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Mucin thin layers on top of model membranes as a model environment for mucosal delivery

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Mucus is a highly viscoelastic secretion, covering the epithelia surfaces of the gastrointestinal, pulmonary, oral, nasal and genital tracts. Its function and composition differs at different locations of our body, but the general task of mucus is to protect mucosal tissues from dehydration, mechanical stress, and to act as barrier against microorganisms and toxic substances. Mucus is mainly composed of water (90%), lipids, small proteins and nucleic acids, but its mechanical and viscoelastic properties are due to the presence of high molecular weight glycoproteins, identified as mucin. Mucin can establish adhesive interactions with particulates via electrostatic interactions, van der Waals forces, hydrophobic forces, hydrogen bonding, or chain entanglement. Therefore, the development of mucosal drug delivery vehicles is a great challenge because little is still known about the interactions between mucin and other macromolecules: they can either penetrate rapidly or establish prolonged contact with mucus, depending on their specific formulation. We worked [1] on the development of model mucus environments to deepen the understanding of mucin interactions with polymers used in pharmaceutical formulations by applying complementary techniques. Beside SAXS and SANS characterization in the bulk, we carried on investigations also on thin mucin layers depositions, by applying QCM-D and neutron reflectivity. Further, we developed a bio-inspired complex model system consisting in a mucin layer deposited on top of a single supported model membrane, structurally investigated by neutron reflection. Since complexation between mucins and biomacromolecules takes place close to the cell membrane surface, the present model is potentially predictive of the fate of nanodrugs intended to cross mucus and enter epithelial cells.

1. Rondelli V., Di Cola E., Koutsioubas A., Alongi J., Ferruti P., Ranucci E., Brocca P. *Int. J. Mol. Sci.* 20(15) (2019) 3712-3726.

Primary author: RONDELLI, Valeria (Università degli Studi di Milano)

Co-authors: DICOLA, Emanuela (Università degli Studi di Milano); KOUTSIOUBAS, Alexandros (Forschungszentrum Juelich GmbH); BROCCA, Paola (Università degli Studi di Milano)

Presenter: RONDELLI, Valeria (Università degli Studi di Milano)

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