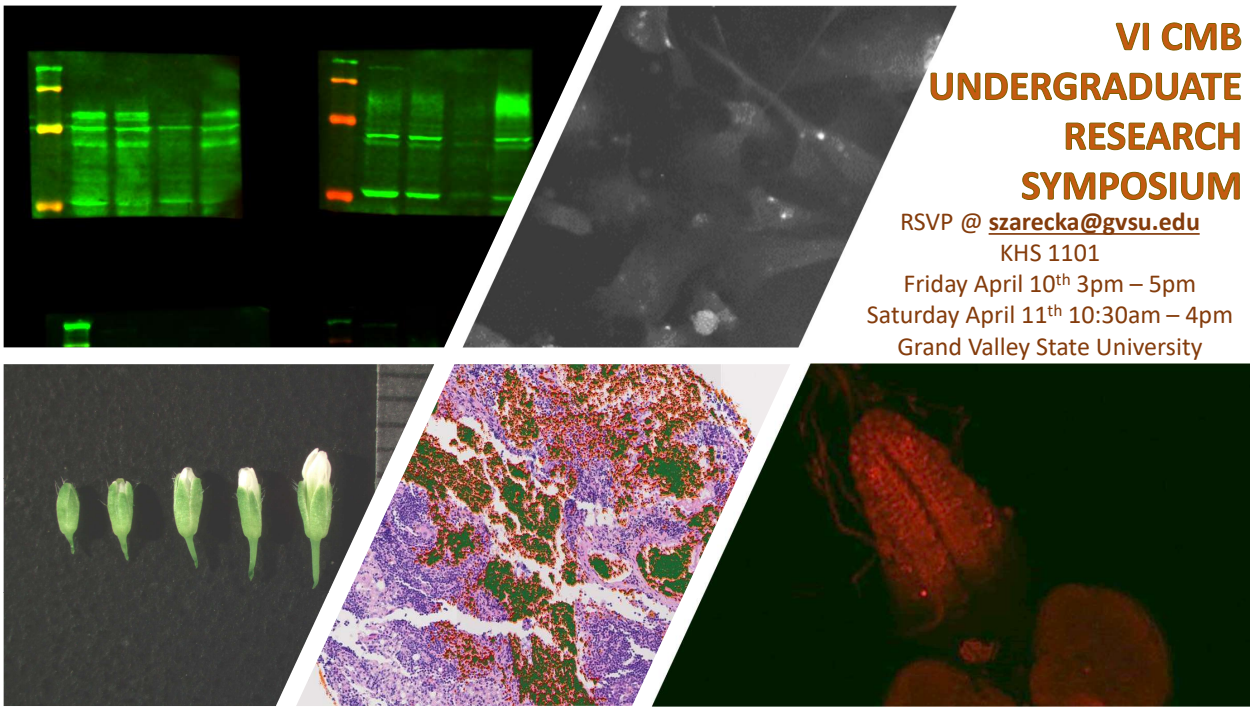


VI CMB UNDERGRADUATE RESEARCH SYMPOSIUM

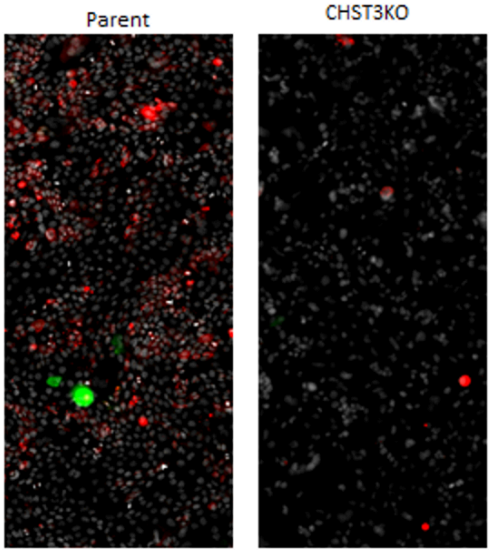
RSVP @ szarecka@gvsu.edu
KHS 1101
Friday April 10th 3pm – 5pm
Saturday April 11th 10:30am – 4pm
Grand Valley State University

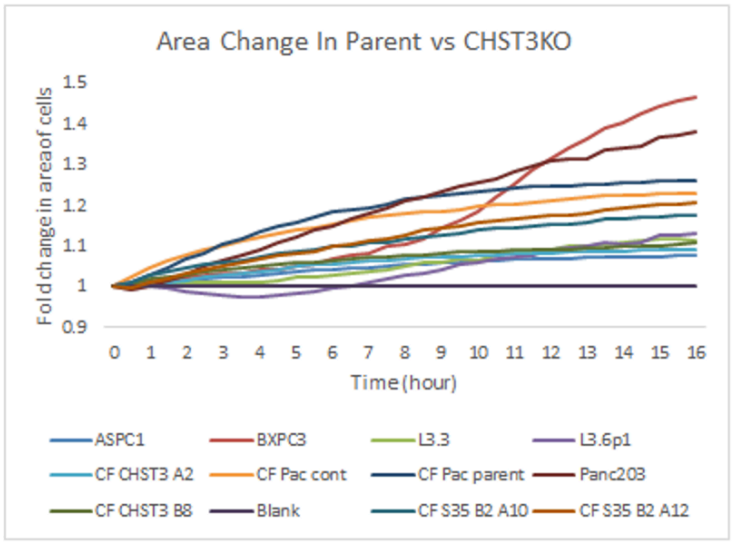
Book of Abstracts

Galactose 6-Sulfation by CHST3 as a Marker for Increased Cell Migration in PDAC

David Ayala-Talavera[1,2], Kevin Maupin[1], Chong-Feng Gao[1], Johnathan Hall[1], Nicole Burmeister[1],
Mentor: Dr. Brian B. Haab[1]

[1]Van Andel Research Institute, Grand Rapids MI
[2]Department of Cell and Molecular Biology, Grand Valley State University, Allendale MI



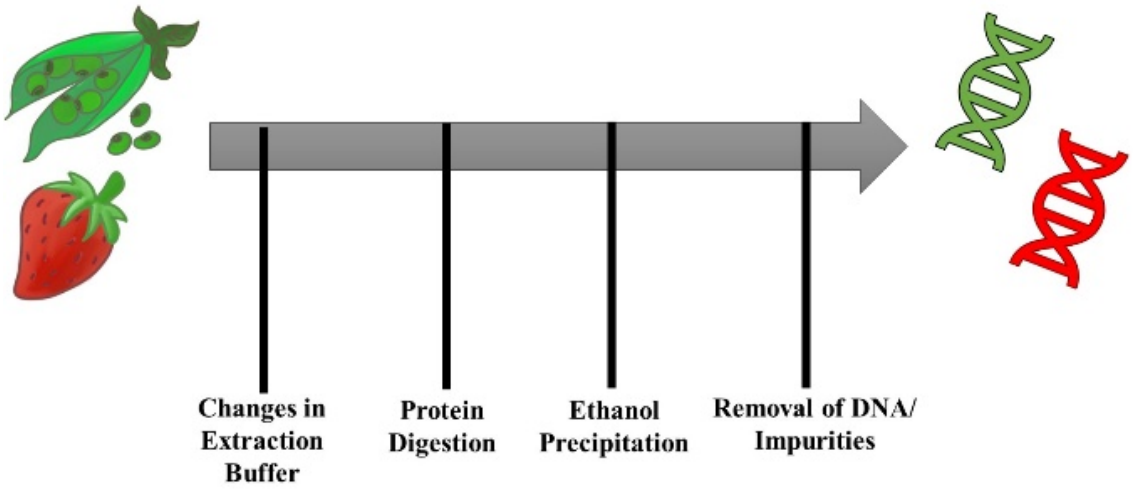


Molecular markers to detect subtypes of cancer cells could facilitate more effective treatment of Pancreatic Ductal Adenocarcinoma (PDAC). The current widely accepted makers are only able to detect 70% of PDACs and therefore complementary markers are needed. Current research focused on improving these detection methods for both diagnostic and prognostic purposes. We recently identified a galactose 6-sulfated glycan detected by sialic-acid-binding immunoglobulin-like lectin-F (Siglec-F) that could be a serological prognostic biomarker of migratory pancreatic cancer types. In this project we sought out to identify if cancer cells producing the sulfated glycan are migratory and if removal of the glycan by knockout of carbohydrate sulfotransferase 3 (CHST3) eliminates the 6-sulfated glycan along with migratory characteristics. Immunofluorescence staining of Siglec-F in PDAC tissues showed that the Siglec-F binding is elevated in metastatic tissue when compared to other PDAC tissues. Wound healing assays of 27 pancreatic cancer cell lines showed positive correlation with rapidly migrating cell lines and cell lines that were elevated with the Siglec-F antigen. A knockout of CHST3 was performed on a portion of the highly migratory cell lines migration ability was significantly decreased if not eliminated in the CHST3KO when compared to the parent. The galactose 6-sulfated glycan detected by Siglec-F defines a separate subpopulation of cancer cells and could have value for classifying migratory subtypes of PDAC.

Refinement of simple and rapid strawberry gDNA extraction method with further investigation of quality of DNA generated during experimentation

Mikaela A Berg[1],
Mentor: Dr. Patrick Thorpe[1,2]

Grand Valley State University, Department of Cell and Molecular Biology[1],
Department of Biology[2], Allendale, MI

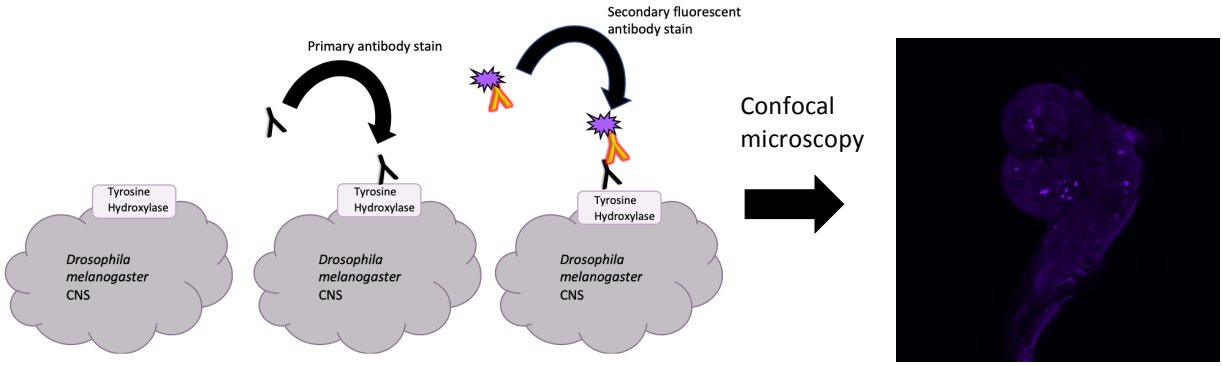


DNA extraction from strawberries may be achieved utilizing commonly found household chemicals to demonstrate the molecular lab experience. The questions being addressed here are: A) how and in what ways can we improve on this method while maintaining a simplicity and cost effectiveness, B) contents of the final extract and the quality of the DNA that is extracted using this method? Others have been able to show this method being used in multiple lab settings; however, they have failed to use the extracted DNA any further; like restriction digest and PCR. We set on a standard method of DNA extraction and tested variations of the method to answer A and then used multiple verification tests to answer B. By changing individual variables and stages in the standard method we were able to compare the outcomes of these changes directly through agarose gel electrophoresis, spectrophotometry readings, and digestions to verify the quality of DNA obtained. With our data obtained the changes we found to be most effective were; decrease in initial pH of the extraction buffer, and direct addition of chelex to the sample. With the work done so far, those using this method (for introductory scientific settings) use this method as an inexpensive and still reliable way to carry out and understand the molecular lab experience while maintaining a tight budget.

Evaluation of a Parkinson's Disease-Related Protein in *Drosophila melanogaster*

Alexis Ellis, Cory Gemmen, Gage Paul, Isabel Thompson[1]
Mentor: Dr. Sok Kean Khoo

Department of Cell and Molecular Biology, Grand Valley State University, Allendale, MI



Parkinson's disease (PD) is a neurodegenerative disease characterized by alpha-synuclein (α-syn) protein aggregation and loss of dopamine, a neurotransmitter that regulates motor functions. Currently, there is no treatment to stop or slow the disease progression. In this study, the fruit fly *Drosophila melanogaster* with inserted human α-syn genes is used as an animal model to evaluate the expression of tyrosine hydroxylase (TH), a protein required for dopamine synthesis in dopaminergic cells. We aim to investigate whether depletion of dopaminergic neurons can be observed in our transgenic flies with A30P and A53T α-syn mutations of familial PD. Using immunofluorescence staining that targets tyrosine hydroxylase as a marker for dopaminergic cells, we found clusters of dopaminergic neurons in the central nervous system (CNS) of larva flies. Further TH staining in adult fly CNS and execution of locomotion assays will determine the potential of using these transgenic flies to study PD.

Perceptions of Fear and Anxiety Throughout Chemistry Laboratories

Mackenzie Canfield
Mentor: Brittland DeKorver

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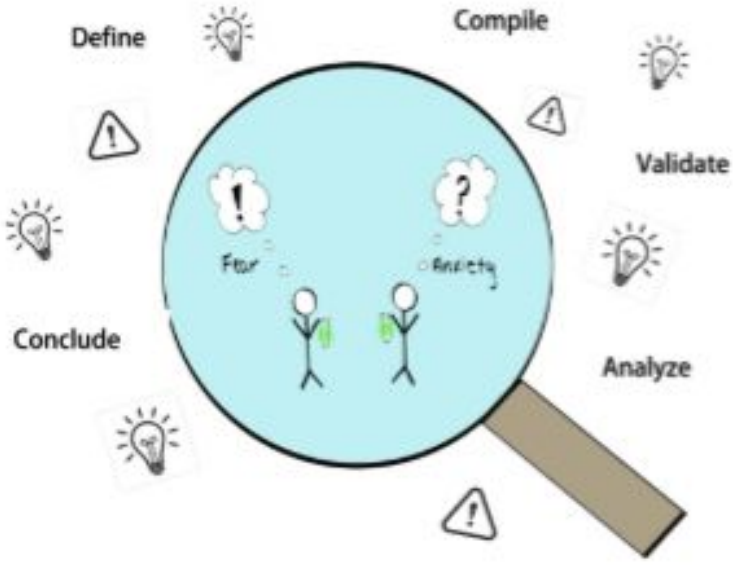
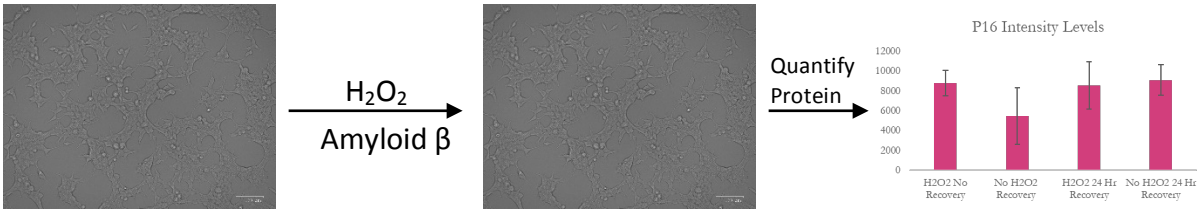


In chemistry education, it has been observed that students' learning can be impacted by their emotions and perceptions; some perceptions, such as risk and danger can vary depending on the students' demographics. Our study seeks to know how gender and race influences the students' perceptions of risk, danger and fear. Previously surveys that have looked at these negative feelings but have not distinguished between fear and anxiety. This study investigates whether students describe their own perceptions of chemistry laboratories as fear or anxiety as defined by previous research in psychology. Data was collected through the qualitative technique of one-on-one structured interviews and analyzed through deductive coding. The findings of this research could lead to improvements in laboratory curricula, resulting in a more equitable experience for all students.

Role of Amyloid Beta in Cellular Senescence Associated with Alzheimer's Pathology

Marcia Gordon[1], Diego Flores[1,2], Dylan Fineran[1], Jennifer Westerhuis[1], Dave Morgan[1]
Mentor: Marcia Gordon [1,*]

[1]Department of Translational Neuroscience, Michigan State University, MI 49503, USA.
[2]Department of Cell and Molecular Biology, Grand Valley State University, Allendale, MI.



Cellular senescence was originally identified as a stable cell cycle arrest, but it is now recognized that senescent cells secrete toxic molecules, such as cytokines, proteases and inflammation stimulators that could contribute to the risk of Alzheimer's disease. It was recently demonstrated that selective removal of senescent cells with senolytic drugs improved Alzheimer-like pathology in mouse models. To elucidate direct mechanisms by which Alzheimer-type pathologies might induce cellular senescence, we treated HEK 293T and human dermal fibroblast cells with oligomeric amyloid-beta. As a control, we treated another group of cells with hydrogen peroxide to induce oxidative stress as shown in previous studies. The experimental design included cell culture techniques, treatment with hydrogen peroxide or amyloid beta for 2 hours, collecting over several time points, and measuring expression levels of $p16^{INK4A}$ (a senescence marker using) western blots. We hypothesize that amyloid and hydrogen peroxide will induce $p16^{INK4A}$ and allow increased understanding of the interaction of amyloid- β pathology and its possible role for cellular senescence in Alzheimer's. This could lead to further therapeutics measures and drugs targeting this interaction.

National Institute Health – National Institute Aging (Grant No.: 5R01AG062217-02)

The Gravitational Pressure Model in Rice Roots Grown in Varying Densities of medium.

Andrew Hankiewicz
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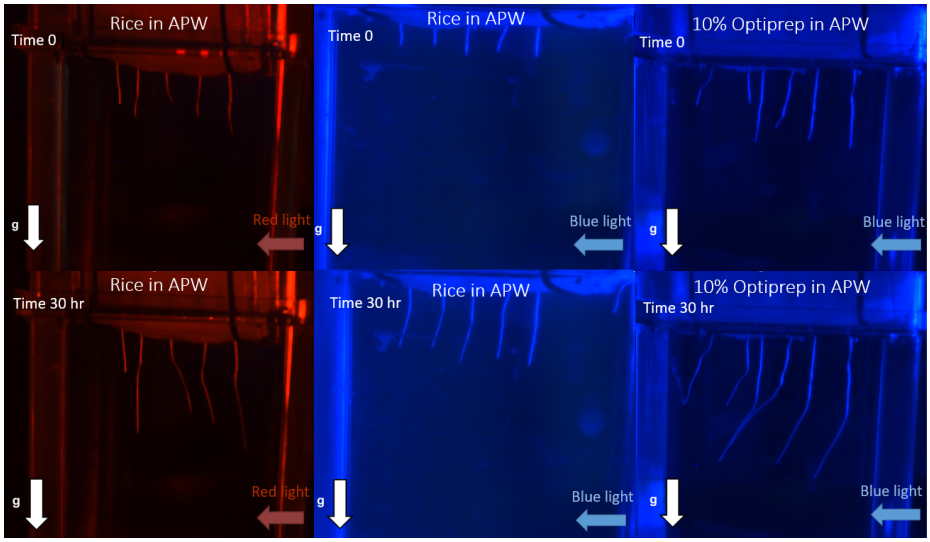

The exact mechanism by which plants can sense gravity is still debated. The starch-statolith model hinges on statoliths (sedimenting starch granules) for gravisensing. However, the gravitational pressure model can be used to explain gravisensing in cells with or without statoliths. We have demonstrated that increasing the density of the external medium with Optiprep inhibits the gravity response (and increases the phototropic response) of roots exposed to blue light and gravity. Assuming that Optiprep is impermeant to the plasma membrane, these results support the gravitational pressure model of gravisensing while invalidating the statolith model. To test whether the plasma membrane is indeed impermeable to Optiprep, and Optiprep treatment doesn't make statoliths buoyant within the cell, we fixed and sectioned roots subject to both Artificial Pond Water (APW) and Optiprep solutions. Specifically, APW and a 10% Optiprep/APW solution (more dense) were used to make solutions of different densities for the rice roots to grow in. The roots were subsequently fixed using FAA, dehydrated in a succession of alcohol solutions, imbedded in paraffin wax, sectioned using a microtome and then viewed using a light dissecting microscope. This was done to determine whether Optiprep treatment caused statoliths to become buoyant with in the cell. This data will add depth to the evidence supporting how plants use gravitational pressure within the cell to sense gravity.

Characterization of Deletion Mutations Induced in the *Hdc* Gene in *Drosophila Melanogaster*

MaryAnn Jaquith[1], Selina Ruiz Mendoza[1],
Mentor: Dr. Martin Burg[2]

[1] Grand Valley State University, Department of Cell and Molecular Biology, Allendale, MI
[2] Grand Valley State University, Department of Biomedical Sciences, Allendale, MI

Histamine is synthesized by the enzyme Histidine decarboxylase (encoded by the *Hdc* gene) and mutations in the *Hdc* gene result in lack of histamine synthesis, leading to numerous defects. While most mutants of the *Hdc* gene show lowered levels of histamine, they still exhibit residual levels of transcriptional activity. In order to remove *Hdc* function completely, the *Hdc* gene was subjected to *Minos* transposon-excision mutagenesis to remove the *Hdc* gene. Candidate deletion mutants that demonstrated disrupted *Hdc* activity were isolated. Oligonucleotide primers specific to the *Hdc* gene region and *Minos* transposon element were created to generate fragments using PCR, to locate where the deletion in *Hdc* is located. Current results suggest deletions obtained are restricted to the *Minos* element and do not remove the *Hdc* gene as anticipated. Further analysis of the deletions obtained to understand how these lead to disruption of *Hdc* gene function is ongoing.

Examination of Overexpressed Gene(s) Relating to Filamentation and Biofilm Formation in *Candida albicans*

Justin Mason[1,2]
Mentor: Derek Thomas[2]

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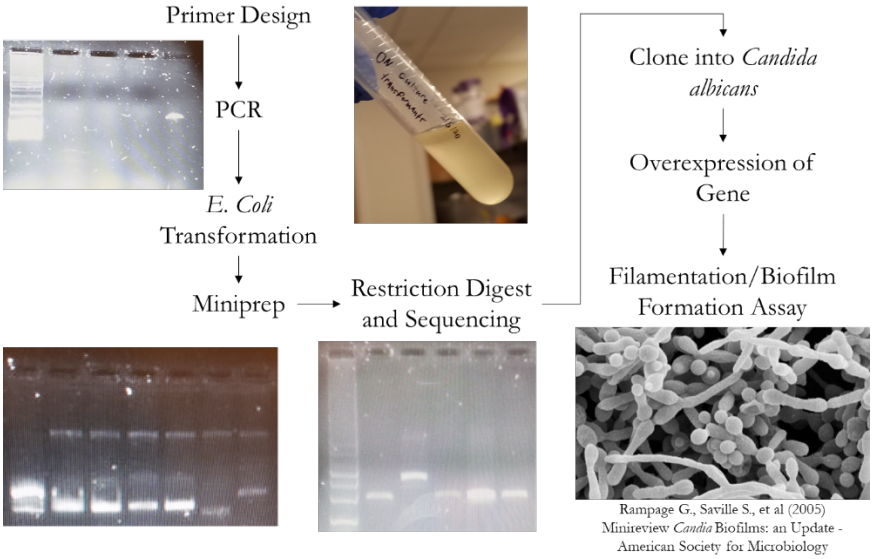
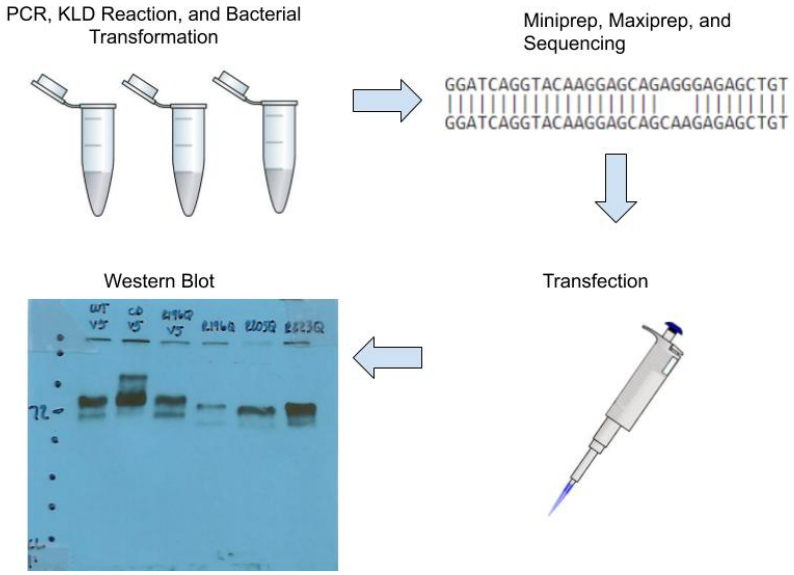


The opportunistic fungal pathogen, *Candida albicans*, commonly resides in the human gut flora. *C. albicans* is ubiquitous in the environment; however, infections appear to typically come from one's own population. Pleomorphism, filamentation, and the formation of biofilms is thought to be crucial in *Candida's* virulence. The formation of *Candida* biofilms is especially of clinical interest because resistance to antifungal drugs and host immune defenses is greater than any morphology on its own. Yeast to hyphae switching is a complex process which involves numerous proteins. A greater understanding of these proteins is crucial in combating *Candida* diseases. Our approach is to overexpress these genes (currently, *CAR2* and/or *PGK1*) relating to morphology and filamentation. Transformation of *E. coli* and subsequent plasmid extractions have been successful; currently, we're assessing the plasmid quality and will ultimately overexpress the uncharacterized gene in *C. albicans.*

The Role of TMPRSS13 in Breast Cancer: Identification of Potential Cleavage Sites

Alaina Norrito[1], Carly Martin[2,3], Kimberley Sala-Hamrick[3], Jacob Mackinder[3], Hiwot Lessanework[3], Tommy Hyland[3]
Mentor: Karin List[2,3]
[1]Grand Valley State University, Department of Cell and Molecular Biology[1], Allendale, MI, [2,3]Wayne State University, Departments of Cancer Biology[2] and Pharmacology[3], Detroit, MI,



Breast cancer is the second most diagnosed cancer and the second leading cause of cancer-related deaths in U.S. women. Many forms of breast cancer can be treated with hormonal therapies that target the estrogen receptor, progesterone receptor, and HER2 protein. Triple-negative breast cancer (TNBC) is unique because patients lack all three targets, reducing treatment options. Transmembrane proteases increase the progression of cancer through the degradation of the extracellular matrix. TMPRSS13 is a type II transmembrane serine protease that has been shown to be upregulated in breast cancer cells as compared to normal tissue and is a promising therapeutic target. Our previous investigation of catalytic and glycosylation mutants of TMPRSS13 has revealed the potential for an additional cleavage site within the protease that we hypothesize may lead to shedding and substrate cleavage. Our objective was to investigate potential cut sites and determine if cleavage was occurring. We performed site-directed mutagenesis on four arginine residues located in the extracellular domain of TMPRSS13. The mutations were confirmed by Sanger sequencing and inserted into a plasmid vector. We transfected HEK293T cells with the mutant plasmid and performed Western blotting. We have identified R223Q as an additional site of cleavage. Further understanding of the functional and oncogenic role of TMPRSS13 in breast cancer in addition to its biochemical properties may assist in drug design for TNBC.

Generation of α-synuclein transgenic fruit flies to study Parkinson's disease

Gage Paul[1,2], Cory Gemmens[1], Alexis Ellis[1], Diego Flores[1],
Mentor: Dr. Sok Kean Khoo[1]

[1]Grand Valley State University, Department of Cell and Molecular Biology, Allendale, MI,
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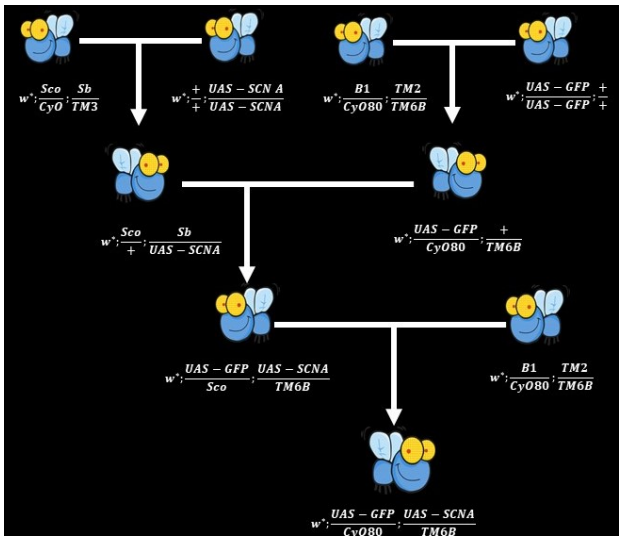

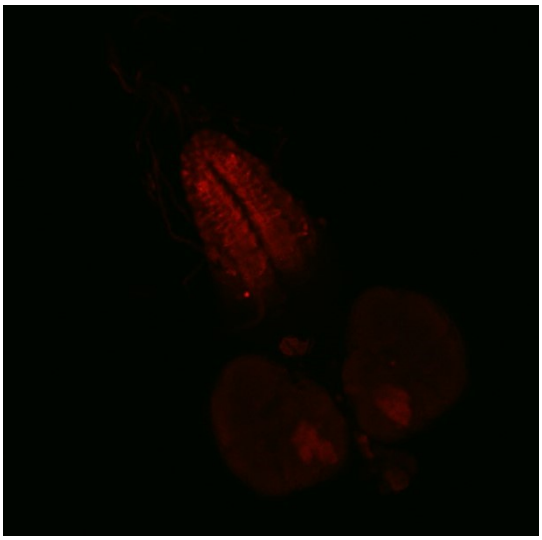

Parkinson's disease (PD) is the second most common neurodegenerative disorder impacting 1-2% of the elderly population. PD is characterized by the loss of midbrain dopaminergic neurons and the formation of α-synuclein (α-syn) protein aggregates, also known as Lewy bodies, along with loss of motor function in the extremities. Currently, there is no cure for PD and its medications only provide symptomatic relief. Thus, an effective animal model that allows visualization of α-syn aggregates within the central nervous system (CNS), along with loss of motor functions, is required to investigate potential PD treatments. Here, we generate fruit flies *Drosophila melanogaster* with human α-syn expression within their CNS along with a GFP reporter to indicate where α-syn is expressed. The generation of a robust fly model will allow for the acceleration of novel treatment research for PD.

Fully funded by the Arnold and Mable Beckman Foundation Beckman Scholars Program at GVSU.

The Impact of Stratification Duration and the Absence of Group 1 LEA Proteins on the Germination Rate of *Arabidopsis thaliana*

Ben Randall[1]
Mentor: Dr. Sheila Blackman[1]

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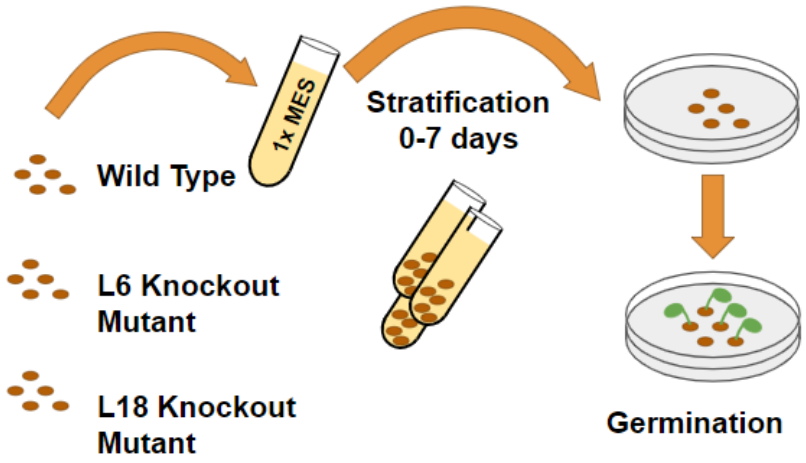

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Adequate germination time is a critical variable for crop survival and some plants require an additional period of stratification for proper germination. Stratification is a period of cold storage that simulates winter conditions before planting in spring, but little is known about the mechanisms of stratification. Late embryogenesis proteins (LEA) are highly expressed during seed development and are thought to be involved in germination. Many studies have demonstrated that storage conditions impact seed viability, but none have addressed the impact of whether LEA proteins affect the stratification times necessary for successful germination rates. Here, we investigate this by stratifying wild type, LEA 6 and LEA 18 knockout mutant *Arabidopsis thaliana* seeds for different times and subsequently planting the seeds in sterile media to monitor germination rates. We report an inverse relationship between duration of stratification and germination period. Seeds that were stratified for at least 72 hours showing a 50% reduction in average germination time compared to seeds that were not stratified, and seeds stratified for the longest duration, 168 hours having the shortest germination period. We also show that the absence of LEA 18 lengthens the germination period and reduces survival rates, while the absence of LEA 6 shows no noticeable change in either. Our results provide crucial insight for further study of stratification mechanisms that can be used for improving crop regulation and increasing yield.

Using transgenic flies containing an altered *Hdc* promoter fusion with GFP to examine *Hdc* promoter function in *D. melanogaster*

Selina Ruiz Mendoza[1], Elizabeth Croff, Elise Miller, Erik R. Anderson
Mentor: Dr. Martin G. Burg

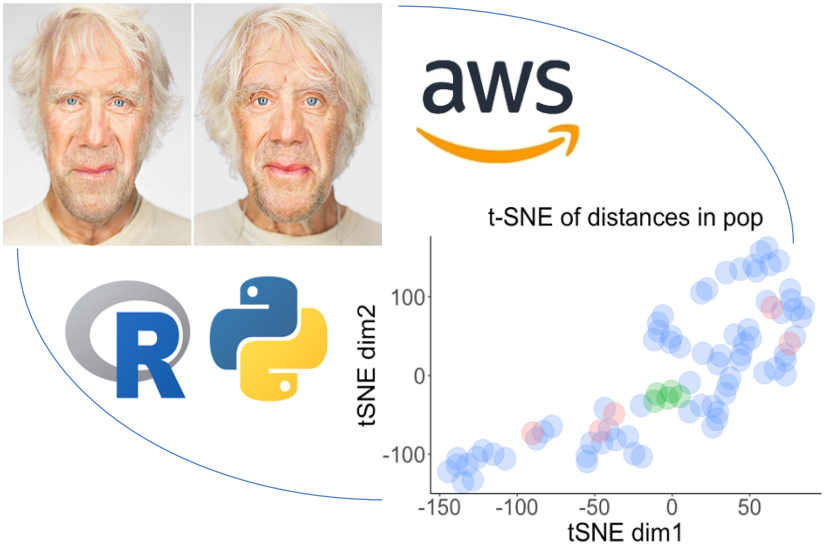
Grand Valley State University, Department of Cell and Molecular Biology, Allendale, MI 49401
Grand Valley State University, Department of Biomedical Sciences, Allendale, MI 49401

The *Hdc* gene encodes for histidine decarboxylase, an enzyme that synthesizes histamine. This study's goal is to identify functional domains of the promoter region for *Hdc*, since 4 separate transcription start sites (TSS) are identified. Previous work, using the presumed fully functional promoter region (pHdc^{L}), indicates that the pHdc^{L} fragment directed Green Fluorescent Protein (GFP) expression in all histamine containing cells, a product of HDC enzyme activity. However, it is not known if the 4 promoters induce expression in different tissues, which could be answered using the pHdc^{S} (short form) which eliminates one TSS from the promoter region. To conduct this study, the full promoter (pHdc^{L}) or short promoter (pHdc^{S}) region were cloned into a transformation plasmid to create a direct fusion with the GFP reporter gene. Plasmids were injected into embryos and germline transgenic flies were isolated. We examined GFP expression patterns in the pHdc^{L}-eGFP and pHdc^{S}-eGFP transgenic flies. The pHdc^{S}-eGFP flies did not have GFP expression in some cells, particularly in the brain regions, when compared to GFP expression induced in the pHdc^{L}-eGFP transformant flies. The importance of this study is to demonstrate the role of various transcriptional isoforms in the spatial regulation of gene expression, refining our understanding of how promoter structure affects expression of a gene.

Reproducible Differences in the Facial Features of Monozygotic Twins

Warren Sink[1], Dr. Brej Muhire[1], Dr. Luca Fagnocchi[1]
Mentor: Dr. Andrew Pospisilik[1]

[1]Van Andel Research Institute, Grand Rapids, MI, 49403, USA

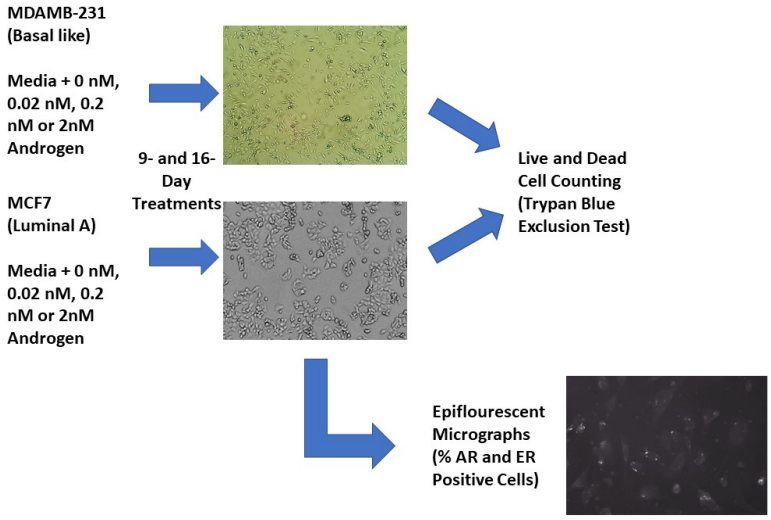


Polyphenism is the consistent and predictable presence of discrete or continuous phenotypic variation across a population in an environmentally variant but isogenic system. No polyphenism in *Homo sapiens* has been hitherto described, partly because of the youthfulness of NGS sequencing and the lack of a large sample of a genetically controlled population being conducted in an longitudinal analysis. Using photographic portraits of monozygotic cotwins from Martin Schoeller's *Identical* (n = 110) and those provided by the Michigan State University (MSU) Twin Registry (n = 298), we report the presence of consistent differences in cotwins' facial features, separating them into concordant and discordant groups. To make sense of the large number of variables, generated from the amount of landmarks provided by the facial recognition technology per individual (p = 27), computation of each individual cotwins' pairwise facial landmark distances (p = 351), and pairwise ratio of distances (p = 61425), we performed Principal Component Analysis (PCA) and sparse PCA along with the visualization techniques t-SNE and UMAP on the differences between cotwins. Additional images of various ages of cotwins and data related to the zygosity of the MSU cotwins are needed to refine the conclusion of this small study; although evidence suggests cotwins' facial features diverge similarly.
Funding was provided by the Frederick and Lena Meijer Student Internship Program and by the Pospisilik laboratory.

Effect of androgen supplementation on proliferation and receptors of triple-negative and MCF-7 breast cancer cells

Nicholas A. Terrell ,
Mentor: Dr. Osman V. Patel

Department of Cell and Molecular Biology, Grand Valley State University, Allendale



Currently, there is no standard therapy for breast cancer classified as triple-negative cells (TNBC) that lack the expression of the three key receptors that prompt breast cancer growth, estrogen (ER), progesterone (PR), and epithelial growth factor (HER2) receptors. This aggressive form of breast cancer has higher rates for metastases and recurrence, therefore a decreased prognosis. However, TNBC cells are known to express androgen receptors (AR), a site of our recent investigation as a target for therapy. Our objectives were, (i) to evaluate the short- and long-term effects of androgen supplementation on MDA-MB 231 (TNBC) and MCF-7 breast cancer cells proliferation rates, and (ii) to evaluate the short- and long-term effects of androgen supplementation on TNBC and MCF-7 breast cancer cells hormone receptor expression (AR and ER). Culture flasks (T-25 and T-75) were seeded with approximately 4×10^5 cells and exposed to 0 nM testosterone (control), 0.02 nM testosterone, 0.2 nM testosterone, or 2 nM testosterone for 9 and 16 days (n=3). The number of live and dead cells and the percent AR- and ER-positive cells were estimated. Most notably, in 16 days of 2 nM androgen exposure, TNBC live cell counts decreased by about 75% ($P<0.05$), AR-positive cells increased by 25% ($P<0.05$), and ER-positive cells increased by 20% ($P<0.05$) in comparison to the control. In 16 days of 2nM androgen exposure, MCF-7 live cell counts decreased by about 25% ($P<0.05$), AR-positive cells increased by 10% ($P<0.05$), and ER-positive cells increased by 5% ($P<0.05$) in comparison to the control. In 16 days of 2 nM androgen exposure, no significant difference in dead cell counts were observed in MDA-MB 231 or MCF-7. Our results indicate that androgen is an effective inhibitor of TNBC cell growth and merits further investigation.

Exploring an alternative role for the COP9 Signalosome in the ethylene response pathway

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Mentor: Dr. Matthew Christians[1]

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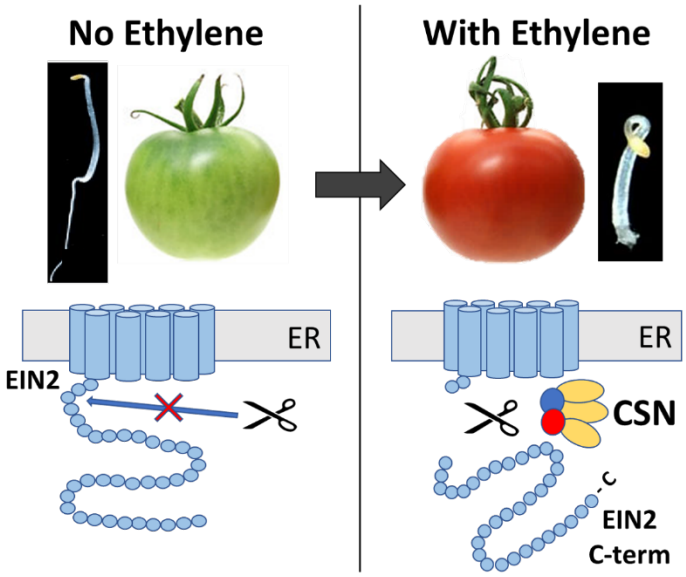
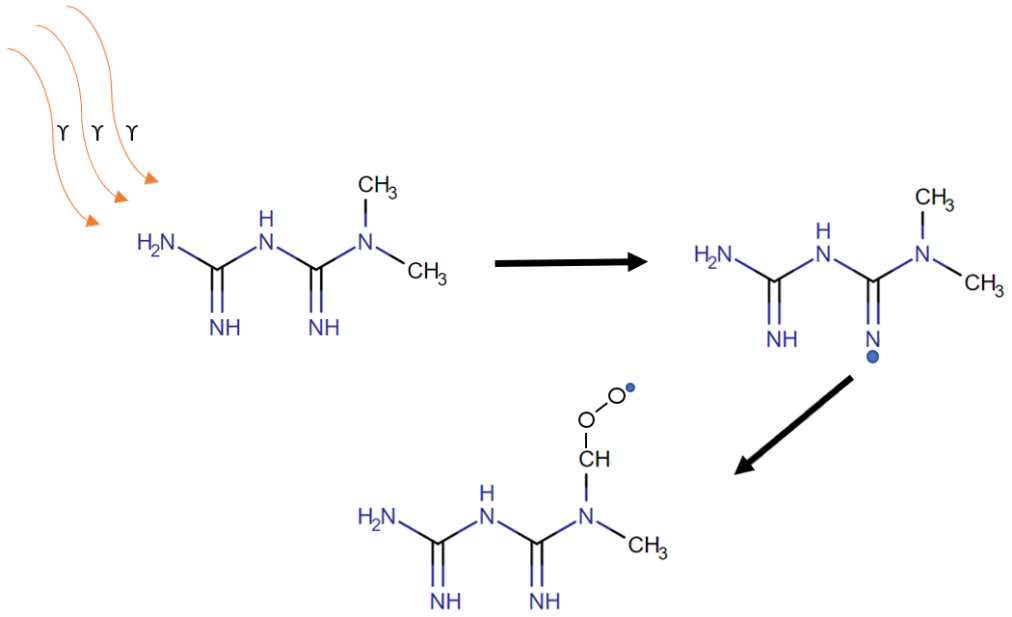


The gaseous hormone ethylene regulates various responses in almost all developmental stages of all plant species. A key protein in the pathway for sensing ethylene is the ER membrane protein Ethylene Insensitive 2 (EIN2), which is cleaved via an unknown interaction and travels to the nucleus. The protein responsible for this cleavage is unknown, however EIN2 has been shown to co-purify with a subunit of the COP9 Signalosome (CSN), a well characterized protease complex. In this project, we investigated CSN involvement in the cleavage of EIN2 using genetic knockouts of CSN subunits and Western blots of EIN2 mutants. We have found that the mutant *csn5a-1* has a significant shortened hypocotyl, and an abnormal phenotype. Through trials of protein extraction and Western blots, we have shown EIN2 C-terminus, which can be used to quantify EIN2 cleavage. Through characterization of this interaction, we can gain information on critical regulation pathways that are present in all plant species.

Electron Spin Resonance and Cyclic Voltammetry Analysis of Radical Mechanism Products of Metformin

Samuel Ward[1], Ifra Maqsood[1], Katherine Ward[1], Ke Qu[1], Anil Kumar[1], Piotr Ulanski[2], Michael D. Sevilla[1]
Mentor: Amitava Adhikary[1,*]

[1]Department of Chemistry, Oakland University, Rochester, Michigan 48309, USA.
[2]Institute of Applied Radiation Chemistry, Faculty of Chemistry, Łódź University of Technology, Łódź, Poland.



When excess prescription drugs enter an environment, their presence can have unknown effects on the environment and other organisms. Metformin is a biguanide drug often used with insulin and other prescriptions to treat those with type 2 diabetes. Metformin is taken in high doses that may not be completely absorbed. These unabsorbed chemicals may leach into the water system and can affect water quality. When metformin is metabolized, it can form free radicals; the effects of which outside of the body have not been researched. We hypothesized that metformin can react and create byproducts through the intermediate neutral peroxyl radical, which can have detrimental effects. Frozen, non-oxygenated and oxygen-saturated metformin solutions were irradiated to create the free radical form. The samples were warmed in stages to allow the reaction to progress. Electron spin resonance was used to identify the products in each stage of the reaction between oxidized metformin molecules. It was found that two biproducts were created. Cyclic voltammetry was used to determine the oxidation potential of the byproducts. Byproducts of these reactions need to be characterized to further determine potential detrimental effects on the environment.

NIH NCI (Grant R01CA045424), Research Excellence Fund (REF), Center for Biomedical Research, and Statutory Funds of CMMS PAS, and National Science Foundation under Grant No. CHE-1920110.

Role of the calpain system in adipocyte mediated proteolysis in metastatic prostate cancer

Alexis Wilson[3], Erandi Rajagurubandara, Mackenzie Herron,
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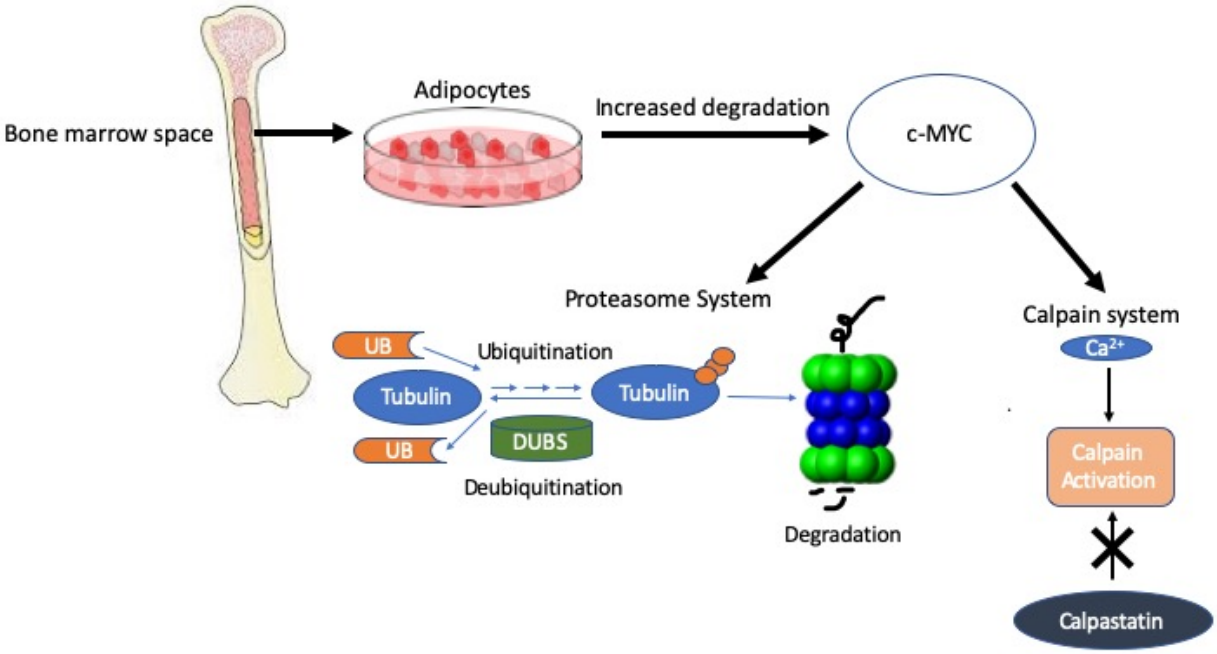

Prostate cancer (PCa) is the most common cancer amongst males and is effectively treatable only until metastasis. Metastasis to the bone occurs most often, due to the rich microenvironment of bone marrow. Prostate cancer cells thrive due to the bone marrow adiposity, which promotes pro-survival pathways. Preliminary data, from our lab show that proteolytic degradation of c-MYC is accelerated in tumor cells grown in co-culture with adipocytes, but the mechanism of degradation is unknown. To identify factors that might be involved in c-MYC degradation, we focused on the calpain system and ubiquitin-proteasome system. Investigating gene expression of CHIP, a ligase in the proteasome system, demonstrated no alteration when ARCaP and PC3 cells are exposed to adipocytes. However, calpain activity in PCa cells was confirmed by casein zymography, suggesting involvement of these cysteine-based proteases in c-MYC regulation. Understanding the source and the mechanisms of regulation of calpain activity in the bone, and its impact on key oncoproteins such as c-MYC may have important therapeutic implications for metastatic PCa.