

Ulp1-SUMO Crystal Structure and Genetic Analysis Reveal Conserved Interactions and a Regulatory Element Essential for Cell Growth in Yeast

E. Mossesso and C.D. Lima (Biochemistry Department, Weill Medical College of Cornell University)

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Modification of cellular proteins by the ubiquitin-like protein SUMO is essential for nuclear processes and cell cycle progression in yeast. The Ulp1 protease catalyzes two essential functions in the SUMO pathway: (1) processing of full-length SUMO to its mature form and (2) deconjugation of SUMO from targeted proteins. Selective reduction of the proteolytic reaction produced a covalent thiohemiacetal transition state complex between a Ulp1 C-terminal fragment and its cellular substrate Smt3, the yeast SUMO homolog. The Ulp1-Smt3 crystal structure and functional testing of elements within the conserved interface elucidate determinants of SUMO recognition, processing, and deconjugation. Genetic analysis guided by the structure further reveals a regulatory element N-terminal to the proteolytic domain that is required for cell growth in yeast.

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