

## **NMR Structure of Syndecan-4L reveals structural requirement for PKC signalling**

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### **ABSTRACT**

Syndecans, transmembrane heparan sulfate proteoglycans, are coreceptors with integrin in cell adhesion process. It forms a ternary signaling complex with protein kinase C and phosphatidylinositol 4,5 bisphosphate (PIP2) for integrin signaling. NMR data indicates that cytoplasmic domain of syndecan-4 (4L) undergoes a conformational transition in the presence of PIP2, forming oligomeric conformation. The structure based on NMR data demonstrated that syndecan-4L itself forms a compact intertwined symmetric dimer with an unusual clamp shape for residues Leu<sup>186</sup>-Ala<sup>195</sup>. The molecular surface of the syndecan-4L dimer is highly positively charged. In addition, no inter-subunit NOEs in membrane proximal amino acid residues (C1 region) has been observed, demonstrating that the C1 region is mostly unstructured in syndecan-4L dimer. However, the complex structure in the presence of PIP2 induced a high order multimeric conformation in solution. In addition, phosphorylation of cytoplasmic domain induces conformational change of syndecan-4, resulting inhibition of PKC signaling. The NMR structural data strongly suggest that PIP2 promotes oligomerization of syndecan-4 cytoplasmic domain for PKC activation and further induces structural reorganization of syndecan for mediating signaling network in cell adhesion procedure.