How can progesterone modify the folding and N-glycosylation of a protein?

Silvia E Miranda
Universidad de Buenos Aires, Argentina

The glycosylation pattern of many proteins can influence their physicochemical and biological properties leading to pathological consequences. Moreover, folding and glycosylation are interdependent processes. We have studied the effects of progesterone on the glycosylation of IgG and on two critical endoplasmic reticulum enzymes: The oligosaccharyltransferase complex (OST) which catalyzed the N-linked glycosylation and the UDP-Glc:Glycoprotein glucosyltransferase (UGGT) which is a central component of the Endoplasmic Reticulum (ER) glycoprotein folding quality control system. We first employed a murine hybridoma cell cultured with a physiological range of progesterone doses and analyzed: The expression of two isoforms of the OST catalytic subunit, STT3-A and STT3-B which are endowed with distinct enzymatic properties, the glycosylation pattern of the secreted IgG and the expression and activity of UGGT. We found that P4 increases IgG N-glycosylation by means of a switch of STT3 isoform expression through a progesterone-induced blocking factor (PIBF) dependent mechanism. We also described the expression and activity of two UGGT isoforms both of them differentially regulated by high P4 doses through nuclear and membrane receptors. To investigate the in vivo modulation of OST, we next employed a sound stress mouse model which increased the abortion rate due a decrease in progesterone levels and in serum glycosylated IgG. We investigated the OST isoform expression in intestine and in implantation sites. In both tissues, sound stress induced an inflammatory response and a switch of STT3 isoform expression. These findings demonstrate that progesterone can regulate both the IgG glycosylation and the glycoprotein quality control mechanism.

simir2@gmail.com

Colorful chemical glycobiology: Simple construction of sweet glycoprobes

Xiao-Peng He
East China University of Science and Technology, China

Inter cellular glycoligand-receptor recognitions are fundamental biological processes, harnessing numerous dynamic cellular events. The better understanding of these interactions may aid both the decipherment of the “glycomics” and the progress of targeted theranostics of human diseases. However, owing to the limitations of current biochemical techniques including their complicated manipulation, long detection time and high detection cost, effective probing of glycoligand-receptor recognitions remains a key challenge in chemical glycobiology. By combining the modular click chemistry with judicious (supra) molecular and materials self-assembly tactics, we have developed simple fluorogenic and electro-actively co-probes for glycobiology. With these probes, live cancer cells that over express glycoligand receptors can be specifically captured in situ. The glycoprobes have also proven suitable for monitoring the expression level of pathogenic glycoligand receptors on cancer cells. Meanwhile, the scope of the glycoprobes has been expanded to the imaging of tumor tissues and diagnosis of clinical serum samples. Tracking of the dynamic endocytosis, translocation and recycling processes of the receptors have been made possible. Our research provides economic tools facilitating the decipherment of the glycomics as well as unique insights into the early-stage diagnosis and targeted therapy of human fatal diseases.

xphe@ecust.edu.cn