2025

IOWA
Center for Biocatalysis and Bioprocessing

Conference Program

Center for Biocatalysis and Bioprocessing

Annual Conference

Program

2025

07:30 AM - 08:15 AM	**Reception and Continential Breakfast**	Atrium
08:15 AM - 08:30 AM	**Welcome and Introduction** **Mark Arnold: CBB Director** **Dean Jill Kolesar: College of Pharmacy**	Room 210
Maria Spies Presiding		
08:30 AM - 09:15 AM	**Anthony Pedley**	
09:15 AM - 10:00 AM	**David Minh**	
10:00 AM - 10:15 AM	Break	
Florence Williams Presiding		
10:15 AM - 11:00 AM	**Reza Nejadnik**	
11:00 AM - 11:45 AM	**Maria Spies**	
11:45 AM - 12:00 PM	Relocation	Atrium
12:00 PM - 12:45 PM	**Lunch and Poster Session A**	
12:45 PM - 01:30 PM	**Lunch and Poster Session B**	
01:30 PM - 01:45 PM	Relocation to seminar room	Room 210
Rob Kerns Presiding		
01:45 AM - 02:30 PM	**Christopher Ahern**	
02:30 PM - 02:50 PM	**Jay Phruttiwanichakun**	
02:50 PM - 03:10 PM	**Hossein Zare**	
03:10 PM - 03:30 PM	**Tyler Woodward**	
03:30 PM - 03:40 PM	**Student Poster Awards** **Michael Schnieders**	
03:40 PM - 3:45 PM	**Final Comments** **Mark Arnold**	

Invited Speakers

Anthony Pedley,
Biochemistry and Molecular Biology

Biography

Tony received his B.S. in Chemistry with a Biochemistry and Biotechnology emphasis from Grand Valley State University in 2007 and earned his Ph.D. with Jo Davisson at Purdue in 2013 as a Department of Defense Breast Cancer Trainee. His dissertation uncovered molecular features driving DNA repair enzyme recruitment to PCNA and leveraged high-throughput screening to discover modulators of PCNA-protein interactions. In 2014, he joined Stephen Benkovic's Lab at Penn State to study the regulation of purine biosynthesis. During this time, he also collaborated with several drug discovery startups. In 2025, Tony became an Assistant Professor at Iowa, where his lab continues to investigate nucleotide metabolic control through a combination of microscopy and in vitro biochemistry.

Presentation Title and Abstract

Breaking "Barriers" in Purine Metabolism to Direct Therapeutic Innovation

In many human cancers, both energy and biomass production are elevated to sustain rapid cell proliferation. For nucleotide supply, salvage synthesis alone is insufficient, and cancer cells rely heavily on de novo purine biosynthesis. Recent discoveries have revealed that sequential enzymes within this pathway assemble into dynamic biomolecular condensates known as purinosomes to meet the enhanced purine nucleotide demand. Super-resolution fluorescence microscopy has uncovered the spatial and temporal regulation of the purinosome, and these new findings have provided insights into how liquid-liquid phase separation organizes metabolic flux.

Although the triggers that promote purinosome assembly are well characterized, the molecular events that facilitate its disassembly remain largely unexplored. Here, I will present an emerging model in which acetylation of purinosome enzymes initiates condensate disassembly and the release of key intermediates that function as signaling molecules to activate glycolysis to slow tumor progression. This mechanism underscores a role for post-translational modifications in coupling enzyme compartmentalization with broader cellular physiology. By elucidating the mechanisms of purinosome assembly and disassembly, our studies offer a more comprehensive picture of how condensates can control metabolic processes, and ultimately, generate insights into whether disrupting the "barrier" of the purinosome might provide a therapeutic strategy to curtail cancer metabolism.

David Minh, Illinois Institute of Technology

Biography

David Minh is the Robert E. Frey, Jr. Endowed Chair in Chemistry at the Illinois Institute of Technology in Chicago, IL. His research is in the computer modeling of the interactions between small molecules and biological macromolecules. His group develops and applies new methods that may be helpful for drug design.

Presentation Title and Abstract

Computational Molecular Pharmacology

Computer modeling of structural, thermodynamic, and pharmacodynamic properties can accelerate drug design by inspiring new designs and prioritizing those that are most likely to be successful. My research group has recently made significant progress in binding pose, affinity, and signaling efficacy prediction. Based on a statistical mechanics framework that I derived, we have developed a method that exploits multiple rigid protein conformations to quickly compute protein-ligand binding poses and free energies. For a series of 130 ligands from a drug lead optimization campaign against the SARS-CoV-2 main protease, the method achieves a Pearson R of 0.55 and RMSE of 1.6 kcal/mol in comparison to experiment. In what could be a significant breakthrough in GPCR signaling, we have also developed a computational method that combines molecular simulation and machine learning to model structural mechanisms of activation and calculate the signaling efficacy along multiple pathways. It computes the signaling efficacy of G protein signaling along multiple subtypes and of arrestin recruitment for a diverse set of mu opioid receptor and cannabinoid receptor 2 ligands with a mean absolute error of less than 30%. I am excited about opportunities to further validate these technologies and apply them to accelerating the discovery of safe and effective therapeutics.

Reza Nejadnik, Pharm Sciences and Experimental Therapeutics

Biography

Dr. Reza Nejadnik received his PhD from the University of Groningen in the Netherlands in 2009. After a few years of research in the area of proteins, nano and biomaterials at The University of Texas, Northwestern University and Radboud University Nijmegen, Reza joined the Leiden Academic Center for Drug Research as a co-lead in a European public-private partnership project that addressed industry-wide challenges with the formulation and delivery of macromolecules. He then joined the Global Biologic Drug Product Development team of Sanofi and headed their formulation and process development laboratory. Reza is currently a faculty member in the Department of Pharmaceutical Sciences and Experimental Therapeutics (PSET) at the University of Iowa. His research focuses on protein pharmaceuticals, their formulation and characterization.

Presentation Title and Abstract

Predicting Solution Behavior: Insights into the Developability of Proteins
Wednesday, October 15, 2025

Despite the increasing availability of protein products including monoclonal antibody (mAb) drugs and their proven success in treatment of rheumatoid arthritis, multiple sclerosis, asthma, atopic dermatitis, and many other diseases, the early identification of the protein candidate molecules with desirable manufacturability, stability and delivery attributes remains a big challenge. Self-association and poor solution behavior, manifested in high viscosity/opalescence at relevant concentrations or in phase separation and stability issues, are major limiting factors in development of protein products.

Solution behavior is believed to be governed by protein self-association, however, measurement of these associations experimentally and prediction of the solution behavior are challenging using the current methods. The quartz crystal microbalance with dissipation monitoring (QCM-D) technique often detects a loosely interacting layer on top of the irreversibly adsorbed layer of molecules/particles. In this work, we demonstrate that this layer provides a plethora of information about molecular/particulate self-association and can be used to predict colloidal stability of macromolecular systems and solution behavior of monoclonal antibodies and other proteins. Unlike currently used approaches, this method is capable of measuring the metrics of protein self-association under relevant formulation conditions. In addition, we show that the reliability of this method is significantly superior to that of DLS-based diffusion interaction parameter.

Maria Spies, Biochemistry and Molecular Biology

Biography

Graduate of the Peter the Great St. Petersburg Polytechnic University, St. Petersburg, Russia (MS in physics/biophysics, summa cum laude), Maria Spies carried out her graduate studies in Osaka University (Osaka, Japan, PhD). During her postdoctoral training with prof. Steve Kowalczykowski at UC Davis where she acquired a lifelong interest in single-molecule biophysics.

She is a Professor of Biochemistry and Molecular Biology and of Radiation Oncology in 2018. She plays a leadership role at the University of Iowa Center for Bioprocessing and Biocatalysis where she is an Associate Director and a PI on the NIH T32 training grant in biotechnology. She is a Co-Leader of the Experimental and Redox Therapeutics Research Program at the Holden Comprehensive Cancer Center.

Throughout her career, Spies' research has been focused on structure-function aspects of genome stability. Lately, her lab started to extend the SAR of the key DNA repair proteins to development of novel small molecule inhibitors targeting cancer and neurodegenerative diseases.

Presentation Title and Abstract

Structure-activity relationship and pharmacological targeting of an enigmatic DNA repair protein RAD52

Human RAD52 is a coveted anticancer drug target. Its pharmacological inhibition is lethal to cancer cells displaying BRCAness phenotype and those deficient is ATM kinase fuction, while the RAD52 loss of function is well tolerated in normal cells. The challenges in targeting RAD52 include disrupring complex and extensive protein-DNA interactions, paucity of structural information and unsertainly as to exact cellular function of human RAD52 important to cancer cell survival.

RAD52 is involved in several cellular events that support genome stability including mutagenic single-strand annealing, mitotic DNA synthesis and maintenance of stalled DNA replication forks. As a gatekeeper of DNA replication forks RAD52 binds to and stabilizes stalled forks during replication stress protecting them from reversal by motor enzymes and subsequent degradation. Our structural, biochemical and single-molecule analyses revealed that the replication fork DNA promotes a unique nucleoprotein structure containing a spool-like, head-to-head arrangement of the two undecameric RAD52 rings with an extended positively charged surface that accommodates all three arms of the replication fork. In contrast, the strand annealing activity proceeds through side-by-side RAD52-ssDNA complexes and is enhanced by a phosphorylation event that disrupts the two-ring arrangement.

I will discuss our structural insights into RAD52-containing nucleoprotein complexes and our ongoing drug discovery campaign targeting human RAD52.

Christopher Ahern,
Physiology

Biography

Christopher Ahern received B.S degrees in Chemistry and Molecular Biology and a PhD in Physiology from UW-Madison. He was a postdoctoral fellow with Dr. Richard Horn in ion channel biophysics at Thomas Jefferson University, with additional training at the California Institute of Technology with Dr Henry Lester and Dr Dennis Dougherty in chemical biology. His lab at the University of Iowa in the Department of Molecular Physiology and Biophysics uses protein engineering and biophysical methods to study ion channel proteins that support electrical signaling in the cardiovascular and nervous systems. He has over 100 research articles, reviews, and book chapters.

Presentation Title and Abstract

Genetic Code Expansion for Mechanistic Studies in Ion Channels: An (Un)natural Union of Chemistry and Biology

Ion channels play central roles in biology and human health by catalyzing the transmembrane flow of electrical charge. Recent advances with single particle cryo-EM have made significant advances in depicting the remarkable and diverse structures of these proteins while many questions remain unanswered regarding their mechanisms of function and pharmacology.

These proteins are ideal targets for a method that is broadly termed genetic code expansion (GCE), whereby new types of synthetic amino acids can be encoded within an expressed protein. Ion channels are an ideal test-case because it is feasible to measure ion channel activity from miniscule amounts of protein and to analyze the resulting data via rigorous, established biophysical methods.

In an ideal scenario, the encoding of a synthetic, noncanonical amino acid via GCE allows the experimenter to ask questions inaccessible to traditional methods. For this reason, GCE has been successfully applied to a variety of ligand- and voltage-gated channels wherein extensive structural, functional, and pharmacological data exist.
I will provide an update of recent progress from my lab in the application of GCE methods as applied to ion channels. Data vignettes will be presented on the use of main-chain mutagenesis via the encoding of alpha-hydroxy acids, as well as fluoro-aromatics to study ligand, drug and protein-protein interactions, and caged-serine to study phospho-regulation. These examples will highlight the promise and challenges of GCE as applied to ion channels with a path towards future advances.

Biography

Pornpoj “Jay” Phruttiwanichakun is a PhD candidate in Pharmaceutics from Dr. Aliasger Salem’s laboratory at University of Iowa College of Pharmacy, and a CBB predoctoral fellow (2023-25). Prior to joining the PhD program, Jay obtained a PharmD from Mahidol University (Bangkok, Thailand) and an M.Sc. in Pharmaceutics from University College London (London, United Kingdom). At University of Iowa College of Pharmacy, Jay’s research focuses on nanoparticle formulation for gene delivery and drug delivery for regenerative medicine and cancer therapy.

Jay Phruttiwanichakun,
Pharm Sciences and
Experimental Therapeutics

Presentation Title and Abstract

Biodegradable Polymer-Drug Conjugates for Colorectal Cancer Therapy

Some of the most potent chemotherapeutic drugs cannot be used as-is due to their unacceptable off-target side effects. One common solution to this issue is to covalently link the drug molecule to biomolecules or biodegradable polymers to allow targeted drug delivery to solid tumors, thus reducing the off-target toxicities and enabling clinical use.
In this study, we synthesized a polymer-drug conjugate (PDC) comprising of poly(lactic-co-glycolic acid) (PLGA), a biodegradable polymer, and monomethyl auristatin E (MMAE), a highly toxic drug. The MMAE content in the PDC was analyzed using ^{1}H-NMR and PLGA-calibrated GPC techniques. The PDC was used in combination with PLGA derivatives to fabricate nanoparticles. The nanoparticle surface was subsequently decorated with cetuximab, giving tumor-targeted nanoparticles (TTNPs). Cetuximab is a clinically relevant monoclonal antibody that targets human epidermal growth factor receptor (EGFR) with an indication for colorectal cancer treatment. Similar nanoparticle fabrication was also performed without cetuximab to make non-targeted nanoparticles (NTNPs).

The anti-tumor efficacy of NTNPs was assessed in vitro in a HT-29 human colorectal cancer cell line and in vivo in a heterotopic HT-29 xenograft mice model. The tumor-bearing mice (~200 mm^3 tumor volumes) were treated twice weekly for two consecutive weeks with either TTNP, NTNP, or left untreated via intravenous injection. The tumor volume was measured throughout the treatment, and the survival rate of the animals was tracked after treatment cessation. The animal body weight was also monitored for safety.

We found that the mice treated with TTNP showed significant tumor growth inhibition compared to the NTNP and the untreated control. TTNP treatment also resulted in an extended median survival time (31 days) compared to the NTNP group (17 days) and untreated controls (21 days), with no appreciable weight loss. These findings support the potential of TTNP for further development as a safe and efficacious treatment for colorectal cancer.

Hossein Zare, Chemistry and Biochemistry Engineering

Biography

Hossein Zare is a third-year Ph.D. candidate in Chemical and Biochemical Engineering at the University of Iowa in Prof. Eric Nuxoll's lab. With a background in Materials Engineering and a Master's in Bioengineering from Iran University of Science and Technology. He researches thermal shock strategies to eradicate Pseudomonas aeruginosa biofilms on medical implants while minimizing bacterial dispersion. His work integrates microbiology with custom-built thermal devices for precise heat transfer control and bacterial response analysis in vitro and in vivo. His broader interests include bioprocessing, biomaterials, and biotechnology applications in healthcare.

Presentation Title and Abstract

Dispersion of Pseudomonas aeruginosa Biofilms on Implant Surfaces: Effect of Thermal Shock

Biofilms formed on medical implants remain a major clinical challenge due to their resistance to antibiotics and the host immune system. Conventional treatments often fail, leaving residual bacteria that persist and re-establish infection. Thermal shock, applied as localized heating of implant surfaces, has emerged as a promising strategy to eradicate biofilms. Even before applying thermal shock, planktonic bacteria disperse continuously from mature biofilms, and this process can be strongly influenced by local stimuli such as temperature. The underlying mode of this phenomenon remains unclear, as bacterial reduction may result either from in-situ death within the biofilm or from dispersion of live cells responding to thermal stress. Dispersed bacteria, however, pose a risk of entering the bloodstream.

This study investigates P. aeruginosa PAO1 biofilms under in-vitro conditions with and without thermal shock. We quantified bacterial departure into surrounding media and tissue mimics. Results show that dispersion into liquid media reached equilibrium within one minute, indicating rapid dynamic exchange between biofilm and planktonic population. Flow-cell experiments with minimized chance of re-adhesion showed that residual biofilm populations persisted, highlighting the resilience of attached bacteria.

In tissue mimics, bacterial penetration followed an active transport mode rather than passive diffusion, with dispersion coefficients comparable to small molecules but extending deeper than expected. Application of thermal shocks (50–80 °C, 1–20 min) enhanced dispersion into deeper PVA layers, with bacteria detectable up to 12 mm at sub-lethal exposures (60–70 °C). Notably, an 80 °C shock for 3 minutes eradicated both surface biofilms and dispersed populations, preventing regrowth during subsequent incubation—even in the presence of tobramycin. By contrast, milder treatments promoted dispersal, leading to biofilm regrowth within one day.

Biography

Tyler Woodward is a PhD candidate in Biochemistry and Molecular Biology at the University of Iowa. Tyler earned his BS in Chemistry from Creighton University in 2018 and received a predoctoral training fellowship from the Center for Biocatalysis and Bioprocessing in 2023. His research centers on mechanisms of DNA damage suppression and bypass, with projects focused on the tardigrade protein Dsup and the Rad6/18 ubiquitin ligase complex. Through his work, he seeks to better understand how cells maintain genome stability. After his graduate work, Tyler is interested in a career in science policy.

Tyler Woodward,
Biochemistry and Molecular Biology

Presentation Title and Abstract

Biochemical and Structural Analyses of the Tardigrade DNA-Damage Suppressor Protein, Dsup

DNA damage is a central feature of many genetic disorders, including cancer and cardiovascular disease. Living organisms have evolved a repertoire of molecular strategies to prevent or mitigate such damage. By studying these strategies, we can gain understanding into disease progression and novel therapies. Tardigrades, extremophiles capable of surviving harsh environments, employ unique protective mechanisms. Among them is the Damage Suppressor (Dsup) protein, which is known for its ability to protect DNA from radiation-induced damage. Interestingly, when expressed in human cells, Dsup increases radiotolerance, underscoring its potential pharmaceutical relevance.

Despite this relevance, the biochemical and structural features that underlie Dsup's protective function remain poorly understood. To address this gap, we investigated its biochemical and structural properties using a variety of approaches, including mass photometry, biolayer interferometry, small-angle X-ray scattering, and microfluidic modulation spectroscopy. Our results show that Dsup is largely intrinsically disordered yet binds DNA promiscuously and with high affinity through a multivalent interface. This interaction induces conformational changes in both Dsup and the DNA itself, suggesting a potential structural mechanism of protection. We posit that Dsup modifies DNA structure—possibly by inducing partial unwinding—to reduce its vulnerability to radiation-induced damage. Together, these findings provide new insights into one of the key mechanisms that Tardigrades evolved to survive immense radiation. By revealing a potential structural mechanism for Dsup-mediated DNA protection, this work not only advances our understanding of tardigrade biology but also highlights the broader potential of Dsup-inspired strategies to enhance radiotolerance in human health and disease.

Poster Presentations

Poster No.	Presenter	Poster Title
1	**Antonu Chakrabortty**	*Decoding Drug Resistance Mechanisms in Ovarian Cancer Through ABC Transporter Regulation*
2	**Zhenru Wang**	*Adipocyte-Conditioned Medium Induces a Transcriptionally Distinct Myofibroblast Phenotype with Enhanced Remodeling and Reduced Fibrosis*
3	**Emily Jansen**	*A Novel Engineered Mixed Microbial Culture for Self-Sustained 1,4-Dioxane Bioremediation*
4	**Sarah Preston**	*Modulation of Organophosphate Metabolism and Toxicity via NRF2 Signaling*
5	**Rhea Fisch**	*Molecular analysis of Cupriavidus necator biodiversity*
6	**Parham Parnian**	*Multimodal Characterization of Protein–Protein Interactions in Monoclonal Antibodies Using kD, B22, and DLVO*
7	**Sarah Jordan**	*Biochemical Studies of the Interactions and Novel Activities of Non-Classical Polymerase η*
8	**Samuel Yu**	*Combination Therapy Targeting PI3K and Hippo Pathways in Sarcoma*
9	**Rose Gogal**	*A Biophysics-Informed Bayesian Framework for Hearing Loss Missense Variant Classification*
10	**Jasmyn Hoeger**	*Discovery and Initial Characterization of a Diverse Family of Microproteins Derived from Alternative Open Reading Frames in SCN(NaV) Genes*
11	**Souradip Sinha**	*The ATAC histone acetyltransferase complex is a key oncogenic driver in sarcomas*

12	**Reza Amouzandeh**	*Specific Salt Ion Effects on 3D-Printed Silk Fibroin Tissue Scaffolds*
13	**Luke Handlos**	*Structural and Biophysical Insights into DNA Translocation by TLS Polymerases Iota and Eta*
14	**Mona Maalouf**	*Synthesis of isoprenoid triazole bisphosphonates*
15	**Zoe Kramin**	*In-line Diffuse Reflectance Spectroscopy Enables Rapid Monitoring of Full-Scale Anaerobic Co-Digestion*
16	**Sophie Granger**	*Probing Allosteric Control of Native Enzyme Dynamics in H. pylori Glutamate Racemase with Single-Molecule Approaches*
17	**Elham Taherian**	*New fluroquinolone derivatives combined with Paclitaxel against Colorectal cancer*
18	**Prateek Aryal**	*Breakdown of Lignocellulose Using Boron Trihalide Reagents*
19	**Kshitija Kale**	*The Interleukin-1β pathway in T helper 17 Polarization and Effector Resistance*
20	**Jacob Miller**	*Relative Binding Free Energy Differences for Transcription Factor-DNA Complexes Using the Polarizable AMOEBA Force Field*
21	**Paras Gaur**	*Pharmacological Modulation of PARP1-G4 Interplay and Replication Integrity*
22	**Elizabeth Walker**	*Designer Bioplastics: Exploring Biodiversity of Cupriavidus necator for next generation PHA producers.*
23	**Sarah Torrence**	*Recombinant Prohibitins Mitigate Pro-inflammatory Priming Response and Acute Kidney Injury Induced by Lipopolysaccharide*

24	**Minou Emmad**	*Protonation Coupling in Zinc Finger–DNA Recognition Explored by Polarizable CpHMD*
25	**Masayoshi HONDA**	*BCRABL1–Mediated Phosphorylation of RAD52 Switches Its Role from Replication Fork Protection to Mutagenic Single-Strand Annealing*

Even numbered posters = Session A 12:00 – 12:45

Odd numbered posters = Session B 12:45 – 1:30

Poster #1

Antonu Chakrabortty	Decoding Drug Resistance Mechanisms in Ovarian Cancer Through ABC Transporter Regulation

Background: Chemoresistance remains a major obstacle in treating ovarian cancer, leading to relapse and poor patient outcomes. My research focuses on understanding how ATP-Binding Cassette (ABC) transporters drive drug efflux and therapy resistance. By combining molecular biology with transcriptomic and functional analyses, I also aim to identify isoform-specific regulatory mechanisms that could be exploited for targeted therapy. This work directly supports the Center for Biocatalysis and Bioprocessing's (CBB) mission to bridge biological discovery with translational innovation. By elucidating transporter-mediated drug metabolism and response, this research contributes to the development of rational, biocatalytic strategies for precision drug design and resistance reversal, ultimately advancing patient-focused therapeutic interventions.

Objectives: This research aims to elucidate how networks of ATP-Binding Cassette (ABC) transporters regulate drug resistance in ovarian cancer. By integrating gene expression profiling, epigenetic mapping, and functional validation, the study seeks to identify key transporters and regulatory pathways that contribute to altered drug efflux and reduced therapeutic efficacy. Understanding these mechanisms will enable the development of strategies to reverse chemoresistance through targeted modulation of transporter activity.

Methods: We will interrogate ABC transporter networks across ovarian cancer models (e.g., TOV-21G, OVCAR3, OVCAR8, OV90) and their paclitaxel/cisplatin-resistant derivatives. Baseline and drug-induced changes will be quantified by qPCR (ΔΔCt) and RNA-seq, with alternative splicing analysis (rMATS) to capture isoform shifts. To map regulation, we'll perform epigenetic assays (e.g., ATAC-seq/ChIP-qPCR for activation/repression marks) and perturb key regulators using siRNA/CRISPRi. Transporter function will be tested via drug-accumulation/efflux assays and viability/IC_{50} curves (CellTiter-Glo), alongside apoptosis readouts and combination tests with selective transporter modulators. We'll extend validation to 3D spheroids to better model tumor context. An integrated analysis pipeline (differential expression/splicing with FDR control, pathway/network enrichment, and mixed-effects modeling) will prioritize actionable targets that can restore drug sensitivity.

Results: Following 48-hour paclitaxel and cisplatin perturbation, our in-vitro ovarian cancer models exhibited distinct alterations in ABC transporter expression reflective of an early adaptive response. ABCB1 and ABCG2 were markedly upregulated, indicating increased drug efflux capacity, while ABCA8, involved in lipid transport and membrane remodeling, also showed elevated expression. Additional members such as ABCA2, ABCA12, ABCA13, and ABCC1 demonstrated variable induction, suggesting activation of a broader transporter network under stress. Conversely, TAP1 expression was reduced, pointing to possible suppression of immune-related pathways during drug treatment. These rapid transcriptional shifts reveal how cancer cells initiate resistance programs during acute exposure, laying the groundwork for chronic adaptation and stable chemoresistance. Understanding these early regulatory events will be critical for identifying predictive biomarkers and designing interventions that can disrupt transporter-mediated resistance before it becomes irreversible.

Conclusion: This study provides early mechanistic insight into how ovarian cancer cells rapidly reprogram ABC transporter networks in response to chemotherapeutic stress. The observed induction of ABCB1, ABCG2, ABCA8, and other transporters highlights a coordinated, multi-gene defense strategy that promotes drug efflux, metabolic adaptation, and survival. By linking these acute transcriptional changes to the potential establishment of chronic resistance, the work underscores the importance of targeting transporter-mediated pathways early in therapy. Ultimately, this research sets the stage for developing precision strategies to predict and prevent resistance in ovarian cancer treatment.

Poster #2

Zhenru Wang	Adipocyte-Conditioned Medium Induces a Transcriptionally Distinct Myofibroblast Phenotype with Enhanced Remodeling and Reduced Fibrosis

Background: Human dermal fibroblasts (HDFs) are key regulators of tissue repair, responsible for regulating extracellular matrix (ECM) remodeling, and supporting wound closure. Typically, fibroblast activation is driven by TGF-β1 signaling, which promotes fibroblast differentiation into contractile myofibroblasts that repair the wound site. Chronically active myofibroblasts can also lead to excessive ECM deposition, matrix stiffening, and fibrosis.

Objectives: Previous studies, including our own, have shown that adipose-derived factors can influence fibroblast behavior. Our studies indicate that adipocyte conditioned medium (ACM) promotes the conversion of HDFs into highly contractile, alpha-smooth muscle actin positive myofibroblasts through a TGF-β1 independent mechanism. Here, we used RNA-Seq to compare the transcriptome of ACM-induced myofibroblasts to TGF-β1-induced myofibroblasts, focusing on the expression of ECM remodeling markers and typical myofibroblast contractile genes.

Methods: Adipocyte conditioned medium was generated by culturing 3D adipocyte spheroids in differentiation medium (PDM-2, Lonza) for 10 days, followed by a 48-hour incubation in Rooster CollectTM-EV medium, a protein-free, low-particle formulation designed to enable clean collection of conditioned media and minimize interference from extraneous proteins as a treatment medium. Human dermal fibroblasts (HDFs) were cultured in DMEM with 10% FBS for 48 hours, then treated for an additional 48 hours under the following conditions: (1) ACM, (2) Rooster Collect with 1 ng/mL TGF-β1 and 50 µg/mL ascorbate-2-phosphate (A2P) (positive control), (3) Rooster Collect alone (control) (n = 5 per culture condition). Total RNA was extracted using the Qiagen RNeasy Mini Kit with on-column DNase digestion (Zymo RNA clean & Concentrator-5 Kit). RNA libraries were prepared using poly(A) enrichment and sequenced on the Element Aviti24 platform to generate paired-end reads (2 × 75 bp). Sequencing quality was assessed using FastQC and MultiQC; adapter trimming was performed with Flexbar, and rRNA contamination was removed using SortMeRNA. Clean reads were aligned to the human transcriptome (GRCh38 reference) using HISAT2, and gene-level counts were quantified with featureCounts. Differential expression and enrichment analyses were conducted using DESeq2 and clusterProfiler.

Results: Principal component analysis (PCA) revealed distinct transcriptomic profiles among control, ACM-, and TGF-β1-treated fibroblasts, with most variation explained by treatment conditions. Both ACM and TGF-β1 significantly altered gene expression relative to control, yet they also diverged from each other, indicating activation of different transcriptional programs. Differential expression and pathway enrichment analyses showed that ACM primarily induced genes and pathways related to ECM remodeling, focal adhesion, cytoskeletal organization, and epithelial morphogenesis—features linked to tissue repair and regeneration. In contrast, TGF-β1 treatment predominantly enriched profibrotic and contractile pathways associated with fibrosis progression.

Conclusion: These results clearly show that ACM induces a transcriptionally distinct myofibroblast phenotype compared to TGF-β1 induced myofibroblasts. ACM appears to promote ECM remodeling and enhance migratory potential while avoiding the same level of fibrotic gene expression seen in TGF-β1 exposed HDFs, which suggests adipocyte secreted factors could favor a more balanced, wound-healing fibroblast state. These findings provide new insights into adipose-fibroblast interactions and highlight the therapeutic potential of ACM-derived factors in modulating fibroblast behavior, which may offer new strategies for promoting healthy tissue repair.

Poster #3

Emily Jansen	A Novel Engineered Mixed Microbial Culture for Self-Sustained 1,4-Dioxane Bioremediation

Background: 1,4-Dioxane is a cyclic ether that is used as a stabilizer for chlorinated solvents, (e.g., 1,1,1-trichloroethane (TCA) and trichloroethene (TCE)) in many industrial processes. It is an emerging contaminant of particular concern, as it is classified as a probable human carcinogen by the US EPA. Because of its high solubility and stability, dioxane plumes are often large and dilute. Biodegradation with dioxane-metabolizing bacteria is a promising, cost-effective strategy for treating large and dilute dioxane plumes.

Objectives: Our group has identified that Rhodococcus ruber 219 can metabolize dilute 1,4-dioxane to below health advisory levels (0.35 µg/L) when supplemented with thiamine (Vitamin B1). However, vitamin supplementation has proven difficult in lab and field settings. In response, we have developed an engineering syntrophic mixed culture, combining R. ruber 219 with VB1 hyper-producing mycorrhizal bacteria.

Methods: Both a batch experiment and genomic sequencing were completed in the laboratory to examine 1,4-dioxane degradation activities and microbial community analysis, respectively. The batch experiment was carried out in flasks, with each inoculated with either R. ruber 219 or the mixed culture. 1,4-Dioxane concentrations, optical density, and protein measurements were taken through time. Additionally, a pellet was frozen to use for future DNA extraction and qPCR analysis.

For metagenomic analysis, a MinION flow cell from Oxford Nanopore was used to perform long-read sequencing of the mixed culture. Basecalling and trimming were completed using Dorado. Taxonomic IDs for the unassembled reads were assigned using Lemur, and associated software MAGnet was also used to validate the taxonomy from a whole-genome standpoint. Flye was used for de novo assembly. DNA extractions from two different dates were used to analyze how the culture has changed over time.

Results: This mixed culture has demonstrated the ability to completely degrade initial 1,4-dioxane (500 mg/L) to below detection limits (0.05 µg/L) without additional VB1 supplements. Despite slower kinetics than R. ruber 219 under the same growth conditions, the mixed culture exhibited significantly higher 16S rRNA gene copy numbers and optical density measurements, suggesting greater overall biomass. The mixed culture also produced more thmA gene copies, the 1,4-dioxane degradation gene in R. ruber 219, indicating a higher dioxane-degrading capacity.

The resulting metagenomic assemblies identified five different genera (Rhizobium, Ralstonia, Rhodococcus, Microbacterium, and Cupriavidus) present in the culture, including an exact match to R. ruber 219. The relative abundance of R. ruber 219 was between about 30% and about 55%, with the remaining four genera comprising between about 70% and about 45% of the mixed culture at the different sample dates. Additionally, three complete genomes for R. ruber 219, Cupriavidus spp., and Microbacterium spp. were extracted from the metagenomes.

Conclusion: Together, these results demonstrate a promising approach for 1,4-dioxane bioremediation that eliminates the need for vitamin supplementation in the field. This also addresses the need for an inexpensive and scalable solution for in situ 1,4-dioxane treatment.

Poster #4

Sarah Preston	Modulation of Organophosphate Metabolism and Toxicity via NRF2 Signaling

Background: Human exposure to organophosphate (OP) pesticides such as chlorpyrifos (CPF) occurs in agricultural, occupational and military settings worldwide. OP pesticides, such as CPF, can lead to cholinergic crisis via acetylcholinesterase (AChE) inhibition and accumulation of the neurotransmitter acetylcholine. Downstream effects of OP intoxication include seizures and production of reactive oxygen species (ROS), likely due to glutamate (Glu) excitotoxicity. Furthermore, there is evidence that CPF exposure correlates with additional adverse outcomes, including depression and neurodegenerative diseases. Molecular mechanisms for such conditions are elusive and may involve targets other than AChE. Metabolism of CPF is critical to cholinergic toxicity as it can yield either bioactivation to the toxic chlorpyrifos-oxon (CPO) or detoxication via glutathione (GSH)/glutathione-S-transferase (GST; dechlorination) or hydrolysis of CPO via the esterases, paraoxonase 1 (PON1) and carboxylesterase 1 and 2 (CES), with CES serving as a “sink" to protect AChE. Interestingly, several of the enzymes critical to the metabolism of CPF are under the control of the transcription factor NRF2, including: GSH/GST, PON1 and CES. Activation of NRF2 is known to induce expression of numerous antioxidant enzymes to mitigate aberrant ROS production, however, the possibility of NRF2 as a therapeutic pathway for OP poisoning is unexplored.

Objectives: The goal of our work is to explore the role of NRF2 modulation in mitigating risk of toxicity and adverse effects to CPF/OP agents and the therapeutic potential to target this pathway to mitigate CPF/OP toxicity. Our central hypothesis is that NRF2 activation alters CPF disposition and potential for toxicity via induction of enzymes that modulate OP metabolism and cellular damage.

Methods:
Genetic - qPCR, RNA-seq
Protein-Based - Enzymatic Assays, Western Blots, Cellular Thermal Shift Assays
Other - MTT assays (cell viability; mitochondrial activation)

Results: Preliminary work found that pretreatment of PC12 cells with potent activators of NRF2 provides protection against acute CPF/CPO treatment at sub-micromolar concentrations. In addition, we have shown that NRF2 activators induce the expression of both CES and PON1 in HepG2 cells (liver). Finally, we found that NRF2 activation increases esterase activity in HepG2 cells. NRF2 activation also appeared to confer protection in HepG2 cells against the OPs paraoxon and Chlorpyrifos.

Conclusion: These data indicate the potential for NRF2 as a target to mitigate short- and long-term OP/CPF toxicity, via the induction of key enzymes involved in the degradation and excretion of OPs and their metabolites.

Poster #5

Rhea Fisch	Molecular analysis of Cupriavidus necator biodiversity

Background: Plastics are a major threat to the environment, as their production produces greenhouse gases and they produce waste which is difficult to dispose of. Bioplastics are a potential solution to both of these problems, and polyhydroxyalkanoates (PHA) are a viable alternative to single-use polyethylene plastics provided metabolic engineering is used to scale up production so such a replacement becomes profitable.

Objectives: Cupriavidus necator is a bacterium which natively produces PHA, the most studied strain of which is H16/DSM 428. However, H16 has issues with transformation stability, which makes industrial modification difficult. However, there are several other strains of C. necator which have potential to be more stable. By studying these strains, the optimal traits can be selected from different strains and transformed into the most stable strains, creating a strain with the ideal properties.

Methods: By sequencing each strain, the differences in their genomes can be analyzed, and the genes which contribute to the desired traits can be compared. Illumina sequencing was used to analyze DNA fragments from the full genome of five C. necator strains. FastQC was used to confirm the accuracy of these reads, before de novo assembly with SPAdes. The contigs provided by SPAdes were then assembled using RagTag with H16 as the reference and annotated using Prokka. Genomic analysis was then conducted with these complete genomes.

Results: The pHG1 megaplasmid is found in both C. necator H16 and N-1, the two sequenced type strains of C. necator. However, this plasmid is not found in all strains. C. necator DSM 4182 and DSM 30029 do not have this plasmid. However, they do have a newly-discovered plasmid which we have named pCnec3, which contains mostly regulatory genes. This plasmid was also found in C. necator DSM 2625, which also had a newly discovered megaplasmid we have named pCnec1978_1. These plasmids were both attested in strains with high growth rates and high stability, indicating the regulatory genes stored on these plasmids may have an effect on these difficult to modify desirable effects. However, this has not been tested in vivo and remains a hypothesis.

Conclusion: Using the newly discovered plasmids in C. necator DSM 2625, among other strains, it may be possible to modify C. necator H16 to become more stable and grow faster, eliminating the two main bottlenecks inherent to metabolic engineering in that strain, and allowing for metabolic engineers to use its higher yield and higher molecular weight to their advantage in further modification. This new platform may allow for better modification of C. necator H16 in the future, allowing for further pushes towards profitable bioplastic production in the strain.

Poster #6

Parham Parnian	Multimodal Characterization of Protein–Protein Interactions in Monoclonal Antibodies Using kD, B22, and DLVO

Background: Reliable characterization of protein–protein interactions (PPI) is essential for identifying monoclonal antibody (mAb) candidates with desirable colloidal stability and formulation behavior. However, relying on a single biophysical characterization tool often results in an incomplete or misleading picture, especially for complex cases. This study evaluates the combined application of three orthogonal approaches, the diffusion interaction parameter (kD), the osmotic second virial coefficient (B22), and DLVO (Derjaguin–Landau–Verwey–Overbeek) modeling, in characterizing PPI in three IgG1 mAbs with distinct physicochemical properties. Each method captures different aspects of intermolecular interactions: kD reflects the influence of thermodynamic and hydrodynamic interactions on diffusion, B22 reveals non-ideal solution behavior from pairwise solute interactions, and DLVO decomposes total interaction energy into mechanistic components.

Objectives: This study aims to evaluate the combined application of kD, B22, and DLVO modelling, in elucidating PPI behavior in three IgG1 mAbs with distinct physicochemical properties.

Methods: Three IgG1 mAbs were buffer exchanged into histidine (pH 6.0) and tested across a range of ionic strengths. Dynamic and static light scattering were used to determine kD and B22, while DLVO modeling fitted B22 values to estimate double layer repulsion and van der Waals contributions to the total interaction energy.

Results: At low ionic strength, one mAb displayed strong repulsion, while the others showed attraction-dominated interactions. Addition of electrolyte substantially reduced kD values, with the extent of reduction correlating with antibody charge, reflecting charge-screening effects. At higher ionic strengths, nonmonotonic behavior and decoupling of kD and B22 indicated contributions from transient clustering and hydrodynamic effects. DLVO modeling further revealed mechanistic differences, including a secondary energy minimum consistent with reversible self-association.

Conclusion: This study demonstrates the power of integrating kD, B22, and DLVO modeling as complementary tools for characterizing PPI in therapeutic mAbs. This multiparametric strategy provides a more complete understanding of colloidal behavior and a stronger basis for guiding formulation decisions and developability assessments.

Poster #7

Sarah Jordan	Biochemical Studies of the Interactions and Novel Activities of Non-Classical Polymerase η

Background: DNA polymerases are a versatile set of enzymes that are necessary for replicating DNA and maintaining genome stability. They function in DNA replication, DNA repair, and damage bypass pathways. DNA polymerases synthesize DNA by incorporating nucleotides opposite templating DNA. Some polymerases are high fidelity, like classical polymerases involved in DNA replication and repair. Other polymerases are low fidelity, like non-classical polymerases involved in damage bypass. In addition to synthesizing DNA, some polymerases contain endonuclease and pyrophosphatase activity. Polymerases containing endonuclease activity often use this activity in proofreading DNA to increase fidelity. Furthermore, DNA polymerases interact with multiple proteins throughout DNA replication, repair, and bypass pathways. Protein-protein interactions are shown to regulate DNA polymerases through localization, increasing their processivity, and increasing catalytic efficiency. The goal of our lab is to gain a comprehensive understanding of DNA polymerase mechanisms. Specifically, we are examining how pyrophosphatase activity and protein-protein interactions change the overall mechanism of DNA polymerases. My project focuses on non-classical polymerase η which is involved in bypassing DNA damage. I am examining protein-protein interactions of polymerase η and its ability to carry out pyrophosphatase activity, the hydrolysis of pyrophosphate into two monophosphates.

Objectives: Non-classical polymerase η interacts with Rad6-Rad18, an E2/E3 ubiquitin ligase complex, but the consequence of this interaction is not understood. We aim to biochemically and structurally understand this interaction.

Two related non-classical polymerases, Iota and Rev1, contain pyrophosphatase activity which leads us to ask whether polymerase η also contains this activity. We aim to biochemically and structurally investigate polymerase η for pyrophosphatase activity and identify residues important for catalyzing this reaction.

Methods: We utilized steady-state kinetics to investigate the biochemical effects of the interaction between Rad6-Rad18 and polymerase η. We found that this interaction increases polymerase η's catalytic efficiency – the ability of the polymerase to extend DNA.

Using malachite green assays, we examined whether polymerase η contains pyrophosphatase activity. We found polymerase η contains a robust pyrophosphatase activity. Additionally, this activity is independent of nucleotide incorporation and allows us to identify residues important for catalyzing the hydrolysis of pyrophosphate.

Results: Results and Methods are combined in the methods section.

Conclusion: Interactions with Rad6-Rad18 may dictate the recruitment of non-classical polymerases to the replication fork and increase the catalytic efficiency. Increasing the catalytic efficiency of each non-classical polymerase may maximize efficiency of bypass, preventing replication fork collapse.

With the pyrophosphatase activity in polymerase η being independent of nucleotide incorporation, we can identify residues that catalyze hydrolysis of pyrophosphate. This will be important for understanding how non-classical polymerases conduct pyrophosphatase activity.

Overall, information from these studies will be important in providing a comprehensive understanding of how protein-protein interactions and additional activities influence the mechanism of non-classical polymerases. Additionally, this information could facilitate the development of drugs to prevent genome instability and/or increase the potency of chemotherapy agents that block DNA replication.

Poster #8

Samuel Yu	Combination Therapy Targeting PI3K and Hippo Pathways in Sarcoma

Background: Sarcomas are a heterogeneous group of cancers with limited effective targeted therapies. One frequently dysregulated pathway in sarcomas is PI3K signaling, often due to PTEN loss in 30–60% of patient samples. PI3K activation promotes tumor growth through both the canonical Akt-mTORC1 axis and a parallel PI3K-TAZ/YAP-TEAD axis. TAZ and YAP are transcriptional co-activators that drive oncogenic gene expression and are regulated by the Hippo pathway which consists of the core kinases MST1/2 and LATS1/2. TAZ/YAP lack DNA binding domains and complex with TEAD transcription factors in the nucleus. The TAZ/YAP-TEAD axis is regulated by PI3K in a LATS1/2 dependent manner. In sarcomas, epigenetic silencing of upstream Hippo kinases MST1/2 and MAP4 kinases via histone deacetylation reduces LATS1/2 activity, leading to aberrant TAZ/YAP activation in 30–50% of cases. Preliminary data show that HDAC inhibition with Romidepsin restores MST1 expression and reduces TAZ/YAP transcriptional activity, suggesting a therapeutic opportunity to target both PI3K and Hippo pathways.

Objectives: This study aims to determine whether dual inhibition of PI3K-Akt-mTORC1 signaling (via Akt or mTORC1 inhibitors) and TAZ/YAP transcriptional activity (via TEAD or HDAC inhibitors) can synergistically suppress sarcoma cell proliferation and survival. We hypothesize that combination therapy will be more effective than single-agent treatment due to the convergence of these pathways on tumor-promoting transcriptional and translational programs.

Methods: We utilized three sarcoma cell lines: RD (embryonal rhabdomyosarcoma), A204 (malignant extrarenal rhabdoid tumor), and RH30 (alveolar rhabdomyosarcoma). Cells were treated with MK2206 (Akt inhibitor), Everolimus (mTORC1 inhibitor), Romidepsin (HDAC inhibitor), and VT-107 (TEAD inhibitor), alone and in combination. Proliferation was assessed via CCK-8 cell viability assays, and clonogenic outgrowth was measured to evaluate long-term survival. Western blotting was used to assess phosphorylation of downstream targets and MST1 expression.

Results: MK2206 treatment reduced proliferation in A204 and RH30 cells at concentrations greater than 1 μM over 72 hours, with corresponding decreases in phosphorylation of Akt-mTORC1 substrates. Clonogenic assays showed reduced colony formation in both lines. Combination treatment with MK2206 and VT-107 further suppressed proliferation, suggesting additive or synergistic effects. In RD cells, Romidepsin at 5–10 nM significantly reduced proliferation and clonogenic outgrowth, consistent with increased MST1 protein levels and reduced TAZ/YAP activity. These findings support the hypothesis that dual targeting of PI3K and Hippo pathways enhances anti-tumor efficacy.

Conclusion: Our data demonstrate that PI3K and Hippo pathways are frequently dysregulated in sarcomas and that combination therapy targeting both axes can more effectively inhibit tumor cell growth. TEAD inhibition disrupts TAZ/YAP transcriptional activity downstream, while HDAC inhibition restores Hippo signaling and suppresses TAZ/YAP-driven transcription, and PI3K pathway inhibitors reduce survival signaling. These findings provide a rationale for further investigation into dual-pathway inhibition as a therapeutic strategy in sarcoma, including mechanistic studies and in vivo validation to define therapeutic windows and potential clinical applications.

Poster #9

Rose Gogal	A Biophysics-Informed Bayesian Framework for Hearing Loss Missense Variant Classification

Background: Hearing loss is the most common sensory deficit disorder affecting ~5% of the world's population. 1 to 3 in every 1000 infants tested will be diagnosed with some form of hearing loss, and 65% of those cases will be due to genetic causes. The Deafness Variation Database (DVD) is an open-access resource of variants associated with hearing loss, containing over 380,000 missense variants (a single, downstream amino acid change to protein sequence) across 224 genes. DVD variants are labelled per the American College of Medical Genetics and Genomics (ACMG) criteria as benign, likely benign, likely pathogenic, pathogenic, or variants of uncertain significance (VUS). VUS comprises 79% of the missense variants in the DVD. It is currently intractable to experimentally investigate over 320,000 VUS, highlighting the need for in silico methods to investigate variants. With the emergence of protein structure prediction methods, we evaluate a variant's biophysical effects to protein structure to better inform our assessment of VUS.

Objectives: We hypothesize evaluating genetic effect predictors in conjunction with biophysical data about a missense variant's associated downstream changes to protein structure will improve our ability to identify VUSs that are likely to cause hearing loss.

Methods: We applied AlphaFold3 to predict protein structures for all genes in the DVD. We optimized these structures with the AMOEBA polarizable force field to resolve steric clashes, repack sidechains, and improve backbone conformations. The optimized protein structures were used as input to the folding free energy difference (ΔΔG_Fold) prediction tool DDGun3D where high, positive ΔΔG_Fold indicates a missense variant leads to protein misfolding. We used this data in combination with the genetic tool REVEL to prioritize VUS as likely pathogenic. We applied our prioritized list to patients at the University of Iowa who previously did not receive a diagnosis to select the most likely genetic cause of their hearing loss.

Results: Using guidelines set in Pejaver et al. for determining the strength of computational evidence from genetic effect predictors like REVEL, we constructed a likelihood function that combines ΔΔG_Fold and REVEL and establish a biophysics-informed threshold for selecting VUS likely to cause hearing loss. ΔΔG_Fold with REVEL identified ~29,000 missense VUSs with very strong evidence of causing hearing loss at a false positive rate of <0.2%. We compared the >29,000 variants to patients sequenced at the University of Iowa in the last five years and selected three variants to highlight here.

Conclusion: Using deep learning protein structure prediction models, sequence-based genetic predictors, and biophysical evidence, we identified >29,000 missense VUS likely to be pathogenic. These variants will publicly be known as VUS' to guide genetic researchers to variants with additional evidence for being pathogenic. We highlighted three patients for which this work would aid in a diagnosis for the genetic causes of their hearing loss. Our work is applied here to hearing loss, but the pipeline is not limited to a specific disease and can be applied in other contexts.

Poster #10

Jasmyn Hoeger	Discovery and Initial Characterization of a Diverse Family of Microproteins Derived from Alternative Open Reading Frames in SCN(NaV) Genes

Background: Microproteins (MPs) are a growing class of short peptides that can arise from upstream open reading frames. Recent advances in ribosome profiling have uncovered a myriad of MPs that serve vital functions in ion channel modulation, cell signaling and energetics, and more. However, there remains a need to continue characterizing novel MPs to determine their expression, function, and disease relevance.

Voltage-gated Na+ channels (NaVs), encoded by SCN-family genes, are critical for membrane excitability and action potential propagation. Pathogenic mutations in SCN(NaV) genes cause a widespread spectrum of channelopathies, several of which can be fatal. Thus, there remains a critical need for continued investigation of their complex regulatory nature.

Objectives: Ribosomal profiling and mutational analyses support the translation of an alternative open reading frame (altORF) in the 5′ untranslated region (5′UTR) of SCN5A. We aim to validate the translation of this altORF and determine its biological relevance as a translational regulator of NaV1.5 expression and as a microprotein. We subsequently identified that this altORF is conserved in most SCN family genes, therefore we aim to expand our studies to include the entire SCN gene family. Finally, a commonality between the altORFs is they contain the conserved motif CAGGATG, across genes and species, five nucleotides upstream of the canonical ATG start codons in nearly all SCN(NaV) genes. We aim to determine the function of this element. Interestingly, several humans have mutations in this region. We aim to characterize these mutations effect on NaV1.5 expression in vitro and in vivo.

Methods: To demonstrate that these altORFs are translated and regulate translation of NaVs expression in vitro we generated a myrid of plasmid constructs, including C-terminal V5-tagged and full-length reporters. We also generated constructs harboring the mutations in the conserved motif to understand how these effect NaV translation. Next, we created an altATG>altAGG KI mouse model to further investigate this altORF translational regulatory mechanism in vivo.

Results: We discovered eight novel MPs that are encoded by the SCN altORFs and primarily localize to the mitochondria. These altORFs act to universally repress downstream NaV translation. Variants in the conserved motif seemingly have a context-dependent ATG selection. Furthermore, knock-in mutation of the SCN5A altATG in mice elevates NaV1.5 protein levels, enhances peak Na+ currents, and alters cardiac conduction.

Conclusion: Overall, this work has uncovered the potential for several SCN(NaV) gene family members to encode a diverse panel of MPs that regulate NaV expression. With respect to relevant human mutations, we identified a probable association between altATG mutations and prolonged QT, highlighting the need to expand considerations for possible profound and clinically relevant effects of SCN5A non-coding variants. Based on our current data, it is a likely possibility that SCN(NaV) gene family altATG mutations leading to gain-of-function could plausibly modify related phenotypes in patients (e.g. epilepsy for SCN1A, SCN2A and SCN3A, arrhythmias for SCN5A, and pain for SCN9A).

Poster #11

Souradip Sinha	The ATAC histone acetyltransferase complex is a key oncogenic driver in sarcomas

Background: Sarcomas are diverse mesenchymal neoplasms originating in soft tissues and most sarcomas lack effective therapies. Our lab has previously shown that gene fusions of TAZ/YAP; TAZ-CAMTA1 and YAP-TFE3 drive the vascular sarcoma Epithelioid hemangioendothelioma (EHE) by recruiting the Ada2A-Containing (ATAC) histone acetyltransferase complex. YEATS2 and ZZZ3 are key scaffolding subunits of the ATAC complex and have been emerging as oncogenic drivers in multiple cancers including sarcomas. The ATAC complex promotes gene transcription by acetylating H3K9 via its histone acetyltransferase (HAT) module containing either GCN5 or PCAF as the catalytic subunit.

Objectives: We are studying the role of the ATAC complex as an oncogenic driver in both fusion protein-positive (EHE) and -negative sarcomas (the majority of sarcomas). In EHE, TAZ-CAMTA1 drives cancer hallmarks in vitro and in vivo. Hence, we are investigating whether genetic/pharmacological inhibition of the ATAC complex can decrease the transformed phenotype. Similarly, we are investigating the ATAC complex in other sarcomas and exploring how to inhibit its oncogenic properties.

Methods: To study the ATAC complex, YEATS2/ZZZ3 were genetically knocked down in various human sarcoma cells lines. For siRNA knockdown, cells with si-YEATS2/ZZZ3 were compared with si-non targeting control(si-NT). For shRNA-mediated knockdown, cells with sh-YEATS2/ZZZ3 were compared with sh-empty vector(shEV) and sh-NT controls. We performed a cell-line derived xenograft experiment, where we injected NSG mice with SW872(TAZ-CAMTA1) cells with sh-NT(negative control) or sh-YEATS2#1 or sh-YEATS2#3. For the in vitro drug studies, sarcoma cells were treated with varying drug concentrations and compared with vehicle control(DMSO). We also performed a miniTurbo ID-mass-spectrometry experiment to identify transcription factors interacting with the ATAC complex.

Results: siRNA-mediated knockdown of YEATS2 in SW872(TAZ-CAMTA1) cells decreased H3K9-acetyl levels. We observed that YEATS2 knockdown significantly reduced tumor progression in vivo as compared to non-targeting cells. Previously, data from The Cancer Genome Atlas showed that high YEATS2/ZZZ3 RNA levels corelated with worse overall survival in sarcomas. We have observed that YEATS2/ZZZ3 protein levels are significantly upregulated in various human sarcoma cell lines as compared to their negative controls. In SKLMS-1 and HT1080 cells, we observed that YEATS2/ZZZ3 knockdown significantly decreases H3K9-acetyl levels, reduces 2D proliferation, and colony formation on soft agar. We have also observed that PU139 (pan-HAT inhibitor) or GSK4027 (GCN5/PCAF-specific inhibitor) significantly decreases cell proliferation and H3K9-acetyl levels in SKLMS-1 and HT1080 cells. Mass spectrometry and subsequent co-immunoprecipitation identified E2F3 as a transcription factor that interacts with the ATAC complex.

Conclusion: In sarcomas, the ATAC complex is a key acetyltransferase complex required for the maintenance of H3K9-acetylation levels, a critical histone post-translational modification associated with transcriptional activation. We show that YEATS2 drives tumor progression in vivo, which suggests that TAZ-CAMTA1 drives hallmarks of cancer in an ATAC complex-dependent manner in EHE. We also show that the ATAC complex promotes 2D proliferation and anchorage-independent growth in SKLMS-1 and HT1080 cells that is associated with H3K9-acetylation. In fusion protein-negative sarcomas, E2F3 appears to be the main transcription factor interacting with the ATAC complex, which might be a critical oncogenic pathway that can be therapeutically targeted in sarcomas.

Poster #12

Reza Amouzandeh	Specific Salt Ion Effects on 3D-Printed Silk Fibroin Tissue Scaffolds

Background: 3D-printed silk fibroin structures are promising scaffolds for tissue regeneration and drug delivery, primarily due to their manufacturing flexibility, protein-based composition, and minimal immunogenicity. However, the properties of these silk scaffolds are often difficult to control precisely and can be compromised by harsh processing conditions. Salt ions play a central role in the natural silk-spinning process of both silkworms and spiders by constituting the solvent environment of their native spinning glands.

Objectives: We propose a bioinspired approach that exploits salt ions to tune the molecular assembly pathway of silk proteins, thereby controlling the morphological and other macroscopic properties of the resulting scaffolds. The ability to modulate silk fibroin scaffolds using salt ions under ambient and aqueous conditions holds great potential for directing cell differentiation and promoting tissue morphogenesis in vitro.

Methods: silk films were printed by extruding a monolithic silk fibroin ink to a 4.4 M sodium chloride bath, as described in our previous work. The impact of potassium, sodium, ammonium, chloride, hydrogen phosphate, and sulfate ions on 3D-printed silk fibroin films was studied by a 24-hour treatment in various salt baths composed of these ions, followed by an additional 24-hour treatment in a 2.3 M ammonium sulfate solution to stabilize the proteinaceous structures. We used a microplate reader, scanning electron microscopy (SEM), Raman spectroscopy, and uniaxial tensile test to characterize the transparency, morphology, molecular conformation, and mechanical properties of the 3D-printed silk fibroin films, respectively. Human primary bronchial epithelial cells were cultured on the treated films to evaluate their cytocompatibility using confocal microscopy.

Results: The properties of 3D-printed silk films can be manipulated via tuning salt composition and concentration. In particular, the β-sheet content of silk films decreases at higher concentrations of Na_2HPO_4 and K_2HPO_4, which correlates with lower cross-sectional porosity, lower elastic modulus, and higher transparency of films. We also found that salt composition can manipulate the molecular conformation, transparency, mechanical properties, and morphology, such as porosity. KCl-treated silk films showed the highest beta-sheet content among the studied salts, which correlates with a lower transparency. Also, NaCl-treated films showed the highest elastic modulus among the studied salts. More importantly, we found there is a correlation between the rank of salt ions in the Hofmeister series, transparency, morphological features, and mechanical properties, thus implying a salt ion-based mechanism for manipulating silk fibroin scaffolds. The cytocompatibility of silk films manufactured by salt treatments is confirmed by the formation of a monolayer of human primary epithelial bronchial cells on silk films after two weeks.

Conclusion: Our study demonstrates the effect of salt ions, inspired by silk spinning, on the properties of 3D-printed silk films. Most likely governed by the Hoffmeister series, salt ion composition dictates silk protein assembly pathways, affecting surface and cross-sectional morphology and thus, macroscopic properties. These findings highlight the potential of monolithic proteinaceous compositions and ambient, aqueous 3D-printing for various biomedical applications such as bioengineered airway patches.

Poster #13

Luke Handlos	Structural and Biophysical Insights into DNA Translocation by TLS Polymerases Iota and Eta

Background: DNA replication is frequently disrupted by lesions caused by oxidative stress and ultraviolet (UV) radiation. When replicative polymerases such as polymerases delta and epsilon stall at these sites, cells rely on translesion synthesis (TLS) polymerases to bypass the damage and maintain fork progression. TLS polymerases, such as polymerases iota and eta, possess flexible, lesion-tolerant active sites that can accommodate DNA lesions. Each TLS polymerase handles specific DNA lesions: polymerase eta bypasses UV-induced pyrimidine dimers and 8-oxo-guanine (8-oxoG), while polymerase iota specializes in minor-groove and exocyclic purine lesions through Hoogsteen base pairing. Although structural studies have clarified how TLS polymerases insert nucleotides opposite lesions, the subsequent translocation step, where TLS polymerases move to the next DNA register, remains poorly understood. Because translocation dictates lesion bypass fidelity, resolving this process is essential for understanding and comparing the mechanisms of different TLS polymerases.

Objectives: The goals of this study are: (1) to determine structural features distinguishing pre- and post-translocation states of polymerase iota using X-ray crystallography; (2) to characterize the conformational pathway of polymerase eta translocation using molecular dynamics (MD) simulations; and (3) to construct Markov State Models for determining energetics and transition rates.

Methods: Polymerase iota-DNA complexes were crystallized using self-annealing oligonucleotides of increasing length, both with and without dTTP. Addition of a single thymidine nucleotide mimics one-step primer extension, generating binary complexes that emulate post-translocation states and ternary complexes that trap pre-translocation conformations. Diffraction data are being processed and refined using Phenix and WinCoot to obtain high-resolution structural models.

For polymerase eta, pre- and post-translocation structures (PDBs 3TQ1 and 3MR2) were used to generate ten linearly interpolated guide structures for stepwise Targeted and Steered MD simulations in CHARMM, producing a continuous biased trajectory. Representative intermediates were selected using a TICA-assisted clustering workflow incorporating DNA phosphate-phosphate distances and base-pair geometry. Selected snapshots were prepared for unbiased simulations through minimization and equilibration. Initial unbiased runs (three 50-ns replicates per intermediate) are now underway, along with biased simulations of polymerase iota with 8-oxoG-containing DNA.

Results: For polymerase iota, two binary and two ternary structures have been refined to 2.58-2.17 Å resolution. These models exhibit distinct pre- and post-translocation-like arrangements, providing strong structures for future dynamic studies. As for polymerase eta, biased simulations have successfully produced a continuous translocation pathway, where DNA RMSD progressively shifted toward the post-translocation state. Polymerase RMSD exhibited transient elevation consistent with domain adjustments, with RMSF analysis identifying two flexible regions, residues 125-200 (palm domain) and 350-400 (little-finger domain), that accommodate DNA motion. Representative intermediates from this biased trajectory are now undergoing unbiased simulations for MSM construction.

Conclusion: Polymerases iota and eta adopt distinct translocation strategies shaped by their active site architectures, catalytic processes, and lesion specificities. Structural refinement of polymerase iota datasets will enable detailed comparisons across DNA registers, while the integrated biased-simulation and unbiased MD workflow for polymerase eta will establish a foundation for MSM analysis. Together, these approaches will map the energetic landscape of TLS polymerase translocation and inform future studies involving other TLS polymerases (e.g., Rev1) and experimental time-resolved crystallography.

Poster #14

Mona Maalouf	Synthesis of isoprenoid triazole bisphosphonates

Background: Our efforts to develop inhibitors of geranylgeranyl diphosphate synthase (GGDPS) have focused on isoprenoid triazole bisphosphonates. Our structure-activity relationship (SAR) studies have determined that isoprenoid chain length, olefin stereochemistry, and the nature of the alpha substituent impact inhibitory potency as well as in vivo biodistribution. In the best-case, the alpha methylated homoneryl triazole bisphosphonate, effective concentrations as low as 20 nM have been observed in cellular assays involving a panel of human myeloma and osteosarcoma cell lines.

Objectives: To investigate SAR further, we have prepared a family of novel derivatives that have a fixed phosphorus position by virtue of vinyl or cyclopropyl groups at the α-carbon position. Additional modifications include compounds with homocitronellyl chains instead of homogeranyl or homoneryl chains.

Methods: Synthesis of bisphosphonate targets from commercially available isoprenoids requires several steps, including regioselective hydroboration of a terminal olefin and a click reaction to assemble the triazole bisphosphonate.A selective conjugate reduction of vinyl bisphosphonate esters affords monoalkylated bisphosphonates. All new compounds were evaluated in GGDPS enzyme assays and in cellular assays involving a panel of human myeloma and osteosarcoma cell lines.

Results: The homocitronellyl derivatives displayed markedly reduced activity in both enzymatic and cellular assays. While all of the homogeranyl/homoneryl vinyl/cyclopropyl compounds had similar activity in the enzyme assay (IC50's 0.37-2.87 mM) , the cellular potencies varied more dramatically (ranging from 10 nM to no activity at 100 mM), depending on the olefin stereochemistry, the specific α-carbon modification and tumor cell type.

Conclusion: Of this set of compounds, the alpha methylated homoneryl derivative 4 proved to be the most active. The focus of future work will be to prepare gram amounts of bisphosphonate 4 to allow for animal testing.

Poster #15

Zoe Kramin	In-line Diffuse Reflectance Spectroscopy Enables Rapid Monitoring of Full-Scale Anaerobic Co-Digestion

Background: Anaerobic digestion is a biological process that breaks down organic materials to produce both biosolids suitable for agricultural use and bioenergy. Common feedstocks include municipal sludge and livestock manure, while energy crops and food waste can also be added through a process known as anaerobic co-digestion. Intensifying anaerobic co-digestion can increase the production of renewable resources but can also destabilize the process. In more aggressive anaerobic co-digestion applications, the physicochemical conditions of both the feedstock and digester can shift more rapidly than traditional monitoring programs are designed to oversee. Maintaining stable anaerobic co-digestion operations requires frequent monitoring of key physicochemical parameters to prevent process disruptions like organic overloading, pH drops, and ammonia accumulation. Incorporating more heterogeneous feedstocks, such as food waste, via anaerobic co-digestion should be encouraged to reduce landfill burden, lower greenhouse gas emissions, and enhance renewable energy production.

Objectives: The objectives of this study were to conduct an in-line diffuse reflectance spectroscopy pilot at a full-scale anaerobic co-digestion facility to inform operator decision-making by 1) generating rapid predictions of key physicochemical parameters in both feedstock and digestate; 2) applying these predictions to assess digester stability under dynamic operating conditions; and 3) determining the minimum reference dataset size required to achieve acceptable prediction accuracy for each parameter.

Methods: In-line diffuse reflectance spectroscopy was piloted at a full-scale municipal anaerobic co-digestion facility to evaluate rapid monitoring of heterogeneous feedstocks and digestate. Spectra and physicochemical analyses from 42 high-strength waste samples and 146 digestate samples were used to train and test partial least squares regression models. Partial least squares models establish relationships between measured spectra and corresponding physicochemical properties. Spectra were preprocessed with a Whittaker smoothing filter and a standard scaler. The datasets were partitioned with the Kennard-Stone 70:30 train:test split. Datasets were downsampled systematically, with each scenario repeated 20 times.

Results: Models developed from high-strength waste samples and digestate samples yielded operationally useful predictions (root mean square error 10–27%) for total solids, volatile solids, fats, chemical oxygen demand, volatile acids, and alkalinity. Protein and carbohydrate predictions were less accurate due to limitations in reference data. Importantly, predicted volatile acid:alkalinity ratios provided rapid indicators of digester stability. Downsampling analysis demonstrated that effective models could be developed with fewer than 50 training samples for several parameters, highlighting opportunities to reduce analytical costs. Field deployment during periods of digester instability, including foaming and failure, further validated the robustness of diffuse reflectance spectroscopy models under dynamic operating conditions.

Conclusion: These results establish that diffuse reflectance spectroscopy when paired with partial least squares regression, can provide operationally valuable predictions of parameters in full-scale systems. Downsampling analysis revealed that effective modeling can still be achieved with relatively few training samples for certain parameters, offering a cost-effective path forward for utilities considering diffuse reflectance spectroscopy implementation. Furthermore, the ability to assess digester stability in real-time supports more responsive and stable digester operation, offering pathways to greater digester stability, higher biogas yields, and improved treatment performance.

Poster #16

Sophie Granger	Probing Allosteric Control of Native Enzyme Dynamics in H. pylori Glutamate Racemase with Single-Molecule Approaches

Background: One of our greatest challenges in drug design is understanding and effectively utilizing cryptic allosteric pockets in flexible enzyme targets. Drug leads that do bind to these cryptic pockets are often discovered during high-throughput screening campaigns, but the mechanisms of action are rarely understood. A confluence of molecular dynamics studies and experimental structural work has implicated a dynamic source for this allosteric inhibition, which centers on a small molecule-associated abolition of essential monomer-monomer coupled motions.

Objectives: In a campaign for new, potent, antibiotics targeting Helicobacter pylori (H. pylori), but sparing the healthy gut microbiome, we focused on HpMurI, a cofactor-independent glutamate racemase from H. pylori essential for converting L-and-D-glutamate in peptidoglycan biosynthesis. Catalysis of this stereoinversion must proceed via a pre-activation step, which is dependent on HpMurI's flexibility. Furthermore, our recently published structure-based drug design study that focused on optimizing a pocket at the monomer-monomer interface has proved highly fruitful in developing a new class of selective inhibitors that target HpMurI's native motions through a novel allosteric mechanism.

Methods: To biophysically establish the first dynamic signatures of this mechanism, we developed a correlated optical tweezers and fluorescence microscopy (CTFM) strategy, as well as characterized HpMurI dimer stability using Mass Photometry (MP).

Results: Using CTFM, we quantified the mechanical stability of individual HpMurI dimers under different ligand conditions; dimer rupture forces increased approximately three- to four-fold upon addition of the native substrate, consistent with substrate-induced stabilization. Conversely, the addition of an allosteric inhibitor compound reduced rupture forces to approximately apo levels, suggesting this inhibitor disrupts stabilizing inter-subunit contacts despite its allosteric pocket being located far from the dimerization and active site. MP experiments complemented these results, demonstrating a shift in the equilibrium toward dimer formation in the presence of substrate and toward monomer in the presence of inhibitor.

Conclusion: Together, the findings thus far indicate a direct biophysical link between small-molecule binding and HpMurI conformational flexibility.

These analyses of the mechanism of allosterically inhibited protein plasticity will define how compound engagement modulates enzyme structure and function, laying the mechanistic groundwork for how protein dynamics can be manipulated or fine-tuned for functional outcomes.

Poster #17

Elham Taherian	New fluroquinolone derivatives combined with Paclitaxel against Colorectal cancer

Background: Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer-related death worldwide, according to global cancer statistics (2020). Recently, the incidence rates of CRC in younger adults (20-49 y) are alarmingly increasing, while they are decreasing in older populations (50-85 y). The therapeutic outcome and 5-years survival associated with the use of current chemotherapeutic protocols in patients with stage III (inoperable) and stage IV (metastatic) are not satisfactory, and the search for innovative therapeutic approaches is thus highly needed.

Paclitaxel, despite being the first line of treatments in various cancers including gynecological and pancreatic cancers, is not used in CRC, nor included in therapeutic guidelines according to the American Cancer Society due to the emergence of resistance and poor efficacy as a single agent. Furthermore, PTX is associated with several side effects, including peripheral neuropathy and myelosuppression, both of which are dose-related and dose-limiting. In the recent years, our lab has developed several approaches to tackle chemoresistance developed against PTX in uterine cancer and melanoma, enabling the use of lower doses to achieve the same therapeutic efficacy. The use of a relatively non-toxic adjuvant in combination with PTX has the potential to improve the quality of life for cancer survivors by reducing PTX-related, dose-dependent adverse events.

Fluoroquinolones are a well-tolerated and highly effective class of antibacterial agents. Recent research highlights their potential as repurposed anticancer agents, with structural modifications enhancing cytotoxicity and selectivity toward cancer cells. CIP2b, M1, and G1 are new p-chlorophenyl carbamoyl methyl derivatives of ciprofloxacin, moxifloxacin, and gatifloxacin, respectively. We previously showed that the combinatorial therapy comprising of PTX and CIP2b exhibited synergistic cytotoxic activity in vitro and superior antitumor activity in vivo against p53 mutant human endometrial cancer.

In this study, we aimed to evaluate the synergistic effect of PTX in combination with fluoroquinolone derivatives—CIP2b, M1, and G1. Furthermore, to explore the underlying mechanisms, we performed cell cycle analysis and uptake studies in the CRC cell line, CT-26

Objectives:
1. To evaluate the cytotoxic effects of PTX and fluoroquinolone derivatives (CIP2b, M1, G1) against colorectal cancer cells.
2. To determine the synergistic activity between PTX and the fluoroquinolone derivatives.
3. To analyze the effect of these combinations on cell cycle distribution.
4. To assess whether fluoroquinolone derivatives enhance intracellular accumulation of PTX.
5. To explore the potential mechanism underlying the observed synergy.

Methods: The toxicity of single treatments with PTX, CIP2b, ciprofloxacin, G1, gatifloxacin, M1, and moxifloxacin, as well as combinations of PTX with each fluoroquinolone derivative and their corresponding parent compounds, was evaluated against CT-26 cancer cell lines using the MTS assay. To evaluate the synergistic effects of these combinations, Bliss analysis was performed. Based on this method, a Bliss score greater than 10 indicates a synergistic interaction. To further investigate the impact of these drug combinations on the cell cycle, CT-26 cells were treated with either single agents or combinations of PTX with the fluoroquinolone derivatives for 24 hours. After treatment, cells were collected, fixed, and stained with propidium iodide. Flow cytometry (FACSCalibur, BD) was then used to analyze cell cycle distribution, and the percentages of cells in each phase (G0/G1, S, G2/M) were determined.

To test whether these fluoroquinolone derivatives improve the PTX intracellular accumulation, CT-26 CRC cells were treated with fluorescently labeled PTX (PTX-OG) alone or in combination with fluoroquinolone derivatives. After a 2-hour incubation, cellular uptake of PTX-OG was measured by flow cytometry. This experiment aimed to determine whether fluoroquinolone derivatives enhance the intracellular accumulation of PTX, which could contribute to overcoming drug resistance in cancer cells that overexpress P-glycoprotein (P-gp) efflux protein, of which PTX is a substrate.

Results: Cytotoxicity studies demonstrated strong synergy between CIP2b, M1, G1, PTX against the CT-26 cell line. This synergistic effect was evidenced by a significant reduction in the IC_{50} of PTX and an increase in cells in G2/M cell cycle arrest. Specifically, the percentage of cells in the G2/M phase increased from 25% in PTX-treated cells to 35%, 75%, and 85% when PTX was combined with CIP2b, M1, and G1, respectively. The Bliss synergy scores for CIP2b, M1, and G1were 15, 20 and 17 respectively, indicating powerful synergistic interactions with PTX. In contrast, the synergistic score for unconjugated fluoroquinolones was less than 10, suggesting no synergistic activity when combined with PTX. Furthermore, uptake studies revealed that the CIP2b doubled the intracellular accumulation of PTX in CT-26 cells, while M1 and G1 increased it threefold when combined with PTX, compared to PTX treatment alone. This suggests that fluoroquinolone derivatives may enhance the delivery and efficacy of PTX in CRC models.

Conclusion: Overall, these findings highlight the ability of fluoroquinolone derivatives to synergistically enhance the anticancer effects of PTX against CRC and that this may at least be partially due to enhanced cellular accumulation of PTX.

Poster #18

Prateek Aryal	Breakdown of Lignocellulose Using Boron Trihalide Reagents

Background: Plant cell walls are made of lignocellulose, which is composed of the abundant biopolymers cellulose, hemicellulose, and lignin. Cellulose has a huge commodity market with several applications in the textile industry, the biomedical industry, diagnostic sensor design, electro-optical device design, energy storage, and others. Lignin is a polyphenolic aromatic polymer whose monomer products can be valorized for chemical feedstock materials, bio-oils, pharmaceuticals, specialty chemicals, resins, and many more. Our lab has demonstrated that boron trihalides, which are Lewis acid reagents, break down lignocellulose into its lignin and polysaccharide components at room temperature and under mild reaction conditions.

Objectives: From this separation protocol, we obtain nanocellulose (~400 nm) in the aqueous fraction and a lignin-rich solid. The lignin can be further depolymerized to obtain a monomer-rich oil. In this way, we utilize both components and add value to a cheap and abundant plant material.

New work focuses on the application of this separation method to lignocellulose samples derived from hemp, which is a regenerative and value-added crop for farmers in Iowa. Further, we report new characterization of the molecular features of the separated cellulose fractions.

Methods: Lignocellulose material is subjected to 4-5 subsequent BCl_3/BBr_3 treatments. The efficiency of polysaccharide removal is monitored using calcofluor white stains and fluorescence imaging. The solid residue that remains at the end is lignin-rich. The residue is subjected to hydrogenolysis in a Parr reactor, from which we obtain lignin monomer-rich oil that can be analyzed by GC-MS (gas chromatography-mass spectrometry). The cellulose obtained in the aqueous fraction is mixed with boric acid. It is dialyzed by a dialysis tube for removing boric acid. The cellulose obtained is further characterized by NMR (nuclear magnetic resonance spectroscopy) and XPS (X-ray photoelectron spectroscopy). The morphology of the cellulose is observed by SEM (scanning electron microscopy). Dynamic light scattering (DLS) is used to determine the dimensions of the nanocellulose formed afterwards.

Results: We observe a gradual decrease in fluorescence intensity after sequential boron trihalide treatments of hemp samples, indicating efficient separation of polysaccharide from the lignin-rich solid. X-ray photoelectron spectroscopy showed that extracted cellulose was halogenated. Dialysis performed using a 0.1-0.5 kDa dialysis tube shows that up to 45% of nanocellulose is recovered from the polysaccharide/boric acid aqueous extract after 24 hrs. with near complete removal of boric acid. EDS analysis shows that the cellulose sample has 16-18% bromination. The halogenation of cellulose is also confirmed by HSQC NMR (Heteronuclear Single Quantum Correlation) and suggests bromination at the 6 position of the glucose monomer unit.

Conclusion: This study demonstrates an efficient boron trihalide-based process for valorizing plant lignocellulose into functional nanocellulose and lignin-derived products, advancing sustainable material innovation. The approach supports renewable biopolymer utilization and promotes hemp as a regenerative, value-added crop for bioeconomy development.

Poster #19

Kshitija Kale	The Interleukin-1β pathway in T helper 17 Polarization and Effector Resistance

Background: Autoimmune diseases such as multiple sclerosis, type 1 diabetes, and rheumatoid arthritis are characterized by an imbalance between pro-inflammatory and regulatory immune responses. Among the effector subsets, $CD4^+$ T helper 17 (Th17) cells play a central role in mediating chronic inflammation through secretion of IL-17A and IL-17F. Our laboratory has previously demonstrated that Th17 cells are resistant to suppression by $CD8^+$ regulatory T cells ($CD8^+$ Tregs). Furthermore, naïve $CD4^+$ T cells exposed to IL-17A/IL-17F acquire a similar resistant phenotype, suggesting an autocrine reinforcement mechanism. Bulk RNA sequencing of these IL-17–exposed cells revealed enrichment of IL-1β signaling pathways, leading to the hypothesis that IL-1β produced by activated $CD4^+$ T cells might act in an autocrine or paracrine manner to promote Th17 differentiation and effector resistance.

Objectives: The overarching objective of this study is to elucidate the role of IL-1β in the differentiation and effector resistance of Th17 cells, particularly focusing on IL-1β produced endogenously by $CD4^+$ T cells. Building upon transcriptomic and preliminary functional evidence, we aimed to clarify whether IL-1β operates as a T cell–intrinsic autocrine factor that promotes Th17 polarization and confers resistance to $CD8^+$ T cell–mediated suppression.

Methods: To test this, we first examined IL-1β expression across human $CD4^+$ T cell subsets. Peripheral blood mononuclear cells from healthy donors were magnetically sorted to isolate naïve, memory, and effector $CD4^+$ T cells. Upon stimulation with anti-CD3 and anti-CD28, IL-1β transcripts peaked within 48 hours, and protein levels in culture supernatants rose steadily over 72 hours, confirming that activated $CD4^+$ T cells endogenously produce IL-1β. We next asked whether this intrinsic IL-1β production was required for Th17 polarization. Naïve $CD4^+$ T cells were cultured under Th17-polarizing conditions with IL-6 and TGF-β1, in the presence or absence of exogenous IL-1β, or with IL-1β/IL1R blockade. Surprisingly, neither neutralization of IL-1β nor IL1R inhibition impaired IL-17A production or the emergence of the effector-resistant phenotype, indicating that Th17 differentiation proceeds independently of IL-1β signaling. To directly test the necessity of T cell–derived IL-1β, we used CRISPR-Cas9 to knock out IL1B in naïve $CD4^+$ T cells. Edited cells failed to produce IL-1β protein upon activation, confirming successful deletion. Yet, IL1B-deficient cells polarized normally into Th17 cells, with comparable $IL\text{-}17A^+$ frequencies, RORγt expression, and cytokine profiles relative to controls. Moreover, these IL-1β–deficient Th17 cells remained resistant to $CD8^+$ Treg-mediated suppression, demonstrating that IL-1β is dispensable for both Th17 differentiation and the development of effector resistance.

Results: Stimulation of $CD4^+$ T cell subsets revealed that IL-1β is indeed produced endogenously upon activation. IL1B transcript levels rose sharply within 24–48 hours, peaking near 48 hours post-stimulation. Corresponding ELISA data confirmed progressive protein accumulation over 72 hours, particularly in memory and effector subsets. This finding establishes that $CD4^+$ T cells are a previously underappreciated source of IL-1β.

However, functional analyses challenged the hypothesized necessity of IL-1β for Th17 biology. Under Th17-polarizing conditions, neutralization of IL-1β or IL1R1 blockade did not significantly affect IL-17A or IL-17F expression, RORγt induction, or cell proliferation. Even in the absence of exogenous IL-1β, robust Th17 differentiation occurred, suggesting IL-1β is dispensable for lineage polarization under IL-6/TGF-β1-driven conditions. CRISPR-mediated IL1B knockout confirmed these findings. IL-1β-deficient $CD4^+$ T cells exhibited normal Th17 differentiation, with comparable frequencies of $IL\text{-}17A^+$ cells and similar transcriptional profiles of key Th17-associated genes (RORC, IL23R, STAT3). Suppression assays further revealed no restoration of $CD8^+$ Treg–mediated regulation in the absence of IL-1β, indicating that effector resistance persists independently of intrinsic IL-1β. Bulk RNA-seq pathway analysis, which had initially highlighted IL-1β signaling enrichment, was thus reinterpreted as reflecting correlative activation rather than causative necessity. Preliminary scRNA-seq data now reveal distinct transcriptional modules among Th17 subsets, some enriched for metabolic reprogramming, oxidative stress responses, and TNF–NF-κB signaling, implicating alternative regulatory circuits driving suppression resistance.

Conclusion: In conclusion, our data refine current understanding of Th17 biology by demonstrating that T cell–intrinsic IL-1β is not required for Th17 differentiation or effector resistance. These insights highlight the complexity of T cell–intrinsic regulatory circuits and suggest new directions for targeting Th17-driven inflammation in autoimmune disease.

Poster #20

Jacob Miller	Relative Binding Free Energy Differences for Transcription Factor-DNA Complexes Using the Polarizable AMOEBA Force Field

Background: Transcription factors (TFs) regulate gene expression by binding specific DNA sequences to activate or repress transcription. Variants in either the TF protein or its DNA binding site can alter binding affinity and potentially disrupt gene regulation. Loss of binding may prevent transcription, while unusually strong binding may impair timely dissociation, both of which can have functional consequences. Experimental characterization of variant effects is costly and time-intensive, motivating the use of computational methods to estimate changes in binding free energy (ΔΔGbind) due to a variant in the TF or the DNA. One of the most robust methods to compute a free energy difference is using molecular dynamics. Previously, efficient protocols have been published using fixed-charge force fields. These often struggle to represent the highly charged and electrostatically complex environment of DNA-protein interfaces, limiting their predictive accuracy. This limitation can be mitigated by using a polarizable force field such as AMOEBA (Atomic Multipole Optimized Energetics for Biomolecular Applications).

Objectives: The goal of this work is to compute variant-induced changes in TF-DNA binding free energy with high accuracy while maintaining computational efficiency. Specifically, we aim to develop and validate a protocol capable of reliably computing ΔΔGbind values for base-pair variants in DNA-bound transcription factor systems.

Methods: To compute free energy differences, we implement the first fully GPU-accelerated dual-topology framework with AMOEBA. This force field describes electrostatics using permanent multipoles (monopole, dipole, quadrupole) and induced dipoles to model polarization. This approach provides a more detailed representation of charge distribution compared to fixed-charge force fields.

The first molecule we tested was the 12-base-pair palindromic Drew-Dickerson DNA. The initial test of our protocol was done on “pseudo-variants,” in which a base pair is alchemically transformed into itself (e.g., an A-T base pair is changed to an A-T base pair). Since the two end states are the same, the resulting free energy change is zero. The other test performed with this molecule was computing zero-sum thermodynamic cycles. Due to the palindromic symmetry, two different variants can be introduced, and the sum of their free energy differences will be zero. Finally, we started testing the method’s success on calculating ΔΔGbind. The system consisted of transcription factor AtERF1 interacting with a canonical DNA sequence used to produce an NMR structure (PDB ID: 1GCC).

Results: The two pseudo-variants, A5A/T20T and G4G/C21C, have free energies of -0.06 ± 0.07 and -0.31 ± 0.07 kcal/mol, respectively. Four zero-sum thermodynamic cycles were calculated with an overall MUE of 0.36 ± 0.21 kcal/mol. Lastly, the computed ΔΔGbind values for two DNA variants in the AtERF1–DNA complex. Compared to experiment, the AMOEBA-based results showed a MUE of 1.71 ± 0.24 kcal/mol, versus 5.06 kcal/mol using fixed-charge approaches, indicating improved accuracy over fixed-charge force fields.

Conclusion: This work demonstrates that the AMOEBA force field combined with GPU-accelerated alchemical methods can provide accurate and computationally efficient ΔΔGbind predictions in TF–DNA systems. This approach enables evaluation of the functional impact of DNA variants, including those implicated in neurological disorders, and may help clarify mechanisms by which variants alter transcriptional regulation.

Poster #21

Paras Gaur	Pharmacological Modulation of PARP1-G4 Interplay and Replication Integrity

Background: Cancer is driven by genomic instability, often influenced by G-quadruplex (G4) DNA structures; non-canonical secondary structures that regulate replication, repair, and transcription. When unresolved, G4s cause replication stress and double-strand breaks, further promoting genomic instability. A key knowledge gap is our limited understanding of how genome maintenance proteins recognize and resolve these structures through coordinated action. PARP1, a clinically validated anticancer drug target, has been shown to interact with G4 DNA. This study examines the interaction and activation of PARP1 on these structures. However, the mechanisms of PARP1 activation and their implications for PARP inhibitor (PARPi) response remain poorly understood. Defining PARP1-G4 dynamics at the single-molecule level will provide mechanistic insights that support the broader goal of elucidating G4 DNA processing during replication, revealing therapeutic vulnerabilities and informing strategies to overcome PARPi resistance in cancer.

Objectives: The specific objectives of this study are to: (1) define the mechanism of PARP1-G4 interaction using single-molecule imaging and mass photometry (MP); (2) determine how G4 structures influence PARP1 activation and auto-PARylation compared to canonical DNA substrates; and (3) assess the impact of clinically relevant PARPi (Olaparib, Veliparib, EB-47).

Methods: The methodology involved expression and purification of PARP1 using affinity and size-exclusion chromatography, followed by site-specific fluorescent labeling for single-molecule visualization. Real-time PARP1 binding and retention on G4-containing DNA versus canonical substrates were monitored using single-molecule total internal reflection fluorescence microscopy (smTIRFM). MP defined PARP1-G4 complex formation and stoichiometry, while MP-based PARylation assays measured activation and poly(ADP-ribose) synthesis upon G4 binding. Finally, the effects of clinically relevant PARP inhibitors on PARP1-G4 interaction and activity were assessed to reveal inhibitor-specific modulation.

Results: smTIRFM and MP revealed that PARP1 binds G4 DNA with a 1:1 stoichiometry and exhibits dynamic association and dissociation. The binding of PARP1 to G4-containing DNA or nicked DNA was sufficient to trigger robust auto-PARylation, generating poly(ADP-ribose) chains of several hundred kDa. Clinically relevant PARPi (Olaparib, Veliparib, EB-47) differentially affected PARP1 retention on G4 substrates compared to nicked DNA, indicating structure-specific modulation. These findings uncover a mechanism by which G4 structures regulate PARP1 activity and suggest that G4-PARP1 interactions may influence therapeutic response to PARPi.

Conclusion: In conclusion, PARP1 binds G4 DNA with defined stoichiometry and undergoes robust activation, and clinically relevant PARPi's differentially modulates this interaction. These findings provide mechanistic insight into how G4 structures influence PARP1 activity and drug response. This mechanistic understanding can contribute to the broader picture of G4 processing and will reveal strategies to enhance current PARPi efficacy and enable development of G4-specific therapeutic interventions to overcome resistance. Specifically, this may benefit patients with aggressive, treatment-resistant cancers by identifying G4-driven vulnerabilities and BRCA-independent biomarkers for precision therapy. Ultimately, this work lays the foundation for personalized cancer treatment strategies and informs future efforts to improve therapeutic durability and reduce recurrence risk.

Poster #22

Elizabeth Walker	Designer Bioplastics: Exploring Biodiversity of Cupriavidus necator for next generation PHA producers.

Background: Plastic pollution poses a major environmental challenge, and one promising solution is to replace petroleum-based plastics with biodegradable bioplastics. Polyhydroxyalkanoates (PHAs) are microbial polyesters that possess similar physical properties to conventional plastics but are produced from renewable feedstocks and are fully biodegradable. Developing efficient biological systems for PHA synthesis is essential for transitioning toward a circular, carbon-neutral economy. Cupriavidus necator is one of the best-known natural PHA producers, yet research has largely focused on the type strain H16, leaving much of the species' natural diversity unexplored. Investigating the diversity within C. necator strains could uncover natural variants with superior PHA productivity, transformability, or genetic robustness, required traits for building more efficient and tunable bioplastic production platforms.

Objectives: The objective of this study is to screen and characterize 13 evolutionarily distinct C. necator strains to identify the most promising candidates for high-yield poly(3-hydroxybutyrate) (PHB) production and genetic engineering. The evaluation uses five criteria: growth rate, PHB production, transformation efficiency, gene expression capability, and DNA robustness. Through comparative physiological studies and genomic analysis of top-performing strains, we aim to uncover factors that contribute to strain-specific differences in PHB yield and properties. These insights will inform the design of synthetic constructs for producing PHAs with tailored physicochemical characteristics.

Methods: Each C. necator strain was cultured in minimal media supplemented with fructose to assess growth kinetics and PHB accumulation. For transformation and gene expression studies, a plasmid containing sfGFP under the control of the pBAD promoter was introduced into each strain. Cultures were induced with varying concentrations of arabinose to determine optimal expression levels. Once the induction conditions were optimized, DNA robustness and transformation efficiency were evaluated using the reporter system. Top-performing strains based on PHB yield and gene expression were further analyzed through genome sequencing to identify genetic variations that might explain their enhanced phenotypes.

Results: Preliminary results revealed that three strains exhibited higher sfGFP expression than the reference strain H16, suggesting that these isolates may support stronger or more tunable gene expression. Additionally, two strains demonstrated higher PHB accumulation (grams PHB per gram dry cell weight) compared to H16. Early genomic comparisons indicate sequence-level differences that could be linked to improved metabolic flux or gene regulation, which will be investigated further. These findings confirm that even within a single species, substantial functional and genetic diversity exists that can be leveraged for strain optimization.

Conclusion: This work broadens our understanding of C. necator's genetic and metabolic diversity and identifies new strains that may outperform the standard model for PHB production. By bioprospecting natural diversity and linking genotype to PHA phenotype, we can inform future metabolic engineering strategies to design synthetic constructs that produce a wider variety of PHAs. Ultimately, this research contributes to creating cost-effective, biodegradable bioplastics that can replace petroleum-derived plastics and advance a sustainable, circular bioeconomy.

Poster #23

Sarah Torrence	Recombinant Prohibitins Mitigate Pro-inflammatory Priming Response and Acute Kidney Injury Induced by Lipopolysaccharide

Background: Prohibitins 1 and 2 (PHB1/2) are ubiquitously expressed lipid raft proteins that form a multimeric ring complex in cellular membranes where they regulate numerous processes including growth, signaling, gene activation/transcription, and metabolism. PHB's have biological effects that are independent of each other, but the evidence consistently supports a cyto-protective and anti-inflammatory role for these proteins. Previous research in our lab demonstrated that recombinant PHB1 (rPHB1) has anti-inflammatory and cardioprotective effects in lipopolysaccharide (LPS)-induced endotoxemia in mice and that this effect is PI3K-dependent.

Objectives: In this study we sought to determine whether rPHB1 also protects mice from acute kidney injury (AKI) induced by LPS, and to further investigate the protective effects of rPHB's in HK-2 cells, a proximal tubular cell line derived from human kidney.

Methods: Adult male C57/Bl6J mice were randomized into 5 groups and treated with an intraperitoneal injection of saline (vehicle), LPS (12 mg/kg b.w.), rPHB1 (300 ng), LPS + rPHB1, and LPS + rPHB1 + buparlisib (a PI3K inhibitor), and euthanized 24 hours later. Kidney tissue from the mice were evaluated via standard histological techniques for tubular swelling and injury. We also used a variety of commercial fluorescence-based assays and real-time NADPH monitoring to probe metabolic activity and cytotoxicity in HK-2 cells treated with LPS and rPHB1 and rPHB2.

Results: Kidney tissue from LPS treated mice showed extensive vacuolization, a marker of acute tubular injury. Treatment with rPHB1 reduced the extent of injury, and this protective effect was attenuated by buparlisib. In HK2 cells, LPS treatment increased metabolic activity at low concentrations and induced cytotoxicity at higher concentrations. Treatment with rPHB1 and rPHB2 consistently blunted the effects of LPS across the range of concentrations tested.

Conclusion: These findings suggest PHBs mitigate the pro-inflammatory priming effect of LPS in kidney, and that rPHBs may have therapeutic potential in endotoxemia-induced AKI. Further investigation of the underlying mechanisms by which rPHB's blunt the effects of LPS are ongoing.

Poster #24

Minou Emmad	Protonation Coupling in Zinc Finger–DNA Recognition Explored by Polarizable CpHMD

Background: Accurately modeling zinc coordination and protonation states is essential for understanding transcription factor regulation, as zinc-finger domains play a crucial structural role in DNA recognition. These domains rely on cysteine residues to coordinate Zn^{2+} ions, maintaining structural stability and mediating communication between protein and DNA. However, traditional fixed-charge models struggle to accurately predict cysteine pKa shifts due to their inability to investigate highly polar environments such as those surrounding DNA-binding domains.

Objectives: Our goal is to determine how protonation dynamics within zinc-finger domains influence Zn^{2+} coordination and DNA binding. We examine titration state changes in both the absence and presence of DNA, and then we assess the impact of cysteine protonation state changes on DNA binding with free energy calculations.

Methods: We apply the first constant-pH molecular dynamics (CpHMD) algorithm for the Atomic Multipole Optimized Energetics for Biomolecular Applications (AMOEBA) polarizable force field. After obtaining our CpHMD trajectories, we use the Rao–Blackwell Estimator (RBE) to gather the free energy estimates.

Results: We show that the inclusion of AMOEBA significantly improves the stability of Zn^{2+} coordination and the accuracy of cysteine pKa predictions relative to fixed-charge models.

Conclusion: Application of polarizable CpHMD will improve our understanding of transcription factor binding affinity and inform not only fundamental biophysical theory but also the design of therapeutic interventions targeting transcription factor dysregulation in stress, immune, and neurodegenerative diseases.

Poster #25

Masayoshi HONDA	BCRABL1–Mediated Phosphorylation of RAD52 Switches Its Role from Replication Fork Protection to Mutagenic Single-Strand Annealing

Background: BCR-ABL1 fusion protein causes Leukemia and one of it's crucial target is RAD52

Objectives: How BCR-ABL1 affect RAD52 function and induce genomic instability

Methods: Combination of biochemistry and cell biology

Results: Oncogenic BCR-ABL1 unleashes RAD52's tumorigenic potential through a dual-regulatory mechanism

Conclusion: The BCR-ABL1 fusion oncogene, the hallmark of the Philadelphia chromosome, is a major driver of leukemogenesis in chronic myeloid leukemia (CML) and subsets of acute myeloid leukemia (AML). Its constitutively active ABL1 kinase stimulates proliferative and anti-apoptotic signaling while disrupting the DNA damage response (DDR). A key, yet underexplored, target within this oncogenic network is human RAD52, a DNA- and RNA-binding protein essential for replication fork repair and single-strand annealing (SSA). Prior studies suggest that ABL1 phosphorylates RAD52 at tyrosine-104 (Y104) following genotoxic stress, transiently enhancing error-prone SSA. However, the structural and functional consequences of this modification—and how its constitutive activation by BCR-ABL1 contributes to genomic instability—remain undefined.

To directly assess the impact of Y104 phosphorylation, we employed genetic code expansion using amber suppressor technology to incorporate the stable phosphotyrosine analogue p-carboxymethyl-L-phenylalanine (pCMF) at position 104, generating a constitutively phosphorylated RAD52 mimic (RAD52-Y104pCMF). Biochemical analyses revealed a striking functional shift. RAD52-Y104pCMF retained wild-type affinity for single-stranded DNA (ssDNA) but showed markedly reduced double-stranded DNA (dsDNA) binding. This selective ssDNA engagement accelerated annealing kinetics, suggesting enhanced turnover and remodeling activity.

Importantly, RAD52-Y104pCMF failed to assemble the canonical double-ring oligomers required for replication fork protection and could not shield model replication forks from degradation by the fork remodeler SMARCAL1. Thus, phosphorylation at Y104 disrupts RAD52’s protective architecture and repurposes it toward rapid, error-prone annealing.

These findings support a dual regulatory mechanism by which oncogenic BCR-ABL1 amplifies genomic instability through aberrant RAD52 activation. Constitutive ABL1-mediated phosphorylation enforces a transition from a replication gatekeeper to a mutagenic catalyst, simultaneously weakening fork integrity and promoting SSA-driven recombination. This functional rewiring of RAD52 establishes a direct molecular link between BCR-ABL1 signaling and genomic instability, defining a new mechanism underlying leukemogenesis in Philadelphia chromosome–positive patients.

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