

Abstract Submitted
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Dynamic switching mechanisms of a CC chemokine, CCL5 (RANTES). A simulation study. EMANUEL PETER, IGOR PIVKIN, University of Lugano — CCL5 (RANTES) belongs to the class of pro-inflammatory chemokines which are part of the human immune-response. It is known to activate leukocytes through its associated chemokine receptor 5 (CCR5) and plays a key role in several malignancies, including HIV-1 infections and cancer. In this talk, we present our results from enhanced sampling simulations of the CCL5 (RANTES) monomer. We find that this protein can adopt 2 different conformations : a globular form, with an orthogonal alignment of the N-terminal part, and a 'cis' form, in which the N-terminus is aligned parallel to the β -strand interface. A detailed analysis of the structure reveals that each of these states is stabilized by salt-bridges along the sequence, and corresponds to a defined dihedral-geometry of the 2 disulfide bridges Cys10-34 and Cys11-50. We derive a uniform distribution of transitions from the globular form of CCL5 (RANTES), and find that each of the main conformers adopts different electrostatic patterns.

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