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MECOM-regulated distal super-enhancer activates ETS2 transcription and promotes colorectal cancer progression

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It has long been documented that abnormal activities of distal cis-regulatory elements such as enhancers contribute to the intitation and progression of cancer. Recently, super-enhancer hijacking was found to be esstential for the activation of certain oncogenes. However, the mechanism of action for most tumor-specific super-enhancers still largely remain elusive. Here, we report that a potential oncogene ETS2 was activated by a super-enhancer located at its 3' distal region in colorectal cancer (CRC). The super-enhancer physcially interacts with ETS2 promoter fragments and is required for transription activation of ETS2. Intriguingly, we found that a eQTL site for ETS2 resides in this super-enhancer and genetic variation at the SNP potentailly abolished the binding of a well-known oncogenic trancritpion factor MECOM. Consistently, the expression of MECOM and ETS2 correlated well with each other in CRC cell lines and multiple CRC datasets and silecning of MECOM induced downregulation of ETS2. Moreover, the expression of enhancer RNA (eRNA) from the ETS2 super-enhancer also correlated with the expression of ETS2 in primary CRC samples. Finally, silencing of both MECOM and ETS2 lead to the inhibition of proliferation, migration and sphere formation of CRC cells. Taken together, we uncovered a novel MECOM-super enhancer-ETS2 regulatory axis that might be crucial for activating oncogenic ETS2 in CRC.

Biography

Xing-sheng Shu received his B.S. degree from the School of Life Sciences, Peking University and his Ph.D. degree from the Department of Clinical Oncology, Faculty of Medicine, The Chinese University of Hong Kong. He is currently an associate professor at School of Medicine, Shenzhen University. Dr. Shu has been focusing on study the aberrant transcriptional and epigenetic regulations in digestive cancers, he has published more than 30 papers with >900 citations and an H-index of 15, including research articles in Oncogene, Journal of Pathology, Theranostics and other high level academic journals.