Poster Presentation

MS081.P03

Plasticity at the Septin 9 interface: implications for filament dynamics

Richard Garratt[1], Sabrina Matos de Oliveira da Silva[2], Diego Antonio Leonardo Cabrejos[1], Napoleão Fonseca Valadares[3], Humberto D´Muniz Pereira[1]

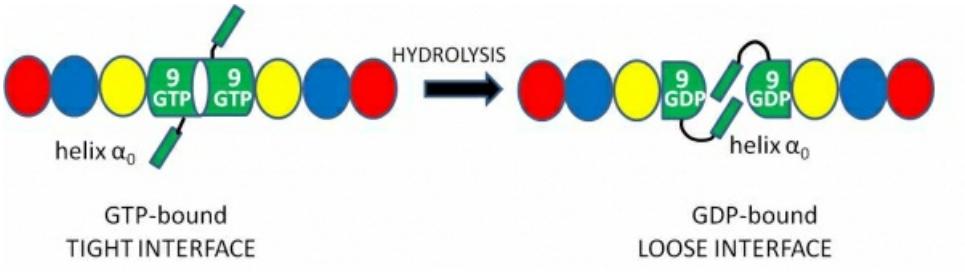
[1]*São Carlos Institute Of Physics - USP, SÃo Carlos, Brazil,* [2]*São Carlos Institute of Chemistry, São Carlos, Brazil,* [3]*Department of Cellular Biology, University of Brasília, Brasilia, Brazil*

E-mail: richard@ifsc.usp.br

Human septins are guanine nucleotide binding proteins that form membrane associating hetero-filaments which result from the polymerization of core particles composed of either six or eight monomers [1]. The resulting filaments are involved in both barrier formation and in a series of membrane remodelling events including cytokinesis. Human septins can be divided into four groups based on sequence similarity and a representative of each is required to build the octameric core particle to which they all provide two monomers. The most widely studied octamer is that composed of septins 2, 6, 7 and 9 which assemble in the following order: SEPT9-SEPT7-SEPT6-SEPT2-SEPT2-SEPT6-SEPT7-SEPT9 [2] generating two different types of inter-subunit interface (G and NC) which alternate along the filament axis. As such it is obvious that interactions formed between adjacent copies of SEPT9 are fundamental to the polymerization process as they form the interface between successive core particles. We have solved the structure of the GTP binding domain of human SEPT9 complexed to both GDP and GTPγS. Two monomers are observed to be squeezed together at the NC interface in the latter leading to a foreshortening of the homo-filament observed in the crystal. This involves a largely rigid body translation together with limited structural rearrangement of the individual monomers. The result is the reduction of the space available at the interface for accommodating a polybasic helix (absent from the construct used in the present study but observed in previous structures [3]) which is known to be involved in membrane association. Based on both the crystal structures reported here and associated modelling studies, we provide a mechanism by which a hetero-filament would bind to a membrane via its polybasic helix in the presence of GTP but would be expected to bury the helix on GTP hydrolysis thus leading to release of the filament from the membrane. This suggests that the NC interface between successive core particles along a filament may have special properties relevant to the dynamics of membrane association which could be related to membrane remodelling events.

Financial support: CNPq and FAPESP.

[1] Mostowy, S. & Cossart, P. (2012) Nat. Rev. Mol. Cell. Biol. 13, 183-194
[2] Kim, M. S. et al. (2011) J. Cell Biol. 195, 815-826
[3] Sirajuddin, M. et al (2007) Nature 449, 311-315



Keywords: Septins, hetero-filaments, NC interface