Summer Research Internship Program

Awards Ceremony

Wednesday, July 30, 2014
Use of Simulations in the LSUHSC-NO Internal Medicine Ambulatory Clinic
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Abstract:

Simulations are a powerful educational tool that can be used to enhance medical education. This poster highlights the use of simulations in the Internal Medicine Ambulatory Clinic at LSUHSC-NO. The simulations were designed to improve residents' skills in patient management and diagnosis. The poster includes a background section, methods and materials section, and patient's data responses section. The figures section contains images related to the simulations.

Methods & Materials:

The simulations were designed by faculty members of the Internal Medicine residency program. They were implemented in the ambulatory clinic to provide residents with practical experience. The simulations were evaluated using pre- and post-tests to assess residents' knowledge and skills.

Patient's Data Responses:

The data collected from the simulations were analyzed to determine their effectiveness in improving residents' skills. The data showed a significant improvement in residents' performance after the simulations.

Background:

Medical simulations are an effective way to train medical students and residents. They provide a safe environment to practice clinical skills and improve patient care. The use of simulations in medical education has been shown to enhance learning and improve patient outcomes.

Figures:

The figures section contains images related to the simulations. These images include diagrams, photographs, and illustrations that depict the procedures and scenarios used in the simulations.

Pictures:

The pictures section contains images related to the simulations. These images include photographs of residents and medical staff using the simulations.

Conclusion:

The use of simulations in the Internal Medicine Ambulatory Clinic at LSUHSC-NO has been effective in improving residents' clinical skills. Further research is needed to evaluate the long-term effectiveness of simulations in medical education.
Tumor-Derived Factors Cause ER Stress in Myeloid-Derived Suppressor Cells Increasing the Stress Sensor Chop Which Mediates MDSCs Suppressive Activity

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Introduction
Myeloid-derived suppressor cells (MDSCs) are a population of immature myeloid cells that accumulate in response to various tumor-derived factors and in the tumor microenvironment. MDSCs accumulate in other diseases linked to chronic inflammation. MDSCs are characterized in mice as cells that co-express CD11b and Gr-1. Although it is accepted that tumors promote MDSC function, there is no clear pathway on how the malignant cells regulate MDSC activity. Our lab has initially suggested the role of the cellular stress sensor C/EBP Homologous Protein (Chop) in the accumulation and immune regulatory function of MDSC. In our study, we sought to determine if there was direct correlation between Chop induction and the suppressive nature of MDSC. To do so, we focused upstream of Chop at Endoplasmic Reticulum (ER) stress and we found that PERK, ER stress and its interaction to Chop was investigated using a pharmacological approach. We demonstrated that Chop expression is upregulated at concentrations below the threshold necessary to initiate apoptosis. We specifically implicate the ER stress sensor PERK in the induction of Chop in MDSC as a small molecule inhibitor of PERK was able to completely abolish Chop induction in BM-MDSC.

Hypothesis
Tumor-derived factors increase stress sensor Chop and promote suppressive activity in MDSC by activating ER stress signaling through PERK.

Methods
MDSC isolation - MDSC were sorted from the tumors (MDSC) and spleens (MSCs) of nude mice bearing SLL-1 leukemia and immature myeloid cells from spleens of tumor-free mice by stick isolation (StemCell Technologies).

T cell suppression assay - CFSE blast assay was performed using 5×105 target T cells with 1×106 of MDSC. The stimulation was performed as described above. The viability of cocultured T cells was determined by 7-AAD viability dye staining and analyzed by flow cytometry.

Bone marrow derived MDSC (BM-MDSC) model - bone marrow was harvested from wildtype and Chop deficient mice. Bone marrow cells were cultured in 10 x 106 cells/mL with GM-CSF (10 ng/mL) for 5 days. MDSC were identified as CD11b+ Gr-1+ and a subset represented the Chop+ phenotype.

Figure 1: Chop induction in the ER stress response is increased in tumor MDSC. A) RT-qPCR of Chop in splenic MDSC isolated from tumor-bearing mice. B) Flow cytometry of Chop expression in splenic MDSC isolated from tumor-bearing mice. C) Western blot analysis of Chop expression in splenic MDSC isolated from tumor-bearing mice.

Figure 2: BM-MDSC induced by tumor-derived factors express high levels of Chop and are more suppressive in the indicated conditions and verified by flow cytometry.

Figure 3: Chop induction in the ER stress response is increased in tumor MDSC. A) RT-qPCR of Chop in splenic MDSC isolated from tumor-bearing mice. B) Flow cytometry of Chop expression in splenic MDSC isolated from tumor-bearing mice. C) Western blot analysis of Chop expression in splenic MDSC isolated from tumor-bearing mice.
Impact of Endocannabinoid Degradation Inhibition on Tight Junction Proteins Following Traumatic Brain Injury

Alana Williams, Paige Katz, Patricia Molina
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Introduction
- In 2010, 2.5 million TBIs occurred either as an isolated injury or along with other injuries.
- TBI contributes to a substantial number of deaths and cases of permanent disability each year.
- Over the past decade, research on endocannabinoids in the brain has revealed that they possess some neuroprotective properties.
- Blood-brain barrier (BBB) disruption follows TBI and is a form of secondary injury facilitated by TBI.
- Previous studies in our lab have shown that EC degradation inhibition post-TBI improved BBB dysfunction.
- BBB integrity is controlled by the tight junctions between endothelial cells, which are composed of proteins such as occludin, zonula occludens (ZO-1), and claudin-5.

Hypothesis
We hypothesize that EC degradation inhibition post-TBI will maintain tight junction proteins involved in BBB function in rats.

Methods
- Tissues used in these studies were previously harvested from sham operated animals and animals that received a TBI and an i.p. injection of either vehicle (TBV/W164), 25, 50, or 100 mg/kg EC, or URB597 (TBV/URB) 30 minutes post-TBI.
- For Western blot analysis, fresh frozen brain tissue lysates were used to measure tight junction protein expression of occludin, ZO-1, and claudin-5.

Summary
- Using brain tissue lysates and Western blot analysis, we see no change in ZO-1 and claudin-5 protein expression across groups.
- Future Studies: Measure ZO-1 and claudin-5 protein expression using immunohistochemistry.
- Measure occludin protein by Western blot and immunohistochemistry.
- Use isolated brain microvessels to measure tight junction protein.

This research was supported by grant 4T32AA007197 from the National Institute of Alcohol Abuse and Alcoholism at the National Institute of Health.
The Effect of Circumcision on Penile Microbiota
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LSUHSC Pediatrics Dept and Children’s Hospital

Introduction
- HPV infections are known to be more common found on uncircumcised males
- Circumcision has been shown to reduce female-to-male HPV transmission
- The exact cause of this reduction is not completely understood
- Circumcision reduces the penile size of how can vary
- Scientists hypothesize that a decrease in the number of penile antibodies reduces HPV viral set movement to the female
- Here we use sequence analysis of PCR-amplified 16S rDNA genes to compare the composition of uncircumcised and circumcised males

Methods
- DNA was extracted from stool using a commercial kit
- Stool samples from 30 circumcised and 30 uncircumcised adult human males were included in the study
- 16S rDNA genes were PCR-amplified from DNA extracted from the stool
- 16S rDNA genes were sequenced using 454 pyrosequencing
- QIIME was used to correct the composition of the microbiota in the two groups of males, to compare the diversity using Chao1 and Shannon’s diversity estimates

Shannon’s Diversity Analysis
- Uncircumcised
  - Chao1: 1.420
  - Shannon: 0.703
- Circumcised
  - Chao1: 1.402
  - Shannon: 0.730

PCoA

Group-Significance Test

Conclusion
- Circumcision does not appear to affect gut microbial diversity
- Circumcision can lower the prevalence of disease
- No reduction in antibiotic bacteria was observed
- No difference in immunoglobulin levels

References
Antiretroviral Therapy Attenuates Dysregulated Hematopoiesis Caused by Chronic Binge Alcohol Administration and SIV Infection in Rhesus Macaques

LSU Health Sciences Center, Department of Physiology,
Comprehensive Alcohol Research Center, New Orleans, LA 70112

INTRODUCTION
HIV infection increases both the innate and adaptive immune response, which increases morbidity and mortality. Treatment for HIV infection with HAART has been associated with increased hematopoiesis. Alcohol consumption negatively affects hematopoietic stem cell function and function in bone marrow. We hypothesized that CBA animals infected with SIV would have decreased HSPC frequency, and we aimed to test this hypothesis.

METHODS
Mice were injected intraperitoneally with SIV and treated with HAART (Ritonavir, 100 mg/kg thrice daily). At 6 weeks postinfection, the mice were sacrificed, and bone marrow and spleen samples were collected.

RESULTS
Hematopoietic progenitor cells (HPCs) were isolated from the bone marrow and spleen and analyzed for their frequency. The results showed a significant decrease in HPC frequency in SIV-infected mice compared to uninfected controls. Moreover, HAART treatment significantly increased HPC frequency in SIV-infected mice.

SUMMARIES & CONCLUSIONS
1. CBA mice infected with SIV had decreased frequencies of HPCs in both bone marrow and spleen compared to uninfected controls.
2. HAART treatment increased HPC frequency in SIV-infected mice.
3. CBA mice treated with HAART had increased frequencies of CD3+ T cells, suggesting a potential role for HAART in modulating immune function.
4. Further studies are needed to understand the underlying mechanisms of HAART in modulating hematopoiesis.

Supported by grants R01AA0223157 and AA018390 from the National Institute on Alcohol Abuse and Alcoholism at the National Institutes of Health.
Chronic binge alcohol administration in SIV-infected female macaques impairs myogenic differentiation

Gabriel Onor Jr., Patricia Molina and Liz Simon
Department of Physiology, LSU Health Sciences Center, New Orleans, LA

Introduction
- In myogenic differentiation, muscle satellite cells (SCs) – progenitor cells beneath the basal lamina – are targeted to differentiate into myoblasts which then form multinucleated myotubes composing the mature muscle fiber.
- Chronic Binge Alcohol (CBA) decreases muscle mass.
- Immunodeficiency Virus (SIV) is known to induce muscle wasting, and we hypothesize that CBA may impair myogenic differentiation.
- Our results suggest that CBA decreases myoblast formation and reduces muscle mass in SIV-infected animals.

Methods
- SIV induces muscle wasting and is used to induce muscle wasting in our model.
- Myoblasts and myotubes are isolated from skeletal muscle.
- RNA is isolated from muscle and subjected to qPCR analysis.
- Immunofluorescence staining is used to visualize myotubes.

Results - qPCR
- Gene expression levels of myogenic factors, such as MyoD and Myf5, are decreased in CBA-treated samples compared to controls.
- Myoblast formation is impaired in CBA-treated samples.

Myogenic Differentiation
- Myoblasts are isolated from skeletal muscle and subjected to qPCR analysis.
- Gene expression levels of myogenic factors, such as MyoD and Myf5, are decreased in CBA-treated samples compared to controls.
- Myoblast formation is impaired in CBA-treated samples.

Summary
- CBA and SIV inhibit myogenic differentiation.
- An effect of ovariectomy at 8 weeks post-procedure was not observed on myogenic differentiation.
- Future studies will investigate the effects of ovariectomy at later time points.

Acknowledgments
- I’d like to thank Dr. Liz Simon, Paul Berner, Curtis Vande Steen, and the Physiology Department at LSU for their support.
The research was supported by grant 8T32AA007101 from the National Institute of Alcohol Abuse and Alcoholism at the National Institutes of Health.
Using Epstein-Barr and Human Papillomavirus Serum Antibodies to Predict Cervical Cancer in HIV Positive Patients

Katie Neil¹, Rebecca Fisher², Hope Oddo², Amelia Ferguson², Michael Hagensee²

¹Southeastern Louisiana University; ²Louisiana State University, Department of Medicine

Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide. Both men and women are susceptible, and this virus can lead to cancers of the cervix, uterine, vulva and anogenital regions, salivary glands, tonsils, larynx, esophagus, lung, skin, and anus. A major goal of the HPV vaccine has been to prevent cancer. The vaccine is effective against the high-risk HPV types (16 and 18) that are responsible for the majority of cervical cancers. However, only a small fraction of those infected with HPV vaccine-preventable strains. Other risk factors may be associated with the development of cervical neoplasia.

HPV infection

The human papillomavirus (HPV) is a small DNA virus that can infect the skin and mucous membranes of the body. There are over 200 types of HPV, and some types are more common than others. HPV can cause a range of conditions, from warts to more serious diseases like cervical cancer.

Study Population Characteristics

80 patients were recruited at the LSU HIV Outpatient Clinic. They received Pap smears and gave blood samples at 3-month intervals to give a total of 36 samples. The average follow-up time was 12 months.

Results

Differences in seropositivity in subgroups are insignificant.

No significant correlation between HPV 16 IgA and dysplasia.

Discussion

HPV 16 IgA data was mixed with previously collected data on EBV IgA antibodies compared to clinical Pap smear results to assess whether HPV 16 IgA correlated with cervical dysplasia. When all visits from all patients were included, a correlation between HPV 16 IgA antibodies and cervical dysplasia was not observed. However, when only the first visit from each patient was analyzed, the correlation was significant.
Effects of QRFP on High Fat Food Intake, Meal Patterns, and Hypothalamic Feeding Circuitry in Female Rats
Mallory C. Lowe, Timothy D. Allerton & Stefany D. Primeaux, PhD.
Department of Physiology, LSU Health Sciences Center

Introduction
Obesity in females is a rising epidemic in the United States and other western countries that has been attributed to alterations in feeding behaviors, which contribute to increased adiposity. An increase in the prevalence of obesity and associated co-morbidities, such as type 2 diabetes and cardiovascular disease, is associated with weight gain and may be a factor in the rising prevalence of obesity. Recent evidence suggests that reduced energy intake and increased energy expenditure may be important contributors to healthy weight management. Evidence from animal studies has indicated that the increase in energy intake and obesity in response to excess high-fat foods is associated with dysregulation of the hypothalamus and associated regulatory systems. Recent evidence from our laboratory has indicated that the reduction of energy intake in response to high-fat foods in female rats is associated with decreased QRFP expression in the hypothalamus. This reduction in QRFP has been associated with obesity and metabolic syndrome, and our findings suggest that QRFP administration may selectively increase food intake and obesity. This study was designed to assess the effects of acute and sub-chronic administration of QRFP on food intake in female rats. We hypothesized that acute QRFP administration would selectively increase food intake in female rats, and chronic QRFP administration would increase the expression of QRFP and its downstream targets.

Methods
Animals
Female and male Sprague-Dawley rats were used in these studies. Rats were individually housed and maintained on a 12/12 light/dark cycle.

Experiment 1
Female rats were randomly assigned to a high fat diet or a low fat diet. After 2 weeks, rats were surgically implanted with osmotic pumps. After 4 hours, food intake was measured. In a separate group of rats, brains were harvested 4 hours following QRFP administration for Real-Time PCR analysis.

Experiment 2
Male and female Sprague-Dawley rats were randomly assigned to a high fat diet or a low fat diet. Rats were implanted with osmotic pumps. After 4 hours, food intake was measured. In a separate group of rats, brains were harvested 4 hours following QRFP administration for Real-Time PCR analysis.

This research was supported by grant #T35AA021097 from the National Institute of Alcohol Abuse and Alcoholism.
Assessment of the Toxicity of Antisense Oligonucleotides Therapy in Usher Mice
Tracy Mai¹, Mette Flaat¹, Hai Tran¹, Frank Rigo², Jennifer Lenz²
¹LSU HSC Neuroscience Center of Excellence, New Orleans, LA; ²BioPharma, Cranford, CA

Introduction

Materials and Methods

References

1. Experimental Model

2. Ush1c.216G>A Genotyping

3. Localization of ASOs in Retina

4. Retinal Histology after Systemic Delivery of ASOs

5. Retinal Histology after Local Delivery of ASOs

6. Results & Conclusions

Funding

- Preliminary results of retinal toxicity indicate no deleterious effects.
- ASOs appear safe and well-tolerated in Usher mice

- ASO treatment reduces retinal degeneration in Usher mice
- ASO delivery methods are optimized for clinical use

- Further studies are needed to determine long-term safety and efficacy
THE EFFECTS OF REPEATED BINGE DRINKING ON ADIPOSE TISSUE INFLAMMATION
Nicholas J. Hourguettes
Mentor: Dr. Flavia Souza-Smith
Department of Physiology, Alcohol and Drug Abuse Center of Excellence, LSUHSC, New Orleans, LA

INTRODUCTION

Alcohol impairs inflammatory signaling by altering cytokine profiles.

Inflammation in adipose tissue can lead to tissue damage and is associated with the development of insulin resistance.

Previous studies in our laboratory have shown that a single binge episode increases inflammatory cytokines and immune cell recruitment in sympathetic adipose tissue.

We tested the hypothesis that repeated binge drinking will impair the inflammatory milieu in epididymal and subcutaneous adipose tissue.

METHODS

Mice, unrestrained male Sprague-Dawley rats were given an intragastric bolus of ethanol in a nutritionally complete diet for 3 days through a feeding gastric catheter.

Thirty minutes or 24 hours after the binge, rats were anesthetized and epididymal and subcutaneous fat pads were isolated and frozen.

Fat was isolated 30 minutes after the last binge.

Histologic analysis of tissue samples was performed.

Inflammatory cytokines were measured using a multiplex kit.

Epidermal and subcutaneous fat pads were also fixed in 4% paraformaldehyde for histological analysis with hematoxylin and eosin (H&E).

Figure 1. Average of weight loss at the duration of the protocol.

Figure 2. Histological analysis of epididymal fat pads from control and ethanol-fed mice.

CONCLUSIONS

Repeated binge drinking appears to impair adipokine profiles in epididymal fat and decrease adiposity in the subcutaneous fat.

Repeated binge drinking may increase inflammation cytokines in both fat pads.

These findings suggest that binge drinking may affect the adipokine profile in both fat pads.

Supported by grant #1 F32 DA 021497 from the National Institute of Alcohol Abuse and Alcoholism at the National Institutes of Health.
Effects of ovariectomy and chronic THC on cannabinoid receptors and their signaling proteins in the striatum of adult female rats

S. Kimbrow, P.F. Weed, MPH, P.J. Winsauer, Ph.D.
LSUHSC-NO Department of Pharmacology and Experimental Therapeutics

Abstract
Previous research from this lab has shown that female rats undergoing ovariectomy and chronic treatment with THC (1-8 mg/kg) show a significant decrease in cannabinoid receptor binding sites in the striatum, a region of the brain associated with learning and memory. To determine the effects of long-term chronic THC treatment on cannabinoid receptor expression, we administered THC to young adult female rats for 4 months. The rats were then administered either control or chronic THC treatment. The results indicate that chronic THC treatment significantly decreases cannabinoid receptor levels in the striatum.

Experimental Timeline

Chaperone Protein Levels

Cannabinoid Receptor Levels

Conclusions
- **CB1R** levels were significantly affected by chronic THC treatment.
  - Chronic THC treatment significantly increased **CB1R** levels.
  - Ovariectomy alone did not significantly affect **CB1R** levels.
- **A2A1** levels were significantly affected by chronic THC treatment.
  - The interaction between THC and ovariectomy significantly affects chaperone protein expression.
  - Chronic THC treatment significantly affects ER receptor levels.
- The interaction between chronic THC and ovariectomy significantly affects ER receptor levels.
CHRONIC BINGE ALCOHOL ADMINISTRATION DISRUPTS INSULIN SIGNALING IN SKELETAL MUSCLE SIMIAN IMMUNODEFICIENCY VIRUS-INFECTED RHESUS MACAQUES
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NIAAA
National Institute on Alcohol Abuse and Alcoholism

BACKGROUND

**PI3K**

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Figure 1. Protein expression of downstream insulin effectors, PI3K. Protein expression data was represented as fold change of control. Bars with * are significantly different (p<0.05) from respective control group. Data are represented as Mean ± SEM.

METHODS

- On day 1, animals were administered chronic alcohol via intragastric gavage.
- On day 7, animals were euthanized and tissue samples were collected for analysis.
- Protein expression was analyzed using Western blotting.

CONCLUSION

These findings indicate discrete changes in insulin signaling pathway(s) evident at 11 months post-SIV infection in CBA-SIV animals. While the ratio of phosphorylated to total 4EBP1 is suppressed only in non-ART treated animals, further pathway characterization is needed to determine our hypothesis.
The effect of high-risk HPV E6 & E7 oncogenes on the STD bacterium Chlamydia trachomatis

Abstract and Introduction

Hela cells have lower Trp levels

A new retroviral vector to make immortalized epithelial cell-lines

Background

Previous Data

Effects of E6/E7 expression in C33A

Construction of new cell-lines

Conclusions
Chronic Binge Alcohol (CBA) Alters Adipokine Production in Cultured Adipocytes Isolated from SIV Infected Macaques

Garth Cook, Stephen Ford, Liz Simon
LSUHSC, Department of Physiology, New Orleans, LA

Introduction
- Nearly 15 million US residents are considered binge drinkers (CDC, 2020)
- Increased fat cell size is a characteristic feature of obesity

Methods
- Methods and procedures for isolation and culture of adipocytes
- Adipocyte isolation and culture conditions

Results
- Adipocyte isolation and culture conditions
- Adipocyte differentiation
- Adipokine production

Discussion
- Adipokine expression in CBA and SIV infection
- Implications for adipocyte function

Conclusion
- CBA alters adipokine production in cultured adipocytes
- Implications for obesity and metabolic health

This research was supported by grant #1T35AA021697 from the National Institute of Alcohol Abuse and Alcoholism at the National Institutes of Health.
Induction of miR-146a through TLR9 signaling

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Introduction

Blasts are the body’s first line of defense against any foreign pathogens. Blast immunity is a non-specific, but a critical line of defense against infection by a wide variety of pathogens, called pathogen-associated molecular patterns (PAMPs), and needs a general lack of specificity. Molecules of the cell can be used to detect PAMPs. PAMPs are recognized by a group of transmembrane proteins called TLR-like receptors (TLR). These are named after the homologous Toll-like receptor that recognizes fungal PAMPs. The TLRs activate a signaling pathway from the receptor that ends in the activation of immune mediators such as cytokines and chemokines.

TLR9 is in the endosomal compartment and is used to recognize the unmethylated CpG DNA of pathogens.

B cells have been shown to participate in innate immunity and release inflammatory cytokines (4). They have also been shown to express TLR9 and respond to CpG DNA.

MicroRNAs (miRNAs) are a group of non-coding regulatory RNAs that function in posttranscriptional regulation by using seed matching sites to inhibit target miRNA expression. In immune cells, miRNAs are used to control the expression of genes involved in immune responses. MiR-146a, for example, has been shown to be involved in TLR signaling in immune cells.

Using immune cell lines derived from mice, we have shown that TLR9 is essential for the induction of miR-146a. We used a reporter gene assay to examine the effects of TLR9 on miR-146a expression in immune cells.

Primary miR-146a transcript expression

Methods

A reporter gene assay, which is a cell line derived from mice, was used to examine the effects of TLR9 on miR-146a expression in immune cells. The results showed a significant increase in miR-146a expression in immune cells treated with TLR9 agonist compared to control cells.
Importance of L-glutamine in Renal Cell Carcinoma Growth-Inhibition

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¹Louisiana State University at New Orleans and ²Stanley S. Scott Cancer Center, LSUHSC-New Orleans, LA.

Introduction
L-glutamine is an essential amino acid that cannot be made in the body and must be obtained from dietary sources. It plays a critical role in various biological processes, including cell proliferation and survival. In cancer cells, L-glutamine is consumed at a higher rate than in normal cells, which has prompted research into its use as a potential therapeutic target.

Objectives
The objective of this study is to determine the role of L-glutamine in the growth inhibition of renal cell carcinoma cells.

Methodology
Cell lines Renca and CI-19 (renal cell carcinoma) were used. Cells were cultured under different conditions to determine the effect of L-glutamine on cell proliferation and survival.

Results
The results showed that L-glutamine significantly inhibited cell proliferation and increased cell apoptosis. This effect was dose-dependent and reversible upon deprivation of L-glutamine.

Conclusions
The results indicate that L-glutamine is a potential target for the treatment of renal cell carcinoma. Further studies are needed to explore the mechanisms of action and the potential of L-glutamine as a therapeutic agent.

Acknowledgements
Dr. Paul Green, Dr. Robert Aronson, and the research team.

References
Regulation of Prefrontal Cortex AMPA Glutamate Receptor 1 Subunits in Alcohol Dependence
Meghan Blackwell, Muhammad Farooq, Kim Edwards, Scott Edwards
Department of Physiology, LSUHSC

Abstract
Our goal is to determine if glutamate receptor signaling is increased in the prefrontal cortex of alcohol-dependent rats.

Objective

Methods

Introduction/Background

Results

Conclusions

This research was supported by grant #1T35AA031097 from the National Institute of Alcohol Abuse and Alcoholism at the National Institutes of Health.