The long non-coding RNA MALAT1 promotes tumour-driven angiogenesis by up-regulating pro-angiogenic gene expression

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Neuroblastoma is the most common solid tumour during early childhood, and accounts for 15% of all childhood cancer death. One of the key features of neuroblastoma is disease progression due to tumour-driven angiogenesis. However, the mechanism through which neuroblastoma cells drive angiogenesis is unclear. Here we showed that the long non-coding RNA MALAT1 was over-expressed in human neuroblastoma cells under hypoxic condition, the condition which triggers pro-angiogenic switch and angiogenesis. In vitro angiogenesis assays demonstrated that conditioned medium from neuroblastoma cells transfected with MALAT1 siRNAs, compared with conditioned medium from neuroblastoma cells transfected with control siRNAs, induced considerably less endothelial cell migration, invasion and vascular sprouting under hypoxic condition. Affymetrix microarray differential gene expression study showed that one of the genes most significantly down-regulated by MALAT1 siRNAs in human neuroblastoma cells under hypoxic condition was fibroblast growth factor (FGF). RT-PCR and immunoblot analyses confirmed that MALAT1 siRNAs reduced FGF mRNA and protein expression, and in vitro angiogenesis assays demonstrated that forced over-expression of FGF in neuroblastoma cells blocked MALAT1-mediated endothelial cell migration, invasion and vascular sprouting. Taken together, our data suggest that over-expression of MALAT1 in human neuroblastoma cells plays an important role in tumour-driven angiogenesis by up-regulating FGF mRNA expression.

Biography
Tao Liu obtained his PhD from The University of New South Wales Australia in 2000. He then worked as a Post-doc with Professor Samuel Breit at St. Vincent’s Centre for Applied Medical Research Sydney. He is now Head of Histone Modification Group at Children’s Cancer Institute Australia, and an Australian Research Council Future Fellow at The University of New South Wales. In the last 5 years, he has been working on the roles of long noncoding RNAs, histone methyltransferases and histone deacetylases in modulating gene transcription, N-Myc-regulated malignant transformation, neuroblastoma initiation and progression in vitro and in vivo.

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