Poster I-85

A Study of SNPs in Sirtuins Structures

Authors:
Beatriz J. Pinto (*Faculty of Medicine of Ribeirão Preto - University of São Paulo*)
André L. T. Vinci (*Faculty of Medicine of Ribeirão Preto - University of São Paulo*)
Marcela C. de Santo (*Laboratory of Bioinformatics - University of Ribeirão Preto*)
Milton Faria Jr (*Laboratory of Bioinformatics - University of Ribeirão Preto*)
Silvana Giuliatti (*Faculty of Medicine of Ribeirão Preto - University of São Paulo*)

Short Abstract: The goal is to locate SNPs in the proteins structures of the sirtuins and verifying if they occur in active sites. Alignment between SNPs and proteins was obtained and it was used to locate SNPs in the structures. However, none of the substitutions had presented alterations affecting the active sites.

Long Abstract:
Introduction: Sirtuins, proteins homologous to SIR2, are present in prokaryotes and eukariotes. All SIR2-like proteins have a sirtuin core domain which contains a series of sequence motifs conserved in organisms ranging from bacteria to human. Members of the eukariotic SIR2 family share a -260 amino acid region of homology flanked by N- and C-terminal extensions. Sequences distantly related to this core region have been found in archaebacteria and prokaryotes. The family has been divided into five classes according to sequence homology. In humans, there are seven known SIR2 homologous, termed sirtuins (SIRT1 throught 7). SIRT1, SIRT2 and SIRT3 are members of class I, of which yeast SIR2 is founding member. SIRT4 is class II, SIRT5 is class III and SIRT 6 and SIRT7 are class IV. Prokaryoteic sirtuins include members of classes II and III (Frye, 2000; Finnin et al., 2001). A Single Nuclotide Polymorphism (SNP) is a DNA sequence variation, occurring when a single nucletide in the genome differs between members of the species. SNPs may fall within coding sequences (CDS) of genes or between genes (intergenic regions). SNPs within a CDS change the codon, which may or may not change the amino acid in the protein sequence. The former may constitute different alleles. The latter are called silent mutations and typically occur in the third position of the codon. SNPs make up 90% of all human genetic variations, and occur every 100 to 300 bases along the human genome. Variations in the DNA sequences of humans can affect how humans respond to diseases, bacteria, viruses, chemicals, and drugs (http://en.wikipedia.org/). SNPs are of great value to biomedical research and in developing pharmacy products. Because SNPs do not change much from generation to generation, following them during population studies is straightforward. Only one amino acid substitution can cause a huge effect in the function of the protein and phenotype of an organism. Therefore, the goal of this project is to locate SNPs (single nucleotide polypmorphism) in the proteins structures of the sirtuins family and to verify if they occur in active site occurring the possibility of modifing the functionality of the protein. Methodology: The human sirtuins proteins were obtained from database National Center for Biotechnology Information – NCBI (http://www.ncbi.nlm.nih.gov/) and the SNPs from database dbSNP (Sherry et al., 2001), accessible from NCBI. The protein structures were obtained from data base Protein Date Base - PDB (Sussman et al., 1998). A alignment

between SNPs and protein sequences was carried through software CLUSTAL_X (Thompson et al., 1997). This alignment was used to locate the SNPs in the protein structures through BioDesigner software (http://www.pirx.com/biodesigner/index/shtml).Conclusion: More than a hundred SNPs were found in the database pbSNP. The analyis has to be done for all of them. So far, the SNPs that had been analyzed had not presented alterations that could affect the active sites, since such substitutions had not occurred between amino acidos of different properties.

References:

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