MOLECULAR MODELING OF THE HUMAN EUKARYOTIC TRANSLATION INITIATION FACTOR 5A (eIF5A) BASED ON SPECTROSCOPIC AND COMPUTATIONAL ANALYSES

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Eukaryotic translation initiation factor 5A (eIF5A) undergoes a unique post-translational modification, hypusination. Such modification is essential for a variety of functional roles for eIF5A, including cell proliferation and synthesis of proteins involved in cell cycle control. Neither a totally selective inhibitor of hypusination nor an inhibitor capable of directly binding to eIF5A has been reported in the literature. Here, we present a molecular model for the human eIF5A protein based on the crystal structure of the eIF5A from *Leishmania brasiliensis*, and compare the modeled conformation of the loop bearing the hypusination site with circular dichroism data obtained with a synthetic peptide corresponding to this loop. Furthermore, analysis of amino acid variability between different human eIF5A isoforms revealed peculiar structural characteristics that are of functional relevance. We concluded that the hypusinated region probably assumes an ordered conformation in hydrophobic environment, which might be a relevant feature for functional interactions of the eIF5A with partner proteins. Additionally, our data suggest that consideration of the eIF5A structure as a protein composed of two functionally and structurally distinct domains might be useful to direct the development of specific inhibitors. Financial support: FAPESP.