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Gene therapy to mitigate radiation-induced bone marrow aplasia: Preliminary study in highly irradiated monkeys

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The hematopoietic syndrome represents the first therapeutic challenge following exposure to high doses of ionizing radiation. Today there is a crucial need to identify/develop new treatments in order to reach the transplantation threshold. The authors propose the concept of a global niche therapy strategy based on local and short-term secretion of selected morphogenes to favor a vascular niche in order to raise the transplantation threshold regeneration and to stimulate residual hematopoietic stem and progenitor cells. The present study was aimed at setting up a monkey model of gene therapy using Sonic hedgehog (Shh) as a first candidate. Multipotent mesenchymal stem cells from adipocyte tissues were nucleofected with mock and Sonic hedgehog pIRES2 plasmids using AmaxaTM technology. 8-Gy gamma irradiated monkeys were given a single intraosseous injection of manipulated or unmanipulated adipocyte stem cells 48 h following total body irradiation. Mock and Shh-grafts were well tolerated. This preliminary study establishes the feasibility of transient gene therapy in highly irradiated monkeys. Ongoing studies will determine the putative efficacy of this therapeutic strategy.

Biography

During her various scientific experiments, she specialized in the optimization of the use of cell therapy in regenerative medicine and more particularly in the case of lesions Induced by ionizing radiation. During her doctorate (IRSN), she studied the plastic capacity of Mesenchymal Stem Cells (MSCs), as part of an innovative therapeutic approach to radiation-induced multi-organ damage. Her work has made it possible to demonstrate for the first time that the MSCs favor the healing of cutaneous radiation syndrome in a xenogeneic transplantation model. As part of her specialization in the field of regenerative medicine through the use of MSC in radiation-induced lesions, she completed a post-doctoral internship (Hôpital Saint Antoine) Have evaluated the safety of MSC transplants after radiotherapy in the context of pelvic cancer. At the same time, she studied the MSCs action in a tumoral environment: early and late stage colonic carcinogenesis. During her last Post-doctoral work, she participated in a clinical study evaluating a compassionate treatment based on the use of MSCs. Finally, taking advantage of her previous scientific achievements, she joined the Radiation Biological Effects Department (RBED) of the French Armed Forces Biomedical Research Institute (IRBA), in which she is currently project leader on the Development of new therapeutic approaches to acute radiation syndrome. Her ten years of research experience have been valued by 22 publications in international journals, 2 national publications and 2 academic books.

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