Analysis of differential glycosylation patterns of human FSH

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Follicle stimulating hormone (FSH) is a glycoprotein hormone with two subunits, α and β, and is required for gamete development. In a process known as glycosylation, oligosaccharide branches are added to specific residues in the protein sequence, and occurs with FSH. Our data suggest that estrogen is responsible for inhibiting the glycosylation of FSHβ in reproductive-age women, thus producing a di-glycosylated FSH with higher biological activity than the tetra-glycosylated form. The difference in glycosylation of two subunits is suspected to be due to activity of different oligosaccharyltransferase (OST) isoforms. OSTs are responsible for the preliminary step in glycosylation. Factors including signal peptide hydrophobicity of α and β maybe contribute to selective usage of OST, and hence modulate glycosylation. Therefore our hypothesis is that glycosylation of FSH subunits is regulated by the differential interactions between OST isoforms and the signal peptides of each subunit, and the differential interaction is modulated by hormones such as estrogen. To test our hypothesis, we will genetically engineer chimeric hFSH subunits by swapping the signal peptide sequences of α and β. Constructs with the chimeric sequences will be introduced into immortalized gonadotrope cell lines. FSH glycoforms expressed in the cell lines will be examined using Western Blot, RIA, and immunoaffinity chromatography. If our hypothesis is correct, then we would expect to detect unglycosylated α subunit in the transfected cell lines. The cell lines will be treated with estrogen and differences in FSHsubunit glycosylation will be examined.