1219 LIPID-COATED MESOPOROUS SILICA NANOPARTICLES (MSN) ACCUMULATE SELECTIVELY IN TUMOR-BURDENED TISSUES IN A MOUSE MODEL OF SEROUS EPITHELIAL OVARIAN CANCER

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Background Nanotechnology for drug delivery to cancer cells is hampered by abundant uptake by myeloid cells, with the majority of nanoparticles ending up in filtering organs.[1] Kupffer cells or other resident macrophages are the main cells that internalize nanoparticles. The dominant internalization of nanoparticles by myeloid cells favors the use of nanoparticles for immune therapy. In this study, we show that intraperitoneal administration of lipid-coated mesoporous silica nanoparticles (MSN) in an advanced mouse model of serous epithelial ovarian cancer results in nearly exclusive accumulation in tumor-burdened tissues.

Methods Nanoparticles were made from a silica base, followed by coating with an optimized cocktail of cholesterol and lipids, the latter including the Toll-like 4 agonist monophosphoryl lipid A (MPL-A). Immunogenic lipid-coated MSN (ILM) with differing surface charges were introduced *in vitro* to a variety of cell types, then flow cytometry was used to compare ILM internalization. Mice bearing advanced ovarian cancer were injected intraperitoneally with ILM and control LM, and then 24 hours later mice were euthanized and organs were evaluated for ILM accumulation. Fluorescent microscopy was used to identify *in vivo* cell targets of ILM.

Results *In vitro* studies showed that ILM with a positive surface charge were internalized by all cell types (endothelial, stromal, cancer, myeloid), while negatively charged nanoparticle internalization was limited to myeloid cells when in the presence of 20% serum.

In mice with advanced ovarian cancer, nanoparticles were selectively localized in tumor-associated tissues, regardless of nanoparticle surface charge, lipid composition, or presence of MPL-A (figure 1). Fluorescent microscopy showed all formulations of ILM were internalized by myeloid cells, regardless of surface charge or the presence of MPL-A.

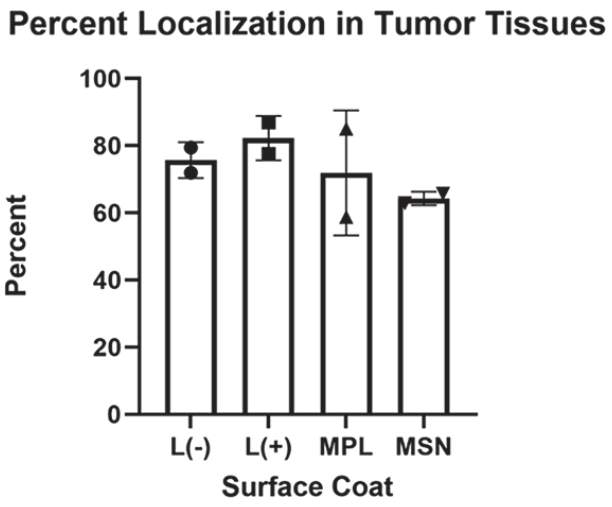
Conclusions When mice with advanced ovarian cancer were injected intraperitoneally with ILM, the nanoparticles localized selectively in tumor tissues, specifically within myeloid cells. While all cell types *in vitro* were able to internalize cationic ILM, robust uptake by myeloid cells appears to out compete other cell populations *in vivo*. We hypothesize that ascites based myeloid cells sequester ILM followed by cell-based trafficked of ILM to immune cell clusters located within tumors.

Acknowledgements This research was partially supported by UNM Comprehensive Cancer Center Support Grant NCI P30CA118100.

REFERENCE

1. Wilhelm S, Tavares A, Dai Q, Seiichi O, Audet J, Dvorak H, Chan W. Analysis of nanoparticle delivery to tumours. *Nat Rev Mater*. 2016;**1**(5):1–12

Ethics Approval This study was approved by the University of New Mexico IACUC, approval number 20-201067-HSC.



Abstract 1219 Figure 1 ILMs selectively localized in tumor tissues, regardless of surface charge, lipid composition, or presence of MPL-A.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1219