Bora Lim, J Cell Sci Ther 2013, 4:4
http://dx.doi.org/10.4172/2157-7013.S1.026

OMICS Group Conferences
Accelerating Scientific Discovery

3rd World Congress on
Cell Science & Stem Cell Research
November 20-22, 2013 DoubleTree by Hilton Baltimore-BWI Airport, MD, USA

Elucidation of TRAIL sensitivity in different subtype of TNBC cell lines and future therapeutic implication

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Triple negative breast cancer (TNBC) comprises 15-20% of breast cancer, and carries a poor prognosis. Recently, efforts to understand heterogeneous group of cancers - TNBC have succeed to recognize different subtypes of TNBC, including basal, mesenchymal, immunomodulatory, and androgen receptor dependent subtypes recently published by Dr. Pietenpol et al. Due to lack of efficient targeting therapeutics unlike other subtype of breast cancers, both subtype based and generalized approach could be used in therapeutic development for TNBCs. TRAIL (Tumor Necrosis Factor-related apoptosis inducing ligand), a member of the TNF-alpha family of death receptor ligands, induces apoptosis by binding death receptors (DR4 and DR5), and can be one of generalized approach in therapeutic development in TNBC, based on the work of Lipkowitz at the NCI. Unfortunately, the majority of breast cancer cell lines including HCC 1937, a basal like TNBC cell line derived from a patient with BRCA1 mutation, are resistant to TRAIL targeted therapy. However, MDA-MB-231 cells with mesenchymal like feature are sensitive to TRAIL targeting therapeutics. The same difference was observed in few other subtypes of TNBC. Understanding of resistant mechanism would offer further direction of overcoming this resistance. We hypothesized this difference of TRAIL sensitivity may be due to difference in cell type of apoptosis. Type I cells have been defined to be independent of mitochondria for the induction of Fas death receptor-mediated apoptosis, whereas Type II cells are mitochondria-dependent. If basal like TNBC cells are type II cells in apoptosis, even with initial process of TRAIL induced apoptosis can be interrupted by mitochondria-dependent resistant mechanism.

Biography

Bora Lim has completed his M.D. at the age of 25 years from Ewha Womans University and further completed Internal Medicine training at Pennsylvania Hospital, University of Pennsylvania Health system. She is currently pursuing clinical hematology-oncology fellowship at Penn State University school of medicine Hershey Medical center, and building up expertise in triple negative breast cancer and solid oncology translational research.

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