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## Developing long acting agonists and antagonists of glycoprotein hormones using gene fusion and gene transfer: From bench to clinics

Peptides are used clinically in the treatment of many diseases. One major issue regarding the clinical use of many peptides is their short life span in the body, due to the rapid clearance of those proteins from the circulation. The low stability of peptides has thus often posed a difficulty to researchers and hindered their adoption in potential medical applications. At the clinical level, there is a need for a regime of frequent injections of the peptides into the patients to overcome this low stability factor. The major strategies for overcoming this problem are based on chemical techniques and using specific peptidase inhibitors or cocktails. To overcome this problem, we used genetic engineering techniques that have been found successful for designing long acting hormones for the treatment of fertility and thyroid diseases. Ligation of a peptide containing 4 O-linked oligosaccharide chains to the carboxyl-end of Follitropin (hFSH), Thyrotropin (hTSH), Growth hormone (GH), Factor VII and to erythropoietin (EPO) resulted in increasing the biological activity and longevity *in vivo*. Moreover, ligation of the subunits into a single gene resulted in active and stable compounds. Designing long acting peptides will diminish the cost of these drugs and perhaps reduce the number of injections for the patients who need them. New analog of hFSH was approved during 2010 by the European Community for clinical use, GH is in clinical trials phase III and Factor VII is in clinical trials phase I. On the other hand, hTSH variants lack of N-linked oligosaccharide chains are less potent than hTSH wild-type on cAMP accumulation and T3 secretion from human cultured thyroid follicles. Moreover, deglycosylated variant compete with normal hTSH and human Thyroid Stimulating Immunoglobulin (TSI) in a dose dependent manner. Thus, this variant, behave as potential antagonists, which may offer a novel therapeutic strategy in the treatment of Grave's disease, the most common form of hyperthyroidism.

### 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 the Director of the Department of Molecular Genetics at Carmel Medical Center and Associate Professor at the Department of Human Biology, University of Haifa. He has published more than 75 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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