GALT-Prot database: a database of the structural features of GALT enzyme and its mutations

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Motivation

GALT enzyme (Galactose-1-phosphate uridylyltransferase) is involved in the galactose metabolism by catalyzing the conversion of galactose-1-phosphate and uridine-5'-diphosphate-glucose into glucose-1-phosphate and uridine-5'-diphosphate-galactose. The genetic disorder called "classical galactosemia" or "galactosemia I" (OMIM: 230400) is linked to the impairment of this enzyme. This disease can be potentially lethal if not detected early and it is revealed through symptoms such as gastrointestinal complaints, hepatomegaly, cataracts, mental retardation, and ovarian failure in females. These last two dysfunctions can persist even with a life-long dietary restriction. Classical galactosemia is characterized by a high allelic heterogeneity, and to date more than 150 different base changes were recorded in several populations and ethnic groups. The three-dimensional structure of the human enzyme has been created by homology modelling methods [1]. On the basis of this model, it is now possible to investigate the position and the influence of each single mutation on the structure and on the dimeric assembly of the enzyme, with the aim of explaining molecular events related to this pathology.

Methods

The 3D model of GALT is available in PDB data base (PDB code: 1R3A). Protein structure analysis software as DSSP, HBPLUS, NACCESS have been used to evaluate secondary structure, H-bond formation, solvent accessibility. Information about gene mutations have been found in literature [2] and in the public data base of GALT mutations at genetic level (GALTdb) [3]. To create the database, the Entity-Relationship diagram has been structured and then translated into a relational model; the database has been then realized using the well know open source RDBMS PostegreSQL [4], paying attention to indexes to be created to improve the whole performance. To realize the Web Application we used STRUTS [5], a well known framework that implements the Model 2 approach, a widely adopted variant of the Model-View-Controller design paradigm. Here a Controller servlet acts as a controller for the whole application while the business logic resides into java beans and other helper classes (the Model). The presentation layer (the View) has been clearly realized using JSP pages and tag libraries.

Results

To model the Web Application we have first of all identified two typical users of the system: the Administrator and the Public User. The Public User, for which login is not required, browses data and has the opportunity to submit new mutations to the Administrator. The Administrator, among other things, inserts, updates and deletes mutations; for the Administrator a login is clearly required. For each typical user, and according to the UML specification [6], we have detailed the Use Cases Diagram. For each Use Case we have also defined the corresponding Sequence Diagram. The data have been modeled using an Entity-Relationship diagram where some entities are worth to be noted. The Protein entity, for example, has been introduced to make to final database capable of storing data not just for the GALT protein; the Chain entity, a weak entity whose occurrences are identified by a number and by the corresponding protein, is used to model amino acids chains. The Analysis entity is again a weak entity, identified by the element of the chain under study, that specializes into several entities (H-Bonds, DSSP, Monomer, etc). The occurrence of the Mutation entity represents a mutation to be stored; for each mutation we also consider an attribute Reference that stores the title of the paper describing such a mutation. The GALT-prot database reports information by the literature about known nucleotide mutations and the related amino acid mutation. The structural features related to this amino acid are visualized with the aim of giving a possible explanation of the effect of the mutation, in terms of structure/function relationships. These information would be

useful for all people involved in the biochemical study of this protein.

References

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Availability: http://bioinformatica.isa.cnr.it/GALT

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