SIII-1

The NMR Studies of Newt Acid Fibroblast Growth Factor : Structure, Dynamics. Folding and Interactions

Chin Yu

Chemistry Department, Tsing Hua University, Hsinchu, Taiwan

Newt acidic fibroblast growth factor (nFGF-1) plays an important role in several cellular processes including cell growth, cell differentiation, angiogenesis, wound healing and other chemo tactic activities. Recently, nFGF-1 was cloned and expressed in *E.Coli* and the double labeled (^{15}N and ^{13}C) protein (nFGF-1) was prepared. A series triple resonance experiments were carried out. The NMR 3D structured of nFGF-1 was calculated by using distance-geometry calculation followed by the dynamical simulated annealing techniques. The backbone dynamics studies on nFGF-1 were accomplished by using ^{15}N relaxation and heteronuclear NOE measurements and data were analyzed by model-free approach. Glycosaminoglycans such as heparin and heparan sulfate are known to activate nFGF-1 by including the dimerization of the receptor tyrosine kinase and thereby triggering the signal transduction cascade. Molecular level understanding of the binding of glycosaminoglycans and its analogs to nFGF-1 is necessary for the design of drugs to inhibit nFGF-1 action. A detailed NMR study using and uniformly ^{15}N labeled sample has been carried out for newt FGF-1 bound to sucrose octasulfate. From the chemical shift perturbation and intermolecular NOEs it was found that those residues belonging to the putative heparin binding domain spanning residues 126 to 142 are involved in the binding of sucrose octasulfate to newt FGF-1. The identification and characterization of an equilibrium intermediate in the unfolding pathway will be also discussed.

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