Stromal vascular fraction for the treatment of the radiation-induced gastrointestinal syndrome

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Accidental or intentional radiation exposures have serious health consequences for exposed individuals and can affect a large number of people. Large volume irradiation at high irradiation doses induces multiple tissue lesions. The gastro-intestinal tract is particularly sensitive to irradiation and lethality. At dose more than 10 Gy results in diarrhea, dehydration, sepsis and intestinal bleeding with mortality within 10 post-exposure. Radiation-induced gastrointestinal syndrome (GIS) results from direct cytocidal effects on intestinal stem cells and crypt stroma impairing epithelial regeneration. Damaged intestinal epithelium significantly reduces the mucosal integrity and promotes systemic bacteria influx resulting in sepsis and death. Given the logistical hurdle and the urgency for treatment in large numbers of casualties, there is a tremendous need for effective therapeutic measures, even if implemented several days after radiation exposure. The stromal vascular fraction (SVF) derived from adipose tissue is an easily accessible source of cells with angiogenic, anti-inflammatory, immunomodulatory, and regenerative properties. We examined whether SVF restores the irradiated intestinal cells niche and mitigates the GIS. At the day of abdominal irradiation (18Gy) mice were injected in systemic with SVF, obtained by enzymatic digestion of adipose tissue. Seven days post-irradiation, SVF treatment limited weight loss and inhibited intestinal permeability [1]. When injected before 24 hours post-irradiation, SVF limited the mortality. SVF has an anti-inflammatory effect in the intestine by repressing pro-inflammatory cytokines, accelerating the maturation of monocyte able to generate anti-inflammatory macrophages. Immunohistological analyses of intestine showed that SVF treatment stimulated the regeneration of the epithelium by promoting numerous hyperproliferative zones. SVF restored the cell population in the intestinal stem cell compartment. The *ex-vivo* intestinal “organoid” model that mimics the clinical response confirmed that SVF treatment stimulated the intestinal stem cell compartment. With pleiotropic effects that contribute to limite radiation-induced lethality, SVF offers attractive prospects for the treatment of emergency GIS.

[1]. Bensemmane, C Squiban, C Demarquay, N Mathieu, M Benderitter, B Le Guen, F Milliat, C Linard, *Stem Cell Res Ther*, 2021,12:309.