doi: 10.4172/1948-5956.10000S6

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Alternative splicing of Kruppel-like factor 4 plays a role in colorectal tumorigenesis

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Most human genes undergo alternative splicing, and many abnormal splicing processes are associated with human diseases. However, the molecular relationship between alternative splicing and tumorigenesis is not well understood. Here, we found novel Krüppel-like factor 4 (KLF4) splicing variants produced by exon skipping in human cancer cell lines as well as colon tumor tissues. To elucidate mechanism of the KLF4 alternative splicing, we developed KLF4 minigene system and found that RNA binding motif protein 5 (RBM5) plays an important role in KLF4 splicing, as assessed by gain and loss of functional studies. Several anti-tumorigenic compounds were also tested for the KLF4 splicing. Interestingly, sulindac sulfide restored wild type KLF4 ($KLF4_L$) expression and this is mediated by dephosphorylation of RBM5. Another splicing variant, small KLF4 ($KLF4_S$), localizes in the cytoplasm and nucleus, and antagonizes transcriptional activity of wild type KLF4. Our data suggest that RBM5 plays a pivotal role in the alternative splicing of KLF4, and these splicing variant forms may impact tumorigenesis.

Biography

Dr. Seung Baek completed his Ph.D from University of Maryland School of Medicine and postdoctoral studies from NIEHS/NIH. He is the director of Lab of Environmental Carcinogenesis. He has published more than 85 papers in reputed journals and serving as an editorial board member of several journals.