M | PHARMACY

MEDICINAL CHEMISTRY SEMINAR SERIES

Topliss Lecture

Activity-based protein profiling – target and ligand discovery on a global scale

Presented by Benjamin F. Cravatt, PhD

October 2, 2025 | 2 PM – 3:30 PM
Weiser Hall – Floor 10

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Advances in DNA sequencing have greatly increased our understanding of the genetic basis of human disease. However, many of human genes encode proteins that remain uncharacterized and lack selective small-molecule probes. To address these problems, we have introduced activity-based protein profiling (ABPP), a chemical proteomic technology that globally profiles the functional state and small molecule interactions of proteins in native biological systems. In this lecture, I will describe the application of ABPP to generate covalent small molecule interaction (or ligandability) maps of human cells and how this information can guide the discovery of first-in-class chemical probes and drug candidates for disease-relevant proteins. Key themes will include: 1) the importance of assaying proteins in endogenous environments to realize their full small molecule interaction potential; 2) the capacity of covalent chemistry coupled with ABPP to extend the druggability of the proteome to reach historically challenging target families like adaptor/scaffolding proteins and DNA/RNA-binding proteins; and 3) the remarkably diverse ways that allosteric small molecules can regulate protein function in cells.