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C/EBP-δ positively regulates MDSC expansion and endothelial VEGFR2 expression in tumor development

P Charles Lin, Yongfen Min, Jingdong Li and **Peng Qu**
National Cancer Institutes, USA

Vascular endothelial cells and Gr-1+CD11b+ myeloid derived suppressor cells (MDSCs) are two important components that constitute the tumor microenvironment. Targeting these cells offers the potential to halt tumor growth. In this study, we report a common mediator in C/EBP-δ that regulates both components and aids in tumor development. C/EBP-δ is elevated in tumor derived MDSCs. Interestingly, genetic deletion of C/EBP-δ in mice significantly impaired MDSC expansion in response to tumor progression, but it had no effect on Gr-1+CD11b+ cell production in normal development. It suggests a specific role of C/EBP-δ in emergency myelopoiesis under tumor conditions. Consistent with the pro tumor functions of MDSCs, loss of C/EBP-δ resulted in reduced tumor angiogenesis and tumor growth. Moreover, we found expression of C/EBP-δ in vascular endothelial cells. C/EBP-δ regulated cell motility, endothelial network formation and vascular sprouting. Notably, inactivation of C/EBP-δ in endothelial cells specifically inhibited the expression of VEGFR2 but not VEGFR1. Ectopic expression of C/EBP-δ increased and knockdown of the gene decreased VEGFR2 expression. C/EBP-δ is recruited to the promoter region of VEGFR2, indicative of transcriptional regulation. Collectively, this study has identified a positive mediator in C/EBP-δ, which regulates tumor induced MDSC expansion and VEGFR2 expression in endothelium. Considering the importance of MDSCs and endothelial cells in tumor progression, targeting C/EBP-δmay provide an interesting means for cancer therapy, killing two birds with one stone.

Biography

P Charles Lin received his PhD in Cell and Molecular Biology (1988) at the Peking Union Medical College, Institute of Chinese Medical Sciences, Beijing, China. In 1992, he joined the Department of Medicine, Duke University Medical Center as a Research Associate. In 1999, he was appointed as Assistant Professor at Vanderbilt University Medical Center. In 2005, he became Associate Professor with Tenure at the Department of Radiation Oncology, Department of Cancer Biology, and Department of Cell & Development Biology at Vanderbilt University School of Medicine. He established the Vascular Biology Section at the Center for Cancer Research in August, 2010.

p.lin@nih.gov

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