Session 1
6th May
11:00 h

Deciphering the interaction of lactoferrin with V-ATPase towards a deeper understanding of its mechanisms of action

Cátia Santos-Pereira[1,2,3], Juliana F. Rocha[3], Henrique S. Fernandes[3], Lígia R. Rodrigues[2], Manuela Côrte-Real[1], Sérgio F. Sousa[3]

[1] Centre of Molecular and Environmental Biology (CBMA), Department of Biology, University of Minho, Braga, Portugal
[2] Centre of Biological Engineering (CEB), Department of Biological Engineering, University of Minho, Braga, Portugal
[3] UCIBIO@REQUIMTE, BioSIM, Departamento de Biomedicina, Faculdade de Medicina da Universidade do Porto, Porto, Portugal

Lactoferrin (Lf), a bioactive milk protein, exhibits strong anticancer and antifungal activities. The search for Lf targets and mechanisms of action is of utmost importance to enhance its effective applications. A common feature among Lf-treated cancer and fungal cells is the inhibition of a proton pump called V-ATPase. Lf-driven V-ATPase inhibition leads to cytosolic acidification, ultimately causing cell death of cancer and fungal cells. Given that a detailed elucidation of how Lf and V-ATPase interact is still missing, in this work we aimed to fill this gap by employing a multi-level computational approach. Molecular dynamics (MD) simulations of both proteins were performed to obtain a robust sampling of their conformational landscape, followed by clustering and protein-protein docking. Subsequently, MD simulations of the docked complexes and free binding energy calculations were carried out to evaluate the dynamic binding process and build the final ranking. This computational pipeline allowed the unraveling of the putative mechanism by which Lf inhibits V-ATPase and the identification of key binding residues that will certainly aid in the rational design of follow-up experimental studies, bridging in this way computational and experimental biochemistry.