



Chemical Biology Seminar

“The Revolution Will Be Compartmentalized: Activity-Based and Cellular DNA-Encoded Library Technology”

Abstract: The NIH Molecular Libraries Program was founded to translate the discoveries of the Human Genome Project into therapeutics through a network of high-throughput screening (HTS) centers. A decade of discovery produced hundreds of probes—highly selective small molecules that modulate cellular function—but centralized HTS bears the same cost and infrastructure burdens of millennial DNA sequencing centers, restricting access to the technology and therefore the rate of probe discovery. We are building a distributable drug discovery platform analogous to next-generation DNA sequencing based on ultra-miniaturized solid-phase DNA-encoded libraries and microfluidic instrumentation for scalable, automated screening. I will overview chemical synthesis and microfluidic screening technology development efforts and describe their application to hit finding for two clinically relevant targets implicated in fibrosis and cancer. Looking toward the future, we are exploring approaches that directly translate genomic sequence into bioactive chemical probes, with the ultimate goal of fulfilling the originally promised pay dirt of the Human Genome Project.

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