

Targeting Macrophages at the Tumor Microenvironment

Maria José Oliveira

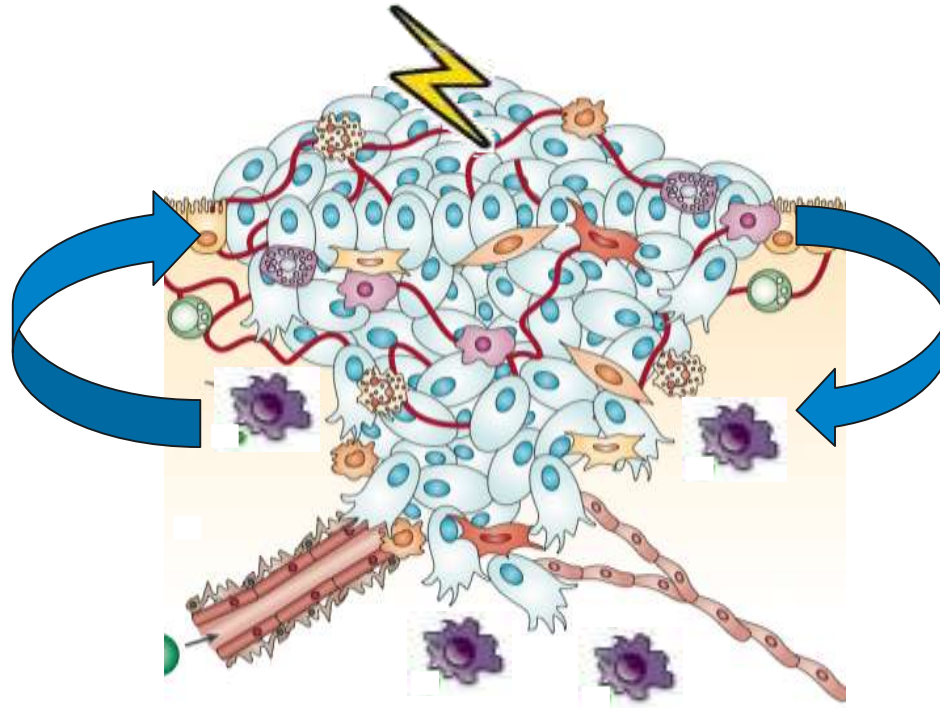
Tumour and Microenvironment Interactions Group

i3S- Instituto de Investigação e Inovação em Saúde

INEB- Instituto de Engenharia Biomédica

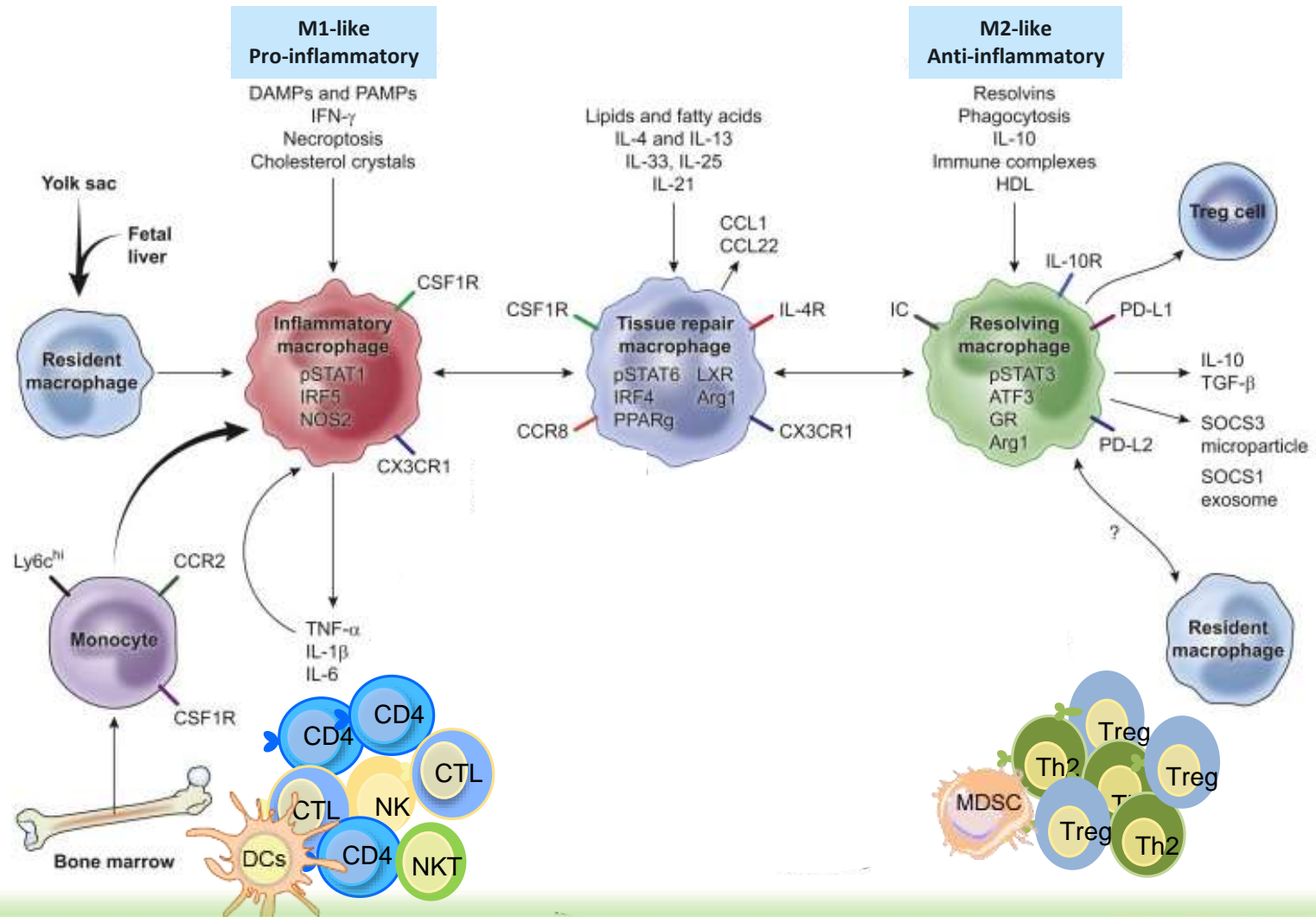
Encontro Ciência 2019, 9th July 2019, Lisboa

How does radiotherapy affect macrophage polarization? How do these effects affect macrophage/cancer cell crosstalk?



**Novel therapies to modulate
macrophage-cancer cell crosstalk**

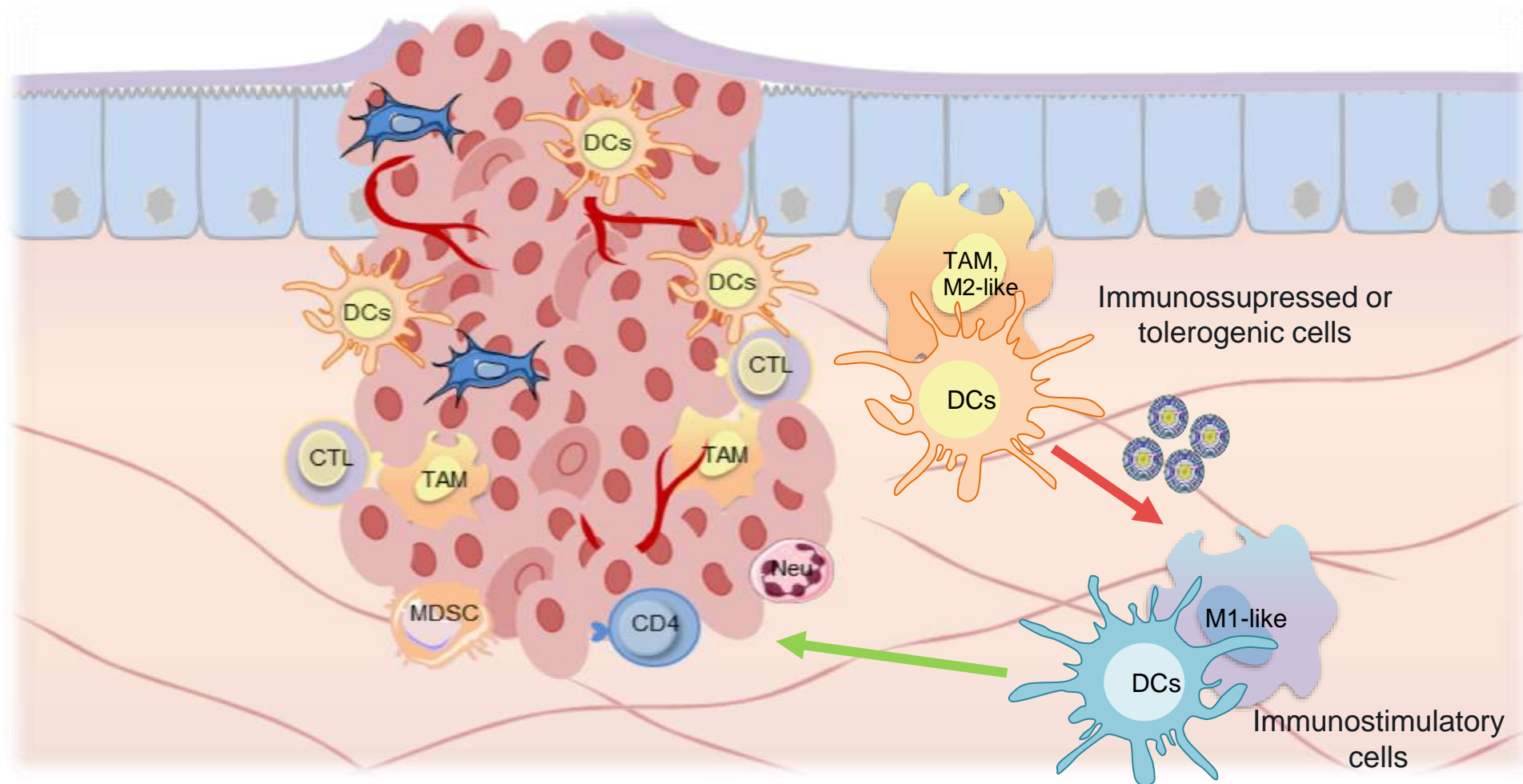
Macrophages plasticity and polarization



Tumour cell elimination

Tumour growth, invasion, metastasis, angiogenesis, immune evasion

Developing an immunomodulatory therapeutic strategy to counteract macrophage-mediated cancer cell invasion and promote immunesurveillance

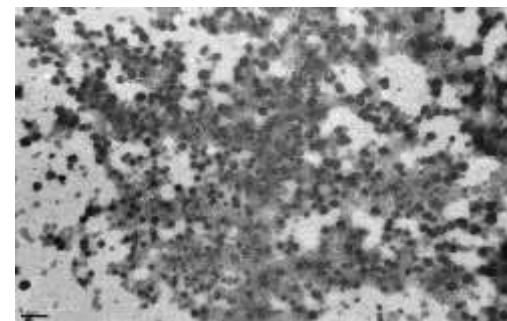
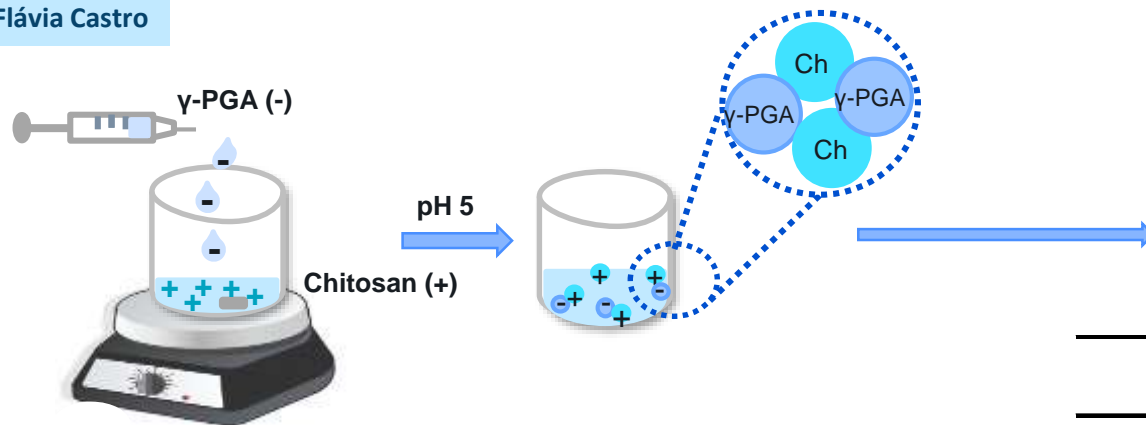




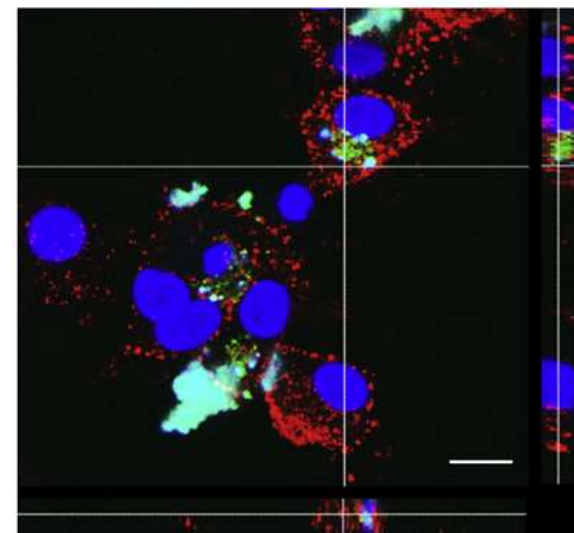
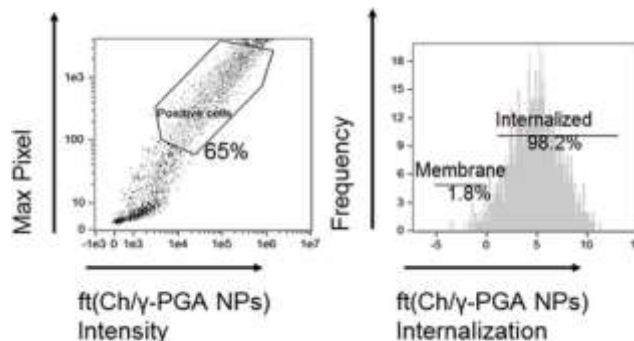
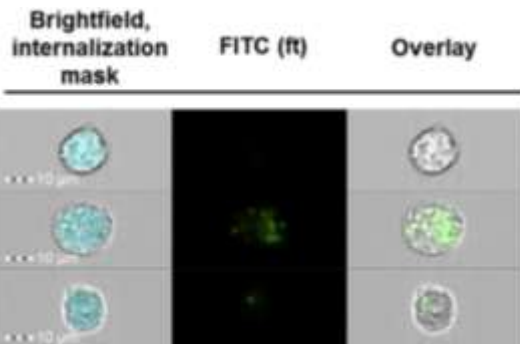
Developing an injectable immunomodulatory therapeutic strategy to counteract macrophage-mediated cancer cell invasion

In collaboration: Raquel Gonçalves, Susana Santos, Mário Barbosa

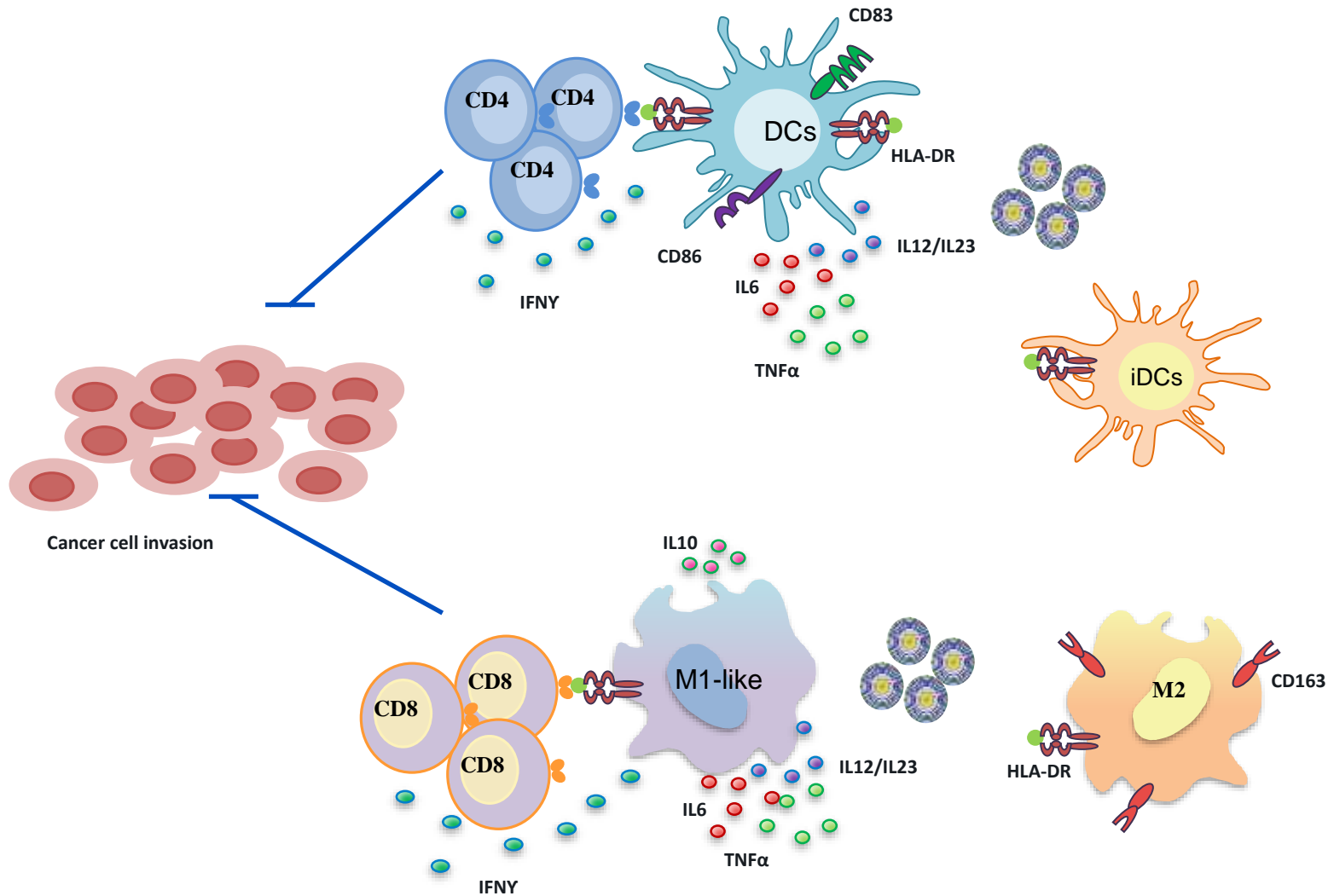
Flávia Castro



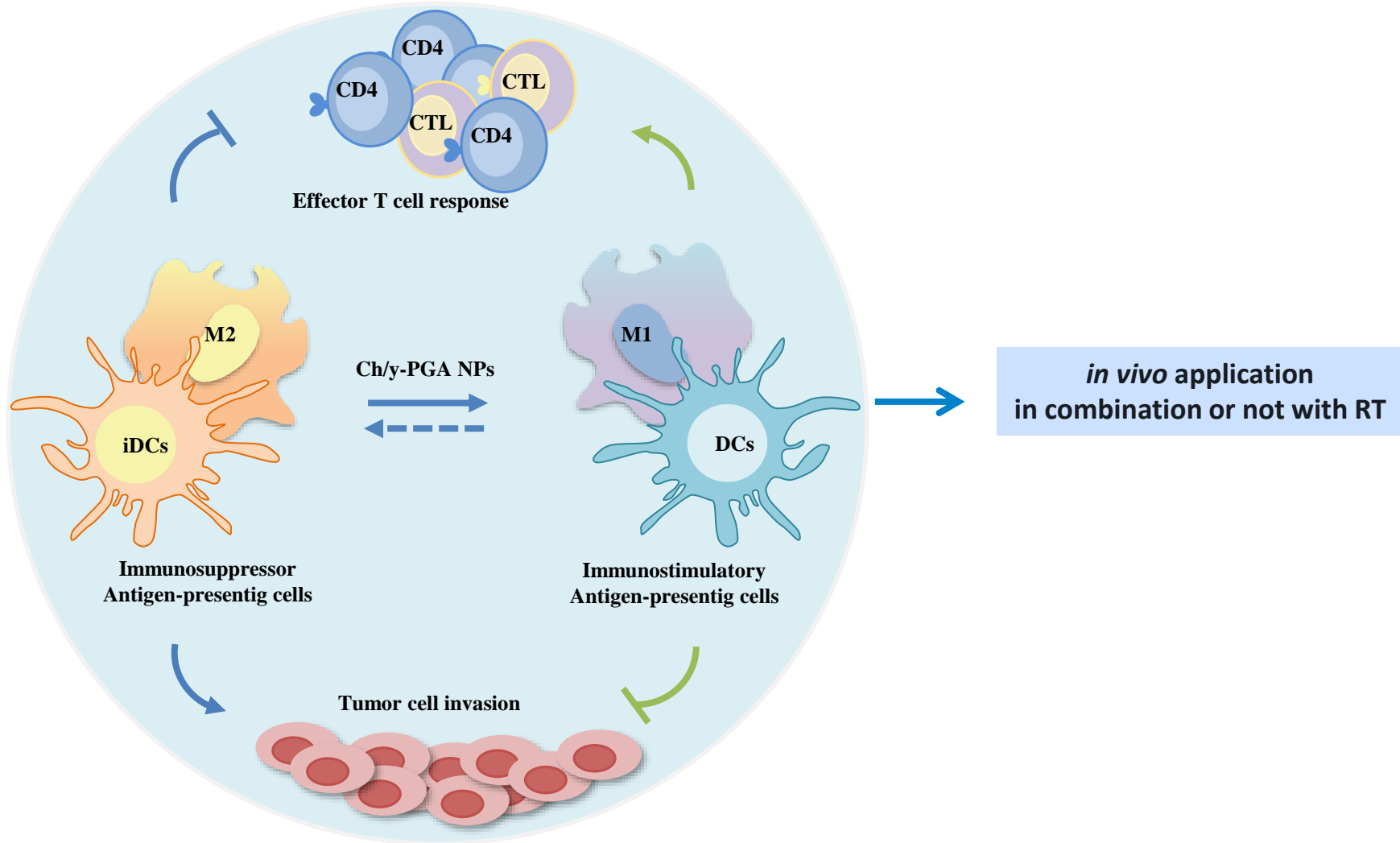
	Particle size (nm)	Polydispersion index	Zeta potential (mV)
Ch/γ-PGA NPs	183.0 ± 2.8	0.2 ± 0.01	18.7 ± 0.8



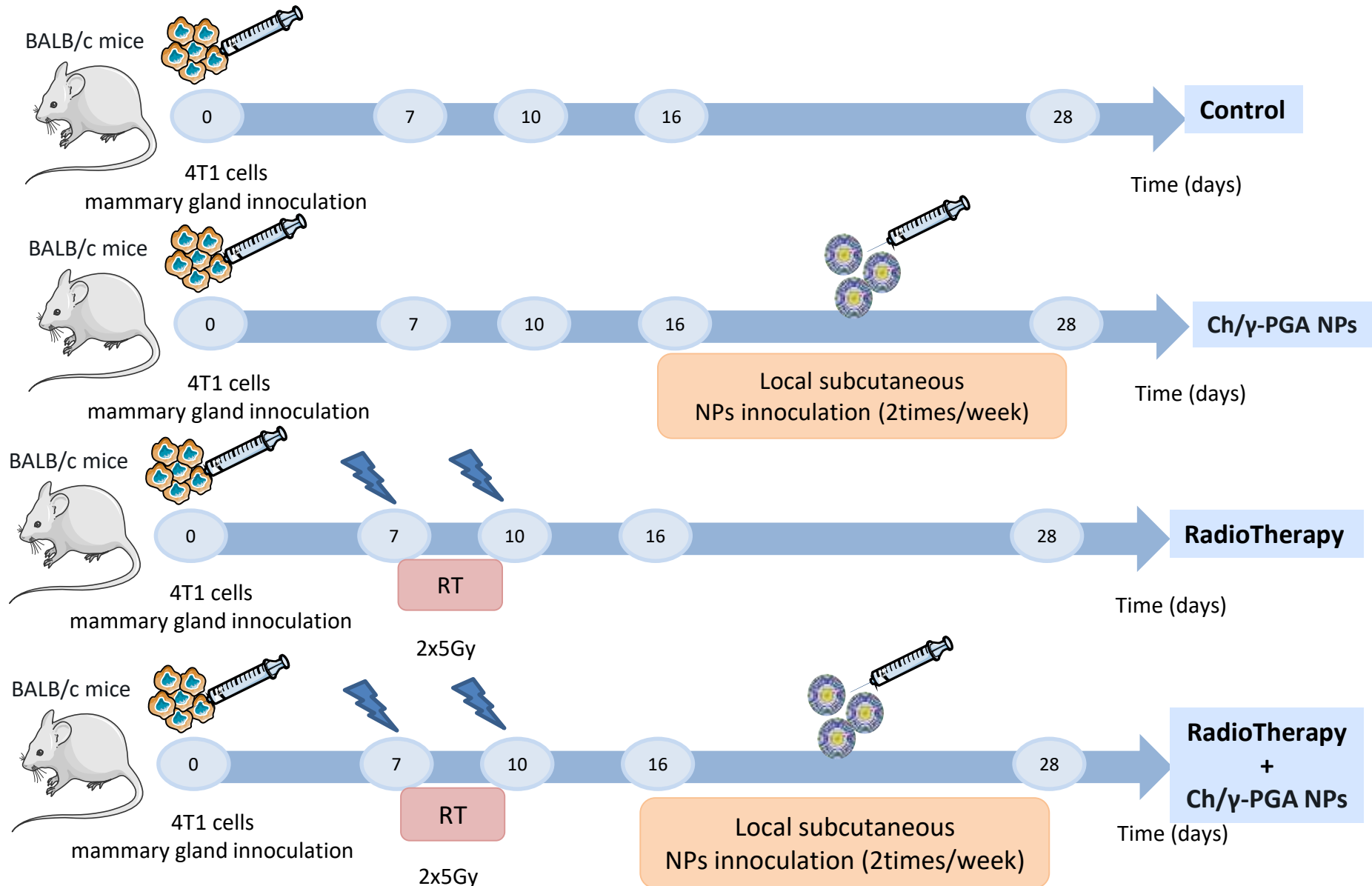
Immunomodulation at the Tumour Microenvironment: basis and challenges



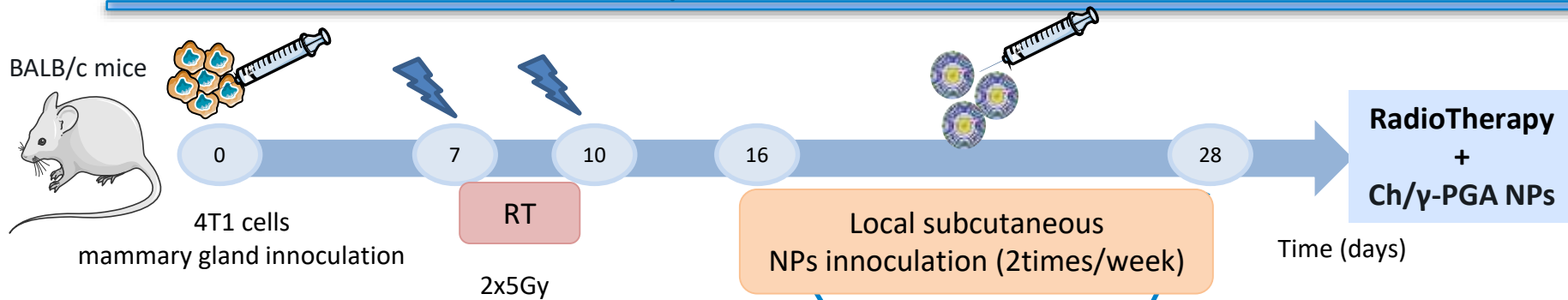
Developing an immunomodulatory therapeutic strategy to counteract macrophage-mediated cancer invasion and metastasis



Establishment of an orthotopic breast cancer model to evaluate the impact of RT or/and Ch/ γ -PGA NPs on cancer invasion and metastasis



Establishment of an orthotopic breast cancer model to evaluate the impact of RT or/and Ch/ γ -PGA NPs on cancer invasion and metastasis

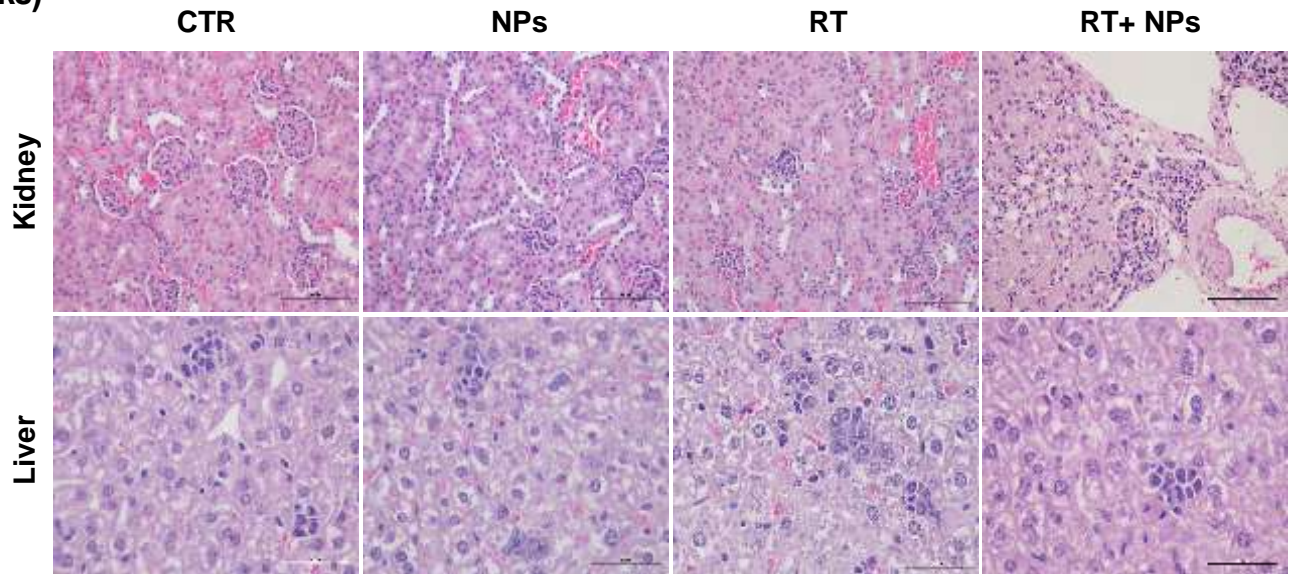
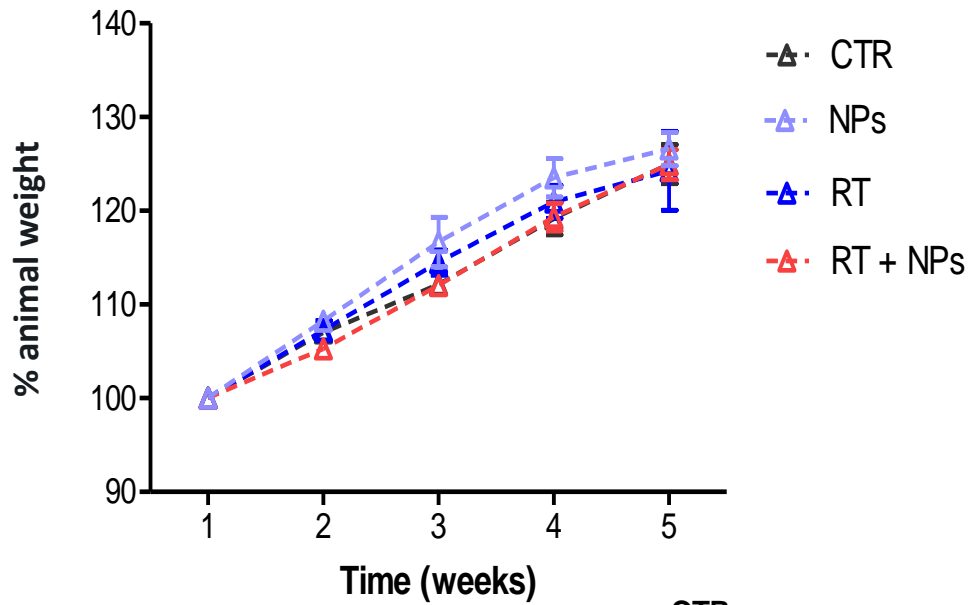


- ✓ Animal weight
- ✓ Tumor growth
- ✓ Lung and LN Metastasis (Bioluminescence)
- ✓ Spleen, Tumor, Lymph nodes FACS (myeloid and lymphoid populations)
- ✓ Histology (H&E)
- ✓ Spleen, Tumor, Lymph nodes RNA
- ✓ Serum (Multiplex ELISA array)

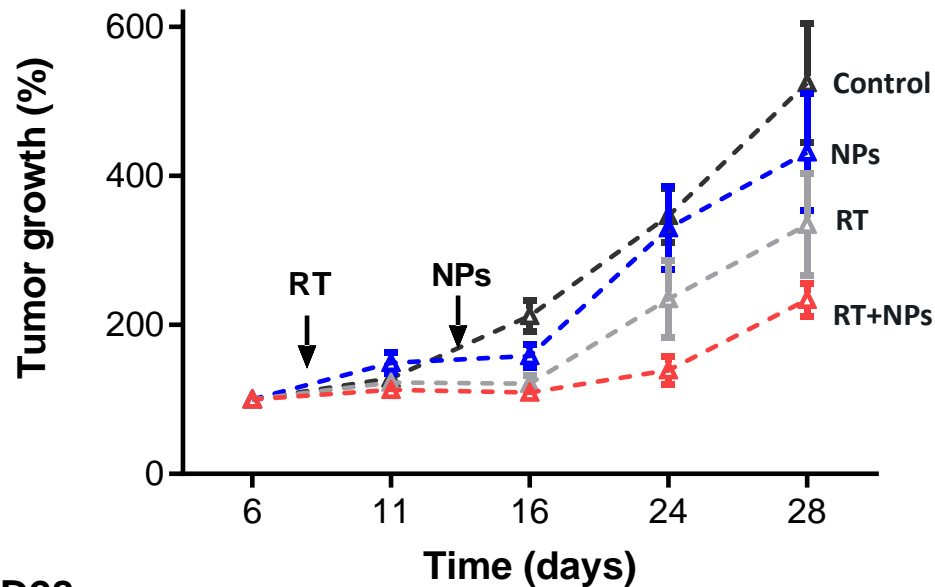
Small Animal Radiation Research Platform (SARRP)



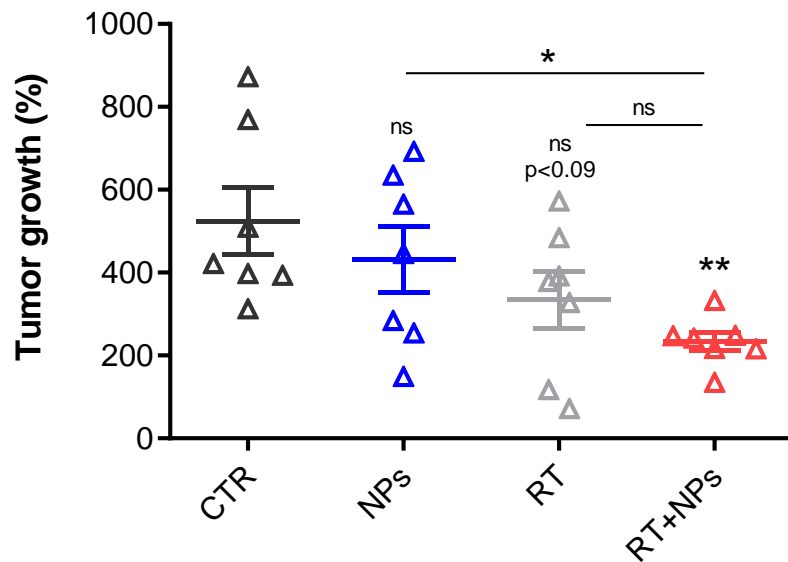
Therapeutic schemes did not affect animal weight nor induce animal kidney or liver toxicity



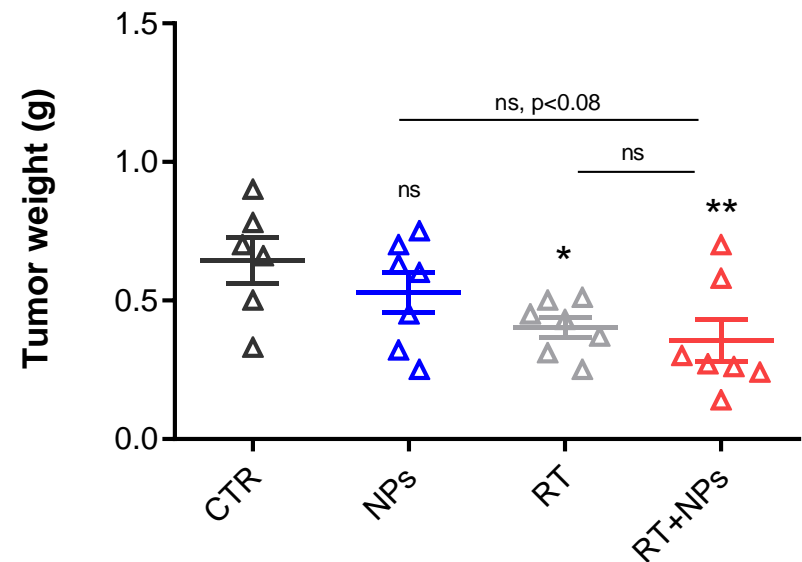
The combination of radiotherapy with the immunomodulatory Ch/ γ -PGA NPs decreased breast primary tumor growth



D28

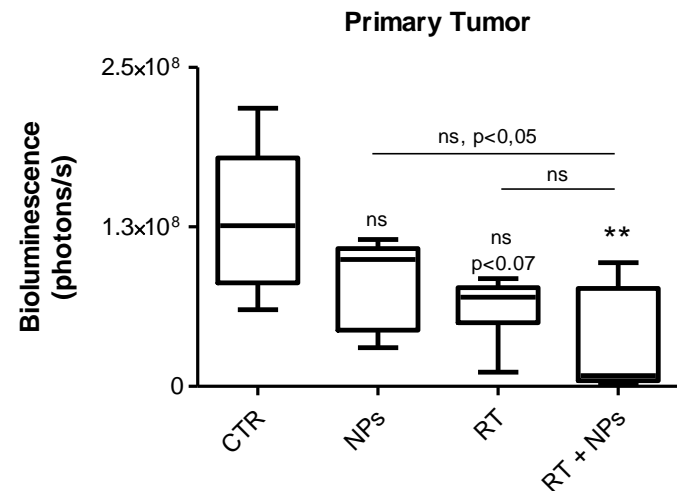
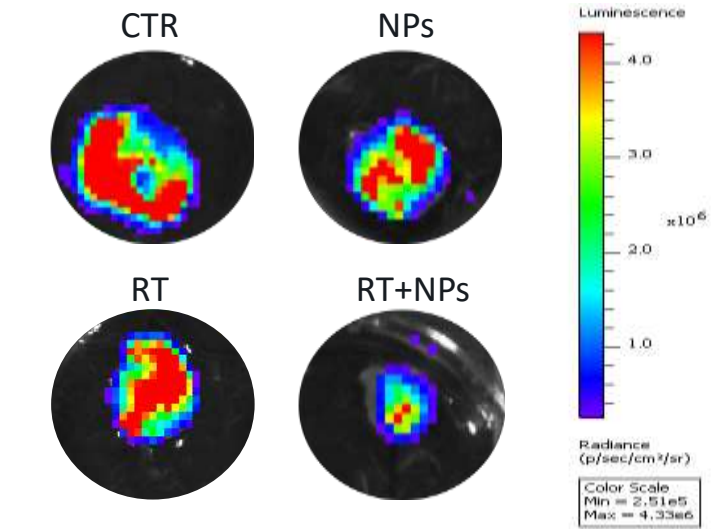
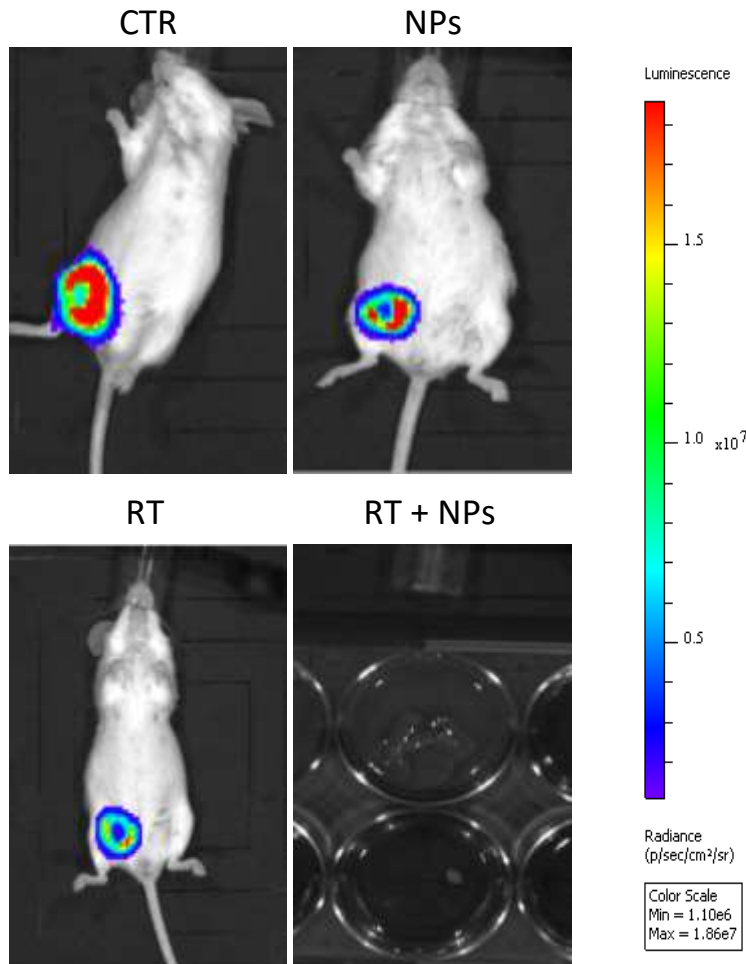


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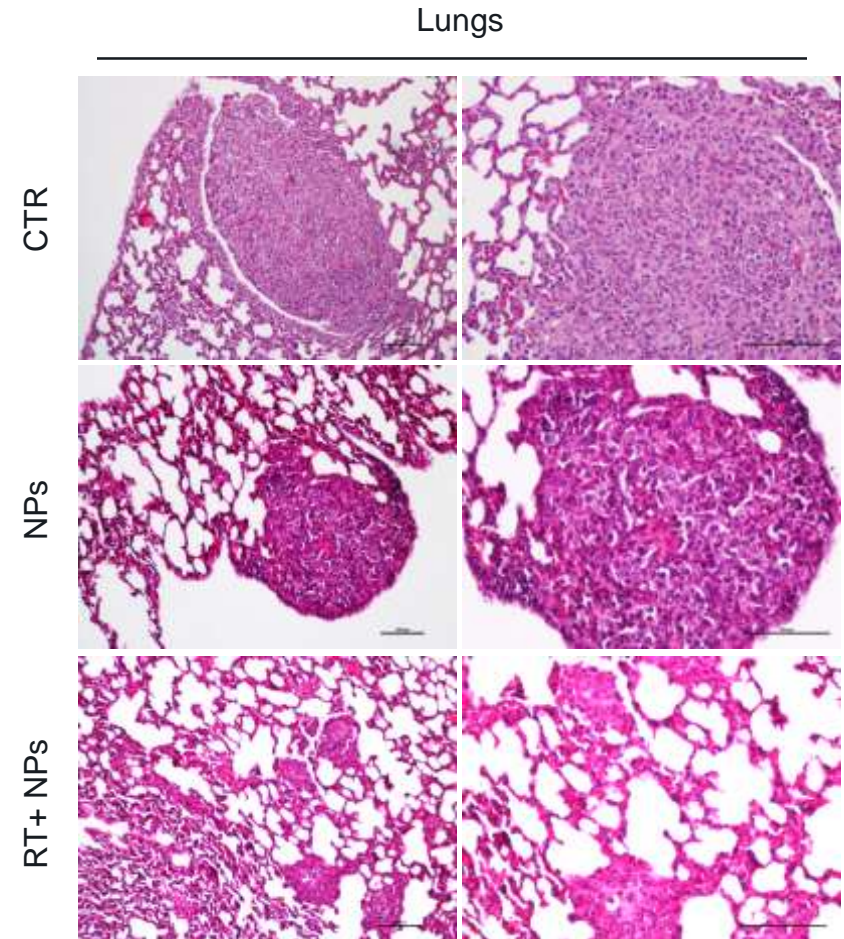
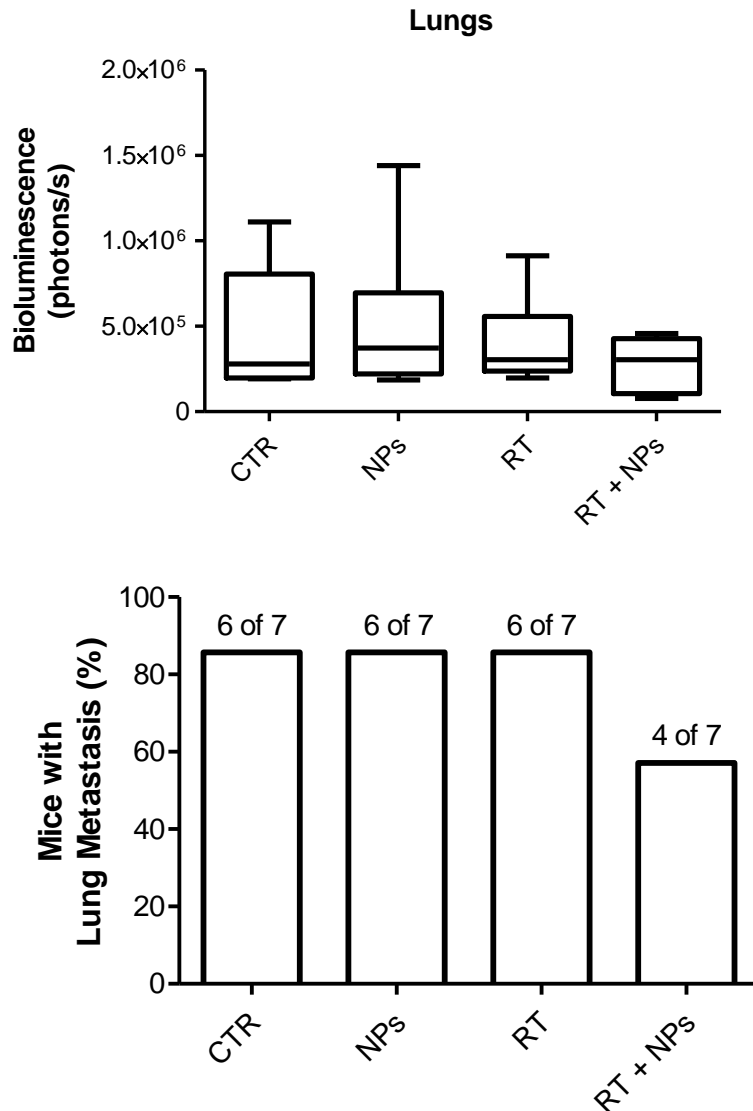


The combination of radiotherapy with the immunomodulatory Ch/ γ -PGA NPs decreased primary tumor burden

Bioluminescence (4T1-Lucifera cells)

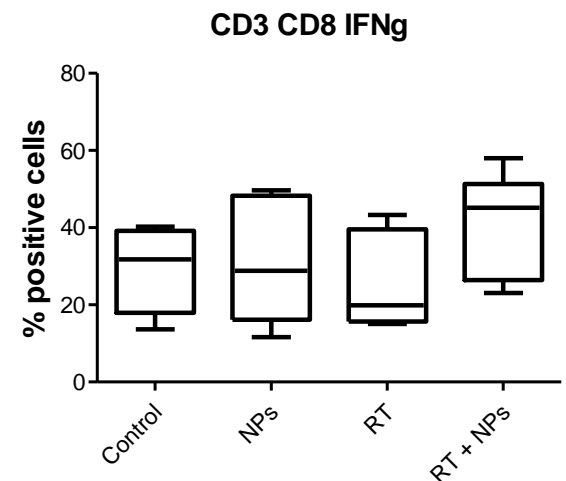
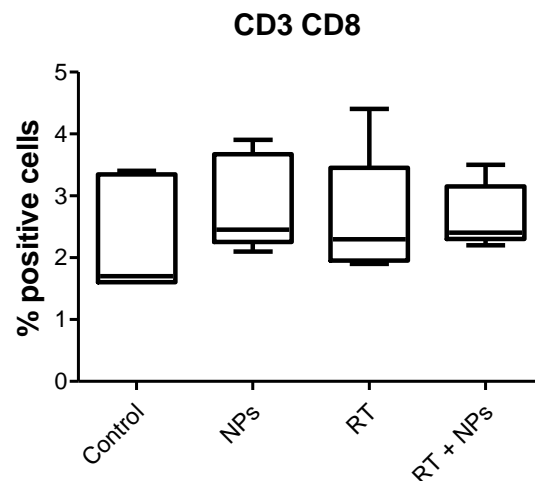
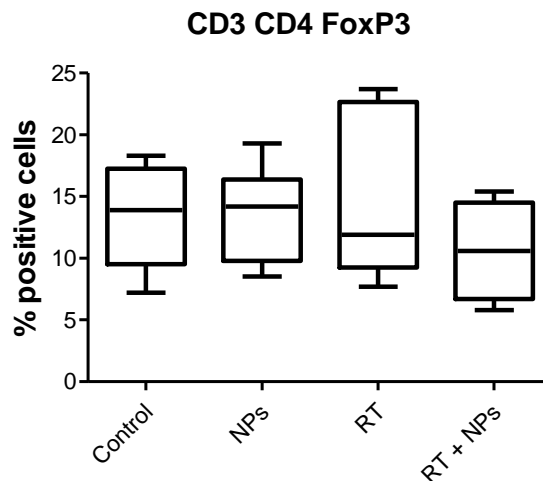
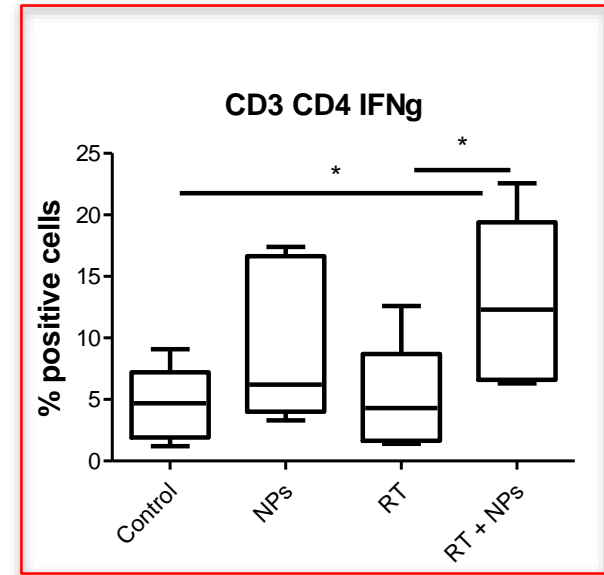
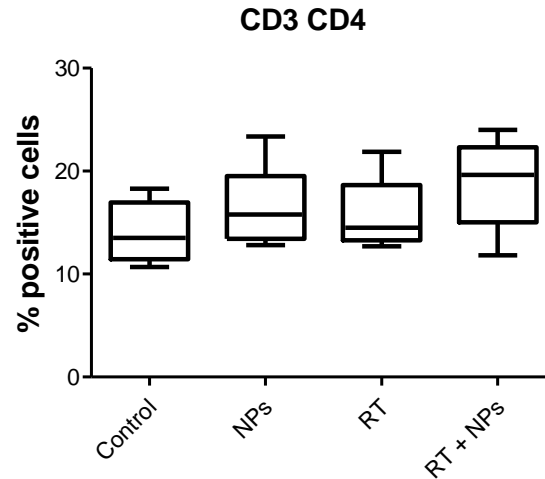
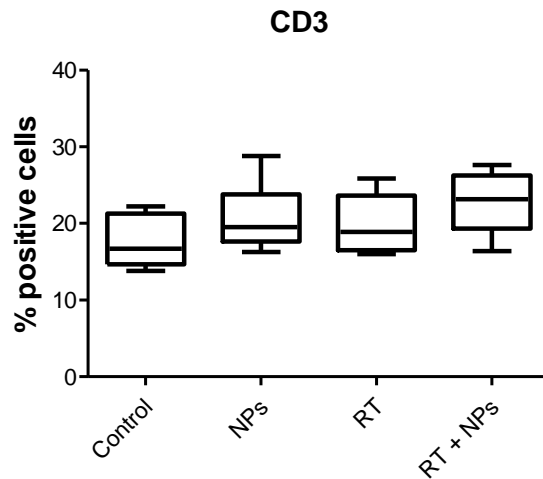


The combination of radiotherapy with the immunomodulatory Ch/ γ -PGA NPs reduced lung metastasis formation

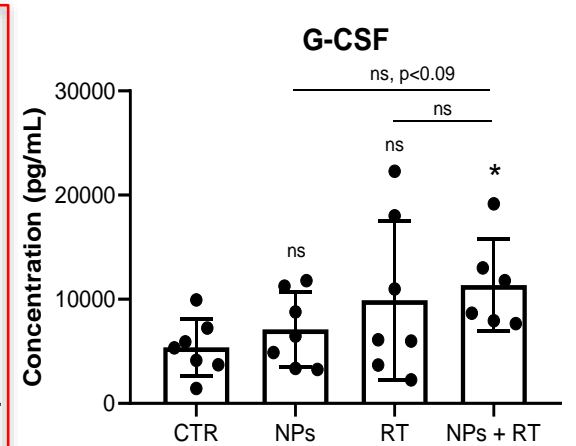
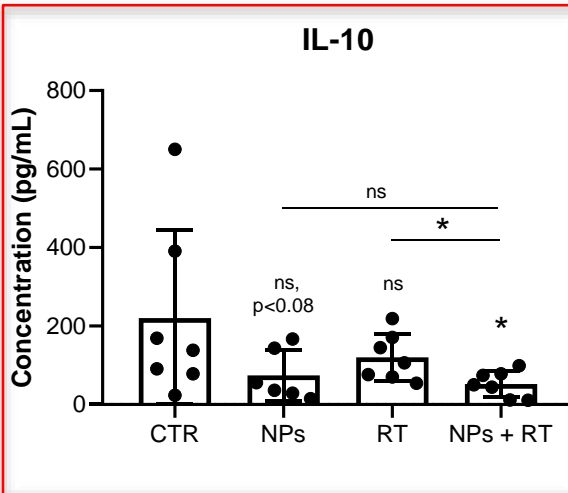
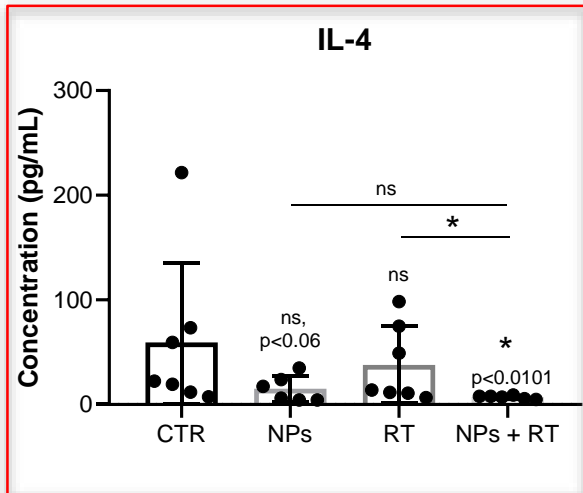
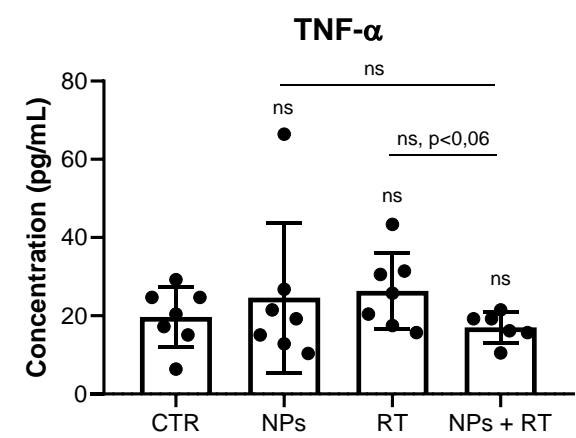
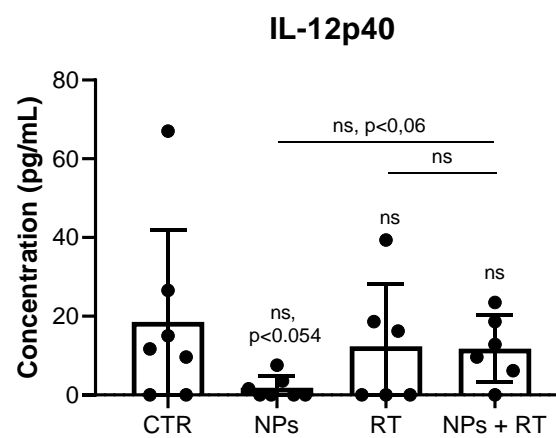
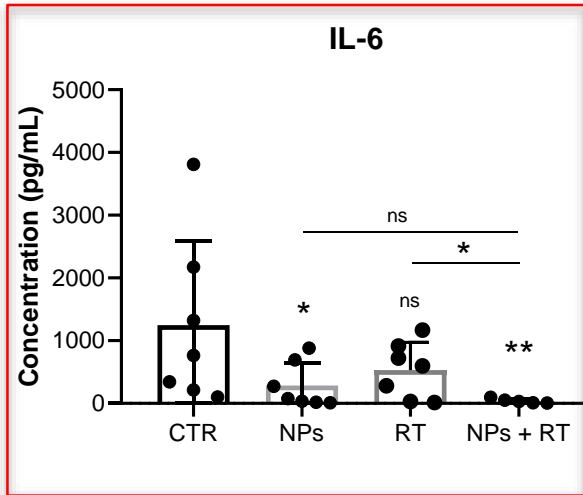


The combination of radiotherapy with the immunomodulatory Ch/ γ -PGA NPs enhanced the splenic population of CD3⁺CD4⁺IFN γ ⁺ cells

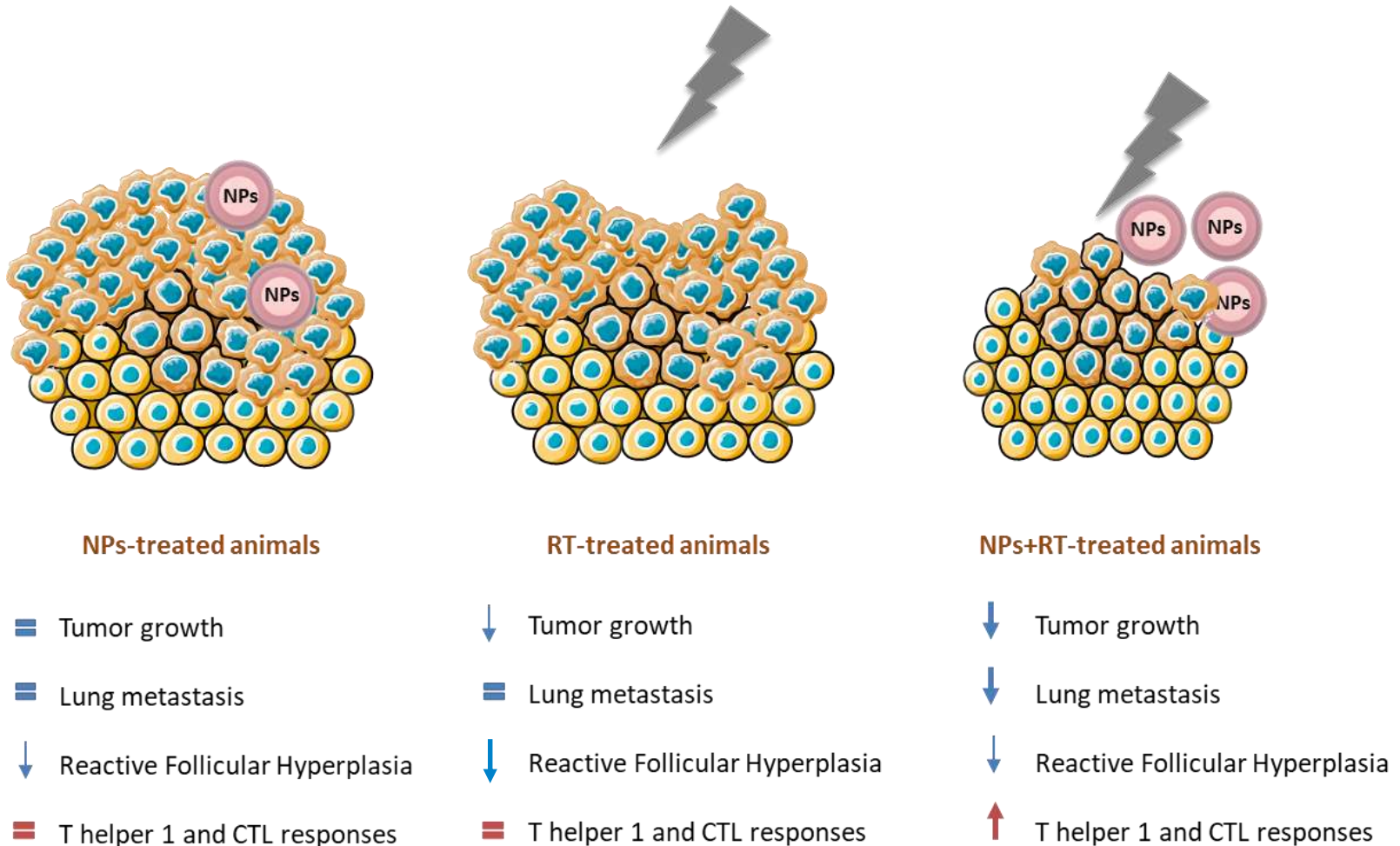
Lymphoid populations at the Spleen



The combination of radiotherapy with the immunomodulatory Ch/ γ -PGA NPs decreased systemic levels of IL-6, IL-4 and IL-10



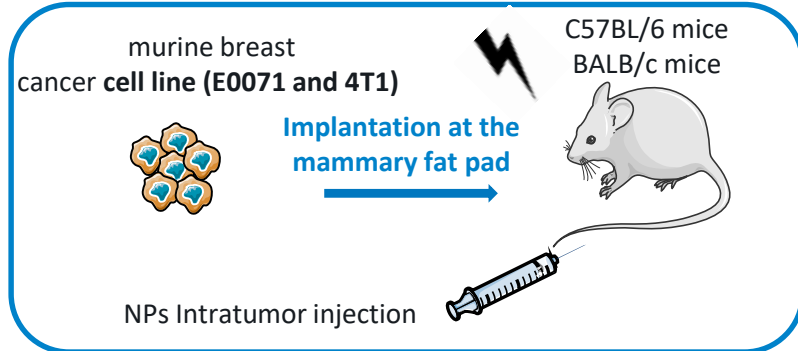
The immunomodulatory Ch/ γ -PGA NPs are promising therapeutic tools to be used in combination with radiotherapy



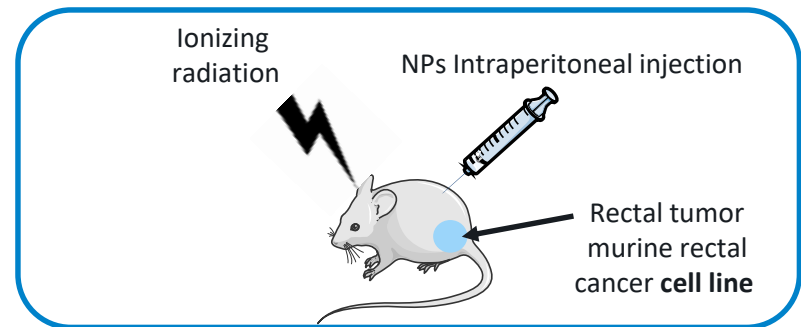
Developing an immunomodulatory therapeutic strategy to counteract macrophage-mediated cancer cell invasion

Ongoing *in vivo* studies
immunocompetent animals

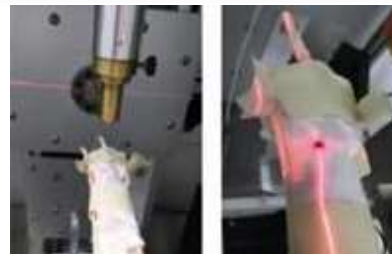
Orthotopic Mouse **Breast Cancer** model NPs + radiotherapy



Orthotopic Mouse **Rectal Cancer** model NPs + radiotherapy



Small Animal
Radiation Research
Platform (SARRP)



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