MICA-TM Peptide Selectively Binds to HLAs Associated with Behçet's Disease

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Abstract : Behçet's disease (BD) is a genetic autoimmune expressed by multisystemic inflammatory disorder mostly occurred at the skin, joints, gastrointestinal tract, and genitalia, including ocular, oral, genital, and central nervous systems. Most BD patients in Japan and Korea were strongly indicated by the genetic factor namely HLA-B*51 (especially, HLA-B*51:01) marker in HMC class I, while HLA-A*26:01 allele has been detected from the BD patients in Greek, Japan, and Taiwan. To understand the selective binding of the MICA-TM peptide towards the HLAs associated with BD, the molecular dynamics simulations were applied on the four HLA alleles (B*51:01, B*35:01, A*26:01, and A*11:01) in complex with such peptide. As a result, the key residues in the binding groove of HLA protein which play an important role in the MICA-TM peptide binding and stabilization were revealed. The Van der Waals force was found to be the main protein-protein interaction. Based on the binding free energy prediction by MM/PBSA method, the MICA-TM peptide interacted stronger to the HLA alleles associated to BD in the identical class by 7-12 kcal/mol. The obtained results from the present study could help to differentiate the HLA alleles and explain a source of Behçet's disease.