

## 2025 PUGS Case Competition: Age-Related Diseases



Cynthia Lei, BMSc Student [1]\*

[1] Department of Physiology and Pharmacology, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada N6A 3K7

\*Corresponding Author Details: [clei28@uwo.ca](mailto:clei28@uwo.ca)



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### Abstract

The 2025 PUGS Case Competition is the first-ever research case competition organized by the Physiology and Pharmacology Undergraduate Society (PUGS) at Western University. This competition served as an opportunity for competitors to gain critical research analysis skills. Teams of two to four undergraduates were paired with a graduate student mentor and presented a novel research proposal that aligned with the competition's theme: Age-Related Diseases (ARD). The competition spanned from March 14, 2025 to March 24, 2025, culminating in a case competition day, where top teams presented their solutions. Abstracts and presentations explored innovative approaches to diagnosing or treating an ARD of choice, which may include modifying existing disease treatment or incorporating a novel component to overcome its shortcomings. Over 100 participants submitted abstracts proposing solutions across interdisciplinary fields, including Physiology and Pharmacology, Synthetic Biology, Pathology, Health Sciences, Biochemistry, Microbiology and Immunology, Molecular Biology and Genetics, and Artificial Intelligence. The top 50% of winning submissions are featured in this conference abstract booklet, with the top six teams delivering additional oral presentations. Awards were presented to the top three teams. Abstract and presentation scoring was facilitated by a panel of faculty judges from the Department of Physiology and Pharmacology.

**Keywords:** age-related diseases; aging; physiology; pharmacology; diagnostic; treatment; undergraduate research; novel research; western university; PUGS

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### Conference Abstracts

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### Top 3 Oral Presentations

#### **Accessible Smartphone App for Early Cataract Detection Using Photonic Properties and Deep Learning Algorithms**

Emma Zhang, BMSc Student [1], Haoyi Wang, BMSc Student [1]

[1] Department of Schulich School of Medicine & Dentistry, University of Western Ontario, London, Ontario, Canada N6A 3K7

Cataract is the most common cause of treatable blindness worldwide, disproportionately affecting aging populations. Cataracts are characterized by opacification of normally transparent eye lens, leading to visual impairment. Although early diagnosis can enhance treatment outcomes, accessibility to ophthalmologists and variability in their experience in detecting early-stage cataracts lead to inconsistent diagnoses. To provide a more accessible and cost-efficient detection of early-stage cataracts, we employed a search strategy using terms related to cataract, photonics, and artificial intelligence (AI). We propose the use of photonic properties of smartphones due to its affordability and availability even in resource-limited settings, and this noninvasive approach with a smartphone flashlight penetrates the eye to reveal internal abnormalities. User-captured images can then be immediately processed by a deep learning algorithm on an app to segment the image and detect potential signs of cataracts. Additionally, recent study showed success in using smartphone images and AI for corneal disease detection, highlighting potential application for early diagnosis of other eye diseases and broad accessibility for the aging population.

#### **Integrating Machine Learning and Bioprinting for Early Diagnosis and Regenerative Treatment of Osteoarthritis**

Shely Kagan, BMSc Student [1], Pavenpreet Brar, BSc Student [2]

[1] Department of Pathology and Laboratory Medicine, University of Western Ontario, London, Ontario, Canada N6A 3K7

[2] Department of Biology, University of Western Ontario, London, Ontario, Canada N6A 3K7

Osteoarthritis (OA) is a progressive disease-causing pain and cartilage degradation, with current treatments focused on symptom relief rather than regeneration. This study integrates a machine learning (ML) driven diagnostic system with Scaffold-Integrated Bioprinting (SIB) for early OA intervention. The ML system detects joint degradation early using imaging – enabling accurate, scalable screening. The SIB approach then uses this data to deliver personalized regenerative treatments. It combines dynamic bioresponsive scaffolds with adaptive 3D bioprinting for cartilage restoration. This method encapsulates patient-derived mesenchymal stem cells (MSCs), chondrocytes, and a "smart" 3D-printed biomaterial scaffold, which adapts to the biological environment, optimizing properties like stiffness and degradation rate to support cell growth and cartilage regeneration. To further reduce inflammation and support joint repair, HAS2-encoding mRNA hydrogels can be injected to upregulate hyaluronic acid production and promote lubrication. This could reduce the risk of ectopic cartilage formation. By combining precise data-driven early detection with personalized regenerative therapy, this dual approach has the potential to delay OA progression, improve long-term patient outcomes, and reduce the burden on healthcare systems.

### **The Gut-Brain Axis: Microbiome Modulation with Inulin for Parkinson's Disease Prevention**

*Amulya Bhagirath, BMSc Student [1], Avin Sharma, BMSc Student [1]*

*[1] Department of Science, University of Western Ontario, London, Ontario, Canada N6A 3K7*

Parkinson's disease (PD) is a progressive neurodegenerative disorder with increasing evidence of onset associated with the imbalance of bacterial composition in the gut (dysbiosis) and chronic inflammation through the bidirectional gut-brain axis. This study proposes a novel microbiome-targeted intervention with inulin-induced metabolic activation and upregulation of *Lactobacillus acidophilus* for restoration of gut homeostasis and reversal of PD-associated neuroinflammation. Our preliminary investigation showed that inulin supplementation on a petri dish with *L. acidophilus* colonies enhanced the metabolic efficiency of *L. acidophilus* as they lowered gut pH more than the control. Hence, they produce more short-chain fatty acids (SCFAs). This state inhibits pathogenic bacteria and inflammatory cascades that are associated with PD. The strategy has two principles: (1) gut microbiome biomarker panel of SCFA content and pH for early risk detection of PD, and (2) individualized prebiotic regimen to reverse dysbiosis before neurodegeneration is established. This strategy offers a non-invasive, scalable solution that unifies nutritional neuroscience with microbiome therapeutics to redefine prevention of PD; this fills an unmet need in current PD interventions and advance personalized care.

### **Top 4-6 Oral Presentations (Unranked)**

#### **Rewriting Cartilage - Epigenetic Reprogramming to Reverse Osteoarthritis: A Research Study**

*Laksavi Rajakumar, BMSc Student [1], Umaiza Ali, BSc Student [2], Lakshan Sivathasan, BMSc Student [1]*

*[1] Department of Interdisciplinary Medical Sciences, Western University, London, Ontario, Canada N6A 3K7*

*[2] Department of Engineering, Western University, London, Ontario, Canada N6A 3K7*

Osteoarthritis (OA) remains a leading cause of disability, with no cure and limited regenerative treatment options. Our solution introduces epigenetic reprogramming as a novel, non-invasive strategy to restore chondrocyte function and reverse OA at the cellular level. By targeting hypermethylated and histone-modified genes that suppress cartilage repair (e.g., *SOX9*, *COL2A1*), we propose using small molecules or CRISPR-based epigenetic editing tools to reactivate youthful gene expression, restoring cartilage's natural regenerative capacity. This approach, delivered via intra-articular injections, is highly scalable, with the potential for widespread application across various clinical settings and patient populations, and offers a cost-effective alternative to implants or stem cell transplants. Unlike conventional treatments that only address symptoms, this method targets the root cause of OA by rejuvenating aged chondrocytes, potentially preventing disease progression. With epigenetic therapies already transforming oncology and regenerative medicine, this innovative strategy holds a breakthrough to redefine OA treatment, ushering in a new era of regenerative medicine.

#### **Personalized Microbiome Banking for Fecal Microbiota Transplantation: Treating Alzheimer's Disease Through the Microbiota-Gut-Brain Axis**

*Saarah Fehmi, BSc Student [1], Fatima Sajid, BMSc Student [2], Hafsa Asim Rao, BMSc Student [2],*

*Safa Awed, BSc Student [3]*

*[1] Department of Biology, University of Western Ontario, London, Ontario, Canada N6A 3K7*

*[2] Department of Medical Sciences, University of Western Ontario, London, Ontario, Canada N6A 3K7*

*[3] Department of Synthetic Biology, University of Western Ontario, London, Ontario, Canada N6A 3K7*

Alzheimer's disease (AD) is the age-related cognitive disorder characterized by the accumulation of amyloid-beta plaques. Emerging research demonstrates that the microbiota-gut-brain axis is a key player in brain A $\beta$  aggregation and neuronal damage. This suggests that the composition of the gut microbiota influences amyloid pathology. This study proposes a therapeutic approach that will use personalized microbiome banking (PMB) to enhance the procedure of fecal microbiota transplantation (FMT). By storing a healthy microbiome at a younger age, PMB allows for transplantation later in life if required. This reduces the risks associated with donor selection compatibility, immune mismatches, and potential transmission of undesirable traits. Restoring gut microbial balance through PMB-FMT could help modulate microbial metabolites, including short-chain fatty acids, which play a role in maintaining gut barrier integrity and support brain function through the gut-brain axis. As a result, PMB-FMT can regulate amyloid beta-protein. Preliminary findings of using FMT for AD indicate that microbiota dysbiosis in AD patients correlates with increased gut permeability and exacerbated neurodegeneration. This personalized, non-invasive intervention offers a patient-specific strategy to mitigate Alzheimer's

progression by addressing underlying metabolic and inflammatory pathways. Future clinical trials will be crucial in validating this PMB-FMT method as an innovative approach to AD therapeutics.

### **Rosmarinic Acid and N-Acetyl Carnosine: A Targeted Approach Through Solid Lipid Nanoparticles for Cataract Treatment**

*Prisha Bhavsar, BHSc & Scholar's Elective Student [1], Gina Chen, BMSc Student [2], Saira Detho, BMSc Student [2], Suhani Panjwani, BMSc Student [2]*

*[1] Department of Health Sciences, University of Western Ontario, London, Ontario, Canada N6A 3K7*

*[2] Department of Science, University of Western Ontario, London, Ontario, Canada N6A 3K7*

Cataracts are the leading cause of blindness, affecting over 10 million people globally. The transparency of the eye lens relies on the tertiary structure and solubility of crystallin proteins. Damage, such as oxidative stress, causes crystallin to denature, forming insoluble aggregates that scatter light and result in age-related cataracts. Solid Lipid Nanoparticles (SLN) safely integrate N-Acetyl Carnosine (NAC), a modified antioxidant for non-invasive cataract treatment into the eye while maintaining appropriate toxicity levels. While helping reduce the presence of cataracts by mitigating oxidative stress, this simultaneously strengthens cancer cells by removing obstacles that would hinder their growth. To combat this, rosmarinic acid, a polyphenolic compound, is used due to its strong antioxidant activity through neutralizing free radicals, chelating metal ions, and modulating antioxidant enzymes. In vitro studies show it inhibits proliferation and reduces cancer metastasis. The methodology behind administration mirrors the standard SLN-NAC, except both NAC and Rosmarinic acid are incorporated into the SLN. This ensures that particles travel through the 's blood-ocular layers of the eye, keeping toxicity, corneal hydration, zeta potential, and impedance at desired levels, resolving both concerns.

### **Remaining Top 50% Abstracts (Unranked)**

#### **Targeted RUNX1 mRNA Delivery for Enhanced Cartilage Regeneration in Osteoarthritis Treatment**

*Akshayaa Thayaparan, BSc Student [1], Laasya Patibandla, BSc Student [1], Raina Jemon, BHSc Student [2]*

*[1] Department of Science, University of Western Ontario, London, Ontario, Canada N6A 3K7*

*[2] Department of Health Science, University of Western Ontario, London, Ontario, Canada N6A 3K7*

Osteoarthritis (OA) is a leading cause of disability for 33% of adults over the age of 65. It involves issues with bone matrix maintenance as hypertrophic chondrocytes mineralize the bone matrix, causing tearing of the cartilaginous surface. We propose a novel treatment using *RUNX1* (runt-related transcription factor 1) mRNA delivery, which regulates chondrogenesis. *RUNX1* influences the expression of genes responsible for chondrocyte differentiation, including Sox9, Ihh, and CyclinD1. Upon promoter binding, *RUNX1* facilitates lineage commitment, enhancing cartilage formation and function. To produce the mRNA, we would clone the *RUNX1* gene into a plasmid vector and perform in-vitro transcription to generate RUNX1 mRNA. Protective polyethylene glycol-polyamino acid block copolymer nanomicelles will encapsulate the mRNA for targeted delivery. The RUNX1 nanomicelles will be injected directly into the knee joint via an intra-articular injection, ensuring precise delivery to the damage site. Injections can be repeated every three days for one month. This delivery method maximizes drug concentration and enhances chondrocyte uptake, enabling personalized treatment matched to an individual's aging profile.

#### **Blood-Based Ev Assay for Early Late Diagnosis: A Novel Tdp-43 Biomarker Approach**

*Shreya Parmar, BMSc Student [1], Rania Saidi, BMSc Student [1], Nirja Soni, BMSc Student [1],*

*Serena Wang, BMSc Student [1]*

*[1] Department of Science, University of Western Ontario, London, Ontario, Canada N6A 3KJ*

Limbic-predominant age-related TDP-43 encephalopathy (LATE) is a neurodegenerative disorder associated with TDP-43 protein accumulation, leading to hippocampal atrophy and progressive cognitive decline. Currently, LATE is often misdiagnosed as Alzheimer's disease due to overlapping symptoms, delaying proper management and treatment. No routine diagnostic test exists, and definitive confirmation requires post-mortem neuropathological analysis, underscoring the need for an early, non-invasive biomarker. This study proposes a blood-based assay detecting TDP-43 accumulation within circulating extracellular vesicles (EVs), offering a minimally invasive diagnostic tool. EV-based biomarkers have successfully detected neurodegenerative disease signatures in Alzheimer's and ALS, demonstrating their potential for TDP-43 pathology detection. This method could distinguish LATE from other dementias at earlier stages by isolating neuron-derived EVs from plasma

and employing ultrasensitive immunoassays. As a scalable and cost-effective solution, blood-based TDP-43 screening could be integrated into routine cognitive assessments, broadening accessibility across clinical and research settings. If validated, this biomarker approach could enable early intervention and personalized management strategies, ultimately improving patient outcomes in LATE and other TDP-43 proteinopathies.

### **Enhancing Parkinson's Diagnosis: Early Detection Methods Using Wearable AI Device**

*Aimee Grace, BMSc Student [1]\*, Paleesa Kapoor, BMSc Student [1]\*, Sarwa Khan, BMSc Student [1]\*,*

*Lily Lu, BMSc Student [1]\**

*[1] Department of Science, University of Western, London, Ontario, Canada N6A 3K7*

*\*All authors were equal contributors to this abstract.*

Parkinson's disease (PD) is a progressive, age-related neurological condition affecting over 100,000 Canadians. Finger tremors are the most common early PD symptom and are best detected during sleep transitions. Patients may also exhibit cardiovascular irregularities and changes in skin conductivity. PD diagnosis traditionally relies on clinical assessments, but the absence of early diagnostic strategies delays detection and treatment. An AI-powered wearable wrist device that incorporates gyroscope technology, electrocardiogram (ECG) electrodes and electrodermal sensors (EDA) would enable early detection accessible to a wider population. Gyroscopes measure angular velocity and rotational movement which enables the detection of subtle hand tremors. Using electrodes, an ECG can monitor the electrical impulses that regulate the heartbeat, detecting irregularities that may indicate PD onset. The EDA sensors track skin conductivity using integrated electrodes and provide information on autonomic dysfunction in PD. Using an AI data analysis application, physiological patterns can be monitored over time to detect first signs of PD. This method of earlier detection allows for timely intervention, potentially slowing disease progression and improving patient quality of life.

### **A Multi-Therapeutic Strategy to Combat Age-Related Atherosclerosis Using Antioxidant and Rapamycin Nano Worm Delivery Systems**

*Prathmesh J. Mishra, BMSc Student [1], Vaidehi D. Sadrani, BMSc Student [2], Sai M. Jaladi, BHSc Student [3],*

*Hashmeet S. Kainth, BMSc Student [1]*

*[1] Department of Neuroscience, University of Western Ontario, London, Ontario, Canada N6A 3K7*

*[2] Department of Physiology and Pharmacology, University of Western Ontario, London, Ontario, Canada N6A 3K7*

*[3] Department of Health Science Honours Specialization, University of Western Ontario, London, Ontario, Canada N6A 3K7*

Atherosclerosis (AS) is an age-related degenerative disease, characterized by plaque buildup and vascular stiffening. Common risk factors include hyperlipidemia, diabetes and hypertension with prevalent cases ( $\geq 61\%$ ) occurring in adults  $\geq 65$  years. Early plaque formation is driven by endothelial damage-mediated inflammation due to oxidative stress. Consequently, dysfunctional endothelial nitric oxide synthase perpetuates stress in a positive feedback loop. Oxidative stress can be combatted using antioxidants such as ascorbic acid and glutathione, while the anti-inflammatory agent rapamycin can reduce plaque buildup. Previously, rapamycin delivered with nanoparticles has revealed limitations such as low specificity and drug loading inefficiencies. Nano worms (NW) overcome these issues via enhanced tissue binding and circulation in the bloodstream, along with efficient drug-loading. Furthermore, NWs are MRI-compatible due to metal-oxide composition which enables diagnostic tracking of disease progression. This approach is scalable due to efficient synthesis procedures. This study uses a multi-therapeutic approach where NWs are co-loaded with ascorbic acid, glutathione, and rapamycin to synergistically target early AS symptoms, potentially increasing treatment outcome.

### **Ultrasound-Activated Nanodroplet Therapy: A Non-Invasive Approach for Early Stroke Prevention and Atherosclerotic Plaque Disruption**

*Aria Parvinnejad, BSc Student [1], Artin Heidarzadah, BSc Student [1], Mohammad J. Balar, BMSc Student [2],*

*Sam Dabir, BMSc Student [2]*

*[1] Department of Health Sciences, University of Western Ontario, London, Ontario, Canada N6A 3K7*

*[2] Department of Medical Sciences, University of Western Ontario, London, Ontario, Canada N6A 3K7*

Stroke remains a leading cause of mortality and disability in aging populations, with ischemic strokes often resulting from atherosclerotic plaque rupture in arteries. Current preventive strategies, including lifestyle modifications, statins, and surgical



interventions, are either insufficient or invasive. A non-invasive, targeted solution is needed to mitigate stroke risk before its onset. We propose a novel ultrasound-activated nanodroplet therapy for the early detection and disruption of atherosclerotic plaques, preventing stroke in high-risk aging individuals. Our approach utilizes plaque-targeting perfluorocarbon nanodroplets, functionalized with ligands that selectively bind to inflamed, rupture-prone plaques. Once accumulated, focused ultrasound (FUS) triggers nanodroplet vaporization, converting them into microbubbles that induce controlled cavitation using FUS. This mechanically disrupts plaques without causing damage to the artery and allowing for ultrasound contrast imaging for real-time monitoring. This dual diagnostic-therapeutic platform enables non-invasive, early stroke prevention, reducing the need for high-risk surgical procedures. By integrating targeted plaque dissolution with real-time imaging, this innovation addresses a critical gap in geriatric cardiovascular care, extending healthy aging and reducing stroke-related disability.

### **Fecal Microbiota Transplantation as an Adjunct Therapy for COPD: Addressing Lung Inflammation in Aging Patients**

Monis Sayyid, BMSc Student [1], Rizwan Tahir, BMSc Student [2], Noor Alvi, BMSc Student [1], Andy Lu, BSc Student [3]  
[1] Department of Biochemistry, Western University, London, Ontario, Canada N6A 3K7  
[2] Department of Pathology and Laboratory Medicine, Western University, London, Ontario, Canada N6A 3K7  
[3] Department of Psychology, Western University, London, Ontario, Canada N6A 3K7

Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of mortality in patients 65 years and older, disproportionately affecting aging populations as they experience higher hospitalization rates and worse outcomes. Despite conventional treatments, COPD progression remains difficult to manage due to chronic inflammation and immune dysregulation. Emerging research highlights the gut-lung axis, linking gut dysbiosis—characterized by decreased Firmicutes and Actinobacteria and elevated Bacteroidetes and Proteobacteria—to systemic inflammation and worsening COPD severity. We propose Fecal Microbiota Transplantation (FMT), which offers a minimally invasive, immune-modulating solution. By restoring microbial balance, enhancing protective metabolites, and reducing proinflammatory markers, FMT may improve lung function in older COPD patients without increasing their treatment burden. Murine models suggest FMT reduces COPD inflammation, however clinical translation requires careful evaluation of age-related microbiome shifts and immune response differences. Given the aging population's heightened susceptibility to COPD-related complications, integrating FMT as an adjunct therapy could provide a novel and accessible strategy to mitigate disease progression and enhance quality of life. Further research can optimize FMT protocols for older patients and test FMT with other lung-related illnesses.

### **A Novel Screen for Epithelial Ovarian Cancer in Postmenopausal Women on Hormone Replacement Therapy**

Aaida Ali, BMSc Student [1], Taylor L. Searle, BMSc Student [2]  
[1] Department of Physiology and Pharmacology, University of Western Ontario, London, Ontario, Canada N6A 3K7  
[2] Department of Pathology and Laboratory Medicine, University of Western Ontario, London, Ontario, Canada N6A 3K7

Hormone replacement therapy (HRT) is a common treatment for postmenopausal women that can improve side effects of estrogen deficiency that accompanies aging. However, the treatment increases risk of epithelial ovarian cancer (EOC), the deadliest gynecologic malignancy. EOC has a 90% survival rate, however, 70% of diagnoses are late-stage, which greatly increases mortality rates. Hence, we propose a novel serum test for EOC measuring lactate dehydrogenase levels, a glycolysis enzyme that increases in serum concentrations due to cancer cells' overuse of the fermentation pathway, as well as MAGE-A1 and SP-17 levels, cancer-testis antigens (CTAs) that are overexpressed in early-stage EOC. Trials would involve xenograft female mice with the SKOV3 EOC cell line while lactate dehydrogenase, MAGE-1A, and SP-17 biomarkers would be tracked throughout EOC development to analyse how serum concentrations change throughout progression. Although ovarian tumor composition varies greatly between patients, this serum antigen test, compared to currently established screens, has wider coverage, higher specificity, and consists of well-defined biomarkers that are prevalent during stages I and II of EOC, allowing for development of an EOC screening program for postmenopausal women.

### **Leveraging the Gut-brain Axis in Bioinformatics for Early Alzheimer's Disease Diagnosis and Personalized Therapies**

*Porousha Shokoofeh, BMSc Student [1], Hannah Zemans-Ronthal, BMSc Student [2]*

*[1] Department of Physiology and Pharmacology, University of Western Ontario, London, Ontario, Canada N6A 3K7*

*[2] Department of Microbiology and Immunology, University of Western Ontario, London, Ontario, Canada N6A 3K7*

Alzheimer's disease (AD) is a progressive neurodegenerative disorder traditionally linked to neuritic plaques and neurofibrillary tangles. However, growing evidence implicates the gut-brain axis, suggesting gut microbiome alterations as early disease indicators. AD patients commonly exhibit increased *Escherichia/Shigella*, decreased *Eubacterium rectale*, and reduced microbial diversity. Studies have revealed that individuals with mild cognitive impairment (MCI) and preclinical AD show distinct gut microbiota compositions, even before symptomatic onset. Cumulatively, these findings reveal the potential for early diagnosis of AD through microbiome analysis, data compilation, and machine learning-driven predictive modelling. Bioinformatics is an emerging, rapidly evolving field with significant implications for early disease detection and personalized therapies. By analyzing fecal-derived RNA data using bulk RNA sequencing, machine learning can assess microbiome composition of normal and diseased patients to establish metagenomic databases to improve predictive modeling for AD risk assessment. Combined with established AD diagnostic tests (i.e. cognitive tests), this approach incorporates a multi-faceted perspective on disease risk, enabling a more holistic understanding of the disease. Clinical applications of this approach through dietary modifications, probiotics, or fecal transplants could help modulate the microbiome and potentially delay the onset of AD as further research emerges.

### **Injectable Hydrogel Therapy with Stem Cell Delivery for Intervertebral Disc Degeneration**

*Helen Pham, BMSc Undergraduate [1], Jessica Truong, BMSc Undergraduate [1],*

*Quanghoon Dao, BMSc Undergraduate [1], Zhilun Yu, BMSc Undergraduate [1]*

*[1] Faculty of Science, University of Western Ontario, London, Ontario, Canada N6A 3K7*

Intervertebral disc degeneration (IVDD) affects up to 80% of individuals at some point in their lifetime. It is the leading cause of chronic lower back pain and contributes to over \$100 billion annually in healthcare costs and lost productivity in the U.S. alone. IVDD is a progressive, age-related condition characterized by loss of disc hydration, reduced extracellular matrix integrity, and increased inflammation. This study proposes a novel injectable hydrogel delivery system as a minimally invasive alternative to surgery procedures such as spinal fusion. Current hydrogels for IVDD primarily function as biomechanical cushions, providing temporary structural support but failing to promote tissue regeneration. Our approach integrates mesenchymal stem cells (MSCs) and controlled-release growth factors within a biodegradable hydrogel. This enables both mechanical restoration and biological repair. Unlike traditional stem cell injections, which suffer from low retention and survival rates, the hydrogel encapsulates MSCs and delivers regenerative factors (e.g., TGF- $\beta$ , IGF-1) in a sustained manner. Furthermore, the hydrogel degrades gradually, allowing functional disc tissue to replace the scaffold over time, a feature absent in most existing biomaterial implants.

### **Epigenetic Profiling and Interventions of Parkinson's Disease**

*Behrad Sharghi, BSc Student [1], Leon Novoslavski, BMSc Student [1], Viona Derakhshani, BMSc Student [1]*

*[1] Faculty of Science, University of Western, London, Ontario, Canada N6A 3K7*

Parkinson's is a disease characterized by progressive neurodegeneration, often remaining undetected until advanced motor symptoms appear. There is recent evidence proving epigenetic ties to Parkinson's disease, specifically the methylation of certain genes and DNA sites, that are precursors to the destruction of dopaminergic neurons. The collection of cerebrospinal fluid (CSF) can enable the detection of methylation sites, such as  $\alpha$ -synuclein intron 1 promoter, and/or differential methylation in the VPS28 gene, both of which trigger chain reactions leading to Parkinson's disease development. Detecting these methylation patterns may propose a method for early diagnosis. Since both genes are methylated at CpG sites, a novel methylation assay of the CSF can be achieved through the Infinium Methylation technique. CSF DNA methylation profiling provides accurate readings and is less invasive than tissue-based methods. This epigenetic approach proposes a scalable technique that can facilitate the early detection of Parkinson's disease, opening a window of opportunity for possible neuroprotective therapeutics and enough time for lifestyle and behavioural adjustments, before the disease becomes more severe.

### **Targeted Degradation of Alpha-Synuclein Using A Supercharged Nanoreactor As A Novel Treatment for Parkinson's Disease**

Rick W. Cui, BMSc Student [1], Andreea C. Murariu, BMSc Student [2,3], Gregory W. Chai, BMSc Student [1], Kyra Y. Li, BMSc Student [1]

[1] Department of Physiology and Pharmacology, Western University, London, Ontario, Canada N6A 3K7

[2] Department of Biochemistry, Western University, London, Ontario, Canada N6A 3K7

[3] Department of Pathology and Laboratory Medicine, Western University, London, Ontario, Canada N6A 3K7

While the etiology of Parkinson's disease (PD) remains an ongoing field of research, a leading theory is the  $\alpha$ -synuclein ( $\alpha$ -syn) hypothesis of PD. It is theorised that mutated  $\alpha$ -syn proteins misfold to form insoluble aggregates and impair cellular processes like proteasomal degradation, leading to the disruption of normal neuronal function and cell death. However, current therapies, like dopamine replacement, do not address the underlying pathology of PD. We propose a novel therapeutic approach utilizing a supercharged nanoreactor to selectively degrade  $\alpha$ -syn. The cage-forming protein *Aquifex aeolicus* lumazine synthase (AaLs) spontaneously forms icosahedral, porous structures capable of uptaking and encapsulating both proteolytic enzymes and their substrates. By modifying AaLs to possess a highly positive lumen, we enhance its preferential uptake of the negatively charged protein  $\alpha$ -syn. To ensure specificity, we incorporate the  $\alpha$ -syn-targeting protease cathepsin D, which degrades excess  $\alpha$ -syn while minimizing off-target cleavage. This approach provides a targeted and adaptable protein degradation system. By strategically tailoring the protease's specificity, this strategy can be extended to other neurodegenerative diseases associated with protein aggregation, such as Alzheimer's disease (Tau) and ALS (TDP-43).

### **Lighting the Path to Vision: Optogenetics As A Breakthrough Therapy for Cone-Rod Dystrophy**

Jason Chu, BMSc Student [1], Douglas Lau, BMSc Student [1], Sandra Xu, BMSc Student [1],

Rysisca Yau, BMSc Student [1]

[1] Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada N6A 3K7

Progressive cone-rod dystrophy (CRD) is an inherited retinal disease-causing vision loss, photophobia, and colour vision disturbance in 1 out of 40,000 individuals. Currently without a treatment, this rare condition manifests through an age-exacerbated fashion that is often predisposed by missense mutations in the ABCA4, PRPH2, and RPGR genes. Translational optogenetics offers a promising therapeutic approach to progressive CRD by introducing opsins into surviving retinal cells via a viral vector. These opsins can be stimulated by specific wavelengths of light, which are externally administered through specialized goggles that illuminate the retina, to enhance the optical activity of retinal cells. To maximize treatment effectiveness, individuals at high risk—those with progressive central vision loss or a family history of progressive CRD—can be identified using Full-Field Electroretinography, the current gold standard for early diagnosis. By integrating early detection with translational optogenetics, this combined approach has the potential to offer a novel therapeutic strategy for progressive CRD.

### **Conflicts of Interest**

The author declares that they have no conflict of interests.

### **Authors' Contributions**

CL: founded the 1<sup>st</sup> annual case competition of the Physiology and Pharmacology Undergraduate Society, served as a planning committee for the conference, drafted the conference abstract booklet, and gave final approval of the version to be published.

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