## Title: Proteasome Dynamics Unleashed: A New Frontier in Cancer Therapy

Cancer cells often display altered proteasome functions, which contribute to their uncontrolled growth and survival. Proteasome inhibitors, such as bortezomib, have been effectively used in treating multiple myeloma by disrupting protein degradation pathways. Extensive research in Prof. Ciechanover's laboratory has revealed a novel mechanism of action based on the dynamic localization and distribution of proteasomes within the cell—a central process in coping with cellular stress. The findings indicate that cancer cells are particularly vulnerable to the manipulation of proteasome localization, positioning proteasome dynamics as a promising target for drug development. Prof. Ciechanover and his team have identified the biological signal responsible for inhibiting proteasome translocation, sequestering it in the nucleus during stress, and eventually leading to cellular death. Additionally, it was also shown that the subcellular distribution of proteasomes may act as a diagnostic biomarker across various cancer types.

Recognizing the therapeutic potential of manipulating proteasome localization, TRDF, Prof. Ciechanover and Dr. Livneh established Tripod Therapeutics to translate these findings into clinical applications.

Tripod Therapeutics is developing orally available drugs that regulate proteasome localization, effectively leading cancer cells to their death.

The company has already demonstrated the efficacy of this novel approach in several animal models of cancer and is now working towards the initiation of pre-clinical and clinical studies.