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In silico assessment of human Calprotectin subunits (S100A8/A9) in presence of sodium and calcium ions using Molecular Dynamics simulation approach

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Abstract

Calprotectin is a heterodimeric protein complex which consists of two subunits including S100A8 and S100A9. This protein has a major role in different inflammatory disease and various types of cancers. In current study we aimed to evaluate the structural and thermodynamic changes of the subunits and the complex in presence of sodium and calcium ions using molecular dynamics (MD) simulation. Therefore, the residue interaction network (RIN) was visualized in Cytoscape program. In next step, to measure the binding free energy, the potential of mean force (PMF) method was performed. Finally, the molecular mechanics Poisson-Boltzmann surface area (MMPBSA) method was applied as an effective tool to calculate the molecular model affinities. The MD simulation results of the subunits represented their structural changes in presence of Ca^{2+}. Moreover, the RIN and Hydrogen bond analysis demonstrated that cluster interactions between Calprotectin subunits in presence of Ca^{2+} were greater in comparison with Na^{+}. Our findings indicated that the binding free energy of the subunits in presence of Ca^{2+} was significantly greater than Na^{+}. The results revealed that Ca^{2+} has the ability to induce structural changes in subunits in comparison with Na^{+} which lead to create stronger interactions between. Hence, studying the physical characteristics of the human proteins could be considered as a powerful tool in theranostics and drug design purposes.

Introduction

Calprotectin is a heterodimeric protein complex which consists of two subunits including S100A8 and S100A9. This protein has a great role in different inflammatory disease and various types of cancers. It is a heterodimeric complex of EF-hand Ca^{2+} binding protein. The protein has two subunits which called S100A8 (MRP8/ Calgranulin A) and S100A9 (MRP14/ Calgranulin B) and are fundamentally expressed by myeloid cells. Thus, they are called