SUPPLEMENTAL MATERIAL FOR

Interaction of chemokine receptor CXCR4 in monomeric and dimeric state with its endogenous ligand CXCL12: Coarse-grained simulations identify differences

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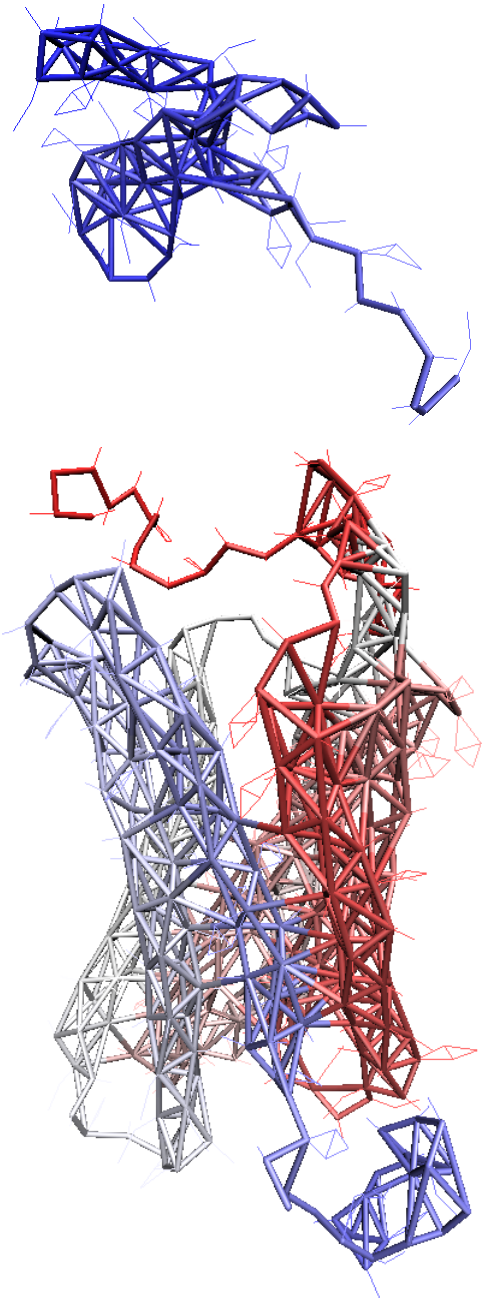

Figure S1: Elastic network models of the CXCL12 (top) and CXCR4 (bottom) proteins. The secondary structures are maintained through dense netwoks of springs, whereas the unstructured terminal tails keep their intrinsic flexibility.

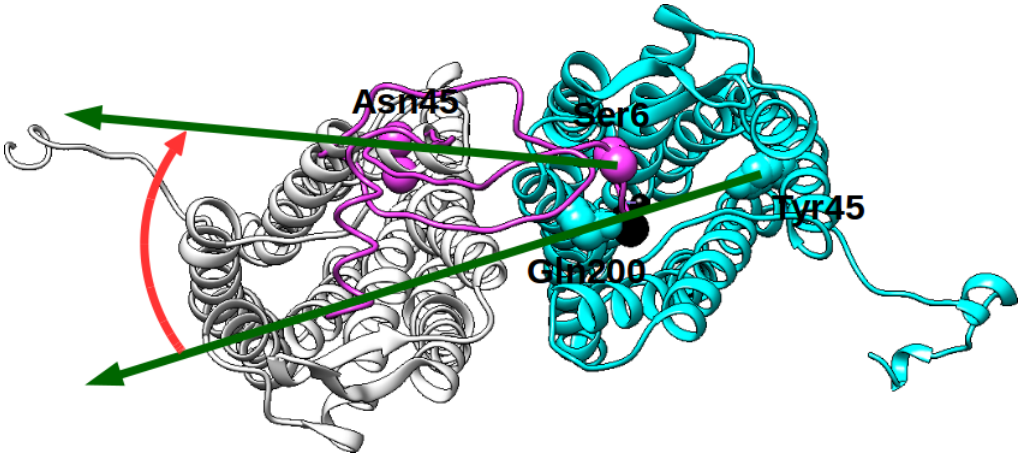

Figure S2: Definition of the angle that characterize the position of the chemokine core domain with respect to the receptor helix bundle. The angle is defined between the vector joining the CXCR4 residues Tyr45 to Gln200 (cyan sheres) and the vector joining the CXCL12 pivotal residue Ser6 to the antipodal Asn45 (magenta spheres).

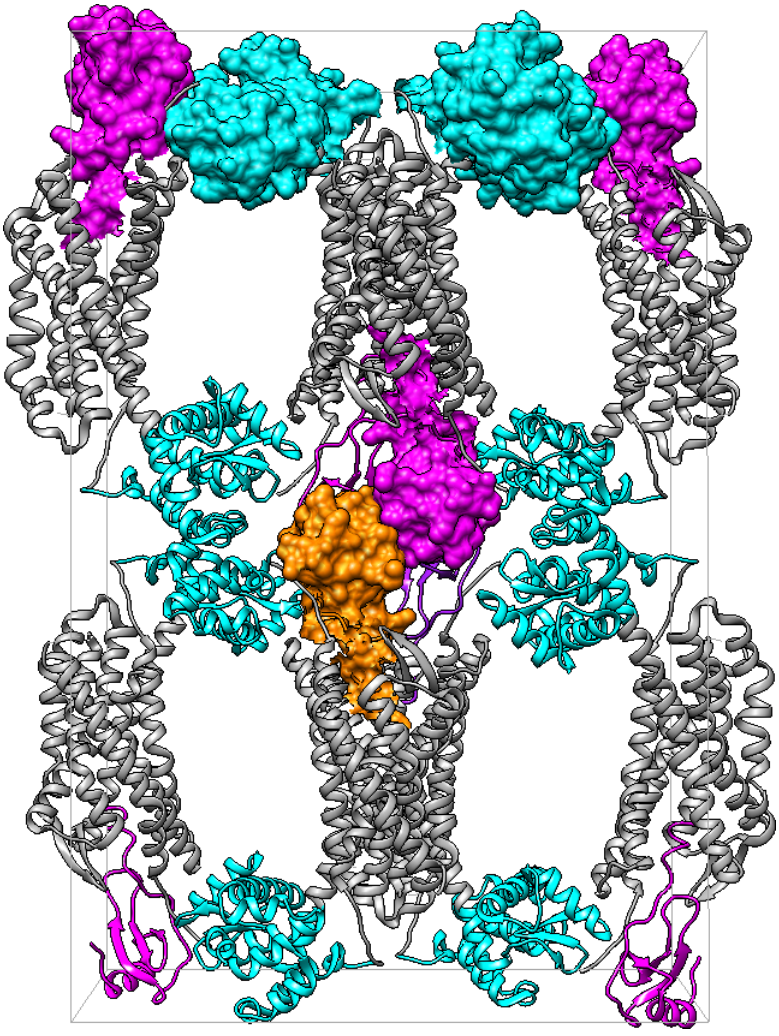

Figure S3: Unit cell of the crystal CXCR4-vMIP-II structure (PDB code 4RWS). CXCR4, vMIP-II and T4 lysozyme are respectively colored in grey, magenta/orange and cyan.

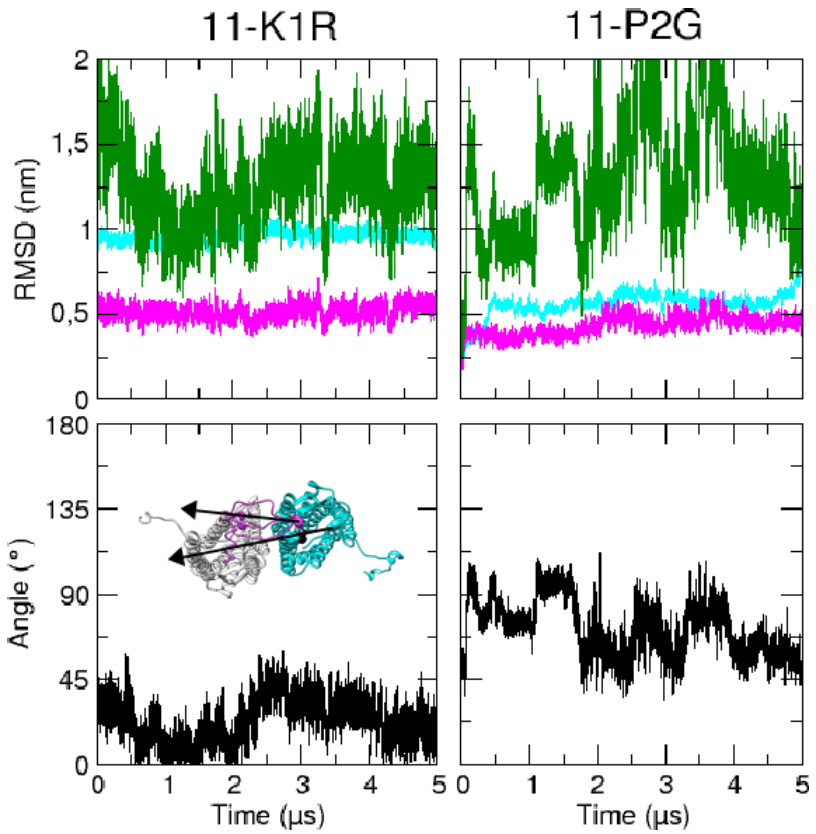

Figure S4: Time evolution of the RMSD (top row) of the receptor (cyan line), the chemokine (magenta line), the chemokine with respect to the receptor (green line), and the chemokine position relative to the receptor (bottom row), for the two chemokine mutant complexes 11-K1R and 11-P2G. The position of the chemokine with respect to the receptor is indicated by the angle between the vector joining the CXCL12 pivotal residue Ser6 to the antipodal Asn45 and the vector joining the CXCR4 residues Tyr45 to Gln200. In the inset picture, the second protomer of the dimeric CXCR4 is represented in white ribbon as a visual reference for the chemokine position. The CXCL12 residue Lys1 is indicated by black spheres and its residues Ser6 and Asn45 by magenta ones.

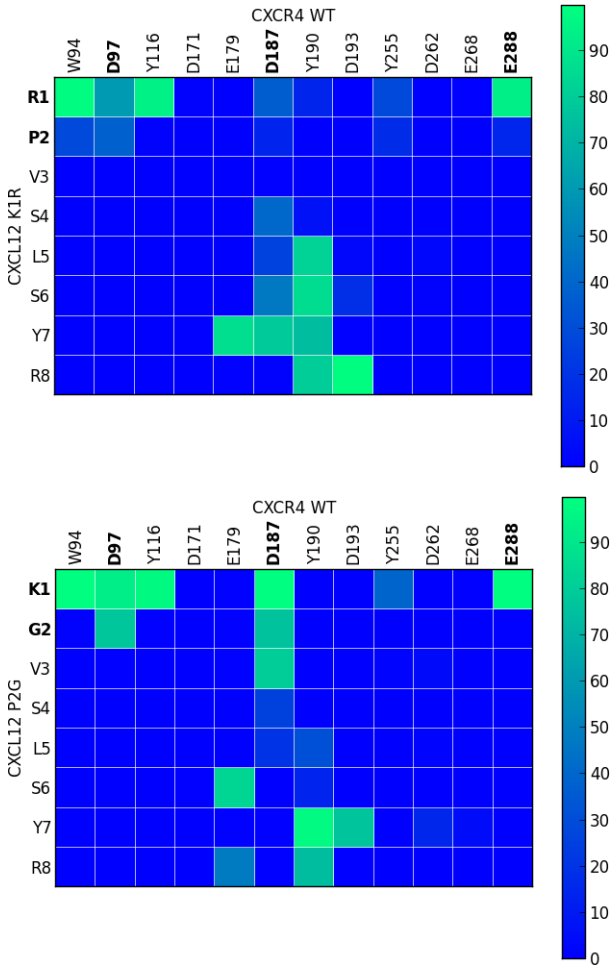

Figure S5: Percentages (right bicolor scale) of the 11-K1R (top) and 11-P2G (bottom) simulation time for which the chemokine N-terminal first eight residues are distant by less than 6 Å to the receptor residues important for activation. Critical residues for CXCR4 activation are emphasized in bold print.

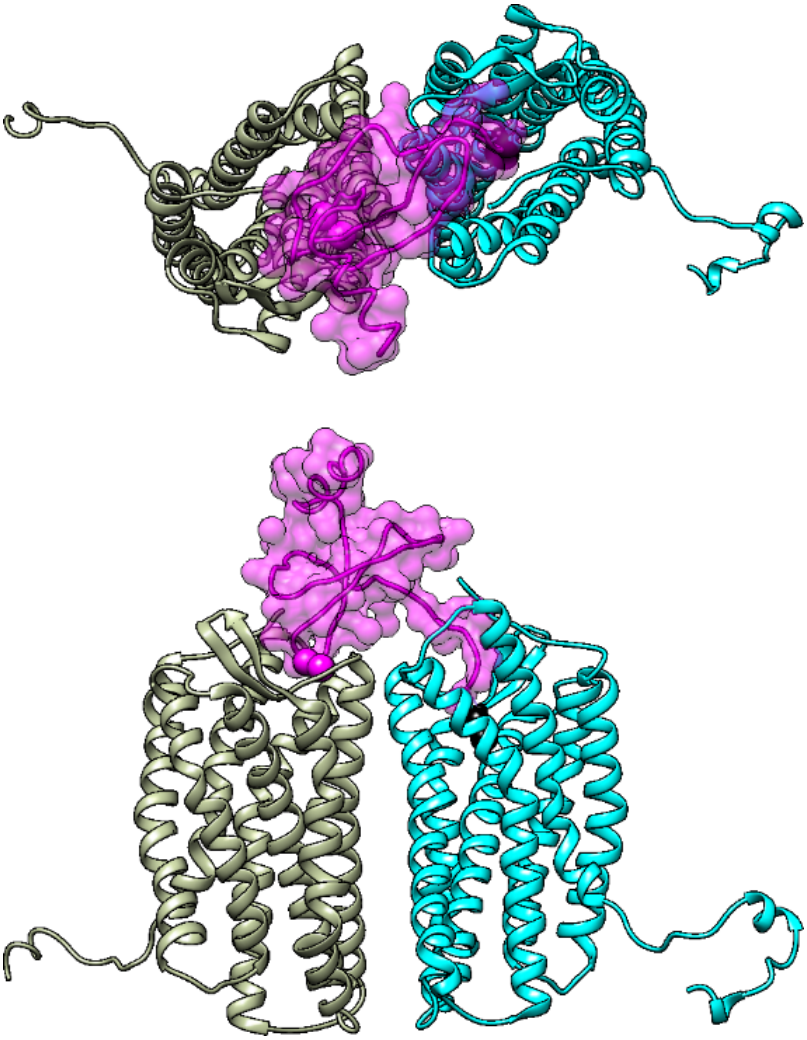

Figure S6: Top and front views of one representative pose of the chemokine CXCL12 (magenta) on the extracellular side of the CXCR4 dimer (cyan and tan).

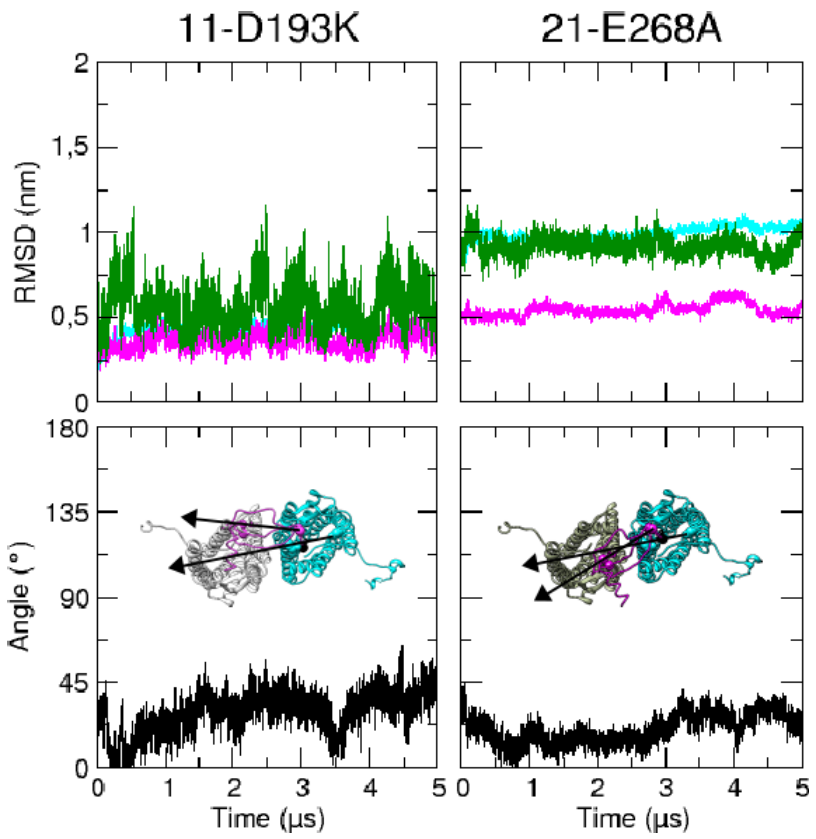

Figure S7: Same as Fig. S4 but for the D193K receptor mutant 1:1 complex (left) and the E268A receptor mutant 2:1 association (right).

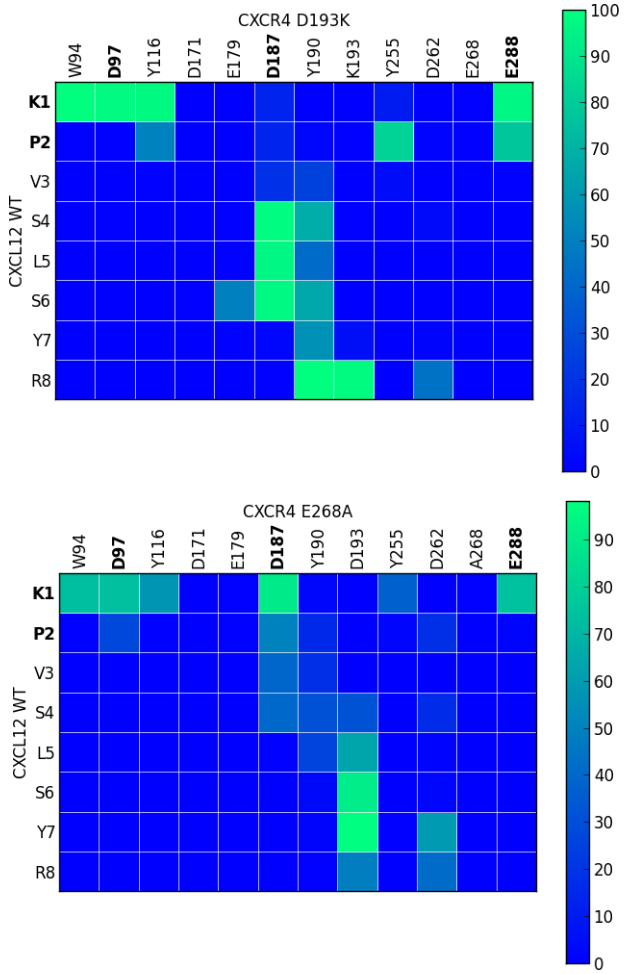

Figure S8: Same as Fig. S5 but for the D193K receptor mutant 1:1 complex (top) and the E268A receptor mutant 2:1 association (bottom).

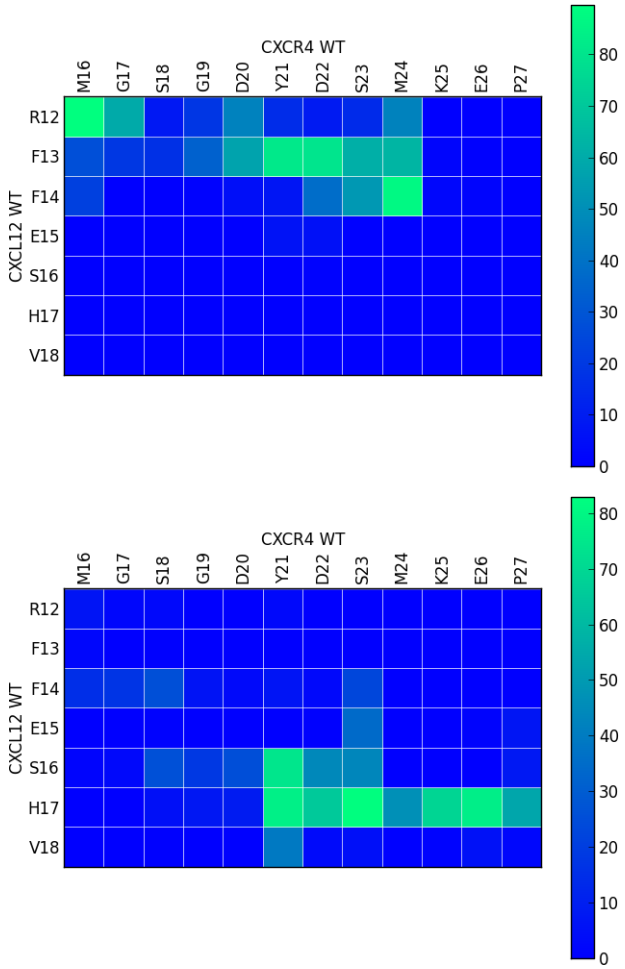

Figure S9: Percentages (right bicolor scale) of the 11-WTC (top) and 21-WT (bottom) simulation time for which the chemokine recognition site residues are distant by less than 6 Å to the receptor N-terminal important residues for binding.