Medical University of Graz

Molecularly imprinted polymers for targeted drug delivery

Summary

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Supervisor:	Dr. Sebastian Schwaminger
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between February 15, 2022 00:00 and March 28, 2022 23:59 (Europe/Zurich)

Description

Background:

Cancer is the second leading cause of death closely following heart diseases. While multiple progresses in immunotherapy treatments seem very promising, the challenge of formulating and administering biological molecules such as monoclonal antibodies still remains.

Thus, there is a need for novel drug delivery platforms which are able to protect these drugs and allow for a targeted delivery. Here, nanotechnology comes in to play. Magnetic nanomaterials allow for targeted drug delivery applications due to their superparamagnetic properties allowing manipulations in magnetic fields.[1,2] While these magnetic materials allow to overcome the transport issue, the biocompatibility and the directed administration are still challenging. Artificial polymers can help to create specific binding sites for peptide-based drugs and stabilize magnetic nanoparticles while improving the biocompatibility. One possibility to create artificial polymers is the synthesis of molecularly imprinted polymers (MIPs) using the target as negative mold.[3,4] Not only the delivery but even cell regulation or protein recognition is possible with such MIPs.[5] These materials can therefore be used as a platform for selective peptide binding and release applications beyond drug delivery. However, the key to the design of high-affinity MIPs lies in an in-depth understanding of surface-peptide interaction sites and mechanisms.

Thus the goal of this project is to develop and investigate magneto-responsive molecularly imprinted polymers for drug delivery of peptide-based drugs.

Hypothesis and Objectives:

The idea behind this project is to identify and create artificial binding sites for cationic drugs based on molecular imprinting of a polymer by a distinct peptide sequence. These MIPs will be used for the binding and targeted release of the cationic drug acting as a carrier system. This system will be enhanced with a magnetic nanoparticles core to allow for targeted drug delivery.

Methodology:

The main focus of this work will be on the organic material synthesis of MIPs as well as their characterization and their application. The synthesis is based on the imprinting process, where the monomer is polymerized in the presence of the respective peptide sequence, which is then removed in a following step. The affinity of the imprinted polymers will be verified by chromatography analysis and the polymer will be characterized with infrared spectroscopy. The MIPs will be validated towards their drug delivery properties by the PhD candidate with biocompatibility assays of cell cultures.

References:

(1) Schwaminger, S. P.; Fraga-García, P.; Blank-Shim, S. A.; Straub, T.; Haslbeck, M.; Muraca, F.; Dawson, K. A.; Berensmeier, S. Magnetic One-Step Purification of His-Tagged Protein by Bare Iron Oxide Nanoparticles. *ACS omega* 2019, *4*, 3790–3799.

(2) Schwaminger, S. P.; Blank-Shim, S. A.; Scheifele, I.; Pipich, V.; Fraga-García, P.; Berensmeier, S. Design of Interactions Between Nanomaterials and Proteins: A Highly Affine Peptide Tag to Bare Iron Oxide Nanoparticles for Magnetic Protein Separation. *Biotech. J.* 2019, *14*, e1800055.

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(3) Mier, A.; Maffucci, I.; Merlier, F.; Prost, E.; Montagna, V.; Ruiz-Esparza, G. U.; Bonventre, J. V.; Dhal, P. K.; Tse Sum Bui, B.; Sakhaii, P.; Haupt, K. Molecularly Imprinted Polymer Nanogels for Protein Recognition: Direct Proof of Specific Binding Sites by Solution STD and WaterLOGSY NMR Spectroscopies. *Angew. Chem.* 2021, *60*, 20849–20857.

(4) Paruli, E., III; Soppera, O.; Haupt, K.; Gonzato, C. Photopolymerization and Photostructuring of Molecularly Imprinted Polymers. *ACS Appl. Polym. Mater.* 2021, *3*, 4769–4790.

(5) Xu, J.; Miao, H.; Zou, L.; Tse Sum Bui, B.; Haupt, K.; Pan, G. Evolution of Molecularly Imprinted Enzyme Inhibitors: From Simple Activity Inhibition to Pathological Cell Regulation. *Angew. Chem.* 2021, *133*, 24731–24738.