DIRNANO

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Polymer composition and functional effects: how to regulate the protein adsorption onto NPs

Grafting polymer brushes onto NPs is a common approach to reduce protein binding and confer a *stealth* character to NPs. Polymer brushes are polymer chains attached at one end to a surface or interface creating a density of attachment points high enough so that the chains are obliged to stretch away from the interface. The fabrication of densely grafted polymer brush shells is among the most effective methods to modulate the interfacial properties of NPs and their interaction with proteins. (1,2)

The design of polymer coatings for NPs has been guided by the *Whitesides rules* for their efficiency in suppressing protein adsorption leading to the formation of an effective polymer shell which provides a hydrated layer that hinders protein adsorption ensuring stabilization of NPs and shielding the core of the NP from the surrounding environment. (3,4)

Polymer brush shells on NPs: poly(ethylene glycol) (PEG)

PEG, a hydrophilic and biocompatible polymer, has the approval from the Food and Drug Administration (FDA) for biomedical applications, establishing it as the gold standard for NP coating. When PEG chains are grafted onto NPs, protein adsorption is reduced, and NPs acquire *stealth* properties. In addition, it has been shown to improve colloidal stability of different nano-systems. (5)

Nevertheless, PEG possesses certain limitations including low stability in physiological environment and potential adverse biological effects. Indeed, further concern is posed by the increasing production of anti-PEG antibodies, because of the *in vivo* accumulation of the polymer, and the recognition of PEGylated NP formulations by the immune system compromising their efficacy. (6,7)

Alternatives

A wide range of polymers are exploited to regulate the recognition features of NP formulations. These polymers share similarities with PEG, *i.e.*, uncharged, hydrophilic, flexible and they provide longer circulation times to NPs when attached to their surface. Some of the polymers that are being investigated in DIRNANO are poly(oligo(ethylene glycol)) methyl ether methacrylate (POEGMA) (8,9), poly(2-alkyl-2-oxazoline)s (PAOXAs) and poly(2-alkyl-2-oxazine)s (PAOZIs) (10–12), and polysaccharides (13,14).
In addition, modulating the structural parameters of polymer brushes represents a versatile approach for adjusting the interfacial and physicochemical properties of macroscopic and nanoscopic materials. Dispersity, which represents the spread of different molecular weight species within a polymeric material, alongside molar mass, topology, and grafting density, has become a crucial tool for tuning properties such as lubricity, biopassivity, adhesion, friction, and steric stabilization. (15,16)

Our goal within the DIRNANO framework

DIRNANO consortium pursues the development of *stealth* NPs for anti-tumour nano-vaccine applications and testing them in human immune cells, *in vitro*, as well as in *in vivo* models. Preparing NPs with widely tuneable immune-interaction qualities—stealth, long-circulating or immune cells-targeted through understanding and controlling the mechanisms operating at the nano-host interface.

In the Laboratory for Macromolecular and Organic Chemistry group (MOC), led by Prof. Edmondo M. Benetti at the University of Padova (Italy), there is a great competence and experience in the synthesis and characterisation of a wide range of different polymers which can be grafted onto NPs for the mentioned purposes.

Within the DIRNANO consortium, we are particularly interested in generating PEG-based ligands by modulating its side-chain dispersity. Despite the numerous reports on controlling dispersity of polymer backbones, the role of dispersity within brushes is still underexplored. Herein, we are investigating the influence of side-chain dispersity of graft polymers constituted by a polymethacrylate backbone and oligomeric ethylene glycol (OEG) side chains, *i.e.*, POEGMAs. Hence, my project focuses on generating a library of POEGMA's with different side-chain dispersity and different OEG side-chain length to regulate the interfacial properties of polymer brushes. These findings open new possibilities for the development of technologically relevant biomaterials.

NEWS in the FIELD

- Young Macromolecular Research Webinars are back! A series of excellent talks aiming to highlight the work of 10 postgraduate and early postdoctoral researchers around the globe in the field of macromolecular chemistry.
All talks are held online on Microsoft Teams.

- EUropean POlymer Conference on *Polymer Brushes* (EUPOC 2024): it will be held in Bertinoro, Italy (26th – 30th May 2024)

- IUPAC MACRO 2024: the 50 th world polymer congress will be held at Warwick University, in the UK (1st – 4th July 2024)

DIRNANO NEWS

The journey of several ESRs within the DIRNANO consortium is about to finish:

- Michele do Nascimento Tomaz (ESR01), Cristina Fontecha Cuenca (ESR03), Ander Eguskiza Bilbao (ESR09), and Tobias Komsthöft (ESR13) have already submitted their thesis, and soon there will be their defences.
The best of luck from the whole DIRNANO consortium!

Regarding secondments:

- Pedro Veloso (ESR02) is currently in Salzburg in Prof. Jutta Horejs-Hoeck's group (Paris Lodron University of Salzburg, Austria) to continue characterising the phenotype of dendritic cells stimulated with poly(oxazoline)-coated NPs.
- Mireia Vilar Hernández (ESR15) will start her last secondment in Prof. Fabrizio Mancin's group (University of Padova, Italy) to continue investigating the physicochemical properties of lipid-coated poly(lipoic) hybrid NPs.

Regarding participation in conferences:

- Carlos Pavón Regaña (ESR05) will attend the EUropean POlymer Conference (EUPOC 2024) and present a poster with his last data.

Stay tuned and follow all updates in our website and in our LinkedIn page!

Carlos Pavón Regaña
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