Aejaz Sayeed, J Cancer Sci Ther 2015, 7:5
http://dx.doi.org/10.4172/1948-5956.S1.043

OMICS International
conferenceseries.com

International Conference on
Prostate Cancer
June 22-24, 2015 Florida, USA

Aejaz Sayeed
Thomas Jefferson University, Philadelphia

Abrogation of b1 integrins in combination with JNK inhibition promotes radiation resistance

Radiation therapy remains an important modality for cancer treatment and ongoing research efforts focus on overcoming radiation resistance to improve patient survival. Here we show that fractionated radiation, 10 Gy for 5 consecutive days (50 Gy total), effectively blocks prostate tumor growth in transgenic adenocarcinoma of mouse prostate (TRAMP) mice. We have previously shown that b_1 integrins suppress c-Jun amino-terminal kinase 1 (JNK1) which plays a crucial role in promoting radiation-induced apoptosis in both cancer cells and in the TRAMP model. Using a selective and reversible JNK-1, -2 and -3 inhibitor (SP600125), we demonstrate that the conditional ablation of b_1 integrins in the prostatic epithelium of TRAMP mice in conjunction with JNK inhibition promotes resistance to radiation as observed in increased tumor growth. While radiation effectively suppresses tumor development in sham-treated b_1 null mice, blocking JNK signaling offsets the effect of radiation resulting in increased tumor growth. We demonstrate that a prominent feature associated with tumor progression driven by JNK inhibition is the up-regulation of Focal Adhesion Kinase (FAK) signaling (enhanced levels of total and phosphorylated protein) in TRAMP prostate tumors. The JNK pathway is not active in irradiated β_1 wild type TRAMP mice; as expected, upon JNK inhibition neither FAK upregulation nor tumor growth is observed. We also demonstrate that b1 integrins and FAK are found in exosomes released from prostate cancer cells, suggesting novel means of acquiring resistant phenotypes. Our study delineates a b_1 integrin/JNK/FAK signaling pathway of radiation resistance in prostate cancer and identifies potential targets for facilitating development of radiosensitizing therapy against PrCa.

Biography

Aejaz Sayeed received his Ph.D. in Immunology in the year 2000. He undertook his post doctoral training in cancer biology and since then he has acquired a broad-based interdisciplinary oncology training with particular expertise in preclinical tumor models of breast and prostate cancer. Using novel primary culture model systems, He studied molecular signatures associated with different histological grades of human breast cancer. He joined TJU as a faculty in 2010 and his current research is focused on understanding the role of integrins and growth factor receptors in radiation resistance of prostate cancer.

Sheikh.Sayeed@jefferson.edu

Notes: