

## Poster Presentation

**MS53.P09**

### *Structural Studies on the SARAH Domain from MST and RASSF Family Proteins*

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Although the recent progress towards the molecular biology of the Hippo signaling pathway, the mechanistic and structural information in this area remains elusive. Intriguingly, RASSFs function both positively and negatively depending on the events in the diverse cellular signals, by the interaction with MSTs through their SARAH domains. The precise mechanism of these sophisticated regulations of cell growth and apoptosis is still largely unknown. Here, we determined the 3D structures of SARAH domains as MST1-RASSF5 heterodimer and MST2 homodimer by X-ray crystallography. Although the structure of MST2 homodimer showed very similar to the previously reported MST1 homodimer, MST1-RASSF5 showed a distinct feature with flexible N-terminal extension of MST1 SARAH domain and a hydrophobic core stabilized by the aromatic interactions. Comparison of the interfaces and computational alanine scanning indicates the more extensive interactions in the dimer interface in MST1-RASSF5 heterodimer than those of homodimer. Monitoring the structural stability by urea denaturation indicated MSTs-RASSFs heterodimers are substantially more stable than MSTs homodimer. These results provide a 3D structural explanation for the preferential binding of MSTs-RASSFs SARAH domains which is a key mechanism of regulation in the Hippo pathway.

[1] Hwang, E. et al(2007) PNAS 104, 9236-9241.

**Keywords:** Hippo signaling pathway, SARAH (SAV/RASSF/HPO) domain, MST (mammalian sterile 20-like) kinase, RASSF (Ras-association domain family), X-ray crystallography