

Long noncoding RNA MALAT1 promotes neurovascular remodeling following TBI by targeting Notch1 via Ezh2

Chongjie Cheng

¹ Department of Neurosurgery, The First Affiliated Hospital of Chongqing Medical University, China



Abstract

As a highly evolutionary conserved lncRNA, MALAT1 was first demonstrated to associate with metastasis of lung tumor by promoting angiogenesis. Activated vasculature was recently indicated to assist neurogenesis by secreting neurotrophic factors. The purpose of this study is to explore the potential role of MALAT1 in angiogenesis and neurogenesis following traumatic brain injury (TBI), as well as its mechanistic connection. The controlled cortical impact (CCI) and oxygen-glucose deprivation (OGD) models were established to mimic neuropathology of TBI, and siRNA, inhibitor, transgenic mice were used to analyse the effects of MALAT1. Our results indicated that silencing of MALAT1 in vitro inhibited endothelial cell viability and tube formation, while increasing migration ability. The mice deficient in MALAT1 exhibited reduced endothelial proliferation, functional vessel density and cerebral blood flow. Furthermore, MALAT1 downregulation suppressed neuroblasts migration, and decreased endothelial production of SDF-1 α and neurovascular coupling niches. RNA pull-down assay validated EZH2 as the downstream element of

MALAT1. And MALAT1 recruited EZH2 to Notch1 promoter regions and epigenetically promoted Notch1 transcription, independent of H3K27me3 activity. Agonist of Notch1 reverses the MALAT1 deficiency-mediated impaired angiogenesis and neurogenesis. Our results suggest that MALAT1 controls key steps of neurovascular remodeling following TBI in EZH2/NOTCH1-dependent manner.

Keywords—Traumatic brain injury; Metastasis associated lung adenocarcinoma transcript 1; Vascular remodeling

Biography

CC has completed his PhD at the age of 30 years from Chongqing Medical University and postdoctoral studies from Harvard Medical School. As an attending neurosurgeon, he has published more than 25 papers in reputed journals on brain injury, including TBI, stroke and SAH.

[31st International Neuroscience Online Event](#); Online Event-July 27, 2020.