UC Irvine Samueli
Department of Chemical and Biomolecular Engineering

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Finding Catalysts of Gut Reactions: The Gut Microbiota in Disease Onset and Treatment

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Abstract: There are trillions of frenemies living in each person's intestines; these are the gut bacteria that compose the human gut microbiota. Whether each is friend or foe depends on the symphony of molecules mingling with gut bacteria and their human host.

A Study of Gut Bacteria as Foe: Accumulation of α-synuclein protein aggregates in brain neurons is thought to result in Parkinson's disease. Despite the clear impact that this disease has on the brain, it seems that the disease as well as α-synuclein aggregates may originate somewhere else—in the gut. Each person's gut houses trillions of bacteria. Our data show that these gut bacteria start a domino-effect that can cause aggregation of α-synuclein in intestinal cells that natively express this protein. Emerging from our discovery of molecular-level mechanisms detailing *how* gut bacteria cause α-synuclein aggregation, we identified diet-derived small molecules as well as existing medicine that inhibit formation of α-synuclein aggregates in intestinal cells. Our discoveries suggest that microbiome-targeted treatments may be developed to slow progression of Parkinson's disease or even stop the disease in the gut before it impacts the brain.

A Study of Gut Bacteria as Friend: While some gut bacteria may cause disease, others are needed for medicines to work effectively. Tamoxifen is an anti-breast cancer drug only effective for 50% of people, and gut bacteria may be the key to unlocking the therapeutic potential of this drug for more people. Our findings show that chemical reactions by gut bacteria are required for tamoxifen to be bioactivated and circulate throughout the body to deliver its anti-cancer effects. The bacteria implicated in this process use fiber to thrive. Eating a diet high in fiber may tailor a person's gut microbiome so they have bacterial enzymes to harvest tamoxifen's benefits for breast cancer prevention.

Together, our findings highlight the importance of a personalized approach to medicine that accounts for the unique molecules in each person's gut microbiome that orchestrate health.

Bio: Elizabeth N. Bess received her B.S. degree from the University of Utah in Biological Chemistry in 2009. In 2015, Elizabeth earned her Ph.D. in Organic Chemistry working with Professor Matt Sigman to develop methods for mathematically describing and predicting outcomes of chemical reactions. As an HHMI postdoctoral fellow of the Life Sciences Research Foundation, Elizabeth worked in the microbiology lab of Professor Peter Turnbaugh at the University of California, San Francisco (2015–2018). There, she discovered how gut bacteria convert molecules abundant in plant-rich diets to new molecules that have anti-breast cancer effects. Elizabeth joined the Department of Chemistry at the University of California, Irvine in 2018. Her lab is fusing chemistry and microbiology to interrogate the chemical mechanisms by which the human gut microbiome impacts human health and disease.

Hosted by: *Prof. Han Li*