Discovering a new subunit for an old complex

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Abstract

The highly conserved COP9 signalosome (CSN) complex is a key regulator of the ubiquitin/26S proteasome degradation pathway. Until now it was accepted that the CSN is comprised of eight canonical components, here we report the discovery of a new integral subunit by using a new mass spectrometry method that combines top-down and bottom-up proteomics. This new subunit, CSNAP (for CSN Acidic Protein), escaped classical analyses methods because it is an intrinsically unstructured low molecular weight (6.2 kDa) protein. We verify that CSNAP is a bona-fide integral member of the CSN complex by several independent biochemical, fluorescence microscopy, native mass spectrometry and cell biology analyses. Most importantly we show that CSNAP promotes the structural stability of the CSN complex by binding to each of the two distinct structural elements in the CSN. Thus, it serves as a flexible 'brace' maintaining the integrity of the complex during the large conformational changes associated with its function. Finally, we show that CSNAP is homologous to a small 19S proteasome subunit, DSS1, completing the perfect one-to-one correspondence between the 19S proteasome-lid and the CSN complex.