

CD9 as a Therapeutic Target in Ocular Diseases

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Background

Angiogenesis, one the main pathogenesis and therapeutic target in ocular disease, is regulated by a variety of hormonal factors, such as vascular endothelial growth factor (VEGF) and hepatocyte growth factor (HGF). CD9, member of tetraspanin superfamily, is abundantly present in endothelial cells, however, its exact role is still unknown. The knock-out animal of CD9 reveals just a minimal functional change, which contrastively differs from other factors such as VEGF. The purpose of this study is to see the role of CD9 in angiogenesis and investigate the possibility of its therapeutic usefulness.

Methods and Results

Migration and invasion assays with Boyden chamber in response to HGF or VEGF were used. Endogeneous expression level of CD9 in human endothelial cells (HVECs) was high, and an infection of adenoviral vector containing CD9 transgene did not alter migration efficiency (vs controls). Next we carried out inhibition of CD9 expression in HVECs by transfection of small interfering RNA targeting CD9 (siRNA). Both migration and invasion of HVECs induced either by VEGF or HGF were clearly inhibited by transfection of siRNA, and interestingly, the degree of these phenotypes well correlated with the degree of CD9 inhibition. Furthermore, pellets containing VEGF or HGF were directly inserted into the rat cornea, and PBS containing either siRNA-CD9 or control siRNA was directly injected into subconjunctiva twice. Neovascularization at 7 days induced by VEGF or HGF were both significantly inhibited by siRNA-CD9.

Conclusions

CD9 can be a novel target protein for the treatment of ocular angiogenic diseases