

P018 An unusual glycosaminoglycan-binding domain in the lymphatic endothelial hyaluronan receptor LYVE-1.
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The lymphatic endothelial hyaluronan (HA) receptor LYVE-1 has been implicated in important functions ranging from leukocyte trafficking to the scavenging of macromolecules from interstitial fluid. In common with its homologue CD44, LYVE-1 is a member of the Link protein superfamily. However, unlike CD44 whose ectodomain structure has been determined by crystallography and NMR spectroscopy, the molecular details of the LYVE-1 HA-binding domain (HABD) are unknown. Here we show by a combination of mutagenesis, molecular modelling and surface plasmon resonance (SPR) that the LYVE-1 HABD is an extended structure encompassing both the consensus lectin-like Link module and flanking N- and C-terminal extensions, similar to CD44. However, the ligand interaction surface differs from that of CD44 in being more compact and dominated by charge interactions rather than H-bonds and van der Waals forces. Finally, SPR data indicate that the minimal oligosaccharide unit for Lyve-1 is longer than that for CD44 and that Lyve-1 monomers have only a low affinity for HA. Overall these findings reveal a distinctly different HA-binding domain in LYVE-1 and predict that receptor self-association will be important in stabilizing ligand interactions.