 22.6 and 45.25 kHz when compared to pre-noise thresholds levels ($p < 0.05$). At 32 kHz, T2DN rats' thresholds were increased but were not significantly different to pre-noise thresholds levels.

Conclusions: The results suggest that T2DN rats are more susceptible to NIHL when compared to Wistar rats. Recovery from noise-induced temporary hearing loss appears to be impaired in T2DN rats. Ongoing studies, including assessment of distortion product otoacoustic emissions, ABR wave I amplitude and afferent synaptopathy, will further elucidate the underlying mechanisms.

Acknowledgements: Supported by NIH R01DC012060 (HZ), R01DC014930 (WZ) R21EY025550 (WZ), R21DC015124 (DEV), R01HL36279 (RJR), R01DK104184 (RJR), P20GM104357 (Core B, C, RJR; Pilot, FF); R21AG050049 (FF).

3. EFFECTIVENESS OF WHOLE SLIDE IMAGE SIMULATION EDUCATION FOR POTENTIAL USE IN PAP TEST INTERPRETATION IN UNDER RESOURCED GLOBAL SETTINGS.

Anas Berneih, M.D., Zelma Cason, Ph.D., Kim R. Geisinger, M.D., Stephen S. Raab, M.D.

Department of Pathology, University of Mississippi Medical Center.

Background: Worldwide, cervical cancer is the third most common cancer among women and the second most frequent cause of cancer-related death, predominantly occurring in under resourced global settings.

Objective: We developed and measured the effectiveness of a Pathology Digital Imaging (PDI) distance simulation-based educational program for potential use in Pap test training of individuals and teams in under resourced settings.

Methods: We developed, pilot-tested, and measured the effectiveness of a distance simulation-based educational program for six university and two high school American students who had no previously experience in diagnostic cytopathology. The entire program lasted 10 weeks with the last six weeks consisting of immersion in conventional Pap test screening using whole slide images retrieved from our files and scanned at 40x. The gold standard diagnosis was the original diagnosis and these slides all had been used for cytotechnologist training. Over the six weeks, the weekly volume increased from 20 to 80 Pap tests and we measured individual and team performance in the detection of high grade squamous intraepithelial lesion or higher abnormality (HSIL+). Subjects were provided feedback of screening results on a daily basis. We evaluated team performance by blinded interpretations of two or three subjects.

Results: The mean individual sensitivity and specificity for HSIL+ detection over the entire six week Pap test screening period was 64.7% and 90.4%, respectively. For the final week, the mean individual sensitivity and specificity was 74.2% and 87.2%, respectively, indicating increased HSIL+ detection. For the final week of training, randomly selected teams of two subjects increased the sensitivity of detection (based on the identification of HSIL+ by one member) to 85% with a slight decrease in specificity to 84%.

Conclusion: Our findings support the hypothesis that a PDI distance simulation-based training program may produce subjects who perform at a relatively high level of competence in 10 weeks. We think that these performance metrics also could be improved with select targeting of subject weaknesses (e.g., lower detection frequency of glandular neoplasia). We hypothesize that under resourced settings, which currently lack cytotechnologists, could adapt this type of training program and different screening models, such as dyad teams, which further would improve HSIL+ detection.

4. APL-LIKE LEUKEMIA WITH AMPLIFICATION OF MYC AND KMT2A BUT WITHOUT PML-RARA REARRANGEMENT.

Anas Bernieh¹, M.B.B.S., Holly H Hobart¹, Ph.D., Siraj El Jamal¹, M.D., Aurelia Meloni-Ehrig², Ph.D., John T. Lam¹, M.D.

¹*Department of Pathology, University of Mississippi Medical Center, Jackson, Mississippi*

²*CSI Laboratories, Alpharetta, GA*

Background: Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML) with relatively favorable prognosis. Timely and accurate diagnosis of APL is required for two reasons. Firstly, patients with APL have a high risk for disseminated intravascular coagulopathy (DIC). Secondly, this disease has a unique and effect treatment: All Trans-Retinoic Acid (ATRA). APL is diagnosed by analysis of morphologic, flow cytometry, and cytogenetic findings. Most important is the pathognomic PML-RARA rearrangement, which is the product of translocation between chromosome 15 and 17.

Objective: We present a rare case which has the morphologic and flow cytometry findings of APL but no evidence of the diagnostic PML-RARA rearrangement. Even more unusual is detection of amplifications of the MYC and KMT2A (MLL) genes. Amplification of MYC is seen in several solid tumors but is an unusual finding in leukemia. Several cases of AML with APL-like features and MYC amplification have been described. These cases have shown both double minutes and homogeneously staining regions (HSRs). The presence of both MYC and KMT2A amplification is another rare finding.

Methods: A 72 year old female who has history of thalassemia with worsening anemia, new onset thrombocytopenia, and peripheral myeloblasts consistent with AML. Bone marrow biopsies, flow cytometry analyses, and cytogenetic testing were performed.

Results: Peripheral blood smear showed many blasts with moderate pale basophilic cytoplasm, large moderately irregular nuclei with homogeneously dispersed chromatin and occasional large nucleoli. Few cytoplasmic granules are noted, but no Auer rods seen. The marrow sample was cellular, had 90% blasts with identical morphologic features. Myeloid maturation was nearly absent. Flow cytometry showed a large (~86%) abnormal blast population with high side scatter and expression of CD4, CD13 (heterogeneous), CD33, CD117, and myeloperoxidase. These cells are negative for HLA-DR, cCD3, CD3, CD19, CD34, and CD64. These results together with the morphologic findings are consistent with AML, and suspicious for APL; fluorescence in situ hybridization (FISH) showed no evidence of PML/RARA gene fusion, t (15; 17). FISH on metaphase cells showed double minutes that are the result of MYC and KMT2A amplification. Amplification of MYC and KMT2A was detected in 84.0% and 70.0% of cells analyzed, respectively (Multiplex probes used and chromosome location: 5'MYC/3'MYC (8q24.2); 5'MLL/3'MLL (11q23), Abbott Molecular.

Conclusion: Although morphology and flow cytometry were suggestive for APL, the cytogenetics confirmed the absence of PML-RARA rearrangement, and the presence of MYC and KMT2A gene

amplification. Double minutes included copies of KMT2A, and copies of MYC. These findings are rarely seen in AML and exclude APL; they are associated with poor prognosis.

5. RHABDOID COLORECTAL CARCINOMA WITH ELECTRON MICROSCOPY CORRELATION: CASE REPORT AND LITERATURE REVIEW.

Anas Berneih, James S. Neill.

Department of Pathology, University of Mississippi School of Medicine, Jackson Mississippi.

Background: Malignant tumors with rhabdoid features were first described in Wilms tumors in children. Colorectal adenocarcinoma with rhabdoid features is a rare tumor type that is characterized by the presence of cells with a large eccentrically placed nucleus, and eosinophilic cytoplasm. These tumors have been associated with a poor prognosis.

Case Presentation: A 69 year old male presented with light headedness, right lower quadrant pain and microcytic anemic. CT scan showed circumferential wall thickening of cecum and proximal ascending colon. A right hemi-colectomy was performed. Gross examination revealed ragged serosal surface with adhesions and a large palpable mass in the circumferential ulcerated mass. Pathology demonstrated a pleomorphic adenocarcinoma with predominant rhabdoid features 90%, glandular pattern 5% and mucinous pattern 5%. Adenocarcinoma involved the serosal surface and a vessel at the circumferential margin. Four of ten mesenteric lymph nodes contained metastatic adenocarcinoma. A low-grade appendiceal mucinous neoplasm involved the appendix. The differential diagnosis of the rhabdoid cells included a lymphoma, melanoma, germ cell malignancy, rhabdomyosarcoma and pleomorphic adenocarcinoma. Positive markers included broad-spectrum cytokeratin AE1/3, CAM5.2, CD10 and EMA (focal). Electron microscopy revealed the presence of numerous cytoplasmic intermediate type filaments. The following immunohistochemical studies were negative: CD20, CD45, CD79a, HMB45, MART1 SOX10, alpha-fetoprotein, CD30, glypican-3, CDX2, CD20, CEA, smooth muscle actin desmin, and synaptophysin.

Discussion: Tumors with rhabdoid features occurring outside the kidneys are recognized as malignant extrarenal rhabdoid tumors (MERT). Seventeen colonic rhabdoid adenocarcinomas have been reported to date. The mean age of diagnosis is 70 years. Eight cases have occurred in the cecum or right colon. Nodal or liver metastases were present in ten cases. One rhabdoid adenocarcinoma was reported with a synchronous mucinous tumor of the appendix. The prognosis of this tumor is poor with most patients' dead of disease within one year. Rhabdoid cells are large, with eccentrically located and large vesicular nucleus, prominent nucleoli, and abundant acidophilic cytoplasm. Electron microscopy shows aggregates of cytoplasmic intermediate filaments. The most frequent immunohistochemical findings are positive vimentin, EMA, pancytokeratins and CAM5.2. One case showed a positive expression of beta catenin. Markers for melanoma, lymphoma muscle and GIST are uniformly negative. Two cases have shown BRAF mutations with loss of MHL1 expression and hypermethylation of promoter genes (MSI high phenotype). Two cases have shown a microsatellite stable profile. Rhabdoid tumors may be mixed or pure adenocarcinomas. Immunohistochemistry expression will vary in the components. Five months (02/17) after initial presentation the patient was admitted at our hospital, he was in a critical situation, and the decision to admit him to hospice care was made (no more information present on his EMR).

Conclusion: This case is an example of a rhabdoid colorectal adenocarcinoma of a mixed type that fits the phenotype of previously described cases. These cases may be recognized by their characteristic histology but melanoma, large cell lymphoma and pleomorphic myoid sarcomas must be excluded.

6. A POSSIBLE ROLE OF MAST CELLS IN THE PATHOGENESIS OF PEDIATRIC NON-SPECIFIC ABDOMINAL PAIN.

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Background: Mast cells (MCs) and a low-grade mucosal inflammatory process are known to be increased in the colonic mucosa of adult patients with irritable bowel syndrome. The number of MCs in the colonic mucosa of children presenting with non-specific abdominal pain has not been investigated before.

Methods: Pediatric patients presented with non-specific abdominal pain, normal colonoscopy findings and apparently histologically normal colon biopsies between May 2015 and February 2017 were studied. The control group consisted of 12 autopsy cases of patients who died of isolated central nervous system diseases. Colonic biopsies from patient and control groups were reviewed and stained with CD117. In each region of the colon, the area with the highest number of MCs (hot spot) was selected and the number of MCs was counted per one high power field (X400).

Results: The patients group consisted of 36 patients (age range 1.7-17 years). The control group consisted of 12 autopsies (age range: 0.4-16.3 years). Clinical presentations of the patients group included abdominal pain (in all patients), abnormal bowel movement, blood in stools and joint pain. Histologic examination of both groups showed no pathologies beside increased number of MCs in the patients group.

Conclusion: Our results show an increased number of MCs in all parts of the colon in pediatric patients with dysfunctional abdominal pain compared to the controls group. It is tempting to hypothesize that these patients may benefit from anti-histamines or other mast cells stabilizers.

7. FACIAL FOLLICULAR SPICULES IN A TRANSPLANT PATIENT.

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Background: A patient with trichodysplasia spinulosa (TS) following heart transplant was successfully treated with topical cidofovir 1% gel.

Case Description: A 57-year-old African American man with hypertension, dyslipidemia, congestive heart failure, and heart transplantation 12 months prior presented to the dermatology clinic with an eruption of multiple, asymptomatic papules on the face. Immunosuppressive medications included mycophenolic acid and tacrolimus. The pin-point papules started on the central face and spread to the ears, arms, and legs. The initial appearance was that of a “nutmeg-grater” with central white spiny excrescences overlying fine papules. Eyebrow alopecia was associated with the eruption. Pathology revealed marked dilatation of anagen hair follicles with a proliferation of haphazard inner root-sheath cells replacing the follicular lumen. Hair shafts were absent and plugged infundibula were observed. The inner root-sheath keratinocytes were enlarged and dystrophic with deeply eosinophilic trichohyaline granules. Transmission electron microscopy (TEM) confirmed the presence of intranuclear viral inclusions within affected inner root-sheath keratinocytes composed of non-enveloped, icosahedral viral particles. These findings were morphologically consistent with polyomavirus. Polymerase chain reaction (PCR) was performed on the tissue but failed to amplify the viral DNA of this polyomavirus.

Discussion: TS-associated polyomavirus is described as a papular eruption that appears on the central face with spiny excrescences and varying degrees of associated alopecia. Histologic features include distended hair follicles with expansion of inner root-sheath cells, eosinophilic trichohyaline granules, and the absence of hair shafts. The clinical differential diagnosis includes follicular spicules of multiple myeloma. Our patient responded well to topical cidofovir 1% gel. Other treatment modalities include reducing immunosuppression.

8. ERB AGONIST HAS A LONGER WINDOW OF ANTIDEPRESSANT EFFECTIVENESS THAN ESTRADIOL (E2) IN RATS AFTER LONG-TERM OVARECTOMY VIA ERB-MEDIATED EXPRESSION OF TPH2 AND MAO-A.

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Background: Estrogen therapy (ET), an effective treatment for perimenopausal depression, often fails to ameliorate symptoms when initiated late after the onset of menopause. Our previous work suggested that this differential effects of ET might be mediated by ER β , but the down stream mechanism is not clear.

Methods: Female Sprague-Dawley rats were treated with estradiol (E2), agonists for ER α and ER β , or vehicle 6-day (Early-ET) or 180-day (Late-ET) after ovariectomy (OVX). We investigated the differential expression of TPH2, an enzyme for serotonin synthesis, and MAO-A, an enzyme in serotonin degradation using RT-PCR and immunoprecipitation, immunohistochemistry, and behavior performance in clinically-relevant early and late ET.

Results: Early-, but not Late-ET increased the expression of tryptophan hydroxylase 2 (TPH2), decreased monoamine oxidase A (MAO-A) level, prolonged the swimming time in the forced swimming test, and reduced anxiety-like behavior in elevated plus maze of OVX rats. In late-ET, only diarylpropionitrile (DPN, an ER β specific agonist), but not E2 (an ER α and ER β agonist) nor propylpyrazole triol (PPT, an ER α specific agonist), achieved similar results.

Conclusion: These data suggest that ER β altered responses in the regulatory system for serotonin may mediate the antidepressant efficacy of ET associated with therapy initiation timing. ER β specific agonist has longer window of antidepressant effectiveness than E2 in rats after long-term ovariectomy.

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9. INTESTINAL PEYER'S PATCH GENE EXPRESSION ALTERED FOLLOWING RODENT VERTICAL SLEEVE GASTRECTOMY.

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Background: The use of bariatric surgery to produce positive metabolic health benefits for long term weight loss continues to rise. The mechanisms that mediate surgical weight loss are not yet fully understood; however, various hormonal, molecular, and neural changes resulting from the surgery have been revealed. In previous studies using our rodent model of vertical sleeve gastrectomy (VSG), it was reported that VSG results in uninhibited gastric emptying resulting in remodeling of the duodenum and various other structural changes within the intestine.

Objective: To investigate the effect VSG has on immune and inflammatory milieu within the immune cell populations of the gut housed within the Peyer's patches (PP).

Methods: We evaluated male Long Evans rats (N=13) having received Sham-Surgery or VSG and fed a standard chow diet post-operatively. VSG animals lost significant amounts of body mass and fat mass and ate less in comparison to Sham males during the first 5 post-operative weeks. During post-operative week 16, animals were euthanized and intestinal Peyer's patches were harvested for gene expression studies. Using real-time PCR, we compared various inflammatory markers commonly expressed by immune cells in duodenal, jejunal, and ileal PPs.

Results: We report increased CD8A (cytotoxic T cell marker) and trend towards increased PTPRC (B cells marker) in VSG PP when compared to Sham. IL4 mRNA expression was increased in VSG PP in comparison to Sham ($P < 0.05$). IL6 and IL1B gene expression were increased in VSG ($P < 0.01$). Furthermore MMP12 was also increased in the VSG PP in comparison to Sham ($P < 0.05$).

Conclusions: These data suggest remodelling within the PP and increased emphasis on maturing T cells within the PP. Further studies are needed to understand the cause of the immune remodelling within the intestine after surgical weight loss.

10. EXPOSURE TO PRIMARY BLAST OVERPRESSURE VIA THE EAR CANAL INDUCES LOSS OF VESTIBULAR STEREOCILIA BUNDLES AND DEFICITS IN THE VESTIBULO-OCULAR REFLEX (VOR) IN RATS

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Background: Primary blast injury, i.e., that due to the pressure shockwave of a blast, is a frequent cause of injury both in military and civilian populations. U.S. soldiers exposed to blast during conflict in Iraq and Afghanistan reported symptoms of vestibular deficits such as dizziness and vertigo during initial treatment and during follow-up examination. In this study, we tested the hypothesis that primary blast induces vestibular injuries by investigating effects of blast exposure on vestibular stereocilia bundles and the vestibulo-ocular reflex (VOR) responses to sinusoidal and transient head rotations.

Methods: Adult female Long-Evans rats were implanted with a head-holder for measuring their VOR responses to sinusoidal (0.2~4Hz) and step (40~90/d/s peak velocity) head rotation. After establishing VOR baseline levels by 3 separate tests, the rats were anesthetized and exposed to a single blast of 275kPa (80% of lethal dose determined in previous studies) to the left ear. VOR responses were measured after 1 day, 3 days, 1 week, and then weekly out to two months. A second group of rats were exposed to blast in the same manner, were allowed to age for periods ranging from one day to two months, and were sacrificed for histology at the same intervals as the VOR tests. The vestibular end organs were dissected and stained with FITC-conjugated phalloidin to mark actin, were imaged on a confocal microscope, and the stereocilia bundles were counted for the five vestibular end organs.

Results: A small number of sheared stereocilia bundles were noted immediately after blast exposure. However, substantial loss of stereocilia bundles in vestibular end organs were observed at 2 weeks after blast exposure. While steady state VORs exhibited little changes over 4 weeks after blast exposure, transient VORs exhibited a substantial reduction at 4 weeks after blast exposure. Interestingly, although blast was delivered into the left ear, reduced transient VOR responses were observed for both leftward and rightward head rotations, indicating that effects of blast exposure on the vestibular system was not confined to the stimulated side.

Conclusions: These results validated our model of blast-induced vestibular injuries. They also provided evidence for the hypothesis that primary blast-induced vestibular deficits were mediated by a progressive process, which induces loss of vestibular stereocilia bundles and deficits in transient VORs over several weeks. Furthermore, compared to steady state VOR responses, transient VORs are more sensitive biomarkers of blast-induced vestibular injuries.

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11. IS LYMPHOCYTIC ESOPHAGITIS IN CHILDREN A PRELUDE FOR EOSINOPHILIC ESOPHAGITIS?

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Background: Lymphocytic esophagitis (LyE) in children remains poorly understood. Here we report 7 patients diagnosed initially with LyE and, upon follow-up, developed eosinophilic esophagitis (EoE).

Methods: All esophageal biopsies performed on children (≤ 18 years-old) in the last 10 years were reviewed. Cases with ≥ 20 lymphocytes/high-power field and rare eosinophils (≤ 2) are included. Demographics, clinical and histological findings are retrieved from pathology reports and medical records in accordance with the institutional research board guidelines. Lymphocytic count was generated by counting the numbers of lymphocytes at 40X in a single hot spot.

Results: The search resulted in 24 patients (age range: 1-17.5 years; mean: 6.9 years). They consisted of 11 males (age range: 1-17.5; mean: 6.9 years) and 13 females (age range: 2-16.5 years; mean: 6.9 years). The most common presentation was dysphagia (33.3%) followed by reflux (29.2%), abdominal pain (29.2%), and nausea and vomiting (8.3%). Esophageal endoscopic findings ranged from normal to erosive esophagitis. Ileal and colonic endoscopy ranged from normal to severe active inflammation. The mean number of lymphocytes was 40.4 (range 21-71 lymphocytes). There was correlation between the number of lymphocytes and a particular final diagnosis. In addition, there was no difference in the number of lymphocytes between males and females. Follow-up showed that 7 patients were diagnosed with gastroesophageal reflux disorder, 7 patients with eosinophilic esophagitis, 3 patients with Crohn's disease, 1 patient with celiac disease, 1 patient with ulcerative colitis, and 3 patients with gastritis. Follow-up in 3 patients did not disclose any particular entity and were labeled as having LyE. EoE developed a mean of 17 months (range 13-21 months) after the first endoscopy that showed LyE. This finding highlights the important of regular endoscopic and histologic follow-up of patients with LyE.

Conclusion: In this series, the largest in the pediatric population, 7 patients (29.2%) developed EoE upon follow-up. Our series suggests that LyE might not be a disease by itself but rather an early histologic feature of several entities particularly EoE. Regular follow-up with histological examination of these patients is necessary in order to unmask the final diagnosis. In this study, EoE developed as early as 13 months after the initial endoscopy and, therefore, follow-up at 6 months interval is probably justified.

12. RADICAL NECK DISSECTIONS: THE NECESSITY AND COST EFFECTIVENESS OF THE STANDARD PROTOCOL.

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Background: Neck dissection in squamous cell carcinomas of the head and neck is therapeutic when nodal metastasis has been found during physical examination and diagnostic when lymph node (LN) involvement has not been found clinically or by imaging. Gross and microscopic evaluation of the neck dissection specimen is therefore critical in staging head and neck carcinomas. In order to conduct a thorough and accurate assessment of the lymph nodes, pathologists typically submit the entire neck dissection specimen and examine it microscopically, including tissue that does not contain palpable LNs. This practice increases the cost of pathologic evaluation and increases the anatomic laboratory's work load, but may not increase the diagnostic yield compared to focused pathologic examination of palpable LN.

Methods: All neck dissections performed for head and neck squamous cell carcinomas between 2014- 2016 were retrieved. Specimens were classified as group I, if they were evaluated grossly by the lead pathologist assistant (PA), or group II, if grossly prosected by pathology residents or physician assistant students. The PA and residents identified LNs using a standard palpation technique. All surgeries were performed by the same surgeon and microscopic evaluation was performed by the same pathologist. Results were tabulated as palpable/non palpable and positive/negative for metastatic carcinoma. The number of glass slides for each group was also documented. For purpose of comparison, bilateral neck dissections were evaluated as separate specimens.

Results: There were 291 radical neck dissection specimens that were received by the Department of Pathology between the years 2014-2016. Of these, 82 specimens were included in group I and 57 in group II. 2,771 palpable LN (levels II to IV) were identified, of which 109 (3.9%) were positive for metastatic carcinoma. 2,088 non-palpable microscopically identified LNs were found in 1174 additional glass slides, costing an additional \$21,202. None of the non-palpable LN was positive for metastatic carcinoma. Soft tissue microscopic deposits were seen in 3 cases with metastatic LNs. There was no major difference in the number of LNs retrieved between the two groups.

Conclusion: While submission of the entire neck dissection specimen increases the number of LN examined, it does not contribute to the pathologic stage of the cancer. The number of palpable LN retrieved is not affected by the level of training of the gross prosector.

13. MELANOSIS COLI IN ANAL HETEROTOPIC GASTRIC MUCOSA: A CASE REPORT AND REVIEW OF THE LITERATURE.

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Background: Gastric heterotopia is the presence of gastric mucosa in a foreign anatomic location. It can occur anywhere in the gastrointestinal tract and has been well documented in the esophagus. Gastric Heterotopia of the anorectum is a rare occurrence.

Case Report: We present a case of an asymptomatic adult male who underwent a colonoscopy during which an anal nodule was biopsied. Microscopic examination revealed oxyntic gastric mucosa with chronic active gastritis and melanosis coli. During a subsequent colonoscopy six years later, an abnormally pigmented area of anus was biopsied. Microscopic examination revealed antral gastric mucosa with chronic active gastritis. A literature review showed that there have been 72 reported cases of gastric heterotopia of the anorectum. Only four of those case occurred in the anus.

Conclusion: To our knowledge, this is the first report of a shift in gastric mucosal type on repeat biopsy as well as melanosis coli associated with gastric heterotopia of the anorectum. We propose the term “outlet patch” for gastric heterotopia of the anorectum.

14. PERICELLULAR INTERPHOTORECEPTOR MATRIX DICTATES OUTER RETINA CRITICAL SURFACE TENSION.

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Background: Retinal detachments create two pathological surfaces, the surface of the outer neural retinal, and an apical retinal-pigmented epithelium (RPE) surface. The physicochemical properties of these two new surfaces are poorly understood. At a molecular level little is known how detachments form, how to optimize reattachment, or prevent extension of the detachment. A major limitation is lack of information about the biophysical consequences of the retina–RPE separation. The primary challenge is determining the molecular properties of the pathological interface surfaces.

Objective: Here, using detached bovine retina, we show that this hurdle can be overcome through a combination of biophysical and ultrastructural approaches.

Methods: The outer surface of freshly detached bovine neural retina, and isolated molecular components of the outer retina were subjected to: 1) Contact angle goniometry to determine the critical surface tension of the outer retinal surface, isolated insoluble interphotoreceptor matrix (IPM) and purified interphotoreceptor retinoid binding protein (IRBP); 2) Mid-infrared attenuated total internal reflectance (MAIR-IR) spectroscopy to characterize the molecular composition of the retinal surface. MAIR-IR depth penetration was established through ellipsometric measurement of barium-stearate films. Light microscopy, immunohistochemistry and electron microscopy defined the structures probed spectroscopically. Furthermore, the data were correlated to IR spectra of docosahexaenoic acid, hyaluronan, chondroitin-6-sulfate and IRBP, and imaging by IR-spectroscopy.

Results: We found that the retinal surface tension is 24 mN/m, similar to isolated insoluble IPM and lower than IRBP. Barium-stearate calibration studies established that the MAIR-IR spectroscopy penetration depth was 0.29 μm . Ultrastructural observations and MAIR-IR studies of isolated outer retina components determined that the pericellular IPM coating the outer retinal surface is primarily responsible for these surface properties.

Conclusions: Our findings suggest that the critical surface tension of detached bovine retina is dictated not by the outer segments, but by a pericellular IPM covering the outer segment tips.

15. THE EFFECTS OF ACUTE AND CHRONIC ADMINISTRATION OF FLUOXETINE ON THE TESTES AND EPIDIDYMIDES OF ADULT SPRAGUE DAWLEY RATS.

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Background: In primary and secondary care settings, antidepressant (AD) drugs are the mainstay treatments in moderate to severe major depression. All second-generation ADs are approved for the treatment of major depressive disorder, except for fluvoxamine (which is approved only for the treatment of obsessive-compulsive disorder), but it is the selective serotonin reuptake inhibitors (SSRIs) that have become the most widely prescribed. While the adverse events of second-generation ADs – SSRIs, specifically – tend to be more favorable than those of the first-generation ADs, they still exist. For instance, fluoxetine seems to have side effects on the male reproductive system, but results are inconclusive. Delivery methods, amount of drug delivered, and what the investigators considered “short-” and “long-term” may play significant roles in the variability of the results reported.

Objective: To determine the effects of acute and chronic fluoxetine delivery on the male reproductive system.

Methods: After a two-week habituation period, the Low Dose (10 mg/kg) and High Dose (20 mg/kg) groups began receiving daily cookie dough mixed with their respective doses while a Control group received cookie dough only, and a Naïve Control group received neither drug nor cookie dough. After two and sixteen weeks, animals in each group were sacrificed. All vital and reproductive organs were harvested, weighed, and stored in 10% zinc formalin prior to processing, embedding in paraffin blocks, sectioning, and staining with H&E.

Results: Change in rate of weight gain was evident after two weeks of drug delivery. The data also shows a significant difference between the Low Dose and High Dose treatment groups at two weeks for the epididymal tissues and at two and sixteen weeks for the testes.

Conclusions: Overall, long-term ingestion of either dose for sixteen weeks shows a visual difference in spermatogenesis in seminiferous tubules of the testes, along with changes in the epididymides, which can impact fertility.

16. URACHAL ADENOCARCINOMA: A RARE ENTITY WITH CYTOHISTOLOGICAL CORRELATION.

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Background: Urachal adenocarcinoma of the bladder (UAB) is a rare malignancy, arising from the urachus, a fibrous remnant of the allantois. The distinction between urachal and non-urachal adenocarcinoma requires correlation of clinical with pathologic findings. UAB occurs in adults (50-60 year) with a slightly male predilection. The clinical presentation of UAB includes hematuria, and/ or mucosuria.

Case report: We present a case of a 29-year-old male with a 6 month history of gross hematuria with cytohistological correlation. The voided urine sample revealed loosely cohesive clusters and scattered pleomorphic cells with hyperchromatic nuclei, high nucleus to cytoplasmic ratio and intracytoplasmic vacuoles, in a background containing necrosis and blood. Based on the cytomorphic features, a diagnosis of suspicious for malignancy was rendered. A computed tomography scan revealed a 5.7 x 3.7 x 4.1 cm bladder mass arising in a peripherally calcified urachovesical diverticulum containing dystrophic calcifications, necrotic iliac lymph nodes and no additional masses. Cystoscopy revealed a 5 cm bladder tumor present at the dome of the bladder. The biopsy showed an adenocarcinoma with mucinous features. Morphology of a UAB resembles colorectal carcinoma with presence of glands and mucin. Hence, the diagnosis of primary UAB should be established only after excluding metastasis from other sites. Immunohistochemical stains were positive for CK20, GATA3, CDX2, and B-catenin (membranous pattern) while they were negative for CK7. Based on the cytomorphology, the immunoprofile, and the location of the tumor, a diagnosis of urachal adenocarcinoma was rendered.

17. ELEVATED EXPRESSION OF HEPATOMA UP-REGULATED PROTEIN INHIBITS GAMMA-IRRADIATION-INDUCED APOPTOSIS OF PROSTATE CANCER CELLS.

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Background: Despite progression in diagnosis and treatment, prostate cancer (PCa) still represents the main cause of cancer-related mortality and morbidity in men. Although radiation therapy offers clinical benefit over other therapeutic modalities, the success of this therapeutic modality is commonly hampered by the resistance of advanced tumors. So far, the mechanisms governing tumor resistance to radiotherapy are not discussed in detail.

Objective: We assessed the resistance of PCa to radiation therapy in relation to elevated expression of Hepatoma Up-Regulated Protein (HURP).

Results: In PCa cells, the induction of HURP expression suppresses γ -irradiation-induced apoptosis. Gamma-irradiation-induced apoptosis of PCa cells is associated with expression of E2F1, p53, p21 proteins together with the phosphorylation of apoptosis signal-regulating kinase1 (ASK1), c-jun-N-terminal kinase (JNK) and Ataxia-telangiectasia mutated (ATM) and histone family member X (H2AX). Whereas, the induction of HURP expression is able to suppress γ -irradiation-induced effects on E2F1, p53, p21, ATM, ASK1, JNK and ATM, and H2AX. Also, inhibition of γ -irradiation-induced- cytochrome c release, cleavage of caspase-9, caspase-3, PARP, and reactive oxygen species (ROS) were noted in PCa cells induced for HURP expression. The observed radio-resistance of PCa is thought to be the consequence of HURP-mediated destabilization of p53 and ATM proteins that are essential for the modulation of γ -irradiation-induced apoptosis.

Conclusions:Based on our findings, PCa resistance to radiation therapy results from the deregulation of ASK1/ JNK; ATM/ H2AX; ATM/p53 and checkpoint kinase 2 (Chk2)/ E2F-1 in response to the elevated expression of HURP.

18. OTC BIOTIN SUPPLEMENTATION NOT LIKELY TO CAUSE CLINICALLY SIGNIFICANT INTERFERENCE WITH MOST ROCHE IMMUNOASSAYS.

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Background: High concentrations of biotin are known to interfere with some laboratory immunoassays. Nutritional supplements containing 100 times the normal daily dose biotin are being marketed and consumed for improved hair, skin, and nail growth.

Objective: This study seeks to characterize the degree of biotin interference in commonly used Roche immunoassays.

Methods: Known concentrations of biotin were spiked into aliquots of pooled human serum, which were analysed using 15 Roche immunoassays: fT3, fT4, T3, TSH, PTH, Cortisol, Prolactin, Testosterone, Progesterone, Estradiol, Ferritin, NT-proBNP, ACTH, AFP and IgE. In a separate experiment, serial serum specimens were collected from an individual that had discontinued an OTC biotin supplement (10,000 µg/day). These specimens were analysed using the afore-mentioned immunoassays prior to the determination of biotin concentrations using liquid chromatography-tandem mass spectrometry.

Conclusions: Increased immunoassay interference was directly correlated to increases in biotin concentrations. Biotin exhibited measureable effects on some assays at 25 µg/L to 50 µg/L, and clinically significant effects at 250 µg/L and higher. Biotin concentrations were less than 40 µg/L in serum specimens collected from a single individual after daily biotin consumption. Of the assays tested, ACTH, Progesterone, PTH, T3 and TSH were most sensitive to biotin.

Conclusion: When taken as directed, OTC biotin supplements are not likely to cause clinically significant interferences with the immunoassays tested. Laboratories should communicate the potential for biotin interference to their clinical providers.

19. METASTATIC NEUROENDOCRINE CARCINOID TUMOR TO LEFT ORBIT.

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Background: Carcinoid tumors, low-grade neuroendocrine tumors, arise from the enterochromaffin cells, predominantly originating in the gastrointestinal or bronchial tracts. With the potential of malignancy relatively low, the rate of metastases for carcinoid tumors is about 50-75% in patients with the most common sites being liver, bone, and lymph nodes. Even rarer is carcinoid tumor metastasis to the orbit which accounts for only 4% to 5%. Here we present a case of metastatic neuroendocrine tumor to the left orbit.

Case Report: A 66-year-old male with a history of neuroendocrine carcinoid since 1 year presented with abnormal left eye movements. Computer tomography angiography revealed persistent and slightly increased inferior oblique insertion presenting as an enlargement. Left orbitotomy and inferior oblique biopsy were performed. The biopsy of the left inferior oblique muscle revealed a metastatic neuroendocrine carcinoma, grade 2 to 3. Appropriately controlled immunohistochemistry showed the tumor cells stained positive for CD56, synaptophysin, and chromogranin. No mitoses were identified. The Ki-67 proliferation index was estimated as 4-5%. The tumor extended to the biopsy tissue edges. The histopathological findings were diagnostic of a metastatic neuroendocrine tumor to the left orbit.

Discussion: Neuroendocrine tumor metastasis to orbital structures is an uncommon event. The most common presenting symptoms of orbital carcinoid tumors are swelling, inflammation, and restriction of ocular mobility from a mass. Upon literature review, there were only a few reported cases of metastatic orbital carcinoid tumors which presented as orbital inflammation and restricted movements. This case report highlights a rare presentation of the metastatic neuroendocrine tumor as an orbital mass. The clinician and pathologist during diagnosis and analysis should be able to make a distinction between an orbital outlet obstruction, an orbital infection, or the rarer systemic carcinoid syndrome.

20. A RARE CASE OF LEIOMYOMATOSIS PERITONEALIS DISSEMINATA WITH ENDOMETRIOSIS.

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Background: Leiomyomatosis peritonealis disseminata (LPD) is a rare benign disorder characterized as numerous smooth muscle nodules in peritoneal cavity. LPD is difficult to diagnose by clinical evaluation due to unknown etiology and incidental findings. To date, less than 200 cases have been reported and one other case of LPD with endometriosis and ascites has been documented. LPD commonly occurs in reproductive age and rarely seen in postmenopausal women. We present LPD in postmenopausal woman with endometriosis.

Case Report: A 54-year-old female presented with pain, nausea, vomiting and weight loss. Physical exam demonstrated palpable mass arising from adnexa. CT scan showed: 6.4cm large multi-loculated heterogeneous mass in right adnexa concerning for ovarian carcinoma, large 17cm fibroid uterus, extensive peritoneal carcinomatosis, small volume of ascites and numerous hypo-dense metastatic liver lesions. CT guided biopsy of peritoneal carcinomatosis of omentum revealed spindle cell neoplasm immunophenotypically consistent with leiomyoma and stained positive for desmin, caldesmon, smooth muscle actin and Ki-67. Microscopy sections of omental mass showed proliferation of poorly circumscribed spindle cells arranged as nodules in short interlacing and haphazard arrangements in omentum. No cytological atypia seen in spindle cell proliferation. No mitotic activity identified. Sections of posterior bladder mass showed endometriosis with adenomyoma pattern of smooth muscle hypertrophy. Immuno-histochemistry confirmed strong positive reactivity in spindle cells to desmin and WT1. Findings consistent with LPD.

Discussion: LPD is not considered in differential diagnosis of multiple peritoneal nodules because of low incidence and unfamiliarity among clinicians. The treatment for this benign condition is conservative because in most cases malignant transformation is rare and tumors regress. For conclusive diagnosis of LPD, radiological imaging proves challenging, thus direct sampling is required to exclude any malignancies. LPD is problematic to identify clinically, so diagnosis is dependent on pathological and surgical results, nevertheless, the prognosis is often good.

21. AN INTERESTING CASE OF METASTATIC ENDOCARDIAL MELANOMA MIMICKING A RIGHT ATRIAL MYXOMA.

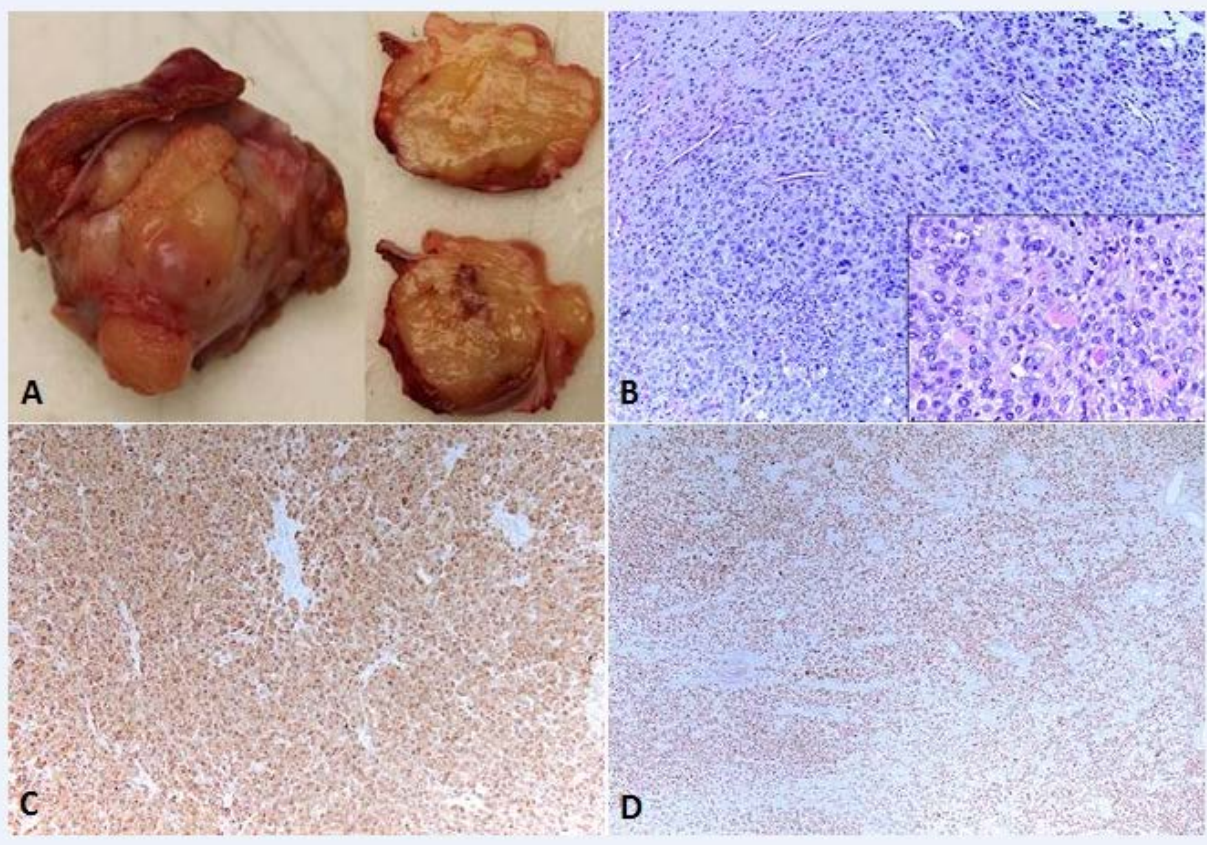
Joy King, M.D., Ph.D., Kristen Adams, M.D., Saeed Bajestani, M.D., Maria F. Gonzalez, M.D.

Department of Pathology, University of Mississippi Medical Center, MS.

Background: Metastases to the heart and pericardium are much more common than primary cardiac tumors and are associated with a poor prognosis. Tumors that frequently metastasize to the heart are those from the lung, breast, melanoma, and lymphoma with the right atrium being the most commonly affected site. Metastatic melanoma to the heart is not infrequent. To the best of our knowledge, this rare presentation of metastatic melanoma mimicking an atrial myxoma has not been documented.

Case report: We report a 64 year old man with a past medical history of myocardial infarctions, coronary artery disease, congestive heart failure, and remote skin melanoma status post resection who presented with shortness of breath. Coronary catheterization demonstrated no significant coronary artery disease. Echocardiogram showed a large right atrial mass adhered to the inter-atrial septum. The chest computed tomography confirmed the presence of a lobulated mass (4.5 x 3.3 cm) occupying the chamber without invasion into the walls of atrium. Both imaging studies favored a diagnosis of myxoma. The endocardial mass was resected and the cut surfaces are yellow-tan, soft and gelatinous with focal hemorrhage (Figure A). Microscopically, sheet of vaguely nested malignant epithelioid cells demonstrate pleomorphic nuclei, eosinophilic cytoplasm, and prominent nucleoli (Figure B). The malignant cells are diffusely positive for S100 (Figure C) and SOX 10 (Figure D). *BRAF* mutations were not detected.

Conclusion: It is important to keep metastatic melanoma in the differential diagnosis of atrial masses especially among patients with a history of melanoma and deterioration of cardiac function to investigate further.



22. ADENOSQUAMOUS CARCINOMA OF THE LACRIMAL GLAND: A RARE ENTITY.

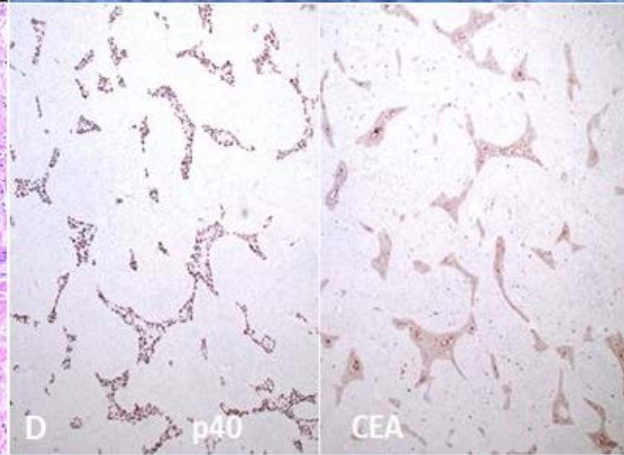
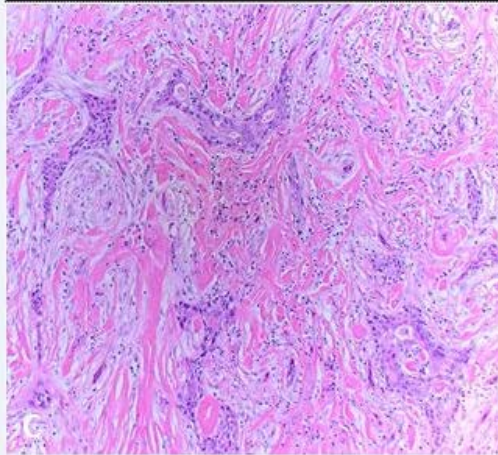
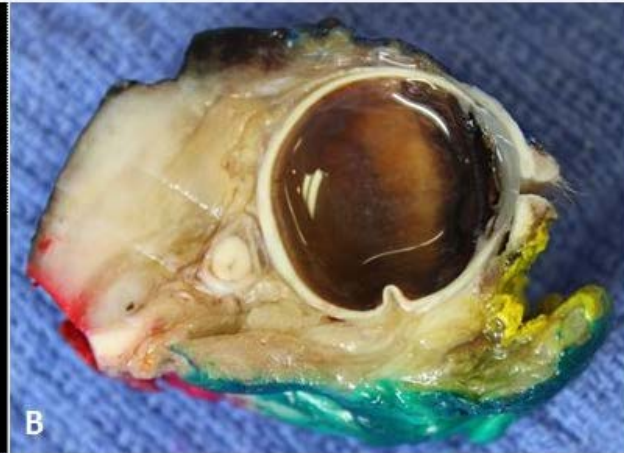
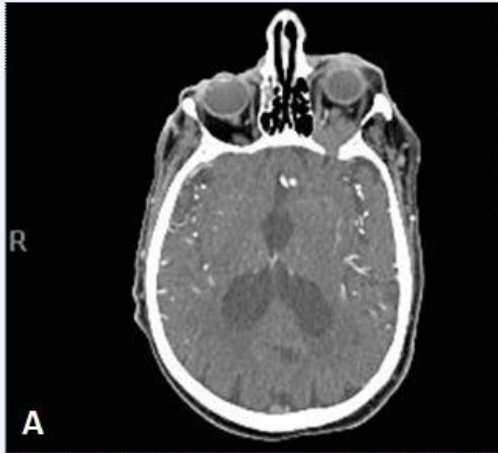
Joy King, M.D., Ph.D.¹, Maria F. Gonzalez, M.D.¹, Lewis Kyle, M.D.², Roberto Rey-Dios, M.D.³, Saeed Bajestani, M.D.¹.

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Background: Adenosquamous carcinoma is a rare neoplasm of the upper aerodigestive tract developing mainly at the nasal, oral and laryngeal cavities with a high propensity to regional lymph node metastasis and a short average survival.

Case presentation: We present an 86 year-old male with a three months history of swelling of the left eye and a subsequent abrupt onset of ptosis, proptosis, diplopia and orbital pain. The patient has a past medical history of prostate carcinoma status post resection as well as an ocular history of herpes zoster, nuclear sclerotic cataract and asteroid hyalosis of the left eye. Computed tomography demonstrates a large left superior orbit mass extending into the brain (Figure A). He underwent a left eye extenteration and craniotomy. A single tan, firm, homogeneous mass (2.5 x 1.5 x 1.2 cm) was identified at the superior-lateral and posterior aspect of the orbit (Figure B). Metastasis was suspected. However, the prostatic specific antigen levels were normal. Histologically, the mass shows a tumor with squamous and glandular differentiation (Figure C). Immunohistochemistry stains for p40 (Figure D) and CEA (Figure D) are positive. Eight months follow up revealed increased enhancing soft tissue extending into left cavernous sinus suspicious of tumor recurrence. Little is known about the associated risks and symptomatology of these cases.

Conclusion: To the best of our knowledge, there are only two reported cases of adenosquamous carcinoma from lacrimal glands in the literature. We present this case with detailed ocular history to contribute to a better understanding of this entity.



23. STEMNESS MARKERS IN COLORECTAL CANCER: ANALYSIS IN A RACIALLY-DIVERSE POPULATION.

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Background: Stemness molecules have the potential to identify patients at high risk of developing aggressive cancers. Herein, Zinc finger E-box binding homeobox 1 (ZEB1), Trefoil factor 3 (TFF3), Hepatoma Up-Regulate Protein (HURP), Mucin 2 (MUC2), and Cystic fibrosis transmembrane regulator (CFTR) are assessed as potential prognostic biomarkers in CRC.

Objective: To analyze the expression of ZEB1, HURP, TFF3, MUC2 and CFTR in CRC tissues, and establish an association with the clinical outcomes.

Methods: A tissue microarray (TMA) with 132 scores from (N=56) cases was created using tumor stage-matched CRC tissues (normal and tumors) including African Americans (AA) (N=32) and Caucasian Americans (CA) (N=24). The TMA was stained for the each biomarker by IHC. The staining score was calculated (area x intensity) obtaining a final score between (0- no expression and 9-high expression). The association with disease-free survival (DFS) in AA and CA separately was calculated.

Results: High ZEB1 expression in CA was associated with higher risk of disease progression or death ($p= 0.015$ for cytoplasm, $p= 0.116$ for nucleus). ZEB1 expression was not found to be a significant predictor of DFS in AA who have worse CRC outcomes. These findings suggest that localization of ZEB1 may represent a marker for CRC prognosis in CA. High nuclear TFF3 expression in AA was marginally associated with poorer DFS ($p=0.089$). However, the cytoplasmic expression of TFF3 was not significantly associated with DFS. Both the cytoplasmic and nuclear expression of HURP, MUC2, and CFTR among the AA and CA did not significantly correlate with DFS.

Conclusions: ZEB1, HURP, and TFF3 have potential as markers for aggressiveness in CRC. Our findings provide evidence of a possible biological basis for ethnicity-related differences with regards to stemness and regulatory factors of CRC aggressiveness.

Acknowledgements: PCRP W81XWH-14-1-0151, UMMC Medical Student Research Program, and UMMC Office of Research.

24. THE MODEL OF INTERDISCIPLINARY COLLABORATION IN PERIOPERATIVE SETTING FROM THE PERCEPTIONS OF THE IDT PROFESSIONALS*.

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Background: Interdisciplinary collaboration (IC) is beheld as the product of synchronization and harmonization of team efforts supporting the move away from fragmentation of care. Research about the model of IC in perioperative setting (PS) is primarily qualitative; it is not sufficient for developing interventions with measurable effects. Often the latest developments in team and collaborative theory are not considered. Further elucidation of ICPS is necessary for better understanding of this phenomenon.

Objective: We aimed to construct the model of ICPS from the perceptions of the interdisciplinary team (IDT) of PS. Questions guiding this research were: 1. what are the significant components of ICPS? and 2. What are the inter-relational patterns of the ICPS factors?

Methods: This research was based on mixed-methods survey design engaging the perioperative professionals at educational and professional meetings. The assumptions of the initial model of ICPS derived from the literature review were tested in analysis of correlations of IC level and its likely factors. Survey data were obtained in REDCap and analysed in SPSS.

Results: Three factor components with eigenvalues >1 and factor loading of >0.40 were extracted with Generalize Least Square (GLS) in SPSS from 32 response sets; 74.606% of variance was explained with this model: Collegial support of adaptability ($r=0.478$), Reflexive decision making ($r=0.457$), and Process development ($r=0.495$). The assumptions of Guardianship-Stewardship Motivational Conflict Model of ICPS were partially supported in testing the correlations.

Conclusions: Significant covariates of ICPS pertinent in describing its model were identified in this study. Guardianship-Stewardship ICPS motivational model was adjusted using these findings. Further research could allow detailing the effects of ICPS factors on levels of IC and technical outcomes.

Acknowledgements: We would to express our gratitude to the study participants in Central Mississippi and the Association of periOperative Registered Nurses (AORN) chapters of Acadiana (Lafayette, LA) and Birmingham, AL.

*Previously presented at Southern Bioengineering Conference (SBEC) 2018, Charlotte, NC.

25. BIOPSY CONFIRMATION OF POROKERATOSIS.

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Previously presented: Medical Student Research Journal, Practice Update Dermatology, Practical Dermatology, Journal of the Mississippi State Medical Society, and SKIN: The Journal of Cutaneous Medicine.

Case report: A healthy 37 year-old male presents with a ten year history of a patchy rash on the trunk and extremities to which he associated with spending a large amount of time in the sun. Physical examination revealed 3-6 mm slightly scaled patches with telangiectasias and a subtle 0.5 mm rim (cornoid lamella) on the chest, arms, and legs. A 4 mm punch biopsy of a lesion on the left upper arm was performed but the lesion was not marked and bisected at the bedside in the manner of Reed.¹ Sections from the left upper arm demonstrated a broad area of compact hyperkeratosis and parakeratosis within a depression within the epidermis. This parakeratosis is contiguous with a widened hair follicle infundibulum at the other pole of the lesion. (Figure 1a and 1b) Dyskeratotic cells are noted at the base of this parakeratotic column typical of a cornoid lamella. (Figure 1c) Sparse perivascular lymphohistiocytic inflammation was also present. The histopathologic diagnosis of disseminated superficial actinic porokeratosis was more difficult to make in this case because a broad area of parakeratosis is present instead of the classic thin cornoid lamella. This is the result of random bisection of this lesion at the pathology lab that ran horizontally along the cornoid lamella rather than the preferred bisection of the specimen perpendicular to the cornoid lamella which is best performed at the bedside. In order to further characterize the nature of cornoid lamella, a three-dimensional model was built to reconstruct the possible spatial parameters of porokeratosis in relation to cornoid lamella. Our model allowed us to observe countless possible cross sections of the parakeratosis. The model also suggested that the cornoid lamella arises from a deep depression in the epidermis then extends upward and superficially continuing horizontally along one side the epidermis. Base on literature searches, this is first attempt of relating the three-dimensional structure of cornoid lamella.

Discussion: Several types of porokeratosis have been described in the literature: classic porokeratosis of Mibelli, linear porokeratosis, disseminated superficial actinic porokeratosis (DSAP), disseminated superficial porokeratosis (DSAP), porokeratosis palmaris et plantaris disseminate, and porokeratosis palmaris plantaris punctate. Each of these disorders are defined by abnormal keratinocytes in the epidermis producing cornoid lamella: a vertical column of parakeratosis produced by atypical keratinocyte clones lacking granularization. Making the diagnosis is important since up to 7.5% of porokeratosis have been associated with a malignancy. In addition, Continued UV radiation exposure in DSAP may increase the risk of malignant transformation to actinic keratosis and squamous cell carcinoma. Thus, it is important for the clinician to perform a proper biopsy with bisection at the bedside to help the dermatopathologist to make a prompt diagnosis of porokeratosis every time.

26. USE OF ESTIMATED CARDIAC OUTPUT TO ASSESS CARDIAC FUNCTION IN OLDER ADULTS.

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Background: Multiple methods have been used to assess cardiac output (CO) in various clinical settings. These may not be practical in the traditional research or rural primary care settings when resources like echocardiography and other instruments are not available. Recent investigations have indicated simple equations, like the Liljestrand and Zander formula ($CO_{est} = PP / (SBP + DBP) * HR$), to be moderately correlated when comparing the estimated CO (CO_{est}) and other accepted methods of determining CO like echocardiographic derived CO (CO_{echo}). CO_{est} can be adjusted by a constant (k) derived by dividing CO by CO_{est} ($k = CO / CO_{est}$). Following adjustment of k, the new estimate ($CO_{est-adj}$) is more comparable to directly measured CO_{echo} .

Objective: The purpose of this investigation was to replicate recent findings in a large sample of older individuals and determine which cardiometabolic risk factors may account for the variation in this formula.

Methods: 1,410 African American participants (71% female, aged 62+9 years, 80% hypertensive, 29% diabetic, and 14% smokers), enrolled in the Genetic Epidemiology Network or Arteriopathy (GENOA) completing an echocardiography exam (2000-2004) participated in this study.

Results: While $CO_{est-adj}$ and CO_{echo} values were moderately correlated (Pearson's $r = 0.43$, $p < 0.001$), there was variation in participants with cardiometabolic risk factors. Overall, $CO_{est-adj}$ was 0.3 L lower compared to CO_{echo} , was slightly overestimated in females by 0.6 L, and was underestimated in males by 0.5 L. Further analyses revealed $CO_{est-adj}$ was 0.4 L higher in hypertensives, 0.7 L higher in diabetics, and 0.1 L higher in smokers compared to CO_{echo} .

Conclusions: These findings suggest that the adjusted Liljestrand and Zander formula can be an inexpensive tool in the primary care and research settings for estimating CO in the presence of risk factors, but further adjustments may need to be developed to improve accuracy and precision.

27. CALCIUM BIOMARKERS WITH BONE MINERAL DENSITY: FINDINGS FROM THE GENETIC EPIDEMIOLOGY NETWORK OF ARTERIOPATHY (GENOA).

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¹*School of Medicine*, ²*Department of Medicine*; ³*Department of Radiology*; *University of Mississippi Medical Center, Jackson, MS.*

Background: Decreased bone mineral density (BMD) in the aging population is associated with a high risk of fractures and a lower quality of life.

Objective: The purpose of this study was to explore the relationship between four serum calcification biomarkers with bone mineral density.

Methods: Computed tomography (CT) images were obtained from 524 Genetic Epidemiology Network of Arteriopathy (GENOA) participants (378 female, 146 male) for assessment of L3 and L4 vertebrae to determine average BMD. Serum biomarkers including osteoprotegerin, osteocalcin, osteopontin, and osteonectin were assessed from stored serum samples. Data were reported as mean±SD for continuous variables or proportions for categorical variables. Multiple linear regression was used to assess the association between the four serum biomarkers in natural log-transformation and BMD. Covariates included age and gender. Alpha level for all statistical tests was set at $\alpha=0.05$.

Results: Our data showed that every 1 unit increase in log-osteopontin was associated with a 6.1 unit decrease in BMD ($p=0.006$); similarly, 2.9 and 8.5 unit decrease in BMD were expected for every 1 unit increase of log-osteoprotegrin ($p=0.498$) and osteocalcin ($p=0.005$), respectively. However, the positive association of log-osteonectin and BMD was not statistically supported ($p=0.153$). Age remained a significant covariant in the prediction of decreasing BMD ($p<0.001$) in all regression models.

Conclusion: These findings provide evidence that osteopontin and osteocalcin may be useful in clinical assessment of osteopenia and osteoporosis because of strong and significant negative associations with bone mineral density.

28. LNCRNAS IN ETHANOL INDUCED NEURONAL CELL DEATH – KNOCKOUT LNCRNA NEAT1 USING DUAL GRNA IN CRISPR-CPF1 STABLE TRANSFECTED SH-SY5Y CELLS.

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Department of Pathology, UMMC.

Background: Our previous work has demonstrated that ethanol increase the expression of Kruppel-like factor 11 (KLF11), a neuronal cell death mediator in brain of rodent treated with alcohol by binge or chronic feeding. Our preliminary data suggest that ethanol induces the functional interaction of KLF11 with Nuclear Enriched Abundant Transcript 1 (NEAT1), a long non-coding RNA playing roles in cell proliferation, growth. NEAT1 consists of two isoforms, a 3.7kb NEAT1-1 and a 22.4 kb NEAT1-2.

Objective: The current work is to decipher the role of these two isoforms of NEAT1 in this ethanol induced interaction with KLF11 and understand its role of the specific protein-RNA interaction in ethanol induced neuronal cells death.

Methods: 1) Construct vectors that contain the nuclease AsCpf1 and gRNAs specifically targeting to the interesting genes; 2) Establish stable NEAT1-1 or NEAT1-2 knockout cells by our recently established CRISPR/Cas mediated dual gRNAs technique; 3) Determine the role of NEAT1-1 and NEAT1-2 in ethanol treated cells; 4) Identify the interaction of NEAT1-1 and NEAT1-2 with KLF11 in ethanol induced cells death.

Results: Our genotyping analysis indicated that we have successfully established a stable transfected CRISPR-Cpf1 SH-SY5Y cells which completely KO the NEAT1-1 from the genome with abolishing both transcripts of NEAT1-1 and NEAT1-2, suggesting that both isoforms share the same promoter; Treatment with 100 mM or 150 mM EtOH significantly increased the expression of NEAT1-2, but not NEAT1-1 in SH-SY5Y cells; There exists the interaction between NEAT1-2, but not NEAT1-1 with KLF11; The treatment of 100 mM or 150 mM EtOH disrupted the combination of KLF11 with NEAT1-2, without changing the co-localization between KLF11 and NEAT1-1.

Conclusion: Our study demonstrates that a dual gRNA guided CRISPR-Cpf1 system is a reliable approach to specifically knock out the lncRNA NEAT1. Establishment of NEAT1 isoform specific cell models provides a critical research tool for better understanding of how NEAT1 and its interaction with KLF11 are involved in ethanol induced neural cell death. As a result, NEAT1 may serve a therapeutic target for intervention.

Acknowledgements: This study is supported by the NIH/NIAAA grants: AA020103 and AA025328.

29. HEAD AND NECK SQUAMOUS CELL CARCINOMA CELLS PRE-TREATED WITH BENZYL ISOTHIOCYANATE BECOME SENSITIZED TO THE EFFECTS OF CHEMO-RADIATION.

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Background: Approximately 90% of head and neck cancers are squamous cell carcinoma (HNSCC). One of the recent approaches in head and neck cancer treatment is the use of naturally occurring plant compounds called phytochemicals. Benzyl Isothiocyanate (BITC) is a phytochemical found in cruciferous vegetables and has been shown to have very potent anti-cancer properties. BITC plays a major role in modulating the activation and detoxification of carcinogens.

Objective: HN12 and HN30 HNSCC cell lines were used to determine if BITC could increase the effectiveness of chemo-radiotherapy treatments. We also wanted to establish if BITC could alter the expression of certain cancer-relevant genes, and to determine if the induction of reactive oxygen species (ROS) played a role in the mechanism by which BITC induces cell death.

Methods: HN12 and HN30 HNSCC cell lines were treated with 10 μ M BITC. Cisplatin was used at 1 mg/ml in 0.9% saline. Glutathione was used at 5mM. Cells were irradiated using an Elekta, Synergy linear accelerator using a 6 MV photon beam. Amount of apoptosis was determined using a Caspase 3/7 activity assay. Intracellular ROS levels were determined using CM-H2DCFDA. Cell Viability was determined using WST-8 reagent. Gene activity was determined using a luciferase battery assay.

Results: Data shows that HN12 and HN30 cancer cells pre-treated with BITC were significantly sensitized to radiation and cisplatin therapy. Cell death was enhanced through the induction of apoptosis. BITC induced levels of ROS which increased cell death. This was reversed by a pre-treatment of the antioxidant GSH. The activity of the transcription factors NF- κ B and STAT-3 were also reduced.

Conclusions: The anti-cancer effects of BITC are of great importance. Results suggest that the use of BITC as a potential adjuvant holds promise in the clinical setting to significantly enhance the effects of chemo- and radiation-therapy in patients with HNSCC.

30. MHC CLASS I POLYPEPTIDE RELATED SEQUENCE A AS CONTRIBUTING FACTOR TO CHEMOTHERAPY-INDUCED RESISTANCE.

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Background: MHC class I polypeptide related sequence A (MICA) is a cell surface protein able to activate natural killer (NK) cells. Cleavage of MICA and generation of its soluble form (sMICA) has been described as an immunoevasion mechanism presented by aggressive tumors. In agreement with this role, recent studies correlated better prognosis for patients with higher levels of MICA expression in different types of cancer. Chemotherapeutic drugs are used to treat a great variety of malignant diseases. However, a fraction of patients under chemotherapy regimen stop responding to the treatment and develop recurrent tumors. We postulate that MICA can be a factor contributing to chemotherapy-induced resistance.

Objective: Our goal was to measure expression of MICA in the context of chemotherapy treatment in PCa cell lines.

Methods: We tested the expression of MICA in prostate cancer-derived LNCaP and E006AA-hT cell lines treated with bortezomib, a proteasome inhibitor chemotherapeutic drug.

Results: Flow cytometry analysis showed baseline difference in the cell fraction expressing surface MICA with 67% in LNCaP against 18% in E006AA-hT ($p < 0.0001$). Following treatment with bortezomib increased the fraction of LNCaP cells expressing surface MICA by 1.3-fold ($p < 0.01$), while the fraction of E006AA-hT cells expressing MICA yielded 2.3-fold increase ($p < 0.001$). Baseline release rate of sMICA was 54pg/ml/ 10^6 cells for LNCaP and 5pg/ml/ 10^6 cells in E006AA-hT cells. Relative to baseline, sMICA release rate dropped 2-fold with bortezomib treatment in LNCaP cells to 22pg/ml/ 10^6 cells ($p < 0.01$). However, sMICA release rate in E006AA-hT rose to 531pg/ml/ 10^6 cells ($p < 0.0001$), more than 100-fold increase.

Conclusions: The release rate of sMICA in response to bortezomib is significantly distinct. These evidences lead us to propose that MICA is a contributing factor of resistance to chemotherapy. This study can open opportunities for new targeted immunotherapies, enhancing the innate immune system and avoiding the undesired effect of chemotherapy resistance.

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31. EVALUATING A QUADRUPOLE GC-MS FOR QUANTITATIVE AND QUALITATIVE TOXICOLOGY.

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Background: Ion trap GC-MS or quadrupole GC-MS are often used for clinical toxicology analyses. The ion trap instruments exhibit high sensitivity and are preferred for qualitative screening, whereas quadrupole instruments exhibit superior linear response and are typically used for quantitative analyses. Unexpectedly high sensitivity was observed with a new quadrupole GC-MS (ISQ, Thermo Scientific Inc.) during quantitative method validation.

Objective: Evaluate the sensitivity of the ISQ quadrupole GC-MS, and determine its effectiveness for unknown toxicology screening via comparison with the Thermo Scientific ITQ ion trap GC-MS.

Methods: The average (n=3) signal/noise ratios were determined from neat solutions of common pharmaceuticals ranging from 224 to 407 amu. The numbers of drugs detected in patient specimens and commercial controls were determined using identical instrument methods.

Results: Signal to noise (S/N) ratios were higher in the ISQ quadrupole instrument, whereas equal numbers of drugs were detected with both instruments. As a result of this study, the Thermo ISQ GC-MS was validated for quantitative drug confirmations as well as general unknown toxicology screening.

Conclusions: The ISQ quadrupole GC-MS exhibited higher sensitivity than the ITQ ion trap GC-MS. The higher sensitivity of the ISQ resulted from improved ion optics and from faster scan speeds. This combination of sensitivity and linear response offers laboratories the opportunity to employ a single instrument for qualitative and quantitative analyses. Use of a single instrument type reduces job complexity by eliminating the requirement to learn multiple software formats, and reduces the number of instruments to maintain and operate.

32. PROSPECTIVE ANALYSIS OF CANCER STEM CELL DRUG RESPONSE ASSAY FOR GLIOBLASTOMA PATIENTS.

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Background: Over the past 20 years even with the aggressive standard of care (SoC) Stupp treatment protocol the prognosis of glioblastoma (GBM) has only minimally improved from 12 to 14 months. This is due in large part to the presence of chemo- and radiation-resistant GBM cancer stem cells (CSCs) that contribute to tumor propagation, maintenance, and treatment resistance. We are using ChemoID, a CLIA certified and CAP accredited drug response assay that identifies the most effective chemotherapy against CSCs and bulk of tumor cells from of a panel of potential treatments, offering great promise for individualized cancer management. A prospective study was conducted evaluating the use of the ChemoID drug response assay in glioblastoma patients.

Objective: **Methods:** Fresh tissue samples were collected for drug sensitivity testing from 41 glioblastoma patients enrolled in IRB approved protocol. Patients were prospectively monitored for tumor response, time to recurrence, progression-free survival (PFS), and overall survival (OS). Odds Ratio (OR) associations of 12-month recurrence, PFS, and OS outcomes were estimated for CSCs, bulk tumor and combined assay responses to treatment; sensitivities/specificities, areas under the curve (AUC) were examined.

Results: The data suggests that ChemoID guided treatment significantly enhanced tumor response. For every 5% increase in ex-vivo cell kill of CSCs by assay-guided chemotherapy, 12-month patient response (non-recurrence of cancer) increased 2.5-fold, OR=2.3 (p=0.01). Bulk of tumor assay was found not statistically significant. Median recurrence time was 20 months for patients with a positive (>40% cell kill) CSCs test versus only 3 months with a negative CSCs test, whereas median recurrence time was 13 months versus 4 months for patients with a positive (>55% cell kill) bulk test versus negative. Similar favorable results for the CSC test were observed for PFS and OS outcomes.

Conclusions: The ChemoID CSCs drug response assay has the potential to increase the accuracy of bulk tumor assays to help guide individualized chemotherapy choices.

33. THE SIGNIFICANCE OF LYMPHOCYTIC ESOPHAGITIS (LYE) IN CHILDREN IS POORLY DEFINED. WE REPORT THE LARGEST SERIES OF PEDIATRIC LYE ALONG WITH THE CLINICAL AND FOLLOW UP FINDINGS.

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Departments of Pathology, Batson Children's Hospital, Jackson MS and Wolfson Children's Hospital, Jacksonville, FL.

Background: The significance of lymphocytic esophagitis (LyE) in children is poorly defined. We report the largest series of pediatric LyE along with the clinical and follow up findings.

Methods: All esophageal biopsies performed on children (≤ 18 years-old) from January 2005 to May 2015 were reviewed. Only cases with ≥ 20 lymphocytes/HPF and rare eosinophils (≤ 2) are included. Immunohistochemistry for CD3, CD20, CD4 and CD8 was performed. Lymphocytic count was generated by counting the numbers of lymphocytes at 40X in a single hot spot.

Results: Twenty one (21) patients fulfilled the search criteria (age range: 1-17.5 years; mean: 6.9 years). They consisted of 11 males (age range: 1-17.5; mean: 6.9 years) and 13 females (age range: 2-16.5 years; mean: 6.9 years). The most common presentation was dysphagia (33.3%), reflux (29.2%), abdominal pain (29.2%), and nausea and vomiting (8.3%). Esophageal endoscopic findings ranged from normal to erosive esophagitis. ileal and colonic endoscopy ranged from normal to severe active inflammation. The mean number of lymphocytes was 40.4 (range 21-71 lymphocytes). There was correlation between the number of lymphocytes and a particular final diagnosis. In addition, there was no difference in the number of lymphocytes between males and females. The vast majority of lymphocytes expressed CD3 and, to a lesser degree, CD8. A minority expressed CD4 and CD20. There was no correlation between the immunophenotype and a particular diagnosis Follow-up showed that 7 patients were diagnosed with gastroesophageal reflux disorder, 7 patients with eosinophilic esophagitis, 3 patients with Crohn's disease, 1 patient with celiac disease, 1 patient with ulcerative colitis, and 3 patients with gastritis. Follow-up in 3 patients did not disclose any particular entity and, therefore, these patients were diagnosed with LyE.

Conclusions: Lymphocytic esophagitis in children remains a poorly defined entity. Our study suggests that a particular diagnosis is often not apparent at the onset of LyE and, therefore, a regular follow-up is required in order to identify the underlying disease. Our results also show that LyE is not associated with a particular disease but rather it represents a prelude to other better defined entities.

34. CHANGES OF NACHRS AND MGLURS IN MEDIAL PREFRONTAL CORTEX AND AMYGDALA ASSOCIATED WITH CUE-INDUCED NICOTINE SEEKING IN A RAT MODEL OF SMOKING RELAPSE.

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Objective: The present study examined expression of the nAChRs and the metabotropic glutamate receptors (mGluRs) in the brain of rats that showed cued nicotine-seeking in the response-reinstatement model of relapse

Methods: Male Sprague-Dawley rats were trained in daily 1-h sessions to intravenously self-administer nicotine (0.03 mg/kg/infusion, free base) on an FR5 schedule. A nicotine-conditioned cue was established by associating an auditory/visual stimulus with each nicotine delivery. After lever-press responding was extinguished by withholding nicotine delivery and its cue presentation, the reinstatement tests were performed with response-contingent re-presentation of the cue without nicotine availability. Thirty minutes after the test session, brains were collected and prepared for western blot analysis of expression of the $\alpha 4\beta 2$ and $\alpha 7$ subtypes of the nAChRs and expression of the mGluRs 2/3, 5, and 7.

Results: Re-exposure to nicotine cue effectively reinstated extinguished responses on the previously nicotine-reinforced lever, indicating the conditioned incentive properties of the cue. Compared to the rats under extinction condition, the cue-reinstated nicotine-seeking animals showed changes in expression of the $\alpha 4\beta 2$ and $\alpha 7$ nAChRs and the mGluRs 2/3, 5, and 7 in the amygdala and medial prefrontal cortex.

Conclusions: These data suggest that the unique change of some subtypes of the nAChRs and the mGluRs may be responsible for cue-induced reinstatement of nicotine-seeking behavior. This work sheds light on fully understanding neurobiological basis of the conditioned incentive motivation by nicotine-associated environmental cues.

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35. A RARE CASE OF METHOTREXATE-INDUCED EPIDERMAL NECROSIS MIMICKING TOXIC EPIDERMAL NECROLYSIS.

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Case presentation: A 52-year-old African American female with long-standing history of rheumatoid arthritis, diabetes mellitus, and obesity presents with sloughing of the oral mucosa and skin for the past 3 weeks. She had been taking methotrexate (MTX) and meloxicam for many years and recently had an increase dosage in MTX and also started on gabapentin for pain. Blisters developed on the skin folds then spread to oral mucosa with subsequent skin sloughing and dysphagic. She was found to have profound pancytopenia and chronic renal failure. We performed 8 mm punch biopsy on the left medial leg with dermal-epidermal blister with epidermal necrosis. Sections showed full thickness epidermal necrosis leading to dermal-epidermal separation and underlying sparse perivascular and interstitial lymphohistiocytic inflammation. MTX was discontinued. She was started on leucovorin for methotrexate toxicity and Neupogen for pancytopenia. Methotrexate-induced epidermal necrosis (MEN) is a rare, but life-threatening cutaneous reaction that mimics Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The early signs of MEN include painful skin erosions, oral ulcers, leukopenia, and thrombocytopenia. Chronic kidney disease is a risk factor as MTX is metabolized by the kidneys. MEN cases frequently had leukopenia (58.3%), thrombocytopenia (66.7%), and hypoalbuminemia (85.7%), but not hepatic toxicity.

Conclusion: The rare report of methotrexate-induced epidermal necrosis mimicks toxic epidermal necrolysis due to chronic kidney disease.

36. SALIVARY GLAND CYTOLOGY; RECLASSIFICATION BASED ON THE "MILAN SYSTEM FOR REPORTING SALIVARY GLAND CYTOLOGY": A TERTIARY CARE EXPERIENCE.

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Background: Fine needle aspiration cytology (FNAC) is highly sensitive and specific in diagnosing salivary gland lesions. However, due to the heterogenous nature of the tumors, nailing the diagnosis can be fairly challenging. Recently the “Milan system” for reporting salivary gland cytology (MSRSGC, Table 1) has been proposed by the international group of pathologists to reclassify the lesions and broadly sub classify into different groups which can facilitate communication between the pathologists and the clinicians in order to triage a lesion and ease the cyto-histologic correlation.

Methods: In order to incorporate MSRSGC into our system we undertook a five year retrospective study in which all salivary gland FNA's performed at our institution, from January 2012 up to December 2016 were retrieved from our laboratory information system. The cytological diagnoses were categorized based on the proposed MSRSGC. A subsequent excision and surgical pathology diagnosis if available was documented and compared with the MSRSGC diagnostic categories.

Results: 322 salivary gland FNA's were retrieved during this time period which were performed on 307 patients. Surgical follow up was available for 124 (38.5%) cases (Table 2). An excellent cyto-histo correlation was identified in non-neoplastic, neoplastic- benign, suspicious for malignancy and malignant categories. Of the non-diagnostic category (6.8%), atypia of undetermined significance category (AUS) (1.5%) and salivary gland tumors of undetermined malignant potential category (SUMP) (5.3%) on subsequent follow up showed 2 (13%), 2 (40%) and 8 (47%) cases as malignant, respectively (Figure 1).

Conclusion: The heterogeneity in the follow up malignant diagnoses in different MSRSGC categories highlights the limitation in making specific cytologic diagnosis in the “SUMP” category especially basaloid neoplasms and low grade cystic tumors of salivary gland. The non-diagnostic and AUS diagnostic categories should be followed up with a repeat FNA. The SUMP diagnosis may be followed by conservative surgical excision in correlation with imaging findings.

Table 1: The Milan system for reporting salivary gland cytology

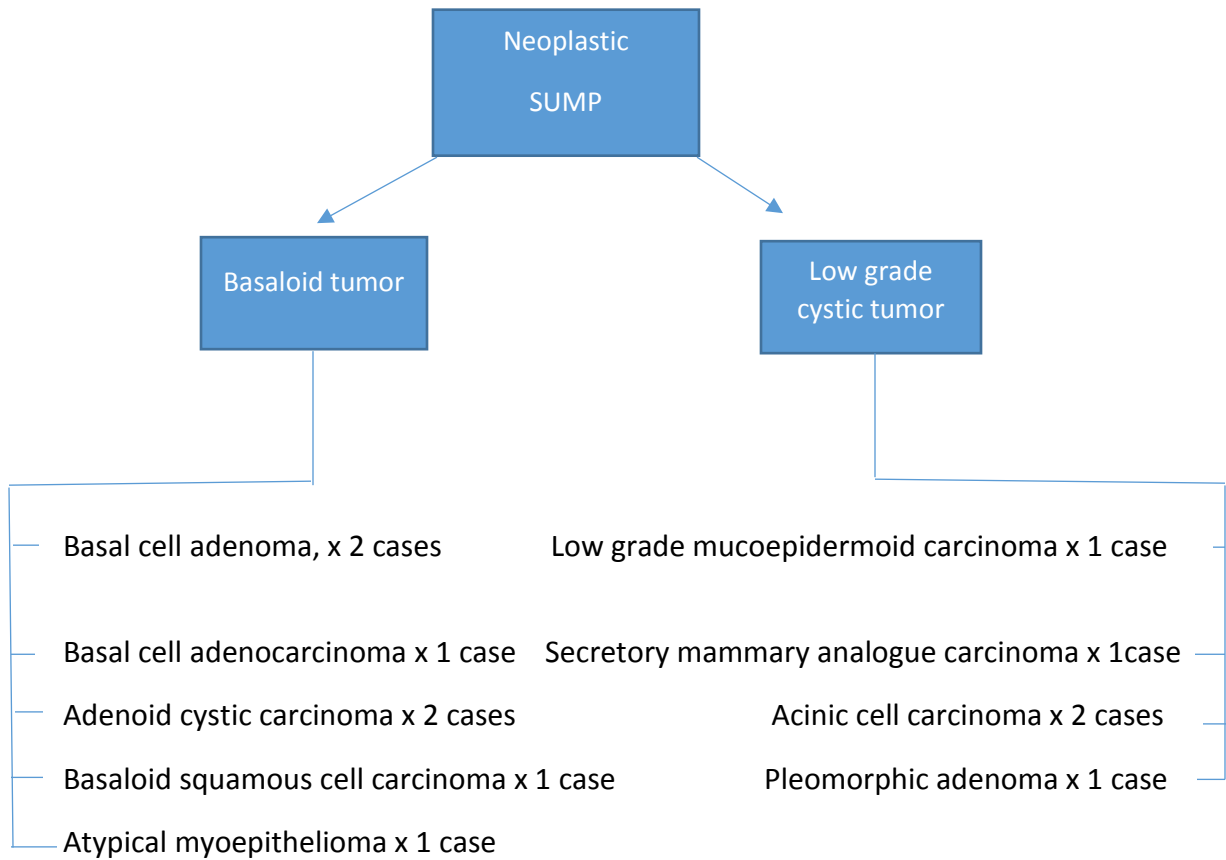
Proposed classification system

- 1) Non-Diagnostic
- 2) Non-Neoplastic
- 3) Atypical
- 4) Neoplasm
 - Benign
 - Salivary Gland neoplasm of undetermined malignant potential
- 5) Suspicious for Malignancy
- 6) Malignant

Table 2: Surgical pathology follow up in MSRSGC categories

MSRSGC					
	Total Number of cases	Non-neoplastic	Neoplastic-benign	Neoplastic-malignant	Histologic subtypes of malignant
Non-Diagnostic	22	0	5	2	Squamous cell carcinoma
AUS	5	2	0	2	Mucoepidermoid carcinoma
Non-neoplastic	117	19	2	1	Squamous cell carcinoma
Neoplastic-benign	120	1	46	0	N/A
Neoplastic-SUMP	17	0	4	8	See Figure 1
Suspicious for malignancy	8	0	0	5	Squamous cell carcinoma
Malignant	33	0	0	27	Squamous cell carcinoma, neuroendocrine carcinoma, adenocarcinoma, adenoid cystic carcinoma, melanoma, lymphoma, carcinoma expleomorphic adenoma and mucoepidermoid carcinoma

Figure 1



37. ROSAI-DORFMAN DISEASE PRESENTING IN THE GASTROINTESTINAL TRACT.

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Introduction: Rosai-Dorfman disease (RDD) is a benign, uncommon, self-limiting disease which typically occurs in children. It is described as a proliferation of unique histiocytes showing emperipolesis and typically occurs in the cervical lymph nodes. Extranodal involvement may arise in some cases. Even more unusual is the involvement of the gastrointestinal tract. Here we report a case of an atypical RDD in a patient who presented with hematochezia and was found to have RDD presenting as a rectal mass.

Case Report: A 59-year-old African American male with hypertension, gastroesophageal reflux disease, and stroke presented with constipation, periodic hematochezia, and decreased stool caliber. Colonoscopy revealed a rectal mass. The mass was found to be possibly involving the prostate and bladder for which an exploratory laparotomy was aborted. Tissue section biopsies were taken from peri-colonic and rectal lymph nodes and from the pelvic mass. The biopsy revealed histiocytic proliferation and focal emperipolesis with background fibrosis and mixed inflammation. Immunostains revealed positivity for CD68 and S-100 in the histiocytes, which were negative for AE1/AE3, confirming the diagnostic and immunophenotypic features of soft tissue RDD.

Discussion: RDD of the gastrointestinal tract is quite rare. Literature reports only 11 reported cases, which was established incidentally or in the course of an autopsy. The diagnosis of RDD is commonly a challenge due to non-specific symptoms, variability of the disease course, and rarity of the disease. Thus patients with similar symptoms must have thorough diagnostic and pathological investigations, keeping RDD within the differential diagnosis of any histiocytic predominant process, for a conclusive diagnosis.

38. THE REGULATION OF DNMT3B EXPRESSION BY LNCRNA-NCRMS IN CANCER.

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Background: 5-aza-2'-deoxycytidine (decitabine; DAC) is an inhibitor of DNA methyltransferases which catalyze the transfer of a methyl group to DNA. It is well known that aberrant hypermethylation occurs in many types of tumors and often contributes to suppression of important genes such as tumor suppressor genes. Reactivation of the methylated genes by DAC has been shown to induce cytotoxicity and cell cycle dynamics. Increasing evidence indicates that lncRNAs may play critical roles in cancer development through epigenetic regulation of gene expression. However, little is known whether and how lncRNAs are involved in regulation of methylation pathways

Objective: In present study, we apply the CRISPR/Cas9-based synergistic activation mediator (SAM) system to a DAC-induced cytotoxicity model to identify potential lncRNAs capable of conferring the resistance to DAC in breast cancer.

Results: This screen identified several potential lncRNA candidates and among them is NCRMS which is capable of promoting resistance to DAC. We further confirmed that ectopic expression of NCRMS causes resistance to DAC whereas knockout of NCRMS increases the sensitivity to DAC. Mechanistically, NCRMS functions as a positive regulator of DNA (cytosine-5-)-methyltransferase 3 beta (DNMT3B). Further characterizations demonstrated that NCRMS promotes the stability of DNMT3B mRNA.

Conclusions: Together, these results suggest that NCRMS may serve as a potential target for cancer therapy. Studies are underway to delineate the detailed mechanism of how NCRMS regulates the stability of DNMT3B mRNA.

39. PROSTATIC FATTY ACIDS CORRELATE WITH THE PROGRESSION AND RACIAL DISPARITY OF PROSTATE CANCER.

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Objective: This study is aimed to correlate the levels of prostatic fatty acids in the forms of total fatty acids (TFA) and free fatty acids (FFA) with the pathogenesis, progression and racial disparity of prostate cancer (PCa).

Methods: Prostatic TFA and FFA were determined in 26 fresh frozen PCa tissues from 13 African American (AA) and 13 Caucasian American (CA) patients, and 21 fresh frozen benign prostatic tissues (BPT) from 12 AA and 9 CA men by GC-FID and ESI-MS, respectively. Methods of biostatistics and bioinformatics were used in data analysis.

Results: Prostatic TFAs were significantly higher in PCa than in BPT in 13 out of 23 TFA parameters in all population. In AA population, prostatic TFAs were significantly higher in PCa than in BPT in only two minor TFA species. In CA population, prostatic TFAs were significantly higher in PCa than in BPT in 19 out of 23 TFA parameters. Prostatic FFAs were significantly higher in PCa than in BPT in 8 out of 17 FFA parameters in all population. In AA population, None of 17 FFA parameters were statistically different between PCa and BPT. In CA population, prostatic FFAs were significantly higher in PCa than in BPT in 11 out of 17 FFA parameters. total TFA was lower in AA PCa than in CA PCa, and higher in AA BPT than in CA BPT, resulting in that AA men had a much narrower "safety window" between BPT and PCa as compared with CA men. Both correlated with the progression of PCa: the higher prostatic concentration of TFAs or FFAs, the higher grade and clinical stage PCa were.

Conclusions: This is the first study to simultaneously quantitate TFA and FFA in individual species, in total and in groups on race-matched PCa and BPT samples. It is concluded that increase in prostatic fatty acids significantly correlates with the risk, progression and racial disparity of PCa.

40. INTERACTIONS OF GENETIC AND ENVIRONMENTAL RISK FACTORS IN ALZHEIMER DISEASE (AD) PATHOLOGY DEVELOPMENT -- APOE4 AND OXIDATIVE STRESS.

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Background: Alzheimer disease (AD) is a multifactorial disease which onset and development may result from environmental risks (i.e., neurotoxins, aging and estrogen depletion) interacting with genetic risks (i.e., ApoE4). However, the underlying mechanisms in the interaction, and how these mechanisms mediating the pathology development in AD brain have not been understood.

Objective: In the present study, we hypothesize that cells carrying the genetic risk ApoE4 are vulnerable to response to the environmental risk induced oxidative stress, leading to the impairment in neurogenesis and new cell differentiation into functional neurons, and the enhancement of neurodegeneration and brain atrophy.

Methods: The ApoE4 Doman interaction mutation, human ApoE4 transgenic mice, and the iPS cells derived from AD patients carrying homozygous ApoE4 are used to evaluate the oxidative stress triggered by an agent that impairs mitochondrial function and increases reactive oxygen species (ROS). The controls are no mutation, no transgenic, transgenic mice with ApoE2, ApoE3, and the isogenic iPS cells with ApoE2/3 in vehicle treatment that do not induces oxidative stress.

Results: In ApoE4 domain interaction mice, oxidative inducer enhanced the accumulation of undifferentiated cells in the sub granular zone (SGZ) of the hippocampus dentate gyrus, while this accumulation of undifferentiated cells was much less in mice that were not treated with oxidative inducer, and in non-mutation mice that were treated with oxidative stress inducer. Meanwhile, human isogenic ApoE4/3/2 neuronal cells are been generating in our lab.

Conclusion: The results suggest that subjects carrying ApoE4 allele are sensitive to oxidative stress. This sensitivity of response to oxidative stress in ApoE4 cells was reflected in higher proliferation of neural progenitor cells, but low differentiation of newly formed cells. This abnormal behavior of the ApoE4 cells with a higher oxidative stress may lead to the exhaustion of the neural progenitor cells and enhance neurodegeneration of neurons later in life of these subjects as well. This hypothesis is now being testing in ApoE4/3/2 isogenic iPS cells to decipher the specific molecular mechanisms, and confirm if the similar response to oxidative stress will occur in human cells carrying ApoE4.