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IGF-1R: A key linker between chemoresistance and cancer stem cells in epithelial ovarian cancer cells

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Generation of chemoresistance and tumor relapse is major therapeutic barriers for successful treatment of ovarian cancer. According to the current notion, a small population of cells (Cancer Stem Cells or CSCs) residing in the tumor bulk aids in drug resistance and tumor relapse. To understand these associations, we developed several drug resistant models against cisplatin, paclitaxel and cisplatin + paclitaxel using A2780 cell line and further classified them into early resistant and late resistant stages. We have previously shown that these early resistant cells possessed high levels of Insulin like Growth Factor 1-Receptor (IGF-1R) expression and Picropodophylin (PPP), an IGF-1R inhibitor potentiated maximal reversal of resistance at early stages (Singh et al, 2014, Cancer Letters). In the present study, an enrichment of CSC like phenotype (biomarker-CD44 & CD133, self-renewal, and Side Population/SP) was observed with gradual increase in resistance. Expression of Oct4, Sox2 and Nanog increased from sensitive to early stage of resistance, which further remained constant at late resistant stages. Non-invasive bioluminescence imaging revealed that SP cells isolated from early resistant stages possessed higher tumorigenic potential than SP cells isolated from the late resistant stages. Interestingly, inhibition of IGF-1R with PPP abrogated the expression of stemness genes and spheroid formation. However silencing of Oct4 and Sox2 did not affect IGF-1R expression indicating IGF-1R as an upstream regulator of these stemness genes. Thus our present data suggests that IGF-1R is a key molecule that governs the cross talk between cancer stem cells and acquired chemoresistance in epithelial ovarian cancer.

Biography

Ram Kumar Singh has completed his masters in life sciences with distinction. He qualified national level exams GATE and CSIR-UGC NET and availed five years scholarship to pursue his Ph.D. Currently he is at the verge of completion of Ph.D. In his entire tenure of Ph.D. programme he has published in high impact peer reviewed journals: one first author paper in Cancer Letters, and two co-author papers in IJBCB and CELL, one book chapter in Engineering in Translational Medicine (Springer publication). He has also presented his work in various national and international conferences.

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