IMS-P13 **Mapping the Protein Interaction Landscape for Fully Functionalized Small-Molecule Probes in Human Cells**

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Phenotypic screening offers a powerful approach to identify small molecules that perturb complex biological processes and organisms. Discerning the proteins and biochemical pathways targeted by screening hits, however, remains technically challenging. Herein we will present the synthesis of an ~60-member fully functionalized probe library, prepared from Ugi-azide condensation reactions to impart structural diversity and introduce diazirine and alkyne functionalities for target capture and enrichment, respectively. In-depth mass spectrometry-based analysis revealed a diverse array of probe targets in human cells, including enzymes, channels, adaptor and scaffolding proteins, and proteins of uncharacterized function. For many of these proteins, ligands have not yet been described. Structure−activity relationships across the probe library will also be discussed.