7th International Conference on

Proteomics & Bioinformatics October 24-26, 2016 Rome, Italy

Solution structure of CUBO, a novel domain that preferentially binds the ubiquitin-like protein NEDD8

Elena Santonico University of Rome Tor Vergata, Italy

A mong the members of the ubiquitin-like (Ubl) protein family, NEDD8 is the closest in sequence to ubiquitin (58% identity). The two modification mechanisms and their functions, however, are largely distinct and the two molecules are not interchangeable. Selectivity is ensured by a complex network of interactions between modifying enzymes and adaptors, some of which are specific while others are promiscuous. Many domains that bind the ubiquitin hydrophobic patch also bind NEDD8 while no domain that exclusively binds NEDD8 has been described so far. Here, we report an unbiased selection of domains that bind ubiquitin and/or NEDD8 and we characterize their selectivity. Many selected domains bind preferentially ubiquitin and to a lesser extent NEDD8. In few cases, the affinity of these domains for NEDD8 can be increased by substituting the alanine at position 72 with arginine, as in ubiquitin. We also identified a unique domain which maps to the carboxyl-end of the protein KHNYN, that has a clear preference for NEDD8 and binds neddylated cullins. Given this ability, we named this domain CUBO (Cullins Binding Domain). We present here the solution structure of CUBO domain in isolation and in complex with NEDD8. The model for the KHNYN-NEDD8 interaction is based on the NMR structure of the isolated domain, mutational analysis and chemical shift perturbations (CSPs) upon binding. The CUBO domain of KHNYN is to date the first example of NEDD8-binding protein that preferentially recognizes neddylated substrates.

Biography

Elena Santonico has completed her PhD and Post-doctoral studies at Tor Vergata University. She is a Research Scientist at the Department of Biology. Her research topic is mainly focused on "Studying the function of ubiquitin and Ub-like binding domains in proteolysis".

Elena.Santonico@uniroma2.it

Notes: