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Vactosertib, ALK5 inhibitor combinatorial treatment with radiation inhibits lung metastasis in syngeneic breast mouse models

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Radio-resistance and relapse after chemotherapy is a life-threatening problem for breast cancer patients. We identified the molecular signatures of the recurrent breast cancer patients after radiotherapy, which showed the up-regulation of TGF-β signaling and the epithelial-to-mesenchymal transition (EMT). In order to find the potential therapeutic strategies to improve radiation therapy, we conducted gene set enrichment analysis, a computational method that determines whether an a priori defined gene set shows statistically significant between two phenotypes, using the breast cancer clinical data with Servant cohort (GSE30682). Since we have proved that EW-7197 showed the inhibitory effect *in vivo* in various breast cancer mouse models previously, we carried out experiments that might test if combinatorial treatment of EW-7197 improves radiation therapy using two syngeneic mouse models. Met 1 cell, which are derived from primary tumors of the FVB/N transgenic mouse with mammary tumor-polyoma virus middle T antigen (MMTV-PyVmt), were injected to fourth inguinal fat pads of FVB/N mice. 4T1 cells, which are derived from primary tumors of Balb/c mice, were injected as same way into Balb/c mice. Mice were treated with the fractionated-radiation (total dose 12 Gy, 4 Gy X3) with or without the combinatorial treatment of EW-7197 (2.5 mg/kg). Conclusion & Significance: Vactosertib (EW-7197), ALK5 inhibitor combinatorial treatment with radiation inhibits tumor growth and metastasis in syngeneic breast mouse models. This effect of Vactosertib (EW-7197), ALK5 inhibitor combinatorial treatment with radiation inhibits tumor growth and metastasis in syngeneic breast mouse models. Vactosertib (EW-7197) maybe related to the breast cancer stem-like phenotype, which is increased by 4Gy irradiation *in vitro*. We need to further study to conclude the therapeutic mechanisms of EW-7197 on improving radiation therapy. This work was supported by the National Research Foundation of Korea grant funded by the Korea government (NRF-2015M2A2A7A01041499) and (NRF-2014R1A1A2005644).

Biography

Yhun Sheen has her research interest in developing new anti-cancer drug. She had participated in the development of TEW-7197 which is currently under clinical trial in USA (NCT02160106).

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