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New materials and reagents for efficient enrichment and identification of glycosylated proteins and peptides

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As one of the most important sub proteomes in eukaryote cells, glycoproteins play crucial roles in various biological processes and have long been considered closely correlated with the occurrence, progression, and metastasis of cancer. Comprehensive characterization of protein glycosylation and association of their aberrant patterns to the corresponding cancer stage may provide a unique way to discover new diagnostic biomarkers and therapeutic drug targets. However, the extremely complex nature of biological samples and relatively low abundance of glycosylated proteins makes the enrichment of glycoprotein/glycopeptide a prerequisite for large scale glycosylation identification. To fulfill this need, we have developed a series of new materials and reagents for the efficient enrichment of glycoprotein/glycopeptides in recent years. (1) We prepared sequence controlled triblock copolymer grafted silica-microparticles (TCP-SMs) by sequential atom transfer radical polymerization (sequential-ATRP) of three different hydrophilic monomers. The triblock copolymer blocks carry densely packed pendent zwitterionic-ions and sugar moieties. Therefore, increased retention of glycopeptides can be achieved by the combination of different HILIC interactions. As a result, 1244 N-glycopeptides were identified after TCP-SMs enrichment from tryptic digests of mouse liver protein. (2) We established a stimuli-responsive polymer system for facile and efficient enrichment glycopeptides from complex biological samples. The soluble polymer supports provide a homogeneous reaction system with fast mass transfer and facilitate interactions between the supports and the target glycopeptides. More importantly, the stimuli-responsive polymers exhibit reversible self-assembly and phase separation under environmental condition variations, which leads to facial sample recovery with a high yield of the target glycopeptides. The hydrazide functionalized stimuli-responsive polymer was successfully applied to the enrichment glycopeptides from tryptic digests of mouse brain protein, which results in the successful identification of 1317 N-glycopeptides corresponding to 458 N-glycoproteins demonstrating the capability of this "smart" polymer system to combine stimuli-responsive and target-enrichment moieties to achieve improved identification of key biological and disease related biomolecules.

Biography

Weijie Qin's research mainly focuses on study of glycosylated proteins/peptides by mass spectrometry. He developed a series of new methods and reagents for efficient glycoprotein digestion, high affinity enrichment and sensitive identification of N/O-linked glycoproteins, glycopeptides and glycans. His recent works include: Talanta 2017, 169 195. Chem. Sci., 2015, 6, 4234 Anal. Chem., 2015, 87, 656 Anal. Chem., 2014, 86, 1452 Anal. Chem., 2014, 86, 482 Anal. Methods, 2014, 6, 2518 Anal. Chem., 2013, 85 2703 Talanta, 2013, 117, 1 Talanta, 2013, 115, 842.

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