Overview

Mitochondrial Disease Working Group: Biomarkers

The National Institute of Neurological Disorders and Stroke (NINDS) Mitochondrial Disease (Mito) Biomarkers Common Data Elements (CDEs) Working Group (WG) lead by WG chair Dr. John Shoffner created a list of biomarkers to be considered as a menu of potentially useful parameters to be used at the routine and research levels of study.

The WG generated the list of biomarkers based on current research of both validated and potentially useful biomarkers studied in mitochondrial disease. The biomarkers included in the CRF do not need to be used in concert with one another and the researcher is at liberty to choose among the recommended biomarkers listed. Due to the diversity of mitochondrial diseases none of the biomarkers is constantly altered or used to assess mitochondrial disease in every study.

To illustrate this point the WG noted that lactate measurements to be significantly altered require an oxidative phosphorylation defect whose metabolic consequences are spread to the investigated metabolic fluid; in clinical practice that means a defect involving both liver and/or multiple organs with severely decreased residual activity. Numerous mitochondrial diseases have a restricted tissue distribution and/or are associated with very mild reduction of residual activity. In these diseases lactate measurements are often not useful and therefore should not be required. Conversely, lactate measurements are clearly essential in most pediatric mitochondrial diseases where the oxidative phosphorylation defect is often both severe and widespread.

The WG also considered some parameters that are absolutely essential, but in only one disease. In the list provided, the best examples are the thymidine and deoxyuridine levels together with the thymidine phosphorylase enzymology. These parameters are only useful in the MNGIE syndrome, a very rare disease, due to thymidine phosphorylase defect. The task of defining these “specific” parameters was found to be difficult by the WG. For example, because it is essential in the analysis of Pearson Syndrome, the WG added the parameter “mtDNA deletion/duplication” in the leukocytes. As a result a muscle biopsy is not required for the diagnosis of the mtDNA rearrangement in Pearson Syndrome.

All biomarkers mentioned in the Biomarker CRF are recommended, are classified as Supplemental, and have been fully defined in a guidelines document to assist researchers in their research studies.