PS-13

NMR Studies on Cyclic OPG Peptide

KIM Youngmee, LIM Sungkil and LEE Weontae

Dept. of Biochemistry, College of Science, Yonsei University, Seoul, 120-749, Korea

Osteoprotegerin(OPG) is a soluble decoy receptor member of the tumor necrosis factor receptor family(TNFR), which has cloned in an expressed sequence tag cDNA project by Simonet *et al.* in 1997. Administration of OPG *in vivo* inhibits osteoclastogenesis and associated bone resorption and blocks the pathological increase in osteoclast numbers and activity seen in animal models that mimic osteopenic disorders in humans. We have designed a peptide ,cyclic OPG, which has similar sequence with OPG. The solution structure of cyclic OPG (Tyr-Cys-Leu-Glu-Ile-Glu-Phe-Cys-Tyr) has been determined by two-dimensional NMR spectroscopy and simulated-annealing calculations in aqueous solution. The NMR data revealed that cyclic OPG forms a turn conformation which has a disulfide bond within the Cys^2-Cys^8. Final simulated-annealing structure of the cylic OPG converged with rmsd of 0.40Å for backbone atoms. This study may establish a new drug design strategy to treat several metabolic bone diseases caused by abnormal osteoclast recruitment and functions such as osteopetrosis, osteoporosis, metastatic bone diseases.