Follicle-stimulating hormone (FSH) plays an essential role in the regulation of reproduction, as FSH KO female mice are sterile. FSH regulates ovarian granulosa and testicular Sertoli cell function by binding to its cognate receptor (FSHR), a member of the G protein-coupled receptor family. Human FSH exists as a heterogeneous mixture of glycoform, differing in the number and location of β subunit glycans. Recently, it has been reported that hypo-glycosylated hFSH binds and activates hFSHR more than fully-glycosylated hFSH (Bousfield et al. Molecular and Cellular Endocrinology 382: 989-997, 2013). We analyzed the kinetics of FSH/FSH receptor complex endocytosis using \(^{125}\)I-hFSH\(^{21}\), \(^{125}\)I-hFSH\(^{24}\) glycoform tracers and recombinant hFSHR-expressing Chinese Hamster Ovarian (CHO) cells as a model system. No difference in endocytic rate was observed for hypo-glycosylated hFSH/FSH receptor complex and fully-glycosylated hFSH/FSH receptor complex. However, a greater endocytic rate for both hypo-glycosylated hFSH/FSH receptor complex and fully-glycosylated hFSH/FSH receptor complex was observed when we use a non-steroidal allosteric modulator 9032A. The mechanism of how the binding of the modulator causes conformational changes of hFSHR remains to be determined.

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