Crystal Structure of Recombinant Human Cyclophilin J and its Complex

Zong-Xiang Xia[a], Li-Li Huang[a], Xue-Mei Zhao[b], Long Yu[b], [a]*State Key Laboratory of Bio-organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, China.* [b]*State Key Laboratory of Genetic Engineering of China, Institute of Genetics, School of Life Science, Fudan University, Shanghai, China.* E-mail: xiazx@mail.sioc.ac.cn

Cyclophilins (CyPs) are a large class of highly conserved ubiquitous peptidyl-prolyl cis-trans isomerase. CyPs have also been identified to be a specific receptor for the immunosuppressive drug cyclosporin A (CsA). CyPJ is a novel member of the CyP family, and human CyPJ (hCyPJ) is the protein encoded by a cyclophilin-like gene from human fetal brain. The three-dimensional structure of recombinant hCyPJ has been determined by molecular replacement using the cyclophilin A (hCyPA) structure as the search model and has been refined at 2.6 Å resolution. The hCyPJ molecule contains four helices and one β-barrel composed of eight antiparallel β-strands. The overall secondary and tertiary structures of hCyPJ are similar to those of hCyPA, but hCyPJ contains an additional disulfide bridge and four segments with conformations that are strikingly different from those of hCyPA. His43 and Gln52 of hCyPJ are expected to be the active sites based on sequence alignment with hCyPA. The hCyPJ structure shows a conserved water molecule close to His43 and Gln52, which appears to support the solvent-assisted mechanism. The crystal structure of hCyPJ in complex with CsA has been determined by molecular replacement and the refined structure will be presented. The crystallization of the complexes of hCyPJ with various ligands is in progress.

Keywords: cyclophilin J, mechanism, complex