Loss of ETV6 expression results in aggressive prostate cancer progression: Modeling through prostate cancer cell lines

Yen-Nien Liu
Taipei Medical University, Taiwan

Loss of heterozygosity of ETV6, an ETS-family transcription factor, in cancer suggests it acts as a tumor suppressor. However, its cellular functions and regulating signaling remain unclear. In this study, we demonstrate that ETV6 represses prostate cancer metastasis. We identified miR-96, a potential oncomiR, as a novel target of epidermal growth factor receptor (EGFR) signaling in prostate cancer cells. We further identified ETV6 as a downstream target of miR-96 and found that EGFR-mediated activation of miR-96 leads to decreased expression of ETV6. Activated-EGFR signaling mediated increases in miR-96 expression directly inhibited ETV6 expression. ETV6 knockdown promotes prostate cancer cells migration and invasion. Moreover, ectopic ETV6 expression was found associated with reduced metastasis of prostate cancer cells to both bone and brain and increased overall survival in a xenograft model. Importantly, we found that EGFR serves as a transcriptional activator for miR-96 expression through nuclear EGFR binding to the primary miR-96 regulatory region. This mechanism is supported by results in clinical samples: low ETV6 levels are correlated with high miR-96 and nuclear EGFR levels in tissue from prostate cancer patients. These studies suggest that prostatic metastasis involves EGFR-mediated miR-96 induction and ETV6 inactivation, resulting in metastatic phenotypes.

Biography

Yen-Nien Liu has completed his PhD from Tzu Chi University, Taiwan and Post-doctoral studies from National Cancer Institute, National Institute of Health, USA. He is an Assistant Professor of Taipei Medical University, Taiwan. He has published more than 19 papers in reputed journals and has been serving as an Editorial Board Member of repute.

liuy@tmu.edu.tw