

## Abstract:

Conjugation of cellular proteins by the ubiquitin-related SUMO modifiers (SUMOylation) has emerged as a crucial regulatory mechanism for maintenance of cell and organ homeostasis. SUMOylation is tightly controlled by the balanced activity of the multi-step SUMO conjugation machinery and the SUMO deconjugation pathway that primarily depends on SUMO-specific proteases of the SENP family. Alterations of SUMO homeostasis are frequently observed in cancer and associated with an aggressive phenotype. Our work links MYC-driven cell biology with activity of the SUMO pathway. We propose biomarker-informed pharmacological SUMO inhibition as rational cancer therapy and target aberrant SUMO activity within cellular and non-cellular immunotherapies.