

BioISI - Biosystems & Integrative Sciences Institute

VERÃO COM CIÊNCIA 2022 | BioISI Internship Projects

Project ID | VC22_4

Project Title | The role of protein knotting role in complex stability and enzyme catalysis

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Number of Fellowships Available | 1 (one)

Abstract | Ubiquitin C-terminal hydrolases (UCHs) are papain-like cysteine proteases that hydrolyze the ubiquitin adduct, countering ubiquitination in proteins. Besides its important role in this proteolytic pathway, UCH-L1 is also highly abundant in the brain and forms one of the most complicated 3D knotted structures yet discovered. There are five crossings of the polypeptide backbone forming a '5 2' or 'Gordian' knot. We have used MD simulations to study several truncated versions of UCH-L1 in complex with its ubiquitin partner. With this protocol, we promote the unknotting process and study its impact on the UCH-L1:Ubiquitin complex stability. In this project, we will calculate the binding affinities of the different truncated complexes using an MM-PBSA methodology (PyBindE) developed in our research unit. The results will provide key evidence of the protein knotting role in complex stability and enzyme catalysis.