

Biodistribution of mesenchymal stem cells derived microvesicles: in vivo and ex vivo analysis

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Background: Microvesicles (MVs) display excellent bio-distribution in the body and some of them can even cross the blood–brain barrier. MVs have immense prospects for clinical application as a vectors for medicines delivery. Therefore, in this study we have investigated their trafficking in vivo. We have determined the bio-distribution of cytochalasin B induced microvesicles (CIMVs-MSCs) derived from murine mesenchymal stem cells in animal model following intravenous, subcutaneous and intramuscular injection.

Materials and methods: CIMVs-MSCs were stained with vital membrane dye DiD and injected intravenously, subcutaneously or intramuscularly (50 µg). Mice were analyzed using IVIS Imaging System.

Results: We found that 1 hour after intravenous injection of CIMVs-MSCs the fluorescence signal was localized in internal organs presumably in lung. To accurately conclude from which organ the fluorescent signal originated the organs were imaged ex vivo. CIMVs-MSCs accumulated mainly in liver and lung, a low signal of CIMVs-MSCs was observed also in spleen and brain. At 48 hours, the fluorescent signal remained in liver and lung and started to increase in brain, heart, spleen and kidneys. These findings may be explained by an uptake of remaining in blood CIMVs-MSCs and their gradual renal excretion. Subcutaneously and intramuscularly injected CIMVs-MSCs could be detected in the injection site up to 14 days, most likely due to incorporation into the tissue and long half-life of the dye.

Conclusions: We have demonstrated that CIMVs accumulated in liver, lung, brain, heart, spleen and kidneys 48 hours after the i.v. injection. We have suggested that the subcutaneous and intramuscular injection of CIMVs-MSCs is more suitable for the local therapy.