Combined therapy for critical limb ischaemia: Biomimetic PLGA microcarriers potentiates the pro-angiogenic effect of adipose tissue stromal vascular fraction cells

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Résumé en anglais	We propose a regenerative solution in the treatment of critical limb ischaemia (CLI). Poly-lactic/glycolic acid microcarriers were prepared and coated with laminin to be sterilized through γ-irradiation of 25 kGy at low temperature. Stromal vascular fraction (SVF) cells were extracted through enzymatic digestion of adipose tissue. Streptozotocin-induced diabetic mice underwent arteriotomy and received an administration of SVF cells combined or not with biomimetic microcarriers. Functional evaluation of the ischaemic limb was then reported, and tissue reperfusion was evaluated through fluorescence molecular tomography. Microcarriers were stable and functional after γ-irradiation until at least 12 months of storage. Mice that received an injection of SVF cells in the ischaemic limb have 22% of supplementary blood supply within this limb 7 days after surgery compared with vehicle, whereas no difference was observed at Day 14. With the combined therapy, the improvement of blood flow is significantly higher compared with vehicle, of about 31% at Day 7 and of about 11% at Day 14. Injection of SVF cells induces a significant 27% decrease of necrosis compared with vehicle. This effect is more important when SVF cells were mixed with biomimetic microcarriers: -37% compared with control. Although SVF cells injection leads to a non-significant 22% proprioception recovery, the combined therapy induces a significant recovery of about 27% compared with vehicle. We show that the combination of SVF cells from adipose tissue with laminin-coated poly-lactic/glycolic acid microcarriers is efficient for critical limb ischaemia therapy in a diabetic mouse model.

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