Effect of PEGylation of Multivalent Polymeric Compounds on Inhibition of Adhesion by Soft Glycocalyx Mimicking Hydrogels

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A myriad of biological processes on the cellular scale are mediated by interactions between carbohydrate ligands and their receptors, e.g. cell-cell communication, pathogen invasion, or cell development. Thus it is of great interest to investigate carbohydrate-receptor interactions in order to gain a deeper insight into their biological functions. Such information could be used to derive new and optimized ligands e.g. to block natural ligand receptor interactions in therapeutic applications such as pathogen inhibition. A potential countermeasure for inhibiting pathogenic adhesion involves multivalent glycomacromolecules.[1] Multivalency and positioning of carbohydrate units on the polymer chain largely controls specific binding to the receptors[2]. Importantly, however, we found that removal of pathogens with competively binding glycomacromolecules is strongly affected by the size of the polymer chain. For example, the adhesion of a soft mannose-presenting particle on a receptor surface can be eliminated with increased efficiency when coupling a non-interacting 8000 Da PEG chain to a trivalent mannose oligomer (Figure 1). In order to quantify the size effect on adhesion inhibition we use soft hydrogel particles as adhesion sensors and a series of glycomacromolecules with different molecular weight and multivalency as anti-adhesion agents. In addition, using a series of charged macromolecules on electrostatically adhered microgels we show that the size effect on adhesion elimination is not exclusive to carbohydrate mediated adhesion but a rather general phenomenon. In order to rationalize potential biological implications, we plan to conduct AFM-adhesion measurements with mannose binding bacteria in a single cell force spectroscopy, which will allow us to study steric repulsion effects of added polymeric inhibitors in great detail.

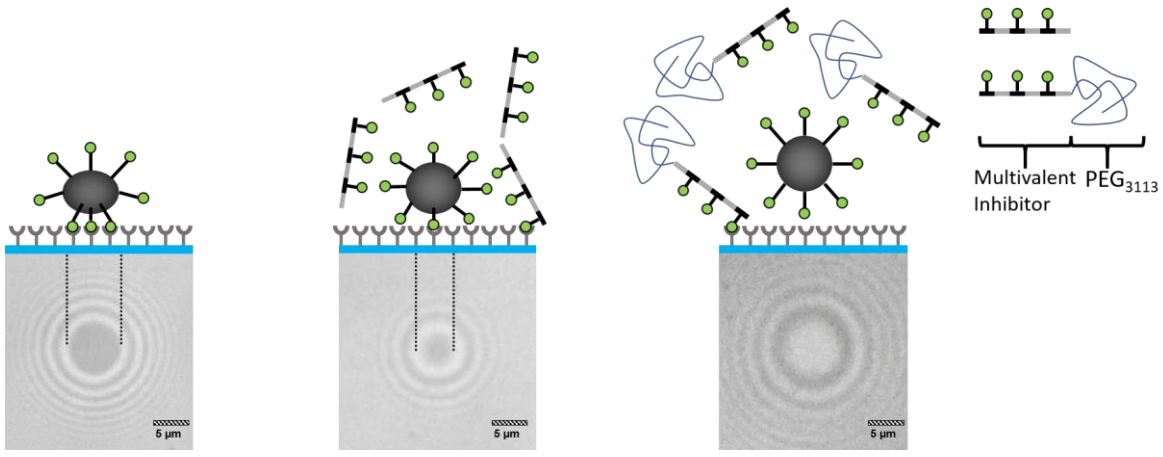

Figure 1. Left: A mannose functionalized soft hydrogel particle adheres on a receptor surface as signified by the large contact area (dark area in the centre of the concentric rings). Middle: Addition of a trivalent mannose presenting glycooligomer partially eliminates the adhesive contact. Right: At the same concentration an inhibitor with an additional PEG chain completely eliminates adhesion.

[1] Kiessling, L., et. al., *Chem. Soc. Rev.*, 2013. **42**, 4476-4491.
[2] Jacobi, F., et al., *Biomacromolecules*, 2018. **19**(8): p. 3479-3488.