MEDICAL STUDENT RESEARCH SYMPOSIUM GUIDELINES

TRAVEL FUNDING FOR CONFERENCES

FUTURE RESEARCH OPPORTUNITIES

Dr. Fern Tsien
Assistant Dean, Medical Student Research
Department of Genetics
LSUHSC

LSU Health NEW ORLEANS

Deadlines:

1. Friday, September 9th
   Abstracts due to: SoMHonorsProgram@lsuhsc.edu
2. Monday, October 3rd
   Posters due to Isché Library (icirc@lsuhsc.edu)
3. Thursday, October 13th, 8am-12 noon, Lions Building, 6th Floor
   Research Symposium and poster judging
3. Tuesday, October 18th, 4-4:30
   Virtual Awards Ceremony (Zoom link: https://lsuhsc.zoom.us/j/96378180422)

Abstract and poster templates, guidelines:

https://www.medschool.lsuhsc.edu/genetics/summer_med_students.aspx

For examples, refer to the 2021 Symposium:

https://www.medschool.lsuhsc.edu/genetics/2020_medical_student_research_virtual_poster_symposium.aspx

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Who is eligible to present at the Virtual Research Symposium?

- Medical students from LSUHSC
- Summer program, MCLIN198, and Honors Program students are highly encouraged
- Only one abstract will be accepted for in-person presentation (if you have additional presentations, refer to slide #24)
- Good practice for national and international conferences, and can be added to your resume/CV
- If co-authoring, each student presents a separate poster with each as first author).
- Student presentations will be judged and awards will be given for each category
  - 1st and 2nd year med students
  - 3rd and 4th year med students

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Important Deadline #1: Abstracts

- Abstracts are due by 11:59pm on Friday, September 9th.
- If you already turned in an abstract this summer, please resubmit it, even if there are no changes to: SoMHonorsProgram@lsuhsc.edu
- Follow the templates and guidelines on our website below:

  https://www.medschool.lsuhsc.edu/genetics/summer_med_students.aspx
- DO NOT change the margins, font size, or font style.

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Sending the abstracts

- One-page summary of your project
- List your name and principal investigator (PI) or mentor's name as described in the template
- Affiliations: department and school
- Use only the template on our website.
- This template has the correct sized fonts and sizes we will use. Do not change the font or size!
- Make sure your mentor approves of your abstract before you send it to us!
- When you submit your abstract in Word format, please be sure to save the file with your last name listed first. For example: BrunoKirstenAbstract.doc
- Send it to: SoMHonorsProgram@lsuhsc.edu

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Your Name (first, middle initial, last)
Classification (High School, Undergraduate, Medical)
Name of School, City, State

Mentor's Name:
Mentor's Affiliation (LSUHSC, Tulane SOM, Xavier, Children's Hospital, etc.)

"Title of Project"

Abstract (summary of project, not to exceed one page)

Body of Abstract: Left Justified, 11 pt Arial font.

Katherine A. Adler
L2
LSU Health Sciences Center, New Orleans, LA

Mentor's Name: Dr. Liz Simon
LSUHSC Department of Physiology

"Circulating myomiR levels as a clinical indicator of alcohol-induced skeletal muscle dysfunction in PLWH"

There are an estimated 1.15 million people living with HIV (PLWH) in the US. The prevalence ofat-risk alcohol use among PLWH is higher than in the general population. Antiretroviral therapy (ART) has significantly reduced patient mortality, and HIV infection has emerged as a chronic disease with associated comorbidities such as myopathy and insulin resistance. Impaired skeletal muscle (SKM) function and mass is a consistent predictor of mortality and contributes to a decrease in quality of life in PLWH. Chronic alcohol and HIV independently and synergistically contribute to significant SKM derangements such as atrophy, weakness, and dysfunction. Previous studies have shown that chronic alcohol exposure alters the epigenome including muscle specific microRNA (myomiR) expression, correlating with alterations in expression of myogenic genes. MicroRNAs are produced in cells and secreted actively or passively into circulation. Abundance of circulating myomiRs is a function of the regenerative and degenerative capacity of the muscle, the overall muscle mass, and tissue expression levels. Our hypothesis was that circulating myomiRs is decreased in PLWH with at-risk alcohol use, and they would correlate with a decrease in SKM mass and function.

Subjects from the LSUHSC HIV Outpatient Program were stratified into low, mid, and high drinkers based on timeline follow back (TLFB) and corresponding AUDIT scores. Circulating myomiR levels were determined and correlated to measures of AUD severity, hand grip strength, 4-meter walk test, and lean mass.

The muscle-specific miRNAs 206 and 133a expression were significantly increased in individuals with mid- and high-drinking. Copy number calculations of these myomiRs revealed they were positively correlated with TLFB. Sex differentially modulated the relationship, with miR-206 positively correlating with hand grip strength in males.

Contrary to our hypothesis, circulating myomiRs were increased in individuals with at-risk alcohol use. This may be due to alcohol-mediated damage or inflammation in SKM tissue. Confounding variables including high BMI, high fat mass, and low physical activity in low-drinking cohort may have impacted circulating myomiRs and further studies will investigate correcting for these variables and using a composite myomiR score to correlate with SKM function.

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Important Deadline #2: Posters

- Posters are due by 11:59pm on Monday, October 3rd.

Preparing the posters 1

- First and most important: make sure that your mentor approves of the information that will be presented in the poster.

- Second most important: Your name should go first, your mentor's name last, and everyone else who helped you (other students, post-docs, etc.) in the middle. Make sure not to leave out anyone who helped you!

Preparing the posters 2

- Make sure that you understand everything you write on the poster. You should be able to explain your project to the judges.
- In general, try to keep text towards the outside and figures and tables in the center.
- The abstract is not necessary for the poster.

Preparing the posters 3

- Use the Power Point poster template on our website :

https://www.medschool.lsuhsc.edu/genetics/summer_med_students.aspx

- Make sure to add the LSUHSC logo and those corresponding to your mentor's affiliation and the funding source.
- The logos on your poster may differ from the ones on your lab mates.
- Use at least a 24 point font size so the printed text will be visible from 3 feet away.
- Feel free to adjust the box sizes and headings depending on the amount of text or figures you have.
- The poster template are already set to 42 x 42 in.

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Preparing the posters 4

- Use any color you want to. Express yourself! Exceptions:
  - Black or deep blue for background of entire poster.
  - Image enlarged to cover the entire background.
- Spell out any acronyms the first time you use them. People outside of your lab may not know what “SIV” or “FSHD” is.
- Refer to guidelines sent to you.

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Once your poster is done:

- Save it as a PPT *and* PDF file.
- When you submit your poster, be sure to save the file with your last name listed first. For example: BrunoKirstenPoster.pptx
- Send it to the Isché Library (icirc@lsuhsc.edu)
- More information is below:
- https://www.lsuhsc.edu/library/services/posterprinting.aspx

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Example of a poster

RNA Binding ability of FUS mediates toxicity in a *Drosophila* model of ALS

Senthil S. Natarajan, J. Gavin Daigle, Nicholas A. Lanson, Jr., John Monaghan, Ian Casci, Udai B. Pandey

Department of Genetics, Louisiana State University Health Sciences Center, New Orleans, LA

LSU Health New Orleans Health Sciences Center

LVC Louisiana Vaccine Center

Abstract

Amyotrophic Lateral Sclerosis (ALS) is a late-onset neurodegenerative disorder characterized by the loss of motor neurons. Mutations in Fused-in-Sarcoma (FUS) have been identified as a major component in both familial (FALS) and sporadic (SALS) ALS cases. FUS is an RNA-binding protein implicated in several processes like RNA splicing and microRNA processing. In normal individuals, the FUS gene is predominantly localized in the nucleus; however in ALS patients, FUS becomes redistributed to the cytoplasm as well, which is believed to be a causative pathway for ALS.

Ectopic expression of human FUS with ALS-linked mutations in fly eyes causes moderate to severe external eye degeneration. Here we examined the role of RNA binding in mediating the neurodegenerative effects of mutant FUS via the RNA Recognition Motif (RRM). The RRM domain in FUS is key to the RNA binding pathway and can be disrupted by total deletion of the domain itself (RRM-D) or by mutating 4 conserved phenylalanine residues within the FUS RRM to leucine (known as 4F-L). The 4F-L mutations have been previously shown to mitigate RNA binding ability in a yeast model of FUS.

We demonstrate that disrupting the RRM-Domain, by way of deletion or by the 4F-L point mutations, can suppress the toxicity of FUS. Interestingly, confocal imaging has shown that disrupting the RNA binding-ability keeps FUS within the nucleus (unlike in ALS cases, where FUS is redistributed to the cytoplasm), further indicating that subcellular mislocalization of FUS is a causative pathway for ALS.

In summary, we have identified a means of rescuing phenotype in our *Drosophila* model of ALS-associated neurodegeneration, which may be relevant for future clinical studies and interventions in ALS.

Introduction

- Familial (genetic) ALS accounts for ~10% of all ALS cases, with mutations in FUS accounting for ~4-5% of FALS cases.
- Victims of ALS display loss of muscle mass, increased frailty, loss of mobility, and eventually death.
- Currently ALS has no definitive treatment in addition to being ultimately fatal, making the study of ALS all the more urgent and important.
- Steve Gleason, former New Orleans Saint and known ALS patient, in a simply a few years, has gone from inciting the loudest recorded noise in the Superdome with his blocked punt all the way to a man confined to a wheelchair and deprived of his former stature.

- Knowing that FUS in itself is an RNA-binding protein, we hypothesized that disruption of its RNA binding ability by deletion of the RRM domain or by 4F-L mutations would reduce the toxicity of mutant FUS.
- We started by transfecting neuronal cells with FUS and corresponding FUS mutations. We then tested our hypothesis by creating transgenic lines with a deletion of the RRM domain in FUS entirely (RRM-D). We next narrowed our focus and created transgenic lines in which we mutated 4 conserved phenylalanine residues within the FUS RRM to leucine (known as 4F-L). Both the RRM-D and 4F-L lines were used in screens in which the FUS trans-gene was expressed in the fly eyes.

I. FUS Gene Model

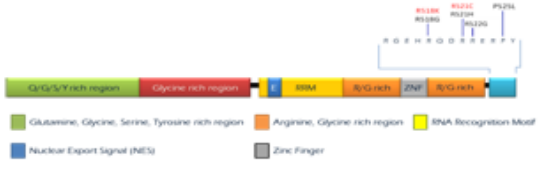


Figure 1: In 2009, ALS-causing mutations in the FUS gene were identified and led to a line of thinking that perhaps errors in RNA metabolism could be involved in ALS pathogenesis.

II. A *Drosophila* model of FUS

Lanson N A et al.

- Recently, our lab developed a *Drosophila melanogaster* (fruit fly) model as a highly useful system for studying FUS-induced proteinopathies such as ALS.
- Fly models of FUS recapitulate several key features of ALS, demonstrating pupal lethality and larval locomotion defects.

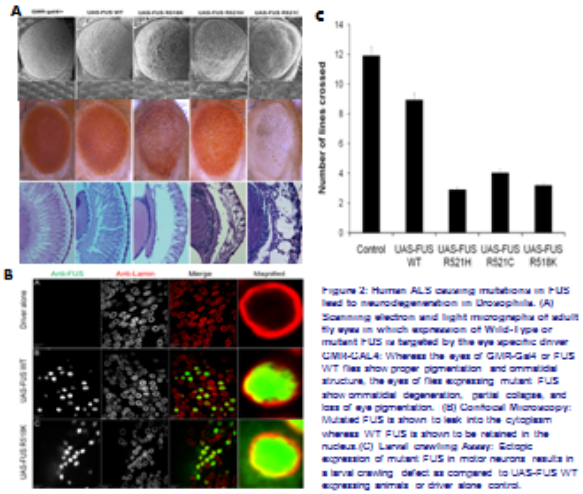


Figure 2: Human ALS causing mutations in FUS lead to neurodegeneration in Drosophila. (A) Scanning electron and light micrographs of adult fly eyes in which expression of Wild-type or mutant FUS is targeted by the eye specific driver GMR-GAL4: Whereas the eyes of GMR-Gal4 or FUS WT flies show proper pigmentation and ommatidial structure, the eyes of flies expressing mutant FUS show ommatidial degeneration, partial collapse, and loss of eye pigmentation. (B) Confocal Microscopy: Mutated FUS is shown to leak into the cytoplasm whereas WT FUS is shown to be retained in the nucleus.(C) Larval crawling Assay: Ectopic expression of mutant FUS in motor neurons results in a larval crawling defect as compared to UAS-FUS WT expressing animals or driver alone control.

III. RNA Binding ability is essential for FUS-related neurodegeneration.

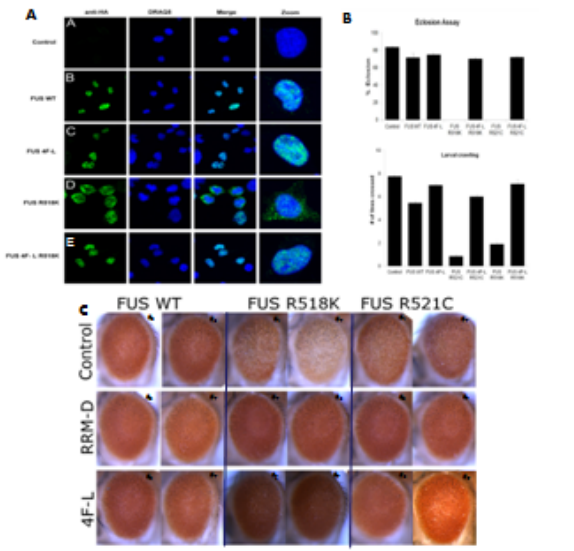


Figure 3: RNA-binding ability of FUS regulates toxicity and subcellular localization. (A) Confocal Imaging: In neuronal cells, WT FUS (B) is predominantly nuclear whereas FUS with ALS-linked mutation (D) is redistributed into the cytoplasm. RNA-binding incompetent FUS along with an ALS-linked mutation (E) is localized in the nucleus. (B) Behavioral Assays: When FUS was targeted by the motor-neuron specific driver (D/K-gal4), we observed greater lethality among pupae with an ALS-linked mutation as opposed to normal eclosion in WT or RNA-binding deficient FUS. Similarly, we observed that expression of mutant FUS in motor neurons results in a larval crawling defect as compared to normal locomotion from FUS WT and non-transgenic controls. Interestingly RNA-binding incompetent larvae also displayed normal locomotion. (C) Light Micrographs of Grossed transgenic Fly lines: Expressing R518K or R521C mutations in fly eyes led to external eye degeneration. However, blocking RNA binding by deleting the RRM domain or by 4F-L mutation rescues the degenerative phenotype.

Conclusions

- Disrupting the RRM-Domain by way of deletion or by 4F-L mutations does indeed seem to significantly rescue phenotype in mutated FUS fly eyes.
- For further research, we want to express RNA-binding deficient FUS mutations in motor neurons of flies and assess neurodegeneration with respect to motility and larval crawling ability.
- We would also like to further investigate the link between subcellular localization of FUS and its toxicity, a point of interest which showed up in these experiments.

- Lanson, N. A., et al. 2011. A *Drosophila* model of FUS-related neurodegeneration reveals genetic interaction between FUS and TDP-43. Human Molecular Genetics. 20, 2510-2523.
- Lanson, N.A., Pandey, U.B., FUS related proteinopathies: Lessons from animal models, Brain Res. (2012), doi:10.1016.2012.01.039

- Acknowledgements: This work was supported by the ALS association and the Robert Packard Center for ALS at Johns Hopkins Medical Center. We would also like to thank the Louisiana Vaccine Center and LSU Health Sciences Center for their generous support.

Example of a poster

AXIN2 Gene Instability In Colon Cancer

Summer Student (you), People who helped you, mentor

Mentor's department and University

LOUISIANA GENE THERAPY RESEARCH CONSORTIUM

LSU Health Sciences Center

Abstract

Colon cancer is one of the most prevalent and fatal cancers in the world. In the United States, 10% of all cancer patients have colon cancer. The disease begins when adenomatous polyps, fleshy growths that line up on the inside of the colon, become cancerous. Colonoscopy is often performed to detect these polyps. Regular testing after the age of 40 can drastically reduce the risk of developing colon cancer.

The AXIN2 gene, located in the region of 17q23-q25, is a gene of interest due to its interaction with the Adenomatous polyposis coli (APC) gene in the Wnt signaling pathway and its association with colon cancer with defective mismatch repair. Mutations in the Adenomatous polyposis coli (APC) gene have been found in about 85% of colon cancer patients. However, not much is currently know about the role of AXIN2 in colon cancer development. By conducting research on AXIN2, researchers are hoping that this gene may assist in distinguishing different subgroups of colon cancer. For this project, we analyzed two colon cancer cells lines to determine their karyotypic differences and for any 17q23-q25 region abnormalities.

The majority of the metaphase cells from both of the colon cancer cell lines analyzed were aneuploid, with one cell line (SW480) having a dramatically higher number of chromosomes reaching hypertetraploidy (103 chromosomes). In addition, the SW480 cell line contained some metaphase cells with an extra copy of chromosome 17 with amplification of the 17q23-25 region. This is the gene location of AXIN2, indicating the possibility of AXIN2 over-expression leading to the colon cancer in this cell line.

Introduction

The colon is the last portion of the large intestine, which also includes the rectum. Colorectal cancer (CRC), also known as colon cancer, is the third most common cancer in the world and the second most fatal cancer in the Western hemisphere. It is reported that approximately 655,000 people worldwide die from this disease every year. It usually arises from adenomatous polyps that line the inside of the colon. Mutations in certain genes are have been associated with this disease.

One significant gene known to cause CRC is the adenomatous polyposis coli gene (APC). The APC gene is located on the chromosome 5 between positions 21 and 22. Its normal function is to provide instructions for the creation of the APC protein, which helps control how and when a cell should divide. Mutations in this tumor suppressor gene can cause CRC, gastric (stomach) cancer, and Turcot syndrome. Approximately 85% of the people who have colon cancer have a mutation in the APC gene. If a person inherits just one defective copy of the gene from one of their parents, then he or she is almost guaranteed that they will develop colon cancer by the age of 40.

A gene that the APC interacts with is the relatively unknown AXIN2 gene, the focus of this project. Located on chromosome 17 between positions 23 and 24, this gene's protein, Axin2, is presumably very important in the regulation of beta-catenin, which is also a function of the APC gene. Since the APC gene and AXIN2 gene interact in the same pathway, it is believed that a mutation to either gene can affect the other gene. About 30% of the people with colon cancer with defective mismatch repair (the mechanism to correct DNA replication errors) have a mutated AXIN2 gene. The region containing the gene shows loss of heterozygosity in breast cancer, neuroblastoma, and other cancers and tumors. Deletions or mutations in this gene can result in truncated proteins which are most likely inactive. There is a possibility that somatic inactivating mutations in AXIN2 can deregulate beta catenin, and therefore, AXIN2 may be tumor suppressor gene.

Colon Cancer Symptoms

- Constipation
- Vomiting
- Stomach cramps
- Thin stool
- Diarrhea
- Hematochezia (Blood in stool)
- Unexplained Weight loss

Figure 1

The AXIN2 gene is located on Chromosome 17 on the q arm (long arm) between positions 23 and 24. The gene spans about 35 kbp and 843 amino acids.

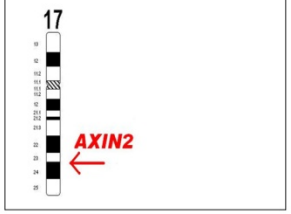
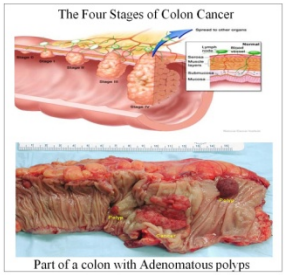


Figure 2



Part of a colon with Adenomatous polyps

Figure 3

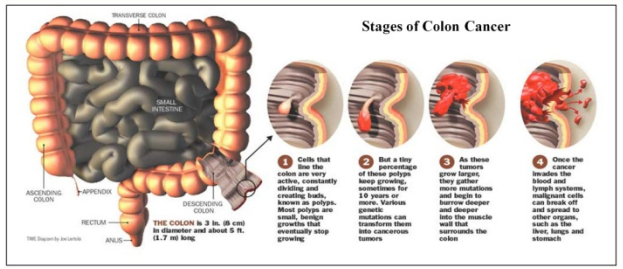
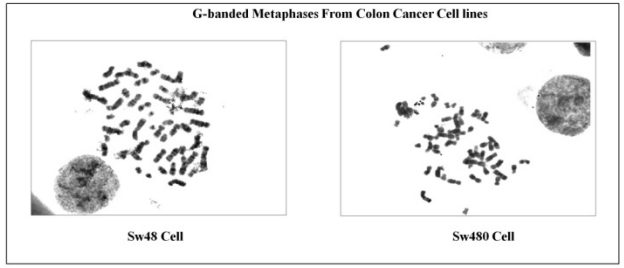


Figure 4

G-banded Metaphases From Colon Cancer Cell lines



Sw48 Cell

Sw480 Cell

Methods and Materials

Samples and Culture Conditions:

Two colon cancer lines were obtained from human patients. The Sw48 cell line was obtained from an 82 year old female and the SW480 cell line was obtained from a 50 year old male. The cells were grown in DMEM with 10% Fetal Bovine Serum (FBS) and 1% penicillin under normal culturing conditions.

Chromosome Preparation:

For solid staining and G-banding, cells were harvested in exponential phase, incubated with colcemid, treated with a KCL hypotonic, and fixed two times with methanol and acetic acid. For solid staining, the cells were dropped onto slides and stained with Giemsa. For G-banding, the cells were dropped onto slides, followed by a short incubation in a trypsin solution prior to staining with Giemsa.

Results

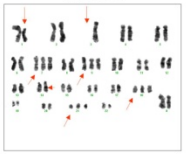
The table to the right shows the frequency of different ploidies in the Sw48 and Sw480 colon cancer cell line.

Ploidy of Human Colon Cancer Cell Lines

	Sw48	Sw480
Total # of cells analyzed	35	20
Diploidy = 46 (Normal #) (%)	2 (6%)	0 (0%)
Hyperdiploidy 47-57 (%)	33 (94%)	6 (30%)
Hypotriploidy 58-68 (%)	0 (0%)	8 (40%)
Triploidy = 69 (%)	0 (0%)	0 (0%)
Hypertriploidy 70-80 (%)	0 (0%)	1 (5%)
Hypotetraploidy 81-91 (%)	0 (0%)	4 (20%)
Tetraploidy 92 (%)	0 (0%)	0 (0%)
Hypertetraploidy 93-103 (%)	0 (0%)	1 (5%)

G-Banded Karyotypes Representative of Colon Cancer Cell lines. The Red Arrows indicate abnormalities.

Sw48 Cell



49, XX, Del (1), (p31), -3, +7, +9, inv (14) (q11q22), +18, +21

Sw480 Cell

57, X-Y, +der X, iso (1q), +2, iso (3q), -4,+6, +8, +10,+11,+11, -12, +13, +15, +17, +add (17) (q23), +21, +22

Conclusions and Future Directions

When compared to normal human diploid cells, the majority of the cells from the Sw48 cell line were hyperdiploids ranging from a total of 47 to 57 chromosomes per cell, while the Sw480 cell line had a wide range of total chromosome number ranging from hyperdiploidy to hypertetraploidy (up to 103 chromosomes). Our results had many similarities with published literature on these cell lines. For example, both previously published and our analysis of sw40 showed the presence of some diploid cells as well as some hyperdiploidy, with an extra chromosome 7 in common.

The sw480 cell line was much more unstable in both studies, with common abnormalities including a missing Y, an extra X abnormal X chromosome, isochromosome 3q, and trisomy 13, 21, and 22. The previous report found one extra chromosome 17. However, our results show four 17 chromosomes, with one of them containing additional genetic material at the q23-qter, the critical region of the AXIN2 gene. Fluorescence *in situ* hybridization (FISH), RNA, and protein analyses should be preformed to determine the extent of AXIN2 amplification in the Sw480 cell line.

Due to the nature of these immortalized cell lines, chromosome abnormalities are acquired with increased cell proliferation. *In vitro* studies such as this one can help to gives an idea of what can occur *in vivo*. More cancer cell lines should be analyzed in order to find genetic differences between the various types of colon cancer.

Geriatric Depression Scale Scores Correlate With Changes in the Oral Microbiota and Abundances of Opportunistic Pathogens in HIV Positive Individuals

William Byerley, Eugene Blanchard, Vincent Maffei
Meng Luo PhD, David Welsh MD, Christopher Taylor PhD
Department of Microbiology, Immunology, and Parasitology
Louisiana State University Health Sciences Center New Orleans

Introduction

Several studies provide evidence that there is a link between depression/mental illness and microbial communities, particularly the gut. However, there has been little research into the link between depression and the population of oral microbiota, especially for individuals with Human Immunodeficiency Virus (HIV).

We hypothesized that there will be a significant difference in the oral microbiota of individuals with depression and those without depression. Furthermore, we hypothesized that HIV positive patients with depression will show a higher abundance of opportunistic pathogens than patients without depression. Similarly, the abundance is expected to be higher for HIV negative patients with depression when compared to those without depression.

Sample Demographic

	0-5	6-15
n	51	25
Male	38 (74.5%)	10 (40%)
Female	13 (25.5%)	15 (60%)
HIV (+)	37 (72.5%)	20 (80%)
HIV (-)	14 (27.5%)	5 (20%)
Age (yr)	50.4 ± 5.5	50.6 ± 7.3
White	19 (37.3%)	6 (24%)
Black	33 (64.7%)	19 (76%)
American Indian	1 (2%)	0 (0%)
Smoking	36 (70.6%)	17 (68%)
Alcohol	51 (100%)	23 (%)
Drug Abuse	32 (62.7%)	20 (80%)

Table 1. Samples were grouped into the categories of those with a GDS score of 0-5, and a GDS score of 6-15. The subgroups (Sex, Race, Female, etc.) are reported as the number of samples that meet the subgroup criteria followed by the percentage.

Alpha Diversity

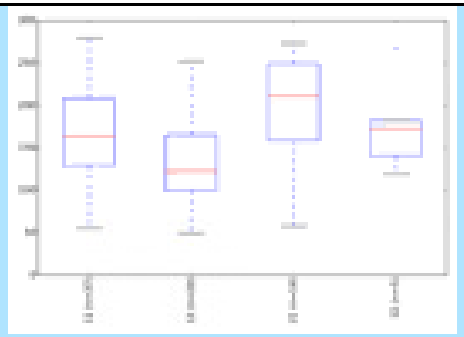


Figure 1. Chao1 Box Plot. The box "between" of the groups, HIV+ (GDS 6-15) and HIV- (GDS 0-5), were the only two groups compared to show any statistical significance ($p = .05$). We expected these groups to differ significantly. However, we did not expect the other comparisons to come back as not statistically significant.

Unifrac Pcoa Plot

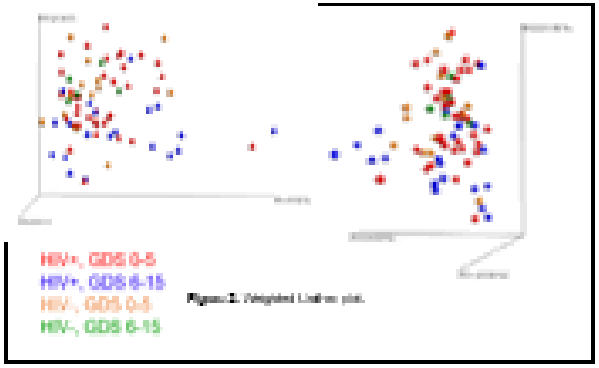


Figure 2. Weighted Unifrac plot.

Taxonomic Summary

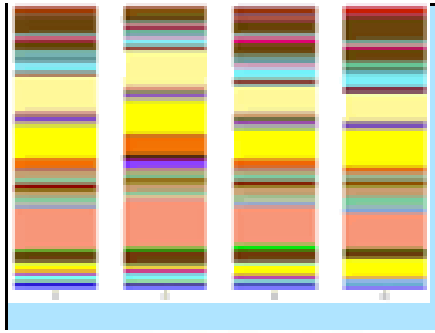


Figure 3. Samples were categorized based on HIV Status, and GDS, Geriatric Depression Scale, score. The x-axis represent these categories. The first number indicates HIV status, a one is positive, two is negative. The second number represents GDS ranking, a one represents those with a GDS score of 0-5, and a two represents a GDS score of 6-15. Only the top 20 pathogens explored showed up above 1% overall abundance. They are listed below with their percentages in each group.

Taxonomy	Total	HIV+, GDS 0-5 (37)	HIV+, GDS 6-15 (20)	HIV-, GDS 0-5 (14)	HIV-, GDS 6-15 (5)
Prevotella Intermedia	0.8%	0.8%	0.9%	1.7%	0.3%
Prevotella Nigrescens	0.8%	0.8%	1.0%	0.7%	0.3%
Prevotella Pallens	1.0%	1.0%	1.0%	1.0%	1.0%
Streptococcus sp.	3.6%	3.6%	4.6%	2.7%	1.5%

Table 2. Out of the 20 opportunistic pathogens standard only 4 were present at higher than 1% total abundance (abundance across all groups). The table is divided into depression status by color. The gold color indicates a GDS score of 0-5, the green indicates a GDS score of 6-15. We hypothesized that those with depression would have a higher abundance of these opportunistic pathogens. This is true for 3 of the 4 in the HIV+ groups. However, this is not true for the HIV- groups, they are in closely same in groups with a leading 3.

Conclusions

- Beta Diversity didn't show an association with GDS scores.
- The majority of subjects with higher GDS scores were HIV positive
- Of the 20 pathogens investigated, only Streptococcus sp., Prevotella Intermedia, and Prevotella Nigrescens demonstrated a relationship with GDS scores and exclusively in the HIV+ groups.
- Alpha Diversity only showed statistical significance for the groups HIV+ (GDS 6-15), and HIV- (GDS 0-5).

This research project was supported by a grant from the US Dept. of Commerce held in conjunction with the New Orleans BioInnovation Center

"Unexpected Results from Hereditary Cancer Panel Genetic Testing: Do Duplications of MMR Genes Matter?"

Sophia Turner[1], Alix D'Angelo, MGC, CGC[1,2].

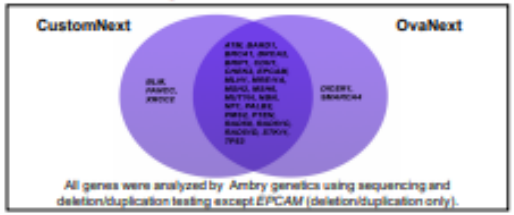
[1]Louisiana State University Health Sciences Center, Department of Genetics

[2]University Medical Center New Orleans, Cancer Center.

Introduction

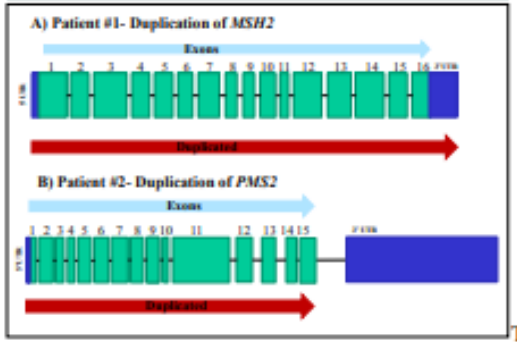
- Lynch syndrome (LS), is the most common form of hereditary colorectal cancer (up to 82% lifetime risk), and also increases the lifetime risk of a variety of cancers, including endometrial (up to 60%), ovarian (up to 24%), gastric, small bowel, hepatobiliary tract, pancreatic, urinary tract, brain and skin neoplasms.[1-3]
- LS is inherited in an autosomal dominant pattern and caused by heterozygous germline mutations in one of five genes: *MLH1, MSH2, MSH6, PMS2,* and *EPCAM*. [4]
- *MLH1, MSH2, MSH6* and *PMS2* are known as mismatch repair (MMR) genes, which play a major role in DNA repair due to replication errors.[5] *EPCAM* is not an MMR gene, however, it impacts the expression of *MSH2*.[6]
- Identifying individuals with LS is crucial, because increased surveillance and preventative surgical options are available.[7]
- We present two patients who were referred to the Genetic Counseling clinic at University Medical Center. Interestingly, both patients met *BRCA* 1/2 genetic testing criteria but were found to have a duplication of an MMR gene.
- A literature search was performed to determine whether these duplications may be of clinical significance, and therefore impact patient management.

Hereditary Cancer Panels

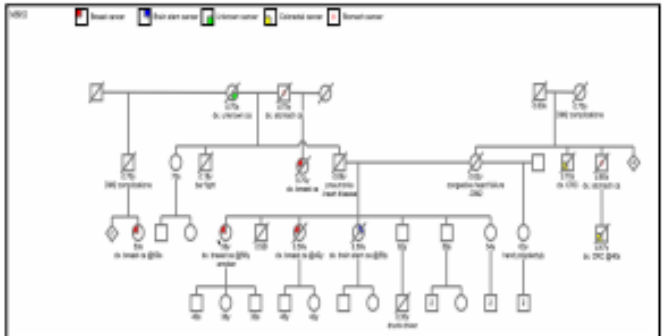


All genes were analyzed by Ambry genetics using sequencing and deletion/duplication testing except *EPCAM* (deletion/duplication only).

Genetic Test Results

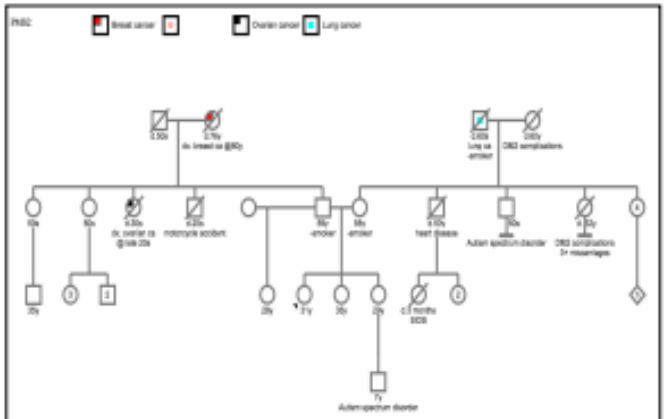


Patient #1



Patient #1 is a 57 year-old post-menopausal female referred to Genetics clinic due to her personal and family history of cancer. She was diagnosed with stage IIB ER/PR+ HER2- invasive ductal carcinoma of the left breast at 56 years-old. She underwent left mastectomy and 6 weeks of adjuvant radiation therapy. She has a history of smoking tobacco (1/2 pack per day since she was 20 years-old). Details of the family history are available in the pedigree above.

Patient #2



Patient #2 is a 31 year-old pre-menopausal, nulliparous, unaffected female referred to Genetics due to her family history of cancer. Details of the family history are available in the pedigree above.

Variant Classification Scheme

- **Pathogenic Mutation**- known to cause a disorder
- **Likely Pathogenic Variant**-strong evidence suggesting it causes a disorder
- **Variant of Unknown Significance** – limited or conflicting data
- **Likely Benign Variant**-strong evidence suggesting it does not cause a disorder
- **Benign**- does not cause a disorder

Discussion

- Next-generation sequencing technology has drastically transformed the genetic testing paradigm, particularly in the hereditary cancer specialty.[8-9] However, this testing has also led to an increase in inconclusive and unexpected results.[10]
- Despite the patients' histories of breast +/- ovarian cancer, both were found to have a whole gene duplication of an MMR gene (*MSH2, PMS2*). The families presented in this report do not meet Amsterdam II criteria, however, they are suspicious of hereditary forms of cancer considering the types of cancers, ages at diagnosis and number of affected relatives in the families.
- A recent study of 528 individuals who have a mutation in one of the MMR genes shows an interesting correlation with breast cancer. Among these individuals, 23.5% had breast cancer (compared to 35.2% who had colorectal cancer and 25.8% who had endometrial cancer), noting that breast cancer was nearly as prevalent. Additionally, individuals who had mutations in *PMS2* or *MSH6* were more likely to meet NCCN guidelines for *BRCA1/2* testing (not Lynch syndrome) than *MLH1* and *MSH2* carriers.[11] This study suggests that the presentation of our patients may be part of the LS phenotypic spectrum.
- Many different types of mutations in the MMR genes are known to be pathogenic, including missense, nonsense, deletions and partial duplications.[12-13] For example, in a report of two individuals with personal and family histories of early- and late-onset colorectal, endometrial and other cancers, exons 7-14 of *MSH2* were duplicated. While the families did not meet Amsterdam II criteria, several tumors were confirmed to have high microsatellite instability, which combined with the presentation of these patients confirmed that the duplication was responsible.[12]
- Unfortunately, evidence of whether whole MMR gene duplications are pathogenic is limited, and they are currently classified as variants of unknown significance (VUS). Pathogenic whole gene duplications have been observed in another gene that is associated with hereditary colorectal cancer/polyposis, *GREM1*.[14-15] However, GREM1 and MMR protein products serve very different functions. Additionally, there are no families that meet Amsterdam II criteria with whole MMR gene duplications that have been reported in literature, to our knowledge.
- Follow-up testing, including chromosomal microarray may be beneficial for our patients in order to further evaluate the size and location of the duplications. Further family and molecular studies are necessary to reclassify these variants, as this may have a dramatic impact on the management of patients and their families.

This research was supported by the Entergy Workforce Training Grant.

Influenza Vaccination Program Requirements of Healthcare Personnel in Louisiana Hospitals

names

LSUHSC-NOLA, Department of Pediatrics, Division of Infectious Diseases and Children's Hospital, New Orleans

Introduction

- Influenza virus causes 24,000 annual deaths in the U.S. Every year 450,000 to 900,000 Louisiana residents are infected and 800 die.
- To prevent high morbidity and mortality, annual vaccination of patients and healthcare personnel (HCP) is recommended. Yet, the vaccination coverage of U.S. HCP in 2010 was only 60%.
- In response, the Centers for Disease Control and Prevention (CDC) is demanding that vaccination rates improve to 90% by 2020, and various Medical Societies are recommending mandatory vaccination programs (i.e., requirement for employment).
- To improve influenza vaccination coverage of HCP in Louisiana hospitals we must first understand what is being done, what is effective and what is ineffective.

Objectives

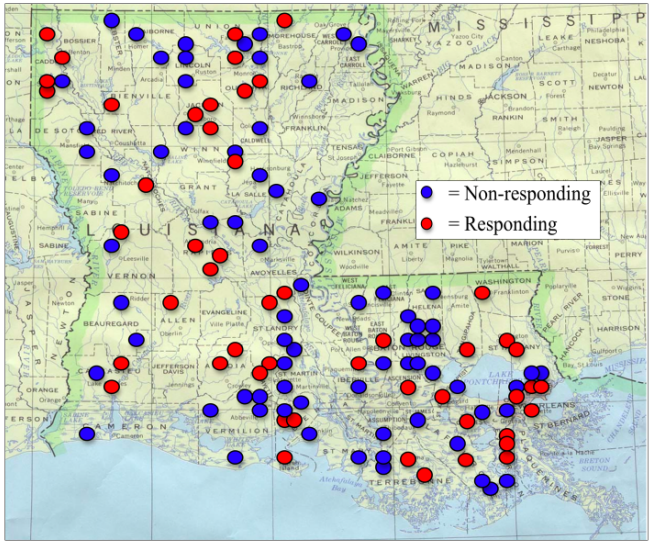
1. To determine influenza vaccination requirements and policies among hospitals in Louisiana, including the prevalence of mandatory requirements and consequences for declination
2. To correlate specific requirements with vaccination rates achieved, and to identify interventions that may increase vaccination rates

Methods

- A survey was sent to all 256 hospitals in Louisiana (under 193 organizations) identified in the Directory of the Louisiana Hospital Association.
- The survey contained questions on type of hospital, patient population served, components of the vaccination program and their estimated vaccination rate.
- Data was inputted into an Excel sheet and analyzed for components that influenced vaccination rates.
- Univariant analysis of categorical data compared the median vaccination rate between hospitals with or without a specific variable using the non-parametric Mann-Whitney test.
- The effect of continuous variables on the vaccination rate was analyzed with regression analysis using the non-parametric Spearman r.
- A p Value of <0.05 was considered significant.

Results: Hospitals Responding

- In the first 4 weeks, 49 (25%) of the 193 administrations responded with a statewide distribution (Figure 1).



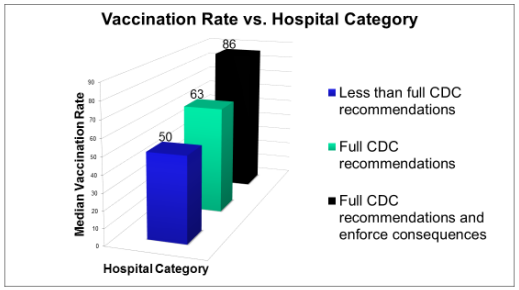
Results: Main Responses

- Most hospitals were private for profit (51%), private non-profit (35%), and public (14%); 22% were teaching and 51% were accredited by The Joint Commission.
- The median number of beds was 60 with a range of 10 – 800.
- All hospitals had a flu vaccination program; 33% had voluntary vaccination and 67% required a formal declination. No hospital demanded vaccination as a requirement of employment.
- All hospitals offered free vaccines; 27% met all CDC recommended activities for vaccination but 73% did not meet all CDC recommendations.
- 24% of hospitals enforced consequences to HCP declining vaccination while 76% had no consequences; the most common consequence was a requirement to wear a mask on patient contact.
- The median vaccination rate reported by the responding hospitals was 61%, with a range from 12 - 98%.

Results: Correlates of Vaccination

Factors Positively Associated with Vaccination Rates

Survey Questions		No. Responses	%	Not Present	Present	Ratio	p Value
				Median (25%, 75%)			
Hospital Type							
	Private	18	37	55 (45, 72)	73 (58, 84)	1.33	0.02
	Acute Care	28	58	50 (45, 72)	70 (57, 81)	1.40	0.02
High-Risk Patient Type							
	Children	29	59	50 (45, 71)	70 (56, 85)	1.40	0.02
	Pregnant Women	23	47	51 (45, 71)	72 (60, 85)	1.41	0.004
	Intensive Care	26	53	50 (42, 70)	71 (57, 85)	1.42	0.006
Number of Beds							
	0 - 99	26	53		50 (45, 71)	0.694	0.0006
	100 - 299	12	24		70 (56, 80)	1.186	
	≥ 300	8	16		85 (61, 92)	1.466	
Vaccination Program							
	Voluntary	16	33	71 (52, 85)	52 (40, 57)	0.73	0.001
	Declination Required	33	67	52 (40, 57)	71 (52, 85)	1.37	0.001
Vaccine Administration							
	Common areas	31	63	48 (37, 52)	70 (59, 83)	1.46	0.001
	Nights/Weekends	38	78	50 (35, 60)	70 (53, 84)	1.40	0.006
Program Promotions							
	Fliers	37	76	43 (33, 56)	69 (55, 80)	1.60	0.005
	Email	34	69	50 (45, 71)	66 (54, 84)	1.32	0.05
Consequences upon Declination							
	None	37	76	86 (82, 93)	55 (45, 70)	0.64	0.0001
	Some consequence	12	24	55 (45, 70)	86 (82, 93)	1.56	0.0001
	Wear mask	10	20	56 (46, 70)	89 (85, 94)	1.59	0.0001

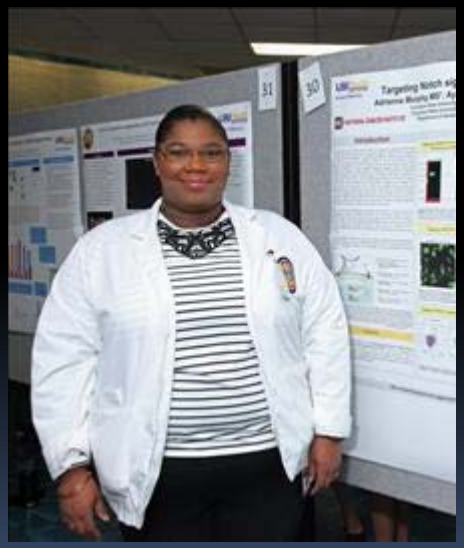


Conclusions

- Preliminary results demonstrate large variability among influenza vaccination programs in Louisiana hospitals. No hospital required vaccination as a condition of employment.
- Hospitals that impose consequences for vaccine declination have a higher vaccination rate than hospitals without consequences.
- Our findings suggest that to reach the goal of 90% vaccination rate by 2020, programs with consequences for declination (e.g. wearing a mask) must be enforced.
- These findings have important public health implications.

Awards:

- Travel awards to present your project at a regional or national conference



Deadlines:

1. Friday, September 9th
   Abstracts due to: SoMHonorsProgram@lsuhsc.edu
2. Monday, October 3rd
   Posters due to Isché Library (icirc@lsuhsc.edu)
3. Thursday, October 13th, 8am-12 noon, Lions Building, 6th Floor
   Research Symposium and poster judging
3. Tuesday, October 18th, 4-4:30
   Virtual Awards Ceremony (Zoom link: https://lsuhsc.zoom.us/j/96378180422)

Abstract and poster templates, guidelines:

https://www.medschool.lsuhsc.edu/genetics/summer_med_students.aspx

For examples, refer to the 2021 Symposium:

https://www.medschool.lsuhsc.edu/genetics/2020_medical_student_research_virtual_poster_symposium.aspx

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Research Symposium and Awards

- The Research Symposium and judging will be in person on the 6th floor of the Lions Building on October 13th, from 8am to 12 noon
- The Awards ceremony will be held on Zoom on October 18th , 4:00-4:30 pm
- Student presentations will be judged and awards will be given for each category
  - 1st and 2nd year med students
  - 3rd and 4th year med students

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Recorded Zoom presentation (not required, but recommended):

- The presentation will be linked on your website next to your abstract and poster.
- Record your presentation using Zoom.
- Present your poster for about 10-15 minutes.
- Send the link to SoMHonorsProgram@lsuhsc.edu by Friday, October 28th .

Recorded Zoom presentation

- Practice with your mentor and lab mates.
- After you create your final PowerPoint presentation, record yourself presenting it using Zoom.
- Before recording, do not save in the computer hard drive; save it on the Cloud
- Refer to the 2021 Symposium:
- https://www.medschool.lsuhsc.edu/genetics/2021_medical_student_research_virtual_poster_symposium.aspx

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What if you want to present more than one project?

- Choose only one for the in-person symposium
  - This is the one which will be judged
  - Follow the guidelines and deadlines previously mentioned.

- Additional presentations:
  - These will not be judged but the presentations will be posted on the website.
  - Turn in the abstract, poster, and Zoom recording between October 18th to October 28th

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Travel

Before submitting an abstract to a conference, please review the guidelines below:

- https://www.medschool.lsuhsc.edu/student_affairs/student_travel.aspx
- https://www.medschool.lsuhsc.edu/student_affairs/docs/Student%20Funding-Travel%20Request%20Form.pdf

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Continuing your research - funding opportunities Zoom Q & A on September 22nd at 5:00 pm

- NIH Medical Scholars Program
  - https://clinicalcenter.nih.gov/training/mrsp/
  - Annual stipend $41,000

Dr. Layne Raborn

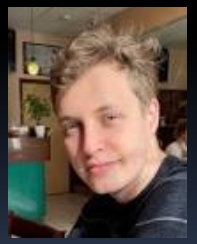
Victoria Huynh

- Center for Clinical and Translational Science (CCTS)
  - https://www.uab.edu/ccts/training-academy/research-fellowships/tl1
  - Annual stipend $25,836 plus $1,500 in travel

Jake Dorion

- Sarnoff Cardiovascular Research Fellowship
  - https://www.sarnofffoundation.org/page/2021-22_Fellows
  - Annual stipend $35,000, up to $8,000 for travel

- Diversity in Research Program, National Medical Fellowships and scholarships
  - https://nmfonline.org/scholarships-programs/programs-portfolio-overview/



Ben Bonner

- Physician Scientist Support Foundation (PSSF) Medical Scholars Research Fellowship; only one per institution, needs to be nominated by the dean
  - https://www.thepssf.org/msrf/
  - Annual stipend $42,000 plus $8,000 for health insurance and travel

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