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The Physiological Environment's Impact on Disease Progression Through the Mucosal Barrier

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Despite the immense contribution to human health, mucus and its respective barrier properties are poorly understood. This biological hydrogel, provides a finely tuned barrier regulating transport of small molecules (e.g., nutrients), particulates, and microbes. We hypothesize that the inherent barrier properties of the mucus lining in the GI tract can be modulated to protect the host against invading microbes. A thorough characterization of physiological conditions' and mucosal strengthening factors' effects on mucus barrier properties, specifically against different pathogens, will provide insight enabling optimization of transport properties.

Mucus collected from a porcine intestine was layered on a slide, and another layer containing fluorescent nanoparticles and mucosal strengthening factors suspended in maleate buffer (MB) was added to the surface in a humidified atmosphere. To examine mucus barrier properties, multiple particle tracking (MPT) technique was used, in which the diffusive motion of polymer nanoparticles was tracked and analyzed to elucidate hydrogel transport properties. Videomicroscopy and an image analysis algorithm are used to capture and analyze particle trajectories in mucus. The outcome of these studies includes characterization of the motion of particulates (diffusive or subdiffusive, indicating hindered motion), effective diffusivities, estimation of time required to traverse physiologically relevant thicknesses of mucus, and microrheological analysis of the mucus gel viscoelastic properties. To examine microbe transport in mucus, the pathogens will be fluorescently tagged and suspended in test media before exposure to mucus and application of the MPT technique to track their motion. Spatial distribution of mucus properties will also be monitored using micro-pH analysis probe and a Ca^{2+} sensitive fluorescent probe. Structural properties will be characterized with electron paramagnetic resonance (EPR) for micro viscosity, micro polarity, and diffusion while quick-freeze deep etch microscopy (QF/DEM) will provide information relating particle/microbe transport and pore/pore network changes.

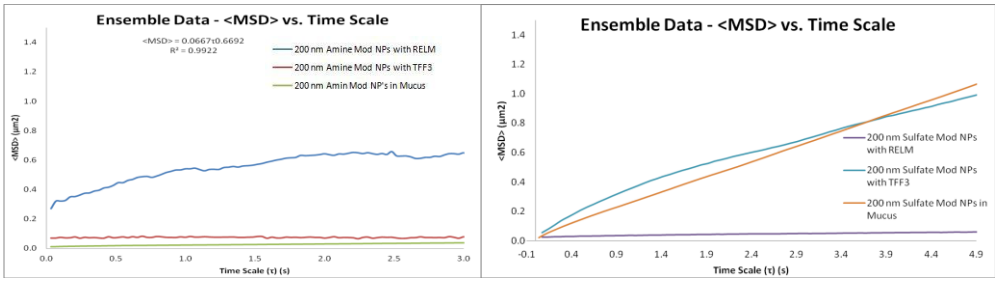

Fig 1- A) TFF3 and RELM effect on amine functionalized nanoparticles in MB. E) TFF3 and RELM effect on sulfoxyl functionalized nanoparticles in MB.

Preliminary data suggest that concentration changes of Ca^{2+}, mucosal strengthening factors, and pH will significantly impact transport through the mucus lining. If the lining was effectively strengthened, the research would show physiological changes and use of mucus strengthening factors can in fact possibly prevent contraction of pathogens or at least slow the transport across the mucus lining providing time to apply additional treatment.