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TITLE

Ei24-mediated Regulation of PKCα Contributes to Carcinogenesis of Skin Cancer

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Etoposide-induced gene 24 (Ei24) is a p53 target gene that inhibits growth, induces apoptosis and autophagy, as well as suppresses breast cancer. To evaluate the role of Ei24 in in vivo tumorigenesis, we generated an Ei24-deficient mouse model. Here, we report that, although Ei24 homozygous knockout mice are embryonic lethal, Ei24 heterozygous null mice are resistant to DMBA/TPA-inducedcarcinogenesis of squamous cell carcinoma due to defective STAT3 and PKCα signaling. Ei24 containsa functional consensus motif, named as an R motif that ishighly analogous to amino acids105-110 of RINCK1, an E3 ligase for protein kinase C (PKC) proteins.We foundthat Ei24stabilizesPKCα via RINCK degradation and competition with RINCK for binding with the C1a domain of PKCα. We also found that Ei24contributes to PKCα-mediated transactivation of EGFR by promoting PKCα membrane localization and interaction with EGFR leading to STAT3 activation. These results suggest that Ei24 is a critical regulator of the PKCα-EGFR-STAT3 signaling pathway in the development of skin cancer.

Biography

Sushil Devkota is a 4th year graduate student in Professor Han-Woong Lee's lab at Yonsei University in the Department of Biochemistry, Seoul, South Korea. He is currently studying and charactering the phenotypes of the Ei24 knock-out mice and the relevant pathways regulated by Ei24.