FOOD-ASSOCIATED STIMULI ENHANCE BARRIER PROPERTIES OF MUCUS

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Mucus, a complex network consists of micro- and nano-scale fluid-filled domains of entangled fibers, mucin glycoproteins, lipids, salts, cellular serum macromolecules provides a barrier through which nutrients and orally delivered drugs must penetrate before entering the circulatory system. Mucus provides a significant, yet poorly characterized barrier to particulate, pathogen, and small molecule transport to epithelial surfaces. It is significantly important to understand the role of mucus barrier in modulating pathogen invasion, drug delivery, and nutrient/toxin absorption. While great strides have been made, the barrier properties of mucus, and how they change with different physiological states and disease, are generally poorly defined. This proposal describes the significant impact of food-associated lipids and physiological changes on model drug carrier transport through intestinal mucus. Lipid content associated with fed state intestinal contents significantly enhanced mucus barrier properties, resulting in a 140-fold reduction in the transport rate of 200 nm carboxylate-modified polystyrene microspheres. Physiologically relevant increases in [Ca^{2+}] resulted in 4-fold reduction of carboxylate-modified particle transport rates, likely due to binding of [Ca^{2+}] to mucin glycoproteins and thus enhanced cross-linking of the mucus gel network. Reduction of pH from 6.5 to 3.5 also affects mucus viscoelasticity, reducing particle transport rates approximately 10-fold. In summary, proposed studies will enable lipid-based delivery of drugs, enhancement in nutrient uptake, or modulate pathogen invasion in diseases such as inflammatory bowel disease, or exposure to bioterrorism agents. A new, relatively facile model for controlling intestinal epithelial exposure will be introduced to the medical community.