yBOTs: Self-Tunable Engineered Yeast for Controlled Therapeutic Delivery

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The Quintana Laboratory is focused on the characterization of signaling pathways that control the activity of the immune system, with the ultimate goal of identifying novel therapeutic targets and biomarkers for immune-mediated disorders.

Current therapeutic approaches are limited to a passive, one-size-fits-all modality that is oblivious to the changing needs of each individual patient, failing to rapidly adapt to changes in disease state and often leading to adverse effects. To address this unmet clinical need, we engineered yBOTs (yeast robots), which provide a new therapeutic platform capable of sensing disease-associated molecules and responding with the release of a therapeutic compound at the right dose, at the right time and in the right location. Specifically, yBOTs are yeast cells modularly engineered to quantitatively detect disease-associated stimuli and respond with the release of therapeutic effector molecules in a self-tunable manner.

We first evaluated the potential of yBOTs-based therapies on Inflammatory Bowel Disease (IBD), a chronic disorder of the gastrointestinal (GI) tract where most available therapies suppress the immune system systemically, increasing the risk of infections and cancer, while not benefiting all patients. Using three independent pre-clinical IBD preclinical models, we demonstrated that yBots could significantly reduce GI tract pathology by targeting 3 important contributors to the disease process: 1) Inflammation driven by innate and adaptive immune cells; 2) fibrosis; and 3) dysbiosis. These findings support the use of yBOTs for the treatment of GI tract inflammation. In addition, yBOTs can be engineered to detect multiple disease markers and release multiple therapeutic effectors.

yBOTs provide a tunable platform for controlled therapy delivery, which can be designed to treat GI and/or systemic inflammation, metabolic and genetic disorders, as well as gut-brain axis related CNS disorders.