CASE COMPETITION ABSTRACT BOOK OPEN ACCESS

The 1st URNCST Journal Case Abstract Competition: New and Innovative Solutions for the Prevention, Diagnosis, Treatment, and Care of Alzheimer's Disease

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Abstract
The URNCST Journal Case Competition provides undergraduate students with the opportunity to experience the peer review and publication process through participate in a case competition. Participants submit an abstract of a research protocol based on a topic proposed by the URNCST Journal. The following abstracts were submitted by undergraduate students to the 1st URNCST Journal Case Competition held during September 2018. This case competition's topic was new and innovative solutions for the prevention, diagnosis, treatment, and care of Alzheimer's disease. To learn more about this abstract competition and submit your own, please visit: https://urncst.com/index.php/competition/about.

Keywords: Alzheimer's disease; case competition; URNCST Journal

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Conference Abstracts
Note: These abstracts were peer-reviewed for quality of research content following being submitted to the URNCST Journal Case Competition. Abstracts are ordered alphabetically by last names of first authors.

URNCST Journal Case Competition

New and Innovative Solutions for the Prevention, Diagnosis, Treatment, and Care of Alzheimer's Disease Abstracts

Cleaning up Alzheimer's disease with biosurfactants

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Introduction: Alzheimer's disease (AD) is a prevalent form of dementia characterized by degenerating physiological and neurological function. A common trait of AD is the accumulation of extracellular β-amyloid (Aβ) plaques, associated with increased tau protein phosphorylation, which creates neurofibrillary tangles that disrupt neuronal nutrient supply. This study explores the therapeutic use of biosurfactants: surfactant molecules secreted by microorganisms. Surfactants disrupt the surface tension of solvents or living membrane surfaces, dissolving any aggregates that rely on this surface tension.
Methods: 10-month-old wild-type mice and Tg2576 transgenic (tgAD) mice will be divided into four groups: tgAD mice injected with biosurfactant in the cerebrospinal fluid (treatment-AD), tgAD mice given a sham injection (control-AD), wild-type mice administered the biosurfactant treatment (treatment-control), and wild-type mice given a sham injection (full-control). Half of the mice (immediate) in each group will be sacrificed for immediate quantification of Aβ concentration. After a week, the remaining mice (deferred) will undergo behavioural examination and then be sacrificed. Toxicological analysis will detect residual biosurfactant and the safety of its degradation.
Results: Treatment mice, in both immediate and deferred conditions, are expected to have lower Aβ concentrations than their control counterparts. Regarding the deferred condition, treatment mice should show better behavioural test results than control

mice. The biosurfactant concentrations should be negligible from the brain samples due to its half-life and non-toxic degradation.
Conclusion: In determining the significance of the biosurfactant treatment on mice with AD and verifying the safety and short *in vivo* half-life of this treatment, clinical trials can test the success of the biosurfactant therapy in humans.
Implications: Exploring the use of therapeutic biosurfactants could improve the prognosis of those affected by AD and even eradicate the disease. If successful, biosurfactants can be utilized as treatment for many other diseases characterized by accumulation of plaques and other toxic aggregates.

Standardization of circulating microRNAs as clinical biomarkers for reliable, non-invasive, cost-effective Alzheimer's disease diagnosis: A projected protocol
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Introduction: The successful prevention of the onset or progression of Alzheimer's Disease (AD) relies on early and accurate detection. Circulating microRNAs (miRNAs) have received heightened attention as highly conserved, stable, and reproducible biomarkers that allow for discrimination between non-AD, AD, vascular dementia (VD) and mild cognitive impairment (MCI) patients. This study aims to design a diagnostic protocol that can be standardized and applied to clinical practice.
Methods: Recruitment, screening, followed by blood collection from healthy (n = 50), MCI (n = 50), AD (n = 50) and VD (n = 50) patients will provide the required biological specimen. Next generation sequencing will be used to screen miRNAs differentially expressed between the cohorts as candidate miRNAs. qRT-PCR will be performed to validate the expression profile of top 10 candidate miRNA in individual blood samples. Student's t-test will be used to compare the expression of miRNAs between cohorts.
Results: Previous studies that profile circulating miRNA expressions have discovered promising biomarkers predictive of AD with high diagnostic values. The top 10 candidate miRNA levels in this study are expected to be significantly up- or down-regulated in AD when compared to healthy controls, VD, and MCI. A diagnostic/prognostic guide can thus be established as we compute each cohort's miRNA means and ranges, adjusted for other factors.
Conclusion: Plasma/serum miRNA detection assays can be employed to obtain quantifiable and reproducible biomarkers from individuals suspected or at risk of AD. The diagnostic/prognostic guide, with established standardized miRNA predictive scores, can better inform clinicians in selecting the appropriate clinical treatment.
Implications: miRNAs satisfy a number of qualifications of an ideal biomarker, including reproducibility, sensitivity and specificity. A rapid clinical assay is therefore beneficial for AD diagnosis especially due to its progressive nature.

Collaboration of hyperbaric oxygen therapy and $A\beta_{42}$/p-tau_{181} as new Alzheimer's Preventative treatment: A research study
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Introduction: Alzheimer's Disease (AD) is a progressive form of dementia caused by beta-amyloid ($A\beta_{42}$) accumulation between neurons in the brain. Hyperbaric Oxygen Therapy (HBOT) is a novel approach to AD treatment which involves the administration of 100% oxygen, and is proven effective for elevating cognitive function and decreasing $A\beta_{42}$ concentrations in the brain in early stages of AD. The presence of protein tau (p-tau_{181}) in the cerebrospinal fluid (CSF) represents a link between $A\beta_{42}$ deposition and cognitive decline. $A\beta_{42}$/p-tau_{181} will be collected from the CSF to act as a biomarker of the progression of AD. Montreal Cognitive Assessment (MoCA) will be used to determine changes in cognition. This study aims to determine a subpopulation that would benefit most from HBOT, which will be reflected by the amount of $A\beta_{42}$/p-tau_{181} in the CSF of the group that shows most cognitive improvement or stability.
Methods: Fifty patients, (both sexes) ages 65-75, diagnosed at various stages of Minor Cognitive Impairment (MCI), an onset symptom of AD, will undergo lumbar puncture to quantify $A\beta_{42}$/p-tau_{181} levels. Patients will be organized into five groups based on similar cognitive impairment. Patients will be randomized into an experimental group that receives HBOT for 1hr/day, or into a control group that receives no treatment. After 14 days $A\beta_{42}$/p-tau_{181} levels will be collected and MoCA readministered.

Results: Through assessment of $A\beta_{42}$/p-tau_{181} levels in the CSF and its impact on cognitive impairment quantified by MoCA, it is anticipated that patients that receive HBOT will show stabilized or slowed cognitive decline. Results will indicate if greater benefit of HBOT is expected at certain $A\beta_{42}$/p-tau_{181} levels.
Conclusion: The results validate further investigation of $A\beta_{42}$/p-tau_{181} biomarker and HBOT therapy as a solution to prevent and slow cognitive decline.
Implications: The opportunity to further establish preventative treatment for AD, which in turn alleviates the cost of care and treatment for patients.

The role of IRE1 signaling in Alzheimer disease: A research study

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Introduction: Inositol-requiring enzyme 1 (IRE1) is an endoplasmic reticulum (ER) stress sensor that triggers the unfolded protein response during disturbance of protein homeostasis. IRE1 has been linked to Alzheimer disease (AD), which is characterized by the accumulation of amyloid-β peptide (Aβ). However, the mechanism and cause-effect relationship remain controversial. This study aims to elucidate the role of IRE1 signaling in AD.
Methods: Wild type (WT) mice will be sequentially treated with ER stress inducers and IRE1 inhibitors. Morris water maze and biomarker panels will be used to examine changes in symptoms of AD and levels of Aβ deposits. Mouse models of AD will be treated with IRE1 inhibitors and assessed for changes in their memory and learning capacities. In addition, knockouts of the downstream mediators of IRE1 will be generated in WT and amyloid precursor protein (APP) transgenic mice. Student's t-test will be used for all comparisons ($p<0.05$).
Results: Previous studies suggest that ER stress is involved in the pathogenesis of AD. ER stress inducers are expected to trigger symptoms of AD and the deposition of Aβ in WT mice. IRE1 inhibition is expected to alleviate symptoms of AD in WT mice and rescue memory and learning capacities in APP mice. The absence of IRE1 downstream mediators in APP mice is expected to have reduced AD symptoms
Conclusion: IRE1 and its downstream mediators could serve as points of intervention for AD. Generation of knockout models and inhibition of signalling molecules may be used to explore the role of ER stress in the pathogenesis of AD.
Implications: Elucidation of the role of ER stress in AD will provide insights into the molecular mechanisms of AD and identify potential therapeutic targets.

Determining the effects of quality sleep in Alzheimer's patients: A research study

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Introduction: Alzheimer's is a neurodegenerative disease that reduces cognitive function and affects millions of individuals annually. Alzheimer's disease is diagnosed by the accumulation of β-Amyloid components extracellularly in the brain and is a significant cause for concern as current methods of treatment cannot keep up with this increasing epidemic. Lack of sleep has been linked to increased levels of the β-Amyloid peptide henceforth advancing the disease. The body utilizes sleep to eliminate β-amyloid peptides from the brain, and sleep deprivation leads to harmful buildup. This study proposes monitoring the amount of sleep newly diagnosed Alzheimer's patients receive through monthly visits, as it will determine the impacts on Alzheimer's progression.
Methods: Twenty patients will be studied, from the time of diagnosis to five years after. The study will comprise of ten patients from each sex aged 65 to 75. Patients will keep daily logs measuring the amount of sleep received per night and stating its quality. PET scans will be administered in monthly visits to monitor changes in β-Amyloid peptide levels. In addition, cognitive testing such as the Mini-Mental State Exam (MMSE) will be used to observe if cognitive decline is present. The recurrent monthly visits will compare patients with the most nights of undisturbed sleep to patients with continuous disturbed sleep cycles.
Results: It will be established that patients with undisturbed sleep exhibit lower levels of β-Amyloid components and the least degeneration in cognitive function.
Conclusion: Patients with greater amounts of nightly undisturbed sleep are expected to have insignificant advancements of disease.

Implications: The data collected from this study may provide evidence to connect daily sleeping habits to the progression of Alzheimer's Disease, and could be used to implement future treatment plans for current patients while providing guidance for at-risk individuals.

Digital application for critical end of life decisions in Alzheimer's disease: A research study

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Introduction: Alzheimer's disease causes progressive decline in cognitive performance and eventually an inability to make meaningful decisions. Recent research shows that substitute decision makers and healthcare providers are mostly unaware of their patients' future health-care choices. As a result, up to 80% hospitalized Canadians may be at risk for overtreatment with life-sustaining measures towards end-of-life, should they have not made prior arrangements to make their choices known. No digital application (app) exists for people with Alzheimer's disease that facilitates an interactive platform to easily discuss, document and disseminate their preferences for future health care choices. This app will allow vulnerable patients, especially with impending Alzheimer's disease to make plans and ensure that their wishes are known to the relevant people in a widely accessible, interactive, updatable and user-friendly format.
Methods: The primary objective is to develop an innovative app that will help all (community dwellers, residents of retirement/nursing homes and long-term care facilities) with impending Alzheimer's to record their end-of-life care wishes online (or their personal devices) facilitating iterative discussions with the people they choose. Thoughts and decisions will be linked to their chosen substitute decision makers digitally and uploaded into a secure public registry accessible to their healthcare providers. The innovation will be advertised through social media, Alzheimer's society and family physician offices. Data collection will take place through the use of the app: this will allow evaluation of content validity and app effectiveness.
Results: It is anticipated that the app will improve patient-centered care with increased certainty amongst substitute decision makers and health care providers.
Conclusion: This novel app will promote autonomy and communication at a time when patients are most debilitated.
Implications: Patients with Alzheimer's disease will have their autonomy respected. Substitute decision makers will be confidant of the decisions made; resource use may be impacted favourably.

Down-regulated expression levels of serum micro-RNAs as prospective biomarkers for early detection of Alzheimer's: A research protocol

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Introduction: With cases of Alzheimer's disease (AD) escalating globally, there is a prompt need for diagnostic measures that will allow clinicians to correctly diagnose individuals anticipated to have AD. Current research has suggested that specific serum-based micro-RNAs (miRNAs) may serve as efficient indicators of AD pathology in patients than amyloid-beta peptides and tau proteins due to their higher concentrations in blood serum and easier availability for extraction. This protocol will examine current literatures focused on the expression levels of six distinct blood serum miRNAs, identified as miRNA-107, miRNA-137, miRNA-181c, miRNA-9, miRNA-29a, and miRNA-29b, in order to evaluate their potential to serve as possible biomarkers for advanced detection of AD.
Methods: Literature searches were conducted using the PubMed database for meta-analytic studies examining the down-regulation of serum miRNAs in prospective patients. Keywords, including "Alzheimer's disease", and "miRNA", were specified within the database to further identify studies relevant to the protocol.
Results: Expression levels of the serum miRNAs across nine meta-analytic studies demonstrated significant down-regulations in subjects, with miRNA-107 showing consistent down-regulation within all experimental groups when compared to the control groups. Further data from additional studies may demonstrate a similar trend towards a potential association between the down-regulations of these miRNAs and early stages of the disease.
Conclusion: Serum-based miRNAs indicate promising results in detecting Alzheimer's at its primary stage. Implementation of this protocol will therefore lead to further breakthroughs in finding the specific miRNA expression levels for early diagnosis of AD in patients.
Implications: In addition to existing medical imaging technology, using serum-based miRNAs will serve as a convenient minimally invasive diagnostic procedure in order to support the treatment and preventative measures taken to halt the progression of Alzheimer's disease in its initial stage.

Donepezil efficacy for Alzheimer's disease: A transgenic model incorporating micro dialysis of acetylcholine

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Introduction: Alzheimer's disease (AD) requires early detection and treatment to delay rapid neurodegeneration into late stages involving severe memory and daily-living impairments. Clinical trials note the utility of acetylcholinesterase inhibitors, medications that compensate for the cholinergic depletion that is characteristic of AD. However, inhibitors only temporarily improve cognitive functioning rather than slow disease progression. This research seeks to apply a transgenic model to identify the average duration up to which the cholinergic inhibitor, donepezil, promotes cognitions and the fluctuations in acetylcholine levels as a function of medication through microdialysis.
Methods: A transgenic mouse model will be used due to its parallels with AD-related pathologies as found in humans. Donepezil, a medication that has been approved to help treat all stages of Alzheimer's, will be administered as mg/kg per day. There will be three arms (n = 10 per arm); placebo, low dose, and high dose. *In vivo* brain microdialysis will be performed at intervals to evaluate acetylcholine fluctuations. Novel object recognition, a test that detects deficits in learning and memory, will serve as the measurement of cognition.
Results: Differences in acetylcholine levels as identified across time through microdialysis between the arms will be compared with the number of object recognition events to provide an accurate estimation of the timespan and dose to which donepezil improves AD-related pathologies.
Conclusion: The effectiveness of donepezil in improving cognitive impairments of AD has yet to be analyzed through comparisons of medication dosage and temporal distance. This protocol aims to measure acetylcholine levels and the duration whereat inhibitors exert alleviating effects upon symptomatology.
Implications: Through this investigation, identification of neurochemical changes will help develop a better understanding of possible neurological adaptations that result in a reduction of medication efficacy, as well as provide a preclinical trajectory for the diagnosis and long-term medicinal availability for individuals living with AD.

Conflicts of Interest
The author(s) declare that they have no conflict of interests.

Authors' Contributions
MHRC: Assisted authors with their abstract submissions, ensured abstracts adhered to correct formatting standards, sourced and assigned peer-reviewers, drafted the abstract booklet, and gave final approval of the version to be published.
AC: ensured abstracts adhered to correct formatting standards, sourced and assigned peer-reviewers, drafted the abstract booklet, and gave final approval of the version to be published.
JYN: Designed and founded the URNCST Journal Case Abstract Competition, ensured abstracts adhered to correct formatting standards, assisted authors with their abstract submissions, sourced and assigned peer-reviewers, reviewed the drafted abstract booklet, and gave final approval of the version to be published.

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