

## **Glycobiology World Congress**

August 10-12, 2015 Philadelphia, USA

## O-glycosylation and protein evolution: The case of the LHB to CGB development

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The glycoprotein hormones LH, FSH and CG are non-covalent heterodimers composed of the common  $\alpha$  and hormone specific  $\beta$  subunit. The subunits contain N-linked glycans, which are important for the folding, heterodimer assembly and bioactivity of the hormone. In addition, the carboxy-terminal region of the CG $\beta$  subunit is O-glycosylated and this unique domain (known as the CTP) extends the circulatory survival of CG relative to the other glycoprotein hormones. While the genes encoding the  $\alpha$ , LH $\beta$  and FSH $\beta$  subunits are generic to vertebrates, the CG $\beta$  gene is restricted to primates and equids. This is curious because the CG $\beta$  gene presumably evolved from the ancestral LH $\beta$  gene following only a small set of mutations, and the resulting O-glycosylated CTP confers new hormonal properties to CG relative to LH that seems advantageous to maintain early gestation. To address this restricted evolution, we combined bioinformatics, *in vitro* and *in vivo* experiments that suggest 1. The potential of the LH $\beta$  to CG $\beta$  transformation is present in several animal phyla and 2. The ability of a CTP domain to have the clustered O-glycans is important for the CG $\beta$  development. Additional studies with the equine CTP-extended  $\beta$  subunit suggest that this subunit, which is expressed in both in the pituitary and placenta of equids integrates intracellular properties that diverged in the LH $\beta$  and CG $\beta$  subunits of primates that are expressed in different tissues. Our studies demonstrate a potential role for the CTP O-glycosylation in the LH $\beta$  to CG $\beta$  evolution and a link between tissue expression and subunit characteristics.

## **Biography**

David Ben-Menahem has completed his PhD at Tel-Aviv University in Tel-Aviv Israel and did his Postdoctorate studies at Washington University Medical School in St. Louis Missouri, USA. He is at the department of Clinical Biochemistry and Pharmacology at Ben-Gurion University of the Negev in Beer-Sheva, Israel. His major research focus is related to structure-function studies of the gonadotropins which are members of the glycoprotein hormone family.

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