Poster Presentation

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Crystal structure of the human COP9 signalosome

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The COP9 signalosome (CSN) is a multifunctional ~350 kDa eight-protein complex with highly-specific isopeptidase activity, which regulates the vast cullin-RING family of ubiquitin ligases (CRLs). Ubiquitin ligases direct target-specific ubiquitination and are involved in a multitude of regulatory processes, ultimately linked to protein turnover by the proteosome. Humans have a repertoire of approximately 240 CRLs, more than any other ubiquitin ligase family. The entire human CSN has been structurally characterised de novo using low-resolution (4-Å) X-ray crystallography. The crystallographic analysis was complicated by rotational pseudo-symmetry and twinning, non-isomorphism as well as the absence of experimental phase information beyond ~8 Å resolution. Details of the structure determination procedures, which combined a cluster compound-based phasing strategy, analysis of seven differentially substituted selenomethionyl derivatives, multi-crystal averaging among non-isomorphous data sets with a multi-crystal co-refinement approach, will be described. Some implications of the structure and insight into the regulation of CSN will also be presented.

Keywords: protein complex, low resolution methodology