GALACTOSEMIA Web DB:
A web Accessible database of Galactosemia related proteins

Antonio d'Acierno[1], Angelo Facchiano[1], Anna Marabotti[1,2]

[1]*Institute of Food Sciences, National Research Council, Avellino, Italy*
{dacierno.a, angelo.facchiano}@isa.cnr.it
[2]*Department of Chemistry and Biology, University of Salerno, Fisciano (SA) 84084, Italy*
amarabotti@unisa.it

Extended Abstract

Galactose is a monosaccharide present in several foods and, once introduced into the body, it is metabolised by a biochemical pathway involving three enzymes: galactokinase (GALK), galactose-1-phosphate uridylyltransferase (GALT), and UDP-galactose-4'-epimerase (GALE).
Hereditary deficiencies of these three enzymes in humans are related to three different forms of the genetic disease globally called "galactosemia". The impairment of GALK causes Galactosemia Type II, whereas GALT deficiency causes the disease called Classic Galactosemia, and finally GALE deficiency is linked to Galactosemia type III or Galactose Epimerase deficiency. The clinical manifestations of each enzyme deficiency differ markedly: patients with GALK deficiency, for example, have the mildest clinical consequences, while Classic Galactosemia is potentially lethal in infancy, if undiagnosed and/or untreated, and is also associated with long-term, organ-specific complications.
The impairment of these enzymes is linked to the presence of mutations in their genes. The most common ones are missense mutations, causing the replacement of a residue on the protein sequence with another one. This kind of mutation can have different effects depending on whether the original residue is replaced with a very similar or very different one, and depending on the place where the original residue is located on the protein structure. It has been shown elsewhere that it is possible to infer the severity of a mutation by using computational approaches that can predict its impact on protein structure and function, provided that the structure is known. This kind of knowledge can be thus of help to correlate the severity of symptoms with the effect at protein level, to better understand and, possibly, to predict, the outcome of a mutation on individuals carrying it.
The aim of the proposed web-accessible database is to collect and provide information about the predicted structural and functional effects of missense mutations of the enzymes linked to the different forms of galactosemia, in order to help researchers to reach a deeper comprehension of these genetic diseases. At time of writing, we are working to develop an unique database that includes the variants of GALT enzyme, already described in the GALT protein DB [1][2], and the variants of GALK and GALE enzymes, and to allow the users to extract information about structural and functional effects of each variant by several kinds of combinable filters. The perspective of this work is to have a tool suitable for investigating with a similar approach also other proteins subjected to variations.

References

[1] A. d'Acierno, A. Facchiano, A Marabotti, GALT protein database, a bioinformatics resource for the management and analysis of structural features of a galactosemia-related protein and its mutants. Genomics, Proteomics & Bioinformatics, 7(1–2), 2009, Pages 71–76.
[2] A. d'Acierno, A. Facchiano, A Marabotti, GALT protein database: querying structural and functional features of GALT enzyme. Human Mutation, 35 (9), 2014, 1060–1067.