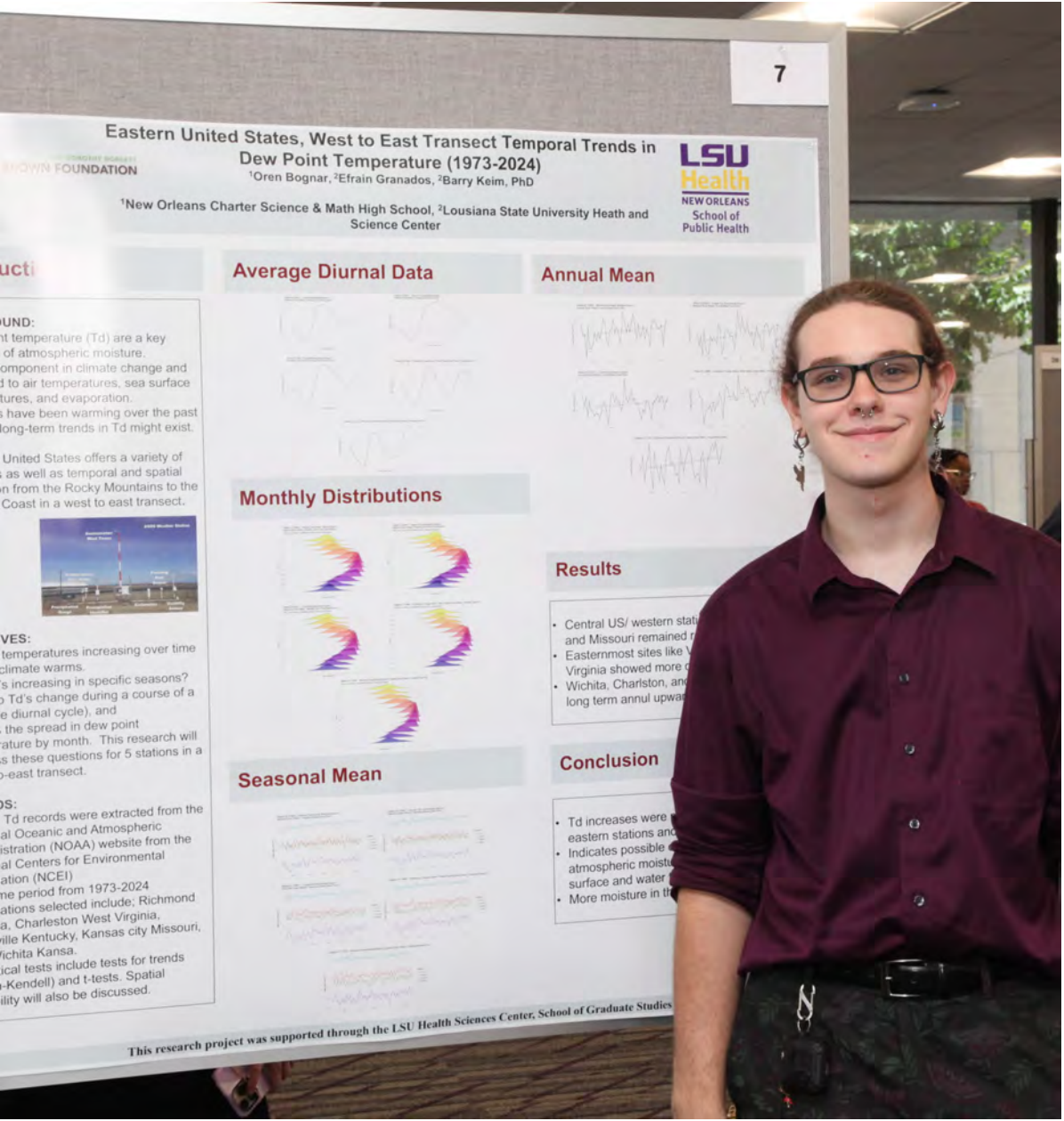
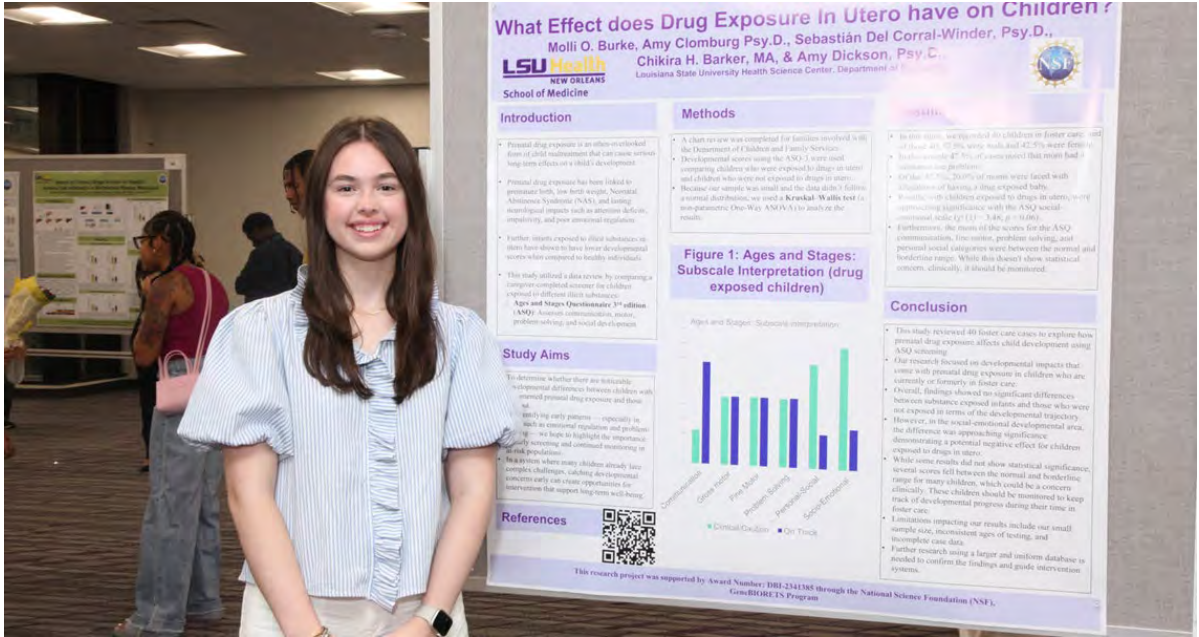


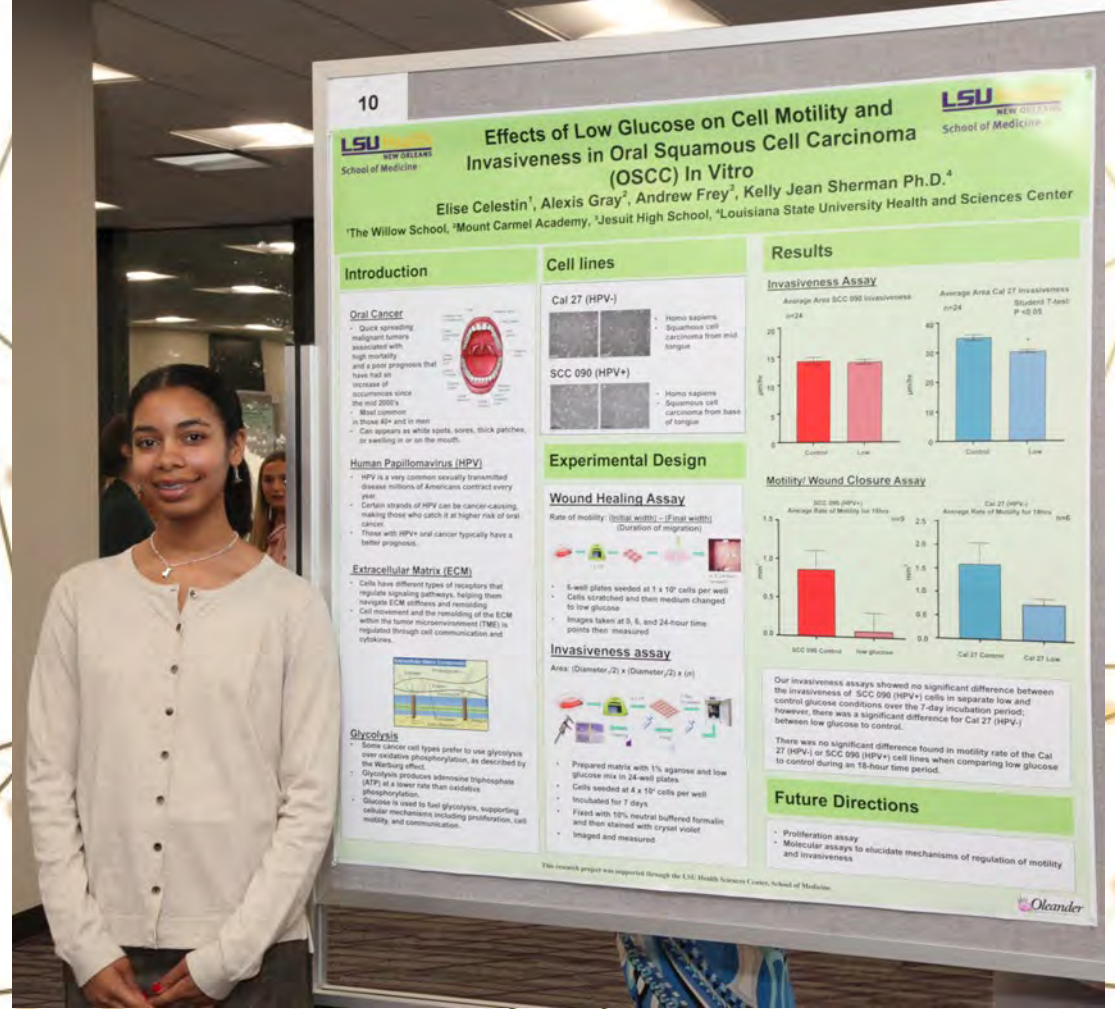
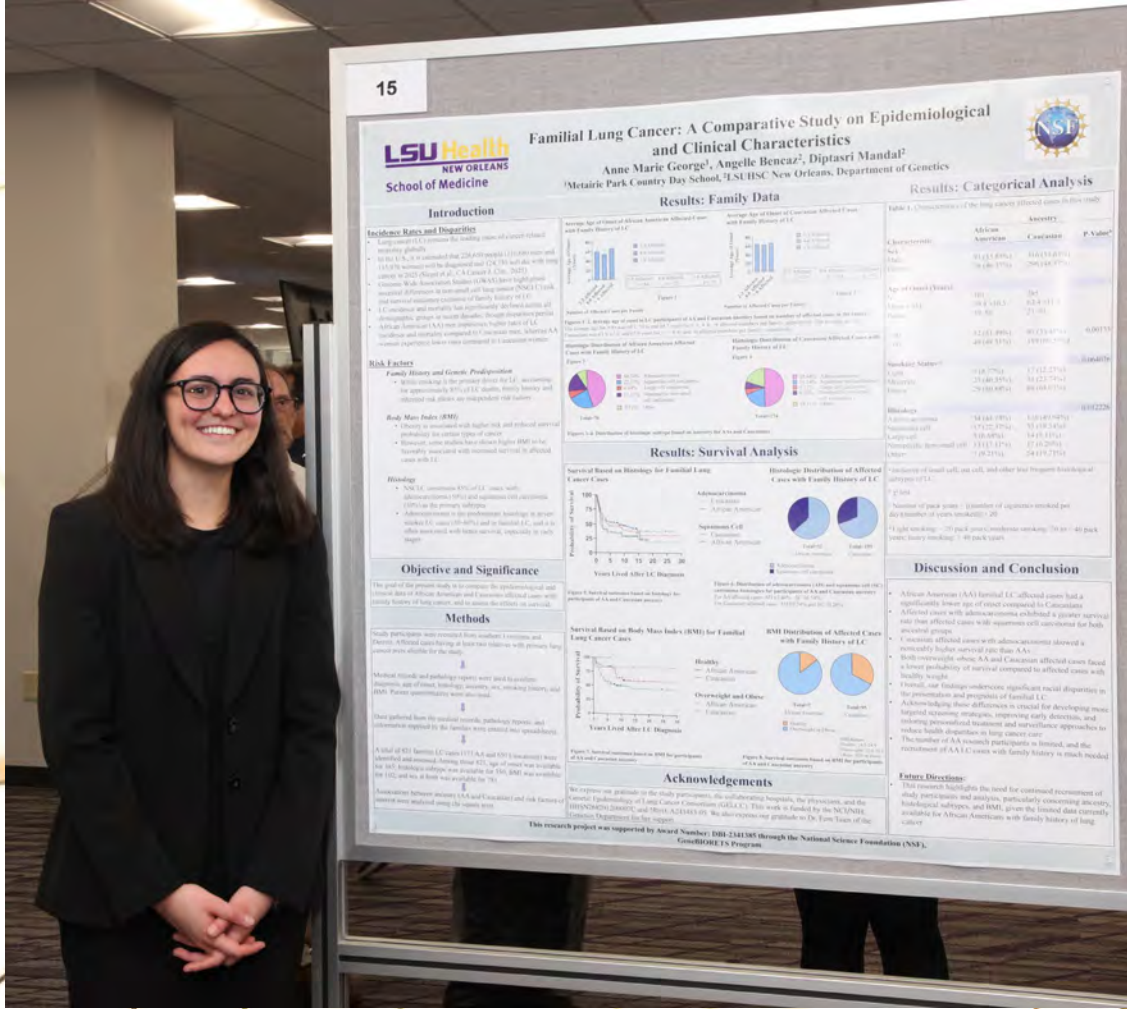
The background of the image is a complex, abstract network of thin, light brown lines connecting numerous small, solid brown dots. The dots are scattered across the frame, with some acting as central hubs from which multiple lines radiate outwards. The overall effect is a sense of interconnectedness and a web-like structure, typical of network diagrams or molecular models.

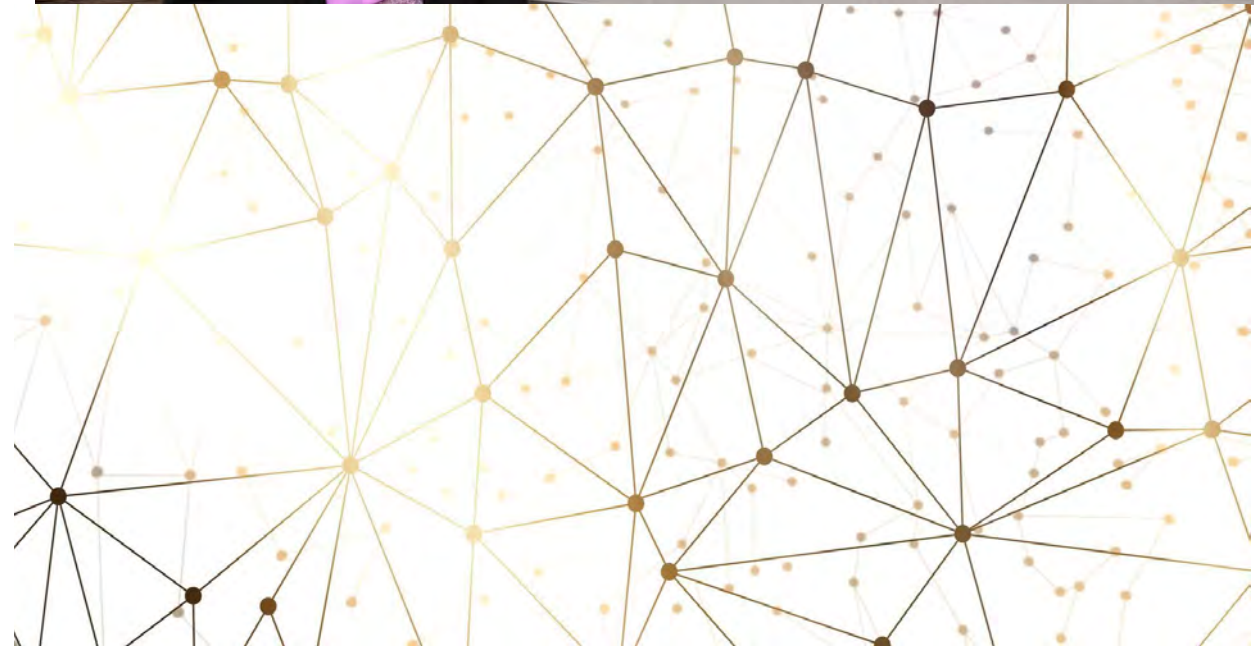
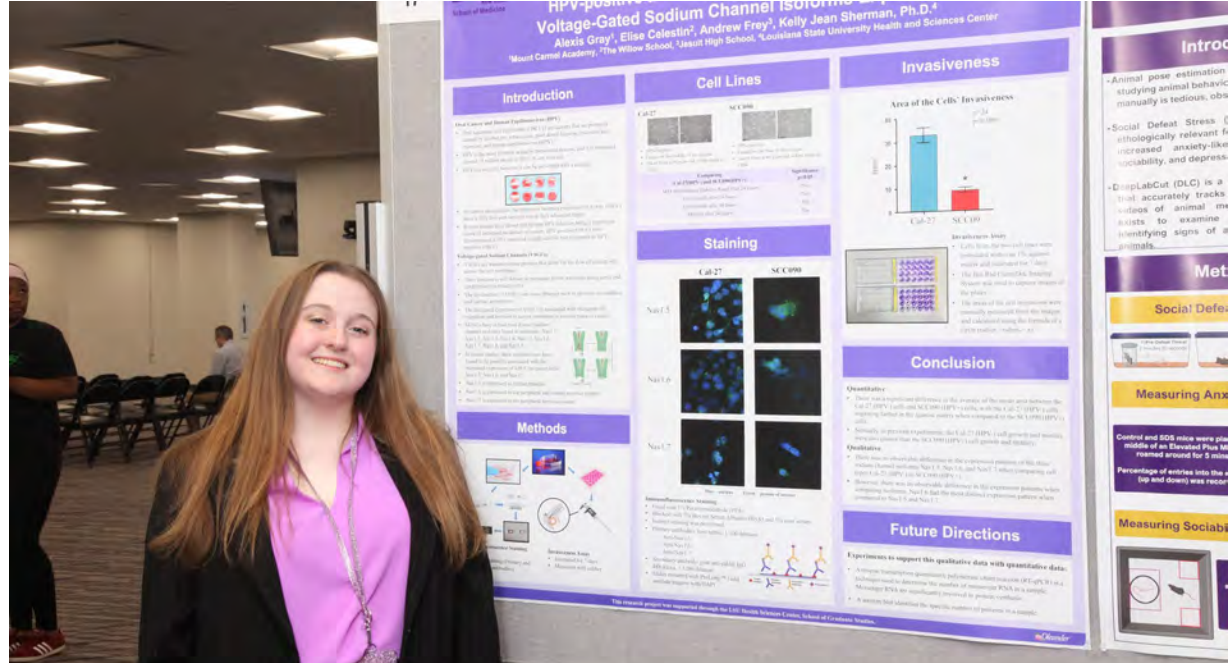
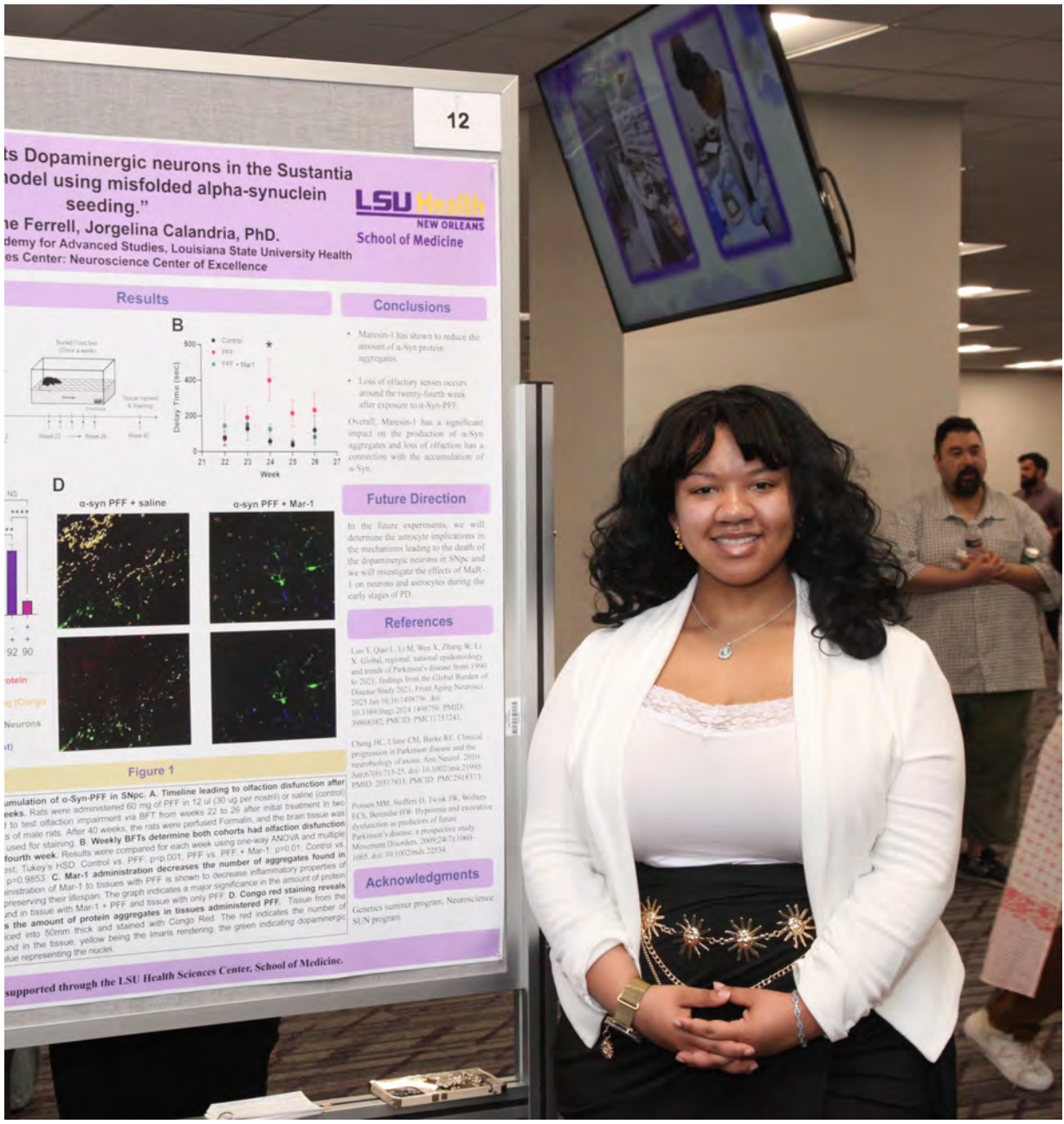
2025 Summer Research Program Symposium

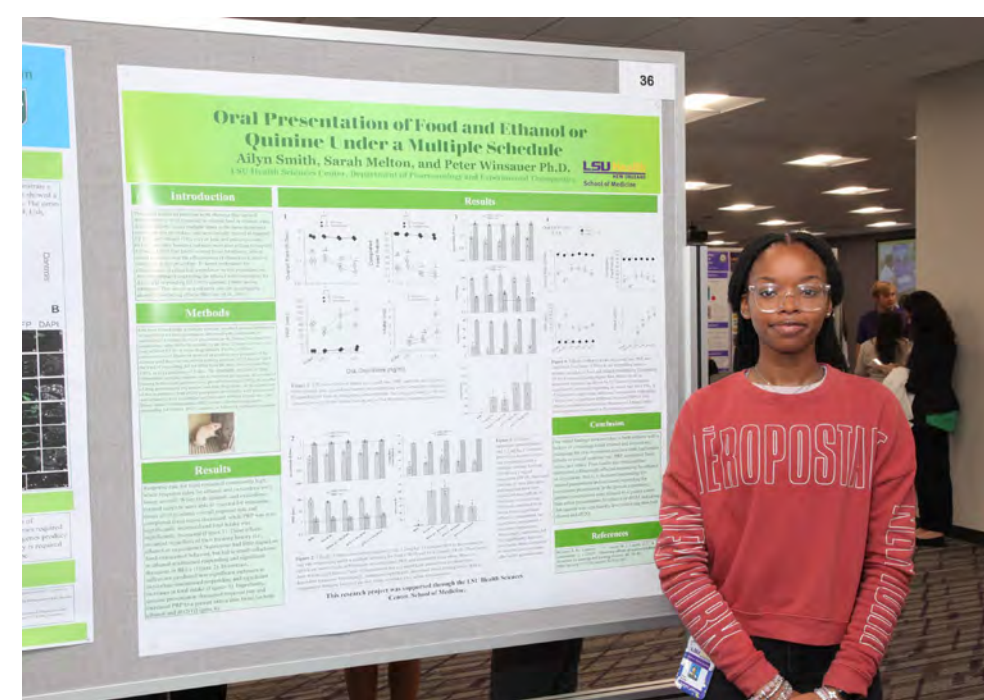
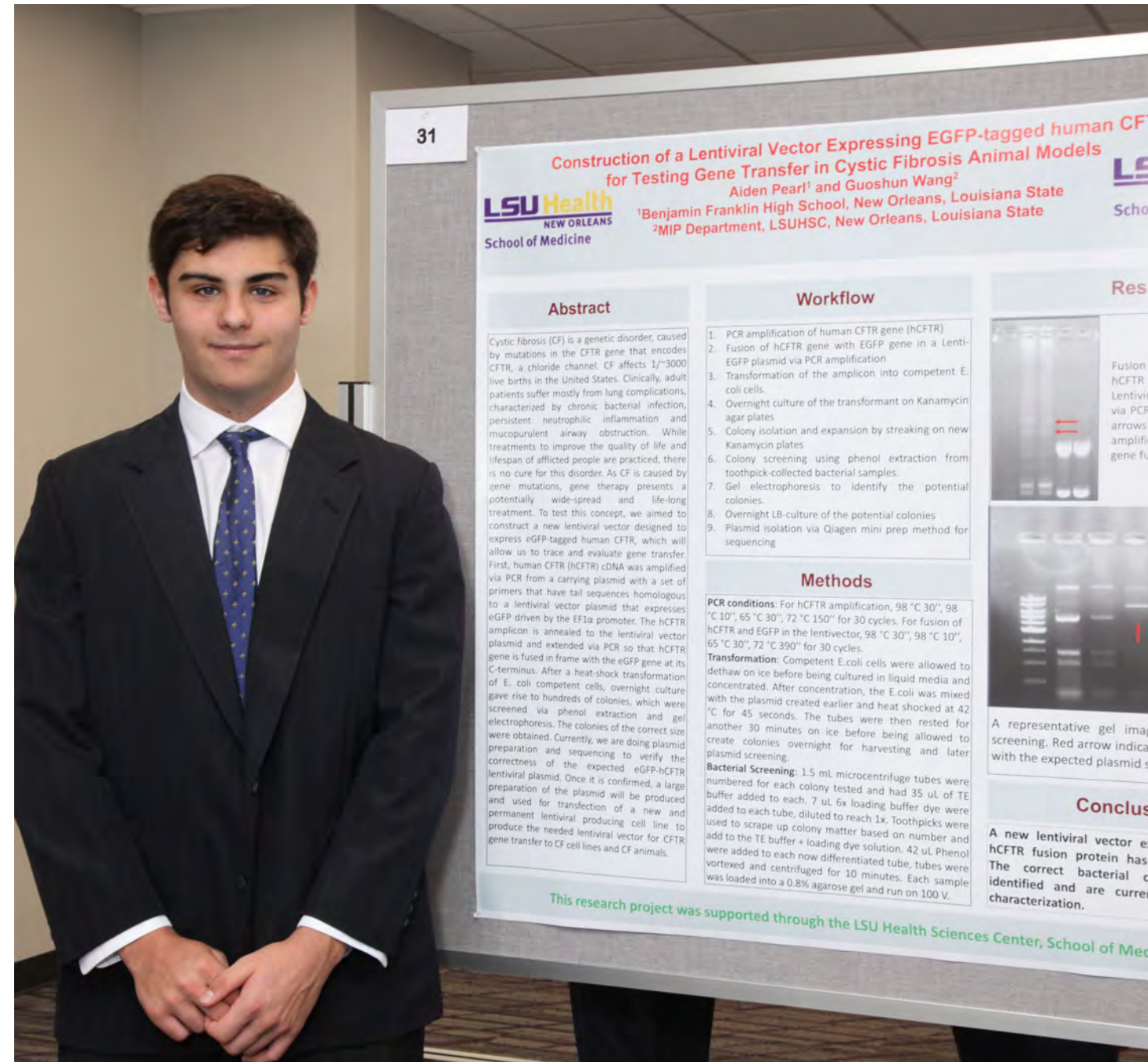
High School & Undergraduates

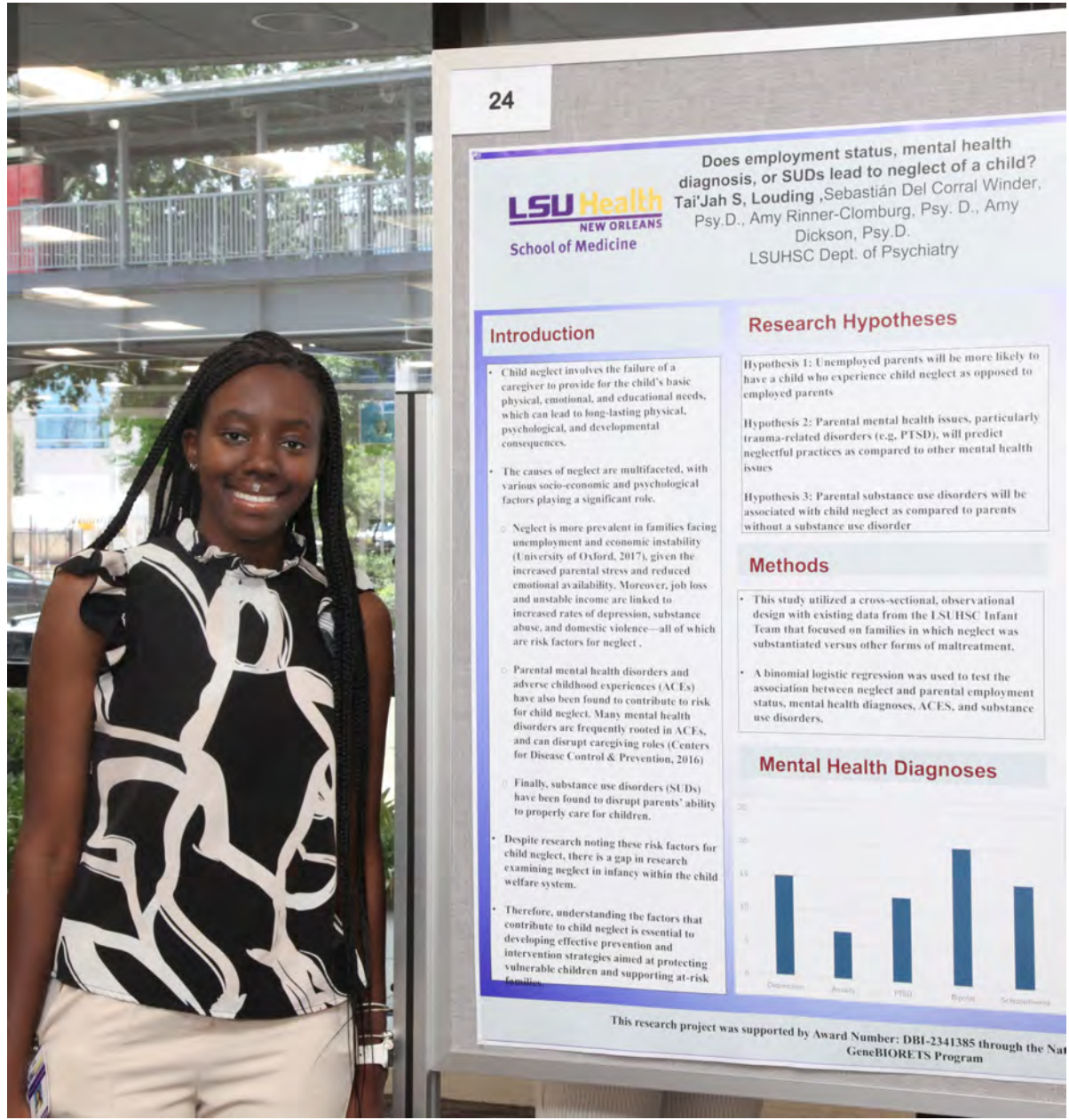
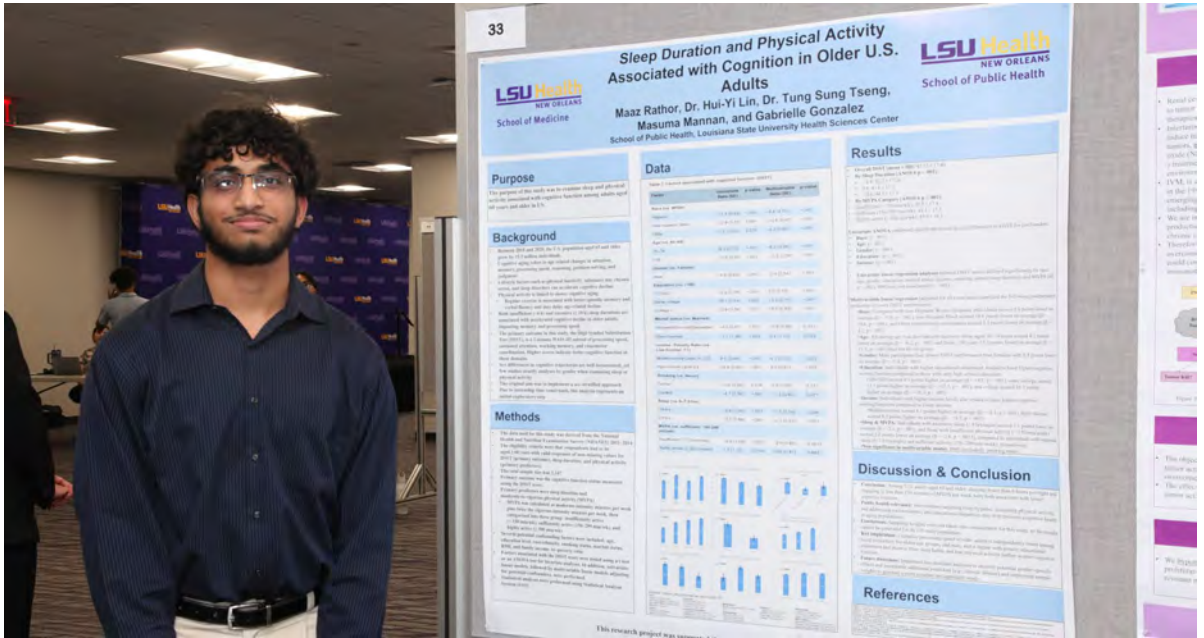


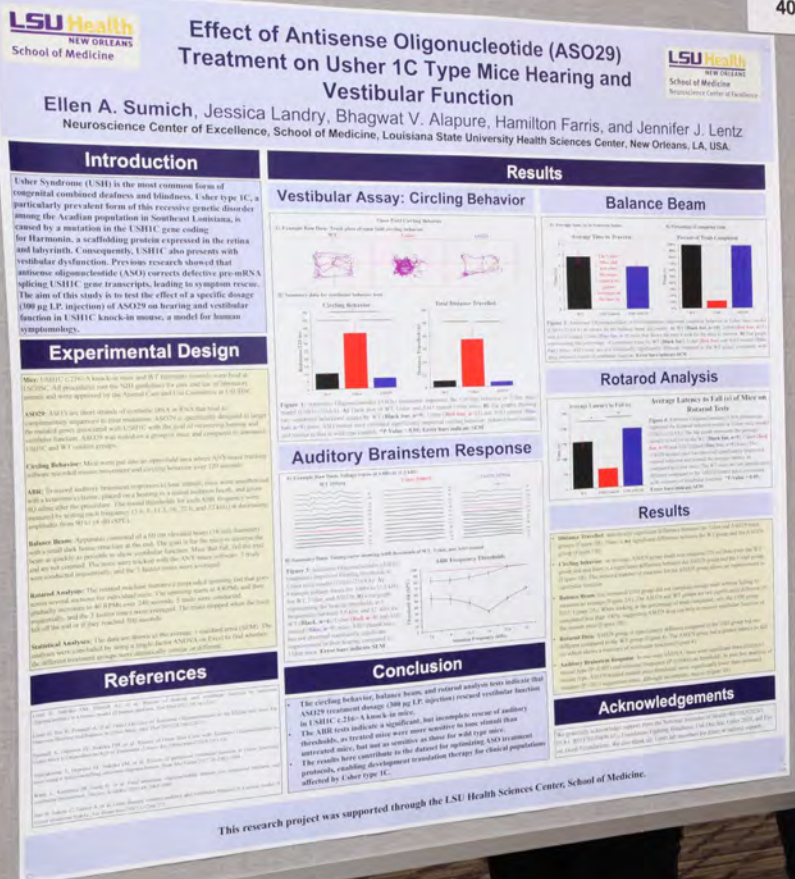
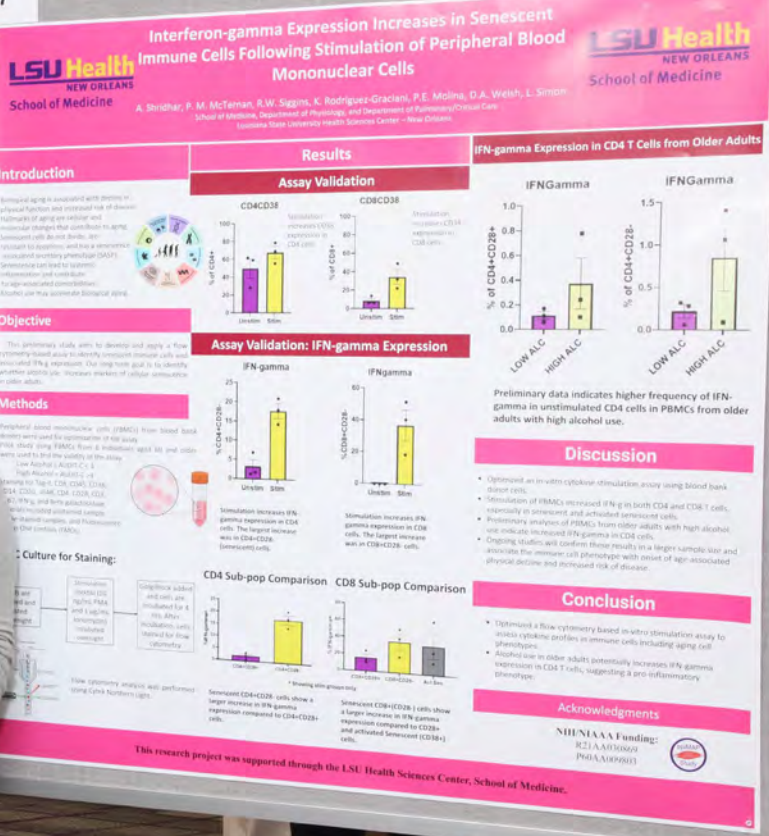


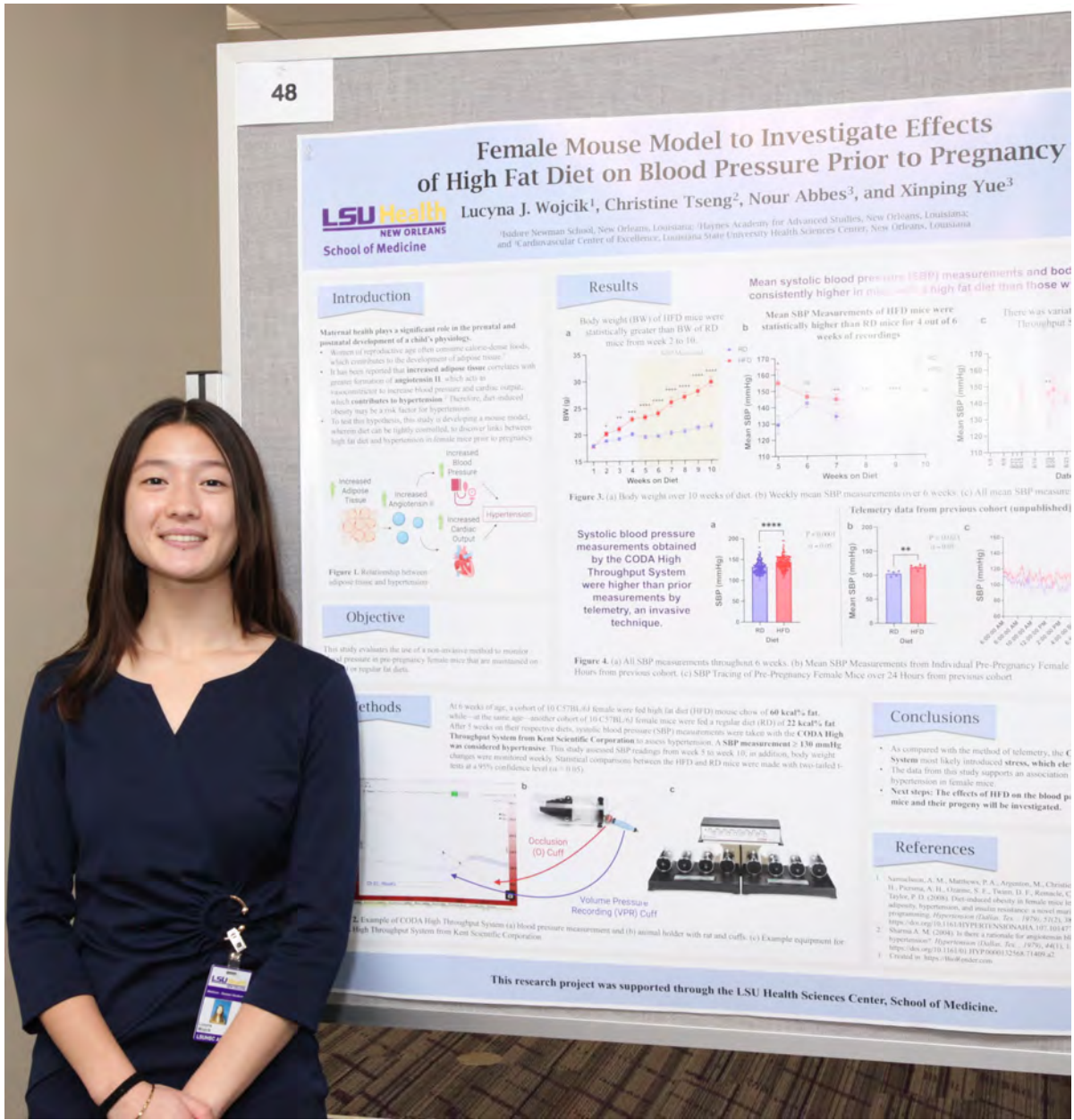
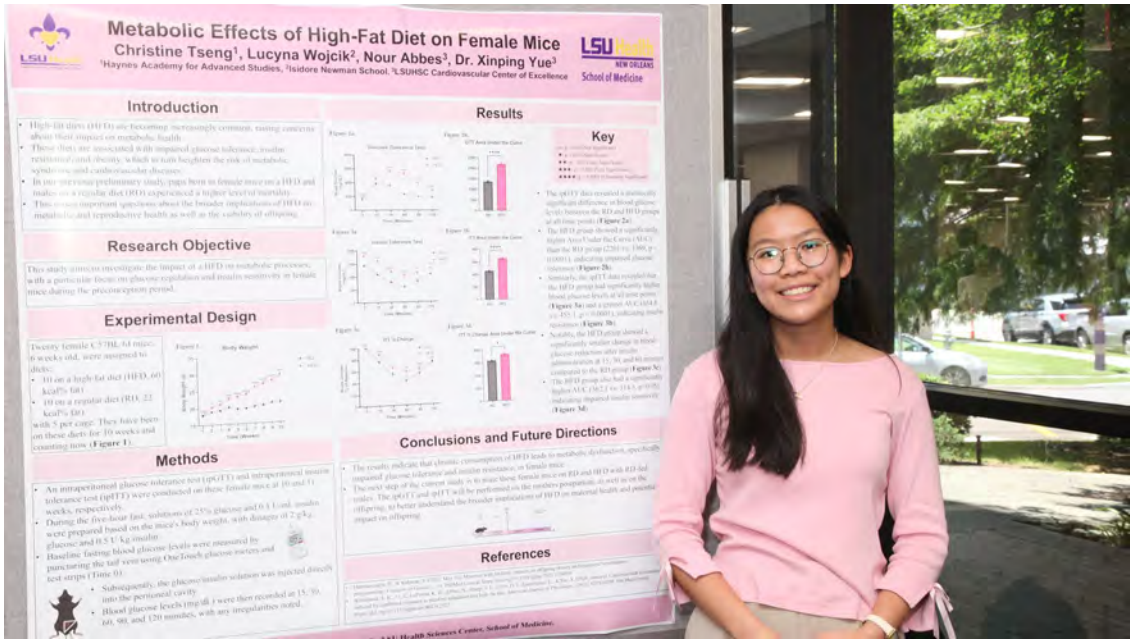














Development of Opioid Withdrawal as a Discriminative Stimulus in Rats

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Introduction

According to NIDA, there were over 105,000 drug-related overdose deaths in the United States during 2023 (2024). These tragic data show the need for reducing opioid abuse and dependence and for understanding the effects of withdrawal from opioids on the body. Whether it is precipitated or spontaneously initiated, withdrawal is accompanied by a range of adverse effects (e.g., diarrhea, gastrointestinal upset, muscle cramping, and chills) produced by a disruption in the body's neurochemical balance (Kintner, 2002). Symptoms of withdrawal are the primary reason opioid-dependent individuals continue administering opioids. Understanding a subject's ability to discriminate between a withdrawal and non-withdrawal state could, therefore, provide new insights into both the objective and subjective effects of opioid withdrawal.



Methods



A cohort of ten rats (7 male and 3 female) were first trained to lever press under a fixed-ratio 20 (FR-20) schedule for food reinforcers.

Physical dependence on the opioid morphine was then established by administering each rat 10, 20, 30, and 40 mg/kg twice daily over four days and were then maintained on 40 mg/kg of morphine once daily.

Withdrawal was initiated during sessions by either saline or 1 mg/kg of naloxone administered interperitoneally (i.p.) on which of two levers. The rat was trained under the FR-20 schedule to respond to the right lever, a NTX lever, and the left lever, a saline lever.



NTX

administer morphine

Results

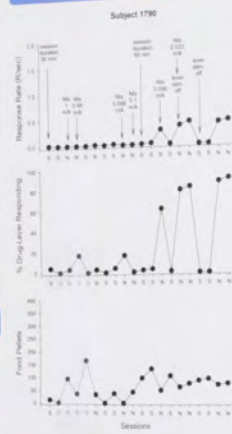


Figure 1: Subject 1790 showed some responding when given 0.056 mEq of NTX but there was more consistent responding once the dose was changed to 0.032 mEq NTX. There was also a subsequent increase in percentage drug-level responding on the days that NTX was administered. This subject has not yet consistently discriminated between the drug and saline lever on the appropriate days (N= NTX day, S= saline day) as shown by the ~95% percent NTX-lever responding following NTX administration.

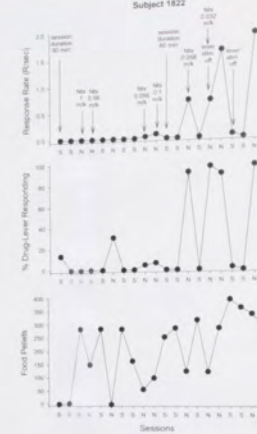


Figure 2: The 0.032 mEq dose of NTX has been shown to be effective as subject 1822 showed gradual improvement in their responding after the dose was lowered. There was also subsequent increases in the percentage of drug-level responding on the days that naloxone was administered. This subject has not yet consistently discriminated between the drug and saline lever on the appropriate days (N= NTX day, S= saline day) as shown by the ~95% NTX-lever responding following NTX administration.

Figure 3: Subject 1822 showed some responding when given 0.056 mEq of NTX but there was more consistent responding once the dose was changed to 0.032 mEq NTX. There was also a subsequent increase in percentage drug-level responding on the days that NTX was administered. This subject has not yet consistently discriminated between the drug and saline lever on the appropriate days (N= NTX day, S= saline day) as shown by the ~95% percent NTX-lever responding following NTX administration.

Conclusion and Future Directions

1. We established opioid dependence using chronic injections and confirmed dependence by showing precipitated withdrawal with naloxone.
2. Training is still in progress; saline and NTX injections will continue until the subjects meet two training criteria for 9 out of 10 consecutive days: (1) less than 20 responses on the incorrect lever prior to the first reinforcement, and (2) at least 95% responses on the correct lever for the entire session.
3. Subjects are reliably responding for food reinforcement during the behavioral sessions irrespective of the injection and subject learning to consistently discriminate between a withdrawal state and a non-withdrawal state.
4. The proper dose range to precipitate withdrawal without causing a drastic decrease in response rate has been identified.
5. These findings show that opioid withdrawal produces subjective effects that can serve as discriminative stimuli for behavioral responses. Therefore, this research creates a model for testing new therapies for withdrawal.
6. Future work will test NAD (nicotinamide adenine dinucleotide) as a treatment for withdrawal. This would ideally lead to better strategies for managing dependence and improving recovery outcomes.

This research project was supported through the LSU Health Sciences Center, School of Medicine.

Protein S Facilitates Clot Retraction through Tyro3 Signaling on Platelets

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Introduction

Platelets are small, anucleated cells that play a critical role in hemostasis and thrombosis. They are involved in the initial stages of clot formation and retraction. The process of clot retraction is essential for wound healing and preventing excessive bleeding.

Protein S, a natural anticoagulant, is known to facilitate clot retraction. It is a vitamin K-dependent protein that acts as a cofactor for protein C. The mechanism of action involves the activation of protein C, which then inactivates factors V and VIII, leading to the dissolution of the clot.

Platelets express Tyro3, a member of the Src family of tyrosine kinases. Tyro3 is involved in various cellular processes, including signal transduction and cell adhesion. It is hypothesized that Tyro3 signaling may play a role in the interaction between Protein S and platelets.

The goal of this study was to investigate the role of Tyro3 signaling in the facilitation of clot retraction by Protein S on platelets. We used a combination of biochemical assays and cell-based models to study this process.

Our results show that Tyro3 signaling is essential for the facilitation of clot retraction by Protein S on platelets. We observed that the inhibition of Tyro3 activity led to a significant reduction in the rate of clot retraction. Conversely, the activation of Tyro3 signaling enhanced the retraction process.

These findings suggest that Tyro3 signaling is a key component in the mechanism by which Protein S facilitates clot retraction. Further studies are needed to elucidate the downstream signaling pathways involved in this process.

This research project was supported through the LSU Health Sciences Center, School of Medicine.

Results

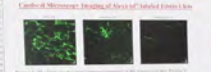


Figure 1: Confocal microscopy images showing the localization of Tyro3 and Protein S on platelets.



Figure 2: Bar graph showing the percentage of clot retraction for different conditions.

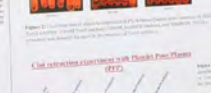


Figure 3: Bar graph showing the percentage of clot retraction for different conditions.



Figure 4: Bar graph showing the percentage of clot retraction for different conditions.

Conclusion

Our results demonstrate that Tyro3 signaling is essential for the facilitation of clot retraction by Protein S on platelets. This finding provides new insights into the mechanism of action of Protein S and the role of Tyro3 in platelet function.

These findings have important implications for the treatment of thrombotic disorders. Further studies are needed to explore the potential of Tyro3 inhibitors as therapeutic agents for these conditions.

This research project was supported through the LSU Health Sciences Center, School of Medicine.



