J Cancer Sci Ther 2014, 6:10
http://dx.doi.org/10.4172/1948-5956.S1.035

OMICS Group Conferences
Accelerating Scientific Discovery

4th World Congress on
Cancer Science & Therapy
October 20-22, 2014 DoubleTree by Hilton Hotel Chicago-North Shore Conference Center, USA

Targeting WNT1-inducible signaling pathway protein 2 (WISP2) alters human breast cancer cell susceptibility to specific lysis through regulation of KLF-4 and miR-7 expression

I Akalay and **S Chouaib**
Institute Gustave Roussy, France

The molecular basis for the resistance of tumor cells to cell-mediated cytotoxicity remains poorly understood and thus poses a major challenge for cancer immunotherapy. The present study was designed to determine whether the WNT1-inducible signaling pathway protein-2 (WISP2, also referred to as CCN5), a key regulator of tumor cell plasticity, interferes with tumor susceptibility to Cytotoxic T Lymphocytes (CTL)-mediated lysis. We found that targeting WISP2 signaling in human breast adenocarcinoma MCF7 cells impairs CTL-mediated cell killing by a mechanism involving Kruppel-like factor-4 (KLF-4) induction and microRNA-7 (miR-7) downregulation. Inhibition of TGF-β signaling using the A83-01 inhibitor in MCF7-shWISP2 cells resulted in a significant reversal of the Epithelial-to-Mesenchymal Transition (EMT) phenotype, the expression of stem cell marker KLF-4 and a partial recovery of target susceptibility to CTLs. More importantly, we showed that silencing of KLF-4 was accompanied by a reduction in MCF7-shWISP2 resistance to CTLs. Using human breast cancer tissues, we demonstrated the coexpression of KLF-4 with EMT markers and TGF-β pathway. More importantly, we found that KLF-4 expression was accompanied by miR-7 inhibition, which is partly responsible for impairing CTL-mediated lysis. Thus, our data indicate that WISP2 plays a role in regulating tumor cell susceptibility through EMT by inducing the TGF-β signaling pathway, KLF-4 expression and miR-7 inhibition. These studies indicate for the first time that WISP2 acts as an activator of CTL-induced killing and suggests that the loss of its function promotes evasion of immunosurveillance and the ensuing progression of the tumor.

History, significance, and potential prevention of radiation-induced heart disease in breast cancer and other malignancies

Gabor T Gyenes
University of Alberta, Canada

Radiation-Induced Heart Disease (RIHD) is a relatively recently recognized condition. It affects patients having received radiation to the chest 10-15 years before the manifestation of symptoms such as those of coronary artery disease, heart failure, and more rarely, valvular disease and conduction abnormalities. This is an important problem because RIHD was shown to counteract benefits of adjuvant radiation therapy for early breast cancer in the 70s. Young patients with Hodgkin's disease had an increased risk of myocardial infarctions up to 44-fold compared to untreated people. Radiation techniques have been modified over the next decades and recently this problem has been affecting many less patients. However, a recent study showed a 7.4% increased risk of coronary artery disease with every Gray of radiation, and without an apparent low threshold. The risk also seems to be associated with traditional coronary risk factors such as age, male gender, hyperlipidemia, smoking, diabetes, positive family history and hypertension. As aggressive risk factor management including smoking cessation, antihypertensive therapy with ACE inhibitors in particular and statins have been all shown to curb cardiovascular risks it would be prudent to undertake a large prospective multicenter study to investigate risk reduction opportunities in this patient population.

Biography

Gabor T Gyenes received his MD at Semmelweis University, Budapest in 1984 and his PhD on the topic of Radiation-Induced Heart Disease in 1997 at the Karolinska Institute in Stockholm, Sweden. He moved to Canada in 1998. Currently, he is Associate Professor in Cardiology at the Mazankowski Alberta Heart Institute, University of Alberta. He is the interim Director of the Rehabilitation Center of the MAHI and he is also involved in several international multicenter research studies. He has about 60 peer-reviewed publications including a textbook on the 25 Landmark Trials in Cardiology.