

**Table S1.** Examples of EV biodistribution time in the liver in mouse models.

EV source	EV concentration/ type of imaging	EV administration route	Type of Liver disease/cell type uptaking EVs	Time taken to reach the liver/ Permanence in the liver/ in vivo or ex vivo analysis	References
Red blood cell -EVs loaded with miR-negative control (NC)-ASOs or miR-155-ASOs	100 µg ≈ 2.3 × 10 <sup>10</sup> particles/ IVIS imaging	Intravenous	Acute liver failure/macrophages	12 hours/24 hours (last time point analysed)/ex vivo	[166]
MLP29 (murine liver-derived cells)- [124 I] NaI-labelled EVs	1.8 ± 0.5 MBq/ PET-CT imaging	Intravenous	Healthy/ n.a.	15 mins/72 hours (last time point analysed)/in vivo	[167]
	0.6 ± 0.2 MBq/ automatic gamma counter	Into the hock			
HEK293T- Duramycin labeled EVs	99mTc-HYNIC- 12 ± 3 MBq/ SPECT/CT imaging	Intravenous	chronic hyperlipidemia/ Kupffer cells and liver sinusoidal endothelial cells (from in vitro data)	60mins/90 mins (last time point analysed)/ in vivo	[70]
Thyroid cancer (CAL-62) and breast cancer (MDA-MB-231) cells -Rluc- labelled CAL-62 EVs or Rluc- labelled MDA-231 EVs	25 µg of protein/ IVIS Lumina II	Intravenous	Naïve nude mice	10 mins, with a peak at 30 mins /9 days/ in vivo	[168]

PET: Positron Emitted Tomography; CT: Computed Tomography, MBq: Megabecquerel; n.a.: not available.