Experimental and theoretical study on converting myoglobin into a stable domain-swapped dimer by utilizing a tight hydrogen bond network at the hinge region

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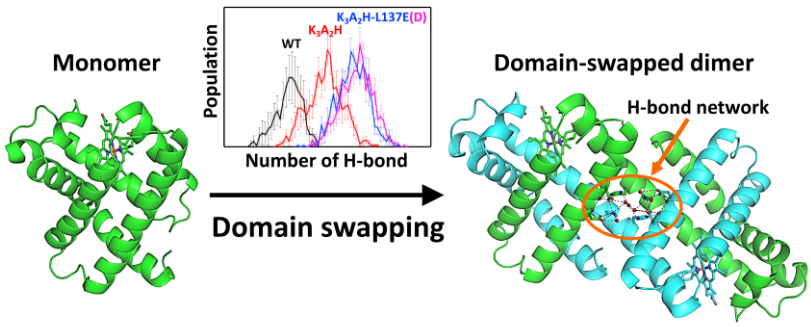
Various factors, such as helical propensity and hydrogen bonds, control protein structures. We have previously shown that a frequently used model protein, myoglobin (Mb), can form a domain-swapped dimer, and we succeeded in obtaining monomer–dimer equilibrium in the native state by introducing a high α-helical propensity residue, Ala, to the hinge region.[1] In this study, we focused on another factor that governs the protein structure, hydrogen bonding. X–ray crystal structures and thermodynamic studies showed that the Mb dimer is stabilized over the monomer when the H-bond network at the hinge region of the dimer is enhanced by keeping His82 to interact with Lys79 and Asp141 and mutating Leu137, which is located close to the H-bond network, to a hydrophilic amino acid, namely, Glu or Asp.[2] Molecular dynamics simulation studies confirmed that the number of H-bonds increased for mutants with a tighter H-bond network. The simulation also showed that the distance between the helices at the hinge region becomes shorter as the H-bond network is enhanced, supporting the hypothesis that the helices at the hinge region become tighter and the Mb dimer is stabilized when the H-bond network at the hinge region is enhanced. This reveals the importance and utility of hydrogen bonds for designing a protein dimer from its monomer.



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