zēlosDx

WINDOW INTO THE BRAIN™

TOOLS TO ENABLE BREAKTHROUGH DISCOVERIES IN BRAIN DISEASE

SEEKING OUT-LICENSING PARTNERS

THE MARKET NEED IN NEUROLOGICAL DISEASES

Neurologic disease and trauma affect over 10 million patients in the US alone and is on the increase [1] associated healthcare costs of $1.3 trillion annually. Brain disorders are the second leading cause of death, and the first cause of severe long-term disability in the world. Unfortunately, this market is challenged by failed drug trials, ineffective treatments, and delayed diagnoses.

A critical missing piece is the lack of low-cost blood testing products that can be used as tools to enable breakthrough discoveries in research and drug development where failures to advance drugs to the market have been notorious. The use of neurological biomarkers can reduce the time required for drug development and improve the success rate of a drug trial. This is the primary market focus of ZelosDx.

TECHNOLOGY OVERVIEW

PHAGOCYTIC CELLS IN PERIPHERAL BLOOD AS A NOVEL DIAGNOSTICS TOOL FOR BRAIN HEALTH

A discovery made by ZelosDx presents a unique opportunity to combine the need for easy access to brain biomarkers with a sufficiently high level for their detection. ZelosDx, with its patented cellular technology termed **WINDOW INTO THE BRAIN**™ (WIB™) was the first to demonstrate that phagocytic cells carrying brain biomarkers can reenter the blood stream, presenting a novel and unrecognized source of molecular biomarkers for neurodegeneration. These phagocytic cells can be detected in peripheral blood, not only in patients with neurologic disease, but even in healthy donors. With their cargo of neurological protein breakdown products these peripheral blood phagocytes provide a novel enriched source of brain-derived biomarkers.

Background:

It is well known that phagocytic cells are recruited to inflamed brain tissue where they engulf debris resulting from disease or trauma [2,3]. More recently it has been shown that such debris is also generated in cognitively normal brains [4,5]. We have shown that phagocytic cells can reenter the blood stream, presenting **a novel and hitherto unrecognized source of molecular biomarkers for neurodegeneration in the aging, diseased, or traumatized brain**.

Neuronal biomarkers have been demonstrated to be useful for the diagnosis of brain trauma (TBI) [7-10], dementia [6,11] or disease [12-18], presenting the potential for early detection of neurodegeneration. But harmful metabolites are also generated in the healthy brain and are cleared through the glymphatic pathway, which allows drainage of solutes from the brain tissue [19]. Glymphatic dysfunction may result in the accumulation of toxic proteins such as A-beta and tau, leading to the invasion of phagocytes and

subsequent neuroinflammation [20], thereby generating a path toward conditions prodromic for neurodegenerative diseases [21,22]. Typically, these molecules cannot spill directly into the blood stream due to the action of the blood-brain barrier (BBB), but even when the BBB breaks down as a result of trauma or disease, their concentration in serum or plasma is near or below detection limits for standard enzyme-linked immunosorbent assays (ELISA).

WINDOW INTO THE BRAIN Commercial Objective is to Out-License

Our goal is to provide such a tool to enable breakthrough discoveries in research, drug development and patient care through single cell analysis. The most efficient approach to reach this research market is to out-license manufacturers the patented ZelosDx technology for incorporation into their blood testing assay systems. **While this technology can be used across a broad set of instrument platforms, we believe there is a unique opportunity to bring this novel cellular approach to flow cytometry.**

This requires a source for the key reagents, i.e. antibodies, which are combined with other reagents into kits, and with appropriate assay development and instrumentation for an instrument reagent package. We are therefore seeking partners with expertise in the development of antibodies, reagents, as well as instruments for the application to flow cytometry. Given the number of potential biomarkers for the detection and monitoring of neuroinflammation, the ideal partner would already have antibodies for various brain-specific biomarkers or can easily develop or acquire them. We have so far focused on biomarkers GFAP, Tau and NfL but various additional biomarkers can be developed, Candidates include polyclonal and monoclonal antibodies for APP, APOE, alpha-synuclein, GFAP, NSE, Tau, pTau-Ser199, pTau-Ser262, pTau-Thr231, and UCH-L1, NfL, TDP-43, and Tau proteins phosphorylated on positions 181, 202, 105, 217, and 396.

We have found that for single cell flow cytometry analysis a blood sample as small as 0.1 - 0.2 ml is sufficient, which may allow for shorter intervals for blood draws in rats, and importantly allows the application of this technology to mice. During our customer discovery interviews the need for better techniques in the study of animal models for neurologic disease have been pointed out as well. These findings have encouraged us to consider the application of ZelosDx's technology and the development of specific products for the rodent market in addition to the human testing applications.

INTELLECTUAL PROPERTY

ZelosDx has one US issued patent relating to the (**WIB™**) technology. (Nayak, R. Methods of detecting a neurological condition via analysis of circulating phagocytes. *US Patent #8,506,933* (2013). Several additional patent applications have been filed by ZelosDx. One is a continuation in part focused on broadening and strengthening the coverage in our issued patents. The second new provisional patent was filed covering our new findings with the goal of lengthening our patent validity timeline.

CONTACT INFORMATION

We hope you are interested in learning more about the ZelosDx technology. You can reach Marie Wesselhoft, President, at 1-520-907-3267 or mwesselhoft@zelosdx.com .

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