Tracking platinum-loaded nanoparticles at single-cell resolution: Drug delivery, biomarker modulation, and immune cell fate in ovarian cancer co-cultures by mass cytometry

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Ultrasmall iron oxide nanoparticles (IONPs) conjugated with platinum (IV) (Pt(IV)) prodrugs show great promise as targeted nanocarriers for ovarian cancer (OC) therapy. This nanoplatform is known to enhance drug delivery, leading to increased DNA platination and better cancer cell killing compared to conventional cisplatin. However, the impact of these IONP-Pt(IV) on key tumour biomarkers and the immune microenvironment has been largely unexplored.

To address this, we used a co-culture model of A2780 OC cells and healthy donor peripheral blood cells, treating them with 20 μM IONP-Pt(IV) for 24h. We employed high-dimensional CyTOF analysis (CyTOF XT instrument) to profile intracellular platinum accumulation, the expression of OC biomarkers — human epidermal growth factor receptor 2 (HER2) and transferrin receptor 1 (TfR1)— and nanoparticle distribution within 37 distinct immune cell subsets using the 30-marker Immune Profiling Assay™ kit (Standard Biotools).

Our results confirmed near-universal platinum incorporation within the cancer cells, demonstrating highly efficient tumour-specific drug delivery. Interestingly, high-dimensional analysis revealed a marked increase in the proportion of $HER2^{-}/TfR1^{-}$ cells post-treatment, suggesting the nanocarrier uptake dynamically modulates biomarker expression. Crucially, nanoparticle uptake in blood cells was restricted mainly to monocytic subsets and some B cells, suggesting limited systemic distribution.

Collectively, this work underscores the critical need to integrate nanoparticle uptake profiling with the parallel assessment of biomarker and immune cell dynamics. Our successful application of CyTOF provides a robust platform for unravelling the complex performance mechanisms of next-generation nanotherapeutics.