## Poster I-86

**Comparative Analysis of Human SIRT Proteins Tertiary Structures**


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**Short Abstract:** Humans have proteins homologous to SIR2, the sirtuins. Some sirtuins have unknown function. The aim is a comparative analysis of the sirtuins structures. A alignment determinated a consensus for each sirtuin. The conserved regions were located in the tertiary structures. It was found amino acid presenting chemical properties replacement.

**Long Abstract:**

Introduction: Normal human somatic cells in cluture have a finite replicative lifespan. SIR is a NAD+-dependent protein deacetylase that extends lifespan in yeast and worms. Humans have seven proteins homologous to SIR2, the sirtuin family (SIRT 1 throught 7), that share the catalytic domain with SIR2 (Michishita et al., 2005). Enzyme SIRT 1 is most characterized sirtuin, but it is not the only one that has been found in mammals. Related genes to SIRT 1 originate similar enzymes that act in different parts of the cells. SIRT1 operates in the nucleus and cytoplasm, removing acetil of other proteins, thus modifying its behavior. Many of its targets are transcription factors that activate genes directly or are regulators of these factors, giving SIRT1 the control of a great variety of basic functions (Sinclair & Garente, 2006). Scientists have been identified the rolls of the sirtuins and discovered if they also influence the longevity. It is known that SIRT2, for example, modifies the tubulin, a component of the internal structure of the cell, being able to affect the cellular division. SIRT3 acts in the energy generators of the cell, the mitochondrials, and seems to participate of the temperature regulation of the body. The functions of SIRT 4 and SIRT5 are not known. Mutations in the gene that codifies the SIRT6 had been associates to the premature aging. No data have been available for biological functions or cellular localizations of the sirtuins 4, 5 ,6 and 7. Comparative protein modelling uses previously solved structures as starting points, or templates. This is effective because it appears that although the number of actual proteins is vast, there is a limited set of tertiary structural motifs most proteins belong. It has been suggested that there are only around 2000 distinct protein folds in nature, though there are many millions of different proteins. Homology modelling is based on the reasonable assumption that two homologous proteins will share very similar structures (Rigden & Mello, 2002). Therefore, the aim is to carry out a comparative analysis of the sirtuins tertiary Methodology: Using the regions conserved from the homologous sequences as probe, the localization of these regions in the tertiary structures can be used in order to determinate possible biological functions. The primary structures of the sirtuins of human beings were obtained through search in the data base National Center for Biotechnology Information - NCBI (http://www.ncbi.nlm.nih.gov/). A multiple alignment was carried through software CLUSTAL_X (Thompson et al., 1997). This

alignment made possible the determination of a consensus for each sirtuin. The protein structures were obtained from data base Protein Date Base - PDB (Sussman et al., 1998). Using BioDesigner software (http://www.pirx.com/biodesigner/index/shtml), these conserved regions had been located in the tertiary structures of sirtuins. Conclusion: Through its localization, it can be analyzed if such regions represent a significant alteration in the structure. Pairs of amino acids can have more or less similar chemical properties. In two homologous proteins, a positively charged amino acid is more likely to be replaced by another positively charged amino acid than by a large hydrophobic residue. In our results we have found this kind of amino acid replacement. The results of this important computational analysis is important for prediction of protein structure and function. References:

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