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A Novel in-silico driven Approach to Determine the Structure and Therapeutic Potential of Cystatin C from *Danio rerio*

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Abstract

Cystatins, a superfamily of evolutionary related proteins are classified as housekeeping proteins vital for the inhibition of Papain-like cysteine proteases. Over expression of cysteine proteases have been related to the development of diseases. These facts result in the realization of Cystatins importance as regulators of protease activity and their role in the body's immune system. The Cystatin C protein understudy was identified from a pre-established transcriptomic database of D. rerio using the NCBI database and the NCBI-BLAST algorithm. Cystatin C belongs to the Type 2 Cystatin family and is the most powerful cysteine protease inhibitor effective against Papain like proteases. The research study aims to develop an economical in-silico based approach to analyze the structure and functionality of novel proteins with a comprehensive revelation of their clinical significance. Therefore, we report on novel in-silico tools to generate a model of the Cystatin C protein expressed by *D. rerio*, prove its functionality through molecular docking techniques and discover its immune potential against diseases caused by Cathepsin over expression through the use of gene-gene interaction mapping. Through the computational procedure a 99.99% accurate protein structure was predicted through homology modelling techniques followed by successful inhibition of Papain and mammalian Cathepsins B, H, L1 and S with therapeutic potential present for diseases caused by Cathepsin B and L1 overexpression. Analysis of the Cathepsin inhibition zone revealed a common binding site on the Cystatin C proteins' surface amoung seven closely related amino acids. In conclusion *D. rerio* produces a Cystatin C protein that can successfully act as a cysteine protease inhibitor in addition to bearing valuable therapeutic potential. Further analysis is required to confirm its tissue specific expression, modulation under pathogenic conditions.

Keywords: Danio rerio, in-silico, Protein-protein docking, Virtual screening, Therapeutics