

Industrial & Physical Pharmacy Seminar

IPPH 69600

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3:30 PM in RHPH 164

“A synthetic approach to 'smart' microbial-based therapeutics”



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Current therapies for treating inflammatory bowel disease (IBD) and other chronic intestinal illnesses are effective in less than 30% of patients due to the lack of adherence to onerous prescription schedules and off-target effects. Synthetic biology offers a unique opportunity to engineer microbial drug delivery platforms that can significantly enhance drug safety and efficacy by overcoming current IBD treatment limitations. The engineered systems can colonize the gut and provide *in situ* surveillance by monitoring changes in the local environment. As an immunotherapy strategy, we aim to implement a synthetic circuit in probiotic *E. coli* strain Nissle 1917 capable of sensing chronic conditions and modulating host immune responses. Here, we adopt the previously characterized split activator AND logic gate to multiplex two input signals: the inflammatory biomarker tetrathionate and the IPTG inducer signal. We report 4 to 6-fold induction with a minimal leak when both stimuli are present. We also demonstrate the tunability of the logic-based genetic circuit by varying the ribosome binding site sequences. We are currently engineering the split activator to drive the expression of an anti-inflammatory effector. In future work, we will test if the engineered circuit can protect against intestinal inflammation in IBD mouse models. Long-term, we will design strategies to sense the onset of chronic disease and engineer immune-modulating responses in commensal microbial chassis.