2.1 The rise of molecular glues and bifunctional compounds
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Efforts to translate novel biological findings have revealed a need for new approaches to drug discovery. The methods we are now pursuing trace back to the revelation that the cyclosporin and FK506 act in a way previously not seen – as “molecular glues” that induce protein–protein associations (Cell, 1991, 66, 807-815). The realization that additional medicines act as molecular glues has fueled the surge of interest in strategies for inducing functional protein–protein associations. I will discuss advances in the discovery of binders and molecular glues that alter their targets’ cellular lifetimes and localizations and may facilitate the translation to novel therapeutics having tissue and substrate selectivity. See also “The Rise of Molecular Glues”, Cell, 2021, 184, 3-9

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2.2 Mapping the Degradable Kinome: A Resource for Expedited Degrader Development
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Small molecules that induce protein degradation through ligase-mediated ubiquitination have shown considerable promise as a new pharmacological modality. We and others have demonstrated that efficacious degradation of kinases and other targets can be achieved in vitro and in vivo, however, many targets remain recalcitrant to degradation. In this presentation, I will discuss the use of large-scale chemical-proteomics approaches to map kinase degradability and accelerate the development of degraders as novel chemical probes for kinases.

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