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**“CHEMOPROTEOMIC PROFILING AND DISCOVERY OF
PROTEIN ELECTROPHILES IN HUMAN CELLS”**



The functions of proteins often derive from the chemical reactivities of specific amino acid side chains. Accordingly, chemical probes can target functional residues on the basis of their enhanced reactivity. Activity-based protein profiling (ABPP) couples probes with protein mass spectrometry to discover enzymes, inhibitors and new drug therapies in native biological systems. This powerful approach and branch of chemical biology, to date, has mainly targeted nucleophilic functionality using electrophilic probes. However, Nature does indeed exploit protein-bound electrophiles for function. In this seminar, I will describe ‘reverse-polarity’ ABPP, a chemically unbiased screen that deploys nucleophilic probes to capture and identify protein electrophiles in human cells.

Dynamic regulation of electrophilic enzyme cofactors can be monitored and novel electrophilic modifications can be discovered by this method.

