

# INTRODUCTION TO MEND™ PROTOCOL

## PERSONALIZED PROTOCOL FOR ALZHEIMER'S DISEASE

MEND™ Protocol simultaneously applies multiple medications and lifestyle changes in a highly-personalized manner to attempt to halt and reverse mild cognitive impairment (MCI) and early stage Alzheimer's disease. MEND Protocol utilizes existing FDA-approved drugs, supplements, lifestyle changes, and medical markers and tests in a novel manner. Personalization of the protocol depends upon an individual's genome, medical test results, comorbidities, current medications, medical history, and other inputs.

MEND Protocol is designed to address the active underlying pathways for Alzheimer's disease including metabolic issues, toxicity, inflammation, and mitochondrial damage. Due to the complexity of the personalization process, the Protocol is realized via health management software. The algorithms are able to incorporate logic to process a wide range of data on an individual's health status and recommend specific interventions matched to the etiology of an individual. The recommendations are different for each individual and change over time.

The analysis algorithm recommends both pharmacological and non-pharmacological components. For example, if synaptic reconstruction and maintenance is needed, then multiple biological mechanisms may require normalization, enhancement, or administration. Examples of these underlying biological mechanisms include: periodically activating autophagy, blocking prionic tau amplification, increasing beta-amyloid clearance, inhibiting beta-amyloid oligomerization, minimizing inflammation, normalizing neurotrophic factors, reducing ApoE E4-mediated signals, reducing stress, reducing tau phosphorylation, restoring cholinergic neurotransmission, and reversing memory loss. Assessing the status of these biological mechanisms involves quantifying and observing hormonal balance, citicoline, C-reactive protein and other inflammation-related markers, diet, exercise, homocysteine, omega-3 acids, sleep, and so on. Interventions targeting specific biological mechanisms are then prioritized and prescribed to optimize key biological mechanisms. Medication doses are specified to an individual's needs. Individuals are re-tested periodically and the protocol is updated as necessary.

## RESEARCH BEHIND THE MEND PROTOCOL

It is increasingly being recognized that the mechanisms in Alzheimer's disease comprise a complex system that a mono-therapy cannot sufficiently treat. The use of combination therapies has increased in the treatment of multiple diseases, such as cancer and HIV.<sup>1,2,3,4</sup>

Research at UCLA's Mary S. Easton Center for Alzheimer's Disease Research has shown that people, symptomatic of cognitive impairment, placed on the MEND Protocol showed improved cognitive function and a reduction in Alzheimer's disease-related symptoms within 3-6 months. Results of this study were published in *Aging* titled "Reversal of cognitive decline: A novel therapeutic program" (Bredesen, 2014). The results suggest that early in the course of the disease, cognitive decline may be driven largely by metabolic processes. Furthermore, the failure of monotherapies to date suggests that a therapeutic system may be a useful platform on which drugs that would fail as monotherapies may succeed as key components of a therapeutic system.

<sup>1</sup>Bredesen, Dale E. "Reversal of cognitive decline: A novel therapeutic approach." *Aging*. September 2014.

<sup>2</sup>Bredesen, Dale E; Varghese, John. "Next generation therapeutics for Alzheimer's disease." *EMBO Molecular Medicine*. June 2013.

<sup>3</sup>Doraiswamy, Murali P; Steffens, David C. "Combination Therapy for Early Alzheimer's Disease: What Are We Waiting for?" *American Geriatrics Society*. 1998.

<sup>4</sup>Stephenson, Diane, et al. "Charting a path towards combination therapy for Alzheimer's disease." *Expert Review Neurotherapy*. January 2015

## WHY OTHER THERAPIES ARE FAILING

Accumulated research is showing that Alzheimer's disease is far more complex than previously thought. Dozens of biological mechanisms need to be brought into a state where they're enhancing a person's cognitive health. There is not a single therapeutic that exerts anything beyond a marginal, unsustainable, symptomatic effect, with little or no effect on disease progression.<sup>1,2,4</sup> Additionally, Alzheimer's disease is rarely seen in isolation; a half-dozen other chronic diseases (and their medications) are often seen in the same person, which must be addressed in concordance with one another.

Of the more-than-40 ongoing Phase 1, Phase 2, and Phase 3 clinical trials for Alzheimer's disease, virtually all involve single-therapy approaches. No such approach is likely to be right for treating Alzheimer's disease. Complexity is the culprit. There are dozens of biological mechanisms, with hundreds of interventions, involved in addressing this disease; and the necessary therapeutics vary by person and change over time. However, the past few decades of genetic and biochemical research have revealed an extensive network of molecular interactions involved in Alzheimer's disease pathogenesis, suggesting that a network-based approach, rather than a single target-based approach, may be feasible and potentially more effective for cognitive decline due to Alzheimer's disease.

## OVERVIEW OF MUSES LABS

Muses Labs, Inc. is located in Research Triangle Park, North Carolina, and is dedicated to helping individuals dealing with a class of chronic diseases with multiple underlying medical causes. This class of diseases is not solved by a single medication; rather, a set of therapeutics must be personalized to the needs of each individual.

Muses Labs applies sophisticated data-driven techniques, in collaboration with deep medical expertise, to address Alzheimer's disease. Muses Labs' infrastructure can reach every person with Alzheimer's disease, as well as their physicians and researchers in the field.

The solution to Alzheimer's disease is an example of a systems-software optimization problem. A new set of algorithms were invented to create personalized therapeutic recommendations. The combination protocol it implements is based on a broad understanding of the pathogenesis of Alzheimer's disease, and aims to achieve Metabolic Enhancement for NeuroDegeneration (MEND) by targeting multiple interrelated biological mechanisms simultaneously.

Muses Labs' information service is used to create and update a personalized protocol, track participant progress, and motivate adherence. This pinpointed protocol can slow the progression of Alzheimer's disease and reverse previous damage, letting individuals return to a normal and productive life.

The infrastructure gathers clinical data from a range of sources – individual's themselves, an individual's medical team, and even Internet-connected devices – to assess the state of their disease, track progress against the disease, and evolve an ongoing set of therapeutic recommendations.

Muses Labs' team comprises prominent Alzheimer's researchers, as well as experts in behavioral science. The seed for the personalized combination protocol has been shown to roll back cognitive decline in a first set of carefully-studied human subjects. Chief Technology Officer, Dr. John Q. Walker, leads the team building the groundbreaking algorithms and managing the data in a high-security, HIPAA-compliant environment.

## THE PROTOCOL PROCESS

The current "state" of the participant is assessed in specific areas pertinent to the biological mechanisms related to the disease, in order to propose a set of prioritized interventions. The assessment information comes from many sources: medical histories, genome sequencing, blood tests, cognitive evaluations, and so on. A genomic assessment that

shows a mutation indicating a strong likelihood for early-onset Alzheimer’s disease will lead down a different logic path than for a participant lacking that mutation. This broad set of values serve as input to the analysis algorithm. The algorithm is designed to 1) describe the condition of the participant, and 2) recommend what should occur next.

Recommendations include best-practice interventions for addressing the goals: medications, supplements, dietary changes, behavioral changes, and even recommendations for additional tests or more details of their medical history (as these can illustrate trends, ranges, effects, or correlations). Inputs from family members are also sought, as well as general input gathered across the entire population. The analysis algorithm learns, has feedback loops, and creates output tailored to a participant and their team – and its output changes over time, as more input is received. This complexity is generally far beyond the constraints of a physician’s practice, thus requiring a system as described here.

The analysis algorithm can determine appropriate biological mechanisms to target based on the data, and use analytics to identify therapeutics that have related performance characteristics that together form a highly effective combination. This avoids less efficacious monotherapies and dynamically adjusts to have a better probability of success.

## GETTING STARTED

Physicians first sign an investigator agreement with Muses Labs. Each individual signs an informed-consent form. Physicians are provided with a list of all needed medical and cognitive tests. It is important that these tests be done quickly, as the protocol cannot be started until they are all completed and the results shared with Muses Labs.

After the baseline tests are completed, Muses Labs generates the personalized MEND Protocol Report for the individual. This is sent to the physician for review and approval, and will be prescribed in a follow up visit (or phone call) with the physician.

## FURTHER READING

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