Summer Research Symposium:

A Collaboration Among PC Summer Fellows, SC-INBRE, SCICU, and the PC Pharmacy School

Presentation Abstracts

Presbyterian College

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Multidrug Resistance in Cancer Cells

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It has been established that individuals diagnosed with cancer and a comorbid mental illness have an increased mortality and shorter survival time, than those diagnosed with cancer alone. Although there are several contributing factors, such as a later overall stage of diagnoses and other contributing comorbidities, an avenue that is likely a neglected contributor to these poorer outcomes is multidrug resistance (MDR), defined as a resistance to multiple drugs with similar mechanisms of action. Patients diagnosed with a mental illness, such as schizophrenia, are often treated with psychiatric medications for various times and at differing concentrations at length prior to being diagnosed and treated for cancer. An increase in expression of P-glycoprotein (Pgp), a drug transporter encoded by the ATP-binding cassette subfamily B member 1 (ABCB1) gene, has been linked to MDR due to its ATP-dependent efflux of cytotoxic drugs. Interestingly, many drugs utilized for the treatment of mental illnesses are substrates for Pgp, potentially explaining poorer outcomes of patients with both mental illness and cancer. An in vitro model was established to assess the impact of long-term treatment of human cancer cells with common schizophrenia medications.

Gilberto Freyre, Racial Democracy, and Contemporary Race Relations in Brazil

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This project explores the sociohistorical discussion of racial mixing (miscegenation) and race relations in Brazil, famously discussed by Gilberto Freyre in a trilogy, the seminal work being *The Masters & the Slaves*, in which the idea of "Racial Democracy"–a society without racial tension and completely harmonic–gained precedence. Moreover, I analyze academic literature outside of Freyre's corpus throughout the twentieth and into the twenty-first century as scholars, more recently, come to terms with on-the-ground realities facing Afro-Brazilians, whom Freyre, like some predecessors, argued were paramount in shaping a powerful, harmonic race of Portuguese, African, and Indigenous descendants. Thus I explore the historiography and socio-anthropological theory of race relations and Racial Democracy as well as the premise of Freyre's racial harmony against more recent sociological or historical explorations of topics ranging from racial identity, Afro-Brazilian resistance, to immigration. In this survey, I have found that "cordial racism" is persistent socially, and various governments' lionization of culture effectively silenced discussions of racial inequality and discrimination. Thus socioeconomic, political, and cultural barriers challenge authentic "Racial Democracy" in Brazil. Phenomena such as police brutality, *favelas*, sociocultural discrimination, post-abolition anti-blackness and pro-immigration polity challenge Brazil's unique adherence to historical myth and memory as a way to silence discriminatory practices on the micro- and macro-scale seeping into the twenty-first century.

Coronal Mass Ejections and Human Physiology

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Coronal mass ejections (CMEs) are large rapid ejections of matter from the surface of the sun. Billions of tons per second of matter are constantly erupting from the sun, but at times they erupt with especial violence and lash out at the earth with speeds approaching anywhere up to 5000 kilometres per second. We have 20 years' worth of data from a human subject who has measured heart rate as well as systolic and diastolic blood pressure every 15 to 30 minutes. Our CME data are from NASA satellites. We have done a correlation analysis to compare the variability of these physiological variables with the coronal mass ejections to see if there is any merit to the idea that CMEs may affect human organisms.

Investigating the Unjamming Transition for the Development of a Soft-Robotic Gripper

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As innovations are made in the field of prosthetics, the quality/cost ratio continually increases. While there are open-sourced prosthetics, most lack the ability to grip uniquely-shaped objects or require arduous coding efforts to do so. Therefore, there is a need for affordable prostheses with universal grippers that can perform everyday tasks. Various styles of grippers exist, including both hard-robotic and soft-robotic designs. Generally, hard robots have a solid form that is rigid and fixed. The most common hard-robotic grippers utilize complex jointed fingers, which resemble a hand, or enveloping grippers which can be imagined as devices that "bite down" on objects. However, our efforts have been focused on a soft-robotic design, particularly a "malleable gripper." This design autonomously conforms to objects of all geometries, and is then able to grasp the object through the use of a granular material. Granular materials exhibit properties of solids, liquids, and gasses; and they can transition between phases. Sand, for example, can act like a solid or a liquid within the appropriate conditions. We can exploit this by having our confined granular material conform to the shape of an object while in the liquid state. We then induce jamming to make the granular material solid and grasp the object. This has been previously accomplished with pneumatic grippers which jam the granular materials within a membrane by removing the air. Though useful, pneumatic designs can be cumbersome and sluggish which has led us to explore the advantages of magnetically induced jamming. We can take advantage of granular materials, such as iron filings, that can be manipulated using a magnetic field. Solenoids can be used to produce magnetic fields which then pull the filings together causing them to jam–gripping the object within the granular material. This project design furthers the affordability of prosthetics through the creation of a low cost, open-sourced universal gripper.

Effects of Dietary Iron on Taxonomic Composition and Function of Zebrafish Gut Microbiome

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A healthy gut microbiota is essential to promote host health and well-being, and it plays a crucial role in the gastrointestinal tract. As this system often serves as a major route of infection, it is important to investigate the effects of dietary components on the gut microbiome. Iron, an essential component of heme and iron-sulfur proteins, plays a central role in many biological activities, including oxygen transport and cellular respiration. In particular, the iron homeostasis system is one of the best characterized due to iron's causative relationship with iron-deficiency anemia. Dietary iron supplementation is a commonly used treatment for iron deficiency anemia; however, the known direct impacts of iron on the gut microbiome functional potential remain limited. In the present study, using Zebrafish (*Danio rerio*) as a model organism, we sought to determine if increases in dietary iron would cause changes in taxonomic composition and gut microbiome function. Based on our analysis, an increase in dietary iron significantly altered the zebrafish microbiome taxonomic composition with specific increases in Firmicutes and Proteobacteria. Analysis of taxa for functional potential suggested that iron enriches physiological functions such as aerobic respiration. In addition, gas chromatography mass spectrometry and liquid chromatography mass spectrometry were utilized to measure primary metabolites and lipids, respectively. When considering the primary metabolites, there was found to be a significant increase in amino acids when iron levels were increased. However, there was no significant change within the lipid data when dietary iron was altered. Further studies should elucidate the importance of these observed changes in primary metabolites.

The Potential Correlation Between IL32 Gene Expression and Secreted CXCL2/3 Levels in SUM159PT Breast Cancer Cells

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SUM159PT is a metastatic breast cancer cell line which has shown to be involved in aggressive triple negative breast cancer activity. This specific cell line contains many cancer stem cells which can go undetected causing cancer cells to spread throughout the body. Past research has shown that the IL32 gene is expressed more in triple negative breast cancer cells and may contribute to breast cancer cells' invasive characteristics. The CXCL2/3 ligands increase angiogenesis in the triple negative cell line which provides alternative pathways for the cancer cells to grow. This allows for a high survival rate of the cells. However, it is unclear what the direct correlation is between these two molecular drivers during cancer metastasis. Through our research with the SUM159PT cell line, we believe that there is a possible connection between IL32 gene expression and the CXCL2/3 ligands. To determine a connection, we grew pre-existing SUM159 cells and executed a siRNA knockdown of the IL32 gene. Once the knockdown was completed for 72 hours, we performed an enzyme linked immunosorbent assay (ELISA) for the CXCL2/3 antibody in order to determine CXCL2/3 concentrations in the SUM159PT cell culture media. While we expected to see a decrease in CXCL2/3 levels in siRNA treated SUM150PT cells, our results showed that CXCL2/3 levels in SUM159PT were >3 times higher than our highest standard measurement. In the future, the cell media used in the ELISA will be diluted 20 fold in order to test a more accurate range of effect concerning CXCL2/3 in siIL32-treated SUM159PT cells.

Optimization and Substrate Scope Analysis of Iron Porphyrin-Catalyzed Oxidation of Ketoacids to Aldehydes

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Aldehydes are common raw materials for the manufacture of many valuable products such as flavorings and active pharmaceutical ingredients. Currently, there is a huge toll on the environment due to the industrial preparation of these aldehydes. The use of costly and toxic heavy metal catalysts and starting materials/reagents, compounded by waste management issues are some of the limitations of current methods. Herein, a novel method that eliminates toxic heavy metal catalysts and utilizes readily available resources and biomass-derived substrates and catalysts was sought to be developed. Instead of toxic and expensive heavy metals, oxygen was used as the oxidant with various iron porphyrin derivatives as catalysts, and ketoacids derived from amino acids as substrates. The yield of each experiment was determined by NMR using dimethylmalonic acid as an internal standard. Solvent screening revealed that acetonitrile yields 29 ± 1 % while methanol yields 0%. Exclusion of sodium hydroxide increased the reaction yield from 26 ± 1 % to 29 ± 1 %. Kinetic experiments showed that aldehyde production peaks and levels off at the 6-h time point. Using acetonitrile as solvent, among the three iron-containing porphyrin catalysts used, hemin diester gave the highest yield. Substrate scope analysis revealed that the benzylic carbon on the keto acids is required to synthesize aldehydes in this method. With the goal of suppressing overoxidation of aldehydes, 1% benzyl alcohol, a known radical quencher, was added as an additive. However, yields remained at 29 ± 1 %. Other reaction parameters such as pH, temperature, presence of additives, and catalyst design need to be explored to further optimize the reaction to achieve the end goal of a mild, practical, and scalable method to the industrial preparation of aldehydes.

Histone Proteomic Profiling of EMT-Transformed MCF10A Breast Cells Reveal Dynamic Changes in Epigenetic Modifications

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Metastatic potential of basal-like breast cancers typically is initiated by genetic alterations that lead to a process known as epithelia-mesenchymal transition (EMT). However, much is currently not understood regarding the role of epigenetic modifications that lead to the invasive characteristics and EMT phenotype of metastatic breast cancers. Based on the previous notion connecting epigenetic changes to breast cancer metastasis, we performed DIA-based mass spectrometry of isolated histones from an isogenic panel of MCF10A breast cell lines where the tumor suppressor genes TP53 and PTEN were silenced and induced EMT. With this approach, we determined which histone modifications were differentially enriched in the non-EMT and EMT-induced MCF10A cell lines. From approximately 72 histone modifications identified and annotated from our mass spectrometry, we were able to identify 5 histone events that were differentially enriched in our MCF10A cell line panel. Two events of note were histone H3 lysine-14 acetylation (H3K14ac) significantly increasing and histone H4 arginine 55 dimethylation (H4R55me2) significantly decreasing in our EMT-transformed MCF10A p53-/PTEN- cell lines when compared to the parental, non-tumorigenic MCF10A cell line, showing these events are differentially affected during the EMT process in breast cancer cells. Two arginine methylation events (H4R55me2 & H3.1R83me) were also of note, which demonstrated significant arginine demethylation in the EMT-transformed MCF10A p53-/PTEN- cell lines. JMJD6 is a known arginine demethylase gene, which is also overexpressed in basal-like breast cancers. These histone modification events corresponding with overexpression of JMJD6 could highlight the potential for targetable epigenetic drivers in breast cancer metastasis.

Reactive Oxygen Species (ROS)-Triggered Carbon Monoxide (CO) Prodrugs for Targeted Delivery

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Carbon monoxide (CO), an established endogenous signaling molecule, shows huge potential as a gaseous therapeutic, with demonstrated ability to slow inflammation, defend tissues from oxidative stress, and protect against various disease pathologies. However, making CO-based therapeutics available in the clinical setting is hampered by the inherent challenges associated with the controlled and targeted delivery of a gaseous drug. Currently, there is no targeted CO delivery approach for diseased states such as osteoarthritis characterized by high levels of reactive oxygen species (ROS), specifically hypochlorite. To this end, we have designed and synthesized ROS-triggered CO prodrugs by installing an alkyne arm to an oxidizable pyrrole ring for an intramolecular cascade of reactions leading to the release of CO. The preparation of the prodrugs was achieved via a practical, one-step synthetic route starting from readily available starting materials. Five CO prodrugs were successfully synthesized (25 - 80% yield) that can be potentially used in diseased states with elevated levels of ROS, such as osteoarthritis, chronic inflammation, atherosclerosis, and some types of cancers, like lung and gastric cancer. In-vitro testing of this ROS-triggered CO prodrug system is currently in the works. Future work entails validation experiments using cell and tissue culture models and eventually animal models.

Evaluation of Best Practice Agreement to Generate Anticoagulation Clinic Referrals

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Background: The Prisma Health Anticoagulation Clinic (ACC) is a pharmacist-run clinic that offers support in the use of anticoagulants through referrals. Anticoagulants are high risk medications that, without sufficient monitoring, can be associated with high medical costs and worsened morbidity and mortality. The ACC deployed a best practice advisory (BPA) alert at the time of prescribing to encourage providers to recognize and refer patients deemed at high risk for an adverse event related to direct oral anticoagulant (DOAC) use to the ACC for assistance with DOAC management.

Objective: Determine patient and prescriber characteristics that result in a referral to the DOAC clinic.

Method: Retrospective chart review of patients who had the DOAC BPA fired at the time of DOAC prescribing, including refills, by a Prisma Health prescriber between May 2022 and December 2022. Patients were categorized by their BPA status and whether they participated in the DOAC clinic or other ACC services. The BPA fired based on: Age >80+ and serum creatinine ≥ 2.5 in the last year; Last patient weight ≤ 50 kg; Hepatic disease AND bilirubin ≥ 2.4 mg/dL; OR chronic liver disease; Anemia and/or history of bleed; BMI > 70 in the last six months. Charts excluded from analysis included those with an ACC visit within the last year, prescribing from a non-Prisma Health Upstate department, or restricted chart access. Descriptive statistics and Chi-Square testing was utilized to describe and assess outcomes.

Results: Of the 400 charts reviewed, 80% of the BPA firings did not result in referral to the ACC. A majority (65%) of BPAs fired because of anemia. Physicians and midlevel practitioners referred to ACC in similar proportions. A newly prescribed DOACs were more likely result in referral than refilled prescriptions ($p < 0.001$).

Conclusion: The Prisma Health DOAC BPA did not result in a referral to the ACC clinic for many patients who were deemed high risk of adverse events. The DOAC BPA needs to be reviewed and likely revised to achieve its intended goal of encouraging pharmacist involvement in DOAC use and management.

Using Acoustics to Probe the Granular Jamming Transition

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Granular materials, such as gravel, sand, and flour, are abundant on Earth and throughout the universe. While they are abundant, there are still many open questions related to granular materials. Granular materials can act like a solid, liquid, or gas; however, a unified equation of state remains elusive. Of particular importance is the transition from the solid-like to the liquid-like state, known as the jamming transition. A classic example of the jamming transition is when flour is poured into a funnel. The flour begins to flow like a liquid, but occasionally the flour jams at the neck and begins to act like a solid. To study the jamming transition, we conduct experiments using a granular material composed of 6 mm and 8 mm airsoft beads confined in a 25 cm x 25 cm x 25cm box. At the top of the box is a screw used to apply pressure to the system, effectively moving the granular material away from the jamming transition. We investigate how the impedance of a piezoelectric embedded in the granular material changes as the granular material moves away from the jamming transition. Using this embedded piezoelectric transducer, we excite acoustic vibrational modes throughout the granular material, and then measure the impedance of the piezoelectric as a function of frequency and distance from the jamming transition. These impedance measurements represent a non-invasive way to potentially analyze how close a material is to jamming or unjamming.

Leveraging the Capabilities of AI Enhanced Learning Tools for Pharmacy Education: Optimizing ChatGPT to Generate Drug Knowledge Test Questions

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ChatGPT, an emerging artificial intelligence (AI) tool, facilitates rapid expansion of user knowledge by generating quick responses to questions posed by the user. AI's potential is under debate due to its experimental nature, resulting in a divide amongst educators on its ability to improve learning. In this study, we aim to evaluate AI's educational potential by creating a comprehensive AI-generated database for fundamental drug knowledge. Using ChatGPT-4, we generated over 3,000 valid pharmacy related questions across 70 topics, which were cross-checked by both Bard, another AI algorithm, and a member of the pharmacy faculty, representing human intelligence. The correct answers were ranked based on difficulty and uploaded to an emerging pharmacy education app, Pharmacynary. The high level of accuracy, combined with the speed at which ChatGPT-4 produced questions, enhanced the case for using AI to generate testing material across all educational fields. In the future, we aim to utilize the knowledge obtained from this study to increase question complexity and explore its application in other study areas.