

Glucose Transport Structure/ Function Studies in *Saccharomyces cerevisiae*: Characterization of Hxt2p

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Glucose is the preferred carbon source for most eukaryotic cells, but how it is sensed and signaled in the cell remains unknown. Defects in glucose signaling, transport, and metabolism can lead to diseases such as type 2 diabetes, therefore it is important to understand these processes. *Saccharomyces cerevisiae* is a good model system for glucose transporter studies, because yeast shares similar components and pathways of glucose signaling with prokaryotic and mammalian counterparts. In *Saccharomyces cerevisiae* glucose uptake is regulated through facilitated diffusion in the plasma membrane by hexose transporters, or Hxts. The proteins of interest for this study are Hxt1-4, each of which are expressed under different levels of glucose. A sequence alignment showed that these proteins are highly conserved everywhere except the N- and C- termini. Therefore, it is hypothesized that the non-conserved regions of hexose transporters, i.e. the N- and C- termini, are involved in glucose sensing and signaling. Due to the circumstances surrounding COVID-19 a more computational approach was employed to study these interactions and Hxt2p became the main protein of interest. The 3D structure of Hxt2p, and its N- and C-termini, were predicted using a variety of homology modeling and threading tools. Molecular dynamics was then used to analyze the physical movements of atoms and molecules of the disordered regions. Looking at these interactions will help the understanding of how cells sense and signal glucose, and how they may interact with other Hxts. These results have potential significance in not only understanding the structure, function and regulation of glucose transporters, but also in how cells sense and signal glucose in a variety of other organisms.

Comparative Analysis of Functional Activity of SSD in NPC1 and NPC1-Like Protein

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Cholesterol (CLR) is essential in the survival of the cell because it reduces passive permeability through the rigidification of the fluid membrane. Niemann-Pick type C1 (NPC1) is a large multidomain transmembrane protein involved in the transportation of CLR from lysosomes/endosomes to cellular compartments. Its known paralog, NPC1-Like-1 (NPC1-like), while performing similar functions, is located within the cellular membrane and transfers CLR from extracellular space towards cytoplasm. Mutations in NPC1 have a high probability to be a disease-causing. In contrast, the majority of documented mutations in NPC1-like are benign. The exact mechanism of CLR transfer by NPC1/NPC1-like is unknown. It is speculated that the sterol-sensing domain (SSD) forming a pore with five transmembrane helices facilitates CLR transfer through the membrane. With evolutionary analysis we compared residues conservation within orthologous sequences of both proteins. We modeled SSD of NPC1/NPC1-like embedded in a membrane and applied a steered molecular dynamic simulation to pull CLR through the pore. With structural and energetic analysis, we proved that SSD indeed can transfer CLR at natural conditions. We also described the path of CLR moving through the SSD and show that it is similar for NPC1 and NPC1-like.

Expression Analysis of Cancer Cell Lines Treated with Omeprazole

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The American cancer society estimates 16,170 deaths in 2020 with 20% survival rate five years post esophageal cancer diagnosis. This poor prognosis is associated with chemotherapy resistance within cancer cells. A known mechanism for the chemotherapy resistance is overexpressed MDR1. MDR1, also known as Pgp, is a transport protein that utilizes ATP for active transport of cytotoxins out of the cell. Studies have shown that the initiation of chemotherapy treatment causes MDR1 expression to increase, resulting in decreased drug effectiveness and patient prognosis. Pgp overexpression prior to chemotherapy treatment also results in resistance. However, the effects of ppg overexpression in chemotherapy naïve cells has not been fully explored. In vitro experiments have identified drugs that are Pgp substrates and induce expression of efflux pumps in cells not treated with chemo. We explored the effects of the reflux drug Omeprazole (OM) on the transcriptome of chemotherapy resistant esophageal cell lines OE19 and OE33 as well as colorectal cell line Caco2. Established OM treated cells and untreated cells were harvested from the three cell lines. Total RNA was extracted using a Qiagen kit and samples were prepared into RNA-seq libraries using the TruSeq RNA sample prep kit. We verified with QPCR that the MDR1 gene was induced. Further expression and sequence analysis in collaboration with Novogene revealed that as expected, genes within the drug metabolizing pathway such as CYP1A1 and CYP1B1 were upregulated across all OM treatment groups, indicating efficient drug resistance. We observed significant expression differences of efflux pump ABCG2 as well as genes HSPH1 and CDK6 in the presences of OM. The identification of chemo-resistant markers and alteration of expression following Omeprazole treatment suggests the involvement of reflux drugs in the development of MDR in esophageal cancer. This can provide personalized treatment guidelines for patients that take reflux drug medications.

Modifications to the Rope Braiding Machine at Presbyterian College

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For some time now the Presbyterian College department of Physics has been conducting research on and making modifications to a rope braiding machine obtained from Auburn University. Currently, the machine is being modified to improve the rope braiding performance, the ease of use, and the safety of operating the machine. In order to continue with these modifications, and to obtain more adequate measurements, the modifications being completed are: creation of a permanent circuit board, building of housing for the circuit board and two servo motor control systems, creation of a pulley system for the capstan motor, and integration of an emergency stop button as an improved safety mechanism. Possible included projects will be the correction of the slipping gear system and modification of the grounding system already in place.

Upregulation of Metastatic Genes in HT29 and Caco-2 cells Treated with Losartan and Chemotherapy Drug Therapies

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Colorectal cancer has the third highest mortality rate of all types of cancer, especially if it becomes malignant. Here, we tested colorectal cancer cell lines of Caco-2 and HT29 that were exposed to various ranges of losartan to chemotherapy agents known to be subject to P-glycoprotein efflux compared to untreated HT29 and Caco-2 cells to detect which genes associated with cell migration and malignancy are upregulated in the Losartan group. After four to seven months of treatment, quantitative-PCR was performed and the genes Hmox, Adora2b, and Sparc3 were all statistically significant in multiple of the cultured cell groups; indicating that these genes attributing to malignancy are all being selected for when introduced with Losartan. These present findings suggested that those with hypertension and a predisposition to colorectal cancer should be prescribed an alternative antihypertensive. These findings also suggest that patients with colorectal cancer being treated with the tested chemotherapy agents should be changed to an alternative chemotherapy regimen to increase effectiveness of the cancer treatment.

A computational approach to investigate the role of zinc finger protein, ZF30C in epigenetic repression of *Drosophila engrailed* gene

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Polycomb group proteins (PcG) are conserved epigenetic regulators that function to sustain the transcriptional repression of target genes. PcGs form the multiprotein complexes Polycomb Repressive Complex 1 and 2 (PRC1 and PRC2) which carry the enzymatic activities to chemically modify histone proteins. In *Drosophila melanogaster*, PRCs are recruited to target genes by DNA elements known as Polycomb Response Elements (PREs). PREs act as binding sites for PcG proteins to regulate gene expression and contain DNA-elements that act as recruiters for specific sets of DNA-binding proteins which bind to PRCs by protein-protein interactions (PPI).

In this study, we focused on the epigenetic regulation of *Drosophila engrailed* gene expression, particularly the identification and characterization of PRE-DNA binding proteins. *Engrailed* PREs contain multiple sites for DNA-binding proteins that interact with PcG proteins; however, there are still sites within this PRE that have yet to be identified binding partners. Through prior experimentation, it was found that one of the candidate binding proteins for one of the unknown PRE sites was Zinc Finger Protein 30C (ZF30C), a transcriptional repressor.

A computational approach was taken to further understand the role of ZF30C in PcG-mediated repression. An evolutionary analysis was executed via Blast to identify conserved domains of ZF30C that could bind to DNA or other proteins. A structural analysis was performed to identify homologous structures using the I-Tasser software and Protein Data Bank. The crystal structure of 2KMK, a zinc finger protein that binds DNA, was found and used for molecular dynamic simulation, to investigate the binding of ZF30C to DNA.

The Mexican Revolution and women in post-revolution Mexico

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The Mexican Revolution (1910-1920) was a significant event in Mexican history that impacted millions of people due to the social and political changes that resulted from it. Women were heavily involved in the revolution in a variety of roles as “soldaderas,” nurses, propagandists, and soldiers. While the fighting may have stopped in 1920, the revolution lived on in reforms and the Constitution of 1917, considered one of the most progressive of its time. Yet, the shifting political tides limited the extent of some reforms, and their effects on women varied based on region, race/social class, and occupation as exemplified in matters of divorce and prostitution. This presentation will focus on the avenues of research I investigated to develop my research question for the Honors project I will be proposing for the 2020-21 academic year: how and in what ways did the Mexican Revolution affect societal perceptions of women? In my presentation, I will first examine some historical background on women’s roles within the revolution as well as post-revolutionary historical interactions between women, politics, and society. Then, I will discuss the historiography of women’s involvement in the revolution, the trends that have evolved as a result, and where I place my research within the historiography. I will discuss the primary and secondary sources I used to build this historiography and form my research question, including sources such as newspaper articles, interviews, photographs, artwork, books, and scholarly articles. I will also present the tentative conclusions that I have made thus far, which is that social perceptions of Mexican women expanded beyond the traditional archetypes of whore or mother to include variations on these types as well as new types, such as “la chica moderna.” Additionally, women used these perceptions to their advantage when navigating social and political spheres of post-revolutionary Mexico.

Whisker Occurrence, Counting Methodology, and Lab Improvements

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This project explores three areas related to Sn Whiskers:

- 1) We explored the relationship between an element's chemical properties and its ability to whisker. We are interested in this topic because metal whiskers (especially Sn whiskers) are known to cause failures in the electronic industry via temporary and permanent short circuits. The goal is to provide a chemical view of why some elements whisker and others do not whisker. Understanding the chemical conditions for whiskering will provide a basis for creating solutions to prevent whisker growth or encouraging whisker growth in other areas. We use the R packages "Periodic Table" and "tidyverse" to create a logistic regression model and then visualize our findings with insightful graphs.
- 2) We explored the arena of machine learning to see if it is feasible for a computer to analyze SEM micrographs. The goal is to be able to input several SEM micrographs, and have the computer distinguish between whiskers, hillocks and other topographical features. Then count, and measure the dimensions of those hillocks and whiskers.
- 3) Finally, we explored the feasibility of improving the vacuum system associated with our sputter deposition system.

The Effects of Dietary Iron on the Taxonomic and Functional Composition of the Gut Microbiome in Zebrafish, *Danio rerio*

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The recent development of Next-Generation Sequencing technologies (NGS) has allowed for the sequencing of unculturable microbes by analyzing all total DNA in an environment, the metagenome. This ability has led to a greater understanding of the functional and taxonomic composition of microbial communities in living organisms, known as microbiomes. Iron is an important nutrient that is often rate-limiting for microbial growth. We hypothesized that increased dietary iron would alter the microbiome composition. We used zebrafish as a model organism. To test the hypothesis, zebrafishes were separated into two groups and fed a normal or high iron diet. The gut microbiome was characterized using two approaches: 16s (small subunit ribosomal) and total metagenomic (shotgun) DNA sequences. Preliminary results suggest modest changes in taxonomic and functional microbiome profiles in normal vs. high iron diets.

An investigation on the impact of Hsp90 isoform and co-chaperone inhibitors on lipopolysaccharides (LPS)-induced NF- κ B and Nrf2 activation in microglial cells

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Heat shock protein 90 (Hsp90) is a group of chaperone proteins that consists of 4 isoforms: Hsp90 α , Hsp90 β , glucose-regulated protein 94 (Grp94), and tumor necrosis factor type 1 receptor-associated protein (TRAP1). These proteins are normally involved in the process of protein folding, maturation, and activation with the assistance of co-chaperones, such as Aha-1. Hsp90 also regulates intracellular signaling pathways. Previous studies have linked Hsp90 with numerous inflammatory pathways, such as nuclear factor κ B (NF- κ B) and Nrf2. However, those studies used nonspecific inhibitors, such as 17-N-allylamino-17-demethoxygeldanamycin (17-AAG), and the role of isoforms and/or co-chaperones in the inflammatory responses remains poorly understood. This study aimed to further investigate the roles of the Hsp90 isoforms Hsp90 α , Hsp90 β , and Grp94 as well as Hsp90 co-chaperone Aha-1 on LPS-induced activation of NF- κ B and Nrf2. The impact of Hsp90 isoform and co-chaperone inhibitors on NF- κ B or Nrf2 activation was investigated using BV-2 microglial cells stably transfected with the NF- κ B or Nrf2 reporters. Cells were treated with various concentrations of Hsp90 isoform/cochaperone specific inhibitors for 15 minutes followed by co-treatment with 1 μ g/mL LPS in serum free DMEM medium for 3 hours or 24 hours. The cells were lysed with a luciferase assay buffer, and the activity of luciferase was detected by adding luciferase substrates. We found that treatment with Hsp90 β inhibitor for 24 hours dose-dependently reduced NF- κ B activation, which mimicked the effect of 17-AAG treatment. The Aha-1 inhibitor increased the Nrf2 activation in both 3-hour and 24-hour treatment. In contrast, treatment with other isoform inhibitors for 3 hours or 24 hours showed modest or no impact on the activation of NF- κ B or Nrf2. These findings indicate that β isoform of Hsp90 and co-chaperone Aha-1 play key roles in LPS-induced inflammatory responses in microglial cells.

Pain Associated with Heat Shock Protein 90 Inhibitor Use: A Systematic Review and Meta-Analysis

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Advisor: Dr. Wei Lei

Cancer has been a public health issue worldwide. There are numerous challenges impeding the discovery of novel cancer therapies. Heat shock protein 90 (Hsp90) is a molecular chaperone and plays an essential role in tumor growth. Numerous Hsp90 inhibitors were discovered and tested in preclinical and clinical trials. Recently, several preclinical studies demonstrated that Hsp90 inhibitors could modulate the generation of pain which is a significant cause of decreased quality of life in cancer patients. However, no studies have reported the impact of Hsp90 inhibitors on pain in the patients. This study aims to summarize the pain events reported in clinical trials evaluating Hsp90 inhibitors and to determine the effect of Hsp90 inhibitors on pain in cancer patients. We searched PubMed, EBSCOhost, and clinicaltrials.gov for Hsp90 inhibitor clinical trials. The pain related adverse events reported in the trials were summarized. Further, we performed a meta-analysis to evaluate the impact of Hsp90 inhibitors on different types of pain reported in randomized controlled trials. We found 93 clinical trials that reported pain as an adverse effect, including five randomized controlled trials. The most common types of pain reported in all trials included headache (15.1%), abdominal pain (10.8%), back pain (8.1%), neuropathy peripheral (6.4%), and myalgia (6.4%). The meta-analysis determined that treatment with an Hsp90 inhibitor significantly increased the risk of abdominal pain compared to the control group. Hsp90 inhibitors also showed a trend to increase the risk of back pain, but not headache, neuropathy peripheral, or myalgia. In conclusion, Hsp90 inhibitor treatment increases the risk of pain based on data from the limited number of randomized controlled trials. These findings provide some evidence to support the discovery of better Hsp90 inhibitors for cancer therapy.

Impact of Pharmacist counseling at discharge

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Advisor: Dr. Erika Tillery

Background: Hospital readmission rates may be affected by the inclusion of discharge counseling. In 2009, nearly 20% of Medicare patients were readmitted within 30 days. Pharmacist-led discharge counseling has shown to increase medication adherence, thus improving patient outcomes and contributing to reduced hospital readmission rates.

Objective: The purpose of this systematic review is to examine the evidence regarding how the implementation of pharmacist discharge counseling affects the number of readmissions.

Methods: A search was conducted using EBSCOhost and the National Library of Medicine databases for articles published through June 10, 2020, with the keywords discharge, discharge counseling, medication education, medication reconciliation, pharmacist, psychiatry, and readmission rates. Two authors independently screened citations and applied inclusion/exclusion criteria. Articles published in the English language with human subjects and adults (18 years and older) involving pharmacist-led discharge counseling and/or medication reconciliation were included.

Results: All of the studies examined reported improvement in readmission rates post-discharge with the implementation of pharmacist services in the discharge process. Not all of the results were significant but there was a downward trend in the number of readmissions.

Conclusion: Implementation of pharmacist discharge counseling may decrease the number of hospital readmissions.

Cosmic Rays and Galactic Motion

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As the solar system travels it oscillates across the dense galactic plane with a periodicity much smaller than its galactic orbital period. Assuming current conditions, the disk crossing period is estimated between 30 and 42 Ma. This would mean that galactic cosmic ray fluxes, and other observations on our planet, might also be expected to vary on a similar cycle, with fluxes being much higher during intervals when our solar system is close to the galactic plane. Cosmic rays are in essence fast flying fossils from space. But on our planet, living and dead creatures connect with cosmic rays. This is because several radioactive isotopes are produced in the upper atmosphere when cosmic rays collide with atmospheric molecules at high speed. These isotopes are known as cosmogenic isotopes. The production rate of the cosmogenic isotopes depends on the strength of the cosmic radiation, which again varies with the strength of the geomagnetic field and solar activity. Therefore, the abundance of cosmogenic isotopes in fossils may give a glimpse into the radiation history of our planet. A connection between calcitic fossil shells is claimed to yield a 32 Ma oscillation which would be consistent with the galactic oscillation idea. In this project we propose to examine several datasets: first, the Phanerozoic dataset of almost 25,000 calcitic fossils with their radiogenic isotopes; second, the solar cycle dataset from the space age on planet Earth. Using these data sets we hope to be able to compare the data and learn about the effect that cosmic ray fluxes have on earth and the solar system.

Interpreting Myoelectric Signals via Machine Learning Algorithms

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Advisor: Dr. Eli Owens

As technological advancements continue to be incorporated into the medical field, there is a gap that is created by the quality/cost ratio associated with using technologically advanced medical solutions. Prosthetics are no different, in the sense that many low-cost and open source prosthetics often sacrifice much of the natural mobility that a more expensive prosthetic could provide. The primary goal of this project is to bridge the gap by developing upper prosthetics that are both low-cost and provide a natural control functionality for the user. Our approach uses an open source 3D printed prosthetic hand combined with electronics of our own design to measure and interpret the myoelectric signals generated by the user. These myoelectric signals are used to control the prosthetic giving the user intuitive operation. As we studied the myoelectric signals, we observed that flicker noise ($1/f$ noise) was dominating the myoelectric signals. However, this noise is easily removed in Fourier space leaving a cleaner data set from which we extract machine learning features. Once the noise is removed, several machine learning algorithms were investigated, and it was found that the decision tree algorithm had the highest predictive power. Decision trees classify objects by asking a series of questions where there are only two possible answers. Decision tree questions are typically true/false, where every answer that qualifies as true moves to the next feature. Features are specific characteristics that help the decision tree classify the various types of data. The features for this project include but are not limited to the following: maximum voltage, minimum voltage, and the dominant frequency component of the myoelectric signal. Through this work, we move towards the creation of a low-cost but high functioning upper prosthetic that will enable many children and other amputees to live a life of confidence and mobility.

Cosmic Rays, Space Weather, and Human Chronobiology

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Advisor: Dr. James Wanliss

There is a strong connection between space weather and fluctuations in technological systems. Recent studies also suggest a statistical connection between space weather and subsequent fluctuations in the physiology of living creatures. In previously funded INBRE research [*Wanliss et al., 2018*], we presented support for a response of human physiology to forcing from the explosive onset of the largest of space weather events—space storms. Here, in collaboration with the University of Minnesota colleagues, we propose to extend this study with Japanese measurements of human blood pressure (systolic, diastolic) and heart rate variability to search for correlations with space weather, and include further astrophysical variables, such as cosmic rays. In contrast to previous studies, we will apply a new method to examine residuals of the physiological signals, to remove circadian rhythms.

- a. The main hypothesis is that there is a measurable chronobiological effect on human heart rate and blood pressure due to space weather.
- b. Specific aim 1: Characterize space weather during a decadal interval using various activity indices such as f10.7, cosmic rays, AE, SYM-H and DST, and classify them into operational units for quiet (Q) and active (A) times.
- c. Specific aim 2: Quantify the various nonlinear correlations between space weather and variability in human heart rate (HR) and blood pressure (BP) with data provided by collaborators at the University of Minnesota.

Paleopalynology of the Eocene/Oligocene Transition in the White River Badlands of WY

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The White River Formation stretches across parts of South Dakota, into Nebraska and Wyoming and terminates in Colorado. This formation contains well-preserved vertebrate fossils in sedimentary rock strata, extending from the lower layers of the late Eocene to the upper layers of the early Oligocene. During this period, there was a worldwide climate change event that caused a shift from warm and wet in the late Eocene to cooler and drier in the Oligocene. This climate shift has been previously recognized in the rock strata based primarily on the differences in fossil vertebrate types throughout this stratigraphic section. In some cases these vertebrates were going extinct, and in other cases they were expanding their evolutionary numbers. Whereas fossil plant leaves were not preserved in this specific environment, pollen and spores were, and have been used in numerous studies in nearby localities (Colorado and Nebraska) as a proxy for various environmental conditions. If climatic conditions were changing as suggested by the animal fossil record, then the pollen and spores should similarly have been changing to reflect new plant groups that were moving into this area and emerging as dominant flora. Based on standard palynological procedures, over 52 taxa of pollen and spores were identified, including pine, alder, birch, elm, asters, grasses, and several fern species. The pollen and spore data collected is indicative of an environment that was temperate with moderate rainfall. This is contrasted with the worldwide climate shift in the Oligocene where cooler, arid conditions prevailed suggesting this region of Wyoming was lagging behind the climate shift being experienced by much of the rest of the world. This data coincides well with the Antero locality of the lower Oligocene of Colorado.

Grit and its Relationship with Athletic Performance

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Advisor: Dr. Drew Brandel

Grit, which describes one's trait-like perseverance and passion for long-term goals, has been identified in prior research as an effective predictor of performance in a wide variety of circumstances and environments. Though a few studies have examined the influence of grit in athletic environments, more research in this area is needed. In this study, the relationship between grit and athletic performance was examined. The Short Grit Scale (Grit-S; Duckworth & Quinn, 2009) was administered to each player on the Presbyterian College Women's Basketball team to establish baseline Grit-S scores ($N=13$, $M=3.78/5$). Player Efficiency Rating (PER) scores were also calculated for each returning player from the 2019-2020 season as a proxy measure of athletic performance ($N=9$, $M=-0.23$). For these returning players, a strong negative relationship between baseline Grit-S scores and '19-'20 PER scores was found, but the correlation was not statistically significant due to the study's small sample size ($r=-.287$, $p=.454$). Next, the researchers developed and facilitated a series of virtual "Cognitive Coaching" sessions that targeted several of the best ideas from the current literature related to improving grit (i.e., Team Culture, Growth Mindset, and Deliberate Practice). Using a brief, researcher-developed survey, data regarding the players' perceptions of each session's acceptability, possibility of integration, and likelihood of implementation were collected. Trends among these data were then analyzed to better adapt the "Cognitive Coaching" sessions to the needs and preferences of the team. Further information, results, and implications related to grit, the collected data, and plans for continued research during the 2020 academic year will be discussed.