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Towards a tolerance toolkit: Gene expression signatures enabling the emergence of resistant bacterial strains KEESHA ERICKSON, ANUSHREE CHATTERJEE, University of Colorado - Boulder — Microbial pathogens are able to rapidly acquire tolerance to chemical toxins. Developing next-generation antibiotics that impede the emergence of resistance will help avoid a world-wide health crisis. Conversely, the ability to induce rapid tolerance gains could lead to high-yielding strains for sustainable production of biofuels and commodity chemicals. Achieving these goals requires an understanding of the general mechanisms allowing microbes to become resistant to diverse toxins. We apply top-down and bottom-up methodologies to identify biological network changes leading to adaptation and tolerance. Using a top-down approach, we perform evolution experiments to isolate resistant strains, collect samples for transcriptomic and proteomic analysis, and use the omics data to inform mathematical gene regulatory models. Using a bottom-up approach, we build and test synthetic genetic devices that enable increased or decreased expression of selected genes. Unique patterns in gene expression are identified in cultures actively gaining resistance, especially in pathways known to be involved with stress response, efflux, and mutagenesis. Genes correlated with tolerance could potentially allow the design of resistance-free antibiotics or robust chemical production strains.

Keesha Erickson
University of Colorado - Boulder

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