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Identification and characterization of a novel role for RNA helicase DP103: The key "missing player" and therapeutic target for NFkB-induced metastasis in human breast cancer

Alan Prem Kumar

Cancer Science Institute of Singapore; Department of Pharmacology Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Metastatic breast cancer is generally considered to be incurable; therefore, new prognostic markers are urgently needed. Furthermore, improving our understanding of the molecular mechanisms of the metastatic process might also improve clinical management of the disease. Herein, we will present for the first time, a novel role of DP103 in the breast cancer metastasis and invasion and its link to NF-κB activation. Indeed depletion of DP103 expression in invasive breast cancer cells led to decreased expression of MMP9 and impedes cell migration and invasion. Conversely, forced expression of DP103 in mammary carcinoma and nonmalignant cells increased oncogenicity and cells' capacity to invade. Our mechanistic studies provide undiscovered evidences that DP103-mediated effects are due its ability to activate NF-κB, a master regulator of genes involved in invasion and anti-apoptosis, and a transcription factor known to be constitutively activated in breast cancers. Clinically relevant, we show expression of DP103 directly correlates to increasing malignancy, both in a xenograft-derived breast cancer cells and in breast tumor tissues obtained from patients. Hitherto, demonstrating the suitability of DP103 as a new prognostic marker needed to identify patients who are at the highest risk for developing metastases and possibly drug resistance, which can also be a clinically useful target.

Biography

Dr. Alan Prem Kumar earned his Ph.D. from University of North Texas, USA. From his Ph.D. work, he discovered a novel regulatory protein, PyrR for the pyrimidine biosynthetic pathway in Pseudomonas. Dr. Kumar then pursued Postdoctoral training in Cancer Research at Sidney Kimmel Cancer Center, California, USA. He was awarded a Postdoctoral Fellowship for his work on the role of nuclear receptors. Dr. Kumar relocated back to Singapore to join Cancer Science Institute of Singapore, National University of Singapore as an independent Principal Investigator to continue on his expertise on nuclear receptor and cancer pharmacology. His current research interest includes the role of nuclear receptors involved in the regulation of target genes and to elucidate mechanism and associated signal pathways. Another area of interest is aimed at developing new derivative drugs with hopefully fewer side effects. Over the years, Dr. Kumar and his laboratory have forged relationships with scientists in cancer research and with cancer readvocacy groups in Singapore.

csiapk@nus.edu.sg