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Mechanisms involved in the therapeutic properties of mesenchymal stem cells on intestine damages: Application to radiotherapies side effects

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Patients who undergo pelvic or abdominal radiotherapy may develop high incidence of undesirable acute and/or chronic gastrointestinal complications resulting from radiation induced damages around the tumor. Side effects can also be aggravated following a radiotherapy accident such as an overdose (Ash D. Clin Oncol, 2007). Treatments applied to manage complications of radiotherapy are only symptomatic. Stem cell-based approaches using mesenchymal stem cells (MSCs) are promising for the development of future therapy and are currently among the most advanced cell therapy tools.

We demonstrated in rodent model that intravenously administered MSCs reduced radiation effects on acute gastrointestinal disorders by enhancing functional epithelium self-renewal (Semont A et al. Cell Death and Differentiation, 2010). Our new *in vivo* and *in vitro* experiments seem to show an involvement of Wnt pathway activation in MSC effects on epithelial cell proliferation and therefore epithelium rescue. The colonic motility dysfunction which participates in the process of radiation induced chronic complications was also restored by intravenously infusion of MSCs. This therapeutic effect is partially dependent of MSCs abilities to regulate neurally induced muscle activity by the modulation of enteric nervous system activity and neurochemical coding (regulation of nitric oxide neuron proportion; nNO). Our results suggest that MSC infusion may be used as a therapeutic treatment to limit acute and chronic radiation-induced gastrointestinal damages.