**PROTACs and Targeted Protein Degradation: A New Therapeutic Modality**

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My lab is interested using ‘Applied Chemical Biology’ to develop novel therapeutic modalities. Enzyme inhibition has proven to be a successful paradigm for pharmaceutical development, however, it has several limitations. As an alternative, for the past 20 years, my lab has focused on developing Proteolysis Targeting Chimera (PROTAC), a new ‘controlled proteolysis’ technology that overcomes the limitations of the current inhibitor pharmacological paradigm. Based on an ‘*Event-driven*’ paradigm, PROTACs offer a novel, catalytic mechanism to irreversibly inhibit protein function, namely, the intracellular destruction of target proteins. This approach employs heterobifunctional molecules capable of recruiting target proteins to the cellular quality control machinery, thus leading to their degradation. We have demonstrated the ability to degrade a wide variety of targets (kinases, transcription factors, epigenetic readers) with PROTACs at picomolar concentrations. Moreover, the PROTAC technology has been demonstrated with multiple E3 ubiquitin ligases and now two PROTAC-based drug candidates are being tested in Phase 2 clinical trials for prostate and breast cancer.

