Molecular Recognition of Cell Adhesion Proteins: Is Water the Glue That Holds Pathogens to Host Cells?

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Abstract

Candida species are among the most common fungal pathogens in humans. Candida is able to recognize a variety of peptide sequences on host cells because of its cell-adhesion proteins; however, it is unknown why binding is so promiscuous. X-ray structural data from a cell adhesion protein-peptide complex suggests that water molecules in the binding cavity play a role as the "glue" holding the peptide in the binding cavity. The aim of this work is to determine whether these water molecules play a role in the molecular recognition of cell adhesion proteins to their host cells. We have performed molecular dynamics (MD) simulations of ALS9-2, a cell adhesion protein, without the peptide and characterized the hydration properties of the binding site using solvation thermodynamics techniques. Many of the regions of high water density observed in the MD simulation correspond to the X-ray crystal waters found in the binding pocket of ALS9-2-peptide complex. However, no correlation exists between the experimental B-factors of the water molecules in the ALS-9 peptide complex and the water occupancies/entropies obtained without the peptide. These results suggest that the peptide does play a role in structuring the network of water in the bound ALS-9-peptide complex. Future work will investigate the influence of the peptide on the hydration properties of this cell adhesion protein.