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Influence of glycans on biological activities of pituitary gonadotropins, follicle-stimulating hormone and luteinizing hormone

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The gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) play central roles in the control of reproduction by connecting neuroendocrine hypothalamic/pituitary activities to gonadal function. LH and FSH receptor activation is an important part of assisted reproductive technologies, such as *in vitro* fertilization. Both FSH and LH are heterodimeric glycoproteins, each composed of a non-covalently associated common α - and a hormone-specific β -subunit. Both subunits are N-glycosylated. Although high affinity binding of both hormones to their cognate receptors occurs exclusively by protein-protein interactions, full gonadotropin receptor activation involves N-linked glycans. However, the activation mechanism remains elusive. Part of the problem is the high degree of oligosaccharide micro heterogeneity that challenges even contemporary analysis by high-resolution mass spectrometry. LH possesses three N-glycosylation sites that are always occupied by glycans and can be removed individually, permitting characterization in a site-specific manner. While FSH glycopeptides can be obtained from all 4 potential N-glycosylation sites, only 2 can be thoroughly analyzed by glycopeptide mass spectrometry. Even then, only about a third of the glycan population can be detected. While both FSH α sub-unit glycosylation sites can be interrogated individually by sequential peptide-N-glycanase digestion, both FSH β glycans are released simultaneously. This is unfortunate, because naturally occurring forms of FSH lacking either one of the 2 FSH β N-glycans bind their receptors more rapidly, occupy more FSH binding sites, and provoke a more robust cellular response than fully-glycosylated FSH. Moreover, the ratio of FSH glycosylation variants may be under physiological regulation.

Biography

George R Bousfield completed his PhD at Indiana University in 1981. He then pursued Postdoctoral studies at the University of Texas, M D Anderson Cancer Center with Darrell Ward. He is currently the L M Jones Distinguished Professor in the Fairmount College of Liberal Arts and Sciences at Wichita State University and Director of the WSU Protein Core Facility. He has published more than 56 journal articles.

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