Structural studies of human purine nucleoside phosphorylase: Towards a new specific empirical scoring function

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Human purine nucleoside phosphorylase (HsPNP) is a target for inhibitor development aiming at T-cell immune response modulation. In this work, we report the development of a new set of empirical scoring functions and its application to evaluate binding affinities and docking results. To test these new functions, we solved the structure of HsPNP and 2-mercapto-4(3H)-quinazolinone (HsPNP:MQU) binary complex at 2.7 Å resolution using synchrotron radiation, and used these functions to predict ligand position obtained in docking simulations. We also employed molecular dynamics simulations to analyze HsPNP in two conditions, as apoenzyme and in the binary complex form, in order to assess the structural features responsible for stability. Analysis of the structural differences between systems provides explanation for inhibitor binding. The use of these scoring functions to evaluate binding affinities and molecular docking results may be used to guide future efforts on virtual screening focused on HsPNP.

Keywords: Empirical scoring functions, Docking, Molecular dynamics

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