Chemical Engineering Colloquium

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Goddard Hall, Room 227
12:00 PM – 1:00 PM

Transport Barriers in Oral Drug Delivery: Lipids, Mucus, and Human Intestinal Models

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The intestinal mucosa, a single layer of epithelium covered by mucus, is the surface across which orally delivered drugs and nutrients are absorbed, and it separates the body from a dense microbial community. Transport across this barrier therefore shapes both the performance of oral medicines and intestinal health. Our laboratory is studying the impact of pharmaceutical excipients, including lipids and polymers, on intestinal transport and overall absorption of orally delivered compounds. Our approach includes mechanistic studies paired with systems-based models of processes key to overall oral absorption, including drug partitioning into colloidal species and permeation through intestinal barriers. One aspect of permeation through the intestinal mucosa, transport through mucus, is being investigated in detail. Results to date highlight the dependence of mucosal permeation on physical and chemical properties of penetrating material (drug, particle, microbe) as well as the significance of intestinal lumen contents in altering the mucus barrier. We have also found that mucins, the major structural components of mucus and often overlooked in standard in vitro testing, can influence drug supersaturation and modulate the performance of polymeric excipients, suggesting that mucins may be useful components of drug delivery systems. In vitro human intestinal models that capture essential features of in vivo biology are useful for understanding the function of drug delivery systems as well as ties between intestinal biology, health, and disease. Our lab has demonstrated that organoid-derived intestinal monolayers replicate key features of lymphatic transport, including lipid-driven chylomicron secretion via the 2-monoacylglycerol re-esterification pathway (absent in Caco-2 cells), polarized apoB-48 output, and enhanced drug partitioning into chylomicron-rich fractions. These monolayers offer a potential alternative to animal-based lymphatic transport models. When integrated into a mesofluidic chip, these monolayers allow real-time visualization of drug carrier diffusion through a physiologically thick mucus layer on live human tissue.

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