Structural Studies on Collagen binding Integrin αI Domains

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Integrins are a large family of cell adhesion receptors that mediate cell-cell or cell-extracellular matrix interactions by bidirectional signaling. They are involved in a number of physiological processes such as platelet aggregation, inflammation, tumor metastasis and other diseases. The αβ heterodimeric glycoproteins are composed from 19 different α subunits and 8 differentβ subunits [1]. The collagen binding integrin family consists of four collagen receptors that have a common β1 subunit non-covalently bound either to α1, α2, α10 or α11 subunit. They all have a 200 amino acid inserted domain (I-domain) in the N-terminal region of the αsubunit, which is responsible for recognition of the ligand [2]. The αI domain folds into a "Rossman fold", which forms a metal ion-dependent adhesion site, referred to as MIDAS [3].

The crystal structure of α1I and α2I, and also the complex structure of α2I bound to a collagen-like peptide, have been solved [4,5,6]. Comparison of the α2I in complex with a collagen-like peptide (open conformation) and α2I without ligand (closed conformation) showed that conformational changes occur, when the ligand is bound [6].

We have shown that two peptides, CTRKKHDC and CARKKHDC, bind to α1I and competitively inhibit collagen binding. We have modeled the open conformation of α1I in complex with a collagen-like peptide and characterized the binding of the ligand and the structural changes that are caused [7]. Our aims are to further study the binding of collagen-like peptides to α1I and to characterize the conformational changes that might occur.

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