

- P005** Structural determination of heparan sulfate required for PDGF-BB_L interaction in pericyte recruitment
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Platelet-derived growth factors (PDGFs) encompass a family of cationic disulfide bonded polypeptide chains. The A and B polypeptide chains have a highly basic carboxy-terminal retention motif, through which they interact with heparan sulfate (HS). Impaired interaction of PDGF-BB_L with HS, by knockout of the retention motif, results in severe physiological defects, such as defective investment of pericytes in the microvessel wall. We now show that phenotypes of mice with differential elimination of enzymes in HS biosynthesis point to the importance of HS domain organization in PDGF-BB_L interaction. Further, a biosynthetic library of HS-related oligosaccharides was used to define the structural requirements for HS/PDGF-BB_L interaction. PDGF-BB_L binds across two highly sulfated domains on the HS chain, interspersed by a variably charged region. The binding strength increases with increasing charge of the sulfated domains, with no requirement for any specific O-sulfation pattern. The determining factor is the overall degree of sulfation rather than any specific structural motif.