

Structural Studies of the CLD from Aggrecan

Anna Lundell¹, Anders Aspberg², Derek Logan¹, ¹*Dept. Molecular Biophysics, Lund University.* ²*Dept Connective Tissue Biology, Lund University.* E-mail: anna.lundell@mbfys.lu.se

Aggrecan is an important protein in the extracellular matrix (ECM) in the cartilage and its function is to organize the forming of the hyaluronan-lectican complexes in the ECM. Aggrecan consists of three globular domains and a central region of an elongated glycosaminoglycans-carrying region. The N-terminal domain (G1) binds to hyaluronan and the C-terminal domain (G3) has been shown to be involved in the binding to two types of ligands: sulphated glycolipids on the cell surface and dimeric/multimeric ECM proteins, e.g. fibulin-2 and tenascin-R. The CLD within the G3 domain of aggrecan has been observed to make a tight protein-protein interaction (K_D 12nM) with fibronectin type III repeats (FnIII) 3-5 from tenascin-R (TN3-5). Interestingly it has been shown that, though the complex is totally dependent on Ca^{2+} , as would be expected of a CLD, the interaction does not depend on carbohydrate. This is one of only a few direct protein-protein interactions of CLDs involving Ca^{2+} .

The structural studies will give us a first insight how lecticans use the CLD domain to interact with different ECM proteins. This is the first structure showing a calcium-dependent protein-protein interaction involving a C-type lectin domain that is not mediated by a carbohydrate. We have also solved the CLD of aggrecan in a unbound state, giving clues of the importance of the calcium ions.

Keywords: protein-protein interaction, calcium-binding protein, complex structure