Mitochondrial disorders are among the most common genetic disorders. In contrast to the extraordinary progress in our understanding of the molecular bases, we are still extremely limited in our ability to treat these conditions. Small patient populations represent the major impediment to progress. The development of a web-based register of patients with mitochondrial disease is needed to better understand the phenotypes and the natural history of these diseases.

13 centers with expertise on mitochondrial medicine are involved in this registry. To date, we have registered more than 1400 patients, with both adulthood and childhood onset. The network has reached the following goals: 1. establishment of an Italian network with specific expertise; 2. creation of a validated web-based database; 3. characterization of a big cohort of cases (see publications list).

Our database allows many phenotype-based and genotype-based studies. Two examples are given:

- Phenotype-based approach: exercise intolerance. More than 20% of patients complained of exercise intolerance. This symptom was more strongly associated with specific mutations (i.e., m.3243A>G). CK levels were increased in ≈34% of the patients with exercise intolerance, not confirming the notion that CK are normal in mitochondrial patients. Moreover, all the other myopathic signs included in our database were associated with exercise intolerance. Ragged red fibers and, especially, COX-negative fibers were more frequent in the subjects with exercise intolerance, whereas lactate levels could not predict the presence of exercise intolerance.

- Genotype-base approach: the m.8344A>G mutation in our database. Myoclonic epilepsy with ragged-red fibers (MERRF) is a mitochondrial syndrome mostly caused by the m.8344A>G mitochondrial DNA mutation. In the Italian mitochondrial population, myoclonus was present in one out of five patients, whereas myopathic signs and symptoms, generalized seizures, hearing loss, eyelid ptosis and multiple lipomatosis represented the most common clinical features. Our results showed higher clinical heterogeneity of the m.8344A>G mutation than commonly thought.

References:

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