DEPARTMENT OF CHEMICAL & PHYSICAL SCIENCES
COLLOQUIUM SERIES

Wednesday, September 30, 2020 @ 3:10pm
https://utoronto.zoom.us/j/97184523374

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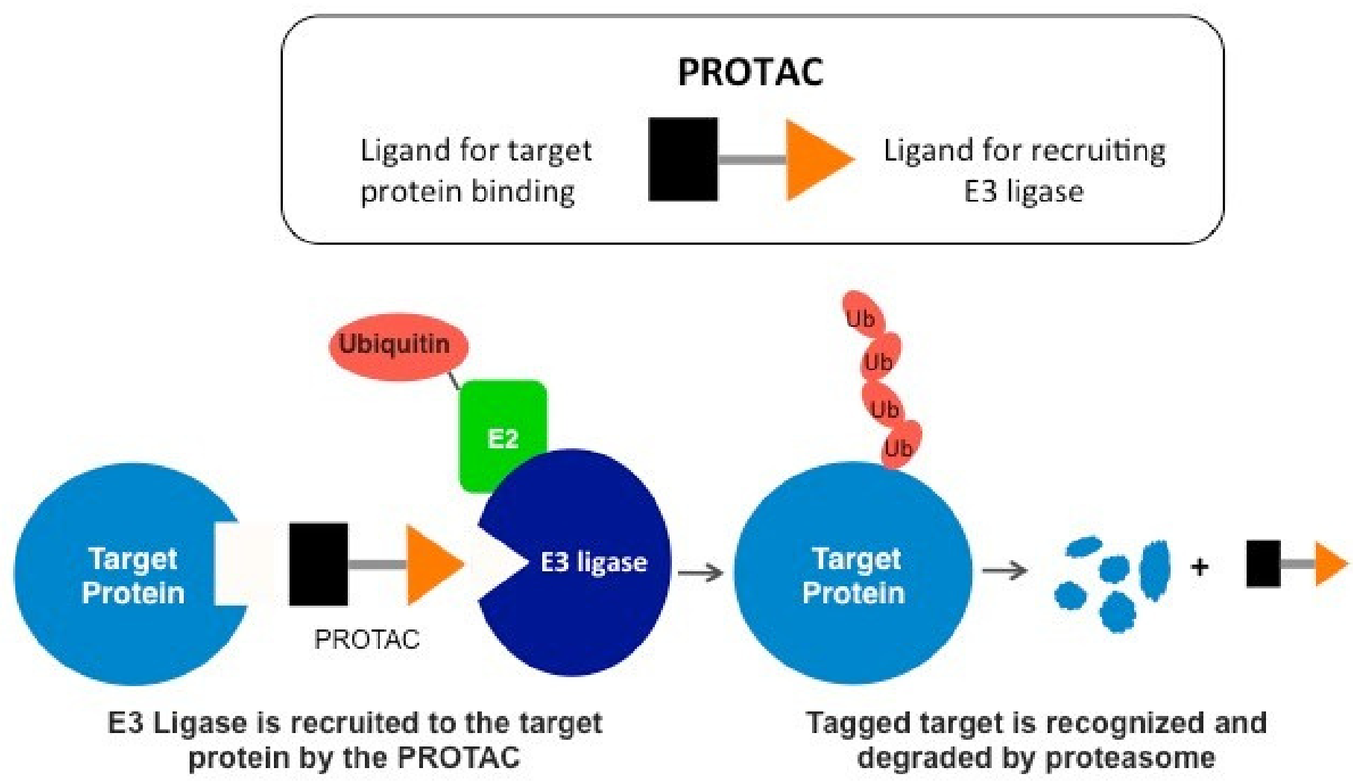
PROTAC-mediated Protein Degradation: A New Therapeutic Modality

PROTAC: PROteolysis TArgeting Chimera



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, included pVHL and cereblon. The first PROTAC-based drugs have entered clinical trials for breast and prostate cancer.