

ABSTRACT – FAOD Consortium

Fat metabolism is an important source of energy for the body during times of fasting and metabolic stress. At least 25 enzymes and specific transport proteins are responsible for carrying out the steps of mitochondrial fatty acid metabolism, some of which have only recently been recognized. Of these, defects in at least 22 have been shown to cause disease in humans and can be fatal if left untreated. In aggregate, these disorders affect 1 in 5-10,000 births. Most of the fatty acid oxidation disorders (FAODs) are now diagnosed pre-symptomatically through expanded newborn screening by tandem mass spectrometry. Among the life-threatening disorders identified by newborn screening, FAODs provide the clearest opportunities to prevent morbidity and mortality. However, little information is available about how best to manage this growing number of patients. Essentially no controlled clinical trials on long term treatment have been performed on these disorders. Moreover, with increased numbers of patients identified, it has become increasingly clear that the spectrum of most of the disorders is far broader than previously recognized. As a critical first step in developing clinical trials to evaluate treatment of FAODs, we propose to capture complete clinical and natural history registry data on a large cohort of patients with FAODs identified through newborn screening as well as onset of clinical symptoms. The registry will take advantage of the largest existing newborn screening outcomes database and expand it into each of the regional genetics networks. It will be developed in alliance with the HRSA funded Regional Newborn Screening Consortia, and the patient advocacy groups Fatty Acid Oxidation Support Group and Saving Babies by Screening. The registry is designed to be dynamic, facilitating collection of information at initial diagnosis, and then collecting information about key data elements at each subsequent visit. A major goal in initiation of the database has been to capture data necessary to monitor long-term clinical health outcomes. The further intent of the information system from its genesis has been to support ongoing development and evaluation of treatment protocols, using a HIPAA-compliant web-based product. This registry will provide a vital resource to conduct outcome studies in order to improve treatment of patients with FAODs, with goals to identify markers predicting a higher risk for poor outcomes as well as preventing potentially detrimental over-treatment in others. As a demonstration project, the registry will be used to examine outcomes in patients with acyl-CoA dehydrogenase deficiencies identified through newborn screening.