TARGETING RETINA MICROVASCULATURE TO IDENTIFY THE LINK BETWEEN DIABETES AND NEURODEGENERATIVE DISEASES (VASCULINK)

GROUND-BREAKING NATURE OF THE PROJECT

The VASCULINK proposes a novel multimodal methodology for the use of photonic technologies in the diagnosis of diabetes mellitus (DM) complications and the development of related dementia, in particular Alzheimer's disease (AD).

In this study, my unique experience in the field of various modern optical imaging techniques and my biomedical background will be used to answer the question of how DM and AD are related, as well as to provide evidence that the eye retina can act as a target for early diagnosis of both pathological conditions. A novel retinal imaging tool will be developed that combines structural and functional retinal imaging techniques, including laser speckle contrast, fluorescence lifetime, hyperspectral and polarization imaging. The Project aims to provide a groundbreaking characterization of retina vasculature in DM and AD, for the first time establishing how cerebral microvasculature and metabolic parameters are altered in these diseases.

KEY CONCEPT AND RESEARCH OBJECTIVES

The Project has **two main scientific challenges (SC)**. The first scientific challenge **SC1** is: **What is the link between DM and AD?** Dementia, in particular AD, and DM are two diseases that are growing at an alarming rate among the world's population. The link between AD and DM has recently been the subject of close study by specialists. Observation of DM patients showed that they were 2 times more likely than other subjects to develop AD for 15 years. These patients were 1.75 times more likely to develop other types of dementia. Among the scientific community, it is increasingly common to find the opinion that AD is the “third type” of diabetes.

Cognitive impairment and dementia associated with DM can be mediated through vascular factors, including primarily the development of microangiopathy. Many studies have focused on altering insulin signaling in the brain as a possible mechanism for the link between AD and DM, but researchers have paid much less attention to the direct effect of vascular dysfunction on the pathogenesis of AD. Vascular problems can contribute to the development of inflammation and oxidative stress in the brain, which in turn can lead to damage to neurons and contribute to the development of AD.

Thus, although the relationship between DM and AD is obvious, it is complex, multicomponent and requires detailed study. At the same time, there are a limited number of instrumental methods that would allow a comprehensive study of the effect of vascular complications of DM on the development of AD.

In this regard, a second scientific challenge **SC2** is: **How to evaluate the development of DM and AD at an early-stage?** It is known the retina and the brain have the same embryological origin. They both originate from the neural tube. Thus, the retina is the only part of the central nervous system that can be noninvasively visualized by optical methods with subcellular resolution and used as “a window into the brain”. Recent studies have shown that people with DM and AD may experience structural and functional changes in the retina. These changes may include thinning of the retinal nerve fiber layer and changes in the retinal blood vessels (changes in stiffness, vessel caliber, branching structure, and fractal dimension). Also, the toxic beta-amyloid peptide (Aβ) was found in the retina of people with AD.

Thus, retinal imaging has the potential as a non-invasive and cost-effective method for detecting early signs of diabetes and dementia and may also make it possible to trace the link between these two pathological conditions.

In this Project, I propose the development of a multimodal optical system that would allow the first time to study a number of parameters of retinal tissue (morphology and stiffness of the vessels, blood velocity and oxygenation, metabolic activity, AGE and Aβ accumulation) *in vivo* and find patterns associated with the development of DM and AD. The Project work program includes ambitious but achievable goals. It has been developed using the track record of my multidisciplinary achievements in biomedical engineering, biophotonics, cell biology, and clinical studies and the unique research environment and world-renowned experts at the Host.