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Improving Binding Selectivity in Molecularly Imprinted Polymers from Templates of Higher Biomolecular Weight: An Application in Cancer Targeting and Drug Delivery

Authors : Ben Otange, Wolfgang Parak, Florian Schulz, Michael Alexander Rubhausen

Abstract : The feasibility of extending the usage of molecular imprinting technique in complex biomolecules is demonstrated in this research. This technique is promising in diverse applications in areas such as drug delivery, diagnosis of diseases, catalysts, and impurities detection as well as treatment of various complications. While molecularly imprinted polymers MIP remain robust in the synthesis of molecules with remarkable binding sites that have high affinities to specific molecules of interest, extending the usage to complex biomolecules remains futile. This work reports on the successful synthesis of MIP from complex proteins: BSA, Transferrin, and MUC1. We show in this research that despite the heterogeneous binding sites and higher conformational flexibility of the chosen proteins, relying on their respective epitopes and motifs rather than the whole template produces highly sensitive and selective MIPs for specific molecular binding. Introduction: Proteins are vital in most biological processes, ranging from cell structure and structural integrity to complex functions such as transport and immunity in biological systems. Unlike other imprinting templates, proteins have heterogeneous binding sites in their complex long-chain structure, which makes their imprinting to be marred by challenges. In addressing this challenge, our attention is inclined toward the targeted delivery, which will use molecular imprinting on the particle surface so that these particles may recognize overexpressed proteins on the target cells. Our goal is thus to make surfaces of nanoparticles that specifically bind to the target cells. Results and Discussions: Using epitopes of BSA and MUC1 proteins and motifs with conserved receptors of transferrin as the respective templates for MIPs, significant improvement in the MIP sensitivity to the binding of complex protein templates was noted. Through the Fluorescence Correlation Spectroscopy FCS measurements on the size of protein corona after incubation of the synthesized nanoparticles with proteins, we noted a high affinity of MIPs to the binding of their respective complex proteins. In addition, quantitative analysis of hard corona using SDS-PAGE showed that only a specific protein was strongly bound on the respective MIPs when incubated with similar concentrations of the protein mixture. Conclusion: Our findings have shown that the merits of MIPs can be extended to complex molecules of higher biomolecular mass. As such, the unique merits of the technique, including high sensitivity and selectivity, relative ease of synthesis, production of materials with higher physical robustness, and higher stability, can be extended to more templates that were previously not suitable candidates despite their abundance and usage within the body.

Keywords : molecularly imprinted polymers, specific binding, drug delivery, high biomolecular mass-templates
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