学 位 論 文 の 要 旨

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主論文の題名：

Tenascin-C Enhances Crosstalk Signaling of Integrin αvβ3/PDGFR-β Complex by SRC Recruitment Promoting PDGF-Induced Proliferation and Migration in Smooth Muscle Cells

主論文の要旨

Neointima formation ocuurs after vascular injurys resulting in restenosis. In the lesions, Migration and proliferation of smooth muscle cells (SMCs) are key events and Tenascin-C (TNC) is upregulated. We evaluated the effects of TNC on responses of SMCs against platelet-derived growth factor (PDGF) stimulation.TNC promoted PDGF-BB-induced proliferation and migration of A10 cell line, which is derived from the thoracic aorta of embryonic rat, in BrdU incorporation and transwell assays. Immunoblotting showed that TNC substrate enhanced autophosphorylation of PDGFR-β after PDGF-BB stimulation. Integrin αvβ3 is known to be a receptor for TNC in SMCs. In immunofluorescence and immunoblot of integrin αv subunit, clustering of αv-positive focal adhesions and upregulated αv expression were observed in the cells on TNC substrate. Immunoprecipitation demonstrated that PDGFR-β and integrin αvβ3 were co-precipitated and that the relative amount of PDGFR-β after the stimulation was increased by TNC treatment. TNC also promoted phosphorylation of focal adhesion kinase (FAK) at tyrosine (Y) 397 and Y925. The phosphorylated FAK was localized at focal adhesions in immunofluorescence. Phosphorylated SRC at Y418 was also seen at focal adhesions. Immunoprecipitation with αv antibody showed increased SRC association with the integrin signaling complex in the cells on TNC after PDGF treatment. In the cells on TNC substrate, crosstalk signaling between integrin αvβ3 and PDGFR-β could be amplified by SRC and FAK recruited to focal adhesions, followed by enhanced proliferation and migration of A10 cells by PDGF-BB.

（注）２，０００字以内にまとめて記入すること。