Single cell analysis of nanoparticle fate and impact in treating triple negative breast cancer

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Triple negative breast cancer remains as one of the most common, yet challenging cancers to treat. Treatment typically includes surgery, chemotherapy and radiotherapy. We have been working towards improved efficacy in the delivery of chemotherapeutic agents and radiosensitizers in a 4T1 BALB/c model of triple negative breast cancer. While we have achieved improved outcomes in terms of animal survival and reduction of metastatic burden we have been challenged in explaining how, especially in terms of promoting beneficial radiobiological responses. Critical to our mechanistic description is elucidating 'where do the nanparticles go in the tumour?' and 'how do they remodel the tumour microenvironment?'

We have been applying a range of single cell analytics for assessing nanoparticle uptake across cell populations in vitro and within the tumor microenvironment in vivo for a range of nanoparticles. Various responses to the nanoparticles and radiation have been assessed such as DNA double strand breaks, protein expression, protein translocation and metabolic profiling. These have been correlated to the quantitative analysis of the number of nanoparticles in the same individual cells. Single cell characterization of ex vivo tumors has further identified cell populations that nanoparticles associate with and alter (**Figure 1a**). We observe that targeted nanoparticles associate with many cell types other than the cancer cells they are targeted towards within the tumour.

In a partnership with the Royal Adelaide Hospital, preclinical radiotherapy studies were conducted with clinical facilities and showed nanoparticle formulations not only modulate the single cell radiobiology but the microenvironment remodeling leads to therapeutic advantage (**Figure 1b**).

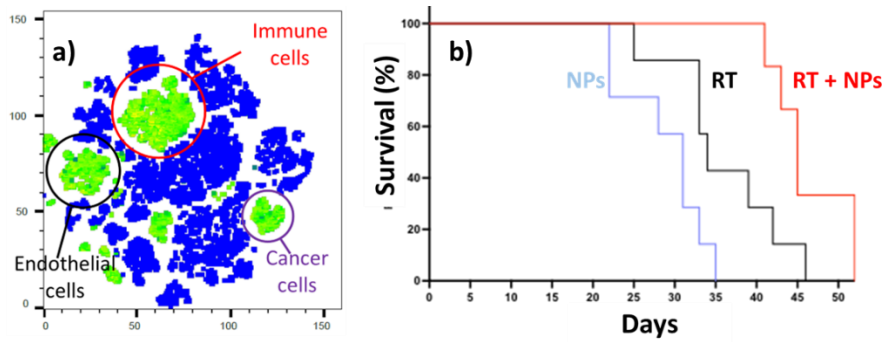

Figure 1. a) Single cell analysis of nanoparticle uptake with mass cytometry quantified the association with specific tumour cell sub-populations. **b)** Nanoparticle remodelling of tumour leads to improved survival in combination with radiotherapy (RT).