Cancer nanomedicine primarily aim to direct drugs delivery to cancer cells but tumor accumulation remains suboptimal (Mitichelheiser et al. Adv. Mater., 2022). To circumvent this limitation, activating immune cells with nanoparticles (NPs) is an emerging concept. However, upon engagement, whether NPs change the fate of immune cells that take them up remains unknown and one needs to thoroughly assess such impact to identify optimal NPs. Here, we characterized the response of immune cells to a selection of nanomaterials classically used in biomedical applications. Doing so, we aim at rationalizing the selection of specific NPs to undergo novel targeted approaches. Through bulk RNA-sequencing and proteomic analyses, we first investigated the impact of 6 NPs (lipidic, polymeric/organic/inorganic) on negatively isolated CD3-CD56+ human NK cells and CD3+human pan-T cells. Amongst all the NPs studied, we observed that the oxidated carbon nanostrabigered wide transcriptome and proteome modifications in both pan-T and NK cells, whereas the other NPs exhibit mild to low impact to both NK and pan-T cells. Interestingly, we observed that only polymeric NPs induced a pre-activated state in NK cells with an overexpression of the CCL5 chemokine and the cathepsin B. Based on these results, we identified one type of polymeric NPs as potential candidates for further NK cell targeting approaches.

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