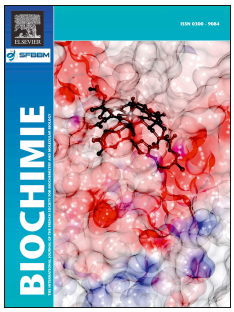
Accepted Manuscript



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PII: S0300-9084(16)30201-2

DOI: 10.1016/j.biochi.2016.09.014

Reference: BIOCHI 5062

To appear in: *Biochimie*

Received Date: 11 May 2016

Accepted Date: 24 September 2016

Please cite this article as: A.E. Zeraik, M. Staykova, M.G. Fontes, I. Nemuraitė, R. Quinlan, A.P.U. Araújo, R. DeMarco, Biophysical dissection of schistosome septins: insights into oligomerization and membrane binding, *Biochimie* (2016), doi: 10.1016/j.biochi.2016.09.014.

Biophysical dissection of schistosome septins: insights into oligomerization and membrane binding

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ABSTRACT

Septins are GTP-binding proteins that are highly conserved among eukaryotes and which are usually membrane-associated. They have been linked to several critical cellular functions such as exocytosis and ciliogenesis, but little mechanistic detail is known. Their assembly into filaments and membrane binding properties are incompletely understood and that is specially so for non-human septins where such information would offer therapeutic potential. In this study we use *Schistosoma mansoni*, exhibiting just four septin genes, as a simpler model for characterizing the septin structure and organization. We show that the biochemical and biophysical proprieties of its *Sm*SEPT5 and *Sm*SEPT10 septins are consistent with their human counterparts of subgroups SEPT2 and SEPT6, respectively. By succeeding to isolate stable constructs comprising distinct domains of *Sm*SEPT5 and *Sm*SEPT10 we were able to infer the influence of terminal interfaces in the oligomerization and membrane binding properties. For example, both proteins tended to form oligomers interacting by the N- and C-terminal interfaces in a nucleotide independent fashion but form heterodimers via the G interface, which are nucleotide dependent. Furthermore, we report for the first time that it is the C-terminus of *Sm*SETP10, rather than the N-terminal polybasic region found in other septins, that mediates its binding to liposomes. Upon binding we observe formation of discrete lipo-protein clusters and higher order

Abreviations: CD- Circular dichroism;CSM- Center of spectral mass; DOPC- 1,2-Dioleoyl-sn-glycero-3-phosphocholine; GUV- Giant unilamelar vesicle; ITC-Isothermal titration calorimetry; SEC- Size exclusion chromatography; PIP2-Phosphatidylinositol 4,5-bisphosphate; SEPT-Septin; ThT- Thioflavin-T