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Mesenchymal stem cell-derived vesicles reverse radiation toxicity to murine marrow stem cells

Extracellular vesicles have great potential for altering cell fate. The vesicles from originator cells are replete with cellular proteins, mRNA, microRNA and non-coding RNA with variable amounts of DNA and change cell fate by entering target cells and inducing epigenetic long-term stable genetic changes. We have evaluated murine and human mesenchymal stem cell-derived vesicles for their capacity to reverse radiation damage to murine marrow stem cells. The addition of vesicles (25 ug of protein total) to liquid culture of control or irradiated marrow cells partially restored engraftment capacity of the irradiated (100cGy whole body irradiation) marrow stem cells, whether administered 24 hours or 7 days after the irradiation. In other studies, C57BL mice were exposed to 500cGy whole body irradiation and then either injected repeatedly with vehicle or with vesicles (15 ug protein per injection) WBC recovery in the vesicle protein injected mice was accelerated. Similar results were obtained injecting human mesenchymal stem cell derived vesicles into 500cGy irradiated mice. The murine hematopoietic cell line FDC-P1 was subjected to either 0 or 500cGy irradiation and then exposed to murine marrow derived vesicles- effects on both growth and apoptosis were reversed. Similar results were obtained with human mesenchymal stem cell derived vesicles. We also showed that homing *in vitro* of CFSE labeled vesicles to marrow cells progressively increase with radiation exposure from 250-1000cGy providing a potential surrogate assay for the healing effects of vesicles in different injury settings. Exposure to extracellular vesicles may provide a unique strategy to reverse radiation damage in different situations.

Biography

Peter Quesenberry is a hematologist/oncologist with a long history of work on stem cell biology and characteristics of the stem cell, especially with regard to cell cycle transit. More recently his work has focused on extracellular vesicles and their capacity to alter cell fate and to restore injured tissue. He is the Paul Calabresi, MD Professor in Oncology and Director of the Division of Hematology/Oncology at the Warren Alpert Medical School of Brown University and Rhode Island and The Miriam Hospitals. He lists 303 publications on PubMed. He is the American editor of the *Journal of Extracellular Vesicles*.

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