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MISA Case Competition 2025

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Abstract
The MISA Case Competition is an undergraduate research conference organized by the Microbiology and Immunology Student Association (MISA) at Western University. It promotes innovation, collaboration, and scientific thinking among students interested in the life sciences. Now in its third year, the 2025 competition challenged undergraduate teams to develop a novel approach using synthetic biology in personalized medicine to address a health issue or disease of their choice. Teams could focus on prevention, diagnosis, or treatment, and were encouraged to enhance existing strategies by introducing innovative elements supported by current scientific literature. The top six teams presented their proposals to a panel of faculty judges from the Department of Microbiology and Immunology at Western University. The top three teams were awarded based on scientific merit, creativity, and feasibility. We hope our competition inspires the next generation of researchers to push the boundaries of science in meaningful ways. To learn more about our initiatives, visit: https://misawestern.wixsite.com/website/resources-and-projects

Keywords: synthetic biology; personalized medicine; undergraduate research; crispr-cas systems; immunotherapy; disease prevention; gene editing; precision diagnostics; microbial engineering; cell-based therapies

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Conference Abstracts

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Top 3 Oral Presentations

Dual-Targeted CAR-T Therapy For B-ALL: A Research Study on Overcoming Antigen Escape and Relapse

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B-cell acute lymphoblastic leukemia (B-ALL) is an aggressive hematological malignancy involving uncontrolled B-lymphoblast proliferation. To treat blood cancers like B-ALL, chimeric antigen receptor T-cell (CAR-T) therapy engineers patient-derived T cells, destroying malignant cells through antigen-specific targeting. However, long-term efficacy is limited by antigen escape, where tumour cells evade immune surveillance by downregulating the targeted surface antigen, leading to disease recurrence. Conventional CAR-T therapies, like CD19-directed constructs, fail to address this challenge, necessitating the development of multi-antigen targeting strategies. Multi-antigen targeting is an advanced synthetic biology strategy that enhances CAR-T cell specificity and persistence by enabling recognition of multiple tumour-associated antigens, reducing immune escape. Other hematological cancers like multiple myeloma successfully exhibited diminished antigen escape and enhanced tumour clearance in contrast to monospecific designs via dual-targeted approaches. In our study, we apply a tandem CAR (TanCAR) design in B-ALL, incorporating dual single-chain variable fragments (scFvs) for simultaneous binding to CD19 and CD22. This ensures robust cytotoxicity despite functional loss of one antigen. Therefore, a dual-targeted approach may improve CAR-T therapy outcomes, reducing relapse in B-ALL and other hematological cancers.

Wearable Biosensors for Early Detection of Chronic Kidney Disease

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Estimated glomerular filtration rate (eGFR) is the standard tool for assessing kidney function due to its non-invasive, simple, and cost-effective nature, using serum creatinine. However, eGFR equations have historically generalized individual physiological variations under race, particularly muscle mass, leading to systemic inaccuracies, especially in Black individuals. This overestimation results in delayed chronic kidney disease (CKD) diagnosis, which is defined as a GFR <60 mL/min for over three months. This proposal introduces a wearable biosensor that eliminates race as a factor in kidney function assessment and instead, focuses on biomarkers such as creatinine and cystatin C, which provide direct indicators of kidney function. The device, worn as a skin patch, uses a microfluidic system to continuously measure creatinine levels in sweat and employs a colorimetric readout for real-time monitoring. Wireless integration with smartphone applications allows clinicians and patients to track kidney health dynamically. By replacing race-based adjustments with direct physiological measurements, this technology enhances diagnostic accuracy, ensuring earlier CKD detection. Leveraging advances in synthetic biology and personalized medicine, this biosensor offers a scalable, non-invasive, and equitable solution to improve CKD management.

Precision Microbiome Editing: Engineered Probiotics With Quorum Sensing-Activated CRISPR for Targeted Pathogen Disarmament

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The gut microbiome plays a crucial role in overall health, but disruptions from infection or antibiotic use can lead to overgrowth of pathogenic bacteria, causing gastrointestinal diseases. Current treatments use broad-spectrum antibiotics that indiscriminately target both harmful and beneficial bacteria, disrupting the microbiome. Instead, we propose a synthetic biology-based therapeutic approach utilizing engineered probiotics equipped with quorum-sensing-based pathogen detection and CRISPR-mediated gene silencing to selectively neutralize virulent bacteria while preserving gut homeostasis. Targeting unique quorum-sensing molecules, short chemical signals that bacteria use to coordinate behavior, allow for precise identification of pathogenic strains. When these molecules accumulate beyond a critical threshold, they bind to specialized receptors engineered within the probiotic host, triggering CRISPR-Cas9 activation. Guided by a carefully designed guide-RNA sequence, the CRISPR complex then selectively silences virulence genes in the pathogen while leaving beneficial bacteria unaffected. Silencing virulence factors rather than killing bacteria allows for the system to avoid selective pressure for antibiotic resistance, allowing the immune system and microbiome to clear infections while maintaining gut homeostasis. This system can be adapted for gut pathogens by modifying quorum-sensing recognition elements and guide-RNA sequences, offering a personalized medicine platform.

Top 4-15 Abstracts (No Particular Order)

STIck It: The Azithromycin Patch That Pokes Back at Chlamydia

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Chlamydia, the “silent killer” of STIs, is the most prevalent and curable sexually transmitted bacterial infection worldwide. However, current treatment methods, including azithromycin oral tablets, are often financially inaccessible or logistically impractical for developing countries. When left untreated, chlamydial infections may lead to pelvic inflammatory disease, ectopic pregnancies, infertility, and epididymitis. To address these challenges, STIckIt introduces a microneedle patch technology that administers a sustained-release injection of a salt form of azithromycin directly into the bloodstream. The salt form is produced by reacting the antibiotic with HCl, creating a stable azithromycin hydrochloride with enhanced absorption rates. Azithromycin delivered through a microneedle patch is a proven effective treatment method for infected wounds. STIckIt leverages this approach to exhibit equally effective results for chlamydia treatment. STIckIt eliminates the inconvenience of repeated tablet ingestion and enhances storage stability in warmer climates, aligning with conditions in developing countries. This reduces the degradation commonly observed in oral tablets. In addition to its convenience and affordability, STIckIt offers personalized treatment through its case-specific dosages, which tailor the treatment to each individual depending on the infection’s severity level.

Novel Synthetic Biology-Based Therapy for Psoriasis: Genetically Modified Microbes for Targeted Salicylic Acid Delivery

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Psoriasis is a chronic autoimmune condition that causes inflammation in your skin, resulting in thick areas of discolored skin covered with scales called plaques. We propose a novel synthetic biology-based therapy using genetically modified microbes, capable of dispensing salicylic acid in response to psoriatic inflammation. Salicylic acid is a topical keratolytic agent that breaks down keratin, resulting in the exfoliation of psoriatic plaques and the reduction of scaling. The ICS gene, responsible for salicylic acid production, can be sourced from plants like Arabidopsis thaliana: to genetically modify microbes using CRISPR, boosting production for therapeutic purposes. A suitable microbe for this process is Cutibacterium acnes, a natural skin bacterium that survives in inflamed areas and can be utilized for salicylic acid production or modulation in psoriasis

treatment. Using a cytokine-responsive gene circuit ensures that salicylic acid production is directly proportional to the severity of inflammation, and will decrease as the condition improves, preventing excessive use and toxicity. This targeted therapy can be applied through probiotic skin cream or supplements, providing an accessible, non-invasive treatment for psoriasis.

Artificial Intelligence-Enhanced Sweat Patch for Real-Time Cortisol Monitoring and Non-Invasive Anxiety Detection: A Research Study

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Anxiety disorders, characterized by dysregulation of stress-responding brain circuits, are linked to excessive hypothalamic-pituitary-adrenal (HPA) axis activation, causing elevated cortisol levels. Healthy cortisol levels in apocrine and eccrine sweat range from 8.16 ng/mL to 141.7 ng/mL. As current anxiety diagnoses involve psychological assessments, cortisol-detecting sweat patches offer a non-invasive approach to diagnosing and tracking anxiety. Wang et al. (2024) engineered these patches with Molecularly Imprinted Polymers (MIP) to mimic cortisol binding sites, and Porous Chitosan Hydrogel for sweat absorption and transport to an electrode. Cortisol binding to the MIP electrode generates an electrochemical signal that is processed to a smartphone via bluetooth; however, these models are passive. We propose a study on a novel approach incorporating artificial intelligence (AI) driven biological analysis, allowing the patch to interpret prolonged hormonal stress responses and analyze biomarker trends. The AI model assesses physiological patterns in cortisol secretion and potential dysregulation of the HPA axis to help medical professionals monitor and diagnose patients with anxiety. By integrating AI hormone analysis, the cortisol sensor patch provides personalized insights into stress patterns to optimize treatment plans.

Integrating Engineered Probiotics and Synthetic Beta Cells for Type 1 Diabetes Treatment: A Research Study

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Type 1 diabetes (T1D) is characterized by the autoimmune destruction of pancreatic beta cells, leading to insufficient insulin production and the need for lifelong insulin therapy. Current treatments, such as insulin injections, do not offer tailored solutions and fail to address the underlying autoimmune attack. This study proposes a novel dual-therapy approach that combines genetically engineered probiotics with synthetic beta cells to manage T1D. Probiotic Lactobacilli, taken orally, will be designed to produce insulin based on blood glucose levels, regulated by a glucose-sensitive promoter (eg. PptsG or PgapA). It will also synthesize engineered TCR-Tregs that target T1D autoantigens, helping prevent the continuous destruction of pancreatic beta cells. The probiotics will transcribe a specially tagged C-peptide as a byproduct of insulin production, which can be detected via urine strip-tests to assess probiotic activity. This in conjunction with other routine tests like blood sugar levels will help physicians determine if the patient requires administration of synthetic beta cells through skin patches, which have been shown to release insulin and respond to glucose fluctuations efficiently. This dual-therapy approach offers a more personalized and adaptive treatment option, combining immune modulation with glucose regulation.

Integrating Synthetic Biology and Eeg Spectrograms for PCOS Diagnosis and Risk Assessment: A Research Study

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Polycystic ovary syndrome (PCOS), a leading cause of infertility, affects 5%–15% of females worldwide. Women with this endocrine disorder experience a higher frequency of sleep disturbances, including sleep apnea and excessive daytime sleepiness (Fernandez et al., 2018; Sam & Ehrmann, 2019). The impact of sleep on PCOS is further emphasized by studies linking the rs10830963 single-nucleotide polymorphism of the melatonin receptor to both PCOS risk and phenotype. As up to 70% of affected women remain undiagnosed worldwide, this study explores a dual diagnostic approach to improve early detection. A synthetic biology-based electrochemical immunosensor with anti-melatonin-specific antibodies immobilized onto electrode surfaces was used for melatonin level detection. Additionally, electroencephalography (EEG) spectrogram analysis was used to detect distinct brain activity patterns. As both melatonin levels and brain wave activity are essential in

sleep regulation, these methods, when combined, serve as diagnostic markers for PCOS. Data from these techniques on patients with PCOS and the MTNR1B SNP were compiled to train machine learning models to identify brain activity patterns and biochemical melatonin markers associated with PCOS. This approach enables the development of a cost-effective diagnostic tool for early PCOS detection using artificial intelligence to assess personalized risk based on a patient's melatonin levels and EEG activity patterns.

Organ-Literally-On-A-Chip: AI Modelling to Project Mesenchymal Stem Cell Therapy Outcomes for Type 1 Diabetes

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Type 1 diabetes mellitus (T1DM) is an autoimmune disease in which insulin-producing pancreatic β-cells are invaded and destroyed by immune cells. Stem cell therapy is emerging as a promising treatment for T1DM that goes beyond managing symptoms to restore β-cell function in patients. While directed differentiation of embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) into functional islets has successfully restored insulin production in clinical studies, immunosuppressive therapy was critical to ensuring that transplanted cells were not destroyed by host alloimmune and autoimmune responses. Mesenchymal stromal cells (MSCs) hold great potential for overcoming this due to their immunomodulatory properties, but they are largely unexplored in therapy because of variances in donor characteristics, posing a need for greater personalization in donor matching. Organoid-on-a-chip technology merges organoids and organ-on-a-chip systems to create personalized models that reflect patient-specific conditions, enhancing disease modeling. It integrates patient-derived tissues and enables personalized therapies but pose challenges like replicating interactions, maintaining functionality, and achieving vascularization. An effective model must replicate the native microenvironment, maintain genomic stability, incorporate ECM component, and control fluid dynamics while accounting for patient variability to ensure precise disease modeling. This complex process demands substantial resources for accurate patient-specific replication. AI has been used in the creation of organoid-on-a-chip, in controlling and monitoring the quality of the final development objects and has been used to predict drug effectiveness, predict drug responses and to choose better therapeutic options, in the line of personalized medicine. Our solution integrates the ability of AI to project and identify signs of potential immune rejection of the donor stem cells used to create the organoid-on-a-chip. The AI will integrate the data collected from various tests and will check the compatibility of the potential organoid with the patient, before the organoid is produced, saving time, resources and improving efficiency effectively.

Living Ink: CRISPR-Engineered Biosensing Tattoo for Real-Time Diabetes Monitoring

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Diabetes is a growing health issue in Canada, affecting approximately 10% of Canadians, with cases predicted to rise by 2% by 2034. The increasing prevalence of diabetes, along with its associated health complications, underscores the need for accessible, cost-effective, and minimally invasive management solutions. Current methods include finger-prick tests and continuous glucose monitors, which are costly, invasive, and require repeated calibration. A novel approach is a CRISPR-based biosensing tattoo, a non-invasive, renewable alternative for real-time glucose monitoring. This system utilizes engineered E. coli Nissle 1917, a skin-safe, probiotic bacterium, programmed via CRISPR-Cas9 genetic circuits to detect glucose imbalances and trigger a visible pigment shift. As glucose levels normalize, CRISPR-regulated gene expression returns to its baseline state, restoring the tattoo's original appearance, making it a dynamic and easily interpretable visual indicator. This technology utilizes guide RNA to activate (or suppress) pigment-producing genes in response to metabolic changes. While similar technology holds promise, it remains in the development phase, calling for further research to assess its long-term efficacy and safety. Nonetheless, it represents an innovative step toward improving the quality of life for individuals living with diabetes.

Combinational Approach to Enhance Type 2 Diabetes Risk Assessment in Indigenous Populations

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In Canada, Indigenous populations have historically faced social and medical disparities. Prevalence of type 2 diabetes (T2D) has declined, but it remains disproportionately higher among Indigenous populations compared to other ethnic groups. T2D is linked to the aggregation of islet amyloid polypeptide (IAPP). While this relationship is less established within Indigenous groups, it is hypothesized that these groups will have elevated levels of IAPP. Surface-based fluorescence intensity distribution analysis (sFIDA) uses antibodies to label IAPP aggregates with fluorescent markers, allowing detection. For Indigenous populations, sensitivity will be increased by adjusting antibody density and fluorescent thresholds to account for increased IAPP levels. This modification ensures accurate, population-specific evaluations of T2D risk. Moreover, we could profile genetic markers such as the HNF-1α G319S variant, linked to an increased risk of diabetes among Indigenous groups in Canada. Concurrently, nascent drugs to overcome IAPP misfolding could create a new axis for treatment in conjunction with sFIDA and genetic marker analysis of indigenous populations. Present drugs such as EGCG prevent misfolded IAPP aggregation, however, do not prevent misfolding. This novel combination of approaches enables a personalized risk assessment, informing early interventions through proteomic and genomic profiling and targeted prevention strategies.

Nanoparticle and Neurotrophic Facilitated Treatment for Tay-sachs Disease: A Research Proposal

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Tay-Sachs is a genetic disorder triggered by a mutation in the hexosaminidase-A (HEXA) gene, impairing HEXA enzyme function that leads to toxic GM2 ganglioside buildup, disrupting brain function. A scalable cure remains undiscovered due to challenges crossing the blood-brain barrier (BBB) and the disease's progressive neurological damage. We propose a bi-faceted treatment utilizing lipid nanoparticle-mediated CRISPR-Cas9 to pass through the BBB and target the HEXA gene mutation, alongside injecting exogenous brain-derived neurotrophic factor (BDNF) to enhance neuronal strength. Building on lipid nanoparticle-mediated CRISPR-Cas9 success in crossing the BBB to edit the Amyloid Precursor Protein gene in Alzheimer's, we aim to synthesize nanoparticles with sgRNA targeting the HEXA gene's 1278insTATC mutation. SgRNA guides Cas9 to the mutation, inducing a double-stranded break and enabling insertion of the wild-type HEXA template, restoring function and preventing GM2 buildup. In addition to gene-editing, exogenous BDNF will enhance neuronal protection against GM2 by binding to tyrosine kinase receptor B. This mechanism has proven to protect newborn neurons in neurodegenerative diseases similar to Tay-Sachs, including Alzheimer's. Together, both mechanisms address the genetic cause and neurodegenerative effects of Tay-Sachs, providing a scalable treatment strategy.

Engineered T4 Bacteriophage With CRISPR-CAS for Targeted Antibiotic Resistance in *Escherichia coli* and *Klebsiella pneumoniae*

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Bacterial infections have become difficult to treat as antibiotic resistance rises. Alternative options such as bacteriophage therapy have shown promise; however, these phages lack specificity. To enhance current phage therapy treatments, we propose the synthetic engineering of a T4 bacteriophage with a CRISPR-Cas system built into the phage's genome to target antibiotic-resistant genes in T4-specific bacteria, *Escherichia coli* and *Klebsiella pneumoniae*. Treatment with modified T4 bacteriophage and antibiotics can combat bacterial infections. The specific CRISPR array was selected to avoid self-targeting of the phage genome and to fit within size constraints of viral packaging. GuideRNA was included to target antibiotic resistance genes in *E. coli* and *K. pneumoniae,* and an active promoter was added to ensure strong expression. Homologous recombination was used to insert the CRISPR array into the viral genome, with flanking elements specific to open regions in the viral genome. Existing Cas systems in the bacteria were exploited with the antibiotic resistance-specific guide RNA to

cleave at targeted sites. Combining phage therapy and CRISPR-based gene editing has the potential to revolutionize bacterial infection treatment and reduce the global threat of antibiotic resistance.

Personalized Detection of Alzheimer's-associated Microbes Using a Multiplex Carbon Quantum Dot Biosensor: A Research Study

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Alzheimer's disease (AD) is a neurodegenerative disease associated with cognitive decline characterized by the accumulation of amyloid-β plaques (Aβ). While common contributors are aging, sex, and genetics, recent findings implicate viral and microbial etiologies such as herpes simplex virus (HSV) and Porphyromonas gingivalis. Current AD diagnostics primarily target Aβ plaques, however, there is a lack of diagnostics for sensing viral and microbial risk factors. Increasing global AD incidence in aging populations propels the need for personalized diagnostic methods. The proposed diagnostic regimen begins with an oral swab of at-risk patients to curate a profile of microbial proteins and viral serotypes contributing to AD pathology. Based on the individual profiles, diagnostic biosensors can be integrated with non-toxic multiplex carbon quantum dots (CQD) embedded in lipid nanoparticles. The CQDs are conjugated to antibodies for serotype-specific viral proteins and P. gingivalis-associated gingipains, allowing for detection. Monoclonal antibodies embedded in the lipid nanoparticle confer access to the blood-brain barrier via receptor-mediated transcytosis. Functional near-infrared spectroscopy can then be utilized for non-invasive in vivo visualization of the localization of risk-associated proteins. Through risk factor detection, AD therapies can be personalized to target microbial contributors to hinder disease progression.

Precision CRISPR Editing of Superoxide Dismutase Genes: Targeting Oxidative Stress and Age-Related Diseases

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Reactive oxygen species (ROS) are highly unstable molecules due to their unpaired electrons causing molecular damage that results in aging, neurodegenerative diseases, and cancer. Superoxide dismutase (SOD), an enzyme that catalyses the breakdown of ROS, can be used as a therapeutic agent and serve as antioxidant defence for the body. Using CRISPR-based synthetic biology, the promoter region of the SOD gene can be modified to control its gene expression and SOD production. CRISPR targets and attaches to the SOD gene using a guide RNA and modifies it using a Cas-9 enzyme. When SOD production is increased, the concentration of SOD rises, which enhances the ability of the cell to neutralize ROS and ultimately prevents damage from oxidative stress. This treatment is especially favorable for older individuals, as the body's SOD production decreases over time. Additionally, it allows for primary prevention of diseases including cancer and diabetes, as the enzyme breaks down ROS before it accumulates. Ultimately, controlling the production of SOD through methods such as CRISPR is both a preventative measure and a therapeutic agent against ROS-linked diseases.

Conflicts of Interest

The authors declare that they have no conflict of interests.

Authors' Contributions

HA: served as a planning committee for the conference, assisted authors with their abstract submissions, reviewed the abstract submissions and ensured that they adhered to correct formatting standards, drafted the conference abstract booklet, and gave final approval of the version to be published.
FN: served as a planning committee for the conference, assisted authors with their abstract submissions, and gave final approval of the version to be published.
TD: served as a planning committee for the conference, assisted authors with their abstract submissions, and gave final approval of the version to be published.
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