

**BioISI - Biosystems & Integrative Sciences Institute**

**VERÃO COM CIÊNCIA 2022 | BioISI Internship Projects**

**Project ID | VC22\_3**

**Project Title | Is the aggregation-prone intermediate of human b2m protein conserved across homologs?**

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**Number of Fellowships Available | 1 (one)**

**Abstract |** We used molecular simulations to predict that the intermediate state, which triggers the amyloid pathway in several human variants of protein b2m (hb2m), displays a conserved core and two unstructured termini. The so-called ‘termini’ intermediate has been confirmed by solid-state NMR for the D76N mutant. We will investigate whether this species is conserved across b2m homologs or exclusively populated by hb2m. We will use an integrative approach that samples conformations with MC simulations and isolates the intermediate states using structural clustering. The student will be involved in the structural clustering task of murine b2m. After intermediate identification, we will posteriorly investigate their structural stability using classical MD and establish a relationship with the in vitro aggregation potential. This work will clarify the role of the ‘termini’ intermediate as a potential therapeutic target for b2m amyloidosis.