BioISI - Biosystems & Integrative Sciences Institute

Mutation database design for mitochondrial rare diseases

Place of work/: BioISI, Chemistry for Biological Systems Group, Computational Laboratory, 8.5.55D

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Rare diseases, such as inborn errors of metabolism, affect less than 1 in 2000 persons worldwide, but although rare it is estimated they affect 6 to 8% of world population. The newborn screening program, "Teste do Pezinho", using tandem MS implemented in Portugal allows the identification of several new cases associated to these rare diseases, including Glutaric Aciduria-type I (GA-I) and Glutaric Aciduria-type II or Multiple Acyl-CoA dehydrogenase Deficiency (GA-II or MADD) cases [1]. GA-I is a neurometabolic disorder of lysine, hydroxylysine, and tryptophan metabolism caused by deficiency of glutaryl-CoA dehydrogenase (GCDH) [2], while GA-II results from deficiencies in the alpha or beta subunit of electron transfer flavoprotein (ETF), or electron transfer flavoprotein:ubiquinone oxidoreductase (ETF-QO) [3].

An enormous gap identified by researchers and clinicians in the field is the lack of a unifying depository for molecular and clinical data on patients, with the majority of cases found disperse in literature, and many not even reported in international journal with full access to all.

In this project we propose to respond to this societal demand, with tremendous impact in the development of new therapeutic approaches, by building a curated database of mutations for Glutaric Acidurias (GA-I and GA-II), with molecular, clinical and treatment data for each case reported all over the world. With the database fully functional we will also build a web-based platform that will be accessibly to researchers and clinicals developing work in this area of research. The platform will function both as a search- based tool and additionally registered users will be able to introduce new validated data.

The work will be developed in a highly multidisciplinary and collaborative environment under the supervision of Dr Bruno L. Victor and co-supervision of Dra Bárbara Henriques at BioISI – Biosystems and Integrative Science Institute, Faculty of Sciences in the University of Lisbon. There are several ongoing funded projects in the host labs by the Fundação para a Ciência e Tecnologia and, also a BioISI internal collaborative projects between the two supervisors. We seek candidates which are highly motivated to tackle a challenging research activity, ability to work independently, and to undertake intensive learning and training in different bioinformatic approaches. For more details, please contact Dr. Bruno Victor (blvictor@fc.ul.pt).

Bibliography

[1] Nogueira, C., et al., Mitochondrion, 2019, 47: p. 309-317
[2] Ribeiro, J.V., et al., Biochim Biophys Acta Proteins Proteom, 2020. 1868(1): p. 140269.
[3] Lucas, T.G., et al., Biochim Biophys Acta Proteins Proteom, 2020. 1868(6): p. 140393.