Fuad Fares, J Proteomics Bioinform 2014, 7:8
http://dx.doi.org/10.4172/0974-276X.S1.071

OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference on
Proteomics & Bioinformatics
August 04-06, 2014 Hilton-Chicago/Northbrook, Chicago, USA

The role of oligosaccharides on structure-function of glycoprotein hormones: Development of agonists and antagonists

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Glycoprotein hormones (FSH, LH, hCG and TSH) are a family of heterodimeric proteins composed of two noncovalently linked subunits, α and β. Oligosaccharides on the glycoprotein hormones have been implicated in several actions including the maintenance of intracellular stability, secretion, assembly, receptor binding, steroidogenesis and modulation of plasma half-life. Glycoproteins are used clinically in the treatment of many diseases. One major issue regarding the clinical use of many peptides is their short half-life due to the rapid clearance from the circulation. To overcome this problem, we used genetic engineering techniques that have been found successful for designing long acting hormones. The signal sequence of *O*-linked oligosaccharides was added to the coding sequence of the hormones. It was postulated that the *O*-linked oligosaccharides add flexibility, hydrophilicity and stability to the protein. On the other hand it was suggested that *O*-linked oligosaccharides play an important role in preventing plasma clearance and thus increasing the half-life of the protein in circulation. On the other hand we found that deletion of N-linked oligosaccharides from hTSH subunits resulted in significant decreased in the bioactivity. Moreover, deglycosylated variants of TSH compete with normal hTSH and human thyroid stimulating immunoglobulin (hTSI) in a dose dependent manner. Thus, this variant, behaves as potential antagonist, who may offer a novel therapeutic strategy in the treatment of Grave's disease, the most common form of hyperthyroidism.

In conclusion, it was found that addition *O*-linked oligosaccharides or deletion of *N*-linked oligosaccharides could be interesting strategy for designing new analogs of glycoproteins.

Biography

Fuad Fares has completed his DSc studies at the Faculty of Medicine, Technion-Israel Institute of Technology, and postdoctoral studies at the Department of Molecular Biology and Pharmacology, School of Medicine, Washington University, St. Louis Missouri. He is associated professor at the Department of Human Biology, Faculty of Natural Sciences and director of the Department of Molecular Genetics at Carmel Medical Center. He has published more than 90 papers in reputed journals and serving as a member of the Israel Council for Higher Education. He is the inventor of "designing long-acting recombinant proteins" and the initiator of PROLOR Biotech Company.

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