Mu Wang, J Cancer Sci Ther, 3:7
doi: http://dx.doi.org/10.4172/1948-5956.S1.13

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Targeting superoxide dismutase 1 for chemosensitization of platinum resistant ovarian cancer cells

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Platinum-based chemotherapy, such as cisplatin, is the primary treatment for ovarian cancer. However, drug resistance has become a major impediment to the successful treatment of ovarian cancer. To date, the molecular mechanisms of resistance to platinum-based chemotherapy remain unclear. In our previous study using a proteomic approach, more than 90 proteins showed significant expression changes when two pairs of ovarian cancer cell lines, A2780/A2780-CP (cisplatin-sensitive/cisplatin-resistant) and 2008/2008-C13*5.25 (cisplatin-sensitive/cisplatin-resistant), were compared. Bioinformatics analysis suggested several potential pathways that may be involved in platinum resistance. Among these potential pathways, a redox regulated pathway involving superoxide dismutase 1 (SOD1) was targeted in order to further explore its involvement in drug resistance. Inhibition of SOD1 activity in the resistant cells by either small-molecule inhibitors or siRNA enabled partial reversal of platinum resistance. Our data suggest that targeting SOD1 can potentially lead to sensitization of platinum-resistant ovarian cancer cells, and SOD1 may be used as a therapeutic target for chemosensitization of ovarian cancer.

Biography

Dr. Wang is the Director of Proteomics and Associate Professor of Biochemistry and Molecular Biology at Indiana University School of Medicine. He received his PhD in Bio-organic Chemistry from Washington University in St. Louis, Missouri, USA and was an NIH postdoctoral fellow studying mechanism of DNA repair in mammalian system. He has published more than 60 peer-reviewed articles in biochemistry and proteomics related journals. His own research involves mechanistic study of drug resistance in ovarian cancer and DNA repair mechanisms in mammalian systems in response to genomic stresses. In his recent study in searching for biomarkers of cisplatin resistance in human ovarian cancer using a proteomic approach, he identified multiple pathways that are involved in cisplatin resistance. His preliminary data suggests that SOD1 is a key determinant of drug resistance. Through inhibition of SOD1 activity, the cisplatin resistant ovarian cancer cells can be sensitized. He is in the process of developing a chemosensitizer to overcome platinum resistance in ovarian cancer. Dr. Wang was a recipient of the HUPO (Human Proteome Organization) 2004 Young Investigator Award.