Capturing Cancer's in It's Early Glow: Pioneering Early Detection Strategies using Light Based Biomarkers (Health Challenge) – *Executive Summary*

The Challenge – Cancer is unique among all global health challenges as it is one of the only diseases that will become *more common* as biomedical innovations eradicate other diseases and extend lifespan. As a leading cause of death worldwide, 2 in 5 people will develop cancer in their lifetime and most surviving patients will experience life altering, negative side effects from current anti-cancer treatments. One unfortunate consequence of such anti-cancer treatment, like chemotherapy, is a syndrome of cognitive impairment that has been colloquially termed "Chemo-Brain" (CB), which remains as the leading source of decreased quality of life amongst the increasing number of cancer survivors. Without predictive and early-detection diagnostic tools, clinicians cannot anticipate which patients are most at-risk of developing CB, thus delaying mitigating interventions. Like the early detection of cancer, without an early diagnosis of CB, the mental health and quality of life of cancer patients declines insidiously, leaving both patients and clinicians with diminishing options. Unfortunately, current cancer diagnostics rely on costly and invasive assays of molecular biomarkers that are highly variable across individuals and must be sufficiently concentrated to achieve detection thresholds, leading to diagnoses at later stages and increased patient mortality. **Thus, there are two challenges that require immediate attention: *ultra early detection of cancer and the early detection cancer-related cognitive impairments like CB*.** Earlier, non-invasive detection is crucial for improved patient survival as current treatments are proving to be much less effective at later stages with known racial disparities of outcomes. Again, what is urgently needed are safe, affordable, and scalable diagnostic tools to detect cancers at earlier stages and monitor side effects of therapies to enhance patient outcomes and quality of life for survivors.

Proposed Project – The main objective of the project is to develop a novel diagnostic imaging platform and signal classification algorithm to non-invasively detect early-stage cancer and chemotherapy-related cognitive impairments, with the ***ultimate goal of reducing mortality rates and enhancing the quality of life for cancer survivors***. We will realize this vision by isolating and characterizing light-based biomarkers of cancer that are naturally emitted from cancerous tissues. While it is well established that all cells continuously emit low-intensity light (10^{-15} W/cm^2), termed ultraweak photon emissions (UPE), their use in biomedicine and early detection technologies is only now being realized. UPEs are a consequence of cellular metabolism, resulting from the oxidation of biomolecules such as lipids, nucleic acids, and proteins. Our group demonstrated that UPE signatures, which span the visible and near-visible electromagnetic spectrum are linked to molecular activity within the cell and can be used as readouts of cell state and behaviour, especially in dysfunctional states like cancer. Advances in single-photon detectors (SPDs) have enabled the unprecedented measurement UPEs from cancer cells at high spatiotemporal resolutions. Our published research indicates that cancer cells express fingerprint-like UPE patterns, and our preliminary data indicate functional brain states correlate with UPE fluctuations. Therefore, ***light-based biomarkers of cancer and CB could represent major breakthroughs toward ultra-early detection***. In Aim 1, we will use in vitro methods to identify light-based biomarkers of proliferation and migration of brain and breast cancer cells. In Aim 2, we will use an array of head- mounted UPE detectors to establish a novel method ("photoencephalography") of predicting cognitive symptoms associated with CB.

Intended Outcomes – The project will deliver a fully non-invasive and affordable biomedical imaging platform and classification algorithm that passively senses naturally emitted light patterns to detect cancer earlier than molecular tests and predict chemobrain before the onset of cognitive symptoms. Unlike current imaging tools (MRI, PET, CT), UPE-based diagnostics use inexpensive and portable optical sensors to capture light-based biomarkers of cell state and fate without the use of external magnetic fields or ionizing radiation. Light-based biomarkers of breast and brain cancer-related proliferation and migration as well as chemotherapy-related cognitive impairment will be characterized. The techniques that we will develop can be applied to detect stroke, metabolic disorders, and many other medical conditions at earlier stages of disease progression. The novelty of the research and its appeal as a biomedical advance will be an important factor in recruiting highly qualified trainees and driving accessible and inclusive scientific innovation. Our team of world-renowned experts will use this opportunity to train the next generation of frontier-pushing scientists to explore equally exciting questions and innovate toward a better world.