

Follicle-Stimulating Hormone Receptor Binding By Glycoforms

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Abstract: Follicle-stimulating hormone (FSH) functions to stimulate ovarian follicle development in the ovaries in females, which is essential for oocyte maturation. In males, FSH regulates Sertoli cell function in the testis. Human FSH exists as a heterogenous mixture of two glycoforms, differing in glycosylation of the beta-subunit. One major glycoform, FSH-24 is glycosylated at all 4 N-glycosylation sites and is indicated in Western blotting by the presence of a 24 kDa band. FSH-21 is characterized by a partially-glycosylated beta-subunit, and seen in Western blotting by the presence of a 21 kDa band. Glycosylation patterns of hFSH can affect receptor binding and activation.

As FSH receptors are known to exist as dimers or as oligomers, FSH binding to one ligand-binding site may influence binding to the other sites in the receptor complex. Our hypothesis was that negative cooperativity would limit FSH-24 to only one ligand-binding site per dimer, whereas FSH-21 would not exhibit negative cooperativity and could bind both sites. We tested this hypothesis by measuring dissociation in the presence and absence of cold FSH glycoforms.

Negative cooperativity was measured by loading FSH membrane receptors with 125 I-hFSH tracer for 24 hours at 25°C, followed by measuring dissociation over the course of 3 hours, at 30-minute time intervals in the absence of cold hormone, or in the presence of either pFSH (FSH-24 only) or eFSH (90% FSH-21). The amount of tracer bound to FSH receptor membranes was measured in a gamma counter and plotted against time.

Dissociation of 125I-hFSH tracer at receptors occurred only in the presence of 1000-fold excess unlabeled FSH glycoform competitors. The dissociation from FSH receptors by both glycoform tracers was consistent with negative cooperativity by both pFSH and eFSH, causing us to reject our current working hypothesis.

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