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**Leveraging microfluidics for linking protein sequence to function in high-throughput**

Recent technological advances in genomics and proteomics have driven an explosion in our knowledge of the molecular parts within cells. Interactions between these parts drive all biological processes: proteins bind DNA and RNA to regulate transcription and translation, dense networks of protein-protein interactions convey cellular signals, and enzyme-substrate interactions allow all of the chemical transformations essential for metabolism and signaling. The strength of these interactions predicts the timing and identity of downstream responses; therefore,quantitative biophysical and biochemical measurements are critical to decipher these networks, predict how they are disrupted in disease, and manipulate them for therapeutic purposes.  To address this, we have developed two new microfluidic platforms that retain the quantitative aspects of traditional, one-at-a-time measurements while dramatically increasing their throughput. The first (HT-MEK, for High-Throughput Microfluidic Enzyme Kinetics) allows quantitative measurement of thermodynamic and kinetic constants for up to 1,500 different enzymes simultaneously. In recent work, we have applied HT-MEK to map the functional effects of amino acid substitutions throughout the enzyme scaffold of a model alkaline phosphatase and discovered surprising evidence that large contiguous groups of residues function in concert to tune particular aspects of catalysis. The second platform (BATTLES, for Biomechanically-Assisted T cell Triggering for Large-scale Exogenous-pMHC Screening) uses spectrally encoded beads comprised of thermoresponsive hydrogels to apply biomechanical forces to 1000s of T cells interacting with 10s of peptides in parallel, facilitating exploration of the force- and sequence-dependent landscape of T cell responses.