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Heteronuclear NMR Studies on Syndecan-4 Cytoplasmic Domain

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The syndecan, transmembrane proteoglycans are involved in the organization of cytoskeleton and/or actin microfilaments and play important roles as cell surface receptors during cell-cell and/or cell-matrix interactions. Our previous studies indicated that the function of syndecan-4 cytoplasmic domain is dependent on its oligomeric status and the conformation of syndecan-4 cytoplasmic domain itself is of importance to understand its biological roles. Gel filtration results show that syndecan-4 cytoplasmic domain(4L) itself forms a dimer stabilized by ionic interaction between peptides at physiological pH. In this report, we present data from heteronuclear multi-dimensional NMR experiments for syndecan-4 cytoplasmic domain using uniformly isotope-labelled peptides. The NMR structures demonstrate that syndecan-4L is a compact intertwined dimer with a symmetric clamp shape in the central variable V region. The molecular surface of the 4L dimer is highly positively charged. In addition, no inter-subunit NOEs in membrane proximal amino acid resides (C1 region) has been observed, demonstrating that the C1 region is mostly unstructured in syndecan-4L dimer. Interestingly, two parallel strands of 4L form a cavity in the center of the dimeric twist similar to our previously reported 4V structure. Based on NMR data, we propose that although the 4V region in the full cytoplasmic domain has a tendency for strong peptide-peptide interaction, it may not be enough to overcome the repulsion of the C1 regions of syndecan-4L.