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Objectives: To develop BMEs that evade elimination by BMDMs.

Methods: Bovine mammary alveolar MAC-T cells secrete MEs and were used to engineer MEs that express proprietary protein features suspected to decrease elimination by BMDMs, denoted UNL1 and UNL2. MAC-T cells were transformed by using lentiviral vectors. BMEs featuring UNL1 or UNL2 were isolated from MAC-T cell culture media supernatant using polyethylene glycol (PEG) precipitation after removing cell debris by using a 0.22-μm filter. The BMEs were labeled using a carbonyl-reactive fluorescent dye and purified by ultracentrifugation. Primary BMDMs was isolated from mouse hind legs (C57BL/6J, aged 8–10 weeks) and seeded in 96-well plates for assessing BME uptake at a physiological concentration (1010 BMEs/mL). Uptake was compared to unmodified BMEs and normalized for BMDM density. Time points were compared pairwise by using t-test, and $P < 0.05$ was considered significant.

Results: The uptake of BME UNL1 by BMDMs was reduced by 37%, 42%, 48% and 47% as compared to unmodified BMEs after 12 h, 24 h, 36 h and 48h, respectively in culture dishes ($P < .05$; $n = 5$). Data are preliminary ($n = 3$), yet encouraging, for BME UNL2: The uptake of BME UNL2 was reduced by 41%, 44%, 46% and 46% compared to unmodified BMEs after 12 h, 24 h, 36 h and 48 h, respectively.

Conclusions: The elimination of BMEs UNL1 and UNL2 is significantly reduced compared unmodified BMEs in BMDM cultures. This is of great importance when using BMEs for delivering therapeutics.

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