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Mesenchymal stem cell (MSC) therapy for the treatment of severe and chronic radiotherapy-induced abdomino-pelvic complications refractory to standard therapy

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Radiotherapy is one of the most used cancer treatment protocols. Although radiotherapy is optimized to avoid damages to healthy tissues within the irradiation field, the secondary effects, such as fibrosis are observed. The most frequent protocols concern abdomino-pelvic radiotherapy. Within this field, colon and rectum are particularly radiosensitive due to the fast renewal of their epithelium. Nevertheless there is no effective therapy against colon and rectum radio-induced fibrosis. Based on the successes of Mesenchymal Stem Cells (MSCs) in cell therapy of radiation injuries, we have decided to investigate their ability to reduce radiation-induced fibrosis after pelvic radiotherapy. In this study, our aim is to investigate the efficacy of MSCs on radiation colon fibrosis in an in vitro model before confirming our results *in vivo* in a protocol close to radiotherapy. We retained to use fibroblasts and smooth muscle cells due to their implication in colon fibrosis. TenG rays ionizing radiation induced fibrogenesis. Using co-culture experiments, we have confirmed MSC anti-fibrotic effect. The effect of MSCs on profibrotic cell lines has been characterized in vitro. Depending on the stage of the fibrogenesis, MSCs act through different pathways. Based on in vitro study we confirmed these results on *in vivo* models of rats. Using a single dose of 29 Grays for pelvic irradiation, we have obtained damages close to those observed in radiotherapy. Finally we observed that the MSC injection may prevent these damages in vivo. We can conclude that MSCs represent a promising strategy in the treatment of severe enteritis, rectitis induced by radiotherapy of prostate, bladder, uterus cancers.

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