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Kinome Profiling to Determine Mechanisms of Drug Resistance

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Kinases are some of the most tractable targets for drug discovery and application. However resistance to kinase inhibitors remains a clinical problem limiting the success of promising therapeutics. Understanding the basis for inhibitor resistance is critical to advancing the field of kinase inhibitor pharmacology. Our lab is applying a mass spectrometry-based kinase profiling technology to study kinome adaptations to select kinase inhibitors. Combined with phosphoproteomics analyses, we have used this approach to identify kinase-dependent mechanisms of drug resistance. Thus these studies provide new opportunities for combinatorial approaches to systematically improve the success of targeted kinase inhibitors.