学 位 論 文 の 要 旨

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主論文の題名主論文の題名

Zinc finger MYND-type containing 8 promotes tumour angiogenesis via induction of vascular endothelial growth factor-A expression

主論文の要旨

Angiogenesis is the growth of new capillary blood vessels, which is essential for tumourigenesis. The zebrafish (Danio rerio) represents a powerful model system in cancer research including tumour angiogenesis. We implanted DU145 prostate cancer cells into the avascular region of the yolk sac in zebrafish eggs at 48 h post-fertilization, which induced tumour angiogenesis in 34% of xenografts at 48 h post-implantation. To identify genes related to tumour angiogenesis, we conducted transcriptome analyses of human prostate cancers (Gene Expression Omnibus) and zebrafish xenografts (DNA microarray). We found that zebrafish and human zinc finger, MYND-type containing 8 (ZMYND8) was a candidate gene that promoted tumour angiogenesis.

We conducted immunohistochemical analysis of human prostate cancer tissue microarrays and revealed that the ZMYND8 protein level was increased at progressive stages of prostate cancer. The zmynd8 knockdown or overexpression in host animals suppressed or promoted tumour angiogenesis, respectively. Experiments in vitro showed that human ZMYND8 knockdown suppressed tube formation of human umbilical vein endothelial cells (HUVEC). qRT-PCR analysis revealed that zmynd8 regulated vascular endothelial growth factor-A (vegfa) mRNA expression in zebrafish xenografts.

In summary, we demonstrated that ZMYND8 promotes tumour angiogenesis in zebrafish xenografts. Furthermore, integrated analysis of human and zebrafish transcriptomes, which identified ZMYND8, might be a powerful strategy to determine also other molecular targets for inhibiting prostate cancer progression.