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NMR structural studies on Osteoprotegerin peptides for Osteoporosis treatment

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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 it is associated bone resorption. It has been reported that OPG blocks the pathological increase of osteoclast numbers in animal models that mimic osteopenic disorders in humans. We have designed two OPG analogue peptides which are short sequences of cystein-rich domain of OPG. The peptides are composed by 9 amino acid residues with and without disulfide bond. The solution structures of two OPG peptides have been determined by two-dimensional NMR spectroscopy and simulated-annealing calculations in DMSO solution. The NMR data revealed that both cyclic and linear peptide formed a stable turn conformation. Final simulated-annealing structures of the cylic and linear OPG peptide were converged with rmsds of 0.94Å and 0.46 Å for backbone atoms respectively. This study could help 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.