MA-6

The Receptor-Ligand Interaction Revealed by a Homology Modelling of the Receptor Binding Domain of Human Thrombopoietin

Jin-Soo Song*, Heung-Rok Park, Hyo-Jeong Hong,
Myeong-Hee Yu and Seong-Eon Ryu
Protein Engineering Research Division, Korea Research Institute of Bioscience & Biotechnology, KIST, Taejon 305-600

Platelet production in blood is regulated by a lineage specific humoral factor called thrombopoietin (TPO). The amino terminal domain of TPO (TPO-N) has a sequence homology to erythropoietin (EPO) and is responsible for the signal transduction mediated by the TPO receptor, c-mpl. We built a three dimensional model of the structure of TPO-N based on its structural homology to other four-helix bundle cytokines. The predicted structure of TPO-N has a well packed hydrophobic core and two disulfide bonds with good geometry. The surface of the structure is mostly hydrophilic except for a hydrophobic patch in the C-terminal side of the four-helix bundle framework. The hydrophobic patch may be involved in the interaction with the remaining C-terminal domain of TPO. From a comparison with the other structurally characterized cytokine-receptor interactions we located residues that have high potential to be involved in the interaction with the receptor.