STEALTH PROPERTIES OF TOPOLOGICALLY DIFFERENT POLYOXAZINE SHELLS ON GOLD NANOPARTICLES

Maria Morbidelli[1,*], Matteo Romio,[2] Carlos Pavon[3], Paolo Pastore[3], Denis Badocco[3], Regina Tavano[1], Emanuele Papini[1] and Edmondo Maria Benetti[3]

[1] Department of Biomedical Sciences, University of Padova

[2] Swiss Federal Laboratories for Materials Science and Technology (EMPA), St. Gallen, Switzerland

[3] Department of Chemical Sciences, University of Padova

*e-mail: maria.morbidelli.1@phd.unipd.it

Introduction

Functionalization of nanoparticles (NPs) with linear, bioinert polymers such as poly(ethylene glycol)s (PEGs), typically hampers immune reactions and prevents interactions in biofluids, additionally providing good pharmacokinetics.

As a promising alternative to PEGs, poly(2-oxazine)s (POZIs) show comparable or even improved biopassivity [1] while being much more chemically versatile.

In this work, we specifically investigate the effect of polymer topology on the stealth character of POZI shells on Au NPs. In particular, the goal is the characterization of the proteins that form the biomolecular corona around the surface of nanoparticles when they come into contact with the host.

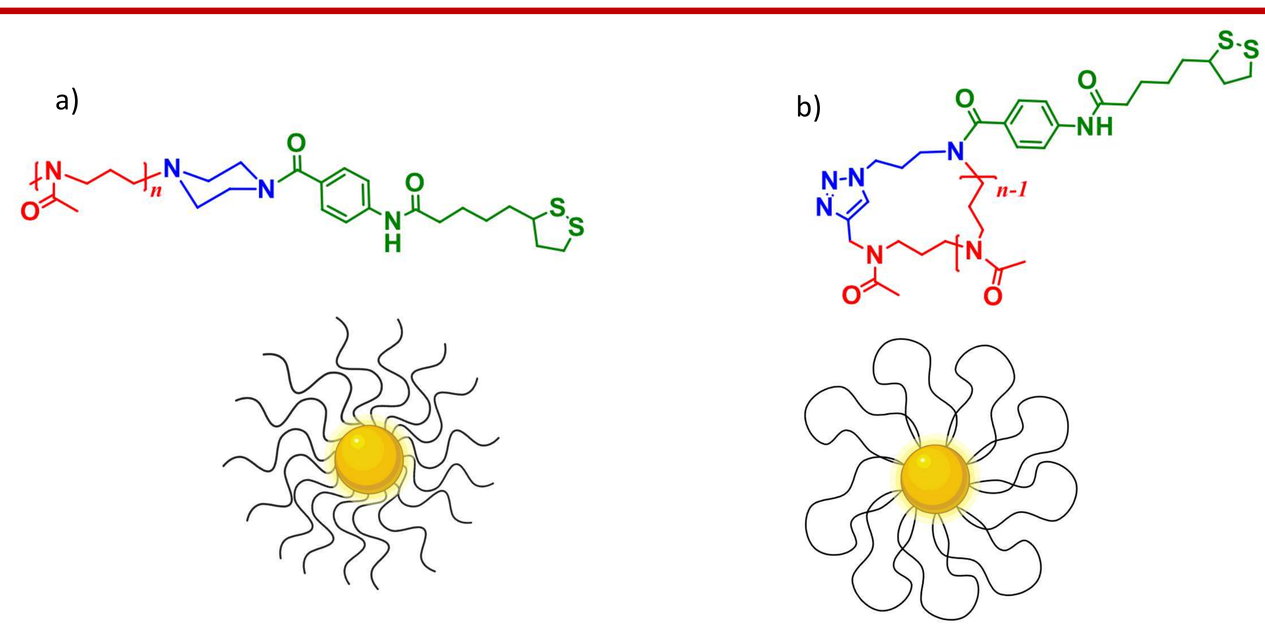

Fig.1: Structure of L-PMOZI (a) and C-PMOZI (b) and their conformation on gold NPs.

Results

1- Protein quantification and proteomic analysis

Citrate, L-PMOZI and C-PMOZI coated gold NPs were incubated with human serum. Then, the protein corona was analyzed using different techniques.

The total amount of protein bound to NPs is significantly different (Fig. 2). L-PMOZI seems to interact more with HS proteins, while C-PMOZI is more "invisible".

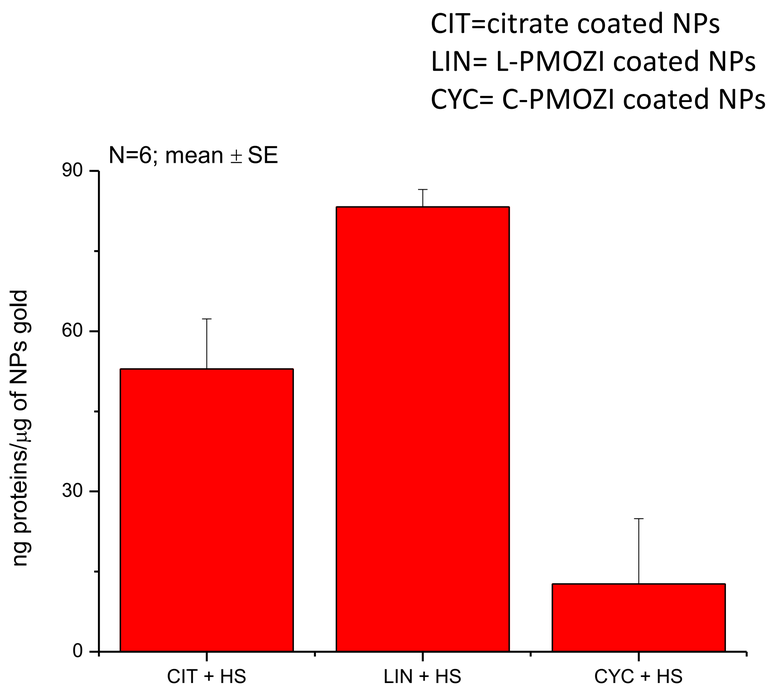

Fig.2: Protein corona quantification.

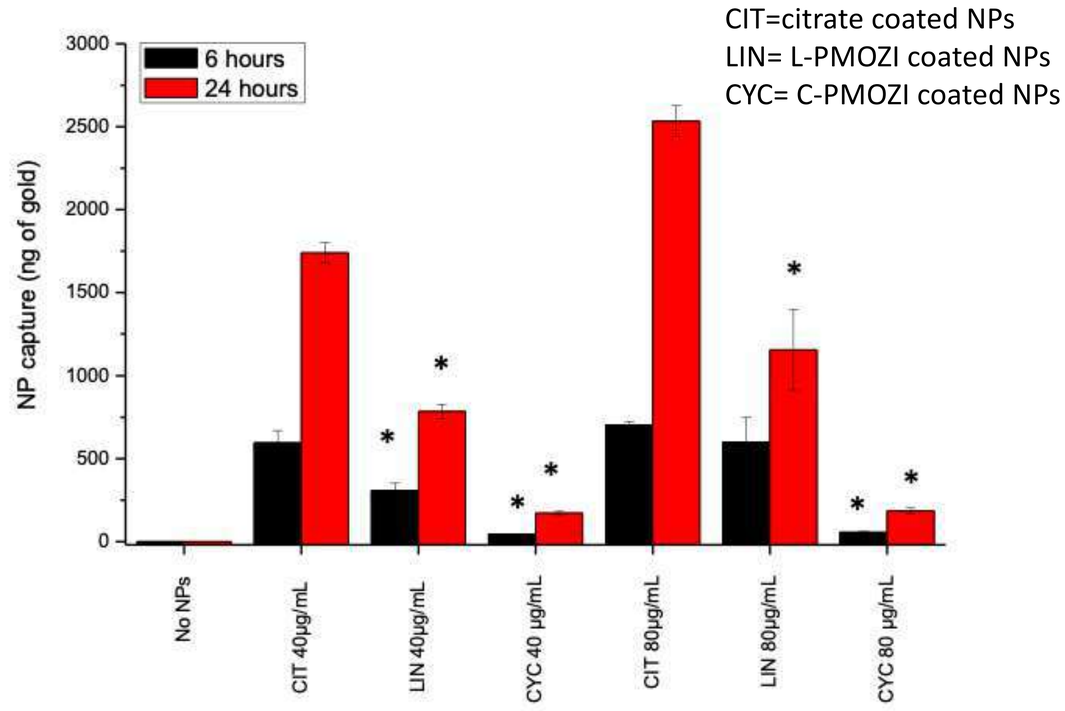

Fig.3: Cell capture experiment. Data shown derives from the ICP-MS measurment.

2- Cell capture experiment

Nanoparticles were incubated with macrophages using two different doses (40µg/mL and 80µg/mL) and two different incubation times (6h and 24h). Then, captured gold was measured using ICP-MS.

Clearly, C-PMOZI NPs are captured less than L-PMOZI NPs for both times of incubation and nanoparticle concentrations (Fig. 3). This data suggests that the cyclic polymer may avoid interactions between opsonin proteins/molecules and their relative receptors on macrophages membranes.

Discussion

The first characterization performed using C-PMOZI and L-PMOZI coated nanoparticles suggests that POZA polymers are extremely promising as stealth coating for nanoparticles. Recent works based on the capture of cyclic and linear coated NPs show the same results that we obtained, confirming that the cyclic topology could decrease the capture by phagocytic cells. In particular, the cyclic topology seems to be more "stealth" than the "linear" one.

Acknowledgment

This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No 956544.

References

1- Morgese et al.,"Chemical Design of Non-Ionic Polymer Brushes as Biointerfaces: Poly(2-oxazine)s Outperform Both Poly(2-oxazoline)s and PEG" Chem.Int.Ed. 2018, 3;57(36):11667-11672 doi: 10.1002/anie.201805620.