Maximizing Access to Research Careers

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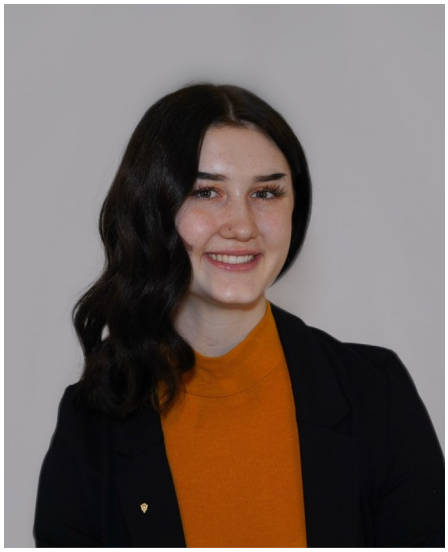

Delivery of Benzene Diazonium Ions (BDIs) to Biological Systems of Interest

ABSTRACT: The biological sciences rely on the ability to target and alter specific elements of a system, including strategies like fluorescent imaging and antibody-drug conjugates. These strategies require bioconjugation chemistry, which entails a reaction that creates a stable covalent bond between a specific site on a biomolecule and another molecule. This reaction can illuminate or change the function of these biomolecules.

Diazonium ions are used in bioconjugation chemistry because they react selectively with tyrosine and histidine residues. Since tyrosine and histidine are both abundant at sites of protein-protein interaction, altering their chemistry with bioconjugation can have a potent impact on the physiological processes in a cell. However, diazonium ions are prepared under very acidic conditions, are bench-unstable, and always reactive, making them incompatible with many biological systems. These challenges can be overcome by using a triazabutadiene scaffold, which releases a diazonium ion at physiological pH. The triazabutadiene can then be protected to prevent the release of a diazonium ion when protonated; after deprotection, the diazonium ion can be released.

My project involves the design of a protecting group for triazabutadienes that deprotects under hypoxic conditions. Hypoxia is characteristic of solid tumor cells. In the past, molecules have been designed to deprotect in the reductive biochemical environment found in hypoxic tissues. Therefore, a reduction-deprotected triazabutadiene is a potentially viable system to probe solid tumors.

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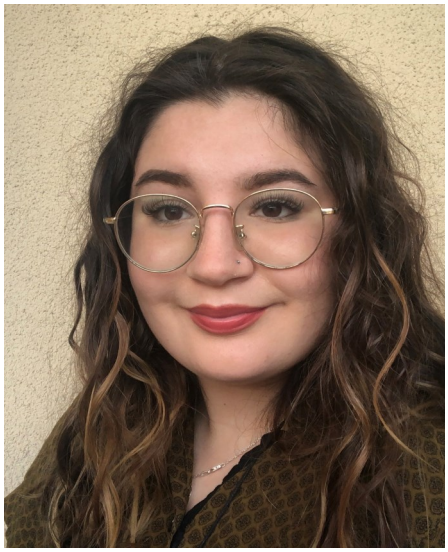

Goal Setting: A Glimpse into Episodic Future Thinking in Young and Older Adults

ABSTRACT: Episodic future thinking allows one to "pre-experience" an event that may occur in their personal future, which has implications for goal success. Research has shown that, compared to young adults, cognitively normal older adults envision the future with less episodic richness. This reduction in episodic richness is exacerbated in older adults with Alzheimer's disease (AD) dementia, raising questions about the effects of higher AD risk on episodic future thinking and goal success. This project seeks to better understand the relationship between goal attainment and future thinking, as well as how episodic future thinking and self-narrative continuity are affected by AD risk in younger and older adults.

In a multi-session study, participants created four goals, and subjectively rated the personal significance and vividness with which they imagined each goal. Ten days later, they rated the degree to which they planned and made progress in their goals. They also completed the prospective and retrospective memory questionnaire (PRMQ).

Analysis of these data showed a moderate positive correlation between goal vividness and goal progress, but no correlation between personal significance and goal progress. Goal planning was positively related to goal vividness, progress, and personal significance. Interestingly, older adults reported significantly more goal planning, personal significance and vividness, but did not make significantly more goal progress. Relatedly, PRMQ data showed no significant age-related differences in reported prospective memory efficiency.

These data reveal part of the relationship between episodic future thinking and goal follow through. Future research will shed light on how this episodic mechanism leads to individual differences in goal attainment, and how higher AD risk affects goal success and future thinking.

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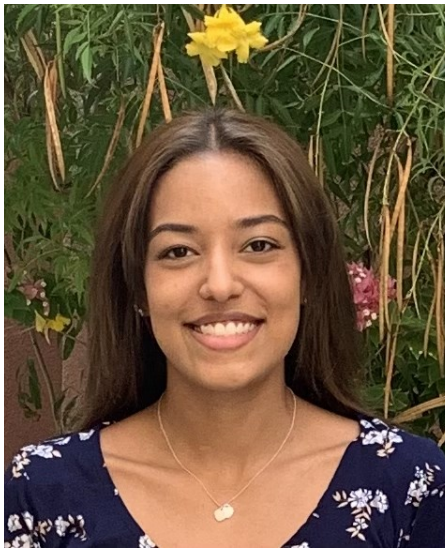

Measuring Integrin Subunit Localization in Prostate Cancer Cell Lines Using Immunofluorescence

ABSTRACT: TBA

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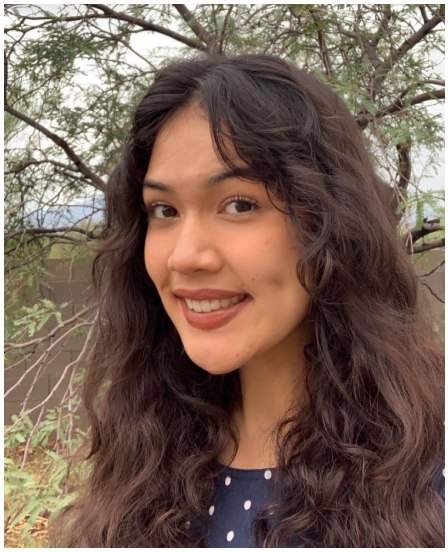

Quantifying Dementia-Relevant Behavioral Phenotypes in a Drosophila Model of TDP-43 Proteinopathy

ABSTRACT: TBA

Shyanne King

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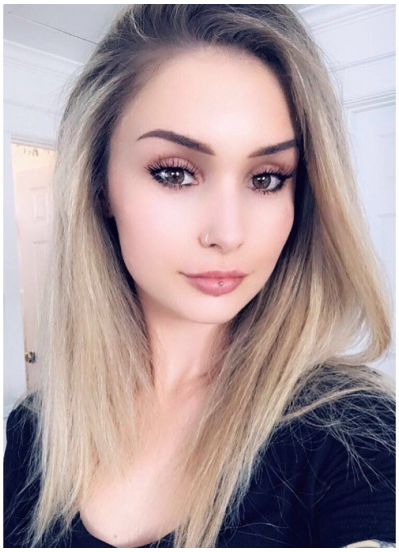

Determining the Role of Nuclear EGFR in Driving Metastatic Breast Cancer

ABSTRACT: Amplification or overexpression of the epidermal growth factor receptor (EGFR) gene occurs in most cases of triple-negative breast cancer. Nuclear EGFR acts as a transcriptional cofactor for several oncogenes and is associated with poor responses to targeted therapeutics and increased metastatic rates. We hypothesize that blocking the nuclear localization signal (NLS) of the receptor will prevent the aggressive metastatic phenotype associated with nuclear EGFR. We established two MDA-MB-468 cell lines to express either EGFR.GFPWT or EGFR.GFP$^{mut.nls}$ with a mutated NLS to block nuclear trafficking. Imaging of the cell lines revealed differential localization of EGFR after treatment with its ligand. The EGFR.GFP$^{mut.nls}$ cells did not appear to contain nuclear EGFR. We then transduced the parental cells with lentiviral particles containing inducible shRNA to knock down their endogenous EGFR to avoid dimerization between wildtype and fusion proteins. After collecting lysates of these cells, we probed for EGFR in a western blot, which revealed successful transduction and knockdown of the endogenous EGFR. In future experiments, we will use these cells to determine if eliminating the NLS of EGFR can prevent the manifestation of a metastatic phenotype in triple-negative breast cancer.

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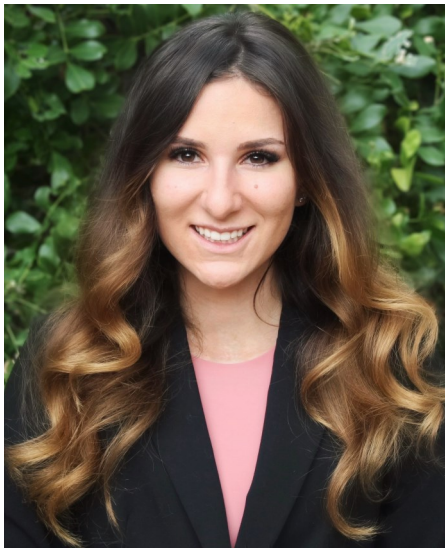

Transcranial Magnetic Stimulation (TMS) of the Default Mode Network as a Treatment for Insomnia

ABSTRACT: Insomnia, characterized by difficulty falling and/or remaining asleep, remains one of the top complaints among military personnel. A large majority (85%) of these individuals exhibit a clinically relevant sleep disorder, and ~42% report getting five hours of sleep, or less, each night. These sleep disruptions diminish optimal alertness, vigilance, and decision-making. The development of nonpharmacological interventions for insomnia is essential for military personnel to perform well in operational environments where alertness cannot be compromised. Insomnia associates with a tendency to engage in self-reflective rumination and worry, which activate the Default Mode Network (DMN), a network in the brain that links the posterior cingulate, precuneus, medial prefrontal, and inferior parietal cortices. This study utilizes targeted noninvasive electromagnetic fields to modestly reduce activation within the inferior parietal lobe (one node of the DMN), a process known as Transcranial Magnetic Stimulation (TMS). TMS creates a current in the brain, via the electrochemical firing of brain cells (neurons), to temporarily reduce the functional connectivity of the DMN. We hypothesize that active TMS will reduced DMN connectivity and improve a night of subsequent sleep compared to a sham treatment. We will evaluate 20 individuals, with self-reported sleep problems to correlate improved sleep metrics and post-sleep cognitive performance with the use of TMS prior to sleep and compare the outcomes to those individuals receiving sham treatment. Results will be statistically analyzed using data gathered through actigraphy, polysomnography, a battery of cognitive assessments, and functional magnetic resonance imaging (fMRI) brain scans.

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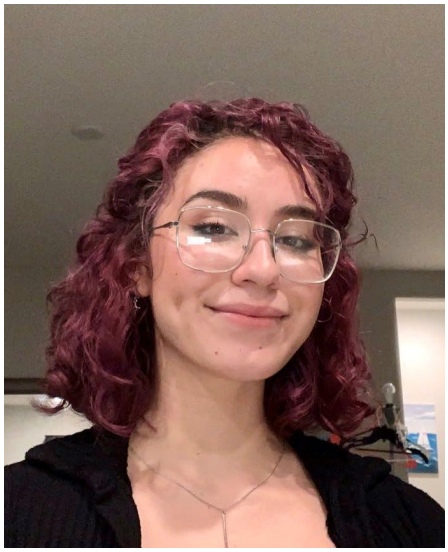

Investigating the Relationship between Aging, Stress, and Stress Granule Dynamics in Drosophila

ABSTRACT: TBA