CDH5 is specifically activated in glioblastoma stem like cells and contributes to vasculogenic mimicry induced by hypoxia

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A portion of glioblastoma stem like cells (GSCs) expressing CDH5 (VE-Cadherin or CD144), a specific marker for endothelial cells (ECs), can trans-differentiate into ECs and form blood vessels in glioblastoma (GBM). However, the implication of CDH5 expression in gliomas, and how its expression is regulated in GSCs remain to be clarified. Here, we demonstrated that CDH5 is overexpressed in gliomas, correlated with tumor grades, and is an unfavorable predictor for GBM patients. Immuno histochemistry analysis revealed that CDH5 expression was observed in tumor cells in addition to ECs in GBM tissues. Interestingly, CDH5 is specifically activated in GSCs but not in non-GSCs or NSCs, indicated by quantitative real-time PCR and western blot. Bioinformatics analysis showed that CDH5 may interact directly with angiogenesis-associated genes and hypoxia inducible factor 2α (HIF2α). CDH5 expression was significantly upregulated in GSCs, but not in non-GSCs or normal NSCs, under 1% O₂ condition. Knockdown of either HIF1α or HIF2α by shRNA significantly decreased CDH5 level in GSCs by about 90%, and abolished the induction of CDH5 under hypoxia. Furthermore, ChIP analysis revealed that both HIF1α and HIF2α can bind to the promoter of CDH5. In vitro angiogenesis assay demonstrated that CDH5 contributes to vasculogenic mimicry of GSCs, especially under hypoxia. Therefore, the specific expression of CDH5 in GSCs may contribute to the GSC-derived neovasculogenesis in glioblastoma, especially under hypoxia conditions. Our results revealed promising mechanisms controlling trans-differentiation of GSCs into ECs regulated by hypoxia, and provided new insights in the mechanisms of hypoxia induced angiogenesis in GBMs.

Biography
Xiang Zhang has completed his Ph.D at the age of 26 years from Xiangya Medical University. He is the director of Department of Neurosurgery, Xijing Hospital, Xian, P.R. China. He has published more than 30 papers in reputed journals and serving as an editorial board member of repute.
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