Impact of nanoparticle size on lymph node biodistribution after subcutaneous injection in mice

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Abstract

Lymph nodes, which are rich in T cells, B cells, dendritic cells, and macrophages, are also primary sites of action for vaccines and immunotherapies. Promoting the delivery of immunotherapies and vaccines to lymph nodes has been found to enhance treatment efficacy.[1,2] In this study, we investigated the particle effect of size on the lymph node uptake and biodistribution of negatively charged Cy5-polystyrene (PS) nanoparticles (NPs) (40 nm, 100 nm, and 250 nm) in mice following subcutaneous (SC) injection at 24 hr. The lymph node uptake and biodistribution were measured through *in vivo* imaging system (IVIS) and confocal microscopy. The concentration of Cy5 in the draining (ipsilateral) and non-draining (contralateral) lymph nodes (inguinal, popliteal, and iliac) is different after SC injection of the three different-sized NPs. The PS 40 nm particles led to significantly higher Cy5 concentration in inguinal draining (ipsilateral) LNs, inguinal non-draining (contralateral) LNs, and iliac contralateral LNs compared to the 100 nm and 250 nm particles at 24 hr. There was also a trend toward higher Cy5 concentrations in all LNs for the PS 40 nm compared to 100 and 250 nm particles. The concentration of all particles was higher on the dosing side than the non-dosing side, suggesting that they were taken up directly into the draining lymphatics. Overall, for all NPs, the concentrations of Cy5 across the lymph nodes were in the order inguinal > iliac > popliteal, which is expected based on lymphatic drainage patterns from the leg side. Consistent with the LN biodistribution data, confocal microscopy images also indicated that Cy5 signals of 40 nm PS NPs were higher in the draining inguinal lymph compared to 100 and 250 nm PS NPs. This work demonstrates the important effect of NP size on lymph node uptake and distribution to immune cells in lymph nodes where the smaller 40 nm NPs were found to yield higher delivery to the LN immune cells. This has important implications for the optimal design of NPs for vaccines and immunotherapies.

References

[1] Trevaskis.; et al. *Nature Rev Drug Discov* **2015,** *15*, 781-803.

[2] Lee, G.; et al. *Molecular pharmaceutics* **2019,** *16* 4987-4999.