

## Biodistribution of membrane vesicles in vivo

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**Background:** Extracellular vesicles (EVs) are important vehicles carrying growth factors, cytokines, chemokines, mRNA, miRNAs and siRNA which mediate intercellular communication. EVs contain the same bioactive molecules and surface receptors similar to donor cells. These properties suggest that membrane vesicles might be a perspective therapeutic instrument instead of mesenchymal stem cells (MSC), which have risk of tumor growth. Therefore, we investigated the biodistribution of allogeneic membrane vesicles in vivo after subcutaneous and intramuscular injection in mice.

**Materials and methods:** We obtained cytochalasin B-induced membrane vesicles (CIMVs) from adipose tissue-derived mouse stem cells (ADSCs) and stained with fluorescent membrane dye DiD (ThermoFisherScientific, USA). Allogeneic CIMVs were injected subcutaneously and intramuscularly in three mice at two different concentrations 1 mg/ml and 0.5 mg/ml. Fluorescence signal was detected in vivo using IVIS Spectrum (PerkinElmer, USA) (3 measurements per mouse).

**Results:** After subcutaneous administration the fluorescence intensity of 0.5 mg/ml CIMVs was 2.705 relative fluorescence units, fluorescence intensity of 1 mg/ml CIMVs - 5.534 relative fluorescence units (through 1 hour). We were able to detect CIMVs injected subcutaneously and intramuscularly after 1 hour, 48 hours and even 14 days. According to the 3D modeling, subcutaneous injection was localized under the skin surface, and intramuscular injection led to the CIMVs spreading and fluorescence signal was located at different focal lengths.

**Conclusions:** The fluorescence intensity of the 1 mg/ml CIMVs was twice greater than the 0.5 mg/ml CIMVs that confirms the specificity of the fluorescent signal. Subcutaneous and intramuscular administration of membrane vesicles derived from MSC may be useful for the therapy of diseases, such as skin damage, lower limb ischemia and others. CIMVs may be used not only for the transfer of bioactive molecules but also for drug delivery to different tissue.

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