Coupling of Dynamics and allostery in the apo MALT1 Paracaspase

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Mucosa-associated lymphoid tissue lymphoma translocation protein 1 (MALT1) is a unique paracaspase protein whose protease activity mediates oncogenic NF-kB signalling in activated B cell-like diffuse large B cell lymphomas (ABC-DLBCLs). ABC-DLBCLs are aggressive lymphomas with high resistance to current chemotherapies. Low survival rate among patients emphasizes the urgent need for alternative treatment options. The characterization of MALT1 will be an essential tool for developing new target-directed drugs against MALT1 dependent disorders.

As the first step in the atomic-level NMR studies of MALT1, we have reported the 15N/13C/1H backbone assignment of the apo form of the MALT1 paracaspase region together with the third immunoglobulin-like (Ig3) domain, MALT1Casp-Ig3 (44 kDa), by high resolution NMR[1]. As the second step, 15N-TROSY based relaxation NMR experiments have been acquired for apo $MALT1_{Casp\text{-}Ig3}$ to study the protein dynamics on different time scales, revealing that $MALT1_{Casp\text{-}Ig3}$ is a dynamic system and that dynamical data is needed to complement the structural data. The allosteric interactions in Malt1 will be discussed.

1 Unnerståle, Sofia, et al. "Backbone Assignment of the MALT1 Paracaspase by Solution NMR." PloS one 11.1 (2016).