Poster Presentation

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Structural characterization of the ASPP/PP1 phosphatase complex

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Serine/Threonine phosphatases such as PP1 generally lack substrate specificity and associate with a large array of targeting subunits (~200) to achieve the requisite selectivity. However, the molecular basis for PP1 recruitment remains unexplored for all but a handful of cases. The tumour suppressor ASPP (Apoptosis-stimulating protein of p53) proteins associate with PP1 catalytic subunits and are implicated in multiple functions from transcriptional regulation to cell junction remodeling. We show that Drosophila ASPP is part of a multiprotein PP1 complex and that PP1 association is necessary for all of Drosophila ASPP's in vivo functions. We solve the crystal structure of the human ASPP2/PP1 complex and show that ASPP2 recruits PP1 using both its canonical RVxF motif and its SH3 domain, which engages the PP1 C-tail. The ASPP2 SH3 domain can discriminate between PP1 isoforms using an acidic specificity pocket in the N-Src domain of ASPP, providing an exquisite mechanism where multiple motifs are used combinatorially to tune binding affinity to PP1. This is the first crystal structure of PP1 showing it's variable C-terminal tail bound to a regulatory/targeting protein.

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