

## Prize4Life ALS Biomarker Track 1 Award Summaries

### *A Novel Biomarker for Measuring Motor Neuron Degeneration and Monitoring Clinical Efficacy of Therapeutic Interventions in ALS*

KineMed proposed an innovative method for measuring a crucial aspect of motor neuron survival that could serve both as a biomarker and a potential therapeutic strategy for ALS. Their proposal was based on the fact that abnormalities in microtubule dynamics have been implicated in the death of motor neurons and the pathogenesis of motor neuron disease. The idea that hyperdynamic microtubules may be an indicator of motor neuron degeneration is not new, but it has gone untested until now because it has been impossible to examine microtubule dynamics in vivo. KineMed has developed a stable isotope labeling technique that involves the use of heavy water, or  $^2\text{H}_2\text{O}$ , to measure microtubule turnover.

### *In Vivo Measurement of Biochemical Skin Properties in Patients with ALS*

Dr. Harvey Arbesman's proposal derived from the observation that ALS patients demonstrate a number of abnormal skin properties. For example, the skin of ALS patients exhibits a "delayed return phenomenon," meaning that the skin has reduced elasticity, and when stretched, it takes a relatively long time to return to its original position. Morphological studies, skin biopsies, and other avenues of research have revealed that many such abnormalities in skin and connective tissue of ALS patients are correlated with the duration of the disease. Dr. Arbesman thus proposed monitoring the biomechanical properties of skin as an ALS biomarker that is cheap, non-invasive, quantifiable, and reproducible. Devices for making such measurements are already on the market.

### *ALS Biomarkers for the Robust Assessment of Disease Progression in Amyotrophic Lateral Sclerosis*

Dr. Giorgia Sgarretta, suggested that the analysis of multiple potential variables simultaneously might bring to light several interdependent biomarkers for ALS that could allow for earlier detection and more precise monitoring of disease progression. For this proposal, the solver considered a number of possible biomarkers, both proteomic and metabolomic, and proposed using an integrated analysis to look at the relationships among several of these possible biomarkers together.

**WWW.PRIZE4LIFE.ORG**

Prize4Life, Inc. 14 Cambridge Center

PO Box 425783, Cambridge, MA 02142

P 617-500-7527 E-MAIL [contact@prize4life.org](mailto:contact@prize4life.org)

## *Carbon Monoxide Related Compounds as ALS Biomarkers*

The solver, who asked to remain anonymous, brings together two potentially related observations:

- 1) there is increased expression of the inducible enzyme heme oxygenase (HO-1) in spinal motor neurons of ALS patients and animal models of ALS, and
- 2) there are increased concentrations of arterial carboxyhemoglobin (hemoglobin bound to carbon monoxide) in ALS patients

to suggest that levels of HO-1 and carbon monoxide may be possible biomarkers for the disease and may be causally related to disease progression. [Heme oxygenase 1 \(HO-1\)](#) is an inducible isoform of the enzyme that is upregulated in response to oxidative stress. HO-1 is responsible for breaking down heme groups and one of the bi-products of this reaction is carbon monoxide. Carbon monoxide competes with oxygen and binds preferentially to hemoglobin, compromising the body's ability to provide oxygen to cells. Levels of arterial carboxyhemoglobin (in the blood) can be measured easily, cheaply, and relatively painlessly using spectrophotometric methods and carboxyhemoglobin measurements in CSF would also be possible (albeit more expensive and invasive). HO-1 activity in the blood (or CSF) would also be measurable using a spectrophotometer.

## *The Measurement of the Enrichment of Several Key Neurochemical Metabolites with Heavy Isotopes within the Glutamate-Glutamine Cycle or Alternative Cycles*

Dr. Anatoly Chernyshev suggested examining subtle changes in the neuronal/glia glutamate-glutamine cycle, based on the hypothesis that ALS may either be caused by and/or lead to abnormalities in the glutamate-glutamine cycle, which researchers could detect and use to track disease progression. Dr. Chernyshev proposed specifically using the kinetic isotope effect, a sensitive measure that compares the ratio of the reaction rates for isotopically pure reactants to the reaction rates when one or more atoms are substituted by heavier isotopes. The proposed biomarker would involve enriching the reactant molecules of the glutamate-glutamine cycle isotopically with  $^{14}\text{N}/^{15}\text{N}$  and  $^{12}\text{C}/^{13}\text{C}$  pairs and then using a combination of chromatographic and spectrophotometric techniques to analyze labeled glutamate and glutamine metabolites thereby revealing any subtle changes in this important biochemical process that correlate with disease progression in patients with ALS.

**WWW.PRIZE4LIFE.ORG**

Prize4Life, Inc. 14 Cambridge Center

PO Box 425783, Cambridge, MA 02142

P 617-500-7527 E-MAIL [contact@prize4life.org](mailto:contact@prize4life.org)