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Venerdì 14 giugno 2024, ore 9:45
CNR-NANO Seminar room 3rd floor,
Dpt. Physics, Informatics and Mathematics, via G. Campi 213/A

Il Dottor Dhawal Choudhary
AMOLF, Science Park 104, 1098 XG Amsterdam, the Netherlands.

terrà un seminario dal titolo

Polyubiquitin conformational dynamics induced by Cdc48

Conformational processing of polyubiquitinated proteins by Cdc48 (p97 or VCP in metazoans) is vital to cells. Cdc48 is thought to translocate the isopeptide bond branches of ubiquitin through its central pore, in order to unfold linked proteins and extract them from molecular complexes. However, the required processive activity has not been established, due to the challenges of measuring Cdc48 and polyubiquitin conformational changes. As a result, the dynamic basis of key processing steps including ubiquitin unfolding and ubiquitin branch point handling is unclear⁶. Here, by following Cdc48 complexes in time, we show that Cdc48 targets polyubiquitin by a combination of repeated non-processive insertion cycles and processive loop extrusion. The insertion of ubiquitin branch points into the Cdc48 pore occurs in burst of trial-abort non-processive cycles that may last up to several seconds. Once started, Cdc48 moves highly processively along the ubiquitinated substrate over hundreds of residues, while generating over 10 pN to unfold ubiquitin monomers, pulling ubiquitin branch points through the Cdc48 pore at 10 nm/s, and extruding ubiquitin polypeptide as loops in trans. We observed that Cdc48 switches between non-processive and processive activity indicating conformational selection by Cdc48, which may be relevant to regulating ubiquitin targeting across the Eukaryotic kingdoms.

Ospitante: Prof. Ciro Cecconi