UNIVERSITY OF COLORADO DENVER ANSCHUTZ MEDICAL CAMPUS

30th ANNUAL STUDENT RESEARCH FORUM

and

STUDENT RESEARCH AWARDS CONVOCATION

COLLEGE OF NURSING

GRADUATE SCHOOL

SCHOOL OF DENTAL MEDICINE

SCHOOL OF MEDICINE

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FEBRUARY 4th, 2016
ANSCHUTZ MEDICAL CAMPUS
Health Sciences Library, 1st Floor Lobby

30TH ANNUAL
UNIVERSITY OF COLORADO DENVER
ANSCHUTZ MEDICAL CAMPUS
STUDENT RESEARCH FORUM

Thursday, February 4th, 2016

Poster Sessions
1:00-2:15 pm
2:15-3:30 pm

Awards Convocation
4:30 - 5:00 pm
Education 2 Auditorium 1102

ANSCHUTZ MEDICAL CAMPUS
Health Sciences Library, 1st Floor Lobby

The Student Research Forum organizing committee wishes to acknowledge, with gratitude, the financial support for medical student research provided by:

The University of Colorado Denver
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And
Undergraduate Medical Education Office

Poster Session Judges

The organizing committee wishes to acknowledge their appreciation to the following serving as judges for the AMC Student Research Forum. Without their generous contribution of time and talent the forum would not be possible. Thank you!

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The organizing committee is especially grateful to the following schools, departments, divisions, and programs for their generous contribution of financial support for the forum and/or a $300 research prize awarded to the top scoring posters at the event.

Cancer Center

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Colorado School of Public Health (CSPH)

Primary Student Presenter: Stefanos Aivazidis

Additional Presenter(s): n/a

Presenting School: Pharmacy

Degree Seeking: PHD

Year: 2nd

Mentor: James Roede

Poster Title: *ER stress in Down Syndrome: A novel mechanism for dysfunction and vulnerability.*

Final Category: Neuroscience 1

Abstract:

S Aivazidis (Ph.D, SOP), A Rauniyar, C Coughlan, JR Roede, Dept. of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado, Anschutz Medical Campus
Down syndrome (DS) is the most common genetic cause of mental retardation occurring at a rate of 1 in 691 live births in the US. It is caused by the presence of a third copy of whole or part of chromosome 21. This triplication results in a variable phenotype that along with several comorbidities, includes dementia and specifically Alzheimer's disease (AD). This is attributed mainly to the presence of 3 copies of the amyloid precursor protein (APP) gene as it is found in the 21st chromosome and is responsible for amyloid plaque formation, a common characteristic of AD pathology. Recent literature in AD is exploring the scenario that ER stress might be a mechanism that promotes AD pathology. However, there is no former research concerning ER stress in the DS population. Our team hypothesized that the presence of an extra chromosome might increase the load in the translational machinery. This can result in increased endoplasmic reticulum stress in DS population that might be responsible for the great percentage of AD appearance in people with DS. Indeed, our data show increased expression of common ER stress proteins (XBP1s, ATF6) at basal levels, in cells derived from DS patients. XBP1s and ATF6 levels were significantly increased in both whole cell lysates and nuclear samples, confirming the presence of increased ER stress. However, IRE1a phosphorylation was not different between CTRL and DS cells. That might indicate that XBP1s overexpression is due to increased presence of ATF6. We also investigated viability after Maneb exposure, a fungicide that causes neurodegeneration, to see if the DS cell lines are more prone to cell death due to the aforementioned ER stress condition. Cell death (LDH) and cell proliferation (MTS) assays results show decreased viability in the DS group after exposure. These results lend credence to our hypothesis, that DS cells are more vulnerable to toxicant exposure compared to the CTRL group.

Primary Student Presenter: Nasser Alsaleh

Additional Presenter(s): n/a

Presenting School: Pharmacy

Degree Seeking: PHD

Year: 2nd

Mentor: Jared Brown

Poster Title: *SIGNALING MECHANISMS OF SILVER NANOPARTICLE-MEDIATED ACTIVATION OF MAST CELL*

Final Category: Immunology and Autoimmune Diseases (Except Arthritis)

Abstract:

SIGNALING MECHANISMS OF SILVER NANOPARTICLE-MEDIATED ACTIVATION OF MAST CELL. Nasser Alsaleh (Ph.D., GS), Abdullah A. Aldossari, Jonathan H. Shannahan and Jared M Brown. Skaggs School of Pharmacy and Pharmaceutical Sciences, Anschutz Medical Campus, University of Colorado, Denver, Colorado The majority of toxicological outcomes of ENM exposure are mediated through immune responses; these allergic immune responses often involved mast cell activation. Mast cells play an important role in allergy and inflammation (e.g. asthma, atopic dermatitis, anaphylaxis, etc.) as they have the ability to immediately release preformed mediators upon activation (e.g. histamine, proteases, eicosanoids, serotonin, cytokines, etc.). Accordingly, mast cells are important regulators of both the innate and adaptive immune responses. Silver nanoparticles (AgNPs) are one of the most prevalent nanomaterials used in consumer products for their antimicrobial/antifungal properties; this leads to an increase in human exposure and risk. We and others have shown previously that AgNPs induce mast cell degranulation/activation which is dependent on the size of AgNPs. Furthermore, we identified a role for scavenger receptor B1 (SR-B1) that might underlie the AgNP-mediated activation of mast cells. Herein, we confirmed the involvement of SR-B1 in mast cell degranulation and provided some insights into the intracellular mechanisms involved in AgNP-mediated degranulation of mast cells. Specifically, our data suggest that AgNP-mediated degranulation of mast cells is dependent on the influx of extracellular calcium, which is at least partially mediated through the ORAI1 calcium channels. Furthermore, we found that both phosphoinositide 3-kinase (PI3K) and phospholipase C gamma (PLCγ) are involved in AgNP-mediated degranulation of mast cells. Taken together, these results provide new insights into AgNP-mediated degranulation of mast cells, which could be of beneficial value for designing novel nanomaterials that are devoid of immune system activation.

Primary Student Presenter: Rachel Ancar

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD/PHD

Year: 2nd

Mentor: Kathrin Bernt

Poster Title: *THE EFFECT OF DOT1L INHIBITION ON RNA POLYMERASE II PAUSING*

Final Category: Hematology and Oncology - Blood and General Mechanisms

Abstract:

THE EFFECT OF DOT1L INHIBITION ON RNA POLYMERASE II PAUSING. R Ancar, (MD/Ph.D., MS), N Fong, D Bentley, T Neff, K Bernt, Department of Hematology and Oncology, University of Colorado, Denver, CO. Re-arrangements of the mixed lineage leukemia gene (MLL) are found in aggressive infant leukemias and adult acute myeloid leukemias. Rearrangements of MLL result in recruitment of DOT1L, a H3K79 methyltransferase, to its target genes. Small molecule inhibitors of DOT1L are in clinical development after they were shown to inhibit leukemogenesis. However, the mechanism of DOT1L activity in leukemogenesis of MLL-rearranged leukemias is not fully understood. Interestingly, MLL-fusion proteins are also known to recruit proteins that regulate RNA Polymerase II (RNA Pol II) pausing on target genes. DOT1L may be recruited with these protein complexes and contribute to increased target gene expression associated with MLL-rearranged leukemias. This study aims to determine the effect of DOT1L inhibition on RNA Pol II pausing in these cancers. Human leukemia cells lines with and without MLL-rearrangements, Jurkat, Loucy, MV4;11, and Molm13, were cultured and treated with DOT1L inhibitor. The control and drug treated cell lines were used for RNA Polymerase II ChIP-seq, to study the effect of DOT1L inhibition on Pol II pausing genome-wide. The ChIP-seq quality was tested with a GAPDH qPCR and sequenced on an Illumina next-generation platform. The Jurkat cell line, a non-MLL rearranged leukemia, produced the expected RNA Pol II ChIP-seq profile. There is a high density of reads just downstream of the transcription start site (TSS) and a smaller increase in read density towards the transcription end site (TES). In the Jurkat cells treated with DOT1L inhibitor, there appears to be slightly more RNA Pol II reads in the body of the gene and less Pol II density near the TES. Inhibition of DOT1L produced some differences in the Pol II profile, especially at highly expressed genes. These results suggest that Dot1l may play a role in the initiation of RNA Pol II pausing. The profiles of RNA Pol II in our MLL-rearranged cell lines are being analyzed in order to further clarify these results, which may provide insight into the mechanism of DOT1L inhibitors as chemotherapeutics.

Primary Student Presenter: Alexandra Antonioli

Additional Presenter(s): n/a

Presenting School: Other (please specify)

Degree Seeking: PHD

Year: Other (please specify)

Mentor: V. Michael Holers

Poster Title: *DETERMINING THE ROLES OF MURINE COMPLEMENT FACTOR H-RELATED PROTEINS*

Final Category: Immunology and Autoimmune Diseases (Except Arthritis)

Abstract:

DETERMINING THE ROLES OF MURINE COMPLEMENT FACTOR H-RELATED PROTEINS AH Antonioli, (M.D./Ph.D., GS), JM Thurman, JP Hannan, P Marrack, VM Holers, Department of Rheumatology, University of Colorado, Denver, CO. The objective of this work is to explore the interrelationships between the complement regulatory protein Factor H (FH) and five closely related molecules known as the Factor H-Related (FHR) proteins. FH primarily regulates complement activation on self-surfaces allowing the innate immune response to discriminate between self and pathogens. FH and the FHR proteins consist in their entirety of compact repeating domains known as short consensus repeats (SCRs). The FHRs share many structural and functional traits with FH including the capacity to bind complement component C3b and glycan markers. However, few functional studies have been carried out on the FHR proteins, and these molecules have not been studied in any in vivo models of inflammatory disease. Our central hypothesis is that murine FHRs act as antagonists of FH function and increase complement deposition whereby inflammation and injury become exacerbated. To test the hypothesis that FHR proteins compete with FH-mediated complement regulation, we: 1) Generated recombinant forms of the murine FHRs. 2) Evaluated the capacity of each of these molecules to inhibit FH function. 3) Developed novel monoclonal antibodies to murine FH and/or murine FHRs in order to further elucidate the plasma concentrations of these proteins and how these molecules may approximate to their human counterparts. Our preliminary data indicate that like their human counterparts, the murine FHR proteins act as antagonists of mouse FH and accordingly are excellent surrogates by which to interrogate the underlying mechanisms linking variations within the human CFH gene family and complement dysregulation.

Primary Student Presenter: Mohammed Assiri

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 2nd

Mentor: Kristofer Fritz

Poster Title: *Chronic ethanol consumption alters SOD2 dynamics via increased lysine acetylation*

Final Category: Neuroscience 2

Abstract:

Alcohol is a leading cause of morbidity and mortality in the western world . It is well known that chronic alcohol consumption induces multi organ tissue damage, including the liver and kidney. Oxidative stress is a central factor in alcohol toxicity and remains an important area of investigation. Previously, superoxide dismutase 2 (SOD2) has been identified as a target of ethanol-induced protein hyperacetylation. SOD2 is a key antioxidant enzyme involved in maintaining a balance in pro-oxidant and anti-oxidant forces within the mitochondria. Post- translation modifications, such as lysine acetylation, alter the activity and physiochemical properties of proteins throughout the cell.. Here we present in vivo data supporting that alcohol increases oxidative stress in liver and kidney through changes to lysine acetylation on SOD2, impacting both structure and function.To further characterize SOD2 acetylation dynamics, we performed In vitro acetylation of recombinant SOD2 followed by activity assay and novel mass spectrometry analysis. These data further support the growing evidence of acetylation-induced changes in SOD2 dynamics.

Primary Student Presenter: Anna Astashchanka

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Britta Jacobsen

Poster Title: *Biology of Mucin-2 (MUC2) In Breast Cancer*

Final Category: Cancer - Below the neck and skin

Abstract:

Purpose of study: Resistance to chemotherapy is a major issue in the treatment of breast cancer. Breast tumors that secrete mucus are especially resistant to chemotherapy. One type of secreted mucin, Mucin-2 (MUC2), is not expressed in normal breast cells but is expressed in some breast cancers such as mucinous breast cancers (MBC). While patients with MBC typically have a favorable prognosis, their tumors are resistant to chemotherapy. Little is known about the effects of MUC2 on the biology of breast cancer. This study examined the role of MUC2 in breast cancer cell proliferation, response to chemotherapy, and how MUC2 expression is regulated in breast tumor cells. Methods used: Two novel model cell lines of mucinous breast cancer were developed from patient derived tumorgrafts called BCK4 and PT12, both of which secrete MUC2. In order to examine the effects of modulating MUC2 levels, MUC2 expression was decreased using shRNA targeted to MUC2 compared to a non-targeting control shRNA. Decreased expression of MUC2 was confirmed using immunoblotting and quantitative immunocytochemistry. Proliferation was measured using the IncuCyte live cell imaging system. Response to chemotherapy was measured by examining apoptosis using cleaved-caspase 3 staining. To examine the regulation of endogenous MUC2 expression, wild-type BCK4 cells were treated with epidermal growth factor (EGF) with or without an EGF-receptor inhibitor or tumor necrosis factor alpha (TNFA) and MUC2 expression was examined using quantitative immunocytochemistry. Summary of Results: BCK4 and PT12 cells both contain MUC2 with cytoplasmic, heterogenous expression. Proliferation was increased in BCK4 cells with decreased MUC2 versus control cells. Docetaxel treatment induced minimal apoptosis in BCK4 control cells, however, it significantly increased apoptosis in BCK4 cells with reduced MUC2. Endogenous MUC2 expression in wild-type BCK4 cells was increased with addition of EGF or TNFA; EGF mediated stimulation of MUC2 was abolished by addition of the EGF-receptor inhibitor, Erlotinib. Conclusions: MUC2 expression plays an important role in mediating cell proliferation and apoptosis in breast cancer cells. Endogenous MUC2 is regulated by EGF and TNFA. These data suggest that MUC2 expression is important in controlling the biology of MBC and MUC2 positive tumors.

Primary Student Presenter: Arezoo Bahramirad

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Al Barqawi

Poster Title: *Validation of UWIN compared to AUA-SS Using Objective Measures*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

Objective: To validate the Urgency, Weak stream, Incomplete emptying, and Nocturia (UWIN) survey for patients with lower urinary tract symptoms (LUTS) by comparing survey scores on the UWIN and the American Urological Association Symptom Index (AUA-SS) to objective cystoscopy data. The hypothesis is that scores on the UWIN and AUA-SS will both equally correlate with objective measures of urine voiding. The UWIN is a more compact version of AUA-SS created to make a less burdensome self-reporting instrument for LUTS, theoretically improving accuracy and minimizing error in assessing LUTS. While shorter and thus taking less time to complete, UWIN scores have been shown to correlate with AUA-SS scores and appear to perform similar to AUA-SS in assessing LUTS. In this study we seek to investigate whether or not subjective self-reported scores on UWIN and AUA-SS correlate with objective measures of LUTS obtained by cystoscopy. Methods: Data was obtained from 94 patients who underwent cystoscopy for LUTS and completed both the AUA-SS and UWIN at the same clinic visit between 2011 and 2012. AUA-SS and UWIN responses were compared to cystoscopy data (bladder compliance, detrusor contraction, urine flow velocity, voided volume and post void residual volume) and evaluated using Pearson correlation coefficients. Results: A statistically significant correlation of -0.18 ($P<.05$) was found between voiding volume and UWIN composite score, however no statistically significant correlation was found between this value and AUA-SS score. Bladder compliance, detrusor contractility, urine flow velocity, and post void residual volume did not significantly correlate with either AUA-SS or UWIN. Conclusion: While shorter and taking less time to complete, the UWIN has been shown to perform similar to AUA-SS in assessing LUTS. The results of this study demonstrate that the UWIN does not underperform the AUA-SS when comparing scores to objective cystoscopy measurements.

Primary Student Presenter: Luke Baldelli

Additional Presenter(s): Ben Flitter

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: G Todd Alonso

Poster Title: *A Survey of Youth Diagnosed with Type 1 Diabetes (T1D): Identifying Opportunities to Reduce the Incidence of Diabetic Ketoacidosis (DKA).*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

Author Block: Luke Baldelli (M.D., CUSOM), Ben Flitter (M.D., CUSOM), Laura Pyle, David M Maahs, Georgeanna J Klingensmith, Robert Slover, G Todd Alonso, BARBARA DAVIS CENTER, Aurora, Co. A Survey of Youth Diagnosed with Type 1 Diabetes (T1D): Identifying Opportunities to Reduce the Incidence of Diabetic Ketoacidosis (DKA). In Colorado pediatric patients with new onset T1D who present with DKA increased from 29.9% to 46.2% from 1998-2012. Because symptoms of T1D are present before DKA, DKA upon diagnosis represents a delay in care. The purpose of this pilot and feasibility study was to compare differences between patients with newly diagnosed T1D who presented in DKA with those who did not across three domains: sociodemographic factors, access to medical care, and medical provider factors, aiming to identify potential targets for intervention. Inclusion criteria were ages < 17 years with diagnosis of T1D in the last 6 months. 61 families completed the questionnaire. Groups were compared using Fisher's exact test or the Kruskal-Wallis test. Parents of 27.8% of patients reported searching their child's symptoms on the internet prior to diagnosis. 22.9% of patients were not diagnosed at the first healthcare visit for symptoms of T1D. There were no significant differences between groups (DKA vs. no DKA) in demographic variables, the type of PCP (pediatrician, family medicine physician, physician assistant, nurse practitioner), first setting for care for T1D symptoms (physician office, urgent care, emergency center), type of provider at diagnosis, insurance status, or specific barriers to care mentioned by families. The DKA group had a longer time between previous well child check and diagnosis (172 vs 263 days, p=.014). Non-DKA patients were more likely to have blood glucose measured and had fewer symptoms prior to the first visit for diabetes symptoms (p=.024, p=.015). Parents in the non-DKA group were more likely to be familiar with symptoms of diabetes and to suspect diabetes (p<.001, p=.010). Further targets for investigation and intervention include glucose and ketone testing by providers, improving public knowledge about diabetes symptoms, and understanding how socio-demographic factors may cause delays in diagnosis of pediatric T1D.

Primary Student Presenter: Alex Barrett

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 3rd

Mentor: Kirk Hansen

Poster Title: *A Rapid and Accurate Method to Study Protein Crosslinking in Cancer*

Final Category: Hematology and Oncology - Blood and General Mechanisms

Abstract:

Despite knowledge that a fibrotic extracellular matrix (ECM) destroys normal tissue architecture and causes organ dysfunction, we still lack a basic understanding of what ECM components contribute to disease progression at the molecular level. Significant hurdles in understanding fibrosis include methods capable of characterizing insoluble ECM components, such as crosslinked fibrillar collagen, as well as downstream analytical techniques to analyze these components. Therefore, this research aims at developing and applying new analytical methods to unravel the complex connection between fibrosis, tissue stiffness, and collagen crosslinking by revealing a more complete and detailed molecular view of how a fibrotic ECM changes during disease progression.

Primary Student Presenter: Colleen Bartman

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 2nd

Mentor: Tobias Eckle

Poster Title: *LIGHT ELICITED METABOLIC ADAPTATION TO HYPOXIA*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

LIGHT ELICITED METABOLIC ADAPTATION TO HYPOXIA: CM Bartman (Ph.D., GS), L Khailova, M Goodman, S Bonney, and T Eckle, Graduate Program in Cell Biology, Stem Cells, and Development, Department of Anesthesiology, University of Colorado Anschutz For over 4.5 billion years, life on Earth has evolved to consistent oscillations of sunlight. As a result, most organisms on our planet synchronize to a 24-h cycle. This is called a circadian (Latin circa = around, and diem = day) rhythm. Modern humans evolved to sunlight as a powerful external stimulus of circadian rhythm. Today, we know that integration between sunlight and internal circadian rhythm does not simply regulate sleep–wake cycles but also influences the molecular biology of individual cells and organ systems, such as the heart. In fact, cardiac cells have a circadian pattern but the role of circadian proteins in cardiac function is not well understood. Our lab investigates the mechanism of circadian rhythm proteins as a cardio-protective strategy in low oxygen environments. Using in vitro and in vivo model systems, we found that the circadian rhythm protein Period 2 (Per2) mediates cardio-protection during myocardial ischemia in mice. Oxygen deficiency from myocardial ischemia requires the heart to metabolically adapt to produce energy and reduce oxidative damage to the tissue in an 'oxygen efficient' manner. In fact, we identified Per2 as a regulator of metabolic flux that enhances oxygen efficient pathways. We generated a novel light-sensing cell line to investigate the effect of light-elicited Per2 on glycolysis and mitochondrial respiration using Seahorse Technology. In addition, data obtained from healthy human volunteers allowed us to begin a clinical trial using intense light to treat patients with myocardial ischemia. This research may lead to using light as a prevention or treatment strategy in diseases affected by disrupted circadian rhythm and metabolic pathways.

Primary Student Presenter: Thomas Beadnell

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 4th

Mentor: Rebecca Schweppe

Poster Title: *INHIBITION OF SRC SIGNALING PROMOTES AN INCREASED RELIANCE ON THE MAPK PATHWAY IN THYROID CANCER*

Final Category: Cancer - Head, Neck, and Brain

Abstract:

Src plays an important role in thyroid cancer growth, invasion, and metastasis. To further understand how to effectively target Src, we generated 2 BRAF- (BCPAP & SW1736) and 2 RAS-mutant (C643 & Cal62) cell lines resistant to the Src inhibitor, dasatinib, and observed increased MAPK pathway activation in all four resistant cell lines, and the drug-resistant c-SrcT341M mutation in the RAS-mutant cell lines. These data indicate that Src inhibition promotes increased signaling through the MAPK pathway as a common mechanism of resistance. Consistent with increased MAPK activity in the dasatinib-resistant (DasRes) cells, here we show the growth of the DasRes cell lines exhibit enhanced sensitivity (3- to 39- fold) to MEK1/2 inhibitor, trametinib, in the presence of dasatinib. Western blot analysis in the BRAF-mutant DasRes cells, indicated that Src and MEK1/2 inhibition is important for increased MEK1/2 inhibitor sensitivity. Whereas, in the RAS-mutant DasRes cells, trametinib sensitivity is likely through dasatinib mediated paradoxical c-Src activation and phosphorylation of pY925-FAK, a Grb2 binding site. In vivo, MEK1/2 inhibition resulted in an initial inhibition of tumor growth in the RAS-mutant Cal62 parental tumors (5.26 fold; p-value = 0.0031). However, the parental tumors became refractory to trametinib after 30 days. In contrast, the DasRes Cal62 tumors exhibited a 5.5-fold greater inhibition of final tumor volume in response to trametinib (DR vs P; p = 0.0009). Finally, up-front dasatinib and trametinib treatment resulted in synergistic inhibition of growth (CI = 0.1-0.3) and increased apoptosis (4- to 19-fold) in vitro. In conclusion, prolonged inhibition of Src reprograms thyroid cancer cells to become more reliant on the MAPK pathway, providing further rational for this combination therapy and a potential mechanism for Src and MEK1/2 inhibitor synergy.

Primary Student Presenter: Christy Beitzel

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 4th

Mentor: Abigail Person

Poster Title: *Non-canonical rubro-cerebellar afferents form both positive and negative feedback loops via diverse postsynaptic targets*

Final Category: Neuroscience 1

Abstract:

The cerebellum is a vital component in motor coordination and learning. The interposed nucleus (IN) of the cerebellum targets the premotor midbrain structure the red nucleus (RN). Retrograde tracing in rats suggests the RN also innervates the IN. This reciprocal innervation of the IN and RN suggests a positive feedback loop may exist between the two structures. However, this view does not take into consideration inhibitory neurons that could limit feedback. We used a combination of tracers and cell type markers in mice to examine whether the anatomical organization of the reciprocal connection. Following injections into the RN, we observed dense terminals in the IN of the cerebellum with very few mossy fibers in the cortex. In stark contrast, terminals for canonical mossy fiber inputs originating from the pontine nuclei preferentially target the cerebellar cortex. Counts of overall bouton numbers in the IN and mossy fibers in the cortex were distinct between the two injection sites, supporting the view that the innervation patterns from these precerebellar sources are distinct. Terminal boutons from RN injections were positive for VGLUT2 suggesting a glutamatergic phenotype. RN terminals formed close contacts with glutamatergic principal output cells, glycinergic and GABAergic inhibitory cells in the IN, indicating heterogeneous connectivity. These results support the view that RN-to-IN afferents preferentially target the cerebellar nuclei over the cerebellar cortex but argue that the RN-to-IN projection do not solely form a positive feedback loop, since inhibitory neurons are also targeted. RN afferents support an emerging view that innervation of the cerebellar nuclei may be independent of the innervation of the cerebellar cortex and could underlie an anatomical substrate for a novel computation made by the cerebellum.

Primary Student Presenter: Deanne Bihler

Additional Presenter(s): n/a

Presenting School: Nursing

Degree Seeking: Other (please specify)

Year: 1st

Mentor: John Welton

Poster Title: *FECAL TRANSPLANTS ARE EFFECTIVE FOR PATIENTS WITH RECURRENT CLOSTRIDIUM DIFFICILE INFTECTIONS*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

FECAL TRANSPLANTS ARE EFFECTIVE FOR PATIENTS WITH RECURRENT CLOSTRIDIUM DIFFICILE INFECTIONS. Deanne Bihler (BSN, College of Nursing), M Almaraz,, M Judczyc, K Monton, K Richards, E Tarsi and John Welton, PhD, RN College of Nursing, University of Colorado PURPOSE: Clostridium difficile (C. diff) has been identified as the leading cause of infectious diarrhea in hospitalized patients. An estimated $4.8 billion nationally is dedicated for the care of Clostridium difficile related infections (CDI). An estimated half million people are infected with C. diff annually with approximately 29,000 deaths attributed to CDI. Antibiotic treatment is currently the standard of care for CDI. However, with continued alterations of the intestinal microbiome through the continued use of antibiotics C. diff infections may recur. This finding prompts the need for further studies and research on alternative treatments for recurrent C. difficile infections. Fecal transplants have been introduced as an alternative treatment for recurrent Clostridium difficile infections in hopes of eliminating continued recurrence of the infection. METHODS: A computerized search through the University of Colorado Health Science library website and Google scholar was completed to compile literature about Fecal Microbiota Transplantation. The search included keywords: 'Recurrent Clostridium difficile Infections', 'fecal transplant' and 'stool flora'. The criteria used to select the articles included scholarly, peer-reviewed journals. The articles selected included longitudinal (retrospective and prospective), decision analytic and convenience sampling studies. RESULTS: Available literature was browsed for similar studies that related to fecal transplants and their effectiveness on patients with recurrent Clostridium difficile infections. This search resulted in 10 articles published in English and these articles were selected based on the effectiveness of the fecal transplant results. The sample size of the studies ranged from 26-94 participants; with 6 of the studies having fewer than 50 participants and 4 of the studies had greater than 50 participants. The findings of the studies with the smaller sample sizes (with less than 50 participants) were consistent with the findings of the studies with the larger sample sizes. The studies included participants with ages ranging from 6-94 years old. The overall effectiveness of the studies ranged from 79 -100%. The types of studies that were included consisted of 6 retrospective studies, 2 prospective studies, 1 decision analytic model study, and 1 convenient sampling study. The results of the studies established the effectiveness of fecal transplants for recurrent CDI. CONCLUSION: The effectiveness of Fecal Microbiota Transplants in the treatment of recurrent Clostridium difficile is undoubtedly high. With new antibiotic resistant strains of this microorganism emerging, it is of high importance to find alternative treatments that exhibit a high cure rate, and just as importantly, are cost effective. Our research favors the Fecal Microbiota Transplant via colonoscopy as the most effective treatment for recurrent Clostridium difficile infections. Fecal Microbiota Transplants are recognized as a viable, effective treatment choice. It is recommended that further research be performed to support Fecal Microbiota Transplants as an effective treatment for recurrent Clostridium difficile infections.

Primary Student Presenter: Nicholas Bishop

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: MD/PHD

Year: 7th

Mentor: Ronald Gill

Poster Title: *Chronic hyperglycemia impairs humoral but not cellular alloimmunity*

Final Category: Immunology and Autoimmune Diseases (Except Arthritis)

Abstract:

CHRONIC HYPERGLYCEMIA IMPAIRS HUMORAL BUT NOT CELLULAR ALLOIMMUNITY N.H. Bishop (MD/PhD, GS), M.K. Nelsen, K.S. Beard, R.G. Gill. University of Colorado Anschutz Medical Campus, Department of Immunology and Microbiology Diabetes impairs immunity to certain infectious pathogens, likely due to impaired innate immunity. However, the effect of hyperglycemia on the adaptive alloimmune response to cells of differing major histocompatibility complex (MHC) haplotype is unclear. The increasing prevalence of diabetes is likely to result in more diabetic patients receiving solid organ transplants. Furthermore, chronic hyperglycemia affects all recipients of islet transplantation, a promising therapy for diabetes. Therefore, we sought to determine the independent effect of chronic hyperglycemia on cellular and humoral adaptive alloimmunity. To isolate the immune effects of chronic hyperglycemia without potentially confounding autoimmunity, we used C57BL-6 ins2akita mice (Akita). Akita mice express the H-2b MHC haplotype and bear a mutated ins2 allele that causes dominant suppression of insulin secretion and lifelong diabetes. We used fully MHC mismatched BALB/c mice (H-2d) as donors in alloimmunization and islet transplantation studies. Surprisingly, chronic hyperglycemia did not affect T cell numbers, cycling (Ki67+) or interferon-gamma production after alloimmunization as measured by flow cytometry. In contrast, serum allo-specific IgG was severely decreased in Akita mice. Despite impaired humoral alloimmunity, Akita islet allograft recipients were fully competent to reject their transplants. On day 7, prior to overt islet allograft rejection, chronic hyperglycemia had no effect on graft-infiltrating regulatory or effector T cell numbers, cycling, or interferon-gamma production. Taken together, our results demonstrate loss of humoral alloimmunity but preservation of cellular alloimmunity in chronic hyperglycemia.

Primary Student Presenter: Aleksandar Blubaum

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Brian Flynn

Poster Title: *Severity of lower urinary tract symptoms predict overall neurologic quality of life among patients with multiple sclerosis*

Final Category: Neuroscience 2

Abstract:

Introduction and objective: Lower urinary tract symptoms, while common, are under reported in patients with MS. It is unclear what the impact of lower urinary tract symptoms due to MS is on the overall quality of life. We aim to define the incidence of lower urinary tract symptoms in patients with MS and their effect on neurologic quality of life. Methods: We identified patients presenting to neurology clinic for routine follow up for multiple sclerosis. Each patient responded to validated questionnaires regarding urinary quality of life (MSQLI) and overall neurologic quality of life (NeuroQOL). Medical records were reviewed to assess for the presence of lower urinary tract symptoms. Overall neurologic quality of life was measured in the presence and absence of lower urinary tract symptoms and p-values were calculated using student's t-test. Urinary quality of life score was correlated to overall neurologic quality of life score by calculating the Spearman's rank correlation coefficient. Results: 91 patients were included in the study. All 91 patients completed the validated questionnaires. 85 patients (93%) described the presence of at least one lower urinary tract symptom. The most common urinary tract symptoms were urgency (84%), frequency (69%), incontinence (54%), and retention (38%). 72 patients reported urologic symptoms negatively impacted urinary quality of life. Presence of lower urinary tract symptoms negatively impacted overall neurologic quality of life (Figure 1). Urinary quality of life was predictive of the overall neurologic quality of life (-0.24, p=0.02). Conclusion: Lower urinary tract symptoms are very common in patients with multiple sclerosis. These symptoms greatly impact and importantly predict the overall neurologic quality of life in patients with multiple sclerosis.

Primary Student Presenter: Sydney Coates

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 2nd

Mentor: Stephanie Wesolowski

Poster Title: *Hypoxia Potentiates Gluconeogenic Activation in IUGR Fetal Sheep Hepatocytes*

Final Category: Child Maternal Health and Arthritis

Abstract:

Introduction: The intrauterine growth restricted (IUGR) fetus produced by placental insufficiency is hypoxic and hypoglycemic, and has increased hepatic glucose production (HGP) not suppressed by insulin. We hypothesized that hypoxia activates fetal HGP and produces insulin resistance. We used isolated hepatocytes to test the effect of hypoxia on gluconeogenic genes, AMPK activation, and insulin signaling. Methods: Primary hepatocytes were isolated from CON and IUGR fetal sheep. Glucose production was measured in the absence or presence of DEX and cAMP (D+C). For mRNA analysis, hepatocytes were studied basally or with D+C or insulin in normoxia or hypoxia for 4 or 24h. For protein analysis, hepatocytes were treated with insulin for 15 min following 4h of normoxia or hypoxia. Results: IUGR hepatocytes had higher glucose production in response to D+C compared to CON ($P<0.05$). In CON and IUGR hepatocytes, hypoxia for 4h increased PCK1 and PGC1A mRNA ($P<0.005$) and D+C further increased PGC1A ($P<0.001$). However, at 24h PCK1 increased with D+C ($P<0.005$) but not hypoxia; this PCK1 increase was higher in IUGR hepatocytes than in CON ($P=0.06$). PGC1A mRNA increased synergistically with hypoxia and D+C ($P<0.001$). Hypoxia increased P-AMPK by 50% in IUGR cells yet the response was 4-fold greater in CON ($P<0.05$). Insulin increased P-AKT and P-FOXO1 ($P<0.001$). P-AKT was further increased with hypoxia in IUGR cells ($P<0.05$). Conclusions: Consistent with increased HGP, IUGR hepatocytes had increased glucose production and PCK1 expression. We speculate this may be due to decreased P-AMPK in response to hypoxia rather than impaired insulin signaling given maintained P-AKT and P-FOXO1 activation. Further, hypoxia alone increased PCK1 and PGC1A expression acutely. Thus, sustained hypoxia-induced PGC1A mRNA and decreased P-AMPK may provide a link to persistently increased HGP in IUGR fetuses with hypoxia.

Primary Student Presenter: Michael Cookson

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Erica Mandell

Poster Title: *Antenatal Vitamin D Preserves Placental Weight and Vessel Density and Fetal Growth After Intra-amniotic Endotoxin Exposure*

Final Category: Child Maternal Health and Arthritis

Abstract:

Background: Antenatal (AN) intra-amniotic (IA) endotoxin (ETX) exposure in fetal rats causes high neonatal mortality and late morbidity, including abnormal lung structure and pulmonary hypertension. Biologically active vitamin D, (1,25-(OH)2D3), improves survival and lung structure in infant rats after IA ETX . Whether the protective effects of IA 1,25-(OH)2D3 are due to direct effects on the fetus or improved placental vascular development remain unknown. Objective: To determine if 1,25-(OH)2D3 treatment improves placental vascularity after IA ETX exposure in fetal rats. Design/Methods: Fetal rats were exposed to IA ETX (10mg), ETX + 1,25-(OH)2D3 (1ng/ml), 1,25-(OH)2D3, or saline at E20 and delivered two days later. Placental vascular development was assessed by CD31 staining and vessel density per high power field (HPF). Results: IA ETX reduced placenta (0.66g v. 0.52g; $p< 0.001$) and birth weight (4.82g vs. 5.69g; $p<0.001$) by 22% and 17%, respectively, compared to controls. IA 1,25-(OH)2D3 increased birth weight by 10% in ETX exposed pups (5.34g vs. 4.82g; $p<0.005$). IA ETX reduced placental vessel density by 24% compared to controls (1114 (±40.65) v. 847 (±16.81) vessels/HPF; $p<0.05$). IA 1,25-(OH)2D3 increased vessel density 2-fold after ETX exposure (847 (±16.81) v. 1739 (±95.88);$p<0.0001$), and increased from controls by 31% (1114 (±40.65) v. 1619 (±67.89); $p<0.001$). Conclusions: IA ETX decreases placental and pup weight at birth. AN 1,25-(OH)2D3 increases birth weight and placental vessel density after IA ETX exposure. We speculate that 1,25-(OH)2D3 treatment improves dysregulated angiogenesis in the placenta caused by ETX exposure.

Primary Student Presenter: MaLaura Creager

Additional Presenter(s): Grace S. Park; Zachary E. Leins; John T. Olson

Presenting School: Pharmacy

Degree Seeking: PharmD

Year: 3rd

Mentor: Roberta Capp

Poster Title: *Optimizing Patient Centered Care: Understanding How we can Help Patients who Receive a Prescription in the Emergency Department get their Medicines. Results from the Student Hotspotters Program II.*

Final Category: Education, Health Care and Public Health

Abstract:

Background: Prescription non-adherence, following a visit to the Emergency Department (ED), is as high as 50% in patients with chronic diseases. Financial barriers make up a large component of prescription non-adherence post ED visit. Patient navigators are trained individuals who help patients breakdown barriers to getting health care services. However, it is unknown if patients with financial barriers want to receive help from a patient navigator in obtaining their prescriptions after their ED visit, in the setting of having a pharmacy available 24 hours, 7 days a week. Objective: To determine the 1. Proportion of patients who cite a financial barrier in obtaining their prescription post ED visit, 2. How many of those patients want to receive help from a patient navigator. We further describe the patient population who wished to receive help from the patient navigator. Methods: This was a quality improvement study, developed through a community-academic partnership and implemented at the University Hospital ED. Students from multiple disciplines were trained as student patient navigators (SPNs), and screened the ED electronic health records for vulnerable patients, defined as those without insurance, or having Medicaid, Medicaid/Medicaid, or Medicare. The SPNs were present in the ED 24 hours, 7 days week from June-August 2015. SPNs administered a socio-health screening survey that guided care coordination efforts for each patient, based on the patient's responses. SPNs inquired about the patient's social determinants health, chronic illnesses, including mental health, and barriers to getting health care services. For this study, we evaluated patients who answered yes to "At the end of your emergency department visit today, if you receive a prescription medication to treat your condition would the cost of the medication prevent you from filling it?" All patients who answered yes to the aforementioned question, were also asked "It sounds like the copay associated with your medications may be an issue for you, would you like me to find out the price of your medications and give you resources for discount programs?" We evaluated proportion of patients who 1. Cited a financial barrier in getting their prescriptions filled in the ED, 2. Wanted help breaking down those barriers. We used chi-square analysis to evaluate differences for categorical variables and t-tests for continuous variables. Results: We approached 1,872 patients in the ED; 348 (18.6%) cited a financial barrier as a potential reason for not getting their prescriptions filled after their ED visit. The mean age was 40 years. Of those who cited a financial barrier, 251 (72.1%) wanted help from the SPN in finding resources that could help with the cost of the prescription medicine. Seventy-two percent of all patients citing a financial barrier also cited having a chronic illness. There were no differences in age or race, in whether or not patients wanted help from the SPN. However, a higher proportion of patients who were uninsured (46% vs. 16%, $p<.001$) and those who cited one more chronic illness (96% vs. 79%, $p=.08$) wanted help from a SPN in getting their prescriptions, when compared with those who did not want help from the SPN. Conclusions: In this study, we find that approximately 1 in 5 vulnerable patients presenting to the ED will cite a financial barrier in getting their ED prescriptions filled, despite having 24/7 access to a pharmacy. The vast majority of these patients want help from a SPN in getting their prescriptions filled, especially those who are uninsured and have chronic illnesses. Implementing patient navigation programs in the ED may help improve ED prescription adherence rates.

Primary Student Presenter: Gargi Datta

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 5th

Mentor: Michael Strong

Poster Title: *Machine learning and genomic analysis to predict drug resistance in Mycobacterium tuberculosis*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

Tuberculosis, caused by Mycobacterium tuberculosis is the second leading cause of death due to an infectious disease. While the incidence of TB cases is declining, an upsurge of drug-resistant strains of M. tuberculosis is a global cause for concern. Understanding the mechanisms associated with TB drug resistance development and quick recognition of resistant strains is critical to limiting the spread of drug resistance disease. We hypothesize that a combination of genotyping and machine learning provides an accurate and efficient way to identify drug-resistance. We have created a fully automated sequence analysis and mutation identification pipeline to identify mechanisms associated with the development of drug resistance. Our training set includes 3502 M. tuberculosis genome sequences with phenotypic susceptibility information from publicly available sources. To characterize existing mutations, we feed these sequences through our mutation analysis pipeline. We have created a diverse feature set that includes different feature types and data types. To combine these different feature and data types into a non-redundant and informative feature set, we are working on a novel way to handle feature selection with mixed data with an existing simultaneous feature selection and classification algorithm algorithm for sparse and imbalanced genomic data, that uses a combination of model based and instance based methods for classification. Finally, we aim to create a publicly available web and mobile application to facilitate fast delivery of drug-resistance profiles to researchers and clinicians.

Primary Student Presenter: Marisa DeGuzman

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 2nd

Mentor: Guido Frank

Poster Title: *Brain response is elevated in adolescent anorexia nervosa to monetary reward receipt and omission when underweight, but only to omission after weight restoration*

Final Category: Neuroscience 2

Abstract:

Understanding the neurobiology of anorexia nervosa (AN) is important in treatment development. Previously, adults with AN showed heightened brain response to unexpected receipt or omission of taste reward, a pattern that improves with recovery. We used a similar paradigm with monetary stimuli to test whether a sensitized brain reward function is seen in adolescents with AN, generalizes beyond taste, and improves with weight restoration. Twenty-four healthy control female adolescents (age = 14.8±2.3 yrs) and 23 female adolescents (age = 16.0±1.9 yrs) diagnosed with and enrolled in treatment for AN underwent functional magnetic resonance imaging (fMRI) before and after the treatment program (mean time between the two scans = 42±14.3 days, mean BMI increase = 2.13±0.96 kg/m2). During fMRI, learned associations between visual and monetary stimuli were violated to evoke a prediction error, i.e., a process linked to the brain reward circuit's dopamine function. Anatomical ROIs at a threshold of $p<0.001$ & 10 voxels with FWE-correction $p<0.05$ were used to assess brain activation. In response to unexpected receipt of monetary reward, AN showed greater activation than controls in the right (R) caudate and R anterior cingulum only before weight restoration. In response to the unexpected omission of monetary reward, AN showed greater activation in left (L) and R medial orbitofrontal cortex (mOFC), which persisted with weight restoration in L mOFC. These novel results suggest reward system responsiveness generalizes in an underweight context. The elevated region-specific sensitivity remits with weight restoration but only for receipt and not omission of the salient stimulus. Altered reward processing and high sensitivity to punishment may pose a treatment obstacle for adolescents with AN, even after weight restoration.

Primary Student Presenter: Ashley Denney

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: MD/PHD

Year: 3rd

Mentor: Michael McMurray

Poster Title: *Mechanistic basis of the recessive behavior of a tumor-derived temperature-sensitive p53 mutant*

Final Category: Hematology and Oncology - Blood and General Mechanisms

Abstract:

MECHANISTIC BASIS OF THE RECESSIVE BEHAVIOR OF A TUMOR-DERIVED TEMPERATURE-SENSITIVE P53 MUTANT Ashley Denney (PhD Candidate, Graduate School), Michael McMurray, PhD Cell and Developmental Biology p53, "guardian of the genome," is a potent tumor suppressor that carries out diverse roles largely through its role as a transcription factor. Mutations in p53 are found in the majority of human cancers and in the inherited Li-Fraumeni syndrome. The budding yeast S. cerevisiae is an excellent model to study p53 oligomerization, localization, and function. This project aims to interrogate the mechanism by which a temperature-sensitive p53 mutation is recessive in a cellular context. The active conformation of p53 is a tetramer composed of two pairs of dimers, and chaperones are thought to mediate tetramer formation as mutant p53s are stably bound by chaperones (Hsp70s) while wild type (WT) p53 is not. We have constructed full-length human p53 constructs with WT, p53-V272M (a recessive and temperature-sensitive mutant), and p53-R273H (a dominant mutant) sequences, each tagged with fluorescent markers mKate (a red fluorescent protein) and split Venus (either Venus-n, Vn, or Venus-C, Vc). Cells carrying both Vn and Vc constructs produce yellow fluorescence by bimolecular fluorescence complementation (BiFC) of Venus if mixed p53 hetero-tetramers are formed. Here we find that less p53-V272M localizes to the nucleus at high temperature relative to p53-R273H. Furthermore, there is decreased BiFC signal for p53-V272M at high temperature, indicating that fewer hetero-tetramers are formed between p53-V272M and WT p53 than between p53-R273H and WT p53. We have additionally identified several chaperones – Hsp26, Hsp104, Ssa2, and Ssb1 – that specifically interact with p53-V272M and not WT p53. These data are in line with our hypothesis that the temperature-sensitive p53-V272M mutant has an earlier structural defect than the DNA contact defect of the dominant p53-R273H mutant.

Primary Student Presenter: Emily Eshleman

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 5th

Mentor: Laurel Lenz

Poster Title: *Suppression of macrophage IFNGR1 by type I IFNs exacerbates bacterial infections*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

SUPPRESSION OF MACROPHAGE IFNGR1 BY TYPE I IFNS EXACERBATES BACTERIAL INFECTIONS Emily M. Eshleman (Ph.D., GS), Staci J. Kearney, and Laurel L. Lenz Department of Immunology and Microbiology, University of Colorado School of Medicine, Aurora, CO 80045, USA. Type I and II IFNs are concurrently produced during infections. Type I IFNs promote antiviral immunity but can exert anti-inflammatory effects and cause increased host susceptibility to multiple bacterial infections, including those caused by Listeria monocytogenes (Lm). Conversely, type II IFN (IFNγ) is critical for resistance to bacterial infections and acts on macrophages to induce both pro-inflammatory and anti-microbial responses. Type I IFNs down regulate the type II IFN receptor (IFNGR) by transcriptional suppression of ifngr1 in myeloid cells. We hypothesized this suppression of IFNGR contributed to increased susceptibility during bacterial infections. To test our hypothesis, we developed a transgenic mouse model (fGR1) in which a functional flag-tagged IFNGR is expressed in macrophages at low levels using a promoter that is not silenced by type I IFNs. Macrophages from fGR1 mice express both endogenous and flag-IFNGR, but overall expression of IFNGR is similar to that of WT congenic C57Bl/6 cells. When treated with type I IFNs WT macrophages lose cell surface IFNGR but fGR1 macrophages maintain normal levels. fGR1 macrophages respond normally when treated individually with type I IFN or IFNγ but show enhanced responsiveness to IFNγ in the presence of type I IFNs. Compared to WT mice, fGR1 mice have significantly reduced Lm systemic burdens and require IFNγ signaling. The enhanced bacterial resistance of fGR1 mice correlates with increased expression of pro-inflammatory activation markers and a reduced frequency of Lm-infected macrophages during systemic infection, suggesting these macrophages have increased bactericidal activity. Our data thus implicate IFNGR down regulation in myeloid cells as a mechanism that impairs macrophage activation and increases host susceptibility to infection by intracellular bacterial pathogens.

Primary Student Presenter: Brent Fitzwalter

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 4th

Mentor: Andrew Thorburn

Poster Title: *Basal autophagy regulation of apoptosis*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

Basal autophagy regulation of apoptosis. Brent Fitzwalter & Andrew Thorburn Dept. of Pharmacology, University of Colorado School of Medicine Aurora, CO 80045. It is widely thought that cell-fate decisions—the choice to live or die—are influenced by macroautophagy (autophagy hereafter), which is an evolutionarily-ancient mechanism by which cytoplasmic proteins and organelles are delivered to lysosomes for recycling nutrients and maintaining organelle homeostasis. However, although numerous studies have demonstrated that autophagy can protect cells from apoptosis, the mechanism by which this occurs is poorly understood. Mitochondrial outer membrane permeabilization (MOMP) is the key commitment step to cellular apoptosis upon which a cell is destined to die. And, previous work from our group suggested that autophagy acts as a principal regulatory mechanism to influence the extent and kinetics of MOMP. The underlying molecular mechanism that we attributed this to was autophagy's ability to regulate levels of the pro-apoptotic protein, PUMA. In basal conditions, SQSTM1/p62-dependent selective autophagy causes PUMA levels to be kept low through an unknown mechanism, reducing the likelihood of efficient MOMP and protecting cells from completing apoptosis. Conversely, genetic or pharmacological inhibition of autophagy leads to increased PUMA mRNA and protein levels, increasing the likelihood of efficient MOMP and making it more likely that cells will undergo complete apoptosis. Here, we describe a mechanism by which autophagy inhibition increases PUMA levels to control tumor cell-fate decisions by testing the hypothesis that homeostatic upregulation of the core autophagy-inducing transcription factor FOXO3a in response to autophagy deficiency leads to increased constitutive expression of PUMA. Our data suggest that FOXO3a is necessary for the compensatory response to autophagy inhibition, and the resulting elevation in PUMA levels. Further, FOXO3a levels are elevated upon genetic or pharmacological inhibition of autophagy. Thus, we propose that upon autophagy inhibition, the cell increases FOXO3a activity as a homeostatic mechanism in an attempt to correct the autophagy deficiency. But, if autophagy is still blocked by other means, the increased FOXO3a activity also acts to increase PUMA levels, thus sensitizing cells to apoptosis. Understanding the effects of manipulating autophagy on cell fate decisions are critical for attempts to improve cancer therapy and other situations (e.g. during degenerative diseases) where too much or too little cell death occurs.

Primary Student Presenter: Greg Fliney

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Enrique Alvarez

Poster Title: *PROTEOLIPID PROTEIN LABELING OF EXTRACELLULAR VESICLES*

Final Category: Neuroscience 2

Abstract:

Authors: Gregory Fliney BS, Katherine Saul MS, Danielle Harlow PhD, Enrique Alvarez MD,PhD; University of Colorado Anschutz Medical Campus, Department of Cellular and Developmental Biology Title: PROTEOLIPID PROTEIN LABELING OF EXTRACELLULAR VESICLES Purpose of the study: Extracellular vesicles (EV's) are currently an intense area of focus for biomarker research involving various diseases like cancer and Parkinson's disease. EV's are small (100-1000μm), protein and RNA containing vesicles that are released from cells into their surrounding media. Further understanding the composition of EV's advances the possibility of finding a biomarker for disease. This study characterizes the EV's that are released from oligodendrocytes by determining if proteolipid protein (PLP) can be labeled and identified on the EV's external surface using immunofluorescent labeling and nanoparticle tracking analysis (NTA). Oligodendrocytes are the targets for autoimmune response in MS, and examining an oligodendrocyte-specific protein like PLP is important for finding a biomarker for this disease. Methods: PLP wt and null mouse oligodendrocyte precursor cell (OPC) cultures were grown and matured for 0-48 hours before the culture media was removed for analysis. EV's were isolated from the media via differential ultracentrifugation. Primary PLP antibodies specific to the extracellular PLP domain were added to the PLP wt and null EV samples in a 1000 antibodies to 1 EV ratio. The samples were then diluted with DPBS 1x to 1mL and incubated overnight before being washed. R-Phycoerythrin conjugated secondary antibodies were then added and incubated for 1 hour before being washed. To determine the orientation of PLP in the EV membrane, a primary PLP antibody specific to the intracellular portion of the protein was used on additional wt and null samples. The Malvern Nanosight NS300 was used to determine the concentration and mean/mode sizes of the EV population for the PLP wt and null samples using a 532 nm laser for the fluorescent capture. Summary of Results: From two trials, the percentage of wt EV's labeled was 9% with the PLP external label and 1.4% with the PLP internal label. For the null EV's, these values were .74% and 1.96% respectively. Conclusion: The percentage of labeled EV's suggests that there is specific labeling of PLP with the PLP external antibody but not the internal antibody. This indicates that PLP in the EV's are oriented in the same manner as they are in the OPCs. In future trials, OPC cultures will mature for 5-7 days to amplify the PLP content.

Primary Student Presenter: Nora Flucke

Additional Presenter(s): n/a

Presenting School: Nursing

Degree Seeking: PHD

Year: 3rd

Mentor: Angela Richard

Poster Title: *DOMAINS OF CARE COORDINATION ACROSS STAKEHOLDER PERSPECTIVES: A REALIST SYNTHESIS*

Final Category: Education, Health Care and Public Health

Abstract:

DOMAINS OF CARE COORDINATION ACROSS STAKEHOLDER PERSPECTIVES: A REALIST SYNTHESIS. N Flucke (Ph.D. GS), College of Nursing, University of Colorado, Denver, CO. Confusion remains about the meaning of care coordination five years after enactment of the Affordable Care Act, in which Congress authorized provisions for care coordination but did not provide a definition. Lack of agreement across stakeholder groups has delayed the development of metrics and incentives to drive value-based care coordination in the intent of health reform. Purpose: The purpose of the study was to improve conceptual clarity of care coordination by identifying shared care coordination domains and associated provider roles, both essential to the delivery of team-based chronic care. Method: This study was designed, conducted, and reported according to RAMESES (Realist And Metanarrative Evidence Syntheses: Evolving Standards) criteria. The scope of the synthesis spanned all levels of involvement, from national expert panels from multiple professional disciplines to direct-care providers, including professionals who cannot currently bill for care coordination services. Findings: Eleven domains of care coordination were abstracted. When plotted onto a matrix against provider roles a grid pattern emerged. The grid allowed for recognition of duplication and gaps in the provision of comprehensive care coordination services according to the involvement of different service providers. Conclusion: This realist synthesis enhanced the conceptual understanding of care coordination by identifying shared domains of care coordination and their relation to the roles and scopes of contributing participants. The subsequently developed tool has utility for optimizing workforce resources and furthering incentives for value-based care coordination.

Primary Student Presenter: Amina Forde

Additional Presenter(s): Alexandra Tsoi

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Hillary Lum

Poster Title: *Needs and Perspective of Elderly Chinese on End of Life Care in Shenyang, China*

Final Category: Education, Health Care and Public Health

Abstract:

Introduction:

End of life care is a growing area of healthcare need in mainland China. Adequate provision of end of life care has been slowed due to cultural factors, lack of education among healthcare professionals, lack of funding, and limited public policies. End of life decision making, though a culturally sensitive topic, is also a part of end of life care, as it is important to understand how these decisions are made so that appropriate care and resources may be provided. This project seeks to answer the research question: What are the current needs and perspectives of elderly Chinese in Shenyang, China on end of life care? We worked with a local organization, Liaoning International General Health Trainers (LIGHT), that exists to provide family medicine education to Chinese medical school students and medical care to underserved populations.

Goals:

Our results will help LIGHT understand the needs that ought to be addressed in the development of their hospice care program and provide insight into cultural issues related to end of life care for the elderly, allowing for a future root cause analysis that explores why some of these cultural issues exist and how to address them.

Methods:

Participants were recruited from LIGHT's clinic and community connections. This was done in several ways. Patients of the clinic who were over 65 years old were contacted via phone and asked if they would be interested in participating in our study. Individuals who worked in the clinic asked family or friends if they would be interested in being interviewed. After some participants had been interviewed, they sent other friends to us, and our recruitment snowballed. Additionally, individuals who worked in the clinic asked other community organizations, such as a local church, for introductions to other elderly Chinese who might be interested in being interviewed.

Primary Student Presenter: Catharina Giudice

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Karen Pierce

Poster Title: *DIFFERENTIAL EXPRESSION OF NEUROPEPTIDE SIGNALING PATHWAYS IN TODDLERS WITH ASD: A DOWNSTREAM IMBALANCE*

Final Category: Neuroscience 1

Abstract:

Background Autism spectrum disorder (ASD) is a male-biased and multifactorial neurodevelopmental disorders characterized by core deficits in social behavior, social communication, and presence of repetitive/stereotyped behaviors. Dysregulation of neuropeptide biology - specifically oxytocin (OT), arginine vasopressin (AVP), and serotonin (5-HT) - have been proposed to explain deficits in social behavior and frequent comorbid conditions in autism spectrum disorders. Methods The study included 333 participants, age 1 to 4 years. 117 subjects were diagnosed as ASD, 71 as control, and 29 as developmentally delayed (DD). 78 females were excluded from the analysis. Toddlers were developmentally evaluated on a longitudinal basis until the age of 3, using the appropriate module of the Autism Diagnostic Observation Schedule (ADOS). Blood samples were collected on the first evaluation and RNA expression levels were obtained using Illumina microarray. Single Gene Analysis: Normalized gene expression values for neuropeptide biomarkers were compared using univariate analysis of covariance (ANCOVA) Pathway Analysis: We tested five KEGG pathways associated with known gene regulatory networks corresponding to neuropeptide activity. We applied the traditional Hotelling's T2-test (T2) and multivariate statistics in the new Fourier space of low dimension (T2[20%F]). Results Single Gene Analysis: Eleven genes coding for ligands, receptors, and synthesizing enzymes within the 5-HT, OT, and AVP pathways were tested. Normalized gene expression values were not significantly different (<0.05) between ASD and Control, ASD and DD, and Control and DD. Pathway Analysis: Between ASD and control subjects, significant differential expression was found for the tryptophan metabolism pathway (T2=0.001, T2[20%f]=0.004), dopaminergic synapse (T2=0.03, T2[20%F]=0.0007), prolactin signaling pathway (T2=0.02, T2[20%F]=0.001), oxytocin signaling pathway (T2=0.0016, T2[20%F]=1.39E-05). Between ASD and DD subjects, the oxytocin signaling pathway reached significance (T2>0.05, T2[20%F]=0.0003). No pathways met significance criteria between Control and DD subjects (contrast group). Each of these correlations were significantly positive using a Bonferroni corrected alpha for multiple comparisons (P<0.0033) Conclusions The neuropeptides serotonin (5-HT), oxytocin (OT), and arginine vasopressin (AVP) are critically involved in social functioning and brain development. Here we provide evidence that, while blood expression of genes directly involved in neuropeptide synthesis and synapse activity (ligands and receptors) are nominally differential between autistic toddlers and their typically developing peers, there is a significant difference in expression of the regulatory networks involved in oxytocin signaling pathways, tryptophan metabolism, dopaminergic synapse, and prolactin signaling pathway. These findings support a downstream variance, which may result in the dysregulation of proper neuropeptide activity.

Primary Student Presenter: Andrew Goodspeed

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 3rd

Mentor: James Costello

Poster Title: *Pan-cancer prediction of sensitivity to EGFR inhibition using a gene expression signature*

Final Category: Hematology and Oncology - Blood and General Mechanisms

Abstract:

Cetuximab, an antibody targeting the epidermal growth factor receptor (EGFR), is approved for the treatment of colorectal and head and neck cancers. Although KRAS mutant tumors have been shown to be resistant to cetuximab, there are limited single biomarkers effective in predicting which patients will be sensitive to treatment. Here, we evaluate if gene expression profiling can be used to identify and predict responders to cetuximab in colorectal cancer, similarly to how gene signatures can predict response to other targeted therapies. Using prediction analysis of microarrays (PAM), we identified an expression signature of 16 Affymetrix probesets that was effective in separating responders and non-responders to cetuximab treatment. In vitro validation confirmed cancer cell lines predicted to be sensitive to cetuximab are indeed more responsive to EGFR inhibition ($P<0.05$) regardless of cancer type. We also found the gene signature could predict overall survival in pediatric glioblastoma patients treated with cetuximab ($P=0.03$). Therefore, a probe expression signature derived from colorectal tumors is capable of predicting sensitivity to similar treatments across cancer type in vitro and clinically. This identifies a novel method using gene expression profiling to predict which individual cancer patients may benefit from cetuximab, regardless of cancer type.

Primary Student Presenter: Oren Gordon

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Curt Freed

Poster Title: *EFFECTS OF HYDROGEN PEROXIDE AND PHENYLBUTYRATE ON MITOCHONDRIAL MEMBRANE POTENTIAL IN DOPAMINE NEURONS*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

While phenylbutyrate has been shown to rescue neurons from oxidative stress by up-regulating the neuroprotective gene DJ-1, the exact mechanism of this protection is uncertain (Zhou et al., 2011). Our recent metabolomics study indicated that phenylbutyrate may be acting to prevent damage to mitochondria, specifically protecting the inner mitochondrial membrane potential (Δψm). In the present study, N27 dopaminergic neurons were incubated for 48 hr with phenylbutyrate 150 uM to which was added hydrogen peroxide 50 uM for an additional 24 hr. In order to measure the Δψm¬ and cell viability, cells were stained using MitoTracker Red (CMXRos), a fluorescent mitochondrial stain, plus Hoechst, a fluorescent nucleic acid stain. To measure Δψm, the MitoTracker Red fluorescence was corrected using the Hoechst fluorescence measurements. In this study we found that cells exposed to H2O2 had decreased cell viability and hyperpolarized Δψm 24 hours after the initial exposure to H2O2. By contrast, cells that were pretreated with phenylbutyrate before being exposed to H2O2 maintained cell viability and Δψm. We conclude that phenylbutyrate may protect dopamine neurons from hydrogen peroxide toxicity by reducing oxidative damage to mitochondria.

Primary Student Presenter: Cindy Ha

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Lisa Schilling

Poster Title: *Data Quality Assessment in a Distributed Research Network*

Final Category: Education, Health Care and Public Health

Abstract:

Introduction

The rise of health information technology has provided many researchers with a wealth of data available for secondary use. Large data sources come with certain challenges. Poor data quality (DQ) leads to inaccurate conclusions. For this reason, assessing a secondary health information dataset is important.

The objectives of this study were to 1) compile and review the methods of DQ characterization and assessment for publically available datasets 2) identify and pilot DQ checks that assess overall DQ and 3) identify and pilot several study specific DQ checks for two studies.

Methods

A literature review was performed to understand the current methods in practice for categorizing DQ checks.

DQ categories, subcategories, and high-level definitions developed by Kahn et al. (publication in preparation) was selected as the basic theoretical framework for the data quality checks piloted in this project.

Results

The literature review consisted of 21 papers. Eight theoretical articles discussed abstract concepts of data quality. Thirteen were applied data quality assessments.

Two data quality checks per category were developed, including overall DQ checks and study specific checks. Internal verification checks confirm that data meets expected values (Table 1). External validation ensures aspects of data are valid when compared to different datasets representing the same information (Table 2).

Conclusions

DQ is a concern when using sources such as EHR data, claims data, and administrative data for secondary purposes. Based on the DQ categories, comprehensive checks were developed to assess the DQ for two different studies. These checks involve both general level and study specific analysis. Such checks allow researchers to determine the value of large secondary datasets for their own purposes and make their own assessments of DQ.

Primary Student Presenter: Tessa Harland

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Kevin Lillehei

Poster Title: *INTRA-CYSTIC BLEOMYCIN FOR RECURRENT RATHKE'S CLEFT CYSTS*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

INTRA-CYSTIC BLEOMYCIN FOR RECURRENT RATHKE'S CLEFT CYSTS. T Harland (M.D., SOM), T Ung, M Wang, T Carlson, R Kumar, M Graner, K Lillehei, Department of Neurosurgery, University of Colorado at Denver School of Medicine, Denver, CO. Rathke's cleft cysts (RCCs) are benign tumors of the pituitary that range between 2 to 40 millimeters in size and can cause neurological deficits that require neurosurgical intervention. Current surgical management of recurrent RCCs often poses a challenge, ultimately suggesting a need for alternative treatment. Intra-cystic application of bleomycin has shown therapeutic potential for cystic craniopharyngiomas and thus may be useful treatment for RCCs. The current study presents our experience with intra-cystic bleomycin for recurrent RCCs. We performed a retrospective chart review of all patients who underwent surgical resection by a single surgeon (K.O.L) for RCCs between January 2010 and May 2015. Review of fifty-nine patients who underwent surgical resection of RCCs identified nine patients with recurrent RCCs. Twelve patients with primary tumors received intraoperative alcohol cauterization and six patients with recurrent RCCs received intra-cystic bleomycin. Intra-cystic application of bleomycin was not associated with an increase in post-operative symptoms or complication rate. No cyst recurrence has been documented in patient's receiving bleomycin (mean = 408 days, range 19 – 876 days). While current treatment of recurrent RCCs is problematic, intra-cystic application of bleomycin is a safe alternative treatment option in patients with recurrent RCCs.

Primary Student Presenter: Erik Hartwick

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 4th

Mentor: Jeffrey Kieft

Poster Title: *INVESTIGATING HOW STRUCTURED 3' UNTRANSLATED REGIONS CAN FUNCTION TO MIMIC POLY(A) TAILS USING THE TYMV TRNA-LIKE STRUCTURE AS A MODEL SYSTEM EW Hartwick, (Ph.D., GS) and JS Kieft. Department of Biochemistry and Molecular Genetics, University of Col*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

Eukaryotic messenger RNAs (mRNAs) contain cis-acting signals that serve to dramatically enhance the rate at which they are translated. Although the most widely known example is the functional synergy that exists between the mRNA's 5' cap and 3' poly(A) tail, there is growing evidence that other signals exist within mRNAs and are important. This includes signals based on specific structured RNA elements within an mRNA's untranslated regions (UTRs) in viral and cellular messages. Despite the growing realization of the importance of these elements, there is little understanding of how non-polyadenylated messages achieve translational enhancement (TE) and increased stability. My goal is to address this by exploring a powerful model system in which a structured RNA serves as a potent translational enhancer element. Specifically, I will use the turnip yellow mosaic virus (TYMV). The TYMV viral RNAs are capped at the 5' end but are not polyadenylated. Instead, they use a highly structured 3' untranslated region (UTR) to enhance translation and stability of the viral genome. The TYMV 3'UTR folds into a structure with two domains: an upstream pseudoknot domain (UPD) and tRNA-like structure (TLS). This structure drives aminoacylation of the 3' end of the viral genome, an event important for its function. Previous results show that the two TYMV 3'UTR domains structurally interact and influence one another in a multi-domained architecture that is not fully understood. This architecture appears to be conformationally dynamic and this ability to switch conformations is likely involved in translation, replication, and stability activities. These features make the TYMV 3'UTR an intriguing model for learning fundamental rules for how a multi-domained, conformationally dynamic, and structured RNA can replace the poly(A) tail to enhance the translation of an mRNA, giving us insight into viral and non-canonical translation events important to disease.

Primary Student Presenter: Nicole Harty

Additional Presenter(s): n/a

Presenting School: Public Health

Degree Seeking: MPH

Year: 2nd

Mentor: Holly Wolf

Poster Title: *Improving Patient Navigation for Cancer Screening: Evidence from the Colorado Colorectal Screening Program*

Final Category: Cancer - Below the neck and skin

Abstract:

Background: The Colorado Colorectal Screening Program (CCSP) has been supporting patient navigation (PN) for uninsured Colorado residents since 2006. With the implementation of the Affordable Care Act, there are fewer uninsured Coloradans, but the medically underserved population remains. Therefore, CCSP is expanding its PN services to all eligible residents. Focusing on increasing the reach of PN services for Medicaid patients, evaluators had two research questions: (1) What are navigators doing to help their patients obtain a colonoscopy? (2) What challenges do navigators experience in providing navigation services to all qualified patients? Methods: Two ten-question key informant interviews were conducted with CCSP PNs to capture program fidelity before and after the PN expansion in order to understand how navigators have increased their reach to include the medically underserved. Results: More overall patient navigation activities occurred for the uninsured, but all patients received the most education activities. Differences in activities by payer source include more determine insurance coverage activities for insured patients and more clinic in-reach/outreach and care coordination for the uninsured. Navigators expressed challenges in securing affordable transportation options for all patients. PNs experience difficulty in identifying providers for Medicaid patients and have limited resources for helping undocumented patients. Implications: The ACA has increased the number of Medicaid patients in Colorado. This evaluation explores the current reach of PN services for Medicaid patients and identifies challenges in providing navigation for all payer sources. The results from this evaluation will inform training and best practices for CCSP PNs, with the ultimate goal to improve navigation services for all cancer and prevention services.

Primary Student Presenter: Rick Heinz

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 5th

Mentor: Jennifer Richer

Poster Title: *FUNCTIONS OF MICRO-RNA 150 IN THE NORMAL MAMMARY GLAND*

Final Category: Child Maternal Health and Arthritis

Abstract:

FUNCTIONS OF MICRO-RNA 150 IN THE NORMAL MAMMARY GLAND. RE Heinz, (Ph.D., GS), H Gu, NS Spoelstra, BL Babbs, KT Butterfield, P Ramanathan, MC Neville, MC Rudolph, MA Gordon and JK Richer, Department of Pathology, University of Colorado Anschutz Medical Campus, Aurora, CO Coordinated changes in protein expression govern progression from pregnancy to lactation during mammary gland (MG) postnatal development. We postulated that these dramatic changes are facilitated by the many micro-RNAs (miRNAs) that decrease significantly in the MG just prior to parturition. Microarray, qRT-PCR, and in situ hybridization identified miR-150 as having the highest fold decrease in mammary epithelial cells (MECs) between pregnancy and lactation, suggesting a primary role for miR-150 during this period of development. Ingenuity pathway analysis of miR-150 predicted targets, shown by microarray to be significantly upregulated between pregnancy and lactation in MECs, suggest that miR-150 may have a function in lipid and cholesterol biosynthesis, critical components of lactation. We tested this hypothesis by crossing WAP-Cre with ROSA26-lox-STOP-lox-miR-150 transgenic mice in order to force expression of miR-150 in the mouse mammary epithelium from late pregnancy throughout lactation. Compared to offspring nursed by control dams, 3-day old pups nursed by the bi-transgenic dams had ~80% decrease in survival ($p<0.0001$). Even foster pups experience an increase in mortality. Forced expression of miR-150 resulted in suppression (~30-70%) of three predicted targets of miR-150 in MECs as detected by western blot, FASN ($p=0.0001$), OLAH ($p=0.0055$) and STAT5B ($p=0.0005$). Using GC/MS lipid profiling, we confirmed forced expression of miR-150 causes a 30% reduction of de novo fatty acids ($p=0.0164$) in MECs at lactation day 2. These results suggest that the pre-lactation decline in miRNAs, such as miR-150, is necessary to release translational suppression of genes critical for lactation.

Primary Student Presenter: Claire Heit

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 5th

Mentor: Vasilis Vasiliou

Poster Title: *Deletion of Catalase in C57BL/6 Mice Results in an Obese Phenotype*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

Catalase (CAT) is the enzyme involved in the detoxification of hydrogen peroxide (H2O2), acting as a defender against oxidative stress but it also metabolizes ethanol to acetaldehyde, using H2O2 as a cofactor. Humans with inherited acatalasemia, a deficiency in CAT activity primarily in red blood cells, have higher risk for numerous pathologies, including diabetes. Catalase knockout mice (Cat-/- or KO) are susceptible to streptozotocin-induced diabetes and diabetic renal injury. We now report that in this communication that Cat-/- mice develop a distinct obese phenotype. Both male and female KO mice exhibit an increase in body weight from fat accumulation, a phenotype that becomes more defined with age. Females displayed a more pronounced body fat accumulation, whereas male mice tended to accumulate more fat in the liver rather than viscerally. Both sexes have increased protein carbonylation, lipid peroxidation, serum and liver triglycerides as well as ALTs. Our RNA-seq analysis in liver tissue shows that, the obesity associated genes Cidec, Osbpl3, Cfd as well as Ppar-γ are in the top ten genes up-regulated in the KO mice. Finally, there is an increase in the size and number of pancreatic islets in the KO mice that is associated with higher fasting blood insulin levels. Our data suggest that CAT plays a more significant role in metabolic disorders than originally thought. We also hypothesize that catalase also plays a more significant role in alcoholic liver disease.

Primary Student Presenter: Jason Hendrickson

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kristine Kuhn

Poster Title: *ALTERATIONS IN THE COLONIC MICROBIOME PRECEDE THE DEVELOPMENT OF RHEUMATOID ARTHRITIS*

Final Category: Child Maternal Health and Arthritis

Abstract:

Purpose of Study: Alterations in resident bacteria, termed dysbiosis, is present in patients in early stages of rheumatoid arthritis. It remains unclear if dysbiosis is causative or occurs as a result of the disease. Using the collagen-induced arthritis (CIA) model in mice and patients at risk for developing RA, we aimed to determine if microbiome changes occur and, if so, at what point during the development of disease. Methods Used: DBA1/j mice were injected intradermally with bovine type II collagen emulsified in complete Freund's adjuvant at days 0 and 21 to induce CIA. Fecal pellets were harvested from the mice at days 0, 21, and 39 after immunization. Patients from the Studies of the Etiology of RA who were CCP+ or CCP- without evidence of arthritis were recruited and fecal samples collected. The microbial DNA was extracted from feces and 16S rRNA sequencing was performed. Microbial ecology such as diversity and relative abundance of the 16S rRNA sequences was evaluated using Explicet software. Summary of Results: The mean severity of CIA at day 39 after immunization was 6.67 ± 1.05; no mice had observable arthritis before day 24. Our microbiome sequencing results demonstrate significant differences in the beta diversity of the microbial community at day 0 (1.000) compared to day 21 (0.866) and at day 39 (0.920). Alterations in the microbiome were concentrated in phylum Firmicutes, class Clostridia, and order Clostridiales. Interestingly, when comparing pre-clinical RA patients, we also observed enrichment in the same microbial order in CCP+ individuals compared to CCP-. Conclusions: These data indicate that dysbiosis occurs during the initial stages of CIA and RA, when immune responses that lead to disease are developing. Such findings suggest that dysbiosis may be causative in pathogenesis of disease rather than reflective of the disease presence. An interesting finding was the observation of the same order of bacteria in both preclinical CIA, in which CCP antibodies are present, and CCP+ individuals at risk for developing RA. Our future directions will focus upon the functional consequences of this bacterial order in driving the development of pathogenic anti-CCP autoantibodies.

Primary Student Presenter: My-Linh Ho

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kristen Demoruelle

Poster Title: *SPUTUM IGG AND IGA ANTI-CPP ANTIBODIES IN SUBJECTS AT RISK FOR RHEUMATOID ARTHRITIS*

Final Category: Child Maternal Health and Arthritis

Abstract:

SPUTUM IGG AND IGA ANTI-CPP ANTIBODIES IN SUBJECTS AT RISK FOR RHEUMATOID ARTHRITIS
Background: Serum anti-cyclic citrullinated protein (CCP) antibodies are specific for rheumatoid arthritis (RA) and are abnormally elevated in the serum years prior to the onset of inflammatory arthritis. As such, anti-CCP antibodies are thought to originate at an extra-articular site. To test whether anti-CCP is generated in the lung mucosa, we examine sputum levels of anti-CCP isotypes. Methods: We studied 28 patients with RA, 115 arthritis-free subjects at risk for future RA based on serum anti-CCP3.1 (IgG+IgA) positivity or familial RA, and 46 healthy controls. Simultaneously collected serum and induced sputum were tested by ELISA for isotype-specific anti-CCP-IgA, anti-CCP-IgG, and anti-CCP-IgM. Serum and sputum positivity was set based on levels present in <5% of controls. Results: We identified 20/28 (71%) RA and 31/115 (27%) At-Risk subjects with ≥1 sputum anti-CCP isotype positive. Sputum CCP-IgG positivity for RA subjects was significantly higher than CCP-IgA (71% vs. 39%, p=0.02), in contrast to At-Risk subjects, who demonstrated similar sputum CCP-IgG and CCP-IgA positivity rates (17% vs. 19%, p=0.73). Also, 22/115 At-Risk subjects had ≥1 sputum CCP isotype positive in the absence of serum CCP isotype positivity suggesting local generation in the lung. In At-Risk and RA subjects, sputum CCP-IgA was more prevalent in ever compared to never smokers (72% vs. 15%, p<0.01), and sputum CCP-IgA and CCP-IgG correlated with sputum absolute macrophage count (p<0.01). Conclusion: Anti-CCP-IgA and CCP-IgG are elevated in the lung of subjects At-Risk for future RA, whereas sputum CCP-IgG was more prevalent in established RA. This suggests that lung generation of CCP-IgA may be an important factor in early loss of tolerance, while CCP-IgG in the transition to articular RA. Longitudinal studies are needed to explore contributing factors in the development of mucosal autoimmunity in RA.

Primary Student Presenter: Tori Holtestaul

Additional Presenter(s): Janine Hoerauf; Alida Ovrutsky

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Janet Meredith

Poster Title: *Youth Community Health Awareness Program*

Final Category: Education, Health Care and Public Health

Abstract:

Since 1997, 3,380 refugees from Burma have fled violence and persecution in their homeland to settle in Colorado, where they must adjust to a foreign culture and a complex healthcare system. This community based participatory research (CBPR) project is a sustainable partnership with a group of local refugee youth from Burma researching personal and community health. Medical students, community leaders, and an advisory board of youth from Burma met once a month and collectively decided to target alcohol use literacy and possible interventions. The project began in January 2014 and is an ongoing effort with the ultimate goal of developing and evaluating an alcohol health literacy intervention specifically for the refugee community from Burma. At this time, we are in the midst of key informant interviews and survey development to formally assess alcohol use and education in this specific community. Longitudinal goals include developing mentorship relationships between refugee youth and medical students, bolstering the relationship between CU School of Medicine and the surrounding community, and improving communication and understanding between refugee communities and the healthcare system.

Primary Student Presenter: Logan Hostetter

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Bryan Haugen

Poster Title: *EXPLORING THIOREDOXIN INTERACTING PROTEIN REGULATED METABOLISM IN ANAPLASTIC THYROID CANCER*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

Authors: Hostetter L, Morrison J, Severson J, Mackie R, Sharma V, Haugen B. Purpose: In the assessment of prognosis of a thyroid cancer patient, tumor PET positivity is associated with a poorly differentiated tumor as well as poor prognosis. Interestingly, thioredoxin interacting protein (TXNIP) expression has been shown to be downregulated during the transition from well-differentiated thyroid cancer to anaplastic sub-types, and is a tumor suppressor in thyroid cells. TXNIP has been shown to inhibit glucose uptake via endocytosis of the GLUT-1 transporter from the cell surface, as well as inhibition of GLUT-1 transcription. Though TXNIP has many functions, we hypothesize that TXNIP's negative regulation of glucose metabolism is critical to tumor suppression. Methods: Multiple ATC (anaplastic thyroid cancer) cell lines were used to model the effects of stable overexpression of TXNIP. To investigate the effects of TXNIP on GLUT-1 expression in thyroid cancer cells, we assessed cell surface expression of GLUT-1 by flow cytometry. GLUT-1 transcript expression was quantified with qPCR, and total GLUT-1 protein by western blot. Results: Cell surface GLUT-1 expression was variable between trials when comparing the control cell line to TXNIP overexpressing cells. Western blot analysis showed minimal changes in GLUT-1 protein in cells with overexpressed TXNIP compared to controls. Conclusions: In an in vitro model of TXNIP overexpression in ATC cells, no significant changes in cell surface expression of GLUT-1, total GLUT-1 protein, or GLUT-1 mRNA were observed. However, there are limitations to these studies (endogenous TXNIP expression, media glucose concentration, etc). Future directions include using the CRISPR Cas9 system to knock down TXNIP expression in thyroid cancer cells lines to further investigate the role of TXNIP as a modulator of glucose metabolism in ATC.

Primary Student Presenter: Marissa Hughbanks

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Evalina Burger - Van der Walt

Poster Title: *SEVERE OSTEOARTHRITIS ASSOCIATED WITH EARLY ONSET MENOPAUSE*

Final Category: Child Maternal Health and Arthritis

Abstract:

SEVERE OSTEOARTHRITIS ASSOCIATED WITH EARLY ONSET MENOPAUSE. ML Hughbanks, (M.D., SOM), E Burger, M.D., Department of Orthopedics, University of Colorado, Denver. Arthritis is the most common cause of disability in the U.S. today and osteoarthritis (OA) is the most common type. This case study and literature review aims to determine whether the role of estrogen (E) and its receptors (ERs) in the onset and progression of OA has been defined in the literature and to demonstrate the need for further investigation into their role in OA. A literature review was done using PubMed with the following key words: osteoarthritis, estrogen, estrogen receptor, articular cartilage, and menopause. The case was reviewed via the patient's medical records. We found the following: ERs are known to exist in human chondrocytes and joint fluid but the effects of life cycle and disease states on their expression is unknown. A 2008 review of studies on ovarectomized animals found an increased risk of OA and a protective benefit for those treated with estrogen replacement (HRT). A study on the effect of ER expression in human cartilage in 18 patients with degenerative spondylolisthesis or spinal stenosis found that patients with more significant joint degeneration had increased ER levels. Case Review: 75y.o. woman presents with cervical and lumbar degenerative disease, bilateral knee and shoulder OA, joint pain, morning stiffness, and inability to walk long distances. PMH significant for menopause onset at 35 without HRT and early onset OA with total left knee replacement at 60 with loosening of the prosthesis. Workup shows age appropriate osteopenia and is negative for inflammatory diseases. There is no known cause for her unusually early onset of severe OA. This study shows that E and its receptors are likely linked to OA development, that the role of E and ERs in the maintenance of articular cartilage is not well understood, and the change in receptors has not been quantified.

Primary Student Presenter: Monica Johnson

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 5th

Mentor: Jared Brown

Poster Title: *THE ROLE OF GENETICS IN SILVER NANOPARTICLE-INDUCED MAST CELL ACTIVATION*

Final Category: Immunology and Autoimmune Diseases (Except Arthritis)

Abstract:

M Johnson (PhD, GS), L Saba, A Bauer, R Podila, J Brown Silver nanoparticles (AgNP) are the most widely manufactured engineered nanomaterial (ENM) due to their antimicrobial properties. However, with their increased use, there is concern that human and environmental exposures may lead to adverse outcomes. Our laboratory previously determined that mast cells are activated following AgNP exposure that is dependent upon key physicochemical properties. Mast cells, central to the innate immune response, are one of the earliest sensors of environmental insult. Genetics are a major contributing factor in many toxicological outcomes, however to date, few studies have examined the contribution of genetics to ENM toxicity. We hypothesized that in addition to ENM physicochemical properties, genetics contribute to regulation of mast cell degranulation following AgNP exposure. We grew bone marrow-derived mast cells from genetically diverse mouse strains, exposed them to AgNP (25μg/mL, 1h) and assessed degranulation. Quantitative trait loci (QTL) mapping was preformed to identify single nucleotide polymorphisms (SNPs) associated with variation in degranulation following AgNP exposure. Mast cells grown from 14 genetically different strains of mice displayed a range of degranulation patterns following AgNP exposure. This suggests that multiple genes are likely regulating the different responses leading to mast cell activation. QTL mapping identified 2 suggestive loci associated with mast cell degranulation; rs32615733 located on chromosome 1 and rs29103777 located on the X chromosome. These regions are currently undergoing annotation. These results provide evidence that a complex set of genes regulate mast cell responses to ENM exposure. Overall, the proposed research will contribute to the field of nanotoxicity by identifying genetic targets that play a role in adverse immune responses to further understand underlying mechanisms of toxicity.

Primary Student Presenter: Diane Kelly

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Brian Berman

Poster Title: *Neural Responses During Reflexive Blinking Are Abnormal In Blepharospasm*

Final Category: Neuroscience 2

Abstract:

NEURAL RESPONSES DURING REFLEXIVE BLINKING ARE ABNORMAL IN BLEPHAROSPASM Diane Kelly, BA, Brian Berman MD, MS, Erika Shelton BS Neurology, University of Colorado Anschutz Medical Campus PURPOSE OF STUDY Investigate the neural mechanisms of reflexive blinking in blepharospasm (BSP) patients compared to healthy controls (HC) using fMRI. METHODS USED 10 BSP patients (7F, 61.7±9.2) and 9 healthy controls (6F, 60.4±5.6) underwent an 8-minute fMRI scan during which air puffs were delivered to each participant's left eye in a pseudo-randomized fashion (40 per scan). Blink elicitation was confirmed using both simultaneous camera visualization and EMG monitoring. Data were analyzed using an event-related design, and groups were compared using a two-sample t test. Pearson correlation coefficients were used to test for relationships between clinical severity and changes in brain activity as measured by BOLD signal. Significance was defined as $p<0.05$, FWE corrected, for the group contrast and $p<0.05$ for the correlations. SUMMARY OF RESULTS BSP patients showed an increase brain activity in their left premotor and inferior parietal cortex, and decreased activity within their left insula and right supramarginal gyrus and superior temporal lobe. Increasing activity in the left premotor cortex and right supramarginal gyrus were correlated with their Burke-Fahn-Marsden score ($r=0.74$, $p=0.01$; $r=0.70$, $p=0.002$) and Blepharospasm Disability Index ($r=0.63$, $p=0.05$; $r=0.63$, $p=0.05$). CONCLUSIONS Preliminary results show that BSP is associated with abnormal brain responses during reflexive blinking. Activity with the supramarginal gyrus is decreased compared to controls, but increases with symptom severity suggesting overactivity in this region during reflexive blinking might serve as an early marker of disease. Enhanced response of the premotor cortex during reflexive blinking may stem from diminished inhibition within the sensorimotor network, and raises the possibility that inhibitory transcranial magnetic stimulation of the premotor cortex could potentially have therapeutic benefit in BSP. Further analysis of the brainstem will be conducted to test for abnormal function of the trigeminal system.

Primary Student Presenter: Charles Kemmler

Additional Presenter(s): Reed Louderback

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: David Richards

Poster Title: *Inter-Rater Reliability in the Evaluation of Increased Intracranial Pressure using Ultrasound Measurement of Optic Nerve Sheath Diameter*

Final Category: Neuroscience 1

Abstract:

INTER-RATER RELIABILITY IN THE EVALUATION OF INCREASED INTRACRANIAL PRESSURE USING ULTRASOUND MEASUREMENT OF OPTIC NERVE SHEATH DIAMETER. CB Kemmler (M.D., SOM), R Louderback (M.D., SOM), A French, and D Richards, University of Colorado School of Medicine and Denver Health and Hospital Authority, Department of Emergency Medicine, Denver, CO Ultrasound (US) measurement of the optic nerve sheath diameter (ONSD) has emerged as a rapid, inexpensive alternative to CT imaging for the detection of elevated intracranial pressure (ICP). To elucidate the potential of ultrasound for this application, it is important to assess the degree of precision among operators measuring ONSD. Furthermore, the development and validation of an optic nerve sheath model could provide a reproducible, accessible method for measurement training. The objective of this study was to evaluate the inter-rater precision of ultrasound ONSD measurement among users with varying degrees of experience, using ultrasound images of both in situ optic nerve sheaths and ONS models. Sixty Emergency Medicine residents, fellows and attendings took part in the study, with 12 of those reporting 0 previous ONSD US measurement experiences, 35 reporting 1-25 and 13 reporting >25 previous experiences. Measurements of all study US images had an average SD of 0.667, 0.627, and 0.612 ($p = 0.878$) among users with 0, 1-25 and >25 pervious experiences, respectively. Sensitivity for the detection of increased ICP, as reflected by detection of an ONSD above 5.5 mm, ranged from 69.2 to 92.3%, with variation due to user experience and in situ vs model sheath measurement. Precision of ONSD measurements did not vary significantly between users based on previous levels of experience. Further evaluations are necessary to elucidate the reliability of ONSD measurement for the detection of increased ICP in users of various experience as well as the efficacy of optic nerve sheath models for the the teaching of ONSD US measurement.

Primary Student Presenter: Brittelle Kessler

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 4th

Mentor: Rebecca Schweppe

Poster Title: *FOCAL ADHESION KINASE ACTIVITY MEDIATES RESISTANCE TO SRC INHIBITION IN BRAF-MUTANT THYROID CANCER*

Final Category: Cancer - Head, Neck, and Brain

Abstract:

FOCAL ADHESION KINASE MEDIATES RESISTANCE TO SRC INHIBITION IN THYROID CANCER BE Kessler (PhD, GS), Q Zhou, J Kim, AC Tan, and RE Schweppe University of Colorado, Department of Medicine There are currently no effective therapies for patients with advanced thyroid cancer. We have shown that Src is a novel, clinically relevant target in thyroid cancer however; resistance mechanisms to single-agent targeted therapies inevitably arise. To more effectively target Src and combat mechanisms of resistance, we generated thyroid cancer cell lines (BRAF- and RAS- mutant) to be resistant to the FDA approved Src inhibitor, dasatinib, in vitro. The effect of FAK kinase inhibition on the cell growth and signaling was evaluated by sulforhodamine B assays and Western blot analysis, respectively. Invasion was demonstrated using Boyden chamber assays. RNA-sequencing was employed to analyze secretome changes and RT-PCR was employed to measure transcript expression. We show an increase in the phosphorylation of FAK at Y397 in both the BRAF- and RAS-mutant DasRes cell lines. Interestingly, only the BRAF-, but not RAS-mutant DasRes cell lines demonstrate increased sensitivity to the FAK kinase inhibitor, PF-562,271. In addition, compared to the DMSO treated controls, invasion is significantly increased in the BRAF-mutant DasRes cells and decreased in the RAS-mutant DasRes cell lines. Dual FAK and Src inhibition in the BRAF-mutant DasRes cells attenuated the increased invasive phenotype. Conditioned media from BRAF-mutant, but not RAS-mutant DasRes cells increases invasion of control cells. Analysis of the secretome using RNA-sequencing data shows increased MMP2 and -9 expression in BRAF-mutant DasRes cells. MMP9 transcript expression is decreased in response to combined FAK and Src inhibition. Taken together, these data show that acquired resistance to Src inhibition promotes a more aggressive phenotype in BRAF-mutant thyroid cancer, mediated in part through increased FAK kinase activity.

Primary Student Presenter: Aaron Kian

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Brooke French

Poster Title: *Sagittal Strip Craniectomy with Biparietal Morcellation in Children with Sagittal Craniosynostosis: 3D Outcome Analysis*

Final Category: Neuroscience 1

Abstract:

Sagittal craniosynostosis is a cranial anomaly treated with surgical intervention that can vary with timing and invasiveness. Although significant differences in protocol exist, current literature indicates that best outcomes result from suturectomy procedures performed before 6 months of age. For infants older than 6 months, the options for intervention may be considered "more invasive". The purpose of our study is to evaluate outcomes in children with sagittal craniosynostosis treated at Children's Hospital Colorado (CHC) who underwent sagittal strip craniectomy with biparietal morcellation (SSCBM) with no post-operative helmeting. Our aim is to establish SSCBM as an acceptable alternative for infants up to 1 year of age at time of surgery. Outcomes in cephalic index (CI), a ratio of maximum cranial width over maximum cranial length, are acquired using the 3dMD imaging system, analyzed with Vectra software, and compared to normal values at 6 month and 1 year post-operative time points. Intracranial volume, head circumference, age at surgery, and blood loss are also compared to published norms for age groups and alternative procedures. Out of 64 patients who underwent SSCBM, 44 patients were < 6 months and 20 were > 6 months at time of surgery. The proportion of successful surgeries, based on CI, in the two age groups will be compared at both the 6 month and 1 year post-op time points with the ultimate goal of demonstrating equivalence. Results of this study will provide more information about the efficacy and timing of SSCBM without helmeting in the treatment of sagittal craniosynostosis in patients up to 1 year of age at time of surgery.

Primary Student Presenter: Greg Kirkpatrick

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD/PHD

Year: 5th

Mentor: Jorge DiPaola

Poster Title: *Germline mutations in ETV6 promote leukemogenesis*

Final Category: Hematology and Oncology - Blood and General Mechanisms

Abstract:

Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, accounting for one quarter of all pediatric cancers. Despite recent advances in genome-wide profiling, the etiology of most leukemias remains unknown, as ALL is a heterogeneous disease. Recent studies have suggested that in some cases, inherited mutations in genes normally regulating hematopoiesis may contribute to leukemogenesis. In the last year, three independent groups, including ours, reported identification of germline mutations in the ETS family transcriptional repressor ETV6, with affected families displaying a disease phenotype including predisposition to leukemia. ETV6 is a frequent actor in cancer, best known for the ETV6-RUNX1 translocation, the most common gene fusion in childhood ALL. We have begun to elucidate the underlying mechanism linking germline ETV6 mutations and predisposition to leukemia, and are also interested in how these ETV6 variants may relate to the ETV6-RUNX1 translocation. We have shown Ras-transformed NIH3T3 cells transduced with germline mutant ETV6 completely lose suppression of colony forming capacity conferred by wild-type ETV6, and have evidence that induction of wild-type ETV6 decreases cell proliferation in leukemia models, while induction of mutant ETV6 does not. Improved knowledge linking alterations in ETV6 and onset of leukemia may guide development of new treatment strategies benefitting patients with both heritable and acquired forms of cancer.

Primary Student Presenter: Robert Kowalski

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 1st

Mentor: Mark Spitz

Poster Title: *Intraventricular Hemorrhage On Early CT Predicts Poorer Short- and Long-term Outcome in Moderate to Severe Traumatic Brain Injury*

Final Category: Neuroscience 2

Abstract:

Intraventricular Hemorrhage On Early CT Predicts Poorer Short- and Long-term Outcome in Moderate to Severe Traumatic Brain Injury Robert G. Kowalski, MD, MS; Alan Weintraub, MD; David Mellick, MS; Tammie Nakamura, MS; Donald Gerber PhD; Cynthia Harrison-Felix, PhD Research Objectives: To evaluate whether intraventricular hemorrhage (IVH) on early CT independently predicts outcome in TBI. Design: Retrospective analysis of prospectively gathered data Setting: Rocky Mountain Regional Brain Injury System. Participants: Patients enrolled in the Traumatic Brain Injury Model Systems (TBIMS) National Database at a single center. Interventions: No study specific interventions Main Outcome Measures: Duration of post-traumatic amnesia (PTA); Glasgow Coma Scale (GCS), Glasgow Outcome Scale - Extended (GOS-E), FIMTM, Supervision Rating Scale (SRS) at acute rehabilitation admission and discharge or at follow up 1, 2 and 5 years after injury. Results: Between 1998 and 2014, 707 adult TBI patients with computed tomography (CT) were enrolled in the TBIMS database. Mean age was 36 ± 14 years, and 77% were male. IVH was observed in 170 (24%) patients. In univariate analyses, patients with IVH were less likely to follow commands at injury onset, and had longer PTA, and lower FIM total scores at rehabilitation admission and discharge. IVH patients were more likely to have concurrent subarachnoid hemorrhage, frontal cortical contusion, and white matter contusion. Independent predictors of poorer outcome (GOS-E scores 1-4) at one-year follow up were higher frequency of Charlson Index comorbidities (AOR, 1.443; 95% CI, 1.099-1.894; p=0.008), IVH (AOR, 2.049; 95% CI, 1.312-3.205; p=0.002), subcortical contusion (AOR, 2.433; 95% CI, 1.447-4.098, p=0.001) and midline shift or cistern compression (AOR, 2.096; 95% CI, 1.389-3.175; p<0.001). IVH also independently predicted longer PTA duration, longer time to resume following commands, and continuing dependence (SRS>1) one year after injury. IVH did not predict outcome at 2- and 5-year follow up. Conclusions: Intraventricular hemorrhage on early CT independently predicts poorer short- and long-term outcome in TBI. These findings may help guide intervention, and prognosis when IVH is present on acute CT imaging. Evidence suggesting that IVH observed on CT may be a surrogate marker for white matter injury warrants further study with MRI imaging.

Primary Student Presenter: Thu Le

Additional Presenter(s): n/a

Presenting School: Public Health

Degree Seeking: MPH

Year: 2nd

Mentor: Lina Patel

Poster Title: *BARRIERS TO EFFECTIVE PEDIATRIC HEALTHCARE: DISCREPANCIES BETWEEN PROVIDER AND PARENT ASSESSMENTS OF DISTRESS AND COOPERATION*

Final Category: Education, Health Care and Public Health

Abstract:

BARRIERS TO EFFECTIVE PEDIATRIC HEALTHCARE: DISCREPANCIES BETWEEN PROVIDER AND PARENT ASSESSMENTS OF DISTRESS AND COOPERATION. TA Le, (MPH, CSPH), K Sturm, and L Patel, Children's Hospital Colorado, Aurora, CO. Healthcare encounters for children, especially those with developmental disorders, can be anxiety-provoking, causing them to have higher levels of distress and lower levels of cooperation with healthcare providers. For the benefit of the pediatric patients and the safety of the healthcare providers, it is important that both parents and providers have similar understandings and perceptions of the patients' anxiety and cooperation levels. In this study, we assessed whether parents and providers of pediatric patients with developmental disabilities perceived distress and cooperation levels similarly. Data were sourced from individuals who participated in the Adaptive Care Plan Project–a funded quality improvement project–at Children's Hospital Colorado between September and November 2015. The current data came from the project's baseline phase, which included pediatric participants (age range = 1.02-25.57 years) with developmental disabilities, their parents, and the patients' providers in seven outpatient clinics (n=86) and on three inpatient floors (n=14). The average age was 10.25 years (SD=4.46) for inpatients and 8.90 (SD=6.05) for outpatients. Results showed that while the average ratings of distress and cooperation levels were similar for parents and providers, there is still a large amount of discrepancy between the actual pairs of assessments made, which ranged from a low of 39.54% to a high of 57.15%; discrepancies were not skewed in any particular direction. While the sample size was too small to determine statistical significance and it is possible that response bias impacted the results, it appears that both parents and providers need more education on identifying distress and cooperation in children with developmental disabilities.

Primary Student Presenter: Tamara Lhungay

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Brian Flynn

Poster Title: *Early Experience With Robotic-Assisted Laparoscopic Sacrocolpopexy (RALS) With Allograft Fascia Lata in Patients with Prior Mesh Complications*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

EARLY EXPERIENCE WITH ROBOTIC-ASSISTED LAPAROSCOPIC SACROCOLPOPEXY (RALS) WITH ALLOGRAFT FASCIA LATA IN PATIENTS WITH PRIOR MESH COMPLICATIONS Tamara P. Lhungay, Nicholas Westfall MD, Stephen Blakely MD, Brian J. Flynn MD Introduction: Sacrocolpopexy (SC) with mesh represents the gold-standard treatment of recurrent pelvic organ prolapse. Prolapse is common in women following mesh removal, and many of these women prefer biological material due to past negative experiences with transvaginal mesh. Objective: We report our early results of RALS with allograft fascia lata (FL) in women with aversion to polypropylene mesh. Methods: A retrospective review of women undergoing RALS for recurrent pelvic organ prolapse in a 3.5-year period was performed. Women who underwent RALS with mesh or those with a follow up less than 6 months were excluded. Clinical information (pre-operative, operative, and post-operative data) was obtained. Y-grafts were created from allograft fascia lata in a standard fashion and fixed to the vagina and sacrum with 2-0 gortex. Patient-reported success was defined as resolution of the complaint of vaginal bulge. Objective outcome was defined as stage I prolapse or less in any compartment. Results: 100 patients underwent RALS in the past 3.5 years, of which 27 underwent RALS with allograft FL. 24 of 27 (89%) had a successful procedure. Average operative time was 310 minutes with mean estimated blood loss of 115 ml across the series. No patient has developed graft-related complications. Bladder incomplete emptying resolved in 3 of 9 patients. Of the 15 of the 18 patients who experienced urge incontinence were cured or improved. Conclusion: RALS with allograft FL appears to be a safe and effective (89%) alternative in the short-term to RALS with polypropylene mesh. Our initial experience with allograft FL for RALS is encouraging, however long-term follow up is necessary to determine if outcomes will be durable.

Primary Student Presenter: Katherine Lind

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: David Schwartz

Poster Title: *Network Identification, Interaction, and Variable Expression in Variant Idiopathic Pulmonary Fibrosis*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

PURPOSE OF STUDY Idiopathic pulmonary fibrosis (IPF) is a complex disorder characterized by pulmonary fibrosis that leads to significant hypoxemic respiratory insufficiency and, ultimately, significant morbidity and mortality. Although there is currently no known etiology of IPF, familial clustering and association of IPF with systemic genetic syndromes suggest that genetics have a critical role in the development of IPF. We have previously shown that the MUC5B promoter variant (rs35705950) is strongly associated with sporadic and familial IPF but the exact mechanism is unknown. A previously published genome-wide association study identified 10 loci of susceptibility (encompassing 66 genes) involved in host defense, cell-cell adhesion, and DNA repair. We hypothesize that these genes are expressed and interact as a network in IPF. METHODS USED In this study, we identified the most promising network from the previously-identified loci by Ingenuity Pathway Analysis (figure 1). In this network, we selected four genes- AZGP1, OBFC1, DISP2, and the Androgen Receptor- to serve as representatives of this network and compared expression of these genes in healthy and IPF tissue by immunohistochemistry (IHC). SUMMARY OF RESULTS These four genes were notably down-regulated in diseased IPF tissue with both wild-type and heterozygous MUC5B variant as compared to healthy lung tissue. Surprisingly, the Androgen Receptor appeared to be strongly expressed in the MUC5B variant and in healthy tissue but lost expression in all other diseased tissue. CONCLUSIONS This data suggests that there is an overall decreased expression of this network in IPF that is somehow altered by the MUC5B variant. Further studies of this network will be crucial to elucidate the mechanism of the MUC5B variant's effect on the development of IPF.

Primary Student Presenter: Reed Louderback

Additional Presenter(s): Bailey Johnson; James Engeln

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Comilla Sasson

Poster Title: *CPR EDUCATION IN SCHOOLS: A NOVEL APPROACH TO BYSTANDER CPR DISPARITIES.*

Final Category: Education, Health Care and Public Health

Abstract:

CPR EDUCATION IN SCHOOLS: A NOVEL APPROACH TO BYSTANDER CPR DISPARITIES. RL Louderback (MD, SOM), C Sasson, MD, Ph.D., J Engeln, B Johnson. Department of Emergency Medicine, University of Colorado, Denver, Colorado Community CPR initiatives represent an important mechanism for increasing CPR awareness, particularly in lower-income areas which tend to have a higher incidence of out-of-hospital cardiac arrest coupled with lower rates of bystander CPR. The goal of this study was to implement a sustainable Hands-Only CPR education program in schools with a focus on schools in lower-income areas, and evaluate the effect of the intervention on student CPR knowledge and comfort. Participants in 16 middle schools in the Denver and Aurora school system underwent a standardized Hands-Only CPR training session using the CPR in Schools Training KitTM, which includes an instructional DVD, 10 inflatable manikins, and additional facilitator resources. Before and after the intervention, participants completed a survey, consisting of 5 questions to assess baseline CPR knowledge and a 6th question to assess overall comfort performing CPR. A McNemar's test was performed on all aggregate paired pre/post-test data and chi square and t-tests were performed on all aggregate unpaired data. Among the 16 participating sites, 12 (75%) returned training data, resulting in 1884 students trained. Analysis of pre- and post-test data demonstrated an increase in the mean number of CPR knowledge questions answered correctly from 2.22 to 4.1 (out of 5) ($p<0.001$). The majority of students (80.7%) felt comfortable performing Hands-Only CPR after the intervention. Thus, middle school students in the Denver and Aurora school system demonstrated increased knowledge and comfort with Hands-Only CPR following standardized instruction with CPR in Schools Training KitsTM. A CPR education program for students is a novel yet promising way of increasing CPR awareness in areas with low rates of bystander CPR.

Primary Student Presenter: Darren Lynn

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Neil Box

Poster Title: *Gene-ultraviolet radiation interactions determining melanoma risk phenotypes*

Final Category: Cancer - Below the neck and skin

Abstract:

Melanoma is known to result from exposure to ultraviolet (UV) light that induces mutations in genes related to cancer; however, genetic risk factors also play a role in predisposing individuals to melanoma. We hypothesize that UV exposure history interacts with inherited genetic risk factors and with the somatic mutations within each cancer to impact the clinical presentation of melanoma. To address this hypothesis, we will determine if genetic variants in melanoma risk genes contribute to sun damage assessed through ultraviolet photography (UV damage score) and if selected SNPs interact with the given UV damage score and with other different measures of sun exposure to alter damage by UV light in a cohort. This study will likely show that the severity of sun damage visualized in UV photographs correlates with skin cancer risk factors. Since UV photographs are an important component of some of the most successful sun protection interventions to date, this would be invaluable knowledge because it would add to the scientific basis of the intervention. As we learn more about how interactions between genetics and sun exposure lead to skin cancer, the integration of a tool that will help quickly assess skin cancer risk while at the same time offering potential as an intervention will be important in focusing skin cancer prevention strategies. We plan to uncover the genetic component to clinical variance and to determine if there is a rationale for the use of genetic information to guide clinical decision making. This information is paramount in the identification of high risk groups based upon genotype type data and UV exposure history.

Primary Student Presenter: Brittney Macdonald

Additional Presenter(s): Cassy Cooper

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Gretchen Domek

Poster Title: *Developing Education Materials for an Early Childhood Health and Development Program in Southwest Guatemala Macdonald B, Cooper C, Cunningham M, Abdel-Maksoud M, Domek G.*

Final Category: Child Maternal Health and Arthritis

Abstract:

The first two years of life are critical for children's physical and mental growth. Our purpose was to pilot test education materials for mothers in southwestern Guatemala regarding child development topics like nutrition, health, hygiene, development, and injury prevention. This was a pre-test/post-test quasi-experimental study. Early childhood education materials from the Colorado Bright Beginnings Program and health and nutrition recommendations from the World Health Organization were adapted to create two 30-page interactive flipchart talks relevant to 0-6 month olds and 6-12 month olds. Three Guatemalan community health workers presented the flipcharts to groups of 5-10 mothers. Demographic surveys were conducted. Short learning assessments were given to the mothers pre-intervention, immediately post-intervention, and 1-2 weeks post-intervention. Thirteen focus groups were conducted with the participants to elicit qualitative feedback about the flipcharts and talks. Mothers (n=76) were an average age of 33.7 years (SD=±11.8) and had an average of 4.1 children (SD=±3.1). Most (71%) had received some primary education only, but 23% had received no formal education. For the 0-6 month flipchart (n=38, 25 questions), scores improved from 77% to 87% ($p<.0001$), and then to 90% ($p=0.01$) for the pre-, immediate post-, and 1-2 week post-assessments, respectively. For the 6-12 month flipchart (n=38, 20 questions), scores improved from 78% to 89% ($p<.0001$), and then to 92% ($p=0.03$). Mothers in this region of southwestern Guatemala significantly increased their knowledge about health and development topics after this intervention. Their knowledge continued to increase 1-2 weeks after the intervention without re-exposure to the materials, presumably by informal reinforcement.

Primary Student Presenter: Alexander Metoxen

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Steven Abman

Poster Title: *Hepatocyte Growth Factor as a Downstream Mediator of Vascular Endothelial Growth Factor-Dependent Preservation of Growth in the Developing Lung*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

Impaired vascular endothelial growth factor (VEGF) signaling contributes to the pathogenesis of bronchopulmonary dysplasia (BPD). We hypothesized that the effects of VEGF on lung structure during development may be mediated through its downstream effects on both endothelial nitric oxide synthase (eNOS) and hepatocyte growth factor (HGF) activity, and that in the absence of eNOS, trophic effects of VEGF would be mediated through HGF signaling. To test this hypothesis, we performed an integrative series of in vitro (fetal rat lung explants and isolated fetal alveolar and endothelial cells) and in vivo studies with normal rat pups and eNOS-/- mice. In comparison with controls, fetal lung explants from eNOS -/- mice had decreased terminal lung bud formation, which was restored with rhVEGF treatment. Neonatal eNOS -/- mice were more susceptible to hyperoxia-induced inhibition of lung growth than controls, which was prevented with rhVEGF treatment. Fetal alveolar type II (AT2) cell proliferation was increased with rhVEGF treatment only with mesenchymal cell (MC) co-culture and these effects were attenuated with anti-HGF antibody treatment. Unlike VEGF, HGF directly stimulated isolated AT2 cells even without MC co-culture. HGF directly stimulates fetal pulmonary artery endothelial cell growth and tube formation, which is attenuated by treatment with JNJ, a c-Met inhibitor. rHGF treatment preserves alveolar and vascular growth after postnatal exposure to SU-5416, a VEGF receptor inhibitor. We conclude that the effects of VEGF on AT2 and endothelial cells during lung development are partly mediated through HGF-cMet signaling, and speculate that reciprocal VEGF-HGF signaling between epithelia and endothelia is disrupted in infants who develop BPD.

Primary Student Presenter: Katie Mishall

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 3rd

Mentor: Rebecca Schweppe

Poster Title: *A CHEMICAL PROTEOMICS APPROACH TO IDENTIFY MECHANISMS OF RESISTANCE TO THE SRC INHIBITOR, DASATINIB*

Final Category: Cancer - Head, Neck, and Brain

Abstract:

Introduction: New targeted therapies are needed for advanced thyroid cancer. Our lab has shown that Src is a key mediator of growth, invasion and metastasis in thyroid cancer cells.However, single-agent Src inhibitors have had limited efficacy in solid tumors. In order to more effectively target Src in the clinic, our lab has generated four thyroid cancer cell lines, 2 BRAF-mutant (BCPAP, SW1736) and 2 RAS-mutant (Cal62, C643), that are resistant to dasatinib (BMS-354,825) through gradual dose escalation. We have further tested two additional Src inhibitors and shown the dasatinib-resistant (DasRes) cells exhibit cross-resistance to saracatinib (AZD0530), but are sensitive to bosutinib (SKI-606), suggesting that unique off-targets of bosutinib play an important role in mediating sensitivity to bosutinib, and therefore resistance to dasatinib. Methods/Case Presentation: To identify the potential targets of dasatinib versus bosutinib, we performed an unbiased compound centric chemical proteomics screen using the BCPAP-DasRes cell line as a model. Briefly, cell lysate was incubated with tagged dasatinib or bosutinib. Proteins that bound to the tagged inhibitors were isolated and identified by mass spectrometry. Results/Discussion: As expected, we identified Src family kinases as targets of both inhibitors, as well as 33 kinases that were pulled down with bosutinib, but not dasatinib. Using the STRING6 database to map protein-protein interactions of the unique bosutinib targets, we identified a signaling axis containing 13 tkinases, including MEK1/2, Focal Adhesion Kinase (FAK), Protein Tyrosine Kinase 2B (PYK2), and a recently identified bosutinib target, Calcium/Calmodulin-dependent Protein Kinase II (CaMKII). We have previously shown inhibition of MEK overcomes dasatinib resistance. Here, we show that a CaMKII inhibitor, KN93, inhibits growth of control and DasRes cells (IC50 1.5-3μM) and increases apoptosis 2-7 fold. Additionally, dual inhibition of FAK/PYK2 with PF-562,271 can overcome resistance to dasatinib (IC50 0.5-1μM). Conclusion: Overall, these results have identified key mediators of Src inhibitor resistance, and provide important information on how to target these pathways alone or in combination with Src-directed therapies.

Primary Student Presenter: Angela Mitchell

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 4th

Mentor: Andrew Fontenot

Poster Title: *Identifying T Cell Antigens in Sarcoidosis*

Final Category: Immunology and Autoimmune Diseases (Except Arthritis)

Abstract:

IDENTIFYING T CELL ANTIGENS IN SARCOIDOSIS. AM Mitchell (PhD, GS)1, MT Falta1, AN Tinega1, J Grunewald2, C Pinilla3, AP Fontenot1, 1University of Colorado, Denver, CO, 2Karolinska University Hospital, Stockholm, Sweden, 3Torrey Pines Institute, San Diego, CA. Sarcoidosis is a multisystem disorder which most commonly affects the lungs and involves the accumulation of CD4+ T cells at the sites of disease. The etiology of the disease is unknown, and the lack of a known antigen has hindered the study of disease pathogenesis. However, there is considerable evidence that CD4+ T cells are involved in the initiation and perpetuation of sarcoidosis. Previous work by our lab and others has demonstrated that particular T cell clones within the bronchoalveolar lavage (BAL) have been preferentially expanded in patients with sarcoidosis. These oligoclonal T cell populations accumulate within the lung and disappear with disease resolution. Furthermore, correlations have been observed between the expansions of CD4+ T cells expressing the T cell receptor (TCR) α-chain variable (V) region Vα2.3 and the presence of the HLA-DRB1*0301 (DR3) allele in certain patient populations. Preliminary data suggest that cells within the BAL expressing TCRs utilizing Vα2.3, Vβ5.1, and Vβ5.3 are preferentially expanded before and after ex-vivo stimulation with IL-2. We hypothesize that sarcoidosis-specific CD4+ T cells accumulate and expand in the lungs of sarcoidosis patients in response to a specific antigen. To determine whether these expanded CD4+ T cell clones play a pathogenic role in disease progression, as well as to address their antigen specificity, the TCRs of these clones have been characterized, and a combinatorial peptide library has been screened to identify candidate antigens that stimulate these clones. These unbiased data will provide clues to the disease-initiating antigens that drive sarcoidosis in a subset of patients and will lead to an extension of our findings to a larger disease cohort.

Primary Student Presenter: Michelle Nelsen

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 6th

Mentor: Ronald Gill

Poster Title: *VACCINE-INDUCED 'INCOGNITO' MEMORY CD8+ T CELLS BLOCK TRANSPLANTATION TOLERANCE WITHOUT HETEROLOGOUS IMMUNITY*

Final Category: Immunology and Autoimmune Diseases (Except Arthritis)

Abstract:

VACCINE-INDUCED 'INCOGNITO' MEMORY CD8+ T CELLS BLOCK TRANSPLANTATION TOLERANCE WITHOUT HETEROLOGOUS IMMUNITY. MK Nelsen (Ph.D., GS), KS Beard, RM Kedl, ET Clambey, and RG Gill. Depts of Immunology & Microbiology, Surgery, and Anesthesiology. Univ. of Colorado, Aurora, CO. Transplant recipients often harbor immunity to vaccines. Unfortunately, through heterologous immunity, vaccine-reactive T cells can cross-react to a donor's major histocompatibility complex (MHC) molecules and drive transplant rejection. Here, we find that memory T cells do not need to be donor MHC-reactive to reject transplants. Instead, 'incognito' memory can covertly drive rejection when donor-derived cells express both donor MHC and vaccine-associated antigens ("linked antigens"). We vaccinated B6 mice with ovalbumin (OVA) to generate OVA-specific host immunity. OVA-immune mice were transplanted with donor BALB/c grafts and treated with a tolerance-induction therapy to promote graft survival. OVA-specific memory did not inhibit tolerance when donor cells only expressed donor MHC. However, when donor cells expressed both vaccine-associated OVA and donor BALB/c antigens, these "linked antigens" readily disrupted tolerance in 11/12 OVA-immune mice (p=.0005 vs. controls). Next, we found that vaccine-induced memory CD8+ T cells, and not antibodies, are necessary and sufficient for 'incognito' perturbation of tolerance. B6 mice were depleted of either CD8+ T cells or CD4+ T cells prior to the OVA immunization. CD8-depleted vaccinated mice generated OVA-specific antibodies that did not block tolerance induction in response to linked antigens. However, CD4-depleted vaccinated mice generated OVA-reactive memory CD8+ T cells that potently blocked tolerance in 7/7 mice (p=.01 vs. controls). Finally, we showed that 'incognito' memory CD8+ T cells do not require donor MHC-reactivity, because non-cross-reactive OT-1 T cells in 9/9 treated hosts rejected their transplants (p=.0001 vs. controls).

Primary Student Presenter: Travis Nemkov

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 3rd

Mentor: Kirk Hansen

Poster Title: *ALTITUDEOMICS: RED BLOOD CELL METABOLIC ADAPTATION TO HIGH ALTITUDE HYPOXIA*

Final Category: Hematology and Oncology - Blood and General Mechanisms

Abstract:

Adjustment to hypoxia is a key challenge for millions of people either living or traveling to high altitude. The physiological process of acclimatization enables adaptation to the low oxygen levels characteristic of high altitudes. Without acclimatization, exposure to low oxygen levels at high altitudes will lead to unconsciousness within minutes. Furthermore, exposure to acute hypoxia in unacclimatized humans results in a marked drop in exercise capacity and impaired cognitive function, which can be reversed upon acclimatization. The AltitudeOmics research program was designed to provide insights into acclimatization to high altitude and the retention of acclimatization after return to low altitude through the application of physiological, neurocognitive and athletic tests. The correlation of physiological readouts with data obtained from omics technologies including metabolomics, proteomics, epigenomics, and transcriptomics can elucidate possible mechanisms of acclimatization. In this study, red blood cells were collected from 21 healthy volunteers at sea level, upon exposure to high altitude (5260 m) for 1, 7 and 16 days, and following reascent after 7 days spent at 1525 m. UHPLC-MS metabolomics analyses were performed and the raw data were correlated to physiological, cognitive and athletic performance parameters recorded within the framework of the AltitudeOmics study. As a result, we could monitor for the first time 250 metabolites from human red blood cells exposed to acute hypoxia. Hypoxia induced increases in the levels of glycolytic byproducts, accompanied by a deregulation of the pentose phosphate pathway. Glutathione homeostasis was up-regulated, suggestive of increased de novo biosynthesis. Correlations between varying metabolites suggest a strong metabolic linkage between pathways, providing possible avenues for therapeutic intervention to promote acclimatization.

Primary Student Presenter: Tuan Dung Nguyen

Additional Presenter(s): Tuong Phan

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jamaluddin Moloo

Poster Title: *Soil Transmitted Helminths Prevalence in Refugees Arriving to Colorado in 2009-2012*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

Soil-Transmitted Helminths Prevalence in Refugees Arriving to Colorado in 2009-2012 Tuan Dung Nguyen; Tuong Phan; Paul Gillenwater, MPH; Lori Kennedy, MSPH; Jamaluddin Moloo, MD, MPH. Background: Refugees are at high risk for contracting Soil-Transmitted Helminths (STH) infections. The CDC advises presumptive pre-departure albendazole treatment to reduce STH infection rate. Objective: To determine the rate and prevalence of STH infections among refugees arriving from countries providing presumptive pre-departure albendazole treatment. Methods: We retrospectively examined CDPHE data, which included results of stool O&P studies on 3,870 newly arrived refugees to Colorado (2009-2012). We examined the rate of STH infection by country and pre-departure albendazole treatment status. We excluded children under the age of 1 for whom albendazole treatment is generally contraindicated. Results: A total of 3,870 refugees underwent screening with stool O&P; 1,668 received treatment with albendazole while 2,202 did not. 478 of 3,870 (12.33%) were positive for pathogenic parasites. Of these, a minority were pathogenic STH (55, 11.51%). Thailand and Malaysia had the highest prevalence of stool samples positive for pathogenic STH (2.12% and 2.59%, respectively) and Ethiopia had the lowest prevalence (0.39%). A lower proportion of overall albendazole treated patients was positive for pathogenic STH infection relative to overall untreated individuals (0.78% vs. 1.91%, $p<0.05$). Conclusion: Among newly arriving refugees to Colorado, more than 1 in 10 was positive for a pathogenic parasite; a smaller proportion was positive for a pathogenic STH infection. Although albendazole pretreatment appears to lower the rate of pathogenic STH positivity on stool O&P, the rate among untreated individuals was lower than prior estimates.

Primary Student Presenter: Vivian Nguyen

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Shi-Long Lu

Poster Title: *The role of AKT and miR-200 in PIK3CA alteration-initiated cancer stemness in HNSCC*

Final Category: Cancer - Head, Neck, and Brain

Abstract:

Head and neck squamous cell carcinoma (HNSCC) arises from the mucosa of the upper respiratory and digestive tracts and is the most common malignant tumor of the head and neck. It presents with 500,000 new cases each year and has a dismal prognosis. The phosphatidylinositol 3-kinase (PI3K) pathway is the most altered signaling pathway in HNSCC. Amplification and/or gain-of-function mutation of PIK3CA, the gene coding for the catalytic subunit of PI3 kinase, is present in more than half of the HNSCC cases. Our previous findings suggest that PIK3CA alteration–initiated cancer stem cell–like phenotype, although unresponsive to PI3K inhibition, can be attenuated by using histone deacetylase inhibitor (HDACi). Further molecular analysis discloses that the knockdown of AKT2, but not that of AKT1 or of AKT1 plus AKT2, synergistically sensitized such effect from HDACis. Recently, the miR-200 family of microRNAs, which is differentially regulated by AKT isoforms has emerged as a major player in cancer stemness. To test the hypothesis that the miR-200 family plays a critical role in sensitizing HDACi to target cancer stemness, we initially determined whether PIK3CA alteration and variation in AKT isoform levels affect expression of the miR-200 family of microRNAs (miR-200A/B/C). We found that overexpression of PIK3CA decreases expression of the miR-200 family. We also found that knockdown of AKT2, but not that of AKT1, increases expression of miR-200A/B. Our findings suggest that abundance of the miR-200 family is mediated by AKT2 and plays a role in PIK3CA alteration-initiated cancer stemness. Further investigation is needed to determine the effects of miR-200 microRNAS in mediating cancer stemness and whether they sensitize HDACi.

Primary Student Presenter: Derek Nhan

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Liron Caplan

Poster Title: *CLINICAL AND DEMOGRAPHIC FACTORS ASSOCIATED WITH FATIGUE IN SPONDYLOARTHRITIS*

Final Category: Child Maternal Health and Arthritis

Abstract:

Fatigue contributes substantially to quality of life in rheumatoid arthritis; however, in the spondyloarthritides it remains poorly characterized. Cross-sectional data from the VA PULSAR database (251 patients) were analyzed to determine associations between clinical factors and self-reported fatigue. We employed multivariable linear regressions to evaluate demographic, clinical, and laboratory factors for associations with fatigue, as measured in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Functional Index (BASFI). The mean fatigue score was 6.15 (SD 2.59) with no evidence of skewing, but a ceiling effect was present. Elevated erythrocyte sedimentation rate (ESR) and current tobacco use were associated with increased fatigue, which was associated with poorer functional outcome, after controlling for numerous variables (Table 1). Psoriatic arthritis patients did not report fatigue scores differently from patients with axial spondyloarthritis ($p > 0.05$). This data demonstrates the necessity for change in the BASDAI/BASFI to better capture fatigue in patient management.

Table 1: Univariate and multivariable regressions of associations between clinical factors and fatigue in patients using the BASDAI (A) and BASFI (B)

	Univariate regression				**Multivariable linear regression**			
Table A	**Coef.**	**P**	**95% Conf. Interval**		**Coef.**	**P**	**95% Conf. Interval**	
Age (years)	-0.005	0.707	-0.031	0.021				
Education (years)	-0.155	0.044	-0.305	-0.004	-0.161	**0.038**	-0.313	-0.009
Current Tobacco Use (yes/no)	1.307	0.001	0.577	2.037	0.962	**0.015**	0.186	1.737
Mean ESR (per 10 mm/hour)	0.354	0.002	0.136	0.571	0.336	**0.003**	0.114	0.558
C-reactive protein (mg/L)	0.030	0.050	0.000	0.060				
Axial SpA (vs. Psoriatic Arthritis)	0.267	0.444	-0.419	0.952				
Table B								
Age	0.040	<0.001	0.017	0.062	0.049	**0.001**	0.021	0.077
Education (years)	-0.098	0.136	-0.228	0.031				
Current Tobacco Use (yes/no)	1.266	<0.001	0.601	1.932	1.250	**0.003**	0.44	2.06
Fatigue (0-10)	0.574	<0.001	0.456	0.692	0.515	**<0.001**	0.381	0.649

Primary Student Presenter: Leila Noetzli

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 5th

Mentor: Jorge Di Paola

Poster Title: *A Dominant Negative Mutation (p.P214L) in ETV6 is Associated with Megakaryocyte and Erythroid Transcript Misregulation*

Final Category: Hematology and Oncology - Blood and General Mechanisms

Abstract:

Our group has recently described a family with autosomal dominant thrombocytopenia, high mean corpuscular volume (MCV) of red cells, and two occurrences of pre B-cell acute lymphoblastic leukemia (ALL) with a mutation in the transcription factor ETV6. ETV6 is a transcriptional repressor which functions through dimerization with itself or with other transcription factors. The missense mutation found in this family (p.P214L) has a dominant negative effect by dimerizing with and sequestering WT ETV6 from the nucleus. This dominant negative mutation causes a phenotype in both platelets and red cells, suggesting a disruption in megakaryocyte-erythroid differentiation. Therefore, we aimed to study the effect of p.P214L ETV6 on megakaryocyte-erythroid differentiation by studying the platelet transcriptome. RNA was isolated from leukoreduced platelets of 2 patients with the p.P214L mutation and 5 controls for whole transcriptome analysis. Platelet transcriptome analysis of patients with the p.P214L mutation revealed significant differential expression of more than 200 transcripts between patients and controls. Seven of the significant transcripts were key erythrocyte transcripts, which were upregulated in affected patients; and 9 transcripts were key platelet transcripts, which were downregulated. Of these, the red cell marker GYPA was upregulated 25 fold in affected patients ($p < 5x10\text{-}5$), and the platelet markers VWF and GPIX were downregulated 6.4 and 5.6 fold in affected patients ($p < 0.05$ and $p < 0.07$), respectively. In conclusion, we find that a dominant negative mutation in ETV6, found in a family with both platelet and red blood cell abnormalities, is associated with differentially regulated red blood cell and platelet transcripts. Our data indicate an important role for ETV6 in megakaryocyte-erythroid differentiation.

Primary Student Presenter: Molly Nowels

Additional Presenter(s): n/a

Presenting School: Public Health

Degree Seeking: DPT

Year: 2nd

Mentor: Lynn VanderWielen

Poster Title: *MENTAL HEALTH AND HIV COMORBIDITIES AND HEALTH DISPARITIES: FINDINGS FROM EMPLOYER-SPONSORED CLAIMS DATA*

Final Category: Neuroscience 1

Abstract:

Disparate outcomes of care for historically underserved populations have been widely documented in the literature. However, few studies have utilized nationally representative employer-sponsored healthcare plan data to examine disparities for individuals experiencing behavioral health and chronic disease comorbidities. Research suggests that health disparities impact HIV transmission, progress, and outcomes of care in the US and beyond. Improved access to quality primary care services is generally thought to offset emergency department and inpatient admissions among individuals with chronic conditions. Research suggests that area-based measures that reflect neighborhood characteristics are important predictors of an individual's morbidity and mortality. The current study examines utilization patterns of care and patient socioeconomic characteristics among patients with anxiety and/or depression and HIV. This study employs 69,380 HIV patients from the Health Care Cost Institute's database of employer-sponsored healthcare claims. This data, along with community-level data from the American Community Survey was employed to conduct regression analyses using measures of healthcare utilization as outcomes, including outpatient visits, ED visits, inpatient stays, and length of inpatient stay. Findings suggest that HIV patients from neighborhoods with greater numbers of individuals with low educational attainment have fewer outpatient visits, but more inpatient and ED visits than their counterparts living in zip codes with higher levels of educational attainment. Additionally, neighborhood level socioeconomic indicators such as race and percentage of female headed households are related to similar utilization patterns among patients with HIV. To address these inequities, the healthcare system may need to focus resources directed towards underserved communities and individual healthcare providers should consider the socioeconomic context in which patients are situated.

Primary Student Presenter: Tyler Okland

Additional Presenter(s): Tyler Okland; Arian Anderson

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Jennifer Adams

Poster Title: *DO ROTATING MEDICAL STUDENTS FIND UTILITY IN DIRECT OBSERVATION FEEDBACK? A QUALITY IMPROVEMENT STUDY*

Final Category: Education, Health Care and Public Health

Abstract:

Direct observation of medical students' clinical skills remains an essential component of the core clinical year. Although direct observation oftentimes takes place organically, the Colorado School of Medicine employs formalized direct observation forms (DOF's), which are used by supervisors to evaluate rotating students. In theory DOF's improve formalized feedback between student and teacher. However, the effectiveness of DOF's at accomplishing this objective has not been assessed. Nor has student impression of DOF utility been evaluated. We hypothesized that students were unsatisfied with DOF's and that we could design an improved form using student feedback. In this two-part study, we first surveyed the Colorado School of Medicine Class of 2017 using an eight-item questionnaire to characterize general opinion of DOF's. Of the 100 responders, ninety-seven said 50% or fewer of DOF's included helpful feedback. Ninety-two of these students said 25% or fewer DOF changed their clinical behavior on rotations. 90% said DOF is not an effective form of feedback. Once these data were obtained, we used student-derived commentary to guide the production of revised DOF models. Finally, we presented these alternative DOF's (AltDOF) to the Class of 2017 alongside a nine-item questionnaire aimed at identifying the utility of these revised models versus DOF. This second questionnaire was answered by 64 students. Only AltDOF 2 and 3 were considered an improvement over DOF. While students preferred AltDOF 2 over both 1 and 3 (41.27%, 22.22% and 36.51% respectively), no majority favorite was established. In addition, neither of the three AltDOF were considered beneficial to student learning by majority. Although two proposed AltDOF were considered improvements by the student body, considerable dissatisfaction with all forms prevailed. These results indicate that medical students do not find significant benefit in the use of proposed direct observation assessments. However, both AltDOF 2 and 3 enjoyed a five-fold increase in student perception of educational utility as compared to DOF. This could represent progress towards an assessment that the majority of students find useful. Further studies are needed to determine if such an assessment can be modeled. Overall, these data may inform competency assessment for future medical school classes.

Primary Student Presenter: Tyler Okland

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Scott Mann

Poster Title: *DEGREE OF SOMATIZATION IN SIX COMMON OTOLARYNGOLOGY CHIEF COMPLAINTS*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

DEGREE OF SOMATIZATION IN SIX COMMON OTOLARYNGOLOGY CHIEF COMPLAINTS. TS Okland (B.S., SOM), and SE Mann (M.D.), Department of Medicine, University of Colorado, Denver, CO. A discrepancy often exists between the symptoms reported by patients and the presence of objective clinical findings. In the field of Otolaryngology, the common symptoms of dizziness, globus and tinnitus may cause significant suffering to the patient, but often have no evidence of disease by physical exam and testing. Many feel these subjective experiences could be a form of somatization, physical manifestations of emotional distress. Another common belief among physicians is that patients with somatization present with wide-ranging symptoms, and will have "pan-positive" results during a standard review of systems interview. In this study we sought to determine the objectivity of findings for six common ENT chief complaints—and also whether a relationship exists between number of positive responses during a review of systems and the presence of objective findings. To achieve these goals, we performed a retrospective chart review of 500 patients who came to ENT clinic at Denver Health over the past 2 years. We included patients complaining of globus, tinnitus, or dizziness (Group 1). We also included patients with a chief complaint of hearing loss, nasal obstruction and hoarseness (Group 2), which are chief complaints often associated with clear objective findings. We compared the clinical objective findings and the number of affirmative responses from a comprehensive 69-point review of systems form (ROS Score). Of the 204 patients in Group 1, only 19.6% were found to have significant objective findings, 45% marginal findings, and 35% had no objective findings. Of the 296 patients in Group 2, 66% were found to have significant objective findings, 24% marginal findings, and 9.5% no objective findings. However, when comparing the ROS score, there were no significant differences between the two groups. This suggests that although some chief complaints may have less objective findings than others, the degree of somatization may be similar across all common presenting symptoms. However, there was also a clear inverse relationship between the ROS score and the presence of clinical findings on physical exam. An excess number of affirmative responses during the review of systems predicted which patients were unlikely to have objective findings. It is important for physicians to understand and recognize when physical complaints may represent emotional distress. These patients would likely benefit most from reassurance and counseling rather than invasive or expensive testing.

Primary Student Presenter: Danielle Ostendorf

Additional Presenter(s): n/a

Presenting School: Public Health

Degree Seeking: PHD

Year: 3rd

Mentor: Victoria Catenacci

Poster Title: *PHYSICAL ACTIVITY AND WEIGHT LOSS MAINTENANCE*

Final Category: Education, Health Care and Public Health

Abstract:

PHYSICAL ACTIVTY AND WEIGHT LOSS MAINTENANCE: DM Ostendorf (Ph.D., CSPH), K Lyden, Z Pan, EL Melanson, HR Wyatt, JO Hill, and VA Catenacci, Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora CO High levels of moderate-to-vigorous physical activity (MVPA) are strongly correlated with long-term weight loss maintenance, however few studies have examined sedentary behavior in successful weight loss maintainers. Our aim was to compare free-living MVPA and sedentary behavior (SB) in subjects successful at weight loss maintenance as compared to normal weight and overweight/obese controls. 114 healthy adults age 18-65 wore the ActivPAL for 7 days and were categorized into three groups: 1) weight-loss maintainers (WLM, maintaining ≥13.6 kg weight loss for ≥1 y); 2) normal weight controls (NC, matched to current BMI of WLM) and 3) overweight/obese controls (OC, matched to pre-weight loss BMI of WLM). Subjects were excluded if criteria for a valid monitoring period were not met (≥3 weekdays and ≥1 weekend day with ≥10 hrs awake). 90 subjects were analyzed (30 WLM, 33 NC, and 27 OC). Age, gender, and ActivPAL wear time were similar across groups. Compared to OC, both WLM and NC spend a lower proportion of awake time in SB (WLM = 61% ± 9.3, NC = 64% ± 9.5, OC = 70% ± 7.5), and spend a higher proportion in light intensity activity (WLM = 30% ± 7.9, NC = 29% ± 8.3, OC = 25% ± 6.7). Compared to both NC and OC, WLM spend more minutes/day in total MVPA (WLM = 95 ± 40, NC = 69 ± 20 OC = 56 ± 20) and bouts of MVPA ≥10 minutes. Findings indicate that not only do WLM spend more time in MVPA than both OC and NC, but compared to OC, they also spend 8.5% (58 min/day) less time sedentary and 4.7% (55 min/day) more time in light activity. Our data indicate that it may be important to increase physical activity (light and MVPA) as well as decrease sedentary time in order to successfully achieve long-term weight loss maintenance.

Primary Student Presenter: Soliman Oushy

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Michael Graner

Poster Title: *GLIOBLASTOMA MULTIFORM-DERIVED EXOSOMES AS A TUMOR DRIVER IN NORMAL HUMAN ASTROCYTES*

Final Category: Cancer - Head, Neck, and Brain

Abstract:

GLIOBLASTOMA MULTIFORM-DERIVED EXOSOMES AS A TUMOR DRIVER IN NORMAL HUMAN ASTROCYTES. BACKGROUND/PURPOSE: Glioblastomas (GBMs) are devastating CNS tumors with abysmal prognoses (median survival < 15 months) amidst a sharply declining quality of life. Our current treatment strategies (maximal surgical resection, concurrent/adjuvant chemo-radiation) have barely altered the natural history of the disease in the past 20 years. We must re-examine GBM biology for novel approaches to disease processes and therapeutic targets. Research into extracellular vesicles (EVs) holds promise for developing and driving such new paradigms. EVs are cell-derived, membrane-enclosed nanospheres released extracellularly as a mean of cell-to-cell communication. EVs possess the capacity to dramatically alter recipient cell phenotypes in both normal cells and tumor cells towards the benefit of the tumor as seen in peripheral blood mononuclear cells (PBMCs). We will extend these analyses towards glial cells/astrocytes with the hypothesis that GBM EVs are able to drive epigenetic changes in normal astrocytes that convert those cells into phenotypically tumorigenic entities. DESIGN: Commercially available human astrocytes will be incubated with different quantities of EVs derived from various GBM/astrocytoma cells. The recipient astrocytes will be examined for cell surface protein changes by FACS, for phospho-signaling changes by antibody arrays, for protein changes by proteomics and Western blotting, for proliferation by MTS, clonogenic, and soft-agar assays, and for in vivo tumor growth in nude mice by subcutaneous and intracranial injections. SUMMARY OF RESULTS: astrocytes that were incubated in 2 different concentrations of glioma EVs were noted to have enhanced tumor-like signaling. Additionally, the astrocytes were noted to migrate in the presence of GBM EVs, as well as improved ability to survive in soft agar. CONCLUSION: Early data suggests that tumor EVs may cause astrocyte migration toward the tumor. Tumor EVs alter signaling pathways in a way that resembles the tumor itself. Generally, the result point to EVs as mean used by GBM to support a tumor microenvironment.

Primary Student Presenter: Grace Park

Additional Presenter(s): n/a

Presenting School: Pharmacy

Degree Seeking: PharmD

Year: 2nd

Mentor: Anne Libby

Poster Title: *PATIENT-LEVEL MEDICATION REGIMEN COMPLEXITY IN BIPOLAR DISORDER*

Final Category: Neuroscience 2

Abstract:

PATIENT-LEVEL MEDICATION REGIMEN COMPLEXITY IN BIPOLAR DISORDER Park, GS (PharmD, SOP); Libby, AM*; Hosokawa, PW; Lee, K; Hirsch, JD. Department of Clinical Pharmacy and Center for Pharmaceutical Outcomes Research, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, CO. To effectively control the episodic symptoms, prevent relapse, hospitalization, and minimize morbidity associated with bipolar disorder, polypharmacy has become remarkably common and is now the rule rather than the exception. The increasingly complex medication regimens can negatively impact adherence and adversely influence pharmacologic efficacy. This cross-sectional, retrospective study investigated patient level Medication Regimen Complexity Index (MRCI) in bipolar disorder. The prevalence cohort was comprised of ambulatory, adult patients ranging from 18-88 years of age diagnosed with bipolar disorder (N=80). A Medication Regimen Complexity (MRC) score was generated using the computerized tool for three medication categories: 1) bipolar mood stabilizing medications, 2) bipolar adjunctive medications, and 3) other medications. The patient-Medication Regimen Complexity Index (pMRCI) for the bipolar patient sample averages 17.78 (range 3-57.5). The defined bipolar adjunctive treatment and bipolar mood stabilizing MRCI average was 6.77 (range 2-21) and contributed to and contributed to 38.1% of the total pMRCI. Using the validated MRC tool the study is able to expand the medication list and look at features that influence patient adherence beyond the medication count.

Primary Student Presenter: Amelie Peisl

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Steven Abman

Poster Title: *Effects of Anti-sFlt-1 Monoclonal Antibody in Experimental Rat Models of Bronchopulmonary Dysplasia*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

Bronchopulmonary dysplasia (BPD), the chronic lung disease that follows respiratory therapy of preterm infants, is characterized by abnormal lung structure due to impaired alveolar and vascular growth. Antenatal factors, such as preeclampsia (PE), are associated with an increased risk for BPD, which may be due to increased soluble Flt-1 (sFlt-1; an endogenous VEGF inhibitor). Past studies have shown that a rat model of PE caused by intra-amniotic (IA) instillation of sFlt-1 decreases alveolar growth and causes pulmonary hypertension (PH) in infant rats. We hypothesized that antenatal treatment with a specific anti-sFlt-1 monoclonal antibody (MAb) would preserve normal lung growth and prevent PH in experimental PE. To address this hypothesis, we studied the effects of anti-sFLt-1 MAb treatment on lung structure and PH in infant rats after exposure to sFlt-1 or saline (controls) by IA instillation at 20 days gestation. Anti-sFlt-1 MAb (1.5 or 15 ug/sac) or saline were administered by IA instillation immediately after sFlt or saline treatment. Rat pups were delivered by c-section 2 days later. Animals were killed at 2 weeks of age for studies. Lungs were inflated and fixed with 4% paraformaldehyde for histology. Alveolarization was assessed by radial alveolar counts (RAC). Right ventricular hypertrophy (RVH) was assessed as the ratio of right ventricle to left ventricle plus septum weights. We found that at 2 weeks of age, sFlt-1 treated rats had reduced RAC by 45% and increased RVH by 50% ($p<0.01$ vs. controls for each value). Concurrent antenatal treatment with anti-sFlt-1 MAb preserved RAC and prevented RVH (p = NS vs. controls). These findings suggest that anti-sFLt-1 MAb treatment preserves normal lung structure and prevents PH in an antenatal model of BPD. We speculate that anti-sFlt-1 MAb therapy may provide a novel strategy for the prevention and treatment of BPD.

Primary Student Presenter: Mario Perez

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Eric Schmidt

Poster Title: *IN VIVO MEASUREMENT OF MOUSE ENDOTHELIAL SURFACE LAYER IN SURFACE CORTICAL MICROVASCULATURE*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

Sepsis, a systemic inflammatory response to infection, is the most common cause of in-hospital mortality in the US. Sepsis survivors often demonstrate chronic neurocognitive dysfunction. However, little is known about the mechanisms underlying the development of neurocognitive dysfunction during sepsis. We previously demonstrated that septic lung and kidney injury is mediated by degradation of the endothelial surface layer (ESL), a thick glycosaminoglycan-rich layer lining the pulmonary and glomerular microcirculation, respectively. We now postulate that degradation of the neurovascular ESL may contribute to septic neurocognitive dysfunction. To pursue this, we adapted a surgical approach to in vivo brain confocal microscopy that allows for direct visualization of the ESL in surface cortical microvasculature. We placed a cranial window in anesthetized mice. After allowing for 4 days of recovery, we re-anesthetized mice and administered an IV bolus of FITC-labeled 150 kDa dextran (excluded by the ESL), followed by TRITC-labeled 40 kDa dextran (inclusive of the ESL). Using an in-focus frame, we identified surface cortical microvessels (< 20 μm diameter); at least 3 microvessels are typically found on a single frame. We performed in vivo confocal microscopy through the cranial window, simultaneously measuring TRITC and FITC microvessel widths. Assuming equal ESL thickness at both edges of the vessel, the ESL size is defined by one-half the difference between TRICT- and FITC-dextran vascular widths. After measurement of baseline ESL thickness, mice were injected with lipopolysaccharide (LPS) to model sepsis. ESL thickness was followed every 30 min thereafter. The baseline ESL thickness of surface cortical microvessels was 0.51 μm, which was less than we previously observed in lungs (1.67 μm) but similar to that of systemic vessels (0.6 – 0.7 μm). Endotoxemia led to a rapid loss of ESL thickness (0.08 μm vs. 0.71 μm 30 min after LPS or saline, respectively).

Primary Student Presenter: Angela Philippus

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: Other (please specify)

Year: 1st

Mentor: David Mellick

Poster Title: *IMPACT OF RELIGIOUS ATTENDANCE ON PSYCHOSOCIAL OUTCOMES FOR INDIVIDUALS WITH TRAUMATIC BRAIN INJURY*

Final Category: Neuroscience 2

Abstract:

IMPACT OF RELIGIOUS ATTENDANCE ON PSYCHOSOCIAL OUTCOMES FOR INDIVIDUALS WITH TRAUMATIC BRAIN INJURY. Philippus, A (MSCS, GS), Mellick, D, Dreer, L, Novack, T, Guller Bodien, Y, Giacino, J, O'Neil-Pirozzi, T, Bergquist, T, and Sander, A, Craig Hospital, Englewood, CO, University of Alabama, Birmingham, AL, Spaulding-Harvard, Boston, MA, Mayo Clinic, Rochester, and TIRR Memorial Hermann, Houston, TX Objectives: Identify demographic characteristics of individuals with traumatic brain injury (TBI) who attend religious services. Understand the relationship between attending religious services and psychosocial outcomes. Examine the independent contribution of religious service attendance to selected psychosocial outcomes while controlling for demographic characteristics at 1-, 5-, and 10-years post injury. Design: Retrospective, secondary analysis Participants: Individuals with TBI living in a private residence who completed a 1-, 5-, or 10-year follow-up phone interview between 10/01/2007 and 10/01/2012; interviews were excluded if completed by proxy or had missing religious service attendance data. A total of 5,573 interviews were analyzed. Main Outcome Measures: Satisfaction with Life Scale (SWLS), Generalized Anxiety Disorder (GAD-7), Patient Health Questionnaire (PHQ-9), PART-O Social Results: Individuals who attended religious services were more likely to be older, identify with a minority status, married, and live in a southern state. Backward stepwise regressions controlling for demographic characteristics were conducted for each outcome at each follow-up period. Analysis revealed a significant, yet small (<1%), unique contribution of attendance at religious services at each time point with the exception of GAD-7 at years 1 and 10. Conclusion: Results demonstrate an association between religious attendance and greater life satisfaction, fewer depressive symptoms, and more frequent social participation for individuals with TBI.

Primary Student Presenter: Haseeb Rahat

Additional Presenter(s): n/a

Presenting School: Other (please specify)

Degree Seeking: Other (please specify)

Year: 4th

Mentor: Stephanie Hsu

Poster Title: *ADRENAL INSUFFICIENCY AND SWALLOWED TOPICAL STEROID TREATMENT OF PEDIATRIC EOSINOPHILIC ESOPHAGITIS*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

Purpose: The aims of our study were to determine how often Adrenal Insufficiency (AI) occurs with chronic Swallowed Topical Steroids (STS) use and to document co-morbid features. Methods Used: We instituted a quality improvement program in our multi-disciplinary Gastrointestinal Eosinophilic Diseases Program to increase awareness of potential chronic STS side effects. Initially, we completed a retrospective analysis of all STS-treated Eosinophilic Esophagitis (EoE) patients seen in the program from 2007 to 2013 and documented how many had an abnormal a.m. cortisol level. This group was labeled as our retrospective group (RG). Cortisol levels measured in a fasting state and drawn between 7 am and 9 am were accepted as valid. As a part of standard of care, we then prospectively measured morning cortisol levels of EoE children treated with STS for over four months. This group was labeled as our prospective group (PG). If two cortisol levels were <5 mcg/dl, then an ACTH stimulation test was performed in order to test for AI. A peak cortisol level of <18 mcg/dl was diagnostic for AI. Summary of Results: Our RG consisted of 166 children. Of these patients, 8 had a morning cortisol drawn, 2 of which were abnormal. One child had an abnormal ACTH stimulation test and was diagnosed with AI. Our PG consisted of 225 children, out of which 106 had a morning cortisol drawn. Of the 106 children, 33 had a normal cortisol (>10 mcg/dI), 45 had an intermediate cortisol (5-10 mcg/dI) and 28 had an abnormal cortisol (<5 mcg/dI). Of this last group, 3 had AI based on their ACTH stimulation test results. None of these 3 patients had clinical features of AI prior to, or after, the AI diagnosis (i.e. fatigue, hypoglycemia, hypotension or cushingoid appearance). BMI percentiles ranged from 43% to 54%, height percentiles ranged from 1% to 49%. All 3 AI patients had been treated with STS as well as with other steroid treatments for asthma and allergic rhinitis. When comparing the RG to the PG, we found that patients were similar in age, sex, and the number of steroid modalities used. More than 70% of patients in both RG & PG groups were males; More than 50% used Fluticasone as STS treatment. Conclusions: A small fraction of children with EoE treated with STS had biochemical evidence of AI.

Primary Student Presenter: Nathan Riechers

Additional Presenter(s): Aubrae Isenhart; Paola Casillas; Eric Webster

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Janet Meredith

Poster Title: *Working to End Teenage Obesity*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

"Working to End Teenage Obesity" examines conversations between healthcare providers and teens surrounding body image and weight. The childhood obesity epidemic results in immediate physical and emotional effects for teens as well as costly long-term health consequences. We hypothesize that teens must be engaged in conversations in ways different than adults, and that dialogue is a crucial component of success. The direct input from teens makes this project novel, with equivalent studies lacking. Methods include a teenager advisory board, focus groups, and qualitative analysis of data. This study is approved via IRB protocol 13-1670. The Teenage Advisory Board is a group of multi-racial community volunteers who helped develop teenager-approved surveys and focus group protocols. Four focus groups have been completed thus far: two female groups (one multi-racial and one Latina group) and two male groups (one multi-racial and one Latino group). Through discussion and surveys, teens relayed their perspective surrounding body image and weight loss, and also shared their experiences discussing weight problems with health care providers. The conversations were recorded and transcribed, with qualitative analysis ongoing. Topline analysis reveals teen recommendations on opening the conversation, tapping into individual motivations, setting realistic expectations, providing relevant and specific suggestions, and demonstrating sincere interest in what the teen is sharing. Future focus groups will include different teen populations, and results will be organized for dissemination to healthcare providers. Additionally, we are developing a survey to distribute among healthcare providers to more fully understand their perspective on conversations with teens about weight. We hope this research will help revitalize the dialogue occurring between teens and their healthcare providers and, ultimately, lead to improved health outcomes in the community.

Primary Student Presenter: Kelli Robertson

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: S. Gail Eckhardt

Poster Title: *PRECLINICAL EVALUATION OF THE TRANSLATIONAL INHIBITOR SVC112 IN COLORECTAL CANCER*

Final Category: Cancer - Below the neck and skin

Abstract:

PRECLINICAL EVALUATION OF THE TRANSLATIONAL INHIBITOR SVC112 IN COLORECTAL CANCER. KM Robertson (MD, SOM), PJ Klauck, JJ Tentler, SM Bagby, TM Pitts, TT Su, SG Eckhardt, University of Colorado School of Medicine. Colorectal cancer (CRC) ranks third in new cases and cancer deaths in the U.S. annually. Current frontline treatments for metastatic CRC (mCRC) are ineffective for an appreciable proportion of patients and cause significant toxicities. Thus, there is an urgent need for the development of new therapeutic strategies. Eukaryotic elongation factor 2 (eEF2) is often overexpressed in CRC causing upregulation of translation, upon which CRC may be dependent. Therefore, it may be possible to differentially target CRC cells vs normal cells by inhibiting translation. SVC112 is a novel inhibitor of translation through its ability to lock eEF2 on the ribosome. As such, this agent may be effective against mCRC by blocking translation of key oncogenes such as c-myc. 44 CRC cell lines were exposed to SVC112 and in vitro viability was quantified by CellTiter Glo. Immunoblotting was performed to assess c-myc and cyclin D1 levels in response to treatment with SVC112. Amino acid incorporation was assessed using the Click-IT AHA kit protocol. Two cell line xenograft models were treated with SVC112. A subset of CRC cell lines were determined to be sensitive to SVC112 in vitro. In these cell lines, c-myc is downregulated by SVC112 in a dose-dependent manner and there was a reduction in amino acid incorporation not seen in resistant cell lines. However, SVC112 has yet to show efficacy in vivo with the experimental dosing regimen. SVC112 shows anti-cancer effects in a subset of CRC cell lines. Resistance to SVC112 in vitro is due to the inability of SVC112 to bind to the drug target as it does not downregulate translation in resistant cell lines. Further analysis of SVC112 binding to the ribosome will be conducted. Additionally, different dosing regimens in vivo may be warranted.

Primary Student Presenter: Thomas Rogers

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 4th

Mentor: Jennifer Richer

Poster Title: *Targeting a Kynurenine-Driven Autocrine Loop to Block Triple-Negative Breast Cancer Metastasis*

Final Category: Cancer - Below the neck and skin

Abstract:

Title: Targeting a Kynurenine-Driven Autocrine Loop to Block Triple-Negative Breast Cancer Metastasis Authors: Thomas Rogers, Jennifer Richer (Dept. of Pathology) Background: Resistance to "anoikis" or detachment-induced apoptosis, is critical for metastasis, facilitating survival of carcinoma cells in transit. Anoikis resistance may contribute to the high propensity of triple-negative breast cancer (TNBC) to rapidly metastasize. Methods: Global gene expression was assessed in TNBC cells in attached versus forced-suspension culture. In addition, global metabolomics of intracellular and secreted metabolites produced by attached or suspended cells was performed using UPLC-MS. Aryl hydrocarbon receptor (AhR) activity was measured using a luciferase reporter and qRT-PCR for endogenous AhR target genes. Results: Profiling of TNBC cells in attached versus forced-suspension culture revealed significant upregulation of AhR itself and downstream targets including CYP1B1. Recently, activation of AhR via the tryptophan metabolite kynurenine (Kyn) has been found to promote brain tumor growth and motility. Interestingly, genes involved in the Kyn pathway, including the rate limiting enzyme tryptophan-2,3-dioxygenase (TDO2), were upregulated in suspended TNBC cells. Metabolite analysis identified a significant increase in Kyn levels in suspended TNBC cells. Therefore, I proposed that upregulated Kyn-AhR signaling promotes anoikis resistance and metastasis of TNBC. Indeed, pharmacological inhibition of TDO2 reduced Kyn production and Kyn-mediated AhR activation in suspended TNBC cells, resulting in reduced survival in suspension. Importantly, TDO2 inhibition significantly decreased lung colonization and outgrowth in vivo. Conclusions: Increased Kyn-AhR signaling may contribute to the TNBC metastasis. Thus, inhibiting TDO2-mediated Kyn production may provide a targeted therapeutic strategy to reduce mortality from this aggressive form of breast cancer.

Primary Student Presenter: Phillip Ross

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Frederic Deleyiannis

Poster Title: *Head Loss As an Explanation of the Steal Phenomenon in Microvascular Surgery*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

Vascular steal has been cited to help explain end-organ ischemia after microvascular reconstruction. Attempts to clarify a mechanism of vascular steal have been made by modeling blood circulation after a simple electrical circuit, suggesting that the free flap provides a path of least resistance for blood flow and thereby compromises end-organ perfusion. We present a case of a posterior medial thigh perforator flap for the reconstruction of a diabetic foot ulcer in a patient with a single vessel providing inflow to the foot. In the context of this case, we provide a novel explanation for the steal phenomenon using the Hagen-Poiseuille law and the property of head loss in fluid dynamics and discuss how the vessel size of the free flap may contribute to a steal phenomenon.

Primary Student Presenter: Ivan Rudenko

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Robert Eckel

Poster Title: *ROLE OF LIPOPROTEIN LIPASE IN NEURONS OF THE BRAIN.*

Final Category: Metabolism, Endocrinology, Pharmacology, Physiology

Abstract:

Authors: Ivan Rudenko, Kimberly Bruce, Hong Wang, Robert Eckel. Purpose of the study: Lipid metabolism in the brain has been implicated in a number of pathological processes including neurodegenerative disease and impaired energy homeostasis. Lipoprotein lipase (LPL) plays a key role in peripheral lipid metabolism by hydrolyzing lipoprotein-derived triglycerides and facilitating free fatty acid uptake, but its role in the brain is less clear. Previously our lab has shown that mice lacking neuronal LPL develop poor cognitive function and obesity, however the molecular mechanisms underlying these phenotypes are unknown. In this study we aim to characterize LPL's role in neuronal function by developing high resolution imaging techniques that accurately measure neuronal lipid accumulation. Methods Used: To determine the function of LPL in the neurons we utilized mHypoE41 (N41) immortalized mouse hypothalamic neurons with variable expression of LPL. N41 cells overexpressing LPL were created by infection of cells with murine stem-cell retrovirus carrying a control or mouse LPL cDNA construct. N41 LPL knockdown cells were created by infection of cells with lentivirus carrying a control or a construct coding for shRNA against the LPL gene. Third Harmonic Generation and AdiporedTM staining were used for imaging of lipid droplets in the cells. ImageJ software was used to quantify the lipid droplets. Summary of Results: N41 LPL overexpressing cells showed a 2-fold increase in number of lipid droplets. N41 LPL knockdown cells showed a 2-fold reduction in number of lipid droplets. Interestingly, while the number of droplets was increased the lipid droplet volume was not significantly different in either cell line. Conclusion: We used a combination of Third Harmonic Generation and AdiporedTM to validate the presence of lipid droplets in individual cells and in the future we will utilize the technique that provides the most robust results in the in vivo setting. We demonstrated that LPL is involved in lipid droplet accumulation in cultured immortalized mouse hypothalamic neurons. However, an in vitro system is not an accurate representation of neuronal microenvironment, which is influenced by the presence of glial cells. Our next step is to utilize viral stereotaxic injections to analyze the function of LPL in neurons of specific brain nuclei to gain critical insights into the pathophysiology/neuronal origins of cognitive and metabolic disorders.

Primary Student Presenter: Anna Schreiber

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: John Arcaroli

Poster Title: *EVALUATION OF MLN0264 AS A NOVEL THERAPY FOR PANCREATIC CANCER*

Final Category: Cancer - Below the neck and skin

Abstract:

Authors: AR Schreiber (MD Candidate, SOM), SM Bagby, AA Nguyen, KS Quackenbush, WA Messersmith, JJ Arcaroli Author's Affiliations: University of Colorado School of Medicine Purpose of Study: Pancreatic adenocarcinoma (PDAC) is the fourth leading cause of cancer deaths annually. Current therapies only minimally improve overall survival, indicating that newer treatments for this devastating disease are urgently needed. An emerging class of targeted cell based biotherapeutics known as antibody drug conjugates (ADC) are currently being developed for the treatment of cancer. MLN0264, a novel ADC that targets guanylyl cyclase C (GCC), consists of a fully human anti-GCC monoclonal antibody conjugated to the cytotoxic microtubule disrupting agent monomethyl auristatin E (MMAE) via a protease cleavable linker (linker/toxin technology licensed from Seattle Genetics). The objective of this study was to determine the efficacy of MLN0264 as a potential target specific agent for the treatment of pancreatic cancer. Methods Used: Seven unique pancreas cancer explants were treated with MLN0264 and treatment responses were determined after 28 days. Tumor size was evaluated twice per week by caliper measurements. Sensitivity to MLN0264 was defined as having a tumor growth inhibition index (TGII) of ≤ to 20%. Expression of p53, CHK2 and GCC was evaluated by immunoblotting. Summary of Results: Three of seven explants showed sensitivity to MLN0264. Evaluation of the effects of MLN0264 revealed a significant increase in p53 and CHK2 activation following treatment in the Panc 150 sensitive tumor. A marked increase in GCC expression was observed in tumor tissue when compared to matching normal tissue. Conclusions: Preliminary results show that MLN0264 has good activity in pancreas tumor explants. These findings support further investigation of MLN0264 for the treatment of pancreatic cancer. Acknowledgements: Takeda

Primary Student Presenter: Katherine Shives

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 5th

Mentor: David Beckham

Poster Title: *Defining how the host mTOR pathway supports viral replication*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

Defining how the host mTOR pathway supports viral replication All viruses are known to be obligate intracellular parasites that are highly dependent upon host factors in order to complete their lifecycles. . Flaviviruses are a group of clinically-important human pathogens including Dengue virus and Japanese encephalitis virus. These (+) sense, 5' capped, single-stranded RNA viruses have limited coding capacity and are therefore obligated to co-opt numerous cellular factors in order to translate their genomes effectively. Our previous work has shown that WNV infection induces the activation of the translational regulator mechanistic target of rapamycin (mTOR). MTOR is a highly evolutionarily conserved serine/threonine kinase that controls vital anabolic and catabolic cellular responses such as protein synthesis and autophagy, respectively. Following inducible genetic knock-out of Raptor, the major mTOR complex 1 (mTORC1) co-factor, we show that mTORC1 supports flavivirus and alphavirus (Chikungunya virus) protein synthesis, but not the translation of the non-capped RNA virus encephalomyocarditis virus (EMCV). This data suggests that WNV utilizes the host mTOR signaling pathway to enhance cap-dependent translation of the viral genome. MTOR governs cap-dependent translation initiation signals through the effector kinase S6K as well as the eIF4E binding protein (4EBP). By utilizing cell lines with stable knockouts of these host factors, we show WNV does indeed require the mTORC1 effector 4EBP for efficient viral growth, while the S6K pathway does not contribute to translation of the WNV genome. Viral growth is further dependent upon formation of the eIF4F pre-initiation complex, as the use of biochemical inhibitors that prevent eIF4F complex formation also results in a significant inhibition of WNV, but not EMCV, growth. In sum, these results demonstrate the central role of the host mTOR pathway in supporting the translation of capped RNA viruses such as WNV.

Primary Student Presenter: Lynelle Smith

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jennifer Richer

Poster Title: *LIPOPLEX DELIVERY OF MICRO-RNA 200C TO OVARIAN CANCER CELLS*

Final Category: Cancer - Below the neck and skin

Abstract:

Ovarian cancer metastasizes by cell shedding and direct seeding to other sites within the peritoneal cavity. Essential steps in the metastatic cascade include the epithelial to mesenchymal transition (EMT) and resistance to anoikis (detachment-induced cell death). Our lab determined that restoration of miR-200c, a non-coding microRNA, decreased ovarian cancer progression by reversing EMT, increasing anoikis sensitivity and also increasing sensitivity to taxane chemotherapeutics. We hypothesize that delivery of miR-200c via direct intraperitoneal injection can be used as an adjuvant to traditional chemotherapeutics to increase anoikis, decrease metastasis, and lower tumor burden. Lipolexes are synthesized from naturally occurring lipid compounds, and can serve as low toxicity delivery vehicles for miR-200c and have the potential to be used in human therapy. We examined the effects of lipoplex-mediated delivery of miR-200c to ovarian cancer cells. The ovarian cancer cell lines HEY and OV-1847 were treated in vitro with 100nM of miR-200c lipoplexes for 48, 72, and 96 hours. We tested four formulations of lipoplex for efficiency of delivery. Gene expression of miR200c and downstream targets were measured by qRT-PCR. Migration/invasion were assessed using an Xcelligence Real-Time Cell Analyzer, and apoptosis/anoikis was measured by Caspase 3/7 assay. Transfection of ovarian cancer cells with lipoplexes containing miR-200c resulted in approximately a 1,000-fold increase of miR-200c levels ($p<0.0001$) as well as expression changes in downstream targets, including ZEB1 and ESRP1. Changes in expression were most significant at time points greater than 72 hours. The formulations did not show equally potent delivery of miR-200c. Cells treated with miR-200c had decreased ability to migrate and invade compared to negative control cells. Finally, the miR-200c treated cells had increased anoikis as measured by Caspase 3/7 assay. The miR-200c lipolex delivery method is effective at introducing miR-200c at high levels and subsequently altering downstream targets and affecting cancer-related cellular functions. Based on the results of the in vitro studies we plan on testing this delivery method in vivo in conjunction with taxane chemotherapy.

Primary Student Presenter: Aria Vaishnavi

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 5th

Mentor: Robert Doebele

Poster Title: *Adaptive survival signaling in oncogenic fusion kinase addicted NSCLC*

Final Category: Cancer - Below the neck and skin

Abstract:

Gene fusions involving the proto-oncogenes ALK, ROS1, RET and NTRK1 are established or potential drug targets in cancer. Although targeted kinase inhibitors induce significant tumor shrinkage, complete patient responses are rare, and it is from that residual tumor burden that drug resistant clones eventually emerge. We have previously shown a role for WT EGFR signaling in ROS1+ cancer cells and their drug resistant derivatives. We hypothesized that EGFR performs a similar role in cancer cells harboring other gene fusions. Stimulation of NSCLC cells that harbor an oncogenic fusion with EGF not only increased downstream signaling, but also rapidly increased phosphorylation of the fusion kinase itself. Additionally, EGFR signaling can dictate the engagement of different downstream signaling effectors, diversifying the signaling and cell fate responses in certain cancer cells. Proximity ligation assays (PLA) were employed to visualize wild-type EGFR-GRB2 signaling complexes in NSCLC cells driven by an oncogenic fusion kinase. We observed two modes of EGFR-GRB2 complex formation, the first in unperturbed cells, and the second only when the fusion kinase was inhibited. The kinetics of the induction of EGFR-GRB2 signaling revealed EGFR can take over the signaling in these cells as quickly as 5 minutes, and this kinase inhibitor-induced rewiring can be reversed by simply washing out the drug, suggesting a preference for the fusion kinase in the signaling circuit of these cells. Analysis of fusion-positive patient samples acquired at the time of progressive disease from treatment with an oncogene targeted monotherapy revealed the presence of EGFR-GRB2 signaling complexes. Additional analyses of patient samples revealed evidence of potentially non-cell autonomous responses to these therapies that may enable the survival of cells that would otherwise be drug-sensitive. The combination of a fusion kinase inhibitor with anti-EGFR therapy provided superior blockage of EGFR and ALK signaling complexes, as well as improved reduction in tumor volume and prolonged survival in an ALK+ xenograft model. Collectively, these results demonstrate a previously unknown role for an unmutated kinase, EGFR, in modulating the oncogenic phenotype in cells addicted to oncogenic fusion kinases. The activation of the EGFR signaling pathway can quantitatively augment fusion kinase signaling, but also diversify it by regulating the engagement of alternate signaling effector proteins. This data provides evidence for a novel role for EGFR as an oncorequisite signaling partner in certain cancer cell populations that harbor an oncogenic fusion kinase. Combination therapy of a fusion kinase targeted inhibitor with anti-EGFR therapy may improve initial tumor cell killing, and delay or prevent the onset of drug resistance in these patient populations.

Primary Student Presenter: Brian Walsh

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Joseph Sakai

Poster Title: *Association of Default Mode Network Activity with Externalizing Behavior Problems in Adolescents with and without Callous Unemotional Traits*

Final Category: Neuroscience 1

Abstract:

Introduction: Adolescents with externalizing behavior problems such as conduct and substance use disorders (CD/SUD) are a source of large social costs. Recent work supports that youths with high levels of callous-unemotional (CU) traits are a distinct CD subgroup. We tested whether activity of the default mode network (DMN), a functional brain network involved in self-reflective thought, empathy, and foresight, is associated with these disorders. Methods: We collected 6 minutes of resting state fMRI for 20 patients with CD/SUD and CU, 21 patients with CD/SUD without CU, and 22 controls. We used independent component analysis to identify networks (clusters of voxels active together across time). We utilized a standard template and spatial correlation to select the DMN. We tested: (1) whether the 3 groups differed significantly in DMN activity, (2) whether DMN activity was associated with severity of externalizing behavior problems in patients, and (3) whether DMN activity was associated with CU trait severity in patients. Results: Three-group comparisons revealed differences in the posterior cingulate cortex (PCC) and precuneus (Brodmann area (BA) 31). Two-group comparisons showed that both patient groups had significantly less activation in this cluster compared to controls. Our within-patient analysis showed that severity of externalizing behavior problems was negatively associated with activity of the ventral and dorsal anterior cingulate areas (BA24/32), and positively associated with activity in the PCC. Finally, severity of CU traits in patients was negatively associated with activity in the inferior parietal lobule (BA40). Conclusions: While both patient groups, regardless of CU, showed less activity in the DMN (BA31), higher levels of CU trait were associated with a distinct pattern of hypo-activity within patients.

Primary Student Presenter: Emily Warnock

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Antonio Jimeno

Poster Title: *IMMUNOLOGIC PROFILE OF HEAD AND NECK SQUAMOUS CELL CARCINOMA CANCER STEM CELLS*

Final Category: Cancer - Head, Neck, and Brain

Abstract:

Purpose of Study: Head and neck squamous cell carcinoma (HNSCC) frequently recurs and metastasizes via cancer stem cells (CSCs). The present study aims to elucidate the immunologic profile of HNSCC CSCs in tissue stroma both in primary tumor sites and metastatic lymph nodes, and to correlate to clinical data.

Methods: We have assembled a tissue bank with over 500 samples of HNSCC, in which a subset of cases have primary cancer and lymph node metastasis samples to compare. In a first set of 10 samples, serial tissue sections were stained for cell markers by IHC including ALDH1, CD44, SOX2, S6K, PD-L1, PD-1, CD3, CD4, CD8, CD19, CD25, CD45, CD56, CD68, CD151. Layered image arrays for each case allow for direct comparison of relative expression. Quantification of a particular stain is performed optically by gating for the stain's color and intensity, thereby selecting all the pixels within the region of interest that fall within the defined limits, as shown in Figure 1. This data was then correlated to clinical data, including tumor staging at presentation and survival data.

Summary of Results: Comparing tumor cells' expression of PDL1 with CD4 lymphocyte infiltration in and around primary HNSCC tumor showed a significant direct correlation between PDL1 and CD4 expression as shown by the scatterplot in Figure 2 (Spearman coefficient 0.598, p=0.002). However, this relationship was only seen in the HNSCCs that had high expression of SOX2 (Spearman coefficient 0.929, p=0.0009, N=8) but not those with low SOX2 expression (Spearman coefficient 0.143, p=0.6, N=16).

Conclusions: Our early data suggests that SOX2 expression is related to PDL1 expression, and increased T-regulatory (CD4) expression. Our workflow enables high-throughput, integrative analyses of multiple tissue factors.

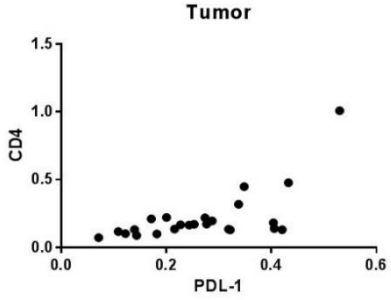

Figure 1. Scatter plot showing relationship of PDL1 expression (percent of image pixels positive) and CD4 lymphocyte infiltration (as measured by percent image pixels).

Primary Student Presenter: Seth Welsh

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: PHD

Year: 6th

Mentor: Jim Hagman

Poster Title: *DOUBLE TROUBLE: FUNCTIONAL ANALYSIS OF A NOVEL ONCOPROTEIN IN B CELL ACUTE LYMPHOBLASTIC LEUKEMIA.*

Final Category: Hematology and Oncology - Blood and General Mechanisms

Abstract:

DOUBLE TROUBLE: FUNCTIONAL ANALYSIS OF A NOVEL ONCOPROTEIN IN B CELL ACUTE LYMPHOBLASTIC LEUKEMIA. Welsh, SJ1, KG Roberts2, CG Mullighan2, and J Hagman1,3. 1Molecular Biology Program, University of Colorado School of Medicine, Aurora, CO. 2Department of Pathology, St. Jude Children's Research Hospital, Memphis, TN. 3Department of Biomedical Research, National Jewish Health, Denver, CO. Genomic sequencing has revealed that B cell Acute Lymphoblastic Leukemia (B-ALL) is a heterogeneous disease. Multiple gene alterations disrupt regulators of B cell development such as the tumor suppressor Early B cell Factor 1 (EBF1). EBF1 regulates >500 genes and is essential for normal B cell development. Genomic deletions resulting in fusion of the nearly complete EBF1 gene with the 3' half of the Platelet-Derived Growth Factor Receptor β gene (EBF1:PDGFRB) were identified in a subset of high risk B-ALL. The resulting fusion protein unifies two drivers of leukemogenesis: (1) loss of hematopoietic differentiation (EBF1 function) and (2) gain of a proliferative advantage due to the unregulated Receptor Tyrosine Kinase (RTK) activity of PDGFRβ. Patients with this fusion have been treated with the tyrosine kinase inhibitor imatinib with moderate success, although the likelihood of relapse has not been determined. Here, we uncover novel molecular mechanisms that contribute to EBF1-associated pediatric B-ALL. Our laboratory has utilized biochemical, cell-based, and fluorescent microscopy approaches to study DNA binding, transcriptional regulation, protein stability and localization of the EBF1:PDGFRβ protein in B cells. EBF1:PDGFRβ transforms progenitor lymphoid cells by removing their dependence on IL-7. Unexpectedly, EBF1:PDGFRβ localizes in the cytosol of transduced B cell progenitors and this localization is dependent upon its transmembrane (TM) domain. Our data suggests the TM domain of EBF1:PDGFRβ could serve as a therapeutic target to supplement kinase inactivating drugs.

Primary Student Presenter: Thomas Wong

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Mary Jesse

Poster Title: *Upsloping lateral sourcil: A novel radiographic finding in clinically unstable hips*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

Hip dysplasia is a phenomenon where insufficiency of the acetabular roof results in pain, hip instability, and early osteoarthrosis. While radiographic findings of frank dysplasia are well defined, there is a lack of diagnostic criteria for patients with radiographically "normal" hips who have borderline morphologic deficit and clinical instability. In this study, we evaluate the upsloping lateral sourcil as a novel radiographic finding in the evaluation of these patients. 316 patient charts were reviewed, including the earliest possible AP-pelvis radiographs with confirmed standard quality parameters. Lateral center edge angles (LCE) were measured bilaterally, upsloping lateral sourcils were documented, and clinical instability was elucidated from notes provided by a hip preservation surgeon. Patients were segmented into the following subgroups: dysplastic (LCE<20 degrees), borderline dysplastic (LCE=20-25 degrees), normal (LCE=25-40 degrees), and pincer (LCE >40 degrees). Chi-square statistical analysis was performed to evaluate the association of the radiographic upsloping lateral sourcil with the degree of dysplasia and the presence of clinical hip instability. Our review consisted of 104 males (32.9%) and 212 females (67.1%), with a mean age of 34y. 49 patients were excluded from analysis due to lack of imaging or for having gross dysplastic deformity, such as femoral head subluxation. Findings are summarized in Figure 1. Of the hips displaying upsloping sourcils, 77.9% had clinical instability (p-value = 0.0258). The upsloping sourcil is a novel radiographic finding that may be useful in identifying patients with borderline hip dysplasia and hip instability. We feel that incorporation of this finding into the assessment of the painful hip will allow for an earlier and more accurate identification of at-risk patients and help to guide treatment.

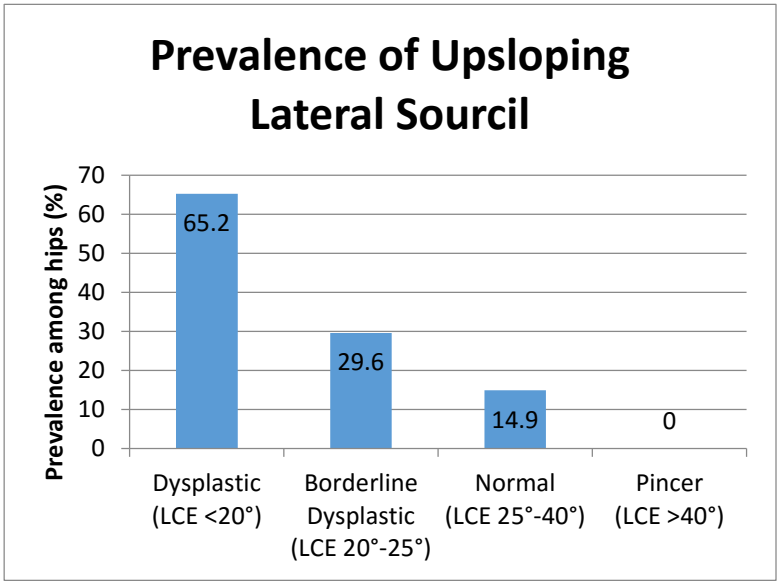

Figure 1

Primary Student Presenter: Mellisa Wu

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Edward Janoff

Poster Title: *ROLE OF IgG SUBCLASSES IN MUCOSAL DEFENSE OF STREPTOCOCCUS PNEUMONIAE*

Final Category: Pulmonology, Microbiology, Infectious Disease, and Critical Care

Abstract:

ROLE OF IgG SUBCLASSES IN MUCOSAL DEFENSE OF STREPTOCOCCUS PNEUMONIAE Unlike the 13-valent Pneumococcal Conjugate Vaccine, the 23-valent Pneumococcal Polysaccharide Vaccine (PVAX23) has not shown pneumonia protection, suggesting the two vaccines may elicit different immunological responses, such as ratios of IgG subclasses. Bronchial alveolar fluid (BAL) and blood samples were acquired from 11 patients with varying smoking status. Using enzyme linked immunosorbent assays, the quantity of IgG1 and IgG2 were measured before and after vaccination. Results showed an increase of IgG1 and IgG2 in serum and BAL fluids, a decrease of IgG2:IgG1 ratio specific to pneumococcal polysaccharide, and an increase in the IgG2:IgG1 ratio in BAL fluids after vaccination. PVAX23 elicits a stronger IgG1 response relative to IgG2 paradoxical IgG2:IgG1 ratio in BAL fluids compared to serum suggest a selective transport for IgG2 from serum across the epithelial layer to the lungs.

Primary Student Presenter: Jingjing Yu

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Xiao-Jing Wang

Poster Title: *Role of TGF-β in regulating inflammation and angiogenesis in Smad4 deficient HNSCCs*

Final Category: Cancer - Head, Neck, and Brain

Abstract:

ROLE OF TRANSFORMING GROWTH FACTOR-β IN MEDIATING INFLAMMATION AND ANGIOGENESIS IN SMAD4 DEFICIENT HEAD AND NECK SQUAMOUS CELL CARCINOMAS. J Yu, (M.D.), A Hernandez and XJ Wang, Department of Pathology, University of Colorado, Denver, CO. Purpose of study: Stromal overexpression of transforming growth factor-beta (TGF- β) is observed in Smad4 deficient head and neck squamous cell carcinomas (HNSCCs) and is known to upregulate inflammation and angiogenesis. Our preliminary studies in Smad4 deficient HNSCC mice have revealed that inhibition of the TGF-β receptor (TGF- βR) did not affect tumor growth but did significantly decrease the number of metastatic lesions. We aim to elucidate the specific mechanisms by which TGF- β signaling promotes this metastatic phenotype of Smad4 deficient HNSCCs. We hypothesize that Smad4 deficient tumors overexpress TGF-β to create an inflammatory microenvironment and promote angiogenesis to drive tumor progression in vivo. Methods: Nude mice were flank injected subcutaneously with Smad4 deficient SCC cells and treated with either a TGF- βR inhibitor (n=5) or a vehicle control (n=6) once primary tumors reached 1mm3. Frozen sections of the primary tumor were analyzed using immunofluorescence. We probed for leukocyte marker CD45, macrophage marker F480, myeloid derived suppressor cell (MDSC) markers CD11b and Ly6G, and endothelial cell marker CD31. Results: Smad4 deficient SCCs treated with the TGF- βR inhibitor showed a decrease in CD45+ leukocytes and CD11b+/Ly6G+ MDSCs compared to the vehicle control group. However, there was no significant difference in F480+ macrophages. There was also no significant difference in angiogenesis as measured by the number of blood vessels/mm2 and the percentage area of the tumor covered by blood vessels. Conclusions: Smad4 deficient SCC tumors treated with the TGF- βR inhibitor showed a decrease in leukocytes, specifically MDSCs, suggesting TGF-β plays a role in mediating inflammation in the stromal environment. Although there was no difference in the total number of macrophages, a subtype of macrophages such as M1 or M2 macrophages could also be responsible for the difference in leukocytes we observed. We would like to examine different macrophage subtypes in the same Smad4 deficient SCC tumors from TGF- βR inhibitor treated mice and the vehicle controls to investigate further the role of TGF-β in promoting tumor progression.

Primary Student Presenter: Jingjing Zhang

Additional Presenter(s): n/a

Presenting School: Graduate

Degree Seeking: MD/PHD

Year: 6th

Mentor: Laurent Gapin

Poster Title: *Regulation of NKT cell development by Schnurri3*

Final Category: Immunology and Autoimmune Diseases (Except Arthritis)

Abstract:

Invariant Natural Killer T (iNKT) cells are a population of TCRαβ-expressing cells that are unique in several respects. In contrast to conventional cells, which are selected on MHC expressed on thymic epithelial stromal cells, iNKT cells are selected on CD1d-expressing double-positive cortical thymocytes. During development, iNKT cells sequentially express surface markers and transcriptional programs that correspond to this cell type's rapid ability to secrete high levels of interferon gamma (IFN-γ) and interleukin-4 (IL-4). Although iNKT cells share some of the same requirements in signaling and transcriptional regulation as conventional αβ T cells in their developmental program, many transcriptional regulators are unique to iNKT cell development. We have found that iNKT cells are dependent on the large zinc finger protein, Schnurri 3 (Hivep3, ZAS3, KRC), for normal development in the thymus as well as proper function in the periphery. While development of conventional T cells and regulatory T cells is normal in the Schnurri 3 deficient mouse, iNKT cells are decreased in number at every single stage and subset of development. In the absence of Schnurri 3, iNKT cells display an altered surface marker and transcription factor profile. Functionally, Schnurri 3 -/- NKT cells secrete less IFN-γ and IL-4 upon stimulation in vivo. Furthermore, the proportions of cells that secrete IFN-γ, IL-4, or both are altered in the Schnurri 3 -/- mouse. Through competitive mixed bone marrow chimeras, we observe that Schnurri 3 exerts its effect in a cell intrinsic manner. Taken together, these results demonstrate that Schnurri 3 plays a critical role in iNKT cell development and function.

Primary Student Presenter: Leonid Zukin

Additional Presenter(s): n/a

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Mark Petrash

Poster Title: *The role of aldose reductase in the development of posterior capsular opacification in a mouse model of cataract surgery*

Final Category: Surgery, Cardiovascular, and Other

Abstract:

Cataracts are among the leading causes of blindness worldwide. They are characterized by clouding of the ocular lens, leading to severely diminished vision. Treatment consists of surgery to remove the lens and implant a synthetic intraocular lens (IOL). However, approximately a fifth of these patients will develop an "after cataract" called posterior capsular opacification (PCO), which is characterized by an aberrant wound healing process that obstructs vision. Recent tissue culture research has demonstrated that inhibition of aldose reductase (AR), an enzyme involved in the generation of reactive oxygen species, can suppress PCO biomarkers. We utilized an extracapsular lens extraction surgery to model cataract surgery and subsequent PCO in a mouse model. Using q-PCR and immunofluorescence microscopy, we analyzed post-operative markers of PCO in three different mouse populations: wild-type, AR knockout, and AR overexpression. Additionally, we tested a pharmacological inhibitor of AR called Sorbinil in these mice. Our results demonstrate that AR knockout suppresses the post-operative induction of PCO biomarkers like alpha smooth muscle actin, vimentin, and fibronectin. Pharmacological inhibition with Sorbinil recapitulated these results. Overall, our study demonstrates an important role for AR in the development of PCO in an in vivo mouse model of cataract surgery.