“Methods to Evaluate and Perturb the Activity of the Human Proteasome with Small Molecules”

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The degradation of proteins is an essential cellular process. The proteasome, a multi-catalytic enzyme, is mainly responsible for degrading proteins that are no longer required by the cell. My lab has focused on the development of activity probes that can monitor real-time proteasome activity biochemically and in live cells. These probes can be applied in variety of analytical methods including confocal microscopy, flow cytometry, and fluorescent plate readers. With these probes, we have discovered a variety of proteasome stimulators and binders to non-catalytic subunits. The recently discovered proteasome stimulators have been applied to determine the effects of increasing the ubiquitin-independent degradation of proteins. Moving forward, we are now analyzing how these small molecule stimulators can affect the accumulation of unwanted proteins, including alpha-synuclein.