Han-Woong Lee, Pharm Anal Acta 3:1
doi: http://dx.doi.org/10.4172/2153-2435.S1.09

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Pharmaceutics & Novel Drug Delivery Systems

20-22 February 2012 San Francisco Airport Marriott Waterfront, USA

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

Professor Han-Woong Lee is in the Department of Biochemistry at Yonsei University, Seoul, South Korea. He is the leading mouse geneticist in the country and is the director of Yonsei Laboratory Animal Research Centre (YLARC). In YLARC, knock-out and transgenic mouse models of various genes relevant to human health are being produced.