

2026 CODE Student Symposium Poster Abstracts

Lemanisha Adams

Oakwood University Bioinformatic Analysis of the KIF1A gene associated with KIF1A-Associated Neurological Disorder (KAND)

KIF1A-Associated Neurological Disorder (KAND) is a rare and progressive neurological condition caused by mutations in the KIF1A gene that encodes for KIF1A, a kinesin motor protein responsible for transporting synaptic vesicles along microtubules in neurons. This transport system is essential for healthy communication between nerve cells and for normal nervous system development. Mutations in the KIF1A gene have been related to transport process disruptions connected to symptoms such as developmental delay, motor dysfunction, spasticity, and intellectual disability. KAND remains an understudied disorder, and a greater understanding of the role of gene variants in the condition's pathogenesis is needed. The purpose of this research is to identify a new KIF1A variant linked to KAND and investigate the implications of the mutation on its encoded mutant KIF1A protein and function. Bioinformatics methods were used for analysis. Simple ClinVar identified two missense variants, Ala255Val (A255V) and Thr99Met (T99M), with CADD scores of 3.89 and 4.03, respectively. PolyPhen-2 predicted the A255V mutation to be possibly damaging (0.524) and the T99M mutation to be probably damaging (1.000). Structural modeling using SWISS-MODEL indicated that the overall motor domain fold of the mutant proteins remained largely conserved compared to the wild-type protein, although localized structural differences near the mutation sites may alter residue interactions. STRING protein-protein interaction analysis revealed that KIF1A functions within a highly interconnected network of motor proteins, including KIF1B, KIF1C, and KLC2, involved in intracellular and microtubule-based transport processes. Collectively, these findings suggest that the A255V and T99M KIF1A variants may contribute to the etiology of KAND through alterations in protein structure and potential disruption of neuronal transport networks. Future studies characterizing the mutant KIF1A protein and investigating its interactions with other proteins may contribute to the development of therapeutic strategies for KAND.

Dillon Adrian

Jacksonville State University

COL4A5 Variant of Uncertain Significance and Alport Syndrome

Alport syndrome is a hereditary disorder characterized by progressive kidney disease, sensorineural hearing loss, and ocular abnormalities, resulting from defects in basement membrane (extracellular) structure and function. COL4A5, located on the X chromosome at Xq22.3, is a primary gene implicated in Alport syndrome and encodes the alpha 5 chain of type IV collagen, a crucial structural component of basement membranes. This alpha chain normally assembles with the alpha 3 & 4 chains to form a stable collagen IV network for the glomerular basement membrane in the kidneys, inner ear, and eye. Mutations disrupt this collagen network, leading to basement membrane functional failure, which leads to the clinical manifestations of X-linked Alport syndrome. The COL4A5 variant examined in this study, c.212C>T (p.Pro71Leu), is a missense mutation that results in the substitution of proline with leucine at amino acid position 71. Bioinformatic analysis including BLAST multiple sequence alignment, consurf conservation, PolyPhen2 and variant pathogenicity tools, protein folding, and molecular dynamic simulation were used to query the effect of this Pro71 Leu variant and its ties to Alport syndrome

Jovia Alexander

Oakwood University

An Analysis of ITGA3 variants associated with Epidermolysis Bullosa Epidermolysis Bullosa (EB) is a rare inherited skin disorder characterized by extreme skin fragility, leading to blistering in response to minimal mechanical trauma. Depending on the subtype, EB may also affect extracutaneous tissues including the oral mucosa, esophagus, lungs, eyes, nails, teeth, and skeletal muscle. Disease severity ranges from mild to life-threatening. In the United States, EB affects approximately 25,000–50,000 individuals. The ITGA3 gene encodes the integrin alpha-3 ($\alpha 3$) subunit, which pairs with the beta-1 ($\beta 1$) subunit to form the integrin $\alpha 3\beta 1$ heterodimer. ITGA3 is highly expressed in epithelial tissues, especially in the basal keratinocytes of the epidermis, as well as in the kidneys and lungs. Proper function of the $\alpha 3\beta 1$ integrin complex is critical for maintaining dermal-epidermal junction integrity and pulmonary epithelial architecture. Pathogenic variants in ITGA3 are associated with integrin $\alpha 3$ deficiency, also known as ILNEB (Interstitial Lung disease, Nephrotic syndrome, and Epidermolysis Bullosa). This rare autosomal recessive condition presents with skin fragility, congenital nephrotic syndrome, and progressive interstitial lung disease. ClinVar was used to identify ITGA3 as a gene associated with EB and its two variants p.Gly541Arg and p.Ala349Ser. Severe missense mutations and other pathogenic variants can reduce integrin $\alpha 3\beta 1$ expression or impair its interaction with laminin, weakening epithelial adhesion. Computational prediction tools PolyPhen-2 and SIFT were used to evaluate the pathogenicity of the two variants. PolyPhen-2 predicted both variants to be probably damaging, suggesting a deleterious effect on protein structure or function. In contrast, SIFT predicted the variants to be tolerated. These conflicting predictions highlight the need for further functional validation.

Yvonne Anderson

Tuskegee University

Pathogenicity of L199T Mutation in Apolipoprotein E

Vascular dementia is a neurological disease that causes a decline in thinking skills by blocking or reducing blood flow to multiple regions of the brain, which deprives them of oxygen and nutrients. One protein that is associated with vascular dementia is Apolipoprotein E (APOE). APOE is a cholesterol carrier that is produced in the brain and other kinds of tissues. The normal function of APOE within the central nervous system (CNS) and the brain consists of clearing debris for homeostasis, inhibiting inflammation, and promoting neuronal network resilience. Defects within the APOE protein can cause abnormal functions, such as the clearance of A β oligomers, the activation of glial cells in response to protein aggregation, and neuronal dysfunction and death. One missense mutation of unknown pathogenicity within APOE is L199T. At the residue position 199, the change from the normal non-polar amino acid leucine to the variant polar uncharged amino acid threonine may or may not impact the proper function of APOE. Several webtools were utilized to predict whether the L199T mutation has a benign or pathogenic impact on APOE's function. The Poly-Phen2 pathogenic prediction tool estimated that the change from leucine to threonine at the 199 amino acid position will have a harmful impact on the protein's function. In addition, the Aminode conservation analytical tool illustrates the moderate conservation of leucine between various organisms, which indicates the importance that the amino acid leucine has on the APOE protein's correct function. These webtool predictions indicate that the L199T mutation has a harmful impact on the APOE protein's appropriate function, even though the YASARA software predicts that there is minimal structural change caused by the missense mutation. The pathogenic impact of this missense mutation can be further researched to find potential treatments for vascular dementia.

Brittany Batiste

Alabama A&M University

Investigating the Structural and Biophysical Properties of HIV-1 Envelope Glycoprotein that Enhance Cell-Cell Transmission

Human immunodeficiency virus type 1 (HIV-1) is the primary cause of AIDS worldwide. However, research understanding how mutations influence HIV-1 Env proteins is critical in the knowledge advancement of viral attachment, entry and evasion mechanisms of the HIV virus.

PDB 6NIJ is a prefusion HIV-1 surface envelope (env) protein trimer structure, that sits on the outside of the virus and can be used to model HIV-1 binding and entry into host cells. The A541V mutation occurs in gp41 of the HIV-1 env protein, which is a key domain for membrane fusion required for viral entry. This may alter env dynamics for cell-to-cell transmission (CCT). The main objective of this study was to evaluate the structural effects of a single amino acid substitution A541V to env trimer structure 6NIJ. YASARA was used to introduce the A541V mutation to PDB:6NIJ Structural comparisons between wildtype and mutant models were performed using RSDM scores to observe the aligning of two proteins, TM scores observing the structural similarity, and molecular dynamic simulations (MDS) to analyze protein stability over time.

Our finding indicates that introducing the A541V mutation PDB 6NIJ structure produced minimal structure difference. These findings suggest that the A541V substitution may have minimal impact on overall structure of HIV-1 Env.

Joshua Bedasse

Oakwood University

Analysis of MECP2 Variants Associated with Bruxism

Bruxism is the subconscious grinding, or gnashing of teeth, mostly happening during sleep but can also happen while awake. It is commonly linked to stress, anxiety, sleep disorders, or an abnormal bite. It is also strongly related to those with Rett syndrome, a rare, severe, neurodevelopmental disorder caused by a genetic mutation in the MECP2 gene, which is what ultimately causes Bruxism. This disease affects around 30-40 million children and adults in the U.S. (Zoe Dental). The purpose of this study is to identify the effects of MECP2 variants associated with Bruxism. No genetic mutations for Bruxism have been reported; however, mutations for Rett's syndrome have been found which is closely associated with Bruxism. We hypothesize that variants associated with Rett's may be associated with bruxism. Genetic and environmental factors are also being investigated. To test our hypothesis, ClinVar was used to identify MECP2 as the genes associated with Bruxism. PolyPhen-2 was used to predict possible impacts of amino acid substitution on the structure and function of a human protein. SWISS Modeling was also used to view the structure of the protein MECP2 codes for. Two variants, p.Val221Leu and p.Pro184Thr, were found using ClinVar and the National Center for Biotechnology Information (NCBI). MECP2 codes for methyl-CpG-binding protein 2 which plays a crucial role in brain development and nerve cell function. Although Bruxism is not directly tied to genetic diseases, Rett syndrome is significant because Rett syndrome is directly tied to most Bruxism cases. This study is still ongoing as conclusive results have not yet been achieved.

Vincent Boutsoukos

Alabama College of Osteopathic Medicine

Desmoglein-2 F833C is Predicted to Disrupt Hydrophobic Interactions of Armadillo Repeat Region 1 of Plakoglobin

Desmoglein-2 (Dsg2) is a cadherin involved in cell-cell adhesion in cardiac tissue [7]. A Variant of Unknown Significance (VUS), F833C, was identified and analyzed for its potential role in disrupting the interaction between Dsg2 and its intracellular binding partner plakoglobin [14,16]. Molecular dynamic (MD) simulations, pathogenicity predictions, and stability metrics were used to assess its impact. The F833C variant showed significantly decreased binding energy and increased per residue Root Mean Square Fluctuations (RMSF) at the Dsg2 interface. These metrics indicate a potential pathogenic effect due to compromised stability and interactions.

India Brame

Oakwood University

Pathogenic Analysis on HBB Variants Associated with Sickle Cell Anemia

Sickle Cell Anemia is a life-long illness of a group of inherited disorders that affects hemoglobin, which is a major protein that carries oxygen in red blood cells. Red blood cells become rigid and misshaped, taking on a “sickle” or crescent shape due to a gene mutation instead of the normal disc-shaped and flexible form. As a result, the blood cells are now less flexible and tend to get stuck in small blood vessels blocking blood flow to the rest of the body, causing very painful episodes. Roughly 1 in 365 African Americans result in this condition. HBB stands for hemoglobin subunit beta and this gene’s type is protein coding. The HBB gene codes for the beta-globin chains, making it essential for proper oxygen delivery and overall cellular function. The purpose of this research is to identify, study, and analyze the pathogenesis of HBB variants associated with Sickle Cell Anemia. SimpleClinVar was used to identify the HBB as a gene associated with Sickle Cell Anemia and three of its variants, single nucleotide missense mutations Val127Gly, Leu107Arg, and His93Asn. . PolyPhen-2 and SIFT were computational tools used to determine the pathogenicity of the three variants. PolyPhen-2 predicted all 3 variants to be probably damaging and SIFT predicted all of the variants to affect protein function. The predicted pathogenicity of the HBB variants suggest that alterations in the beta-globin structure may impair hemoglobin stability and oxygen-binding capacity, which contributes to the characteristics of Sickle Cell Anemia. The findings emphasize the importance of identifying disease-associated mutations, as this can support improved genetic screening, risk assessment, and future therapeutic development.

Kerry Brathwaite

Oakwood University

An analysis of the mutations in the SCAPER gene links Intellectual disability accompanied by Retinitis Pigmentosa. Retinitis Pigmentosa (RP) is an inherited retinal disorder characterized by the progressive degeneration of photoreceptor cells in the retina. The disease typically begins with the loss of rod photoreceptors, which are responsible for vision in low-light conditions, and later affects cone photoreceptors that enable color and central vision. As a result, individuals with RP experience gradual vision loss that may eventually progress to complete blindness. RP represents a group of genetically diverse retinal disorders caused by mutations that disrupt normal photoreceptor structure and function. The S-phase Cyclin A-associated protein residing in the endoplasmic reticulum (SCAPER) gene encodes a cyclin A-interacting protein involved in regulating cell cycle progression. Pathogenic variants in the SCAPER gene have previously been linked to autosomal recessive intellectual disability, and recent studies have also associated SCAPER mutations with Retinitis Pigmentosa. Despite these findings, SCAPER remains a rare and understudied gene. The purpose of this study was to analyze specific SCAPER mutations that may contribute to the combined presentation of intellectual disability and RP. Using Simple ClinVar, two mutations—p.Cys71Trp and p.Ser1219Asn—were identified. Because one mutation was classified as uncertain, additional bioinformatic tools, including PolyPhen-2, SIFT, and Swiss Model, were used to evaluate their pathogenic potential. PolyPhen-2 analysis indicated that p.Cys71Trp had a score of 0.00, suggesting it is likely benign, while p.Ser1219Asn received a score of 1.00, indicating it is likely pathogenic and associated with intellectual impairment. Swiss modeling further demonstrated how missense mutations may alter protein folding. Overall, these findings support the conclusion that the p.Ser1219Asn mutation in the SCAPER gene plays a significant role in the development of intellectual disability accompanied by Retinitis Pigmentosa and emphasize the importance of genetic analysis in rare inherited disorders.

Travis Burrell

Tuskegee university

Computational Characterization of a Missense Variant in the ABCB1 Drug Transporter and its Potential Impacts on Antimicrobial Pharmacokinetics

Interindividual variability in antimicrobial treatment outcomes remains a persistent challenge in infectious disease management and drug development. While microbial resistance mechanisms are well characterized, host genetic variation influencing antimicrobial pharmacokinetics is comparatively underexplored. The human ABCB1 gene encodes P-glycoprotein (P-gp), a membrane-bound ATP-binding cassette transporter responsible for the efflux of numerous xenobiotics, including several clinically relevant antibiotics. Variants affecting transporter function may therefore alter intracellular drug concentrations and contribute to variability in therapeutic efficacy. This study investigates the poorly characterized missense variant p.Gly827Arg (G827R) in ABCB1, a rare polymorphism predicted to be functionally deleterious based on high Combined Annotation Dependent Depletion (CADD) scores and multiple in silico pathogenicity predictors. Computational structural modeling and evolutionary conservation analyses suggest that residue 827 lies within a functionally important region of the second transmembrane domain involved in substrate recognition and transporter conformational dynamics. Substitution of glycine with a positively charged arginine is predicted to disrupt local structural flexibility and potentially alter substrate-binding geometry. Such changes may influence efflux efficiency for P-gp substrates, including several antimicrobial agents, thereby modifying intracellular drug exposure and therapeutic response. Understanding host genetic variants that alter drug transport has significant implications for both academic research and pharmaceutical development. From an academic perspective, this work contributes to the emerging field of host pharmacogenomics in antimicrobial therapy. From an industry standpoint, identifying functionally impactful transporter variants can inform precision medicine strategies, optimize clinical trial design, and guide patient stratification in drug development pipelines. Characterizing underexplored variants such as ABCB1 p.Gly827Arg may therefore bridge translational gaps between genomic discovery and therapeutic application, supporting more individualized and effective antimicrobial treatment strategies.

K'sia Byass

Oakwood university

An analysis of XPO1 variants associated with Neoplasm of the Large Intestine

Neoplasms of the large intestine (NOLI) are abnormal tissue growths in the colon or rectum that range from benign adenomatous polyps to malignant carcinomas. NOLI is highly prevalent, ranking as the third most common cancer worldwide and the second leading cause of cancer-related deaths, with more than one million new cases reported annually. This study aims to identify and assess the pathogenicity of XPO1 gene variants associated with neoplasms of the large intestine. Overexpression of XPO1 results in abnormal nuclear export of tumor suppressor proteins (TSPs) and RNA from the nucleus to the cytoplasm, enabling cancer cells to evade normal growth regulation. We hypothesize that specific genetic variants of XPO1 are pathogenic and contribute to the development of this disease phenotype. ClinVar was used to identify XPO1 as a gene associated with NOLI and to select four missense variants for analysis: Glu571Lys, Glu571Val, Glu571Ala, and Ser387Pro. The XPO1 gene encodes a primary nuclear export receptor responsible for transporting hundreds of proteins and RNAs from the nucleus to the cytoplasm. Through this role, it regulates key cellular processes including tumor-suppressor localization, cell cycle progression, mitosis, and mRNA transport. Pathogenic mutations in XPO1 can function as oncogenic drivers by altering the nuclear export signal (NES) binding groove, leading to improper export of tumor suppressor proteins and increased cell proliferation. Computational prediction tools PolyPhen-2 and SIFT were used to evaluate the pathogenicity of the four variants. PolyPhen-2 predicted Glu571Lys to be damaging, while SIFT predicted Glu571Lys and Ser387Pro to be damaging. Both tools predicted Glu571Val and Glu571Ala to be tolerated. These results suggest that certain XPO1 variants may disrupt the function of the NES binding groove, potentially impairing tumor suppressor regulation, and contributing to colorectal tumor

development. Further experimental studies are needed to confirm the functional impact of these variants.

Legend Cadet

Oakwood University

A study of the IRF5 gene pertaining to Systemic Lupus Erythematosus Systemic Lupus Erythematosus (SLE) is a currently incurable disease

characterized by severe joint pain, chest pain while breathing, hair loss, weight loss, and a distinct “butterfly rash” mostly found on the cheek. It is a disease that mostly affects women, with 90% of patients being female. The purpose of this study is to gain more understanding of SLE. SLE is a mainly misunderstood disease, and more research must be done pertaining to its pathogenicity. With a better understanding of the IRF5 gene pertaining to SLE, it is possible to gain more insight into a cure for the disease. The study of the IRF5 gene in SLE is mostly inconclusive but must be considered when researching SLE. ClinVar, was used to identify the IRF5 gene in SLE. This system identified IRF5 as a gene with a single variant with a single missense mutation, p.Gly502Ser. This gene encodes a member of the interferon regulatory factor (IRF) family, a group of transcription factors with diverse roles, including virus-mediated activation of interferon, and modulation of cell growth, differentiation, apoptosis, and immune system activity. PolyPhen-2 was used to determine the pathogenicity of the IRF5 gene but predicted it to be benign. This concludes that this gene does not have much of an immediate effect on the pathogenicity of SLE but its effect on cell growth plays a role in the spread of the disease. While it is shown that the IRF5 gene is not the most pathogenic protein involved in SLE, it still has an effect on its growth. Because of the lack of knowledge of SLE, the research of every gene and its purpose matters to better understand such a rare disease.

Justice Cadet

Oakwood University

An analysis of the SOCS1 gene in Systemic Lupus Erythematosus

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that affects roughly 0.06% of people worldwide with a strong bias towards women with 90% of SLE patients being female (Lupus Foundation of America). SLE is characterized by inflammation caused by immune cells targeting healthy cells in the body. The purpose of this study is to identify the pathogenicity of SOCS1 variants regarding SLE. There are no known causes for SLE other than theories on hormones, genes and environmental changes. There are ongoing studies to determine which genes have a specific role in the development of SLE but no conclusive evidence has been found. ClinVar was used to SOCS1 as a gene associated with SLE and its three nucleotide missense mutations, p.Gln6Glu, p.Arg22Trp, and p.Pro123Arg. SOCS1 acts as a negative regulator for the JAK/STAT pathway and mediates the cell's responses to cytokines. SOCS1 is very important for immune response and highly expressed in the spleen and thymus. PolyPhen-2 was used to determine the pathogenicity of the three variants and SIFT was used to predict the effect of the mutation on protein function. PolyPhen-2 predicted p.Pro123Arg to be possibly damaging whereas p.Gln6Glu and p.Arg22Trp were benign. SIFT predicted p.Pro123Arg to affect protein function. These mutations suggest a change in the functionality of the SAK/STAT pathway and consequently the body's immune response. This study supports previous findings on the correlation between SOCS1 and SLE.

Kiar-Ra Cameron

Oakwood University

Pathogenic Potential of the VPS13C Variant Associated with Early-Onset Parkinson's Disease

Parkinson's disease (PD) is classified by symptoms including tremors, bradykinesia, and difficulty speaking (motor symptoms), and memory loss, mood disorders such as depression, and difficulty reasoning (non-motor symptoms). It affects many individuals worldwide and has now widened from an old-aged to a middle-aged condition. PD is identified as a lipid-induced proteinopathy where changes in lipid composition or metabolism induce protein alteration. The Vacuolar Protein Sorting 13 Homolog-C (VPS13C) gene encodes for lipid transport proteins that regulate lysosomal function within the cell and VPS13C mutants were linked to PD. This study aims to identify a VPS13C variant linked to PD and the possible implications of the mutation on the mutant protein structure and functions. We hypothesize that the mutation will be associated with structural and functional changes in the mutant VPS13C protein. Bioinformatics tools were used for analysis. Simple ClinVar analysis revealed a missense mutation G1389R VPS13C variant with a CADD score of 34 previously associated with PD. UniProt analysis showed VPS13C isoforms with similar sequences except at sequence positions 152-127 and 3648-3585. PolyPhen2 study predicted the mutation to be probably damaging with a score of 0.986, and a sensitivity score of 0.74. Protein structure analysis suggests modulation in protein structure based on changes from a non-polar amino acid to a positively charged one. STRING studies revealed that VPS13C is involved in a protein network including plasma proteins instrumental in tracking and maintaining homeostasis within the cell such as Synaptojanin-1, F-Box only protein 7, Cation-transporting ATP13A2, and Phospholipase A2. Collectively, our findings suggest an involvement of the G1389R VPS13C variant with PD, with predicted damages to its mutant protein function and possible implications for a protein-protein interactions network. Future studies are warranted to further understand the involvement of the G1389R VPS13C variant in the development of PD.

Azaria Carey

Oakwood University

An Analysis of FSHR Variants Susceptibly Associated with Polycystic Ovarian Syndrome

Polycystic Ovary Syndrome (PCOS) is a common endocrinopathy affecting approximately 6% to 13% percent of females. It is characterized by small fluid filled sacs along the ovarian lining that may develop into cysts. These sacs contain immature follicles that often fail to release during ovulation. The exact cause of PCOS remains unclear, but early diagnosis, treatment, and lifestyle changes such as weight management may reduce the risk of long term complications including type 2 diabetes. The purpose of this study was to identify and assess the pathogenicity of variants in the FSHR gene associated with PCOS susceptibility. We hypothesized that genetic variants in FSHR may contribute to increased risk. Although mutations in FSHR have been linked to ovarian hyperstimulation syndrome and ovarian dysgenesis, their role in PCOS remains inconclusive. PCOS also does not follow a simple Mendelian inheritance pattern, suggesting contributions from genetic and environmental factors. The FSHR gene was identified using the Simple ClinVar database, which reported 103 variants. Three missense variants, p.Ala444Thr, p.Thr449Ala, and p.Thr449Ile, were selected for analysis due to their potential to alter receptor structure and function. The FSHR gene encodes a follicle stimulating hormone receptor involved in ovarian follicle development and hormone signaling. PolyPhen 2 predicted p.Ala444Thr and p.Thr449Ala to be benign, while p.Thr449Ile was predicted to be damaging. SIFT analysis classified p.Ala444Thr with a score of 0.73 and p.Thr449Ala with a score of 0.18 as tolerated, while p.Thr449Ile with a score of 0.00 was predicted to affect protein function. Conserved domain analysis identified functional regions including transmembrane domains and leucine rich repeats involved in ligand binding and signal transduction. A three-dimensional model of the FSHR protein was generated using SWISS MODEL to visualize structural effects. Overall, this study contributes to understanding how FSHR variation may influence ovarian function and play a role in PCOS pathophysiology.

Kayla Carryl

Oakwood University

SCNN1A Variants Role in the Severity of Cystic Fibrosis

The Respiratory and Digestive systems are the main organs affected by Cystic Fibrosis, a genetic illness marked by thick, sticky mucus that can cause airway blockage and persistent lung infections. Although mutations in the CFTR gene are the most prevalent cause of cystic fibrosis (CF), the severity of the disease may be influenced by other genes related to ion transport. SCNN1A is one such gene that codes for the epithelial sodium channel's (ENaC) alpha subunit. In airway epithelial cells, ENaC is crucial for controlling salt and fluid balance. A mutation in SCNN1A may result in ENaC overactivity, which raises the absorption of sodium and dehydrates the surface of the airways, causing thicker mucus and intensifying respiratory symptoms. This study set out to find and examine missense variations in the SCNN1A gene that might be linked to greater severity of cystic fibrosis disease and ENaC overactivity. Variants of the gene were found using ClinVar database whilst also been evaluated by PolyPhen-2 and SIFT which assessed the potential effects of amino acid alterations. The three variants Arg81Cys, Arg181Trp, and Val114Ile were chosen for analysis, which represent amino acid substitutions where arginine at position 81 was replaced by cysteine, the arginine at position 181 was replaced by tryptophan, and valine positioned at 114 was replaced by isoleucine. PolyPhen-2 projected that all three variations were probably damaging, implying that they could have a detrimental effect on protein structure or function. SIFT expected Arg81Cys to affect protein function, however Arg181Trp and Val114Ile were predicted to be tolerated with scores of 0.10 and 0.07, respectively. These findings indicate that certain SCNN1A mutations may affect the function of the ENaC alpha subunit, contributing to increased channel activity. Additionally, SWISS Model Pro was used to simulate the SCNN1A protein's structure showing how possible mutations would affect its structure. This data indicates that some SCNN1A variants may alter ENaC function and lead to higher Cystic Fibrosis Severity.

Blake Carter

University of North Alabama

Deciphering the Unknown: A Computational Characterization of the HEXA Variant Thr467Ala in Tay-Sachs Disease

Tay-Sachs disease is a fatal, inherited neurodegenerative disorder caused by a deficiency in the enzyme Hexosaminidase A which leads to the toxic accumulation of GM2 gangliosides in neurons. The HEXA gene provides the blueprint for the alpha subunit of this enzyme, which must successfully dimerize with a beta subunit to function. While the clinical progression of the disease is well-understood, genomic data from Ensembl reveals that approximately 80% of identified HEXA variants remain classified as Variants of Uncertain Significance (VUS). This lack of classification creates a significant gap in diagnostic capabilities for affected families. This research addresses this gap by using a computational methods to characterize the specific VUS Thr467Ala. The methodology involves structural analysis using AlphaFold models, pathogenicity scoring via CADD and PolyPhen-2, and Molecular Dynamics Simulations (MDS) conducted in YASARA to observe protein stability in a simulated physiological environment. Structural modeling indicates that Thr467 is located within an alpha helix at the C-terminal interface, a region established by literature as the primary dimerization glue for the enzyme. The substitution of a polar Threonine for a non-polar Alanine may disrupt critical hydrogen bond anchors, leading to increased structural volatility compared to the wild-type protein. This suggests that the Thr467Ala variant may act as a structural disruptor that prevents proper subunit binding. These results are significant as they provide a theoretical basis for reclassifying Thr467Ala as a pathogenic variant.

Felyna Charles

Oakwood University

An Analysis of the Gene MYL2 in Association to Myopathy

Myopathy is a skeletal muscle disease in which muscle fibers are damaged, leading to muscle weakness. This disease can be classified as inherited or acquired. In inherited myopathy, the disease is passed down and determined by genotype analysis. Acquired myopathy is developed later in life often due to environmental factors. As an X-linked gene it most commonly affects men. Myopathy is characterized by muscle spasm, weakness, fatigue after exertion, and the inability to perform daily tasks. This study will explore how MYL2 is related to myopathy. ClinVar was used to identify the MYL2 as a gene implicated in myopathy phenotype. MYL2 codes for myosin light chain 2 protein, a sarcomere protein. Mutations in MYL2 result in heart disease due to its effect on cardiac muscle structure and function. PolyPhen-2 and SIFT were used to determine the pathogenicity of three MYL2 variants p.Gln38Arg, p.Leu150Ser, and p.Gly162Glu. PolyPhen-2 predicted that variants p.Gln38Arg, p.Leu150Ser, p.Gly162Glu to be likely damaging. SIFT predicted the variants p.Gln38Arg, p.Leu150Ser, and p.Gly162Glu are deleterious or pathogenic. Pathogenic mutations in this gene affected the structure and function of the myosin light chain protein. Previous research has linked MYL2 with muscle and heart disease such as myopathy because MYL2 plays a role in muscle contraction.

Javan Charles

Oakwood University

The Role of KCND3 Gene Mutation in Brugada Syndrome and Associated Cardiac and Neurological Channelopathies

Brugada Syndrome is an inherited cardiac arrhythmia disorder characterized by ST-segment elevation in the right precordial leads and an increased risk of ventricular fibrillation and sudden cardiac death. Classified as a cardiac channelopathy, it is caused by dysfunction of ion channels that regulate myocardial electrical activity. The KCND3 gene encodes a voltage-gated potassium (Kv) channel protein Kv4.3, which forms that alpha subunit of the transient outward potassium channel responsible for the I_{to} current in the cardiac myocytes and neurons. This current is essential for early repolarization of the cardiac action potential and contributes to the regulation of neuronal firing frequency. KCDN3, based on gene expression data profile, this gene is expressed in multiple fetal tissues, with highest levels in the intestine and stomach, strong expression in the heart, moderate expression in the kidney, and lower levels in adrenal and lung tissues. This study aims to identify and test the pathogenic potential of selected KCND3 variants associated with Brugada Syndrome and other related neurological channelopathies. While ion channel mutations are widely implicated in arrhythmogenic and neurodegenerative disorders, the functional significance of specific KCND3 variants still remains uncertain. The sources, PolyPhen2 and SIFT were used to predict pathogenicity. PolyPhen-2 identified G371R and R549H as probably damaging, while D149G was predicted to be probably benign (0.014). SIFT on the contrary, predicted P269R and R86G to affect protein function (0.00) and R549C to affect function (0.01; low confidence). Overall, these findings show the potential disruption of Kv4.3 channel function and altered electrical signaling, supporting its role in cardiac and neurological disease.

Simone Chotan

Oakwood University

The Analysis of KCNA5 Variants Associated with Hypertension

Hypertension is a chronic condition characterized by blood pressure that is too high, typically defined as a reading of 140/90 mmHg or higher. Often termed as a "silent killer," hypertension presents itself without symptoms while the condition continuously damages arteries, which leads to stroke, heart attack, or even death. KCNA5 (Potassium voltage-gated channel subfamily A member 5) is the gene that codes for the protein that forms potassium voltage-gated channels, which are responsible for regulating cardiac repolarization during an action potential. Mutations of the KCNA5 gene can lead to atrial fibrillation and pulmonary arterial hypertension. The purpose of this study is to identify and investigate the effects of the mutations on KCNA5 variants associated with hypertension. In this study, the Simple ClinVar database was used to identify and analyze missense mutations associated with the KCNA5 gene, and three variants were selected: p. Arg525Trp, p. Ile443Met, and p. Ala576Val. To

analyze the pathogenicity of each KCNA5 variant, the computational tools Polyphen-2 and SIFT were used to predict if the mutation was damaging. The Polyphen-2 results revealed that variants p. Arg525Trp and p. Ile443Met were predicted to be damaging, and p. Ala576Val was benign. SIFT predicted that p. Arg525Trp could affect the protein function, while variants p. Ile443Met and p. Ala576Val were predicted to be tolerated. Further analysis of this data reveals that the replacement of arginine with tryptophan can cause the potassium voltage-gated channel protein to misfold and become dysfunctional. In previous studies regarding the effects of mutations in hypertension, mutations in the genes KLHL3 and CUL3 have been proven to directly cause hypertension; however, gene KCNA5 and its variants should be further investigated for future studies.

Nhael Cinous

Oakwood University

Analysis of the CELSR3 Variants in Tourette Syndrome

Tourette Syndrome is a neurological disorder that causes an individual to perform sudden and repetitive movements that a person can't control. These movements are known as "tics", which can be motor or vocal. They involve blinking, various facial expressions, grunting, words, and/or sounds which can all change over time. In the United States, Tourette syndrome is estimated to affect about 0.3-0.6% of children, which could be anywhere from 1 to 160 children. The purpose of this study is to identify what variants are associated with this disorder. Identifying the underlying genetic mechanisms can clarify how abnormal neural signaling develops, improving early diagnosis, and be able to determine the contributors of TS. We hypothesize that variants, such as CELSR3 variants, may be identified to be associated with this disease. To test this hypothesis, SimpleClinvar was used to identify the different genes associated with Tourette's. The CELSR3 gene, which encodes the "Cadherin EGF LAG Seven-Pass G-Type Receptor 3" protein and plays a crucial role in brain development and has been investigated to associate with Tourette syndrome. Variant Ser255Thr was evaluated with computational tools PolyPhen-2 and SIFT. PolyPhen-2 predicted the variant to be benign with a score of 0.384. The SIFT results displayed a SIFT score of 0.009-0.02 which predicted that the amino acid switch was damaging/deleterious. This differs from the results that were previously received in PolyPhen-2. Previous studies show that, though the connection between CELSR3 and Tourette Syndrome is still being investigated, research into this gene contributes to a better biological understanding of the disorder. By connecting genetic variation to brain development and neural signaling, researchers and healthcare professionals can work toward reducing the stigma, developing better support and treatment strategies for individuals affected by the disorder, Tourette Syndrome.

Donessa Cooper

Oakwood university

An Analysis of CAPN10 variants associated with Diabetes

Diabetes mellitus (DM) is a metabolic disease, involving inappropriately elevated blood glucose levels. DM has many different categories including Diabetes type 1 and Diabetes type 2. Diabetes type 1 is an autoimmune disorder. Meanwhile, type two Diabetes does make insulin, but they are instead the patient experiences insulin resistance where the cells in your body stop responding to insulin. 589 million adults are living with diabetes worldwide – 1 in 9. This study's purpose is to assess the pathogenicity of Calpain10 (CAPN10) variants that can be connected to DM. Studies regarding CAPN10 have shown that polymorphisms in the CAPN10 gene have been associated with an increased risk of developing Diabetes mellitus type 2. ClinVar, was used to identify and confirm if CAPN10 was associated with DM and to identify the variants related to this gene. The two single nucleotide missense mutations that were used were p. Glu238Asp and p. Met31Ile. The PolyPhen-2 mutation was used to find the way the two different variants would affect the des: It was predicted to "probably be damaging" with a score of 1.00 sensitivity. Looking over the results, finding out that the variant is mostly likely damaging to the gene, which means that the gene has a genetic cartoon that stops the function of the CAPN10 function. This research is very significant because it tells us how different variants in certain genes connected to DM effects how the Disease affects our body.

Franyeli Dalmasi Soliman
Oakwood University

An Analysis of CDH1 Variants associated with Breast Cancer

Breast cancer is a disease in which abnormal breast cells grow out of control and form tumors. Breast cancer affects 1 in 8 women, or approximately 13% of the female population in the U.S., will develop breast cancer in their lifetime with an estimated 2.3 millions of women diagnosed with breast cancer globally. The purpose of this study is to analyze the mutations in the CDH1 gene and how it affects the progression of this disease. The cadherin 1 gene, which is found on chromosomes 16, provides instructions for making a protein called epithelial cadherin or E-cadherin. E-cadherin acts as a tumor suppressor protein, which means it prevents cells from growing and dividing too rapidly or in an uncontrolled way. Inherited mutations in the CDH1 gene increasing woman's risk of developing a form of breast cancer have been reported. ClinVar, was used to identify the association of the CDH1 gene with breast cancer and its variants-Gly239Arg and Ser853Leu. The CDH1 gene variants were evaluated using the computational tools, PolyPhen-2 and SIFT. PolyPhen-2 predicted Gly239Arg mutations are most likely damaging while Ser853Leu mutation is predicted to be likely benign. However, SIFT predicted both mutations to be likely damaging. Lastly, a 3D model of CDH1 gene was provide by SWISS MODEL prediction tool. Previous studies have suggested CDH1 variants are associated with several epithelial malignancies like hereditary diffuse gastric cancer and lobular breast cancer. This study contributes to the existing research regarding Inherited mutations in the CDH1 gene implications of woman's risk of developing breast cancer.

Makaila De Velde
Oakwood University

Analysis of NKX2-5 Missense Mutations Associated with Cardiac Development

Hypertrophic Cardiomyopathy (HCM) is a genetic heart condition characterized by thickening of the heart muscle that can impair normal cardiac function. This change makes it harder for the heart to pump blood and can lead to chest pain, heart palpitations, blood flow obstruction, and eventually death. HCM is a common heart disease affecting about 15 million people worldwide but remains severely underdiagnosed. HCM is often inherited but may also arise from new (de novo) mutations. The NKX2-5 gene is expressed in the heart tissue of a fetus around 17 weeks of development. This study evaluates how variants in the NKX2-5 gene may disrupt cardiac development and contribute to congenital heart disease associated with HCM. Previous research shows how the heart and its electrical activity are affected by this gene, but the molecular mechanisms that cause CHD are still not fully understood. The purpose of this study is to evaluate possible variants associated with HCM. We hypothesize that there will be variants that may be associated with or implicated in disruption of proper cardiac development or function. To test this hypothesis, SimpleClinVar was used to identify NKX2-5 as a gene associated with HCM. Three NKX2-5 variants were analyzed: p.Gly298Glu, p.Ala127Val, and p.Gln22Lys. These variants are important for transcriptional activity, protein interactions, and protein stability. Although these variants occur outside of the core homeodomain, alterations in transcriptional activity can still impact the gene. Variant pathogenicity was evaluated using PolyPhen-2 and SIFT. p.Gln22Lys and p.Ala127Val were predicted to be not damaging, while p.Gly298Glu was extremely damaging. These findings suggest that certain NKX2-5 variants may disrupt protein stability and transcriptional activity, helping explain genetic causes of congenital and hypertrophic cardiac disease and why studying these mutations is important for improving future research, diagnosis, and understanding of heart disease.

Jhordana Donaldson

Oakwood University

An Analysis of MSH6 Variants Associated with Breast Cancer

This gene encodes a member of the DNA mismatch repair MutS family. The MutS protein helps in the recognition of mismatched nucleotides prior to their repair. A highly conserved region of approximately 150 aa, called the Walker-A adenine nucleotide binding motif, exists in MutS homologs. The encoded protein heterodimerizes with MSH2 to form a mismatch recognition complex that functions as a bidirectional molecular switch that exchanges ADP and ATP as DNA mismatches are bound and dissociated. We hypothesize that variants associated with this gene may be associated with the breast cancer phenotype. This study's purpose is to identify and assess the pathogenicity of MSH6 variants associated with breast cancer. The MSH6 protein has shown many genetic mutations covering more than one domain. MSH6 and its specific role in Breast cancer show results in high levels of pathogenicity, leading to other diseases/symptoms. To test our hypothesis, ClinVar was used to evaluate the variants of the MSH6 protein. It identified MSH6 as a protein along with its mutations: p.Ala1055Pro, p.Met1Ile, and p.Ser341Ala. The MSH6 gene is expressed in most somatic cells, including the pancreas, etc. Polyphen2 was used, which predicted that the p.Met1Ile mutation was benign, while p.Ala1055Pro and p.Ser341Ala are predicted to be probably damaging. SIFT was then used to predict the effect of the protein function; both p.Met1Ile and p.Ala1055Pro are predicted to affect the protein, and Ser341Ala is tolerated. These results of these mutations showed the functionality of the protein, which may greatly impact the protein function. Studies suggest that pathogenic mutations in the MSH6 gene are associated with increased breast cancer severity and related diseases. In conclusion, findings of this study supports our hypothesis. Variants p.Ala1055Pro and p.Met1Ile may disrupt mismatch repair function by impairing heterodimerization with MSH2, leading to genomic instability and heightened cancer susceptibility.

Jordan Doucet

Athens State University

Potentially Pathogenic Mutant miRNA-142 on its Interactions with Dicer

The function of miRNA is to regulate the production of proteins by silencing a mRNA's code to inhibit the production of proteins. Dicer is a protein that processes a ~78-nucleotide strand of pre-miRNA cleaving it down to a single stranded mature miRNA that is 22 nucleotides in length. A mutation in a miRNA can lead to disease by contributing to an upregulation of a downregulation of a protein if it forms a silencing complex more often or less efficiently. We hypothesized that a mutation in the miRNA will cause a structural difference in the mutant miRNA that could alter the processing of the pre-miRNA by Dicer. This study investigates the 55G>A mutation of miRNA-142. This mutation occurs in the stem region of miR-142 in close proximity to one of the catalytic sites of the Dicer protein and disrupts the base pairing of the nucleotide in the stem of miR-142. We used molecular dynamic simulation studies to determine the change in the RMSD of the backbone atoms of the pre-miRNA in the Dicer bound and the Dicer unbound miR-142 state of both the wildtype and mutant forms of miR-142. From these studies we observed the energy minimized structure of wild-type miR-142 has a slightly wider backbone than the mutant miR-142, which may indicate the wild-type is trending towards A-form. The mutant miRNA-142 energy minimized structure has a slightly wider minor groove than the "dicing state", but the minor groove is less wide than the wild-type. The mutant appears to be trending to A-form at a slower rate, which could potentially indicate the mutant is more stable in the "dicing" state. The difference in stability of the mutant compared to the wild-type may result in a difference in processing by Dicer from the mutant compared to wild-type.

Lillibeth Duberry

University of North Alabama

Bioinformatic Characterization of Variants of COL11A2 Associated with Adolescent Idiopathic Scoliosis

Adolescent idiopathic scoliosis (AIS) is a type of scoliosis characterized not only by the curvature of the spine but also by the age at which it develops. AIS occurs in individuals between the ages of 10 and 18 years old and is defined as a lateral curvature of the spine with an angle exceeding 10 degrees. "Idiopathic" refers to scoliosis without a specific cause; however, the Scoliosis Research Society (2025) found that 30% of AIS patients have family members who have had scoliosis. Having AIS can lead to several physical symptoms, including a back or rib hump, uneven shoulders, and torso lean due to the curvature of the spine. These symptoms can result in discomfort and even back pain, particularly in the lower back. Rebello et al. (2023) found the gene COL11A2 played a key role in vertebral development. While some COL11A2 variants have been classified, 96% of them have not. Classifying these variants can help to diagnose AIS at earlier stages and prevent further spinal curvature. Clinical submissions reported in the Ensembl database categorized pathogenic, benign, and unclassified variants. YASARA modeling of the COL11A2 protein was used to examine the structural characteristics relative to regions with unclassified variants. SIFT, PolyPhen, Revel, CADD and MetaLR scores were normalized and plotted to compare known pathogenic and benign variants with selected R130W and R130Q unclassified variants. Molecular dynamics simulations were performed to model 20 nanoseconds of movement in an aqueous environment for the wild type COL11A2 as well as the two variants, R130W and R130Q. The results of these methods are mixed. The analysis of the in-silico predictor scores, as well as the chemical difference between arginine and tryptophan suggested that R130W may be pathogenic. Swaps between glutamine and arginine appear in 44.8% of pathogenic missense mutations in COL11A2. However, gene conservation analysis yielded low scores for position 130 when over 150 homologues and the molecular dynamics simulations for both R130W and R130Q demonstrated little divergence from the wild type COL11A2. This research will aid future studies into these mutations and other mutations of this gene, which will help to discover any existing links to adolescent idiopathic scoliosis and ultimately improve the ability of physicians to diagnose this condition before it becomes more severe.

Nicholas Earle

Oakwood University

An analysis of HNF1A gene variants associated with Type 2 Diabetes

Type 2 diabetes (T2D) is a chronic metabolic disorder where the body can't effectively use insulin or produce an adequate amount of it, which leads to high blood sugar levels. T2D is associated with roughly 462 million people, which is 6.28% of the world population and around 8.7 million people are undiagnosed. This study's purpose is to identify and assess the pathogenicity of HNF1A variants associated with T2D. Some genetic mutations responsible for T2D have been identified. However, studies regarding HNF1A and its association with T2D have been undetermined. We hypothesize that HNF1A variants may contribute to the pathogenesis of this disease. HNF1A also known as Hepatocyte Nuclear Factor-1 Alpha is a gene that encodes a transcription factor that is vital for the development and functionality of pancreatic beta cells which produce insulin, as well as liver and kidney development. To test our hypothesis, ClinVar was used to help to identify the HNF1A as a gene associated with Type 2 Diabetes and its three variants that are single nucleotide missense mutation, p.Pro447Leu, p.Arg583Gly, and p.Ile27Leu. Computational tools PolyPhen-2 and SIFT were used to determine the pathogenicity and the likely effects of the three variants on humans. According to PolyPhen-2 the variants p.Arg583Gly and p.Ile27Leu had resulted in the mutation predicted to be benign. Additionally, the variant p.Pro447Leu was predicted to be probably damaging. Using the other computational resource, Sift, it resulted in the variants p.Pro447Leu and p.Arg583Gly predicted to be affecting protein function with p.Ile27Leu predicted to be tolerated. Many genetic studies have shown that HNF1A contribution to T2D can vary due to many factors that humans are associated with. However, a conclusive result hasn't been finalized yet. Due to the study that has been taking place, it has helped assist the existing research regarding the implication of the HNF1A gene associated with T2D.

Sara-Michelle Edwards
Oakwood University

Analysis of the UCP3 gene in pathogenesis of Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2D) is a chronic disease caused by the impairment of insulin signaling, leading to decreased insulin secretion and high blood sugar (hyperglycemia). T2D affects an estimated 6.3% of the world's population, ranging from 1 in 10 people in the U.S displaying metabolic warnings (Cleveland Clinic). Examining the UCP3 gene will provide critical insight of its role in diabetes by strengthening fatty acid metabolism while promoting the reduction of insulin resistance. The purpose of this study is to analyze possible variants associated with diabetes. We hypothesize that UCP3 variants may contribute to the pathogenicity of this disease. To test this hypothesis, Simple ClinVar, Polyphen-2, and SIFT, to identify possible variants associated with diabetes. SWISS Model was used to analyze the structure of the protein. ClinVar, was utilized to identify the UCP3 as a gene associated with T2D and its two variants, single nucleotide missense mutations, p.Arg70Trp and p.Met68Val. The UCP3 gene codes for a mitochondrial anion carrier protein that is fundamental in the separation of oxidative phosphorylation from ATP synthesis and the protection of mitochondria against lipid-induced oxidative stress. Computational tools Poly-Phen-2 and SIFT were used to establish the pathogenicity of the two variants. Poly-Phen-2 predicted that both mutations would be most damaging while SIFT predicted the p.Met68Val variant to be tolerated and the p.Arg70Trp to be damaging. The pathogenesis of these mutations entails that the functionality of the mitochondrial anion carrier protein was affected, potentially modifying gene expression and replication within the skeletal muscle. Prior investigations have proposed pathogenic mutations in UCP3 to be related to T2D; however, results are inconclusive. These findings can contribute to existing research in the relationship between UCP3 and Type 2 diabetes.

Mitspah Eshette
Oakwood University

Evaluating the Pathogenic Potential of SDHA Gene Variants in Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is a heart condition that affects the left ventricle, reducing its systolic function. DCM affects an estimated 25–35% of individuals with familial forms of the disease, with most mutations impacting genes encoding cytoskeletal proteins, though some mutations affect other proteins involved in contraction. The disease is genetically heterogeneous, but the most common form of inheritance is autosomal dominant. However, some research has found that DCM can also be caused by mitochondrial inheritance. This research focuses on the assessment and pathogenesis of mitochondrial inheritance regarding DCM, using Succinate dehydrogenase complex flavoprotein subunit A (SDHA) as a model. SDHA is a critical mitochondrial complex II protein that functions in both the tricarboxylic acid (TCA) cycle and the electron transport chain. ClinVar was used to identify SDHA as a gene associated with DCM and its three variants, single-nucleotide missense mutations: p.Lys517Glu, p.Arg589Trp, and p.Met1Leu. Pathogenic mutations in SDHA are known to alter mitochondrial function and disrupt energy metabolism in certain tissues, particularly in high-energy-demanding tissues such as the heart muscle. Computational tools PolyPhen-2 and SIFT were used to determine the pathogenicity of the variants. PolyPhen-2 predicted that p.Arg589Trp and p.Met1Leu are most likely damaging, whereas p.Lys517Glu was predicted to be benign. SIFT predicted both p.Met1Val and p.Met1Leu variants to be damaging, and p.Lys517Glu to be tolerated. Previous studies have suggested that pathogenic mutations in SDHA are associated with DCM, as they have been widely implicated in the disruption of mitochondrial complex II, a phenomenon often observed in those with DCM. However, a conclusive result has not yet been reached. This study contributes to the existing research regarding the implications of the SDHA gene in DCM.

Dennia Estrella-Vargas

University of North Alabama

Investigating the connection between ALS through the mutation R522S in the RNA binding protein FUS Amyotrophic lateral sclerosis (ALS) is a fatal degenerative disorder of motor neurons, with 10% being due to hereditary factors. Fused in Sarcoma (FUS) is a gene that codes an RNA-binding protein by the same name, this protein influences cellular processes, including transcription regulation, RNA splicing, RNA transport, DNA repair and damage response. Mutations in FUS are associated with neurodegenerative disorders, including ALS. This study investigates the arginine to serine swap at the amino acid position 522 in the FUS protein. Results from in silico prediction tools and molecular dynamics modeling provide evidence to support pathogenicity of the R522S missense variant.

Gabriel Fabre

Oakwood University

Analysis of HTRA1 Gene Associated with CARASIL

Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy (CARASIL) is a condition that disrupts the small blood vessels in the brain. CARASIL decreases blood flow, causing damage to brain tissue. Some common symptoms of this disease are small strokes, cognitive decline, difficulty walking, and early hair loss. CARASIL is a rare condition with 100-200 cases being reported in medical literature worldwide. Currently, there is no cure, and treatment focuses primarily on managing symptoms and disease progression. The purpose of this study was to determine whether variants of the HTRA1 gene associated with CARASIL are potentially pathogenic. We predict variants of CARASIL may be associated with the pathogenesis of this disease. To test this hypothesis, the ClinVar database was utilized to identify four different single-nucleotide missense variants, Arg302Gly, Asp320Asn, Arg401Trp, and Val417Ile, to be analyzed. NCBI helped with identification of the conserved domains revealing their localization inside the critical serine protease and PDZ domains. PolyPhen-2 predicted all four variants to be probably damaging with high-confidence scores of 0.999 to 1.000. SIFT, predicted the mutations to affect protein function, with significant scores ranging from .00 to .02, which was supported by high median sequence conservation. Additionally, the RPKM data found peak expression in the fetal heart and stomach, proving that the HTRA1 gene is a vital blueprint for building and maintaining healthy blood vessels throughout your entire body. The software SWISS-MODEL revealed that these mutations to the catalytic domain of the HTRA1 protein severely damage the protein's 3D structure and its enzymatic function. This explains the development of blood vessel decay and the symptoms that occur in CARASIL patients.

Anique Fayette

Oakwood University

An Analysis of the SNTA1 gene associated with Duchenne Muscular Dystrophy

Duchenne Muscular Dystrophy (DMD) is a severe, genetic disorder that causes progressive muscle weakness and wasting. DMD occurs primarily in male adolescents due to the lack of the essential protein, dystrophin, needed for muscle strength. Duchenne Muscular Dystrophy affects 1 in every 3600 male live-born infants. (National Institute of Health). One of the genes associated with this disease is the SNTA1 gene. According to an article published by the National Institute of Health, the SNTA1 gene is a member of the syntrophin gene family, which are cytoplasmic peripheral membrane scaffold proteins that are dystrophin-associated protein complex. Additionally, this gene encodes the most common isoform found in cardiac tissues. The purpose of this study is to identify how the SNTA1 gene's mutations affect the disease, DMD. When determining the genes associated with DMD, SimpleClinVar was used to show all missense mutations associated with the SNTA1 gene. The missense mutations further investigated were Ser335Asn and Ala496Pro. PolyPhen-2 and SIFT were used to determine the damage of the mutations. Ser335Asn was shown to be likely benign, while Ala496Pro was shown to be most likely damaging in Polyphen-2. SIFT also showed the same result that Ala496Pro was likely to affect protein function, while Ser335Pro was tolerated. Conclusively, a likely damaging mutation in the SNTA1 gene can hinder the building of the dystrophin protein in a patient with DMD which is what leads to muscle weakness and abnormal heart arrhythmias. This study

is important because it helps to further understand why the SNTA1 gene is crucial in the discussion of DMD.

Hazel Frazier

Tuskegee University

Functional Impact of a Missense Variant in the CACNA1A Gene Associated with Familial Hemiplegic Migraine. Familial Hemiplegic Migraine (FHM) is a rare inherited neurological disorder characterized by severe migraine attacks accompanied by temporary paralysis or weakness on one side of the body. This study investigates a variant in the CACNA1A gene, which encodes the voltage-dependent P/Q-type calcium channel subunit alpha-1A. This protein plays a critical role in regulating calcium ion flow into neurons and is essential for normal neurotransmitter release and brain signaling. The analyzed variant results in a missense substitution in which the amino acid arginine is replaced by serine at position 88 of the protein. Bioinformatics databases including PolyPhen-2, VarSome, and UniProt were used to evaluate the potential pathogenicity of this variant, all of which suggest that the mutation is likely pathogenic. Structural and biochemical analysis shows that this substitution represents a non-conservative amino acid change, replacing a large, positively charged arginine with a smaller, polar, uncharged serine. This change may disrupt electrostatic interactions and alter the structure or function of the calcium channel. Multiple sequence alignment and conservation analysis using UniProt and the ConSurf server revealed that this amino acid position is highly conserved across homologous sequences, suggesting that it plays an important functional role. Because conserved residues are often essential for protein stability and activity, the arginine-to-serine substitution may impair normal calcium channel function. Disrupted calcium signaling in neurons is a known mechanism underlying Familial Hemiplegic Migraine, supporting the hypothesis that this variant contributes to disease pathology.

Em'Maya Freeman

Tuskegee University

Investigation of a missense mutation (Val12Phe) on the HBB gene in Sickle Cell Anemia

This project explores a missense mutation on the HBB gene with a currently not known outcome. This gene encodes for beta-globin, which is a subunit of a larger protein, hemoglobin. Hemoglobin is very important in transferring oxygen around the body by red blood cells. The most known mutation associated with this gene is Sickle cell anemia. This project focuses on a missense mutation a few amino acids down from this disease at the 12th position. The mutation consists of a change of amino acid from Valine to Phenylalanine; this change can have possible pathogenic effects on the subject. Software's such as PolyPhen 2, Aminode, YASARA 3D, and SIFT were used to explore the possible effects this mutation can have on the body.

Mario Fuentes

Oakwood University

Genetic Variability of the CCL2 Gene and Its Implications in Tuberculosis Progression

Tuberculosis is a contagious infectious disease caused by *Mycobacterium tuberculosis* that primarily affects the lungs but may also involve other organs such as the kidneys, spine, and brain. The gene associated with the illness is CCL2, which encodes a chemokine responsible for recruiting monocytes and other immune cells to sites of infection, playing a critical role in inflammation and granuloma formation, key mechanisms in controlling tuberculosis infection. The hypothesis of this study is that some specific amino acid substitutions in the CCL2 gene reduce chemokine functionality, impair monocyte recruitment and granuloma formation, and therefore increase susceptibility to active tuberculosis. To test this hypothesis, we evaluated the functional impact of selected amino acid substitutions in the CCL2 gene and assessed their potential association with tuberculosis susceptibility and progression. Computational prediction tools, including SIFT, PolyPhen-2, and Simple ClinVar, were used to analyze four specific variants based on sequence homology and evolutionary conservation. The analysis involved four variations of the gene and demonstrated a median conservation score of 3.09, indicating that the evaluated positions are relatively conserved. SIFT

predicted three substitutions: position Thr55Ser (score 0.04), position Cys35Trp (score 0.00), and position Ala15Pro (score 0.01) to be deleterious, as scores below 0.05 indicate a high probability of affecting protein function. In contrast, the substitution at position Ala49Val (score 0.12) was predicted to be tolerated. PolyPhen-2 analysis further supported the potential damaging effect of the deleterious variants. Overall, these findings indicate that specific CCL2 variants may impair chemokine function, disrupt immune cell recruitment, and influence inflammatory responses, potentially contributing to differences in tuberculosis susceptibility, disease progression, and overall host immune effectiveness. This study is significant because it links genetic variability in the CCL2 gene to potential differences in tuberculosis susceptibility and it will enhance the development of targeted immunomodulatory treatments that enhance host defense against *Mycobacterium tuberculosis*.

Kayla Fulford

Oakwood University

An Analysis of NF1 Variants Associated with Ovarian Cancer

Ovarian epithelial cancer is the most lethal type of gynecologic cancer in much of the industrialized world. It is a morphologically and biologically heterogeneous disease. It has been estimated that overall, 5-year survival of (EOC) is only 30% and the poor situation has not been improved in 30 years. The NF1 protein functions as a negative regulator of the raw signal transduction pathway. The purpose of this study is to help identify the infectiveness of the NF1 variants related to ovarian cancer. Simple clinical trials were used to identify the NF1 as a gene related to ovarian cancer and its 3 missed mutations, P.Cys93Trp, P.Ala219Pro, and P.Ala3Val. The NF1 gene has been linked to neurofibromatosis type, Myelomonocytic Leukemia, and Watson syndrome. Computational tools PolyPhen-2 and SIFT were used to determine the infectiveness of the 3 variants. Polyphenus-2 predicted all three mutations to be damaging. Previous studies have suggested pathogenic mutations in the NF1 to be associated with ovarian cancer. The NF1 gene is strongly associated with defects in about 22% of cases, including splicing and deletion. This study contributes to the existing research regarding implications of the NF1 gene associated with ovarian cancer.

Misiel Garcia

Oakwood University

KIF1B Variants and Their Role in Melanocyte Dysfunction in Vitiligo

Vitiligo is an autoimmune skin disorder characterized by the progressive loss of melanocytes, resulting in depigmented patches on the skin. The condition affects millions of individuals worldwide and approximately 1.9 to 2.8 million adults in the United States, significantly impacting patients' quality of life. While autoimmune mechanisms contribute to melanocyte destruction, the genetic factors underlying susceptibility to vitiligo remain unclear. Identifying genetic variants associated with melanocyte dysfunction may help clarify the disease mechanisms.

To investigate potential genetic factors, variants in the gene KIF1B were identified using the database ClinVar. KIF1B encodes a kinesin motor protein involved in the anterograde transport of mitochondria and synaptic vesicle components along microtubules, a process essential for cellular organization and survival. Disruption of this transport system may affect pathways relevant to melanocyte homeostasis. Three missense variants, Gln98Leu, Ser49Tyr, and Glu825Lys, were selected for functional prediction using SIFT. SIFT predicted that substitutions at positions 98 (Q to L) and 49 (S to Y) may affect protein function, with a median sequence conservation score of 3.48 and low-confidence warnings due to limited sequence diversity. In contrast, the substitution at position 825 (E to K) was predicted to be tolerated, with a score of 1.00 and a median conservation score of 4.32.

KIF1B has previously been associated with Charcot-Marie-Tooth disease and Neuroblastoma, suggesting a broader role in cellular homeostasis. These findings highlight KIF1B variants as potential contributors to melanocyte dysfunction and support further investigation into their role in vitiligo pathogenesis.

Madison Gates

University of North Alabama

Evaluating potential impact of variants R157S and T281M in PSEN1 on Early Onset Alzheimer's Disease via in silico prediction and molecular modeling

Early Onset Alzheimer's Disease (EOAD) is a type of dementia that can affect memory, thinking, and behavior. Of all EOAD cases, 70-80 percent are caused by autosomal dominant mutations, meaning the trait can be inherited by one allele, to the PSEN1 gene. This study is focused on PSEN1 and its involvement in the breakdown of Amyloid Precursor Protein (APP) into potentially harmful Amyloid Beta (AB) peptides. PSEN1, a subunit of gamma-secretase (γ -secretase), is responsible for cleaving APP. This study investigates two variants of uncertain (VUS) significance at position 157 swapping arginine to serine and position 281 swapping Threonine to Methionine. Evidence gathered from in silico prediction tools and other computational tools seem to result in pathogenic classifications for both VUS.

Spencer Graham

Oakwood University

Functional Analysis of an ABL1 Missense Variant Associated with Congenital Heart Defects

Congenital heart defects (CHDs) are structural abnormalities of the heart that occur during fetal development and represent one of the most common birth defects worldwide. These conditions can arise from genetic mutations that disrupt signaling pathways responsible for normal cardiac formation. The ABL1 gene encodes a proto-oncogene tyrosine kinase that regulates cellular processes including cell division, adhesion, differentiation, and response to cellular stress. Although ABL1 mutations are most commonly associated with leukemia, particularly chronic myelogenous leukemia, variants in this gene have also been linked to congenital heart defects and skeletal malformation syndromes. These mutations may disrupt signaling pathways required for proper heart development. The purpose of this study is to assess the potential pathogenicity of ABL1 variants associated with congenital heart defects and evaluate how environmental factors may influence gene function and disease development. ClinVar was used to identify ABL1 as a gene associated with multiple disease phenotypes and to examine missense mutations within the gene. One variant of interest, A506V, represents a single nucleotide missense mutation within the ABL1 protein. The FASTA sequence of ABL1 was analyzed using bioinformatic tools including PolyPhen-2 and structural modeling programs. PolyPhen-2 predicted the A506V substitution to be probably damaging, suggesting the mutation may disrupt normal protein function. In conclusion, mutations in ABL1 may contribute to the pathogenesis or phenotype of congenital heart defects. Understanding how these mutations and environmental factors influence ABL1 activity may provide insight into the genetic mechanisms underlying congenital heart disease.

Rochelle Gunter

Oakwood University

An Analysis of ZAP70 Variants Associated with Bullous Pemphigoid

Bullous pemphigoid is a rare chronic autoimmune skin disorder that affects 10 out of every 1,000,000 individuals per year. This disease is characterized by the abnormal infiltration of B lymphocytes, T lymphocytes, and lymphoid cells into the skin's epithelial junctions. The activity of these immune cells is heightened when they break through the skin's layers, resulting in characteristic symptoms of bullous pemphigoid: chronic blisters and inflammation. The objective of this study is to identify and evaluate the pathogenic potential of ZAP70 variants associated with the development of bullous pemphigoid. ClinVar was used to identify ZAP70 as a gene involved in autoimmune pathogenesis, along with its three variants: p.Ala6Thr, p.Gly45Arg, and p.His158Gln. Gene expression data shows that the ZAP70 gene occurs mainly in T-lymphocytes. PolyPhen-2 and SIFT PolyPhen-2 and SIFT are bioinformatics tools that were used to assess the pathogenicity of the three variants that were selected for analysis. PolyPhen-2 predicted that p.Ala6Thr was likely to be benign. The predictions for

the mutations of p.Gly45Arg and p.His158Gln were likely to be damaging. SIFT analysis predicted that p.Ala6Thr substitutions are to be tolerated. For the mutations of p.Gly45Arg and p.His158Gln, SIFT predicted that they are to affect protein function. The pathogenicity identified by SIFT and PolyPhen-2 indicates that ZAP70 protein function, important for immune system signaling, is inhibited. These mutations could alter the signaling pathways of T-cell receptors and add on to the underlying characteristics that cause bullous pemphigoid. In conclusion, pathogenic ZAP70 variants can be implicated in the pathogenesis of bullous pemphigoid, but further research is needed. This study builds on current research of the genetic and molecular foundation of ZAP70 in autoimmune skin disorders.

Alisia Hackshaw
Oakwood University

Pathogenic Role of SOCS1 Gene Variants in Systemic Lupus Erythematosus

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease in which the immune system attacks healthy tissues, leading to widespread inflammation and damage to joints, kidneys, heart, and lungs. It affects an estimated amount of 3.4 million people worldwide, with 90% of cases occurring in women. This disease is complex and influenced by both genetic and environmental factors. The SOCS1 gene encodes a protein that negatively regulates cytokine signaling and helps prevent excessive immune activation. This study's purpose is to identify and assess the pathogenesis of SOCS1 (Suppressor of Cytokine Signaling 1) variants when associated with SLE. Computational tools such as ClinVar, SIFT, and PolyPhen-2 were used to help analyze data. Simple ClinVar was used to identify the SOCS1 gene associated with SLE, and three of its missense variants, p.Pro123Arg, p.Gln210His and p.Arg193Cys. PolyPhen-2 predicted the selected variants to be most likely damaging. SIFT predicted p.Pro123Arg and p.Gln210His to be damaging and the p.Arg193Cys to be inconclusive. Furthermore, the results suggest that the functionality of the Suppressor of Cytokine signaling 1 was affecting the immune system to become overactive, contributing to increased inflammation and damage to healthy tissues. Earlier studies have suggested that pathogenic mutations in SOCS1 affect IL-2 which helps immune cells grow, and IFN-gamma which activates immune defense and is needed in postnatal growth and survival. These dysregulations contribute to excessive immune activation in the kidneys causing lupus nephritis while continuing to affect the heart, kidney, and lungs. This study adds to the existing body of research by further examining the role and implications of the SOCS1 gene in the development and progression of SLE.

Taylor Hall
Oakwood University

A Bioinformatic Analysis of a ACVR1 variant in Fibrodysplasia Ossificans Progressiva

Fibrodysplasia Ossificans Progressiva (FOP) is a rare autosomal disease that results from the progressive formation of heterotopic growth of bone in soft tissue, contributing to episodic flare-ups, loss of mobility, declines in the respiratory system, and toe malformations. FOP has been linked to a gain-of-function mutation in the ACVR1 gene. This gene encodes a bone-morphogenic protein (BMP), a type 1 receptor. Genetic mutations associated with FOP are found to alter ligand function and receptor conformation, culminating in an aggressive activation of bone-morphogenic protein signaling pathways. The study seeks to identify a ACVR1 variant associated with FOP and investigate possible changes in its mutant protein and function. We hypothesize that an ACVR1 variant linked to FOP will show changes in the structure of its encoded mutant protein, with possible implications for its function. Bioinformatic methods were used for analysis. Simple ClinVar identified two ACVR1 variants, R307Q and A358E, with a CADD score of 29.9 and 24.4, respectively. PolyPhen2 predicted both mutations to be probably damaging, with a score of 0.849 for the R307Q mutant and of 0.993 for the A358E mutant. Structural protein modeling studies showed conformational changes between the mutant and the wild-type proteins. STRING study indicated the ACVR1 interacts with proteins involved in bone-morphogenic protein signaling pathways, supporting its involvement in abnormal bone formation. Taken together, our findings identify two ACVR1 variants encoding for mutant ACVR1 proteins with predicted damaged functions and/or functions, compromising their interactions with proteins involved in bone morphogenesis and possibly contributing to FOP. Future studies on the above

mutant ACVR1 proteins are recommended to better understand the mechanisms contributing to the development of FOP.

Rachel Hampton
Oakwood University

The Role of ROS1 Proto-oncogene in Lung Cancer Pathogenesis

Lung Cancer is a disease that is the product of cells in the lungs that mutate and grow at an uncontrollable rate, forming tumors that can spread throughout the lungs and different parts of the body. Lung cancer has the leading mortality rate of any cancer in the US, for both men and women. There are over 124,000 – 132,000 deaths annually. Thankfully, the number of lung cancer diagnoses has decreased over the last 5 years by 13%. The purpose of this study is to identify and analyze the pathogenicity of ROS1 variants that are associated with Lung Cancer. Some ROS1 variants act as oncogene promoters with 1-2% of non-small-cell lung cancers (NSCLC). This results in Kinase activation and Uncontrolled Multiplication cells. ROS1 is not a hereditary gene but can be developed over time from somatic mutation. We hypothesize that NSCLC variants may have implications in the pathogenesis of the disease. To test this hypothesis, Simple ClinVar, was used to find the ROS1 genes in relation to lung cancer. Many variants were found, the variant used was the Missense mutation p. Gly2032Arg. This was the only possible pathogenic mutation in relation to lung cancer noted. The ROS1 gene codes for a Proto-oncogene tyrosine-protein kinase. The computational tools, PolyPhen-2 and SIFT, were used to determine the pathogenicity of the variant. PolyPhen-2 predicted that the mutation is damaging, while SIFT predicted that protein function could be affected. This data suggests that this specific mutation makes the tyrosine protein hyperactive, resulting in the production of the gene. This study contributes to the existing research regarding relations of the ROS1 gene associated with lung cancer.

Isaiah Harris
Oakwood University

Analysis of ETV6 variants associated with Leukemia

Leukemia is a disease that is characterized by a heterogenous group of hematologic malignancies that come from the dysfunctional proliferation of developing leukocytes. It is classified as either chronic or acute based on the speed of proliferation and as lymphocytic or myelocytic based on its cell of origin. The ETV6 gene is a member of the ETS (E26 transformation-specific) superfamily of transcription factors located on chromosome 12. It encodes a protein that consists of 452 amino acids. ETV6 is affiliated with chromosomal rearrangements in leukemia and congenital fibrosarcoma. It has been reported that ETV6 can be involved with leukemogenesis through point mutations, deletions, and other forms, and they have an important role in prognosis and disease progression. The purpose of this study is to identify the pathogenicity of ETV6 variants that are associated with leukemia. However, the clinical impact of ETV6 mutations in acute myeloid leukemia is not clear. SimpleClinVar was used to identify ETV6 as a gene associated with leukemia and its four variants, missense mutations, p.Ala247Gly, p.Pro325Leu, p.Pro214Leu, and p.Leu201Pro. PolyPhen2 and SIFT were used to identify the pathogenicity of the four variants, two of them being benign and two of them being probably damaging. Previous studies suggest that pathogenic mutations in ETV6 are associated with leukemia, as germ line mutations in ETV6 are able to keep the gene from regulating hematopoiesis. These mutations in ETV6 are strongly associated with familial thrombocytopenia. Leukemia is reported in around 30% of people who carry pathogenic ETV6 mutations, which shows an association between ETV6 mutations and leukemia. However, even with this information, the exact cause of leukemia from ETV6 mutations is still not fully known. This study contributes to research regarding the ETV6 gene associated with leukemia.

Lucas Hasting

University of North Alabama

Computational Approaches using Machine Learning to Predict Functional Impact of SERPINA1 Missense Mutations

Bioinformatics is an important tool for genomics research, lowering the cost and reducing the time to wait for results. This research aims to use machine learning to predict the pathogenicity of variants of uncertain significant (VUS) for the Alpha-1 antitrypsin (AAT) protein associated with the SERPINA1 gene. Data used was collected through the Ensembl database. Moreover, Python was used to clean the data and create/train the models used for prediction. The dataset contains 196 more benign observations than pathogenic, so we removed 196 benign observations for training. However, we used the full data set of 484 observations for testing to determine accuracy over all known missense swaps associated with SERPINA1. Next, four different models were used for prediction with all parameters found using the hold-out method (aside from the neural network) with a generalization gap of 0.015. The first model focuses on using a neural network built using PyTorch. This neural network is a multilayer perceptron (MLP) that will use known cases of missense swaps and their pathogenicity and their mutation accessor score to predict the pathogenicity of all VUS. This is done using linear affine transformations and then passing that information into a Rectified Linear Unit activation function through one hidden layer. The output layer also makes use of a linear affine transformation and then utilizes a sigmoid function to map into the open interval (0,1) and translate that into a Bernoulli distribution to predict benign (0) or pathogenic (1). The model was optimized using the stochastic gradient descent algorithm, with a learning rate of 0.01, a momentum of 0.9, and a batch size of 32. The model was trained using backpropagation with 10000 epochs and a log-loss loss function. The second model utilized K-Nearest Neighbors (KNN) via scikit-learn with $k = 10$. The third model uses a maximum-depth decision tree which also uses the hold-out method. In this model, we used Gini impurity as a measure of information. Our last model uses a random forest with a max-depth of 4 and n -estimators with $n = 4$. We built these random forests using the bootstrap method which builds decision trees by taking out random subsets of our training data for each decision tree. These four models resulted in an accuracy of determining whether any given VUS was benign or pathogenic of 86%, 85%, 89%, and 90%, respectively. These findings contribute to the understanding of how pathogenicity scores influence clinical significance of missense swaps related to SERPINA1 and AAT which is associated with non-cystic fibrosis bronchiectasis while defining the importance of further investigation of these variants for improved diagnostics in clinical diagnosis.

Rondel Hemerding

Alabama A&M University

Structural Insights into HIV-1 Env Mutations That Modulate Cell–Cell Transmission

HIV-1 cell–cell transmission (CCT) enhances viral spread and may reduce susceptibility to neutralizing antibodies compared to cell-free infection. Structural determinants within the HIV-1 envelope (Env) glycoprotein that promote this transmission mode remain incompletely defined. In this study, we seek to understand the structural and biophysical consequences of two Env point mutations, R298K and S162K, relative to the wild-type (WT) Env structure 6NIJ. We hypothesized that these mutations alter Env conformational stability, receptor engagement, or structural dynamics. Using structural modeling based on the WT 6NIJ trimer, we examined the local and global effects of the R298K and S162K substitutions. Electrostatic energy analysis showed that solvation and vacuum energies stayed mostly the same across all variants. However, the total electrostatic energy changed slightly, suggesting that R298K slightly stabilizes the protein, while S162K slightly destabilizes it. R298K, located within the gp120 subunit, preserves positive charge but may alter local side-chain interactions and hydrogen bonding networks that influence CD4 binding or trimer stability. In contrast, S162K introduces a positively charged residue at a position commonly associated with glycosylation, potentially disrupting glycan occupancy and modifying Env surface exposure. These structural perturbations may alter energy landscapes and conformational dynamics critical for virological synapse formation. Preliminary analyses suggest that while both mutations are conservative at the sequence level,

they may induce measurable shifts in Env flexibility, electrostatics, and receptor binding compared to WT 6NIJ. Together, these findings provide insight into how specific Env mutations may modulate structural properties to enhance cell–cell transmission and contribute to viral fitness under selective pressure.

Joshua Henry

Oakwood Adventist Academy

The Role of the ACVR1 Gene in the Genetic Disorder Fibrodysplasia Ossificans Progressiva (FOP)
Fibrodysplasia Ossificans Progressiva (FOP) is a rare and severely disabling genetic disorder characterized by the progressive formation of bone in soft tissues such as muscles, tendons, and ligaments, leading to cumulative loss of mobility and reduced quality of life. FOP primarily affects children, with symptoms often beginning in early childhood, and currently has no cure. The genetic basis of FOP is strongly linked to mutations in the ACVR1 gene, which encodes a bone morphogenetic protein (BMP) type I receptor that plays a critical role in skeletal development, cell growth, and tissue differentiation. Activating mutations in ACVR1—most commonly the R206H substitution—lead to abnormal signaling that causes inappropriate bone formation in soft tissues. In addition to FOP, alterations in ACVR1 signaling have been associated with other conditions, including diffuse intrinsic pontine glioma (DIPG), a highly aggressive pediatric brain tumor, as well as developmental skeletal abnormalities and dysregulated bone growth disorders. This study examines the role of ACVR1 mutations in the pathogenesis of FOP using bioinformatic tools such as SimpleClinVar, SIFT, and PolyPhen2 to analyze missense mutations. Predictive analyses indicate that many ACVR1 mutations are damaging and likely disrupt normal receptor regulation, contributing to disease progression. These findings emphasize the broader clinical significance of ACVR1 and highlight the importance of continued research to improve diagnosis and develop targeted treatments for ACVR1-related disorders.

Darby Holder

Oakwood University

Evaluation of the Association between BRIP1 Variants and Hereditary Breast Cancer

Breast cancer is characterized by uncontrollable cell growth in breast tissue, which is caused by genetic alterations (MedlinePlus). It is the second most diagnosed cancer among women in the U.S. and the second leading cause of cancer deaths (National Cancer Institute). BRCA1 interacting DNA helicase 1 (BRIP1) is one of the top ten genes associated with breast cancer. BRIP1 has been identified as a gene that may contribute to hereditary breast cancer (National Library of Medicine). The purpose of this study is to identify missense variants in the BRIP1 gene and determine their malignancy. This study hypothesizes that missense mutations of the BRIP1 gene are associated with hereditary breast cancer. Simple ClinVar was used to identify BRIP1 as a gene associated with breast cancer and locate missense mutations of that gene. Three variants were selected for further analysis: p.Lys116Asn, p.Ala349Pro, and p.Gln255His. SIFT and Polyphen-2 were then used to determine the pathogenicity of these mutations. The BRIP1 gene codes for Fanconi anemia group J protein, a member of the RecQ DEAH helicase family (National Library of Medicine). It binds with BRCA1 to repair double-stranded breaks in DNA (National Library of Medicine). Alterations in this protein caused by BRIP1 mutations have been associated with hereditary breast cancer (National Library of Medicine). PolyPhen-2 predicted the p.Lys116Asn variant to be benign and the variants p.Ala349Pro and p.Gln255His as likely damaging. SIFT predicted p.Lys116Asn and p.Ala349Pro as tolerated and p.Gln255His to affect protein function. These findings suggest that p.Ala349Pro and p.Gln255His affect protein function and contribute to breast cancer development. In alignment with previous studies, this study suggests that variations in the BRIP1 gene may be associated with breast cancer development and thus contributes to the growing body of research discussing the malignancy of BRIP1 mutations.

Samantha Hunte

Oakwood University

Assessing the Pathogenicity of RHOTB2 Variants in Rett Syndrome

Rett syndrome (RTT) is a rare neurodevelopmental disorder that primarily affects females and causes severe impairments in cognitive, motor, and communication abilities. Symptoms typically emerge between 6 and 18 months after a period of normal development. While mutations in MECP2 are the most common cause of RTT, variants in other genes, including RHOTB2, have been identified in individuals with Rett-like features. The RHOTB2 gene encodes a small Rho GTPase involved in ubiquitination and proteasomal degradation through interaction with cullin-3, which is important for cell cycle regulation. This study aims to identify and assess the pathogenicity of RHOTB2 variants associated with RTT. We hypothesize that genetic variants of RHOTB2 may be pathogenic and contribute to the phenotype of RTT. ClinVar was used to identify RHOTB2 and three single-nucleotide missense variants: Pro153Arg, Asp368Asn, and Arg511Gln. Swiss-Model was used to predict the protein's three-dimensional structure, and computational tools PolyPhen-2 and SIFT were used to evaluate variant pathogenicity. PolyPhen-2 predicted Pro153Arg and Arg511Gln to be damaging and Asp368Asn to be benign. Similarly, SIFT predicted Pro153Arg and Arg511Gln to affect protein function, while Asp368Asn was predicted to be tolerated. These results suggest that specific RHOTB2 variants may disrupt normal protein function and contribute to atypical RTT phenotypes. Although RHOTB2 mutations are rare compared to MECP2, their predicted pathogenicity supports a potential role in RTT-related disorders. This study contributes to the understanding of the genetic heterogeneity of Rett syndrome and supports further investigation of RHOTB2 as a candidate gene.

NICHOLAS JAMES

ALABAMA A&M UNIVERSITY

Decode CXCR4 Variants to Understand HIV -1 Co-Receptor Function HIV – 1 entry into cells requires interactions between a viral envelope's glycoprotein and chemokine receptors, which includes CXCR4. CXCR4 variants are linked to CD4+ T cell decline, but we do not know how genetic variation in CXCR4 influences protein function and HIV – 1's binding. We hypothesized that certain mutations in the human CXCR4 gene can impair receptor structure and potentially change its ability to facilitate viral entry. This study investigates variants of uncertain significance (VUS) in CXCR4 using data sets and integrative computational approaches. We focused on two specific mutations at positions 32 and 2 of CXCR4: glutamic acid to glycine (Glu2Gly) and glutamic acid to alanine (Glu32Ala). We first optimized each variant to its lowest energy conformational state; then, we performed structural modeling of our proteins. Afterwards, we used PolyPhen2, CADD, and SIFT to assess the pathogenicity and overall functional impact of each variant. Findings indicate that genetic variants could potentially impair binding. Genetic variation of CXCR4 plays a role in modulating HIV outcomes. Overall, this work adds to understanding host factors that influence HIV, and it lays a foundation for interpreting CXCR4 VUS in genomics.

Clarissa Jean-Charles

Oakwood University

The role of mutation in the VSX2 gene in the development of Retinitis Pigmentosa

Retinitis pigmentosa (RP) is a group of rare inherited eye diseases characterized by the progressive degeneration of retinal photoreceptors. Symptoms typically appear in childhood, beginning with loss of night vision, and often progress to severe visual impairment or blindness in adulthood. The disease significantly affects patients' quality of life, impacting daily activities, social relationships, and employment and has no definitive cure. The Visual System Homeobox 2 (Vsx2) gene encodes a transcription factor that regulates retinal development, particularly by promoting neural retinal differentiation while repressing retinal pigment epithelium fate. Previous studies have shown that loss-of-function mutations in Vsx2 are associated with congenital stationary night blindness (CSNB), a condition that shares several clinical features with RP. However, the potential role of Vsx2 variants in RP remains understudied. This study aims to identify a Vsx2 variant associated with RP and the implications of the mutation on the mutant Vsx2 protein. We hypothesize that the mutation observed in the variant will compromise the function of the mutant Vsx2 protein encoded by the variant.

Bioinformatic tools were used to identify the Vsx2 variant and study its protein. Simple ClinVar analysis identified the nonsense variant p.Trp203Ter, with a CADD score of 43 to be associated with RP. UniProt analysis indicated that the mutation introduces a premature stop codon upstream of the Vsx2 functional domain, suggesting structural changes that may impair domain interactions and compromise protein function. Additionally, STRING analysis revealed a regulatory network involving interactions between Vsx2 and RP-related proteins RHO and MFRP. Our findings suggest an involvement of Vsx2 variants in RP through alterations in their encoded mutant protein structure and function in protein-protein interactions networks. Future studies are warranted to further our understanding of the biological mechanisms involved therein and possible contributions to treatment strategies.

Kyle Johnson
Oakwood University

Analysis on FGA in association to Venous Thromboembolism

Venous Thrombosis (VTE) is a blood clot that blocks the flow of blood through the veins. This blood clot can form in the deep veins of the arms and legs, or travel through the veins to the lungs, which can lead to complications such as cardiovascular damage, fatal lung blockages, and chronic disability. VTE represents a significant global health burden, with incidence rates estimated at approximately 1–2 cases per 1,000 individuals annually. The purpose of this study is to identify and evaluate the pathogenicity of FGA variants associated with venous thromboembolism (VTE) using genetic databases and protein analysis tools, with a focus on how missense mutations may alter protein function and influence blood clotting. ClinVar was used to identify genes and genetic mutations associated with VTE. FGA was identified as the gene and two missense variants p.Arg35Cys and p.Arg38Gly were chosen for further analysis. The FGA gene codes for the alpha subunit of the coagulation factor fibrinogen, an important glycoprotein produced in the liver that plays a vital role in blood clotting. Mutations in FGA can lead to shortened protein, missing alpha chain, and low Fibrinogen which leads to defective clot formation. Polyphen-2 and SIFT were used to analyze the damage probability, examine the domains of the protein encoded by VTE, and analyze how the substitution affected the function of the gene. Polyphen-2 predicted both mutations to be probably damaging while SIFT predicted both variants to affect the protein function. The pathogenicity of these mutations suggest that they affect the function of the coagulation factor fibrinogen glycoprotein, potentially affecting the blood clot through changing the structure of the alpha chain.

Joshua Johnon
Oakwood Adventist Academy

Calvin Jolly
Spring Hill College

Comparative Study of Missense Variant Ser437Tyr in the MFSD8 Gene Associated with Infantile Neuronal Ceroid Lipofuscinoses

Infantile Neuronal Ceroid Lipofuscinosis type 7 (CLN7) is a rare inherited neurodegenerative disorder that affects the nervous system. The disease is caused by mutations in the CLN7 gene, located on chromosome 7, which encodes the lysosomal protein MFSD8. CLN7 is a subtype of Batten disease and primarily affects children. Mutations in this gene can result in the production of a defective or nonfunctional protein, impairing normal lysosomal function and ultimately leading to progressive neurodegeneration. According to the ClinVar database, the pathogenicity of approximately 90% of variants in the MFSD8 gene remains uncertain. This study aims to investigate a variant of uncertain significance caused by a missense mutation at amino acid position 437, in which serine is substituted with tyrosine. To evaluate the potential structural impact of this mutation, computational molecular dynamics analysis will be conducted to compare the protein structure before and after the amino acid substitution. Understanding the structural consequences of this mutation may provide insight into its potential pathogenicity and contribute to improved classification of MFSD8 variants associated with CLN7.

Megan Joseph

Oakwood University

An Evaluation of COL1A2 pathogenic variants associated with Dentinogenesis Imperfecta

Dentinogenesis Imperfecta (DGI) is a genetic disorder that is characterized by the appearance of translucent, brittle teeth. This disease influences the levels of dentin formation, which then results in the degradation of tooth enamel. This study's purpose is to examine the relationship between the COL1A2 gene variants and DGI. Previous studies have suggested that COL1A2 pathogenic mutations are closely correlated with the development of DGI. We hypothesize that variations within the COL1A2 gene will result in impaired type I collagen function. The COL1A2 gene is responsible for encoding the alpha-2 chain, a component of type I collagen. Type I collagen is the most common form of collagen in the human body, as it's found in the skin, bone, and dentin. Mutations in the COL1A2 gene result in defective tissue disorders, directly influencing oral health. To test this hypothesis, Simple ClinVar was used to identify the gene COL1A2 as a gene associated with DGI and its three variants, p.Gly487Arg, p.Gly256Asp, p.Asp939Asn. Bioinformatic tools PolyPhen-2 and SIFT were used to determine the severity of pathogenicity caused by the three variants. PolyPhen-2 predicted each of the three mutations to be most likely damaging, while SIFT supported these findings for all but p.Asp939Asn, which it labeled as tolerated. These mutations influence the functionality of type I collagen, potentially affecting cohesive gene expression. Prior investigations have revealed pathogenic mutations in COL1A2 correlate with DGI as they prevent the proper collagen formation in dentin. This study expands on the understanding of missense mutations within COL1A2 and its relation to DGI.

Karly Kibble

Oakwood University

An Assessment of COL1A2 Variant Pathogenicity in Patients with Dentinogenesis Imperfecta

Dentinogenesis imperfecta (DI) as hereditary dentin disorder causing discolored, fragile teeth and abnormal dentin formation. DI Type I is associated with osteogenesis imperfecta while Types II and III are isolated from dental forms. DI can be caused by mutations in the Collagen 1A2 gene that encodes the pro- α 2 chain of type I collagen, but the pathogenicity of the many variants remains unclear which limits accurate diagnosis. The objective of this study is to determine the pathogenicity of COL1A2 variants in patients with dentinogenesis imperfecta and find the correlation between the genotype and the dental phenotype. Using SimpleClinVar, COL1A2 was discovered to be involved in dentinogenesis imperfecta as well as other connective tissue disorders. Simple ClinVar showed that the single nucleotide missense variant, p.Gly676Asp in COL1A2 had been submitted. Collagen type I alpha 2 chain is the product of COL1A2. Collagen type I make up most of the structural components of bone, dentin and other connective tissues within the body. Simple ClinVar states that this variant changes a glycine to an aspartic acid at position 676 which is located in the collagen triple-helix domain of COL1A2. SimpleClinVar further shows that the variant is a germline mutation that has been found in patients with heritable disorders of collagen. PolyPhen-2 and SIFT were used to evaluate the pathogenicity of the variant p.Gly676Asp. PolyPhen-2 predicts that p.Gly676Asp is probably pathogenic with a highly damaging score of 0.999 and the SIFT analysis predicted that the variant was likely damaging. The combined clinical, structural, and computational evidence supports the pathogenic role of the COL1A2 missense variant (p.Gly676Asp) in dentinogenesis imperfecta. The substitution of glycine within the collagen triple-helix domain is particularly significant, as glycine residues are essential for proper collagen helix formation and structural stability.

Amir King

Oakwood University

Predicting the Functional Impact of ALK Mutations Associated with Lung Cancer

Lung cancer is one of the leading causes of cancer deaths globally. It is caused by the uncontrolled proliferation of abnormal cells in one or both lungs. Risk factors for the disease include smoking and exposure to secondhand smoke, inhalation of air pollution, in addition to other genetic risk factors. Common symptoms include cough, chest pain, difficulty breathing, fatigue, and unexplained weight loss. The anaplastic lymphoma kinase (ALK) gene encodes a receptor tyrosine kinase that is involved in several intracellular signal transduction pathways. It plays a fundamental role in the growth and development of the nervous system and processes of intercellular communication throughout the body. A mutation in this gene can disrupt cell signaling and result in uncontrolled growth, contributing to cancer pathogenesis. The purpose of this study is to evaluate ALK variants that may be pathogenic. ClinVar was used to identify the association of ALK with lung cancer and to identify particular variants. Bioinformatic prediction algorithms PolyPhen-2 and SIFT, and protein structure prediction, were used to assess the missense mutations in the ALK gene. The substitutions A815S, D1225N, and G1494R were studied using the UniProt reference sequence Q9UM73. PolyPhen-2 predicted that the A815S (0.998) and D1225N (1.000) variants to be probably damaging or damaging, and might have great effect on ALK protein function. Conversely, the G1494R (0.377) variant was predicted to be benign. The SWISS-MODEL program modeled the ALK structure on its template structure (4F0B) using a homologous model. These observations suggest that ALK mutations such as A815S and D1225N can lead to aberrant signaling pathways that may drive the development of lung cancer. The understanding of the features of these mutations may aid precision medicine and the development of targeted therapies resulting from ALK-associated pathologies, including cancers.

Malee Kollie

Oakwood University

The Analysis of TBX21 variants Associated with asthma

Asthma is a chronic inflammatory airway disease characterized by airway narrowing, bronchial hyper-responsiveness, mucus overproduction, and difficulty breathing. It affects over 300 million people worldwide and arises from a combination of environmental and genetic factors. One of the primary contributors to asthma pathogenesis is immune system imbalance, it particularly increased T helper 2 (Th2) activity and reduced T helper 1 (Th1) regulation, which leads to airway inflammation and hypersensitivity. TBX21 is an immune regulatory gene involved in maintaining Th1/Th2 balance and supporting proper inflammatory responses. The purpose of this study was to identify and evaluate the pathogenicity of TBX21 gene variants associated with asthma susceptibility using computational analysis tools. Variant information was obtained from the CLIN Var database and analyzed using PolyPhen-2 and SIFT to predict the possible impact of these mutations on protein function. In this study, the missense variant c.83G>A (p.Gly28Asp) in the TBX21 gene was examined to determine whether it may affect protein structure or activity. Swiss-Model structural analysis was also used to examine how damaging variants could affect protein stability and DNA-binding ability. It was hypothesized that certain variants in TBX21 may change the structure or function of the protein, which could disrupt immune regulation and increase the risk of asthma. Results show that the p.Gly28Asp variant was predicted to be benign by PolyPhen-2, while SIFT classified the mutation as tolerated. Structural modeling suggested that the mutation does not significantly change the overall structure of the TBX21 protein but may still influence protein stability or function. These findings are significant because they provide insight into how genetic variation in immune regulatory genes may contribute to asthma development and progression, supporting further investigation into TBX21 as a potential biomarker or therapeutic target in asthma-related immune dysfunction.

Lauren Kramer

Alabama A&M University Variant Bioinformatics & Analysis: Do CXCR4 VUSs have increased pathogenicity associated with X4-Tropic HIV-1? Approximately 40.8 million people are living with HIV worldwide. For viral entry to occur, a viral envelope glycoprotein (Env) of human immunodeficiency virus type one (HIV-1) must bind with the primary receptor CD4, as well as either the CCR5 coreceptor or the CXCR4 coreceptor. Whereas CCR5-tropic viruses preponderate pathogen transmission, individuals with chronic infections often experience CXCR4-tropic variants correlated with the onset of AIDS. HIV-1's primary coreceptor CCR5 may contain a 32 base-pair deletion (CCR5- Δ 32) allowing carriers to prevent successful viral attachment by inhibiting binding through the truncation of the CCR5 protein, thus promoting innate HIV-1 resistance. Nevertheless, research into whether CXCR4 variants that may congenitally influence protein function or pathogenicity, as well as HIV-1 Env binding, is sparse. Investigating variants of CXCR4 is essential for understanding mechanisms of HIV binding and entry. However, questions remain regarding whether variants of uncertain significance (VUS) of CXCR4 affect Env binding. We hypothesized that CXCR4 VUS Asp262Glu and Glu268Asp will be pathogenic and affect X4-Tropic HIV-1 Env binding. In this study, we analyzed two CXCR4 VUS using bioinformatic software to determine their pathogenicity and impact on Env binding. Variant effect prediction programs were used to evaluate benignness, deleteriousness, or protein tolerance. YASARA was used to conduct simulations investigating protein dynamics, folding, and docking. MEGA12 was used for constructing phylogenetic trees as well as creating multiple sequence alignments. Overall, research into CXCR4 VUS enhances understanding of CXCR4 pathogenesis, as well as providing a foundation for understanding mechanisms of HIV-1 binding and entry.

Kaylani Krigger

Oakwood University

Effects of IL36RN Single-nucleotide missense mutations on IL36-Ra protein and Psoriasis phenotypes
Psoriasis is a chronic autoimmune disease characterized by a rash with scale-like patches on the skin. There are several types of psoriasis, including plaque, guttate, inverse, nail, pustular, and erythrodermic. Genetic and environmental factors can influence this skin condition. According to Mayo Clinic, "Common triggers in people with a genetic predisposition to psoriasis include infections, cuts or burns, and certain medications" (Mayo Clinic Staff, 2025). The evidence indicates that genetic factors are associated with the presentation of psoriasis, as reported in previous research. This may suggest that genetic mutations influence the risk of developing psoriasis. The IL36RN gene provides instructions for a protein that is important for regulating the skin's immune system. from interleukins in order to control inflammation. Therefore, it was hypothesized that missense mutations in IL36RN can be damaging to the IL-36ra protein function. Analysis of the IL36RN gene mutations' effect on protein function was assayed through Polymorphism Phenotyping v2 (PolyPhen-2) and Sorting Intolerant From Tolerant (SIFT). The research included: L3P, A6V, R10Q, L27P, and N47S. For example, Leucine (L) to Proline (P) amino acid substitutions on chromosomes 3 and 27 were likely damaging to protein function. However, an Alanine to Valine missense mutation on chromosome 6 was shown to be benign on Poly-Phen 2, while SIFT predicted deleterious impacts to IL-36ra protein function. In addition, R10Q and N47S were predicted to be damaging by PolyPhen-2 but were tolerated in the protein function. The significance of IL36RN's role in psoriasis phenotypes may stem from null and hypomorphic mutations, which cause complete and partial loss of gene function, respectively. Understanding genetic mutations on IL36RN can assist dermatologists in developing therapies that target inflammation through cell signaling pathways, such as the NF-kb pathway. Therefore, future research is needed to elucidate the role of IL36RN missense mutations in the phenotypic spectrum of psoriasis.

Gabrielle LaDonis
Oakwood University

An Analysis of TNF variants associated with Endometriosis

Endometriosis is a chronic, often painful, and systemic disease characterized by the presence of tissue like the endometrial lining of the uterus growing outside of the uterine cavity, most frequently in the pelvis. Affecting an estimated 10% of women of reproductive age, endometriosis is a leading cause of pelvic pain, inflammation, and infertility (Mayo Clinic). Despite its prevalence, the underlying mechanisms contributing to endometriosis remain incompletely understood, with emerging evidence suggesting a multifactorial etiology involving genetic, immunological, and environmental factors. The aim of this study is to identify and assess the pathogenicity of tumor necrosis factor (TNF) gene variants associated with endometriosis. TNF encodes a multifunctional proinflammatory cytokine critical for immune regulation, homeostasis, and cell signaling. Pathogenic mutations in TNF can significantly alter the expression and function of this cytokine, potentially acting as a biological switch in various tissues. While TNF is predominantly expressed in immune cells, it also has the capability to be expressed in numerous other tissue types. ClinVar was utilized to identify the TNF gene as being associated with endometriosis and to pinpoint two specific single nucleotide missense variants: p.Met6Lys and p.Arg108Trp. The pathogenicity of these variants was predicted using PolyPhen-2 and SIFT. PolyPhen-2 classified both mutations as damaging, whereas SIFT indicated the p.Arg108Trp variant is tolerated. The findings support the notion that endometriosis is not merely a structural disorder of misplaced tissue but a genetically driven inflammatory disease. Previous research has also reported pathogenic TNF mutations in endometriosis, and some endometriotic lesions have been found to harbor somatic mutations in cancer-driver genes, despite remaining benign. This study contributes to expanding research on the genetic and molecular underpinnings of endometriosis.

Joshua Laine
Oakwood University

An Analysis of LDLRAP1 Variants Associated with Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is a monogenic disorder characterized by high levels of low-density lipoprotein cholesterol (LDL-C) in the bloodstream, increasing the risk of premature cardiovascular disease and atherosclerosis. FH is commonly caused by mutations in genes involved in cholesterol metabolism such as LDLR, APOB, and PCSK9. However, rarer cases of familial hypercholesterolemia are associated with mutations in the LDLRAP1 gene. LDLRAP1 encodes LDL receptor adaptor protein 1 in receptor-mediated endocytosis by helping LDL receptors internalize LDL cholesterol particles into liver cells. Mutations in this gene can disrupt the internalization process, thus causing an increasing LDL cholesterol concentration in the blood. The purpose of this study is to find and evaluate variants of the LDLRAP1 gene associated with FH and determine potential pathogenic effects. Research on FH cases linked to LDLRAP1 remains miniscule. ClinVar was used to identify LDLRAP1 as a gene associated with FH and to examine reported variants. Computational tools such as PolyPhen-2 and SIFT were used. These analyses suggest that specific amino acid substitutions affect the structure or function of the adaptor protein involved in LDL receptor internalization. Missense variants Asp287Asn, Pro299Ser, and Ser303Leu were selected for analysis. SIFT predicted Asp287Asn to be tolerated with a score of 0.88, and Pro299Ser to be tolerated; a score of 0.21. The resultant scores suggest that these substitutions are unlikely to effectively alter or disrupt protein function. Ser303Leu in contrast was predicted to affect protein function with a score of 0.02, indicating the presence of a deleterious substitution. Polyphen-2 was also used to evaluate the potential effects of these variants. The Asp287Asn substitution was predicted to be benign with a score of 0.003. The Pro299Ser variant scored similarly with 0.001. In contrast, the Ser303Leu substitution was predicted to be probably damaging with a score of 0.982, implying a high likelihood of negative changes to LDLRAP1. Studies show that mutations in LDLRAP1 can be later attributed to autosomal recessive hypercholesterolemia, a rare form of familial hypercholesterolemia.

Ayanna Liburd

Oakwood University

An Exploration of the Effects of the FCGR2B Gene on Systemic Lupus Erythematosus

Lupus, most commonly referred to as systemic lupus erythematosus (SLE), is an autoimmune disease that causes organ failure and immune hypersensitivity. SLE can manifest in varying types and strengths, and is often characterized by high creatinine ratios in the urine. In the U.S., approximately 1.5 million people have lupus; however, it primarily affects women, especially those of Caribbean descent. The risk of developing SLE is not solely based on inheritance. Environmental factors such as diet, UV light, and stress can significantly influence gene activation, as well as the severity and progression of the disease. This study aims to examine the FCGR2B gene, which encodes Fc gamma receptors and plays a crucial role in clearing immune complexes. Missense mutations in this gene can lead to either suppressed or overactive immune responses. FCGR2B is expressed during fetal development between weeks 10 and 20 in the adrenal glands. ClinVar was utilized to determine the relationship between the FCGR2B gene and SLE, as well as two problematic variants, Glu55Val and Pro48Arg. Computational tools such as PolyPhen-2, SIFT, and SWISS-Modeling were employed to assess the impact of single-nucleotide missense mutations. PolyPhen-2 predicted both variants to be “probably damaging,” and SIFT also indicated that both the P48N and E55V shifts could affect protein function, suggesting that these gene variants may contribute to autoimmune symptoms. Recent studies have demonstrated that the FCGR2B gene influences the expression of lupus, although research remains inconclusive. This investigation adds to the ongoing research on the FCGR gene and its impact on lupus expression.

Angelique Lightbody

Oakwood University

The Molecular Analysis of COL1A1 Mutations Linked to Dentinogenesis Imperfecta 1

Dentinogenesis Imperfecta (DGI) is a genetic disease that interferes with the production of dentin, the calcified matrix beneath the tooth enamel. The lack of dentin causes the enamel of the tooth to break away, which leads to the affected tooth being discolored and fragile. 1 out of 8,000 people are affected by DGI in a population which classifies it as a rare genetic disorder. The purpose of this study is to analyze the pathogenicity of COL1A1 variations and their associations with DGI. Dentinogenesis Imperfecta Type 1, which is linked to osteogenesis imperfecta, is associated with variations in the gene COL1A1. Simple Clinvar was used to identify two missense variants. These gene variations were Gly335Asp and Gly272Ser. COL1A1 codes for collagen, the most abundant extracellular matrix protein, which is integral to maintaining bone integrity. Pathogenetic mutations of this gene lead to major variations in the phenotype of the infected individual. Somatic cells, such as the heart, kidneys, lungs, intestines, and stomach, typically express variations of COL1A1. Computational tools such as PolyPhen-2 and SIFT predicted the 3 mutations to be pathogenic and damaging to the protein. The pathogenicity of the variations suggests that collagen production was reduced, which led to degradation of the connective matrix in the tooth. Previous analyses have been made on the pathogenetic mutations of COL1A1 and the effect it has on Dentinogenesis Imperfecta Type 1. This study contributes to previously established studies involving the effects of the COL1A1 gene associated with Dentinogenesis Imperfecta Type 1.

Neria Lopez

Oakwood University

Analysis of FAN1 Genetic Mutations Associated with Hereditary Ovarian Cancer

Ovarian cancer is a cancer that develops in the tissue within the ovaries and is generally either epithelial cancers or malignant germ cell tumors that have developed (National Cancer Institute). This gynecological malignant type of cancer is typically fatal, as it develops at rapid speeds leading to late detection and treatment. The Fanconi-associated nuclease 1 gene has been tied to monoallelic mutations on BRCA1 and BRCA2 genes (National Library of Medicine), leading to hidden hereditary cancers such as ovarian cancer. This study serves to investigate the impact of FAN1 gene mutations on hereditary ovarian cancers. If mutations of the FAN1 gene lead to harmful mutations on the BRCA1 and BRCA2 genes, then there may be a direct correlation to the FAN1 gene's impact on hereditary cancer such as ovarian cancer. ClinVar was utilized to identify the FAN1 gene and its variants,

p.Met1Val and p.Ser27Phe, which are single nucleotide missense mutations as a gene correlated to hereditary ovarian cancer. Computational tools PolyPhen-2 and SIFT were used to facilitate an analysis of pathogenicity of each variant. PolyPhen-2 identified p.Met1Val as a probable damaging mutation, and p.Ser27Phe as being benign, and SIFT identified p.Met1Val to affect protein function, and predicted that p.Ser27Phe would be tolerated. Previous studies suggest that the impact of the FAN1 gene have been linked to mutations in genes associated with hereditary cancers, although results remain inconclusive. This study contributes to the existing research on the implications of the FAN1 gene's association with ovarian cancer.

Tanyaradzwa Lunga
Oakwood University

An Analysis of the FOXF1 gene associated with Alveolar Capillary Dysplasia with Misalignment of Pulmonary Veins (ACD/MPV)

Alveolar Capillary Dysplasia with Misalignment of Pulmonary Veins (ACD/MPV) is a rare disease affecting the development of the lungs and their blood vessels. When the alveolar capillaries fail to develop normally, the number of capillaries reduces, and the already existing capillaries are positioned improperly. This leads to the disruption of oxygen and carbon dioxide exchange. It presents severe respiratory failure and pulmonary hypertension. The FOXF1 belongs to the forkhead family of transcription factors and codes for the Forkhead box protein. The purpose of this study is to assess the pathogenicity of FOXF1 variants, and its influence on ACD/MPV. The FOXF1 protein is essential for gene expression in the development of tissues in the lungs and gastrointestinal tract. We hypothesize that FOXF1 variants may be associated with this disease. To test this hypothesis, SimpleClinvar was used to identify FOXF1 as a gene associated with ACD/MPV. 3 missense mutations p.Ser101Leu, p.Ala296Thr, p.Ala60Val were further evaluated using computational tools SIFT and PolyPhen-2. PolyPhen-2 and SIFT were used to determine the pathogenicity of the mutations. SWISS was used for protein modeling. PolyPhen-2 predicted that variants p.Ser101Leu and p.Ala60Val would be probably damaging with scores of 1.000 and p.Ala296Thr would be benign with a score of 0. SIFT predicted that mutations of p.Ser101Leu and p.Ala60Val will affect the protein function. The pathogenicity of p.Ser101Leu and p.Ala60Val mutations suggests that they will affect the development of the alveoli and their blood vessels. Previous studies have associated pathogenic mutations of the FOXF1 gene with ACD/MPV. The link between the FOXF1 mutations and ACD/MPV is considered strong but not fully conclusive. This study contributes to the existing research regarding the link between the FOXF1 gene and ACD/MPV.

Gabriella Mcdowell
Oakwood University

An analysis of RINT1 mutations associated with Ovarian Cancer

Ovarian Cancer is a form of cancer that occurs within the ovaries. In its early stages most patients present asymptomatic, often leading to late diagnosis. Ovarian cancer symptoms are often subtle and vague during its early stage; they include persistent abdominal bloating, pelvic or abdominal pain, increased/more frequent urination, pain during sexual intercourse, and abnormal vaginal bleeding or discharge. Primary gene mutations associated with this condition include BRCA1, BRCA2, PALB2, RINT1, and several other genes. The purpose of this study is to identify and assess the pathogenicity of the RINT1 mutations associated with Ovarian Cancer. We hypothesize that there are RINT1 variants that may contribute to the disease pathogenesis. To test this hypothesis, several tools were utilized to identify RINT1 as a gene associated with ovarian cancer including ClinVar, which predicted missense mutations in Ala130Thr, Val217Phe, and Leu662Ser. Polyphen and SIFT were able to predict substitutions to the RINT1 gene at Val217Phe and Leu662Ser, which would affect protein function, while mutations in Ala130Thr were predicted to be more tolerable. Previous studies suggest that pathogenic mutations to RINT1 have been associated with significant risk associated with hereditary breast and ovarian cancer. However, conclusive understanding of its role as a homologous recombinant gene in Hereditary Breast and Ovarian Cancer Syndrome predisposition remains uncertain.

Addie Mclver

Oakwood University

An Analysis of Alzheimer's Associated VCP Variants

Alzheimer's Disease (AD) is the most common form of dementia, affecting around 5.6 million people over the age of 65. This neurodegenerative disease is characterized by amyloid- β plaques and hyperphosphorylated tau accumulation. This aggregation can lead to a loss of neuron connection and damage, resulting in cognitive decline, behavioral changes, and eventually, death. The purpose of this study is to investigate the pathogenicity of VCP mutations and their potential role in AD. VCP codes for the valosin-containing protein, which plays a role in protein degradation and autophagy. With two ATPase domains, and an N- and C- domain, this protein is involved in remodeling, cofactor binding, and cellular localization, playing a critical role in the ubiquitin-proteasome system (UPS). Although decreased VCP expression has been associated with tau accumulation in AD tissue, its underlying mechanisms are not fully understood. To identify potential mutations, VCP was analyzed through Simple ClinVar, and the results showed five mutations: p. Ala232Glu, p. Gly271Ala, p. Arg191Gln, p. Arg155Cys, and p. Lys386Glu. To predict the pathogenicity of these missense mutations, the five variants were investigated using computational tools, PolyPhen-2 and SIFT. Out of these variants, p. Gly271Ala, p. Arg191Gln, p. Arg155Cys, and p. Lys386Glu, were predicted to affect protein function, while p. Ala232Glu was tolerated and predicted to be possibly damaging. VCP is also expressed in the heart, adrenal tissue, intestine, lung, and stomach, and pathogenic mutations may affect protein function in these tissues. Data from this study highlight possible implications of VCP expression and its association with AD.

Shania McKelvey

Oakwood University

An analysis of RAD50 variants associated with breast cancer

Breast Cancer is notable one of the leading forms of cancer in the United States. Characterized by firm lumps or breast morphological changes, breast cancer affects 1 in 8 women today. As of 2026, over 321,910 new cases are estimated to be diagnosed. Breast cancer is associated with inherited mutations linked to supplementary mutations and the BRCA-1 and BRCA-2 genes. This study's purpose is to analyze the pathogenicity of RAD50 variants associated with breast cancer. We hypothesize that RAD50 mutations may contribute to the pathogenicity of this disease. To test this hypothesis, SimpleClinvar was used to identify two RAD50 missense variants, p.Glu47Gln and p.Ile25Thr, and their predicted pathogenicity. RAD50 is a protein coding gene, which codes for a double strand break repair protein. A pathogenic mutation of RAD50 is known to cause the disruption of maintaining genome integrity and DNA repair processes. Analysis of collected data using PolyPhen-2 and SIFT were used to analyze the pathogenicity of this gene and it's variants. Both variants p.Glu47Gln and p.Ile25Thr were predicted to be damaging, with a PolyPhen score of 1.000 respectively. The pathogenicity of these variants suggests that the functionality of the RAD50 protein was affected. Additionally, the produced results suggests that the mutation causes an inability for BRCA complexes to functionally maintain DNA repair and genome integrity, leading to the onset of cancer within somatic cells. Previous studies draw parallels to additional associations with mutations related to MRE11 complex link RAD50 mutations with Ataxia Telangiectasia Like-Disorder (ATLD) and Nijmegen Breakage Syndrome Like-Disorder (NBSLD). This study contributes to the existing research regarding implications of the RAD50 gene associated with Breast Cancer.

Gabriella McPherson
Tuskegee University

Analysis of the Missense Variant His529Arg in Mitochondrial Myopathy

Mitochondrial myopathies are a heterogeneous group of disorders often caused by defects in mitochondrial lipid remodeling and membrane integrity. This study investigates the functional impact of an uncertain missense variant, H529R, in the PNPLA8 gene, which encodes the calcium-independent phospholipase A2- γ enzyme (iPLA2- γ). iPLA2- γ plays a critical role in maintaining mitochondrial homeostasis by hydrolyzing phospholipids, removing oxidized fatty acids from cardiolipin, and regulating lipid derived signaling molecules. Analysis of the canonical PNPLA8 FASTA sequence (782 amino acids) and AlphaFold structural models identifies His529 as a residue located within a structured region of the protein with moderate local confidence (pLDDT $\approx$ 55), suggesting functional but flexible positioning. Importantly, multiple sequence alignment demonstrates strong evolutionary conservation of His529, supporting its biochemical importance. Histidine's pKa ($\sim$ 6) enables reversible proton transfer essential for phospholipase hydrolysis, whereas its substitution with arginine is highly protonated at physiological pH (pKa $\sim$ 12.5), disrupts this catalytic capability. PolyPhen-2 analysis predicts the H529R variant to be "probably damaging" with a maximal score of 1.00, reinforcing its likely deleterious effect. Structural modeling shows that replacing histidine with arginine introduces a larger, permanently charged residue that may destabilize active-site geometry or interfere with substrate positioning. Based on these findings, the H529R substitution is predicted to reduce PNPLA8 enzymatic activity, impair mitochondrial phospholipid turnover, and hinder cardiolipin repair. Consequently, this variant may contribute to mitochondrial dysfunction characteristic of mitochondrial myopathies. Further biochemical validation is warranted to confirm the pathogenic potential of this mutation.

Malachi McRoy
Oakwood University

Analysis of CFTR variants associated with Cystic Fibrosis

Cystic fibrosis is a genetic condition that causes severe damage to the lungs and digestive system. Mucus normally secreted by cells in the lung airways; pancreatic ducts, and reproductive system becomes thickened and blocked, which causes infection and loss of function. This occurs due to a mutation of the cystic fibrosis transmembrane conductance regulator (CFTR), so it cannot reach the membrane. This genetic disease affects about 1 in 2,500- 3,500 white newborns, and 1 in 17,000 newborns of other ethnic groups. The purpose of this study is to identify CFTR variants that could potentially contribute to the cystic fibrosis disease. We hypothesize that specific variants of CFTR will be identified and predicted to be pathogenic and associated with the phenotype of this disease. To test this hypothesis, Simple ClinVar was used to identify the CFTR gene and variants associated with cystic fibrosis. Then The FASTA sequence was used in the analysis tools. Computational tools of PolyPhen-2 and SIFT were used to identify possible variants. SIFT predicted the Leu1242His variant to be damaging, as did PolyPhen-2. A second variant, Asp579His was predicted to be pathogenic by PolyPhen-2 and SIFT predicted the variation to be highly pathogenic. Data from this study supports our hypothesis that other variants may be associated with the pathogenesis of cystic fibrosis. The findings of this study may shed light on other variants associated with this disease and may contribute to development better management of this disease.

Kashmere Miller

Tuskegee University

Computational Analysis of a TSHR Missense Variant (p. Phe97Ser) Associated with Hyperthyroidism

Hyperthyroidism is a condition characterized by excessive production of thyroid hormones. One gene associated with thyroid hormone regulation is TSHR, which encodes the thyrotropin receptor. In this study, a missense variant (p.Phe97Ser) in the TSHR gene was analyzed using bioinformatics tools to evaluate its potential impact on protein structure and function. Sequence analysis, multiple sequence alignment, and structural modeling were used to determine whether the mutation occurs at a conserved region of the protein and how the substitution may influence protein stability. Conservation analysis showed that phenylalanine at position 97 is highly conserved across species. Because phenylalanine is hydrophobic and serine is polar, the substitution may disrupt hydrophobic interactions or introduce new hydrogen bonding. These results suggest the variant may influence receptor structure or function and could potentially affect thyroid hormone signaling.

Kyah Miller

Oakwood University

The Analysis of Variants of the CHEK2 Gene in Ovarian Cancer

Ovarian cancer is a leading cause of cancer related death among women. According to the National Cancer Institute, it claims over 13,000 lives and affects more 19,000 women annually. The majority of these cases are epithelial ovarian cancer and are often not diagnosed until stage III or later, making treatment more difficult. The aim of this research is to analyze how mutations in the CHEK2 gene affect the progression of ovarian cancer. The CHEK2 gene functions as a cell-cycle checkpoint regulator and an important tumor suppressor. It contains a forkhead-associated (FHA) protein interaction domain that is essential for activation in response to DNA damage. CHEK2 is rapidly phosphorylated in response to replication stress and DNA damage. Once activated, the encoded protein inhibits CDC25C phosphatase, preventing entry into mitosis. It also stabilizes the tumor suppressor protein p53, leading to cell-cycle arrest in the G1 phase. In addition, CHEK2 interacts with and phosphorylates BRCA1, one of the primary genes associated with cancers such as breast and ovarian cancer. Mutations in CHEK2 have also been associated with an increased risk of sarcomas, breast cancer, and brain tumors. To investigate potential disease-associated variants, Simple ClinVar was used to identify CHEK2 variants linked to ovarian cancer, including Ile160Thr, Thr168Ile, Asn171Ser, Tyr327Phe, and Ile364Thr. These variants were further analyzed using the prediction tools PolyPhen-2 and SIFT. Polyphen-2 predicted that all identified variants were probably damaging. These findings were largely consistent with the SIFT results, with the exception of Tyr327Phe, which would be tolerated. Finally, the SWISS-MODEL prediction tool was used to generate a three-dimensional structural model of the CHEK2 protein. The findings from this study may help the biomedical community better understand CHEK2 variants associated with ovarian cancer and may contribute to improved early detection and more effective treatment strategies.

Anaiah Mills

Oakwood University

The Analysis of PRNP of Variants linked to Fatal Familial Insomnia

Fatal Familial Insomnia (FFI) is a rare fatal neurodegenerative disease that affects the thalamus, a region of the brain responsible for regulating sleep. FFI affects 1 to 2 persons per million. This disease worsens over time and becomes life-threatening. The disease is caused by a mutation in the prion protein (PRNP) gene. Treatments are available to slow down the progression of the disease, but no cure has been finalized. The breadth of PRNP variants associated with FFI is understudied, limiting opportunities for knowledge and therapeutic strategies. The purpose of this study is to identify a PRNP variant linked to FFI and investigate the implications of the mutation on the encoded mutant prion protein structure and function. It is hypothesized that the mutation in the identified PRNP variant will alter the mutant prion protein structure, compromising its function. Bioinformatic methods were used for analyses. Simple ClinVar was used to identify the Asp178Asn PRNP variant with a CADD score of 26, indicating the mutation to be likely pathogenic. PolyPhen 2 predicted the mutation to be probably damaging, with a score of 1.00. Three-dimensional protein modeling studies revealed the mutant

protein structure to be different than the wild type. STRING analyses showed that the prion protein interacts with a network of proteins involved, such as the interaction of APP, STPI1, NCAM1, CAV1, FYN, SNCA, HSPA5, GRM5, PRND, and RPSA. These are the predicted functional partners. Collectively, our findings reveal the Asp178Asn PRNP variant linked to FFI that encodes for a mutant prion protein predicted to have a damaged structure and function, with possible implications for its role in a network of proteins all related to the development of FFI. Future studies characterizing the above mutant prion protein are encouraged to promote the understanding of mechanisms contributing to FFI and the development of therapeutic strategies for the disease.

Jalayah Milteer Taylor
Oakwood University

Analysis of CDKAL1 gene variants associated with Type 2 Diabetes

Type 2 diabetes (T2D) is a chronic metabolic disorder in which the body cannot effectively use insulin or produce an adequate amount of it, leading to high blood sugar levels. T2D affects millions of people worldwide and can lead to serious complications such as cardiovascular disease, kidney damage, and nerve damage if left untreated. Genetic factors play an important role in the development of this disease. The CDKAL1 gene (CDK5 Regulatory Subunit Associated Protein 1 Like 1) has been identified as a gene associated with Type 2 diabetes. This gene is involved in insulin biosynthesis and helps regulate pancreatic beta cell function, which is responsible for producing insulin. Variants in the CDKAL1 gene may affect insulin secretion and increase the risk of developing T2D. The purpose of this study is to analyze CDKAL1 gene variants associated with Type 2 diabetes and evaluate their potential effects on protein function. It is hypothesized that certain CDKAL1 variants contribute to the development of T2D by impairing insulin production. To test this hypothesis, ClinVar was used to identify CDKAL1 gene variants associated with Type 2 diabetes, two being p.Arg39Gln and p.Tyr452Phe. Computational prediction tools PolyPhen-2 and SIFT were then used to determine the potential pathogenic effects of these variants on protein function. Using PolyPhen-2, variants p.Arg39Gln and p.Tyr452Phe had predicted mutations to be benign. p.Arg39Gln and p.Tyr452Phe analysis suggests that certain CDKAL1 variants may influence insulin secretion in pancreatic beta cells. Additionally, variant p.Arg39Gln was predicted to affect protein function, while variant p.Tyr452Phe was predicted to be tolerated. These findings suggest that genetic variation in the CDKAL1 gene may contribute to the development of Type 2 diabetes. Further research is needed to better understand the role of CDKAL1 variants and their impact on disease susceptibility.

James Mitchell
Oakwood University

An Analysis of IKZF1 gene variants associated with Leukemia

Leukemia is defined as a cancer of the body's blood-forming tissues, affecting the blood and bone marrow. Leukemic cells rapidly and uncontrollably divide, overcrowding functional blood cells and causing anemia, infections, abnormal bleeding, and pain. Leukemia is the leading cause of childhood cancer, accounting for about 30% of pediatric cancer cases (Dana-Farber Cancer Institute). The goal of this study is to distinguish and analyze the potentially damaging effects of IKZF1 gene variants in relation to leukemia. Although there is a significant correlation between IKZF1 gene mutations and leukemia, the specificity of the IKZF1 gene mutations involved and their definitive effect on the progression of leukemia are undetermined. Utilizing NCBI Simple ClinVar, the IKZF1 gene was related to leukemia, and three missense variants, p.Arg162Gln, p.Val53Met, and p.Asn159Ser were chosen for further analysis. IKZF1 encodes the Ikaros family zinc finger 1 protein, an essential transcription factor for hematopoiesis and a regulator of chromatin remodeling. Injurious IKZF1 mutations are known to cause immune dysfunction, impaired lymphocytic differentiation and reduced apoptosis. PolyPhen-2 and SIFT analysis tools were used to assess the pathogenicity of these variants. PolyPhen-2 predicted that p.Arg162Gln and p.Asn159Ser variants were probably damaging, while the p.Val53Met variant was predicted as benign. SIFT results reported that the p.Arg162Gln and p.Val53Met variants would be tolerated, while the p.Asn159Ser mutation was predicted to affect the function of the protein. These results indicate that these mutations affected the protein function and possibly caused immune dysfunction and abnormal lymphocytic activity. While studies have identified a relationship between

IKZF1 mutations and leukemia, further exploration must be done to fully understand the involvement. Conducting this research advances knowledge pertaining to the correlation of IKZF1 mutation and leukemia progression.

Vaughan Mountain
Oakwood University

An Analysis of ANTXR2 Variants associated with Hyaline Fibromatosis Syndrome

Anthrax is a disease caused by the bacteria *Bacillus anthracis*, known to manifest as either cutaneous, gastrointestinal, or pulmonary anthrax. Anthrax can be potentially fatal, with high mortality rates for cases with delayed treatment. The gene ANTXR2 is an anthrax-associated gene which encodes for the cellular receptor of the anthrax toxin, allowing its entry into cells. ANTXR2 mutations are known to reduce susceptibility to anthrax infection. However, they can also cause HFS, a genetic disease characterized by buildup of hyaline substances in the body. While rare, its link to the ANTXR2 gene allows some insight into its expression. This study analyzes the potential for pathogenicity within variants associated with the gene ANTXR2. While several studies have examined ANTXR2 mutations' relationship with HFS, few have explored its relationship to anthrax protection; understanding the nature of these variants' potential for pathogenicity may increase understanding of ANTXR2's relationship with HFS and of its non-pathogenic mutations' potential effect against anthrax infection. ClinVar was used to identify the ANTXR2 gene and three variants, including p.Leu45Pro, p.Asp464Glu, p.Val270Ile – all missense mutations. PolyPhen2 and SIFT were used to further analyze these variants and their pathogenicity. The results yielded by PolyPhen2 determined that variants p.Leu45Pro and p.Asp464Glu were likely damaging, while p.Val270Ile was predicted to be benign. SIFT also determined that p.Leu45Pro and p.Asp464Glu were predicted to affect protein function, while variant p.Val270Ile was predicted to be tolerated. These results suggest that ANTXR2 variants p.Leu45Pro and p.Asp464Glu, predicted to be damaging, may be related to the expression of HFS. Furthermore, they suggest that variant p.Val270Ile may have potential for protection against anthrax. Although no definitive conclusions have been reached regarding the direct relationship between ANTXR2 mutations and HFS/anthrax protection, this research serves to contribute to the wider study of ANTXR2 mutations and their causative/preventative properties.

Gabrielle Murray
Oakwood University

An Analysis of IRF6 Variants Associated with Non-syndromic Cleft Lip and Palate

Non-syndromic cleft lip and palate (NSCLP) is a type of orofacial cleft characterized by openings or separations of the cleft lip and/or palate. It is a complex condition with a genetic predisposition that occurs in 1 in 600-800 babies worldwide. NSCLP is associated with mutations in Interferon Regulatory Factor 6 (IRF6), which is located on the q arm of chromosome 1. IRF6 encodes transcription factors such as IRF6 that are important for embryonic tissue development and is expressed in osteocytes and hypertrophic chondrocytes of craniofacial tissue. Previous studies have reported NSCLP to be associated with Arginine to Glutamine mutation in IRF6 variants at position 9 of a DNA-binding domain, but other mutations such as Arg9Trp have not been studied. It is hypothesized that Arg9Gln and Arg9Trp mutations will compromise the structural configuration of the IRF6 with possible functional implications. This study aims to determine the effects of Arg9Gln and Arg9Trp variants on the pathogenicity, structural configuration and function of IRF6. Simple Clinvar revealed a CADD score of 32 for the Arg9Gln and Arg9Trp variants. PolyPhen-2 predicted the mutations to be probably damaging with a score of 1. YASARA did not show any notable changes in the mutant IRF6 configurations compared to the wild-type. STRING analysis identified the proteins VAX1, MAFB, NECTIN1, and MSX1 to be associated with IRF6 in the development of NSCLP. Since no structural changes were observed in the protein models, the predicted damages to protein function may be solely related to the mutation being located in the IRF6 DNA-binding domain. Collectively, these findings show that the connection between NSCLP and the Arg9Gln and Arg9Trp variants may be due to changes in the DNA binding abilities of the mutant IRF6. Future studies screening for Arg9 mutations in NSCLP patients are warranted.

Corwin Nance

Huntingdon College

Molecular Dynamics of Highly Pathogenic Variants of the Human Prion Protein (PRP) Associated with Creutzfeldt-Jakob Disease

Creutzfeldt-Jakob disease (CJD) is a lethal neurodegenerative disease caused by misfolded prion proteins. The gene associated with the production of prion proteins in humans is the PRNP gene (CD230) located on the p-arm of chromosome 20 in region 13. The native glycoprotein is a cellular isoform known as PrPC with functions in neuron plasticity and copper buffering. The misfolded form is the result of a missense mutation known as PrPSc; named for the ovine disease "scrapie" in which the pathogenic form was first discovered. Given the rarity of CJD (<350 cases per annum) and its resistance to crystallization, the PrPSc structure is mostly unknown. Utilizing PolyPhen-2, we noted three high pathogenic variants of interest to investigate: D178N, T183A, and E200K. Specifically, these mutant types are forms of familial/genetic CJD (gCJD). These mutations occur on the α -helices indicating location may be a major contributing factor. However, previous research points towards multiple variables involved in pathogenicity. Dynamic molecular modeling of the more common variants can help lead towards determining these other variables. These computational methods can predict mutated proteins' stability, behavior, binding affinity, and structural dynamics, ultimately helping researchers develop treatments.

Charity Ncube

Oakwood University

Analysis of PIK3CA variants and its indirect association with Bipolar Disorder

Bipolar Disorder (BPD) is a mental disease that is characterized by extremely frequent and drastic emotional mood swings. Although this disease is genetically inherited, other challenging environmental factors such as trauma, stress, or substance abuse can trigger BPD. The purpose of this study is to analyze the PIK3CA gene, and its variants associated with Bipolar Disorder while analyzing correlation to cancer. Despite ongoing current research, PIK3CA has still not been clearly linked to BPD. However, PROS has been found to negatively affect signaling pathways leading to neurological damage. Simple Clinvar was used to determine the PIK3CA as a prominent gene with potential correlation to BPD. Three variants were then chosen for further analysis: p.Asp91Asn, p.Arg93Trp, and p.Ille31et. PolyPhen-2 and SIFT were then used to analyze the pathogenicity of the variant caused by the mutations. Mutations in the PIK3CA gene cause PROS (PIK3CA Related Overgrowth syndrome) a rare group of genetic disorders. This gene has been found to be oncogenic and has been implicated in many various cancers. Polyphen-2 predicted variants p.Asp91Asn and p.Arg93Trp to be possibly damaging and variant p.Ille31Met to be benign. SIFT predicted p.Asp91Asn and p.Arg93Trp to affect protein function and p.Ille31Met as tolerated. These findings suggest that p. Asp91Asn and p.Arg93Trp contribute to PROS causing cancer and potential BPD. While definite research on BPD's correlation to the PIK3CA gene is limited, research like this highlights its importance and reemphasizes the gene's contribution to the development of cancer and other oncogenicities.

Nandi Ndlela

Oakwood University

Analysis of CYP4F22 in atopic dermatitis Bioinformational analysis of CYP4F22 in atopic dermatitis.

Atopic dermatitis is a disease characterized by chronic inflammation that causes skin pain. Atopic dermatitis affects an estimated 15% of children and 8% of adults worldwide (National Eczema Organization). Eczema is more prominent and severe in African American children than in any other race in the United States. CYP4F22 is a member of the cytochrome P450 enzyme family, CYP4F22 is responsible for processing drugs, fats, and steroids. P450 is a monooxygenase that catalyzes many reactions involved in metabolism. CYP4F22 gene sequence has a mutation, lamellar ichthyosis will cause moderate to severe at. This study's purpose is to identify and assess the impact of the CYP4F22 gene and the likelihood of mutation associated with eczema. Although the role of CYP4F22 in atopic dermatitis is not fully understood, previous studies have demonstrated its involvement in epidermal lipid synthesis and its association with lamellar ichthyosis. Simple Mendelian Inheritance Patterns within the gene are autosomal recessive. Both copies of the gene must be present to replicate. Simple

ClinVar was used for identifying the CYP4F22 gene in relation to eczema mutations. The factors of CYP4F22 are two autosomal recessive mutations. The first is an uncertain missense (Ser406Phe) and a pathogenic missense (Glu292Lys). Computational tools like PolyPhen-2 and SIFT predicted the orientation of the gene variants as well as the likelihood of the mutation being damaging or benign. SIFT predicted that the Ser406Phe variant would most likely be benign, whereas Glu292Lys is most likely damaging. The Swiss Model displayed the orientation of the gene CYP4F22 as well as the pathogenicity of the mutation before and after the amino acid change. In previous research, pathogenic mutations in CYP4F22 have been used in catalyzing drug and cholesterol reactions. CYP4F22 and its gene family are useful in lipid production and liver cancer. CYP4F22 in the family P450 encodes a secondary gene that creates a 12R lipogenase pathway. Analysis of CYP4F22 genes illustrate that the mutations result in skin barrier dysfunction associated with atopic dermatitis. SIFT tools were able to predict that the Ser406Phe variant is benign, whereas the Glu292Lys variant is pathogenic and detrimental to lipid metabolism within the epidermis. CYP4F22 mutations in atopic dermatitis contribute to atopic dermatitis in dermatological diseases.

Micah Norris

Oakwood Univeristy

Heart Failure's Association with PRKAG2

Heart failure is a cardiovascular condition and the leading cause of death in the United States. When the heart cannot pump sufficient oxygen-rich blood to meet the body's needs, pressure increases in the pulmonary veins. This condition is often caused by weakness of the left ventricle. As a result, people may experience symptoms such as shortness of breath, chest pain, and heart palpitations. The PRKAG2 gene encodes the gamma-2 regulatory subunit of AMP-activated protein kinase (AMPK) enzyme, which regulates the body's circulatory demands. This study aimed to explore how mutations in the PRKAG2 gene contribute to heart failure. Protein variants of PRKAG2 were discovered using Simple ClinVar. In addition, computational tools such as PolyPhen2 and SIFT were used to evaluate missense mutations predicted to impact heart failure. The hypothesis was that missense mutations in PRKAG2 will disrupt AMPK protein function and contribute to the pathogenesis of heart failure. The research investigated three variants: Q563R (pathogenic), T174K (likely benign), and H383Q (variant of uncertain significance). PolyPhen-2 and SIFT suggested that the T174K and H383Q mutations may negatively affect protein function, while Q563R was predicted to be benign despite its pathogenic classification. However, results were inconclusive due to the limited sequence of comparisons available in SIFT. These findings suggest that certain PRKAG2 mutations may influence protein function and contribute to cardiac conditions such as glycogen storage disease and cardiomyopathy, which are linked to heart failure. Understanding conditions related to PRKAG2 mutations may improve knowledge of the genetic mechanisms underlying heart failure and related cardiomyopathies. Further research is needed to clarify the role of PRKAG2 mutations in heart failure phenotypes and to develop targeted gene therapies.

Rachael Oke

Alabama A&M University

Structural Analysis of S162K and Q363R Mutations in HIV-1 Envelope Glycoprotein

Human immunodeficiency virus type 1 (HIV-1) infects host T cells through interactions between the viral envelope (Env) glycoprotein and the CD4 receptor. Changes in the Env protein can affect viral entry efficiency and may influence disease progression. Previous studies have identified a set of seven mutations in the HIV-1 Env glycoprotein that arise during in vitro evolution experiments under antiretroviral selective pressure and are associated with increased cell-cell transmission. Among these, the S162K and Q363R mutations were selected for this study because they occur in structurally important regions of Env that may influence receptor binding and conformational stability. We hypothesized that these substitutions may alter local structural stability and nearby residue interactions within Env. In this study, we evaluated the structural impact of S162K and Q363R using structural modeling and sequence comparison. Differences in amino acid charge and side-chain properties were analyzed to determine how these substitutions affect neighboring residues and functional regions of the Env protein. Constructs containing these mutations were further analyzed

using molecular dynamics simulations to assess conformational flexibility and structural stability relative to the wild-type Env protein. Structural assessment suggests that S162K may influence the local environment of the V2 loop, while Q363R may affect interactions within the gp120 inner domain. Electrostatic interaction energy analysis revealed distinct effects for the two mutations. The S162K mutation showed minimal changes in receptor-binding interactions, whereas Q363R produced larger variations in electrostatic interaction energy, suggesting a stronger effect on receptor binding and Env conformational dynamics. These findings provide insight into how Env mutations may influence viral cell-cell transmission.

Erin Oliver

Alabama A&M University

Using an informatics approach to understand the structure, function, and evolution of head-to-tail adaptor proteins in phages Amok and SunnyD

Bacteriophages (phages) are viruses that infect specific types of bacteria. Phages can attach themselves to the bacterial cell membrane or to membrane receptors and inject their genetic material into the cell causing infection. Bacteriophages that infect actinobacteria encode structural proteins to connect different parts of the virus together during infection and assembly. One important protein would be the head-to-tail adaptor protein, which connects the phage capsid to the tail.

In this study, we focus on head-to-tail adaptor proteins from phages that infect two distinct actinobacteria species: Amok (a Cluster CT phage that infects *Gordonia*) and SunnyD (a cluster EB phages that infects *Curtobacterium*). Similarities and differences between these two head-to-tail adaptor proteins were interrogated using informatic tools such as YASARA and MEGA12. The results showed that although the proteins came from distinct phages, they shared similar regions in their sequences, which may suggest that these proteins are highly conserved even across different bacterial hosts. Differences in protein folding and molecular dynamics remained, however. Protein similarities can suggest that the adaptor proteins likely perform the same functions. In sum, these comparisons can help show how structural features are conserved amongst phages, informing their biological and evolutionary histories.

Andrew Page

University of North Alabama

Characterization of SAMHD1 HIS/ASP HD Domain Variants Disrupting Metal Ion Coordination in Aicardi-Goutières Syndrome

The functional domain for the protein SAMHD1 ranges broadly from positions 111–599. Due to the recent finding that metal ions direct catalytic activity for SAMHD1, this study focused on clinical submissions of missense variants from the highly conserved histidine or aspartic acid native state. Attention is appropriately directed to the catalytic activity since these residues coordinate metal ions essential for dNTP hydrolysis, critical for restricting viral replication and regulating immune responses in Aicardi-Goutières syndrome (AGS). We analyzed SAMHD1 missense variants within the functional domain (111–599) using UniProt, ClinVar, and gnomAD databases, representing sequencing data from over a million individuals. The study prioritized clinical submissions of variants altering highly conserved histidine or aspartic acid residues critical for metal ion coordination. In silico tools (PolyPhen-2, 1-SIFT, CADDNORM, metaLR, Mutation Assessor) assessed pathogenicity, molecular dynamics simulations evaluated impacts on catalytic function, and Dynamic Cross-Correlation Matrix (DCCM) mapped pairs of residues moving together or apart during simulation. From analysis of amino acids in the functional domain range with either histidine or aspartic acid in the native protein, several VUS of interest were identified. Variants such as D120Y, D137H, and H215P disrupted the HD domain's catalytic activity, with in silico tools predicting high pathogenicity. Molecular dynamics simulations showed altered structural dynamics, affecting metal ion coordination by His/Asp residues. DCCM correlated variant D120Y with highest value of movement with other residues across the protein. Variants in SAMHD1's HD domain (111–599) altering conserved histidine or aspartic acid residues disrupt metal ion coordination, which impairs catalytic dNTPase activity essential for immune regulation. These changes disrupt SAMHD1's ability to break down nucleotides, causing too many

nucleotides to build up and triggering harmful immune responses that lead to Aicardi-Goutières syndrome (AGS). Further studies of these VUS are needed to enhance AGS diagnosis and therapeutic development, particularly in diverse populations, which remain heavily unexplored.

Joseph Pope

University of North Alabama

Using Bioinformatics to Characterize Missense Variants of SERPINA1 Associated with Bronchiectasis
Bioinformatics is the intersection of statistics, biology, and computer science. The abundance and open-source nature of data from clinical submissions of genome sequencing can allow one to study genetic mutations without the need for expensive lab equipment and wet-lab time. Bioinformatics research is an important tool for lowering cost and reducing time to wait for genomic results. This study investigates missense swaps of the SERPINA1 gene. SERPINA1 is the gene that carries the instructions to produce the Alpha-1 antitrypsin (AAT) protein. AAT is a protease inhibitor created in the liver that protects the airways from pollutants. Mutations in SERPINA1 can result in the AAT protein to not reach its intended destination; the lungs. Such a deficiency in AAT can cause non-cystic fibrosis bronchiectasis. This study aims to predict the pathogenicity of the missense swaps S38F and S69F. These swaps were chosen due to their proximity to an alpha-helix, their possible harmful effects on other bonds throughout the protein, and their relationship to the pathogenicity of other serine to phenylalanine swaps. Pathogenicity scores were compared to the known pathogenic swap S77F and the average of all known benign scores using the in-silico prediction analysis from SIFT, PolyPhen, REVEL, MetaLR, and CADD scores. ConSurf modeling over 150 homologues revealed conservation scores and predicted if the amino acid positions of interest were exposed, buried, structural, or functional. Molecular dynamic simulations were used to predict the movement of the protein, comparing the wild type and the selected variants of uncertain significance to determine differences in movement. These simulations indicate a statistically significant increase in movement for the selected uncertain variants. These findings contribute to the understanding of genetic factors influencing non-cystic fibrosis bronchiectasis and define the importance of further investigation of these variants for improved diagnostics in clinical diagnosis.

Laila Prentice

Oakwood University

Analysis of TERT Gene associated with Melanoma

Melanoma is a skin cancer that occurs when melanocytes, pigment-producing cells in the skin, reproduce uncontrollably. It is a severe form of skin cancer characterized by aggressive proliferation and resistance to treatment. Melanoma poses a significant health risk to the elderly, who may be more susceptible due to cumulative sun exposure and age-related immune system decline. The gene targeted in this research is TERT (telomerase reverse transcriptase), a ribonucleoprotein that synthesizes telomeric DNA and plays an important role in cellular aging and cancer development. The purpose of this study was to identify and assess the pathogenicity of TERT variants associated with melanoma. Bioinformatic tools including ClinVar, PolyPhen-2, SIFT, and SWISS-MODEL were used to evaluate potential changes in protein structure and function. Four amino acid substitutions were analyzed: Histidine to Tyrosine at position 412, Serine to Threonine at position 191, Leucine to Proline at position 77, and Tyrosine to Cysteine at position 772. PolyPhen-2 predicted that the substitutions Tyrosine to Cysteine at position 772 and Leucine to Proline at position 77 were probably damaging to protein function, both producing scores of 1.000. In contrast, the substitutions Histidine to Tyrosine at position 412 and Serine to Threonine at position 191 were predicted to be benign. SIFT analysis supported these findings by predicting that the Y772C and L77P mutations may affect protein function, while the other substitutions were tolerated. SWISS-MODEL structural comparisons showed subtle but noticeable differences in the 3D protein structure among the variants. This study contributes to existing research on the role of TERT gene mutations in melanoma. Understanding how these variants affect TERT function may provide insight into melanoma development and support future research aimed at improving diagnosis and targeted treatments.

Azrielle Privette

Oakwood University

Adolescent Idiopathic Scoliosis (AIS) as a Product of PAX7 Gene Variations

Adolescent Idiopathic Scoliosis (AIS) is a polygenic deformity characterized by the twisting and curving of the vertebral column exceeding 10°. It can be treated by stretching, bracing, and in extreme cases, surgery. PAX7, the gene chosen for this study, is a transcription factor located near the N-terminus of a 40 amino acid long chain that encourages the growth of muscle stem cells. Without proper support from skeletal muscles, the spinal column cannot develop properly. AIS affects about 1-3% of children ages 10-16 worldwide, that is roughly 10-30 million children. Thus, this study was done to observe the most common missense mutations in PAX7 and shed light on three variants: p.Arg56Cys, p.Ile133Thr, and p.Arg215His. It is hypothesized that each of these mutations will be pathogenic and damaging. SimpleClinVar was used to identify these variants and confirm their pathogenicity. All three variants were linked to congenital and progressive myopathy, which has been linked to AIS. However, p.Arg56Cys was the only variant deemed pathogenic. P.Ile133Thr and p.Arg215His were both of uncertain and conflicting clinical significance. SIFT and PolyPhen were applications used for determining the severity of the pathogenicity of each variant. PolyPhen predicted that p.Ile133Thr and p.Arg56Cys were both highly pathogenic with a score of 1.000, while p.Arg215His had a score of 0.987 which is still considered a damaging mutation. SIFT confirmed, providing each variant a score of 0.00. Suggesting these mutations affect protein function. These findings are consistent with the understanding that the PAX7 gene contributes to skeletal muscle growth, and without it there are phenotypic abnormalities. However, measurable differences in pathogenicity between variants were inconclusive.

Paula Ramirez Mejia

Oakwood University

Analysis of CHRNG Gene Variants (Arg86Cys, Ala44Thr, and Gln238His) and Their Potential Role in Rheumatoid Arthritis

Rheumatoid Arthritis (RA) is a chronic autoimmune disorder characterized by persistent inflammation of the synovial joints, progressive cartilage damage, and systemic immune dysregulation. It affects approximately 0.5–1% of the global population and is more prevalent in women than in men. Although environmental factors contribute to disease development, genetic variation also plays an important role in susceptibility and progression. The CHRNG gene encodes the gamma (γ) subunit of the nicotinic acetylcholine receptor, a ligand-gated ion channel involved in neuromuscular signaling and fetal muscle development. Mutations in this gene have been associated with neuromuscular disorders such as Multiple Pterygium Syndrome and Escobar Syndrome, highlighting its importance in receptor structure and signaling.

This study investigates how specific missense variants in CHRNG may contribute to rheumatoid arthritis. Genetic databases such as ClinVar were used to identify reported variants including Arg86Cys, Ala44Thr, and Gln238His (Landrum et al., 2018). Computational prediction tools SIFT and PolyPhen-2 were employed to evaluate their potential impact. Arg86Cys is predicted to be deleterious by SIFT and probably damaging by PolyPhen-2, suggesting a high likelihood of affecting receptor function. Ala44Thr is predicted to be tolerated by SIFT but possibly damaging by PolyPhen-2, indicating uncertain impact. Gln238His is classified as tolerated/benign by both SIFT and PolyPhen-2, suggesting minimal functional effect. Understanding how CHRNG variants influence receptor function may provide insight into molecular mechanisms that contribute to inflammatory pathways involved in rheumatoid arthritis. Identifying pathogenic variants may support future research aimed at improving diagnostics and developing targeted therapeutic strategies.

Jade Ray

Alabama A&M University

From Wastewater to the Clinic: Comparing CTX-M Antibiotic Resistance Proteins from Phages

Antibiotic resistance continues to be a serious and growing public health issue, especially among bacteria in the Enterobacteriaceae family. Species such as *Enterobacter hormaechei* are increasingly associated with hospital-acquired infections and multidrug resistance. One major reason resistance spreads so effectively is because antibiotic resistance genes can move between bacteria, including during infections by bacteriophages. Wastewater systems, including both municipal and hospital sources, contain large populations of bacteria and bacteriophages, making them important environmental reservoirs for these genes. One significant resistance mechanism involves beta-lactamase enzymes, particularly those encoded by the blaCTX-M gene. CTX-M enzymes can inactivate beta-lactam antibiotics such as cephalosporins, reducing treatment effectiveness. While blaCTX-M is commonly identified in clinical Enterobacteriaceae isolates, it has also been detected in bacteriophages found in wastewater. This study uses computational methods to identify and compare CTX-M beta-lactamase proteins from LAU1 and P7. Through sequence analysis and three-dimensional structural modeling, conserved catalytic residues and active-site features are examined. By comparing these structural characteristics, this project evaluates whether environmental phage-associated enzymes resemble clinically relevant enzymes linked to *Enterobacter hormaechei*, helping to assess the potential connection between environmental reservoirs and clinical antibiotic resistance.

Me'Aira Richardson

Alabama A&M University

Investigating two CXCR4 VUS and their impact on protein structure, function, and HIV-1 Env binding
CXCR4 plays an important role in cell signaling and entry mechanisms.

Mutations in CXCR4 have been associated with immune system disorders and disease susceptibility, making it an important target for genetic research. CXCR4 also serves as a co-receptor for Human Immunodeficiency Virus (HIV) entry into host cells. During infection, HIV binds to the CD4 receptor and a chemokine coreceptor such as CXCR4 to gain entry into immune cells. In this study, we examined two Variants of Uncertain Significance (VUS) in the CXCR4 gene to evaluate its potential impact on structure, function, and HIV Env binding. Using prediction tools, we analyzed amino acid substitutions and their location within the CXCR4 protein. We analyzed two variants, ASN33ILE and TRP102TER, using multiple bioinformatic programs, which predicted that ASN33ILE likely had a benign effect, whereas TRP102TER was shown to be strongly pathogenic. Using multiple bioinformatics approaches including creating a phylogenetic tree, calculating total energies, and conducting docking simulations, we were able to interrogate the impacts of the VUS on receptor-Env interactions. Our analysis indicated that the VUS may influence CXCR4 receptor function depending on the structural context, which could potentially affect HIV interaction with host cells. These findings highlight the importance of computational approaches for prioritizing variants for further biological validation. Overall this study contributes to a better understanding of CXCR4 genetic variation and demonstrates how bioinformatic tools can assist in evaluating variants whose clinical significance remains uncertain.

Tierra Russell

Huntingdon College

Genetic Variants, Diagnostic Disparities, and Sudden Cardiac Death Risk in Black Male Athletes with Hypertrophic Cardiomyopathy

Hypertrophic Cardiomyopathy (HCM), an inherited genetic disorder, is the leading cause of sudden cardiac death (SCD) in athletes. Black males athletes appear to be disproportionately affected despite being more than 50-70% of NCAA and professional sports athletes. This raises questions about genetic risk and healthcare access. This study investigates whether African ancestral populations have comparable or higher frequencies of HCM variants and also examines disparities in diagnosis, management, and outcomes in black male athletes.

Maya Saint-Vil

Tuskegee University

Analysis of a Missense Variant in the MECP2 Protein

The MECP2 gene encodes the MECP2 protein, a methyl binding protein that plays an important role in regulating gene expression through its interactions with chromatin. The protein is highly expressed in neurons and is essential for normal brain development and synapse formation, among other things. Mutations in this gene are the primary cause of Rett Syndrome, a neurodevelopmental disorder characterized by regression, cognitive impairment, and motor issues in young girls. Because many variants in this gene have an uncertain clinical significance, computational analysis is helpful in predicting impact on function. In this study, a missense variant in the MECP2 gene was analyzed to evaluate the potential effects on the protein's structure and function. Variant information was obtained from genetic and protein databases including ClinVar and UniProt. Various computation tools were used to predict the pathogenicity of the variant. Multiple sequence alignment and conservation analysis were then performed to determine evolutionary conservation. Structural models of wild-type and variant proteins were visualized and compared using YASARA Structure. The alignment produced an RMSD value of 0 Å, indicating the overall protein backbone structure remains unchanged. However, mixed pathogenicity predictions were observed. The variant also occurs at a highly conserved position, suggesting importance. The findings demonstrate how the integration of sequence analysis, pathogenicity prediction, and structural modeling can provide insight into the potential effects of genetic variants on protein function.

Elaina Seal

Athens State University

Correlation Between Structural Differences of Wildtype and Mutant miR-133 on Dicer Processing

miRNAs are 22 nucleotide RNAs that play an important role in the regulation of protein synthesis. Mature miRNAs function by binding to a specific mRNA through complimentary base pairing to a target mRNA and inhibiting translation of the mRNA. They must be trimmed from their original transcript in two steps. The second step of the processing is where the pre-miRNA is trimmed from a ~75 nt single stranded hairpin to the double stranded duplex 22 nt duplex by the RNase enzyme Dicer. Mutations in a miRNA sequence have been linked to disability, disease, and tumorigenesis. The mutation 79T>C in miR-133 is associated with familial atrial fibrillation. In this study, we look to correlate the differences between the wildtype and mutant version of miR-133's thermal stability with processing by DICER using molecular dynamic (MD) simulations. Simulations of the wildtype and variant mi-RNA were studied in the absence and in the presence of DICER for a period of 20 and 40 ns. Analysis of the data from the MD simulation indicates variation in the RMSD of the 5' and 3' end between the wildtype and mutant forms of the miR-133 in proximity to the mutation. Based on this data, we conclude that mutation 79T>C disrupts the base pairing between the first nucleotide of the 5' end and allows this nucleotide greater freedom of movement compared to the wildtype. The greater movement of the mutant version of the miR-133 could more easily be positioned into the proper cleavage state by DICER and therefore, an increase in regulation of the target mRNA by the mutant miR-133.

Ashlee Simpson

Oakwood University

An Analysis of FGFR3 variants associated with Multiple myeloma Multiple myeloma is a rare, incurable blood cancer that is characterized by abnormal plasma cells in the bone marrow multiplying uncontrollably, crowding out the normal plasma cells that assist in fighting infection. These malignant plasma cells then produce high amounts of an antibody called the M protein, which leads to kidney damage, high calcium levels, weakened bones, and various frequent infections. The purpose of this study is to identify and evaluate the pathogenicity of FGFR3 variants associated with multiple myeloma. Genetic mutations resulting in multiple myeloma have been reported, but whether they are specifically related to the FGFR3 variant is inconclusive. Simple ClinVar was used to identify FGFR3 as a gene associated with multiple myeloma and its three variants, Tyr373Cys, Lys650Gln, and Arg200Cys. The FGFR3 gene is a member of the fibroblast growth factor receptor (FGFR) family. It provides instructions to create proteins involved in cell proliferation, cell determination, angiogenesis,

wound healing, and embryo development. Computational tools PolyPhen-2 and SIFT were used to determine the pathogenicity of the variants. PolyPhen-2 predicted all three variants to be probably damaging. SIFT predicted the Tyr373Cys variant to be tolerated while the Lys650Gln and Arg200Cys variants affected protein function. Studies on pathological variants of FGFR3 mutations are limited; therefore, a conclusive result has not yet been reached. This study contributes to the existing research concerning implications of the FGFR3 gene associated with multiple myeloma.

Jordae Smith

Oakwood university

Analysis of MED12 variant associated with Uterine Leiomyoma

The MED12 gene encodes a critical subunit of the Mediator complex, a multi-protein regulatory structure that plays a central role in transcription by linking transcription factors with RNA polymerase II. Through this function, the Mediator complex helps regulate gene expression across many biological pathways. Because of its key regulatory role, mutations in MED12 have been associated with several human diseases, including uterine leiomyomas (fibroids), intellectual disability syndromes, and certain cardiovascular abnormalities. Investigating genetic variation within MED12 can therefore provide important insight into the molecular mechanisms that contribute to disease development and progression. In this project, publicly available genomic databases and bioinformatics tools were used to examine MED12 variants, protein domains, and predicted structural effects of amino acid substitutions. Variant information was obtained from genomic repositories and analyzed to determine mutation types, predicted functional impact, and reported clinical significance. The analysis revealed that single nucleotide variants (SNVs) represent the most common mutation type identified in the MED12 gene. Among these, missense mutations were the most frequent functional consequence, suggesting that amino acid substitutions may play an important role in altering MED12 protein function. Many variants were categorized as having uncertain or conflicting clinical significance, highlighting the need for additional functional studies to clarify their biological impact. Computational prediction tools, including SIFT and PolyPhen-2, were used to evaluate the potential effects of selected variants on protein function. Structural modeling was also performed to explore possible changes in protein conformation associated with specific mutations. Together, these analyses demonstrate how bioinformatics approaches can help identify and characterize potentially significant MED12 variants and provide a foundation for future experimental research on their role in disease.

Lanisha Smith

Alabama A&M University

Structural Effects of Q363R and V85A Mutations in HIV-1 Env on Cell to Cell Transmission

HIV-1 continues to be a major global health concern, partly because it spreads efficiently through direct cell-cell contact. The viral envelope glycoprotein (Env) is essential for this process, but it is not always clear how individual amino acid substitutions affect its structure and function. In this study, we focused on two Env mutations, Q363R and V85A, to better understand how they might influence Env structure and potentially impact cell-cell transmission. We hypothesized that these substitutions would cause structural changes that could alter Env stability or conformation. Using YASARA, we generated models of the mutant and wildtype Env structures. Each structure was energy minimized to relieve strain and improve stability, and the models were aligned to compare structural differences. Root mean square deviation (RMSD) was used to quantify how closely the mutants matched the reference structure (PDB: 6NIJ). The Q363R mutant showed an RMSD of 0.155 Å across 2002 aligned residues with 99.85% sequence identity, while V85A showed an RMSD of 0.141 Å across the same 2002 residues with the same sequence identity, indicating that both mutants remain structurally very similar to the reference Env structure. We also compared electrostatic energy values to evaluate potential energetic differences between the structures. The reference structure (6NIJ) had a solvation energy (E_{solv}) of 1.45×10^6 and a vacuum electrostatic energy (E_{vac}) of 1.51×10^6 , resulting in a total electrostatic energy change (ΔE) of -6.04×10^4 kJ/mol. The Q363R mutant showed a slightly more negative ΔE of -6.17×10^4 kJ/mol, while V85A remained nearly identical to the reference with a ΔE of -6.04×10^4 kJ/mol. Overall, both mutants show strong structural conservation compared to the reference Env structure, though small localized differences and slight energetic changes—particularly

in Q363R—may influence Env behavior. These results suggest that even subtle structural and energetic changes caused by single amino acid substitutions could contribute to differences in HIV-1 cell–cell transmission.

Joseph Sousa
Spring Hill College

Exploring VUSs in SYNJ1 Synaptojanin 1

(SYNJ1) is a phosphoinositide phosphatase found in nerve endings. It is important in recycling of synaptic vesicles in neurons. One recent study found a missense mutations in SYNJ1 led to autosomal recessive form of early-onset Parkinson's disease. Other missense mutations, variants of uncertain significance (VUSs) were investigated using data from Clinvar and computational tools found in Polyphen2, SIFT, Alaphamissense, CAD, and Franklin to determine likelihood of being pathogenic. The missense mutation of Arginine to Glutamine at position 250 was investigated further and is predicted to be deleterious based on the computational tools mentioned above.

Hannah Stanley
Tuskegee University

Structural and Functional Analysis of the CYBA p.Ala91Thr Variant in Chronic Granulomatous Disease
Chronic granulomatous disease is a rare inherited immunodeficiency caused by defects in proteins that form the NADPH oxidase complex in phagocytic immune cells. In this project, the CYBA gene, which encodes the cytochrome b-245 alpha chain (p22phox), a membrane-associated component required for reactive oxygen species production during microbial killing, was investigated. The selected variant, NM_000101.4(CYBA):c.271G>A (p.Ala91Thr), is a missense mutation that replaces alanine with threonine at amino acid position 91. This substitution changes a small nonpolar residue to a polar residue, which may affect local protein interactions or structural stability. To evaluate the possible impact of this variant, bioinformatics tools were used to examine sequence conservation and predicted functional effects, and YASARA Structure was used to visualize the protein model and identify the location of the mutation within the structure. Structural comparison of the wild-type and variant residues provides insight into how this amino acid substitution could influence p22phox function and potentially contribute to impaired NADPH oxidase activity in CGD. This project demonstrates how computational tools can be used to investigate the possible effects of a missense variant on protein structure and disease-related function.

TaNiya Steele
Alabama A&M University

Analysis of CXCR4 Variants of Uncertain Significance in HIV-1 Co-Receptor Function

Human immunodeficiency virus type 1 (HIV-1) enters host cells through interactions between the viral envelope glycoprotein (Env), the CD4 receptor, and chemokine co-receptors such as CCR5 or CXCR4. While CCR5-tropic viruses are more common during early infection, CXCR4-tropic variants often emerge during later stages of disease and are associated with accelerated CD4⁺ T-cell decline. Although the CCR5Δ32 mutation is known to confer resistance to HIV-1 infection, the functional effects of many naturally occurring CXCR4 variants remain unclear. This study evaluates two CXCR4 variants of uncertain significance (VUS), Tyr184Cys and Asp262Asn, to determine their potential impact on receptor structure and function. We hypothesize that these variants may alter receptor conformation or affect interactions between CXCR4 and the HIV-1 envelope protein. To investigate this, computational approaches such as sequence conservation analysis, structural modeling, and protein interaction prediction will be used to assess potential changes in receptor stability and binding capability. Understanding the functional consequences of these CXCR4 variants may clarify their biological significance and improve the interpretation of variants identified in genomic studies. Ultimately, this work aims to advance knowledge of host genetic factors involved in HIV-1 entry and provide insight into how genetic variation in CXCR4 may influence viral infection mechanisms.

Javon Stewart

Oakwood University

Bioinformatic Analysis of MPZ Mutations in Pheochromocytoma

Pheochromocytoma is a tumor, typically benign, that arises in the adrenal medulla from chromaffin cells, which secrete catecholamines, a group of neurotransmitters and hormones that maintain homeostasis and regulate the body's response to stress (National Center for Biotechnology Information [NCBI]). The purpose of this study is to evaluate the pathogenicity of the myelin protein zero (MPZ) gene variants and their rare association with Pheochromocytoma. Given that MPZ is infrequently associated with this tumor, there is insufficient evidence to conclude a definite role. We hypothesize that variants associated with MPZ can contribute to the pathogenesis of Pheochromocytoma. To test this hypothesis, ClinVar was used to identify the MPZ gene's frequency in Pheochromocytoma and to identify three missense mutation variants: p.Ser63Cys, p.Gly123Ser, and p.Leu172Pro. The myelin protein zero (MPZ) gene is expressed in Schwann cells and encodes a type I transmembrane glycoprotein, a primary structural protein of the peripheral myelin sheath (NCBI). Polyphen-2 and SIFT, predictive bioinformatic tools, were used to determine the pathogenicity of the three variants. Polyphen-2 predicted the p.Ser63Cys and p.Gly123Ser variants to likely be damaging, while the p.Leu172Pro variant was predicted to be benign. SIFT predicted all three variants to affect protein function. The pathogenicity of these mutations shows that the type I transmembrane glycoprotein was affected, likely also causing an abnormal myelin sheath. Previous studies have widely linked pathogenic mutations in MPZ to Charcot-Marie-Tooth disease rather than Pheochromocytoma. A conclusive result for the MPZ gene's role has not been reached. Since little research has linked the MPZ gene mutation to pheochromocytoma, this study contributes to understanding the genetic implications and rare associations with Pheochromocytoma.

Collin Summers

University of North Alabama

Exploring the Impact of COLQ Mutations on Congenital Myasthenic Syndromes

Congenital Myasthenic Syndrome 5 (CMS 5) is an autosomal recessive disorder characterized by muscle weakness and neuromuscular transmission failure. Mutations found in COLQ are a well-documented cause of this specific type of CMS. Efforts have been made to categorize the possible mutations of COLQ, but there are still over 1600 uncategorized variants. The focus of this study is specifically on positions 402 and 234. The variants were assessed using renderings sourced from AlphaFold, conservation scoring from ConSurf, and 6 common pathogenicity scoring models (CADD, PolyPhen-2, SIFT, REVEL, MetaLR, and Mutation Assessor). Additionally, molecular dynamics simulations were performed using Yasara and the 20-nanosecond macro provided by CODE. Results showed very high pathogenicity scores for both variants. Position 234 held a higher conservation score (ConSurf 9) when compared to position 402 (ConSurf 5), possibly due to position 234 being placed on the triple helix of the COLQ protein. By providing evidence for the classification of these variants of unknown significance, this research will improve patient outcomes for those suffering from CMS 5 as well as provide a starting point for future research into COLQ mutations.

Kyla Tucker

Oakwood University

Study of an ACAN Mutation Variant and Its Association with Osteoarthritis

Osteoarthritis is a chronic, degenerative joint disease that causes discomfort to millions worldwide. Mutations in the Aggrecan Core Protein 2 (ACAN) gene are associated with early-onset osteoarthritis, however there is a gap in our understanding of the ways mutations contribute to Osteoarthritis. This study aims to determine ways in which an identified ACAN variant associated with osteoarthritis could be associated with the development of Osteoarthritis. We hypothesize that the mutation in the identified ACAN variant will be associated with structural changes in the resulting mutant ACAN protein, with possible implications for its function. Bioinformatics tools were used for mutation analyses. Simple ClinVar analysis identified the ACAN Gly578Arg variant with a CADD score of 34 to be associated with Osteoarthritis. Polymorphism Phenotyping v2 (PolyPhen2) predicted the mutation to be probably damaging with a score of 1. Three-dimensional protein modeling studies revealed no

notable structural changes in the 3D conformation of the mutant protein compared to the wild type. STRING analyses showed a protein-protein interaction network for ACAN that included RUNX2, ADAMTS5, MMP13, ADAMTS3, ADAMTS4, and COL2A1. Our findings suggest that the predicted damage in the mutant protein function may not be caused by structural changes but chemical ones from a small non-polar amino acid to a large positively charged one. Future studies targeting the chemical effects of the mutation on protein function, including protein-protein interactions, are warranted to further the understanding of possible mechanisms involved in the development of osteoarthritis.

Jordon Vanterppol

Oakwood Adventist Academy

Analysis of CASP3 and BIRC5 Variants and Role in Cancer Cell Survival; A Bioinformatics Approach
Cancer is a powerful disease that negatively affects millions of people worldwide. Recent studies show that survivin (BIRC5), a survival factor, is expressed in cancer cells and can potentially be secreted. Studies also show that caspase 3 (CASP3), a crucial cysteine-aspartic acid protease that acts as a primary executioner in apoptosis, is also expressed in those cancer cells as well. In this study, we focused on pathways leading to survivin abnormal expression in cancer cells. We used a bioinformatic approach to analyzing variants that could be associated with regulating survivin and caspase 3 expression. The purpose of this study is to look at regulatory pathways of BIRC5 and how it is connected to pro-apoptotic factors including caspase 3. The hypothesis of this study is we would be able to create a universal cancer screen using BIRC5 and caspase 3 as the target protein. First, Clivar was used to identify variants associated within the pathway of BIRC5 and CASP3 being activated or expressed. BIRC5 had 33 missense mutations, while CASP3 had 24 missense mutations. Second, PolyPhen-2 was used to predict if the mutations were pathogenic or benign. We decided to choose two mutations from both BIRC5 and CASP3. Third, Sift was used to see if the mutations could impact the protein function. For CASP3, the two mutations that I chose were Met233Val, which was predicted to be pathogenic, and Thr255Ile, which was predicted to be benign. For BIRC5, both mutations that I chose, Asp16Glu and Pro12Leu were predicted to be benign. Even though one mutation from CASP was predicted to be pathogenic, SIFT predicted every mutation to be tolerated. Data from this study suggests that mutations in BIRC5 and CASP3 needs to be further analyzed regarding its impact on the dysregulation of survivin expression, resulting in its expression or overexpression of survivin seen in cancer cells.

Antonio Ward

Oakwood University

An analysis of DMD variants associated with Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a severe genetic neuromuscular disorder primarily affecting young boys. That is caused by a lack of functional dystrophin protein. It leads to progressive muscle degeneration, weakness, and loss of mobility. This disease affects approximately 1 in 3,500 to 5,000 male births worldwide, estimated that about 15,000 to 20,000 people are living with the condition in the United States. The purpose of this study is to assess the pathogenicity of DMD variants associated with Duchenne's Muscular Dystrophy. ClinVar was used to select the DMD as a gene associated with the DMD disease along with 4 variants, single nucleotide missense mutations, p.Arg3571Cys, p.Gln2376Leu, p.Asp2826Asn, and p.Lys534Asn. The DMD gene encodes for the protein Dystrophin, a rod-shaped cytoplasmic protein that acts as a bridge and connects the cytoskeleton of a muscle fiber to the extracellular matrix. The FASTA sequence of DMD was input into Polyphen2, SIFT, and SWISS MODEL PROT. In this study the Polyphen2 for both p.Arg3571Cys p.Asp2826Asn were predicted as probably damaging. From SIFT, two of the chosen mutations p.Arg3571Cys and p.Gln2376Leu were predicted to affect protein function, while the other two, p.Asp2826Asn and p.Lys534Asn were predicted to be tolerated. In conclusion, these mutations influence the DMD gene and contribute to getting the disease. This is important because understanding the mutations of this gene, allows us to greater research its prevention.

Bria Watkins

Oakwood University

An analysis of the pathogenicity of MYRF variants associated with CDH

Congenital Diaphragmatic Hernia (CDH) is a birth defect that results in a partially formed diaphragm that cannot separate the thoracic and abdominal cavities. This causes abdominal organs to protrude into the thoracic cavity, inhibiting normal organ development during infantile growth. The Myelin Regulatory Factor (MYRF) gene is a membrane-associated protein. It encodes an important transcription factor required for the myeline gene expression in the central nervous system and regulates oligodendrocyte differentiation. Mutations in MYRF can lead to issues in muscle tissue. The purpose of this study is to identify and analyze the variants of MYRF to determine pathogenicity and relation to CDH. Previous research has highlighted MYRF; however little exists. Simple ClinVar was used to determine genes associated with CDH, and MYRF was found to have 2 single missense mutations, p.Gly435Arg and p.Val679Ala. Bioinformatic tools SIFT and PolyPhen-2 were used to further analyze the variants and determine pathogenicity. SIFT predicted both variants to be likely damaging, suggesting a disruption of protein function. PolyPhen-2 classified p. Gly435Arg. as likely damaging, indicating a high likelihood of structural or functional impairment. In contrast, p.Val679Ala was predicted to be likely tolerated, reflecting a small chance of pathogenicity, but likely no disruption. These findings suggest that missense variants in MYRF may contribute to CDH pathogenesis through altered protein function that most likely occurs during fetal development. This study supports continued investigation into MYRF as a candidate gene in the genetic architecture of CDH.

Tabiyell Watson

Oakwood University

An Analysis of Genetic and Clinical Features of Turner Syndrome (45,X) An Analysis of Genetic and Clinical Features of Turner Syndrome (45,X)

Jordan Whalen

Alabama A&M University

Investigating the Structural and Biophysical Properties of HIV-1 Envelope Glycoprotein that Enhance Cell-Cell Transmission: Analysis of R298K and V85A Mutations

Early transmission of HIV-1 is influenced by mutations within the envelope glycoprotein (Env) that can alter viral entry dynamics. In this study, we investigated the structural and biophysical effects of two Env mutations, R298K and V85A, using structural bioinformatics approaches. Structural superposition of mutant and wild-type Env proteins demonstrated near-identical global folding, with RMSD values ranging from 0.33–0.37 Å and TM-scores of ~0.99, indicating minimal structural deviation between variants. To further evaluate potential energetic differences, electrostatic calculations were performed using the Adaptive Poisson-Boltzmann Solver (APBS). Total electrostatic energy values were -6.04×10^4 kJ/mol for the wild-type structure, -6.08×10^4 kJ/mol for R298K, and -6.04×10^4 kJ/mol for V85A. These findings indicate that the mutations do not significantly disrupt the global structure of Env but may introduce subtle energetic changes within the protein's electrostatic environment. Such small shifts in electrostatic interactions could influence molecular binding behavior and provide insight into how specific mutations modulate viral protein function

Patrick Wheatle

Oakwood University

The Role of AP1S3 Gene Variants in the Pathogenesis of Psoriasis

Psoriasis is a chronic (long-lasting) disease in which the immune system becomes overactive, causing skin cells to multiply too quickly. Recent genetic studies have identified mutations in the AP1S3 gene as a contributing factor in certain forms of psoriasis, specifically pustular variants (Setta-Kaffetzi, et al., 2014). The purpose of this study is to identify and evaluate variants associated with Psoriasis. We hypothesize that there are variants associated with psoriasis. To test this hypothesis, ClinVar, PolyPhen-2, SIFT, and SWISS Model were used during this study. Using Simple ClinVar, there were 3 detectable variants associated with the AP1S3 gene, but only 2 of them could be used. The AP1S3 variants Arg33Trp and Phe4Cys were evaluated to see if they were damaging or tolerated. Both were predicted to be probably damaging using PolyPhen-2. Both were also predicted to affect protein function using SIFT analysis. These findings support the hypothesis that AP1S3 mutations may contribute to the pathogenesis of pustular psoriasis by altering protein structure and impairing normal cellular processes. Further investigation into the functional consequences of these variants may improve genetic screening approaches and contribute to the development of targeted therapeutic strategies for psoriasis patients.

MiLisiya Williams

Oakwood University

An analysis of ABCA3 variants and its potential link with hypertension

Hypertension (high blood pressure) is a disease that happens when the force of blood pushing against your artery walls is too high. ABCA3, a gene encoding an ATP-binding cassette transporter protein, has been linked to alter lipid homeostasis and inflammation, processes that can influence vascular function and blood pressure regulation. This study aims to investigate the potential association between ABCA3 variants and hypertension. Understanding whether ABCA3 contributes to vascular lipid metabolism or endothelial dysfunction could provide insight into new genetic pathways influencing blood pressure control. Simple ClinVar was used in the identification of ABCA3 gene. PolyPhen-2, used to predict the amino acid substitution from ABCA3 that was damaging. SIFT was used sed to predict if the amino acid substitution affects protein function. SWISS Modeling was used to create a 3D structure of the gene, both with and without the missense mutation. Analysis of the variants also shows that L326P and E292V variants were predicted to be probably damaging. This finding may be significant because these amino acid switches may disrupt how ABCA3 functions in relation to lipids. Since lipids are important for keeping blood vessels flexible, that could mean that there is a connection to high blood pressure (hypertension). Previous studies have shown that lipid imbalance and oxidative stress contribute significantly to hypertension. Although the ABCA3 gene has primarily been studied in pulmonary disorders, this analysis suggests possible vascular implications of its variants. To improve our knowledge of the genetics of hypertension, more research will be needed to determine whether ABCA3 dysfunction causes endothelial inflammation or lipid signaling.

alexander williams

Oakwood University

Analysis of GLUD1 Variants associated with Hyperinsulinism-Hyperammonea

Hyperinsulinism-Hyperammonea (HI/HA) syndrome is a disorder commonly characterized by its stability and lack of acute symptoms. This study's purpose is to identify and assess the pathogenicity of GLUD1 variants associated with (HI/HA) syndrome. Some genetic mutations responsible for (HI/HA) have been reported. However, studies regarding GLUD1 and its specific role in causing (HI/HA) have not been determined completely inconclusive. While the genetic cause-activating mutations in the GLUD1 gene are well established, many clinical facets of the syndrome remain under investigation. ClinVar, was used to identify GLUD1 as the gene associated with (HI/HA). The GLUD1 gene encodes glutamine dehydrogenase, which is a mitochondrial matrix enzyme that catalyzes the oxidative deamination of glutamate to alpha-Ketoglutarate and ammonia. This enzyme has an important role in regulation of amino acid-induced insulin secretion. It is allosterically induced by ADP and inhibited by GTP and ATP. Activating variants impair the inhibition of GDH by GTP, causing the enzyme to become

overactive, leading to overproduction of insulin. PolyPhen-2 was used to determine the pathogenicity of the variants. The variants analyzed include G499D, S498L, R274K, and Y319C. PolyPhen-2 shows that G499D and S498L are predicted to be benign with scores ranging from 0-0.397. R274K is predicted to be possibly damaging with a score of 0.529, and Y319C was predicted to be damaging with a score of 1. AlphaFold was used to visualize the protein structure. Previous studies confirmed mutations to the GLUD1 to be associated with (HI/HA) syndrome as the mutation causes a large amount of insulin to be produced, which is a byproduct of a mutated GLUD1 gene. However, a conclusive result has not been achieved. This study contributes to the existing research regarding implications of the GLUD1 gene associated with (HI/HA) syndrome.

Junia Williams

Alabama A&M University

Attacking Cutibacterium acnes: modeling phage endolysin proteins & their contribution to replication
Acne affects approximately 85-95% of children and young adults. Understanding how to combat acne-causing Cutibacterium using bacteriophages while also uncovering the structural basis of phage-mediated lysis will allow new forms of treatment and open the doors for further research on endolysin mechanisms and functions. However, there are essential questions that still need to be addressed. Diving deeper into how endolysin enzymes break down bacterial walls from the inside during the lytic cycle and why this is important is one of the questions we can analyze during deep research. We hypothesize that endolysin proteins from Phages KIT08 and Pa615 will show conserved results between their sequences and functions. We examined the endolysins using informatics tools such as sequence alignments, molecular dynamics simulations, and protein modeling to study and compare data about their amino acid sequences and protein structures. This helped us to identify the various structures involved in lysis. Our findings suggested these proteins have similar structures and functions between phages, and they also gave us insights into how to analyze the lytic cycle and identify its usefulness when infecting bacteria like Cutibacterium acnes. We can now apply this in future phage therapy-based studies when identifying the best strategies for treating acne and other bacterial infections.

Taylor Willis

Oakwood University

An Analysis of ASAH1 variants associated with Disseminated Intravascular Coagulation Syndrome
Disseminated Intravascular Coagulation (DIC) is a life-threatening acquired syndrome characterized by widespread, uncontrolled coagulation that consumes platelets and clotting factors, leading to both microvascular thrombosis and severe hemorrhage. Acid ceramidase, encoded by the ASAH1 gene, is a lysosomal enzyme responsible for breaking down ceramide into fatty acids and plays a key role in signaling, inflammation, and apoptosis. This study investigated whether ASAH1 mutations and dysregulation contribute to pro-inflammatory and pro-coagulant mechanisms underlying DIC pathogenesis. We hypothesize that variants associated with ASAH1 may contribute to the pathogenesis of this disease. To test this hypothesis, ClinVar was used to identify ASAH1 as a gene associated with DIC, focusing on three missense variants: p.Gln95Pro, p.Ile31Val, and p.Ala120Pro. Functional impact was assessed using PolyPhen-2 and SIFT. Among the variants analyzed, p.Ile31Val was predicted to be damaging, whereas p.Gln95Pro and p.Ala120Pro were predicted to be tolerated. These findings suggest that not all ASAH1 variants equally disrupt protein structure or function. Our results support the hypothesis that acid ceramidase deficiency may enhance inflammatory responses and dysregulate coagulation pathways, contributing to microvascular thrombosis in DIC. However, the pathogenicity of individual variants varies, indicating a mutation-specific effect on disease severity. Consistent with previous studies, ASAH1 mutations are associated with DIC but represent a broader disease spectrum ranging from severe neonatal visceral forms to more attenuated phenotypes.

Journi Wise

Oakwood Adventist Academy

Molecular Characterization of HGSNAT Variants in Mucopolysaccharidosis Type IIIC

Mucopolysaccharidosis type III (MPS IIIC) is a genetic disorder that occurs when there is an enzyme that breaks down heparan sulfate. It is a neurodegenerative disorder often found in children; it can present in many ways including development delays, behavioral issues, and mild facial differences. As it progresses, it can cause severe neurodegeneration, which is why MPS IIIC is often referred to as childhood Alzheimer's. Specifically, the gene HGSNAT produces the enzyme that is needed for the breakdown of heparan sulfate. Eventually, accumulation causes progressive damage to the central nervous system. The purpose of this study is to identify variants of the gene HGSNAT. To investigate the role of HGSNAT in MPS IIIC we used Clinvar, PolyPhen-2, and SIFT to find the data. When using Clinvar we were able to find 181 missense mutations. PolyPhen-2 was then able to predict the gene mutations as either benign or potentially damaging. After that SIFT is used to predict whether the gene mutations protein is likely to affect its function. Out of the variants we analyzed in the gene, 2 were detrimental while one was benign. This showed that the detrimental mutations could contribute to the accumulation of heparan sulfate. Through this analysis, we were able to pinpoint some variants that could potentially influence the progression of the disease so that those can be prioritized for additional testing. MPS IIIC is a progressive neurodegenerative disorder that occurs from mutations in the HGSNAT gene. These findings provide understanding of the HGSNAT gene mutations and may find helpful insight to further develop research on MPS IIIC.

Blake Woode

Oakwood Adventist Academy

My09b And Ctla4's Effects On Celiac Disease

Celiac disease prevents millions of Americans from digesting gluten effectively. This occurs when gluten causes villi in the small intestine lining to be inflamed, causing chronic diarrhea, bloating, vomiting, and nausea within patients. Researchers have been observing genes associated with celiac disease to determine which are pathogenic. The goal of this study is to identify the genes that affect celiac disease, and determine which are pathogenic. The use of Sift, Simple Clinvar, and Polyphen-2 was useful in finding the genes and isolating the variants of those genes. Using Simple Clinvar, two genes that were affected include MY09B and CTLA4. Point shift Mutations of these genes were then investigated with the use of SIFT. In addition to identifying the mutation pathogenicity, the potential to impact protein function was identified. After further investigation, 4 missense mutations were detected in the gene MY09B, and 5 were detected in the gene CTLA4. Using PolyPhen-2 and SIFT, multiple mutations were predicted to be pathogenic and potentially damaging to the protein. The mutations Arg1621Trp and Arg502Gln were predicted to be pathogenic for gene MY09B. Data from this study suggests that the mutations in MY09B tend to overreact and damage the protein. This data supports our hypothesis that the genes MY09B and CTLA4 are pathogenic.

Michael Woods

Oakwood University

Computational Assessment of AMELX Missense Variants and Their Pathogenic Role in Amelogenesis Imperfecta.

Amelogenesis imperfecta (AI) is an inherited disorder characterized by defective or missing tooth enamel. Due to defective enamel, secondary effects of this disease are cracked teeth, early tooth decay, and increased tooth sensitivity. AI effects on average 1 in 15,000 people in the United States. The purpose of this study is to assess the pathogenicity of the AMELX gene associated with AI. It is predicted that mutations in the AMELX gene are involved in the development of AI. This study aims to evaluate variants associated with this gene. We hypothesize that AMELX variants are associated with the pathogenesis of this disease. The AMELX gene codes for amelogenin, which makes up 90% of the extra cellular matrix protein in enamel. However, defects in AMELX is responsible for Type I hypoplastic AI. To test this hypothesis, ClinVar, was used to identify the AMELX as an AI associated gene along with three single nucleotide missense mutations variants, pMet1Thr, pTrp4Ser, and pAsn30His. The AMELX gene is expressed from somatic genes. Computational tools PolyPhen-2 and SIFT were used

to determine the pathogenicity of the three variants. PolyPhen-2 predicted that pTrp4Ser and pAsn40His variants are pathogenic while pMet1Thr is likely benign. SIFT predicted parallel results to PolyPhen-2. The pathogenicity of these mutations suggests that the functionality of the amelogenin protein was affected, potentially leading to defective enamel. Previous studies have suggested the pathogenic mutations in the AMELX gene to be associated with AI. Tooth discoloration, improper bite, and varied enamel thickness are symptoms of Type I hypoplastic AI associated with AMELX gene. This study contributes to the existing research regarding the possible implications of the AMELX gene associated with AI.

Jonathan Zepeda Trejo

Jacksonville State University

Parkinson's Disease: study of PRKN missense variant Asp243Asn

Parkinson's is a dopaminergic condition that leaves those afflicted with debilitating motor-control issues. Commonly associated with juvenile forms of Parkinson's is parkin (PRKN/PARK2), a gene that provides instructions for making the Parkin protein, an E3 ubiquitin ligase crucial for cellular quality control, especially removing damaged mitochondria (mitophagy) and misfolded proteins. Disruption of Parkin function will lead to an accumulation of damaged proteins and mitochondria, contributing to neuronal death. Our research project aims to analyze a missense variant of uncertain significance NM_004562.3(PRKN):c.727G>A (p.Asp243Asn). A missense variant results in the substitution of a single amino acid that may alter protein structure or function. With the assistance of genomic and protein databases, protein visualization, molecular dynamic simulation, and other bioinformatic tools, our study will characterize the location and conservation, analyze function impact, and establish biological relevance of this specific variant with the parkin protein.