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Combined Treatment of PARP-1 Inhibitor and Carbon Ion or Gamma Exposure Reduces the Metastatic Potential in Cultured Human Cells

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Abstract : Hadron therapy using high Linear Energy Transfer (LET) ion beam is producing promising clinical results worldwide. The major advantages are its ability to kill radio-resistant tumor and its anti-metastatic activity. Poly(ADP-ribose) polymerase-1 (PARP-1) inhibitors have been widely used as radiosensitizer, but its role in metastasis is unknown. The purpose of our study was to investigate the effect of PARP-1 depletion in combination with either Carbon Ion Beam (CIB) or gamma irradiation on metastatic potential of cultured cancerous cells. A549 cells were irradiated with CIB (0-4Gy) or gamma (0, 2, 4, 6 and 10 Gy) with and without PARP-1 inhibition. The metastatic potential of the cells was determined by cell migratory assay, expression, and activity of MMP-2 and MMP-9, expression of Cadherin, Fibronectin, and Vimentin. CIB exposure reduced migratory property and activity of MMP-2 and MMP-9 significantly. CIB with PARP-1 inhibition reduced cell migration and Matrix Metalloproteinase (MMPs) activity in a synergistic manner. Expression of MMPs was also down-regulated in CIB and combined treatment. On the contrary, MMP- 2 and MMP-9 activity was significantly increased in gamma irradiated cells but decreased upon combined treatment of gamma and PARP-1 inhibitor. MMPs expression and migration was reduced when gamma irradiation was combined with PARP-1 inhibition. Thus, our study clearly demonstrates that PARP-1 inhibition in combination with either high or low LET can significantly suppress metastatic potential in cancer cells and thereby can be a promising tool in controlling metastatic cancers.

Keywords : high LET, low LET, matrix metalloproteinase (MMP), PARP-1
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