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Objectives: Monocytes are one of the major phagocytic cells that patrol for invading pathogens, and upon activation, differentiate into macrophages or antigen-presenting dendritic cells (DCs) capable of migrating to lymph nodes eliciting an adaptive immune response. The key role in regulating adaptive immune responses has drawn attention to modulate monocyte responses therapeutically within cancer, inflammation and infectious diseases. We present a technology for targeting of monocytes and delivery of a toll-like receptor (TLR) agonist in fresh blood using liposomes with a positively charged surface chemistry.

Methods: Liposomes were extruded at 100 nm, incubated with fresh blood, followed by leukocyte analyses by FACS. Liposomes with and without the TLR7 agonist TMX-202 were incubated with fresh blood, and monocyte activation measured by cytokine secretion by ELISA and CD14 and DC-SIGN expression.

Results: The liposomes target monocytes specifically over lymphocytes and granulocytes in human whole blood, and show association with 75 - 95% of the monocytes after 1 h incubation. Formulations of TMX-202 in cationic liposomes were potent in targeting and activation of monocytes, with strong induction of IL-6 and IL-12p40, and differentiation into CD14+ and DC-SIGN+ DCs.

Conclusion: Our present liposomes selectively target monocytes in fresh blood, enabling delivery of TLR7 agonists to the intracellular TLR7 receptor, with subsequent monocyte activation and boost in secretion of proinflammatory cytokines. We envision this technology as a promising tool in future cancer immunotherapy.

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