



**Supplementary information, Fig. S1: Interhelical packing interactions in HR121.**

**a** Schematic representation of HR121. The corresponding sequences of HR1, HR2 and the linker are shown in diagram. The “e” and “g” positions in HR1 and “a” and “d” residues in HR2 are colored in red. The residues involved in interaction between HR1 and HR2 are marked with a grey background. **b** Left: formation of HR121 between HR1 and HR2. The inner HR1 trimer ( $\alpha 1$ ,  $\alpha 3$ , and  $\alpha 4$ ) is formed through the interaction of residues located at the “a” and “d” positions, and two HR2s depend on the residues located at the “a” and “d” positions to interact with the residues in “e” and “g” positions in the inner HR1 trimer. Another HR1 ( $\alpha 2$ ) depend on the residues at “e” positions to bind with the residues at “g” positions in HR1 ( $\alpha 3$ ), and the residues at “a” positions to bind with the residues at “e” positions in HR1 ( $\alpha 4$ ). Right: formation of the post-fusion structure of SARS-CoV-2 6-HB (PDB code: 6LXT). The HR1 trimer is formed through the interaction of residues located at “a” and “d” positions, and the HR2 depend on the residue located at the “a” and “d” position to interact with the residues in “e” and “g” positions in HR1. **c** A cartoon representation showing superimposition of the inner HR1 trimer ( $\alpha 1$ ,  $\alpha 3$ , and  $\alpha 4$ ) of HR121 with the central HR1 trimer of SARS-CoV2 6-HB (PDB code: 6LXT). The figures below are diagrams of the superimposed helices in top view. **d** List of interacting residues between HR121 helical bundles. The helical fusion core regions are marked with dark blue box.