

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

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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 succeeded to ligate the signal sequence of O-linked oligosaccharides to the coding sequence of the hormones. The cassette gene that has been used contains the sequence of the carboxyl-terminal peptide (CTP) of human chorionic gonadotropin β (hCG β) subunit. The CTP contains 28 amino acids with four O-linked oligosaccharide recognition sites. It was postulated that O-linked oligosaccharides add flexibility, hydrophilicity and stability to the protein. On the other hand it was suggested that the four O-linked oligosaccharides play an important role in preventing plasma clearance and thus increasing the half-life of the protein in circulation. Using this strategy we succeeded to ligate the CTP to the coding sequence of follitropin (FSH), thyrotropin (TSH), erythropoietin (EPO) growth hormone (GH) and thus to increase the longevity and bioactivity of these proteins in-vivo. Interestingly, the new analogs of FSH and GH were found not immunogenic in human and it is already passed successfully clinical trials phase III and phase II respectively. Moreover, FSH long acting was approved by the European Commission (EC) for treatment of fertility. In addition, our results indicated that long acting GH is not toxic in monkeys and the results from clinical trials phase I and phase II seem to be promising. Designing long acting peptides will diminish the cost of these drugs and perhaps reduce the number of injections in the clinical protocols.

Biography

Fuad Fares has completed his D.Sc 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 associated 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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