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Role of Pleiotrophin and its Receptor Protein Tyrosine Phosphatase β/ζ in Vascular Endothelial Growth Factor-induced Endothelial Cell Migration

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SUMMARY

A considerable progress has been made during the past years in elucidating the molecular actors of angiogenesis, with vascular endothelial growth factor (VEGF) representing the major inducer of angiogenesis up to date. VEGF induces several angiogenic functions of endothelial cells through its receptors VEGFR1 and VEGFR2 or KDR. VEGF-induced endothelial cell migration seems to be mediated by KDR, possibly via engagement of integrin $\alpha_v\beta_3$. Pleiotrophin (PTN) is a secreted heparin-binding growth factor that through its receptor protein tyrosine phosphatase β/ζ (RPTPβ/ζ) and $\alpha_v\beta_3$ integrin induces human endothelial cell migration. We have previously shown that exogenous PTN inhibits VEGF-induced endothelial cell migration. In the present work we studied the effect of endogenous PTN and its receptor RPTPβ/ζ in VEGF-induced endothelial cell migration. We found that endogenous PTN is not involved, while RPTPβ/ζ is required for VEGF-induced endothelial cell migration. Although VEGF may directly interact with RPTPβ/ζ, down-regulation of the latter by siRNA does not affect VEGF-induced ERK1/2 activation, but seems to affect the interaction of KDR with $\alpha_v\beta_3$, which is important for VEGF-induced cell migration. Collectively, RPTPβ/ζ seems to be required for VEGF-induced endothelial cell migration through its receptor KDR.