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Cell therapy the allograft to universal transplant and how to transform a concept in a clinical trial also application in the treatment of the side effects of radiotherapy

Cell therapy was demonstrated of main importance in the management of normal tissue radiation damage. Preclinical and clinical trial data suggest that mesenchymal stem cells (MSCs) are a practical and safe source of cells for stem cell-based therapies of severe tissue damage consecutive to radiation overexposure. MSCs were shown to migrate to damaged tissues supporting wound healing through a "cell drug" mode of action restoring skin and gut functions after irradiation. However, technical limits associated with large-scale ex vivo expansion indicate that alternative source is required to obtain sufficient cell numbers of the appropriate lineage to treat patients with severe disease.

Based on this pluripotency and unlimited expansion potential, induced pluripotent stem cells (iPSCs) are considered a promising resource for regenerative medicine. Like naturally occurring stem cells, these artificially induced cells can self-renew and develop into almost any cell in the body (pluripotency). Clinical iPSC banks of selected universal donors should allow their use for large scale allogeneic grafts.

Our consortium describes a GMP-grade system to produce hiPSCs, a cell population capable of reconstituting human hematopoiesis. We demonstrate that i) hiPSC-derived hematopoietic stem cells (HSCs) from healthy donor are capable of reconstituting a functional human hematopoiesis in a radio-induced aplasia preclinical model, ii) hiPSC-derived HSCs from aplastic anemia patients or acute leukemia affected patients retain this ability.

Our study prepares a new approach of autologous graft (from the cells of the patient) of cells for healthy tissue damage after radiation exposure. It could potentially pave the way to the constitution of universal banks of stem cells, which would radically increase the capacity of support and treatment of tissue exposed to high doses of ionizing radiation and in the management of chronic late radiotherapy side effects.

Speaker Biography

Alain Chapel has been developing gene and cell therapy using non-human primates, immune-tolerant mice and rats to protect against the side effects of radiation. He collaborates with clinicians to develop strategies for treatment of patients after radiotherapy overexposures. He has participated in the first establishment of proof of concept of the therapeutic efficacy of Mesenchymal stem cells (MSCs) for the treatment of hematopoietic deficit, radiodermatitis and over dosages of radiotherapy. He has contributed to the first reported correction of deficient hematopoiesis in patients (graft failure and aplastic anemia) thanks to intravenous injection of MSCs restoring the bone marrow microenvironment, mandatory to sustain hematopoiesis after total body irradiation. He is scientific investigator of clinical phase II trial evaluating the efficacy of systemic MSC injections for the treatment of severe and chronic radiotherapy-induced abdomino-pelvic complications refractory to standard therapy.

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