

Séminaire de Radiothérapie Interne Vectorisée
Montpellier 14-16 mars 2022

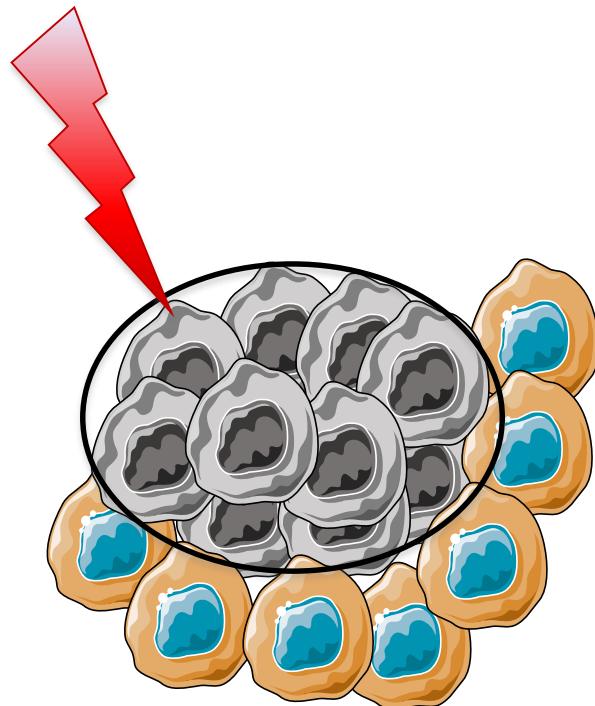
Aspects immunologiques de la réponse à la RIV-alpha

Joëlle Gaschet

UMR Inserm 1307 CNRS 6075 - Nantes

Ionizing radiation and tumor cell eradication

**Ionizing
radiation**



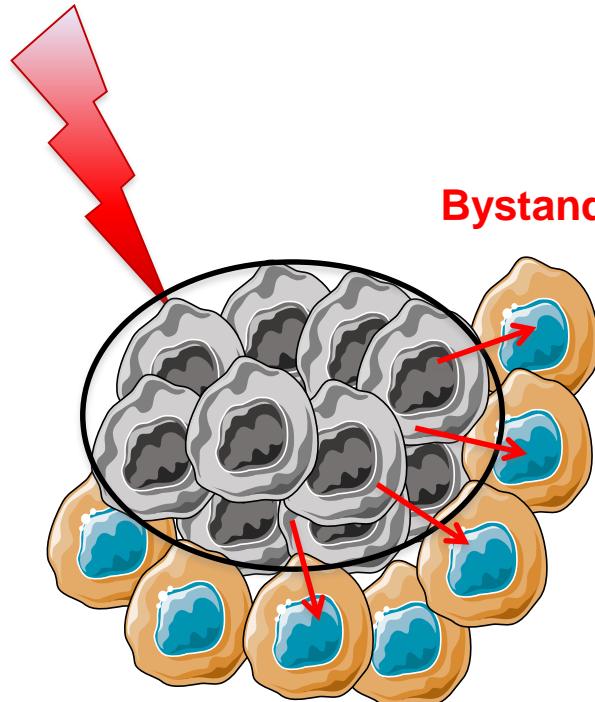
Primary Tumor



Metastases

Ionizing radiation and tumor cell eradication

**Ionizing
radiation**



Bystander effects

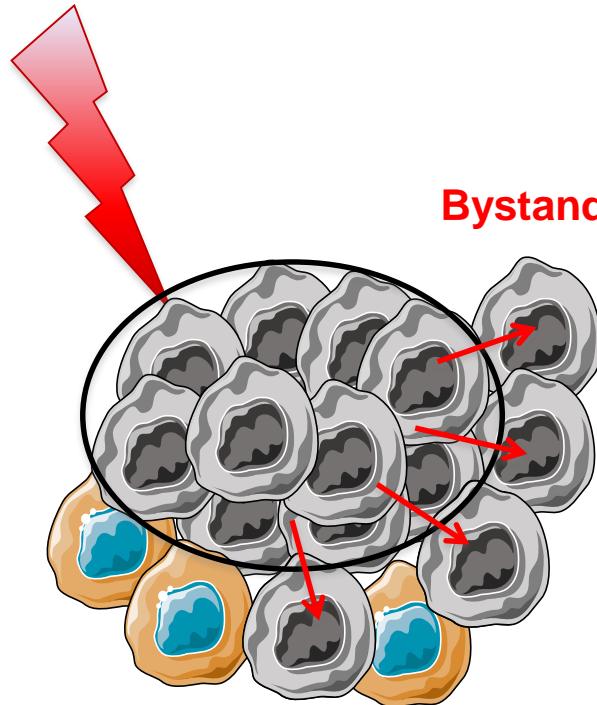
Primary Tumor



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**Ionizing
radiation**



Primary Tumor

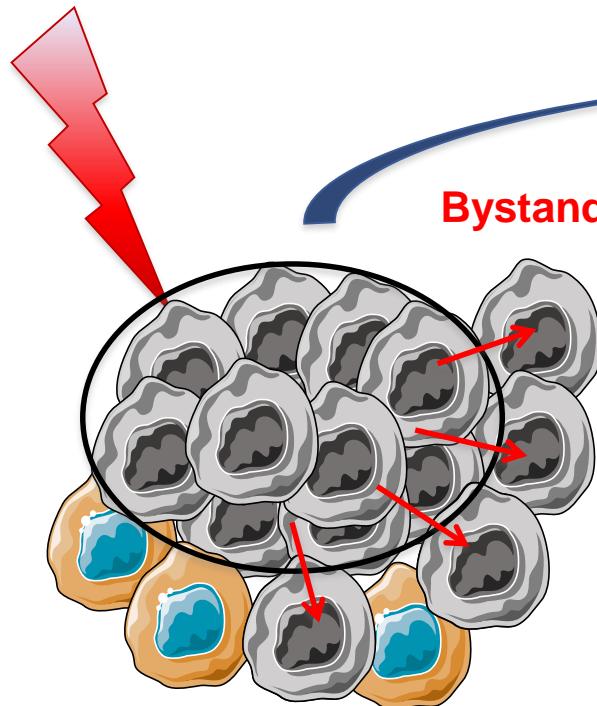
Bystander effects



Metastases

Ionizing radiation and tumor cell eradication

**Ionizing
radiation**



Bystander effects

Abscopal effect

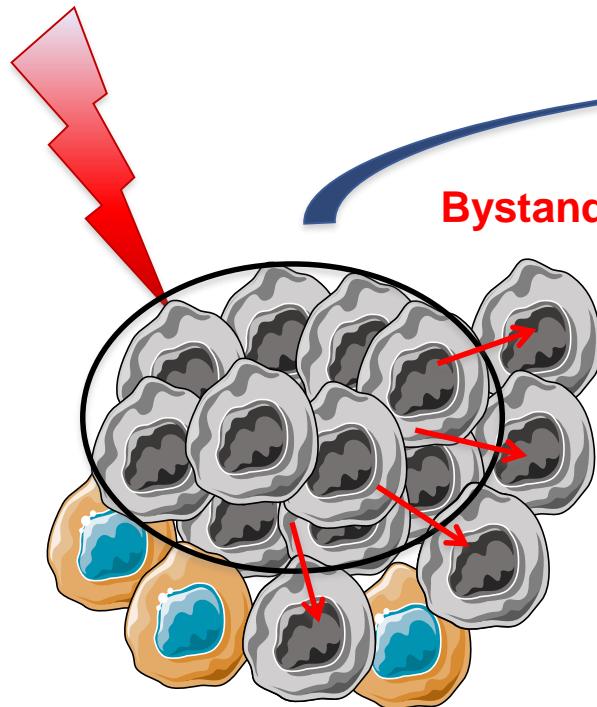


Metastases

Primary Tumor

Ionizing radiation and tumor cell eradication

**Ionizing
radiation**



Primary Tumor

Abscopal effect

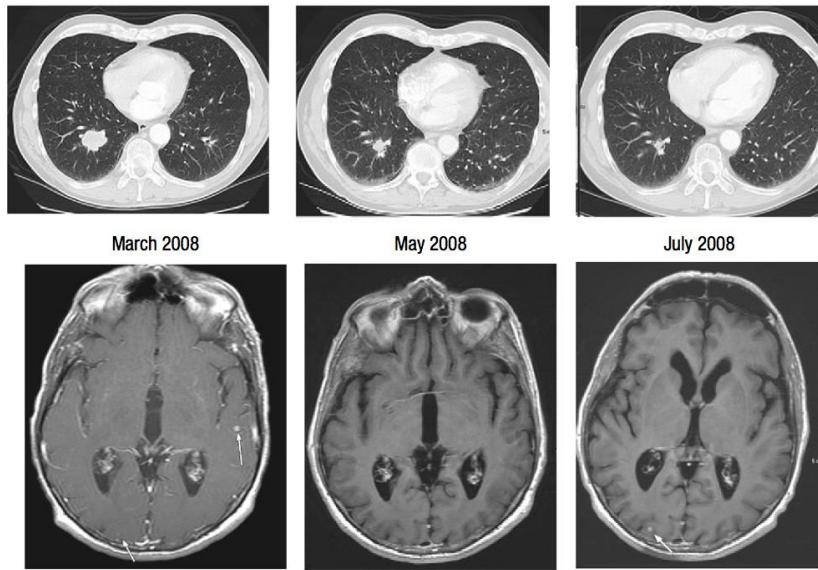
Bystander effects



Metastases

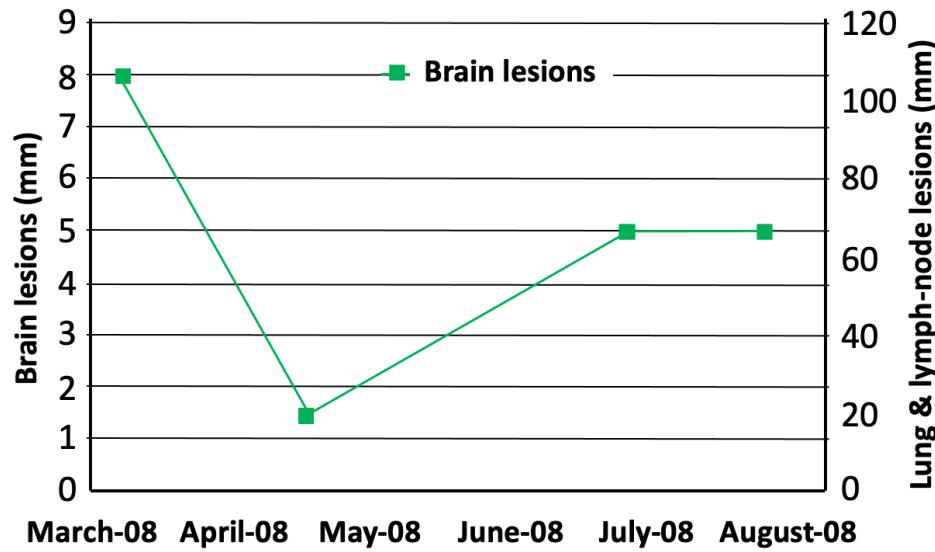
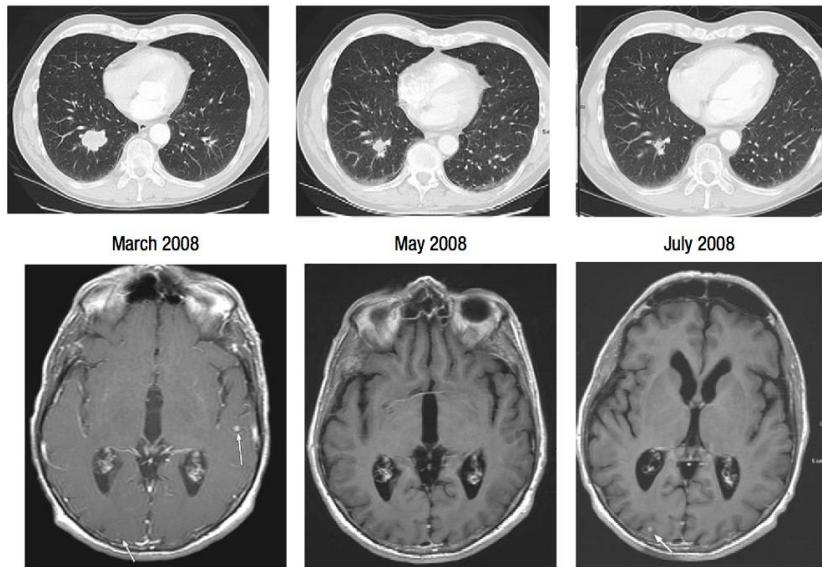
Abscopal effect: clinical example

Patient with a kidney cancer and lung, lymph node, bone and brain metastases



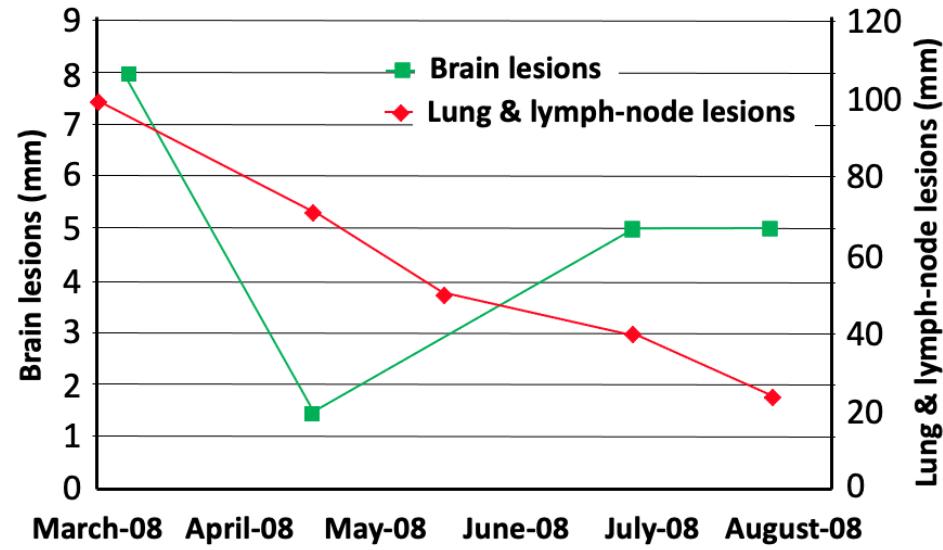
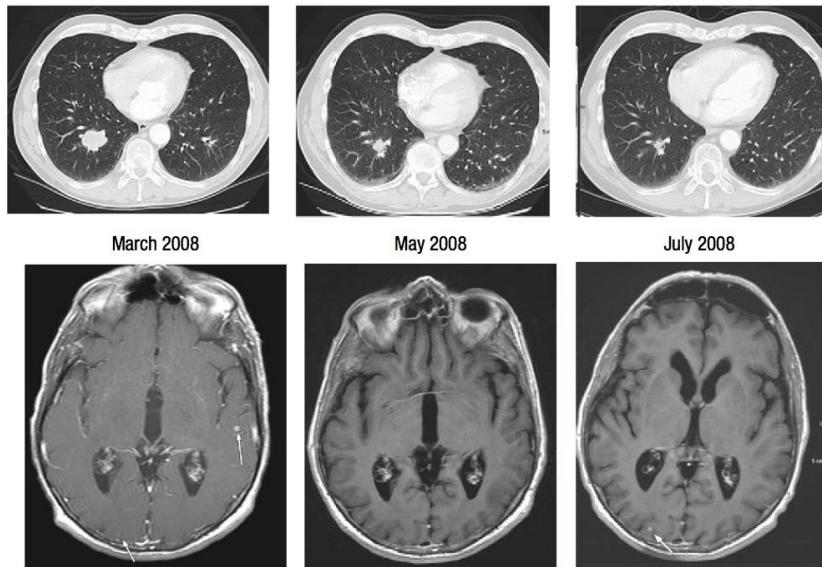
Abscopal effect: clinical example

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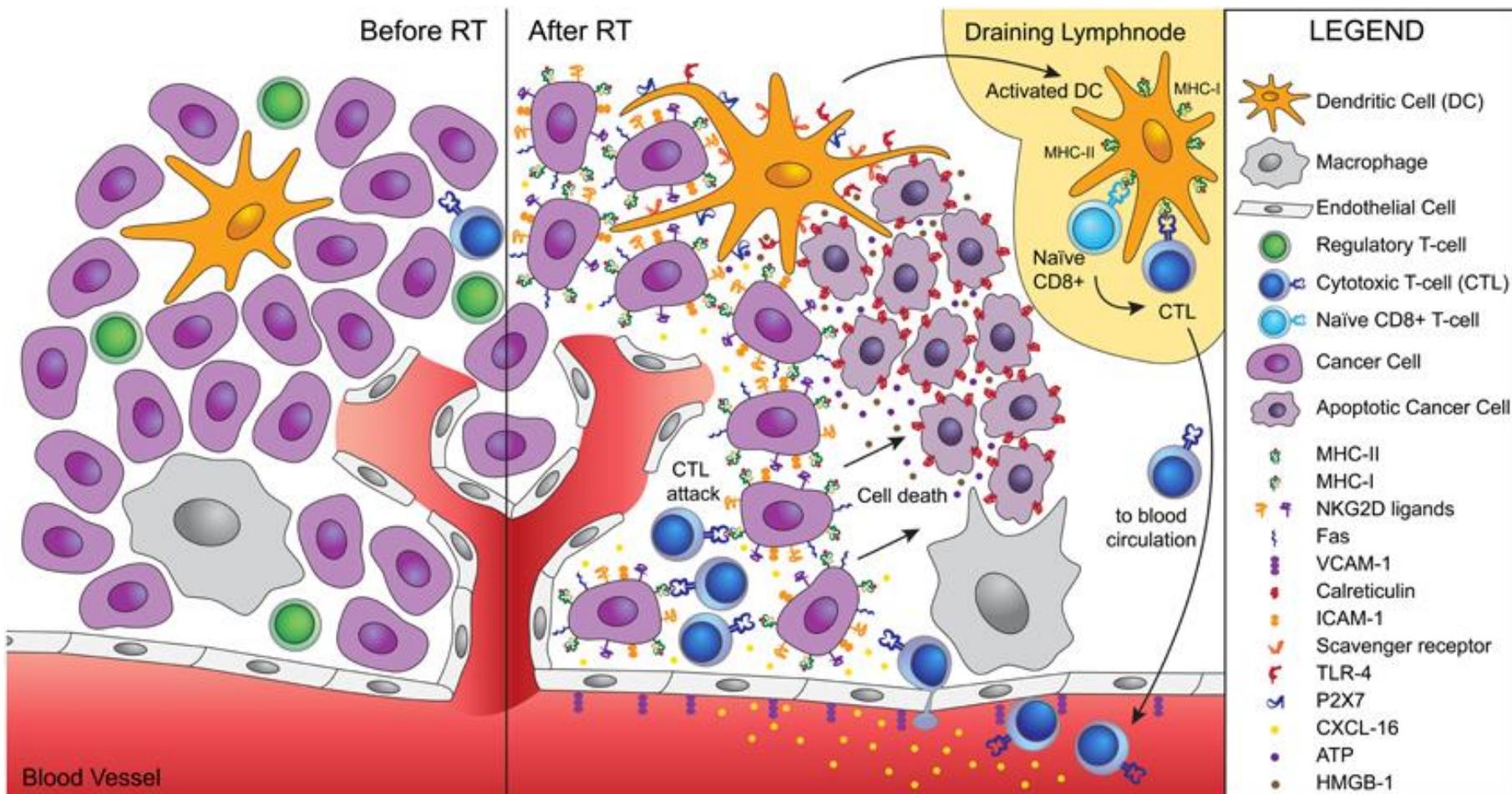


Abscopal effect: clinical example

Patient with a kidney cancer and lung, lymph node, bone and brain metastases

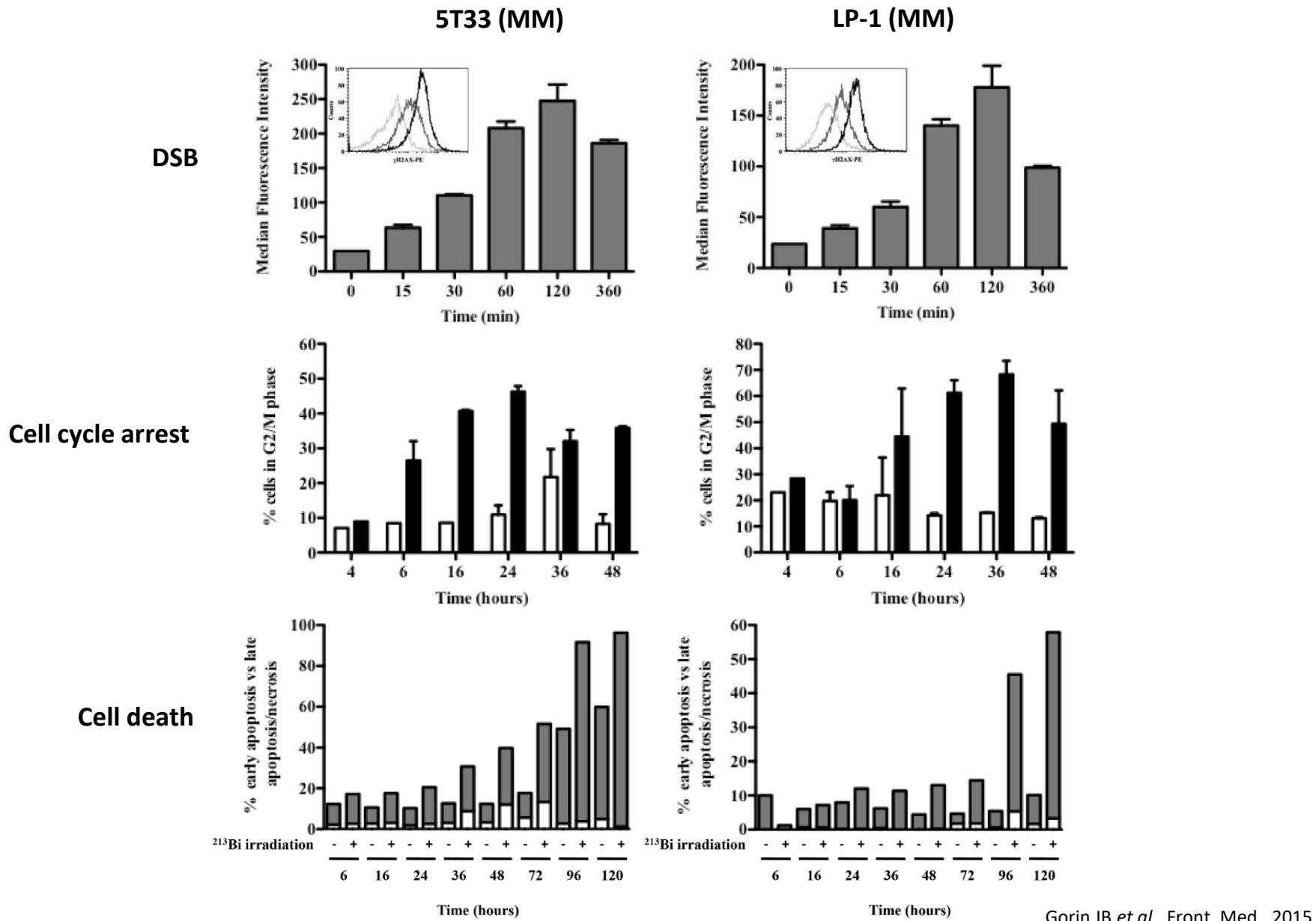


Ionizing radiation and immunogenic cell death

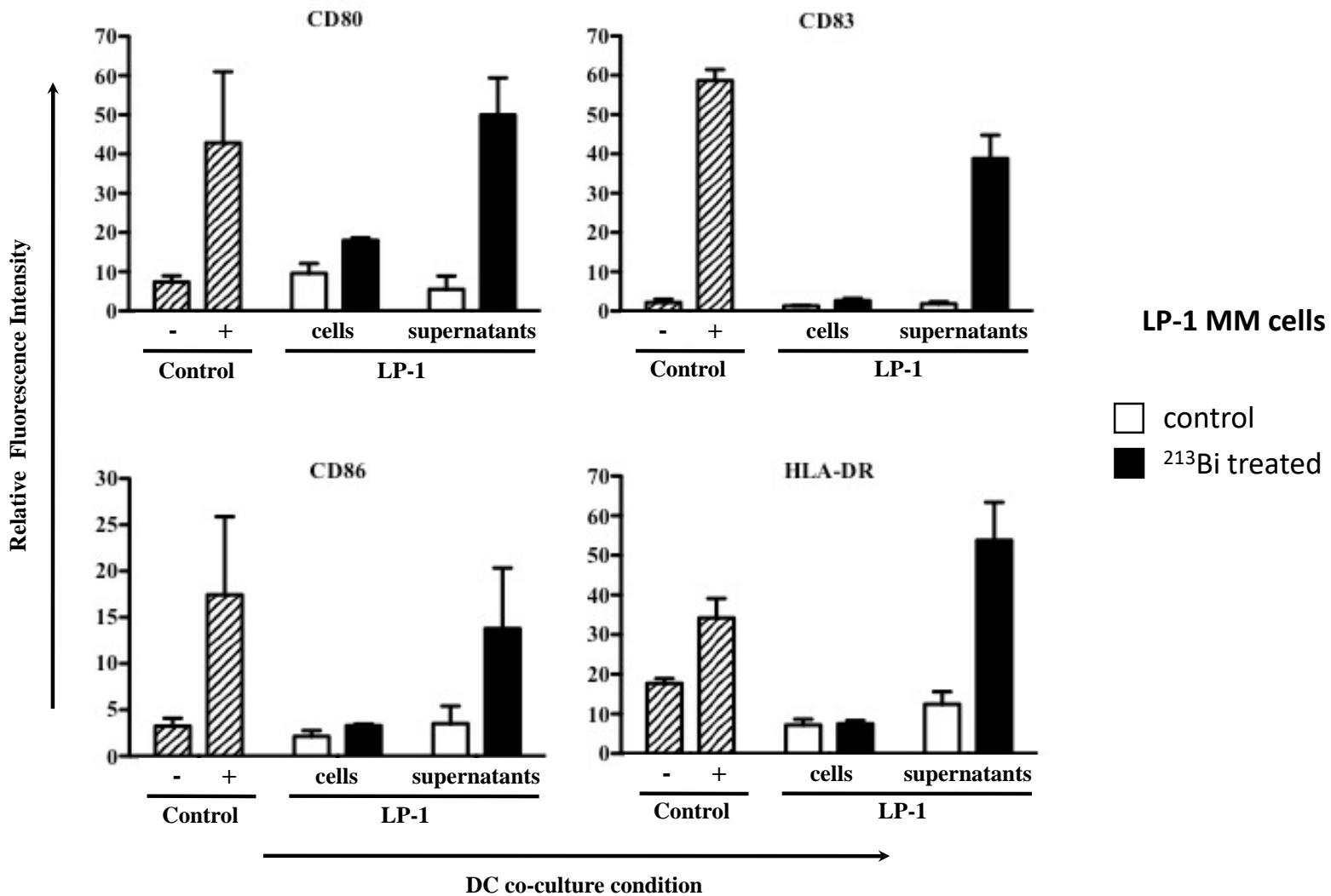


Demaria & Formenti, Front Oncol, 2012

Radiobiology of alpha particles : ^{213}Bi



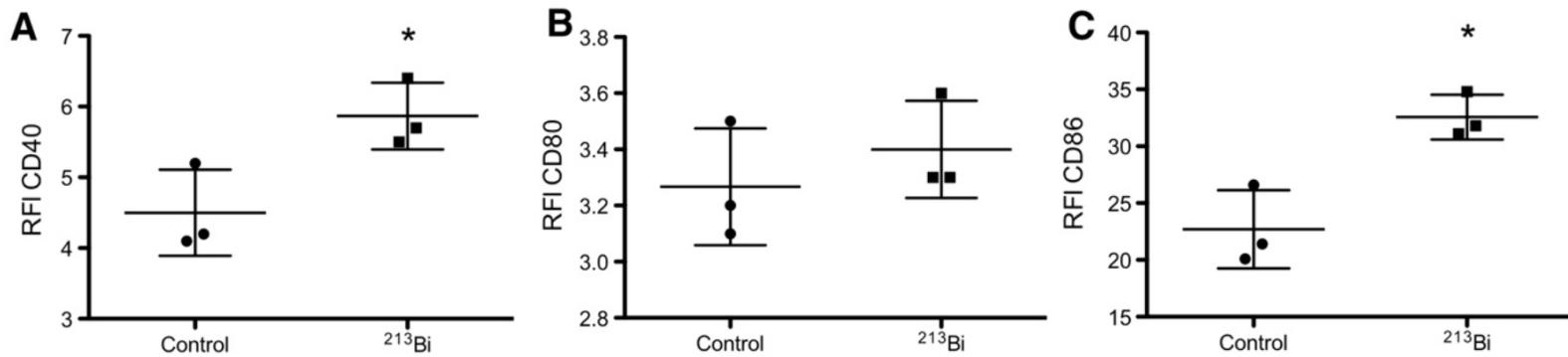
Alpha particles and immunity: DC activation



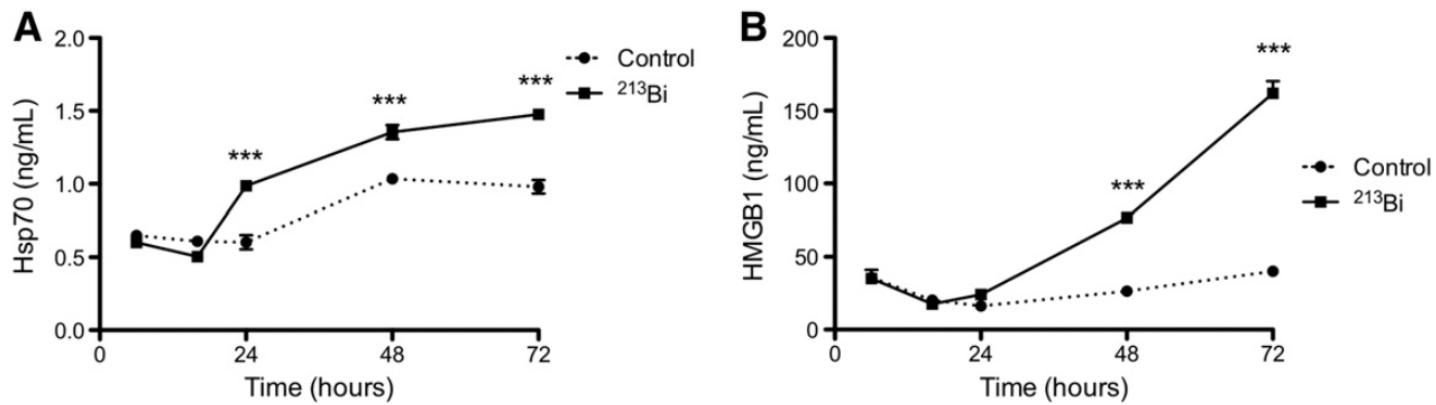
Alpha particles and immunity

MC38 colon carcinoma cells

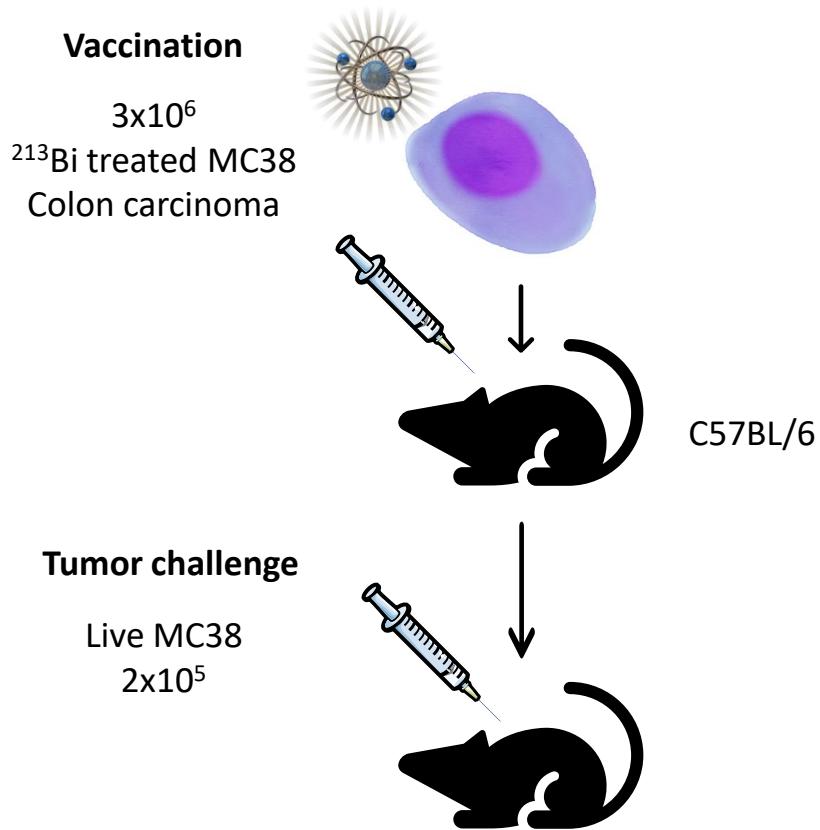
DC activation



Danger signal release

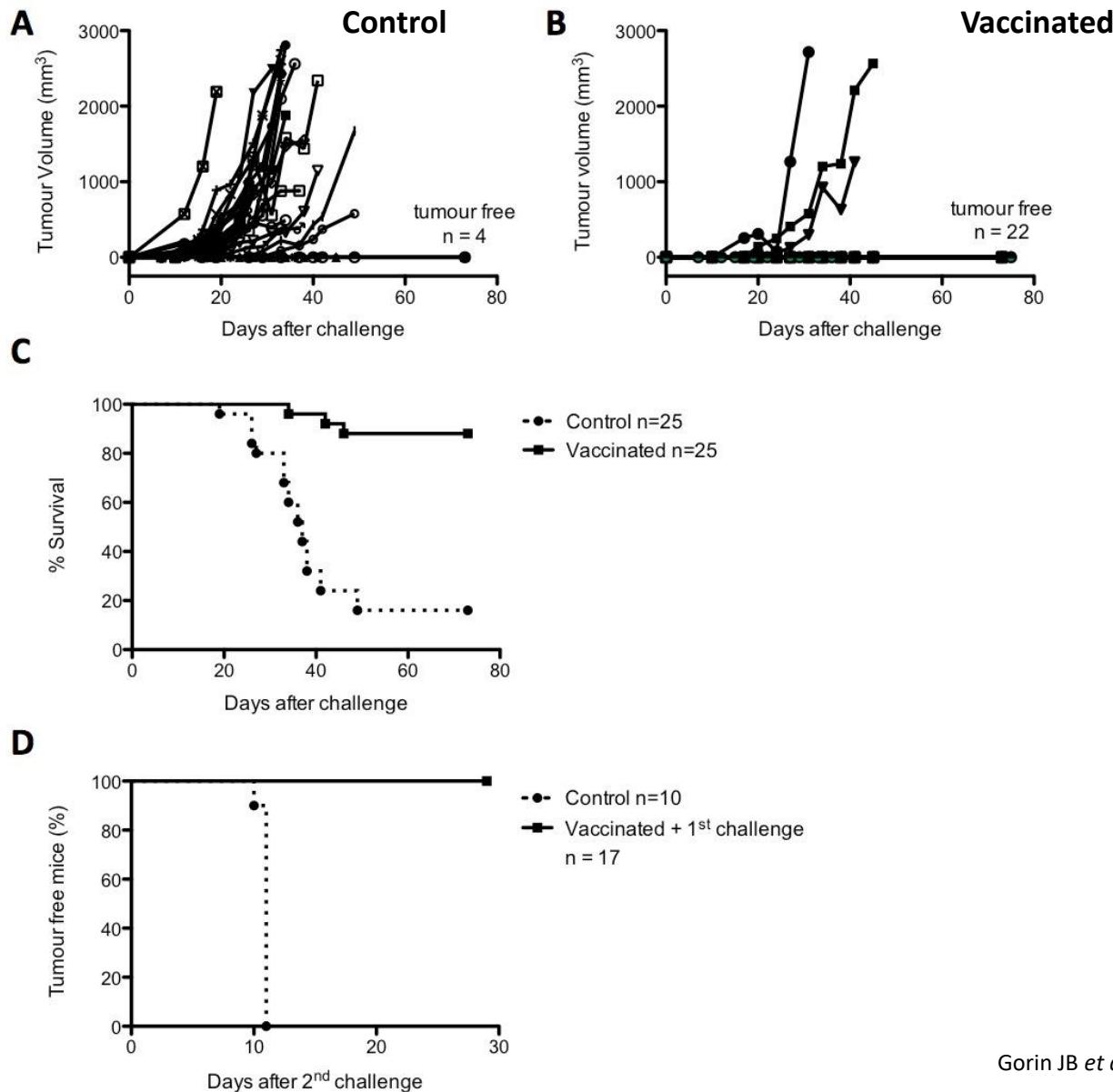


Alpha particles and anti-tumor immune response

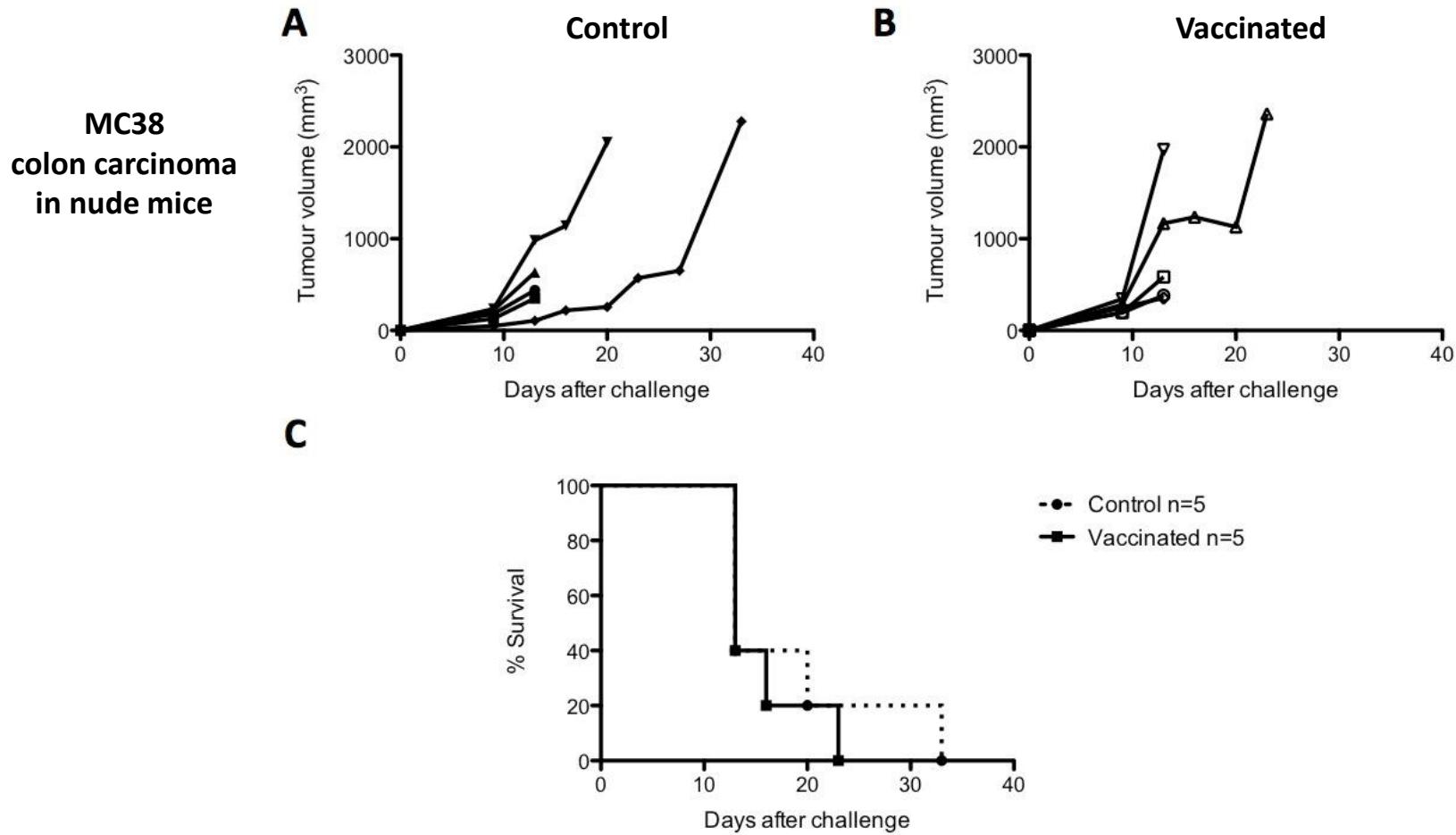


Alpha particles and anti-tumor immune response

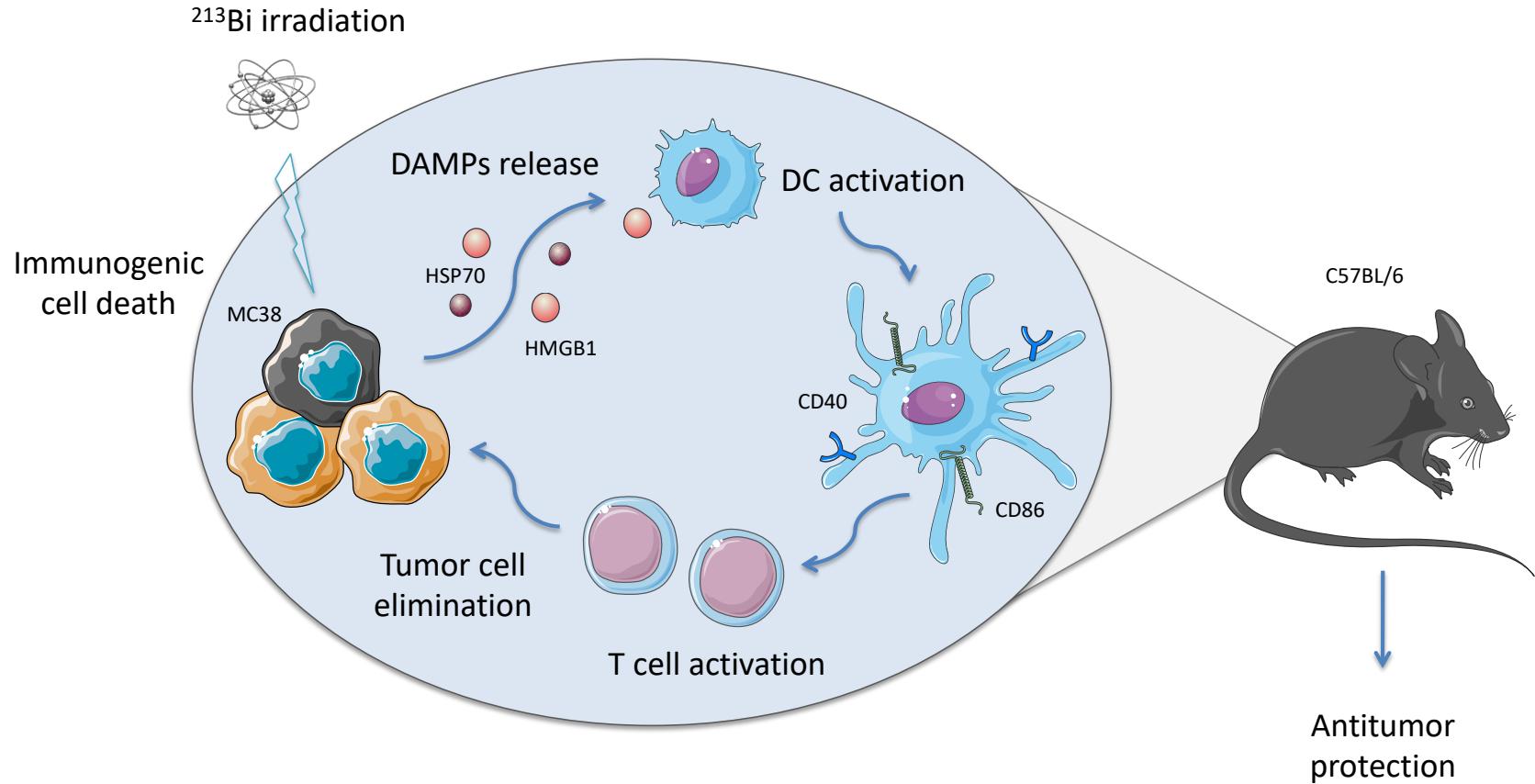
MC38
colon carcinoma
in C57BL/6 mice



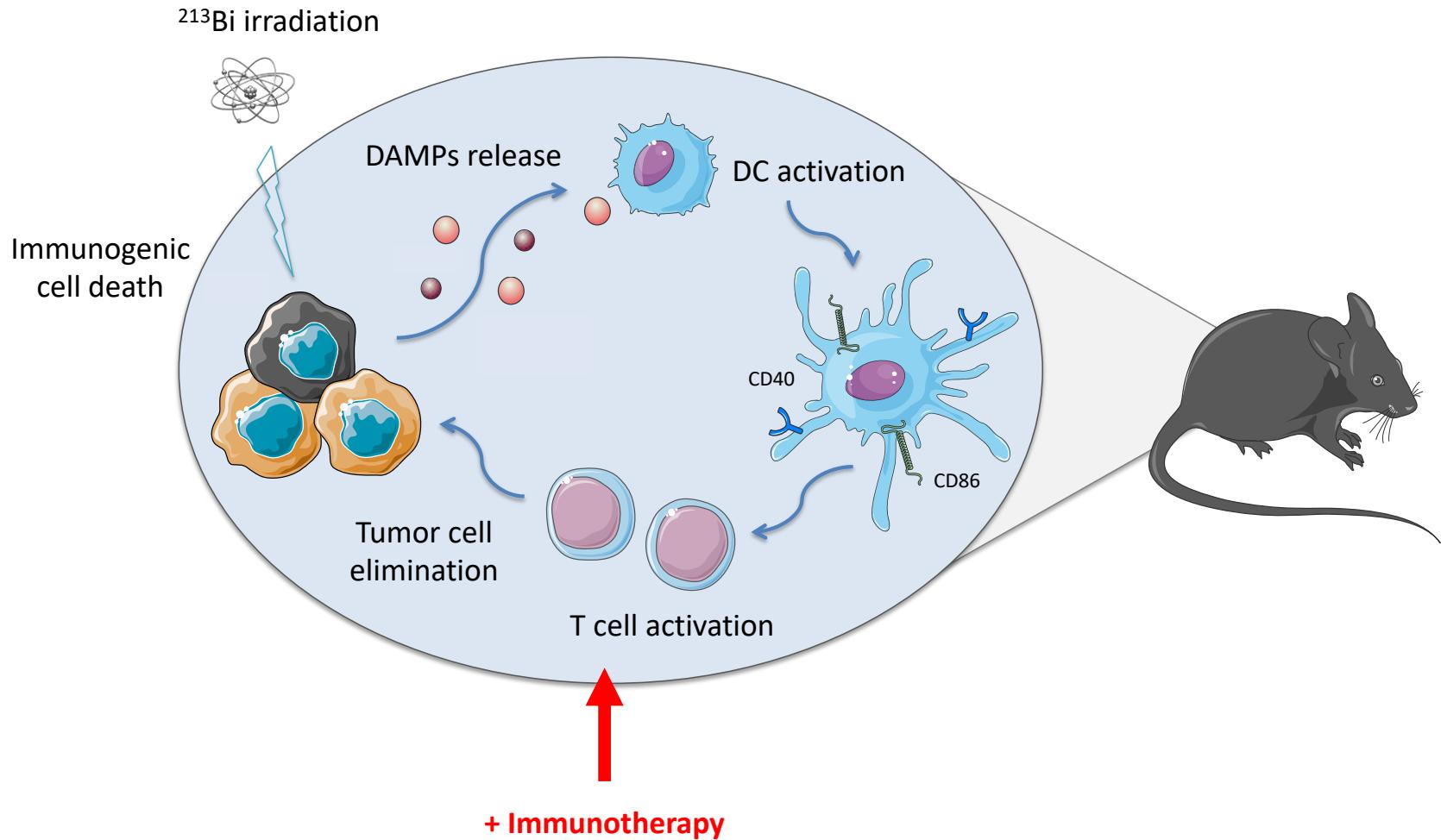
Anti-tumor protection relies on adaptative immunity



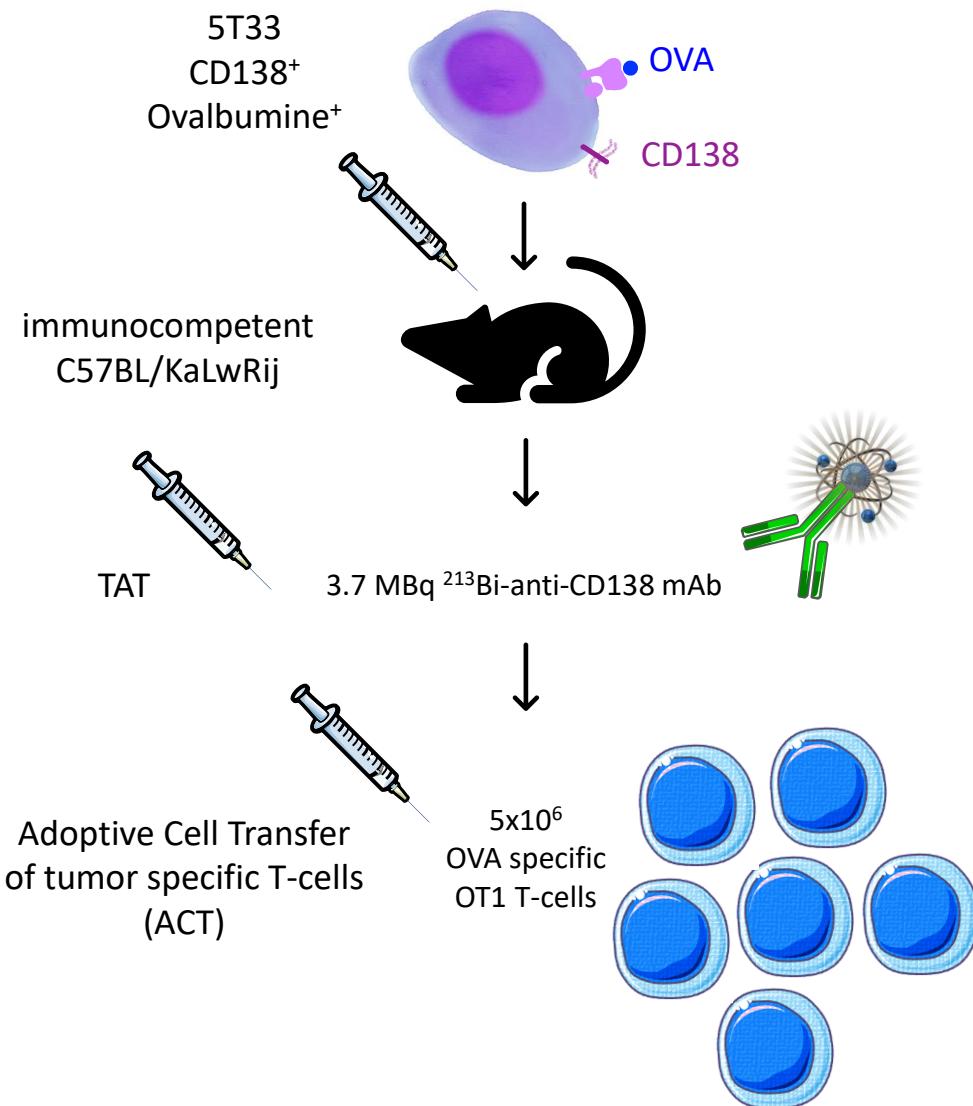
Alpha particles and anti-tumor immune response



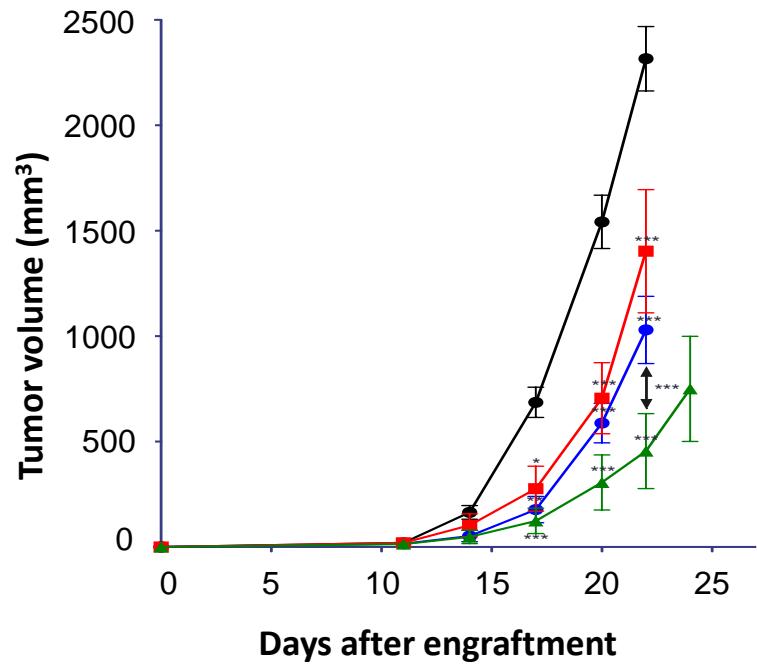
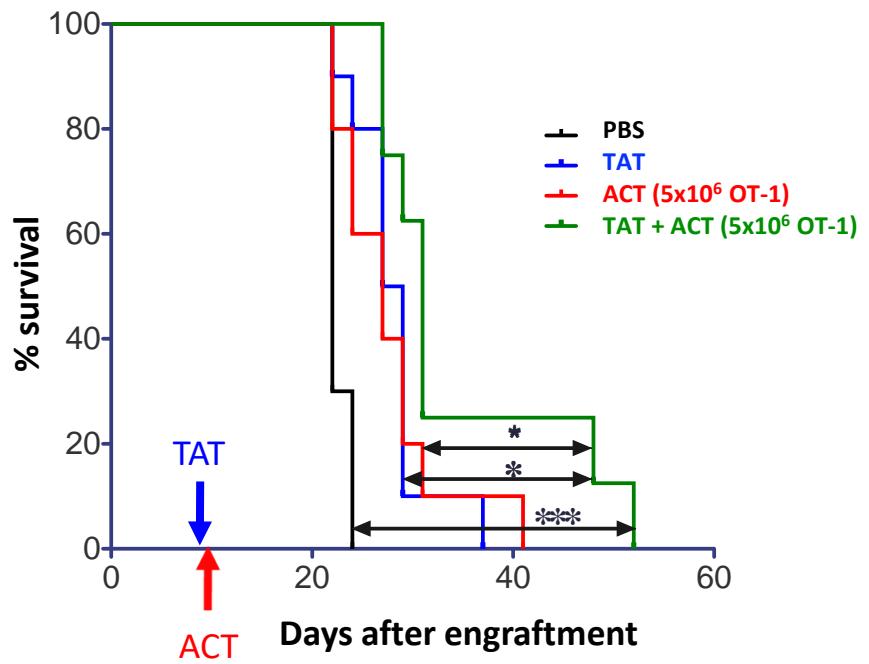
Combination therapy: TAT + immunotherapy



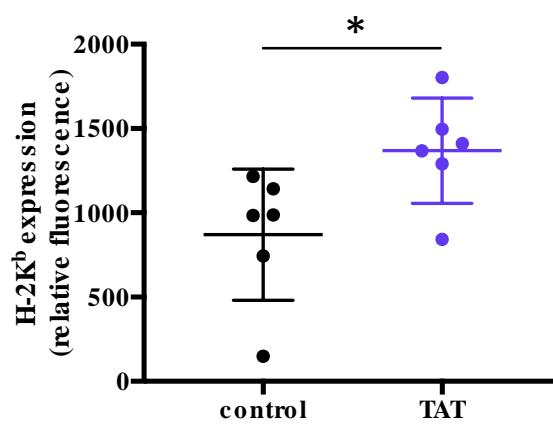
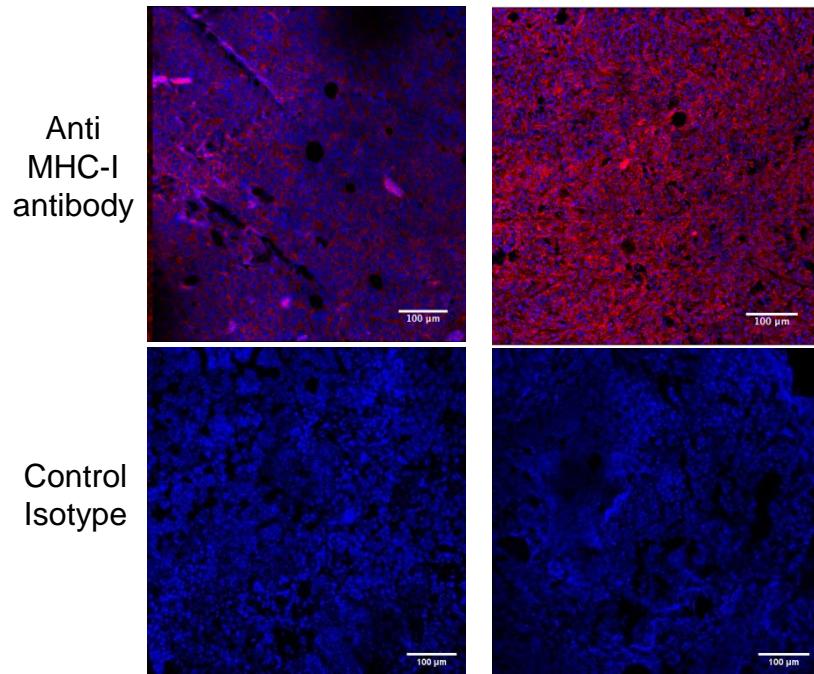
TAT and Adoptive Cell Transfer of Tumor Specific T-cells in Myeloma



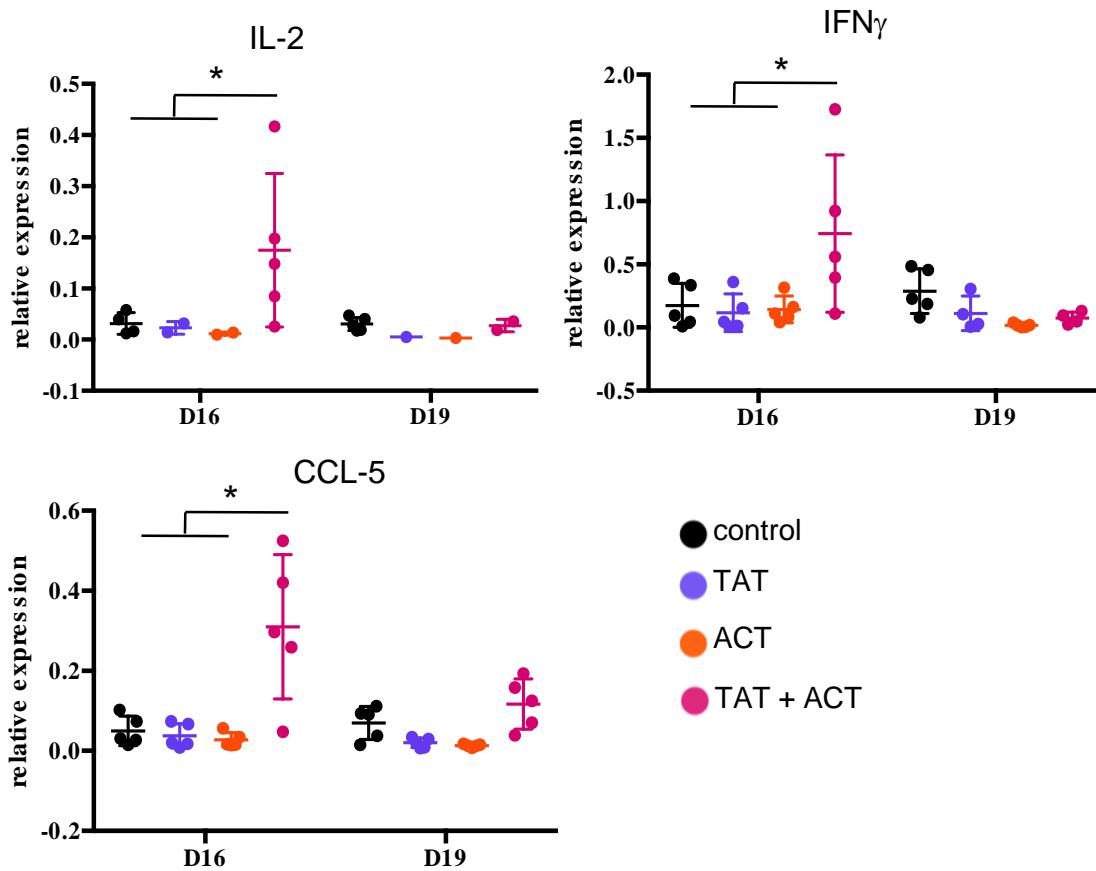
Efficacy of the combinaison therapy



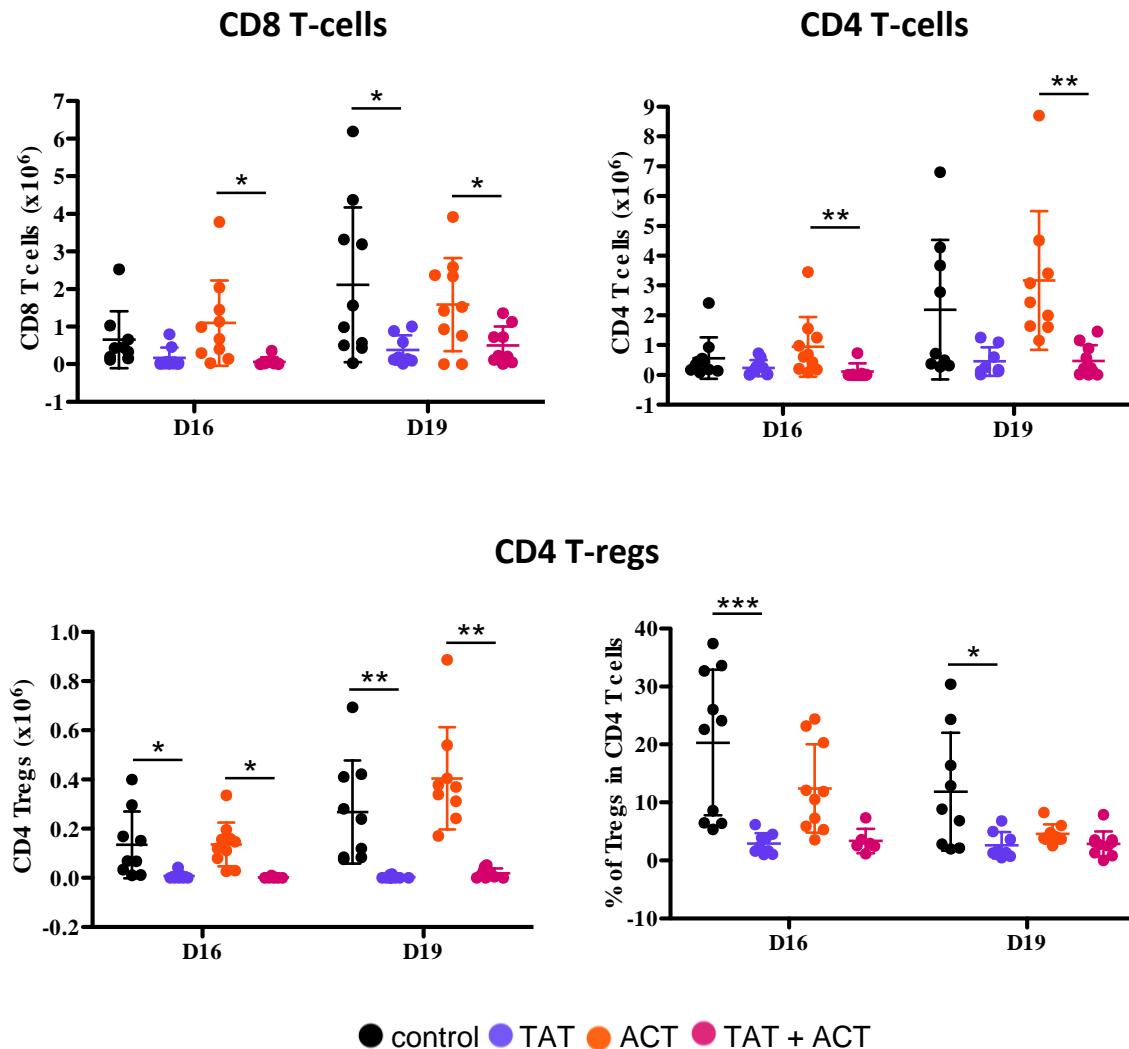
TAT increases MHC class I expression *in vivo* on tumor cells



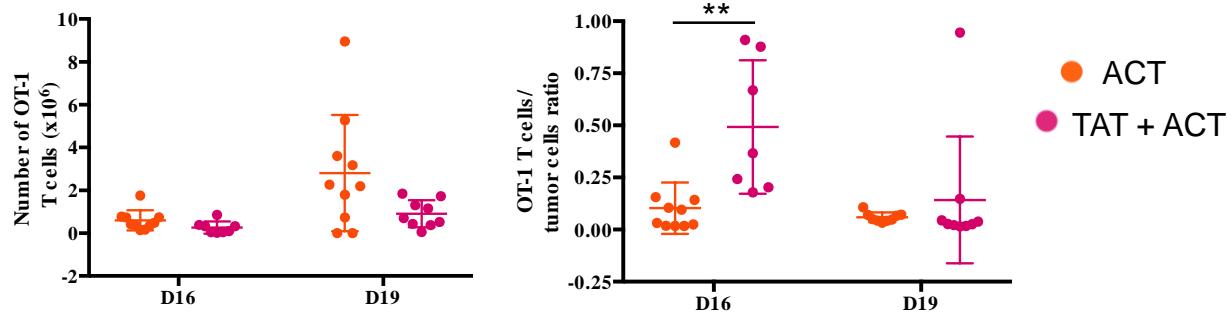
TAT induces release of immune cytokines and chemokines *in vivo*



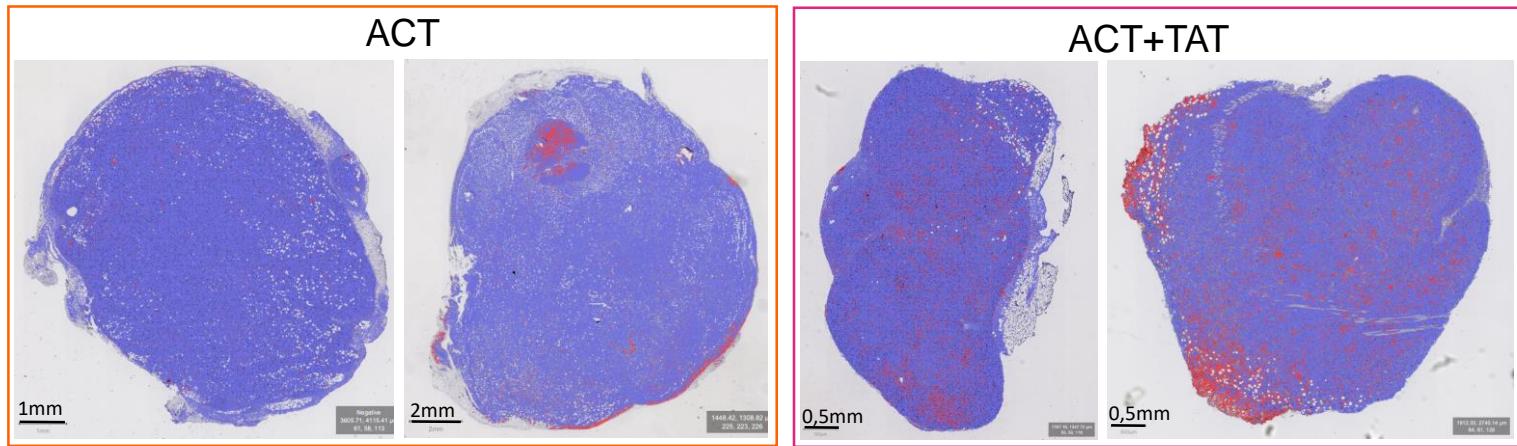
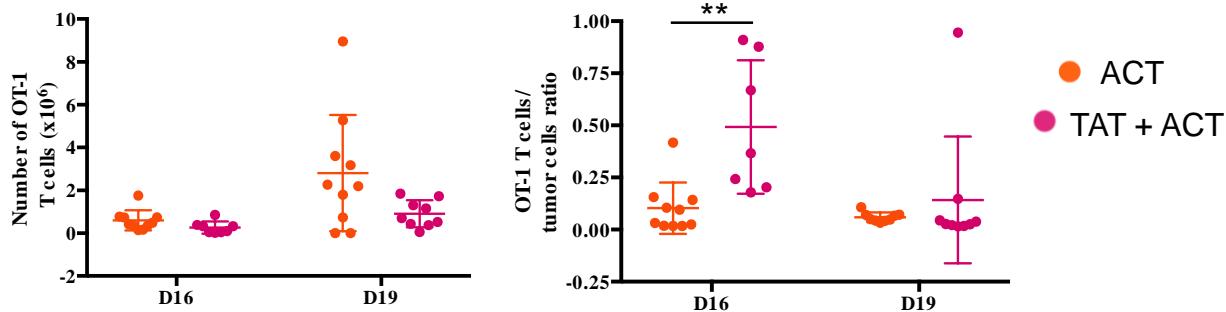
Impact of TAT on T-cell tumor infiltrate



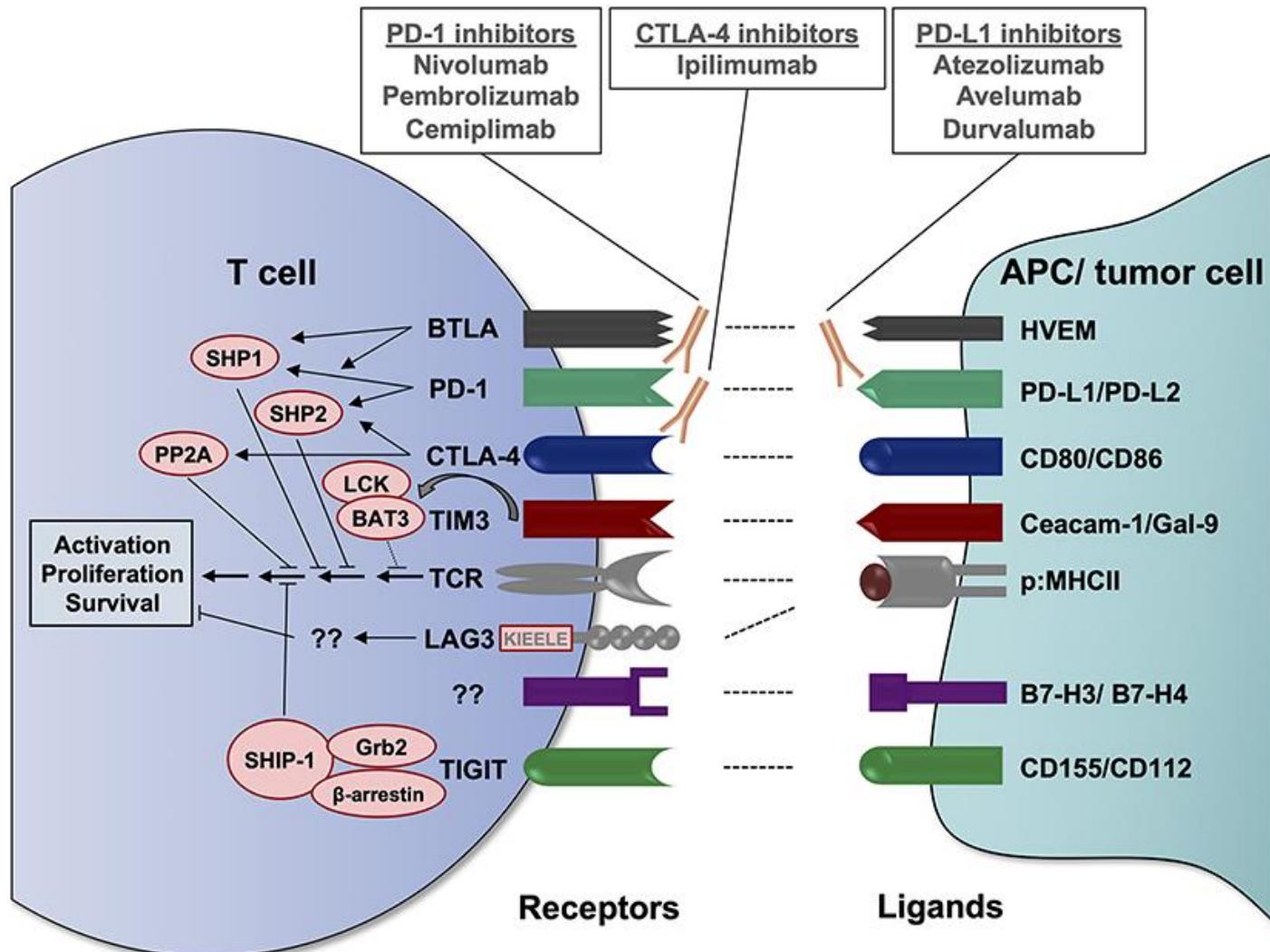
Impact of TAT on OT1 T-cell tumor infiltrate



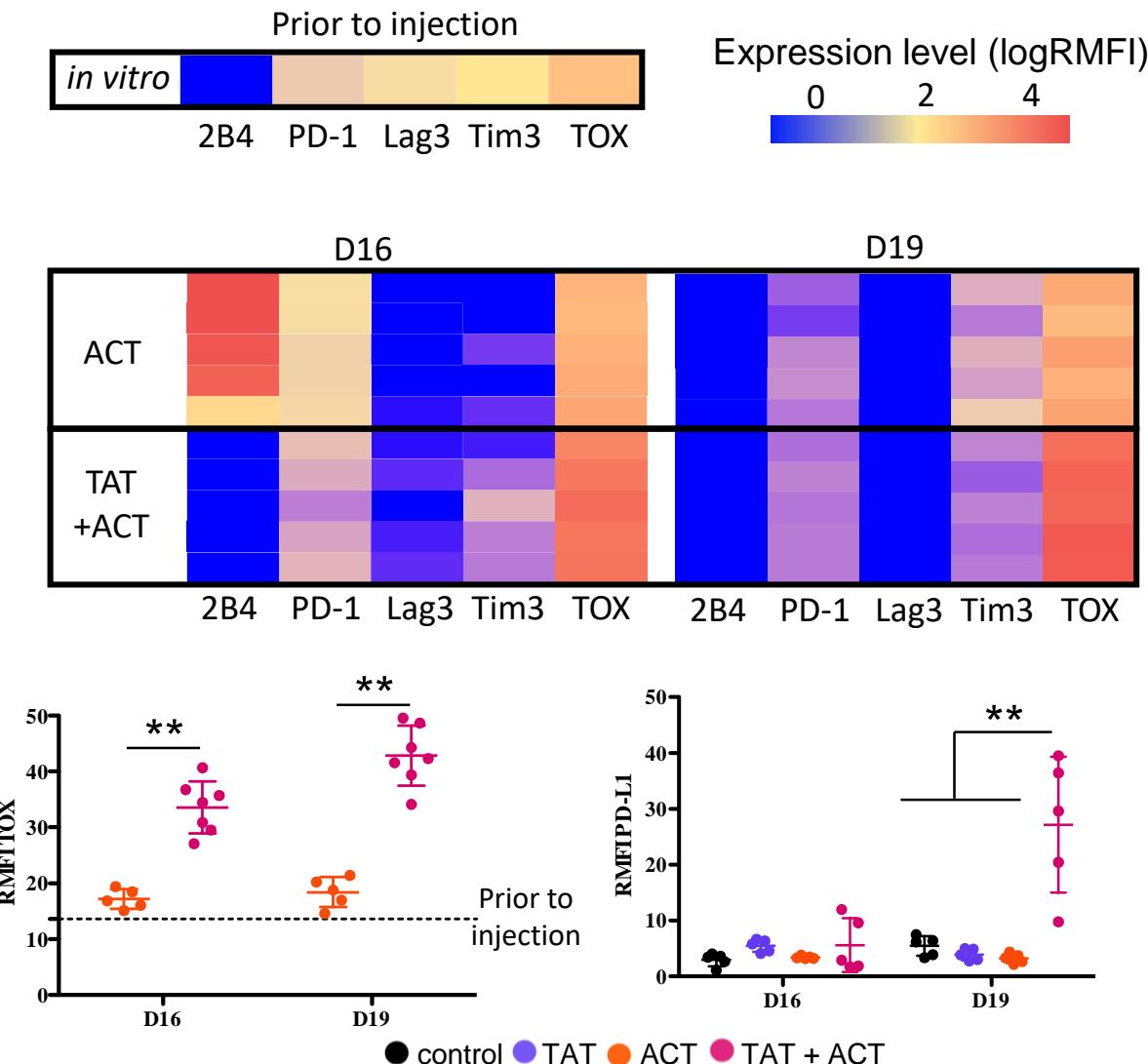
Impact of TAT on OT1 T-cell tumor infiltrate



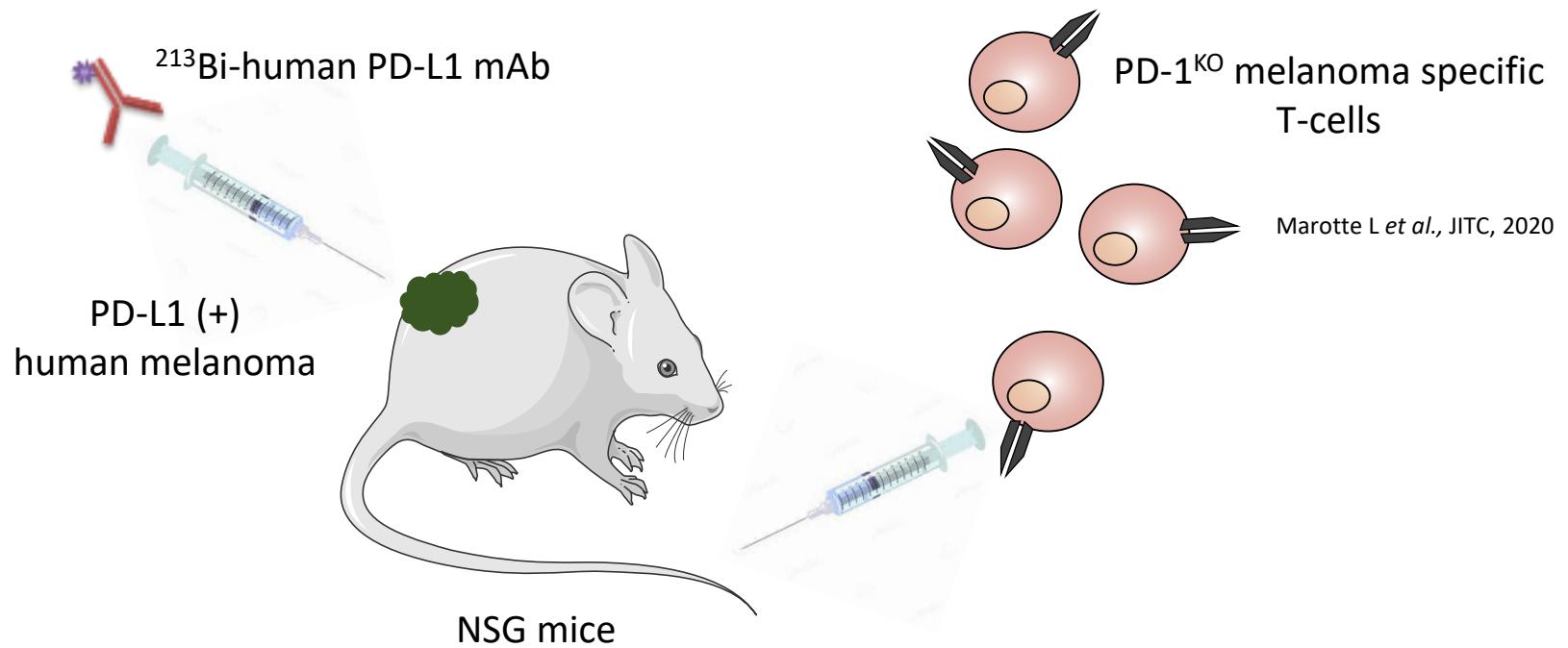
Important inhibitory immunoreceptors (immune checkpoints)



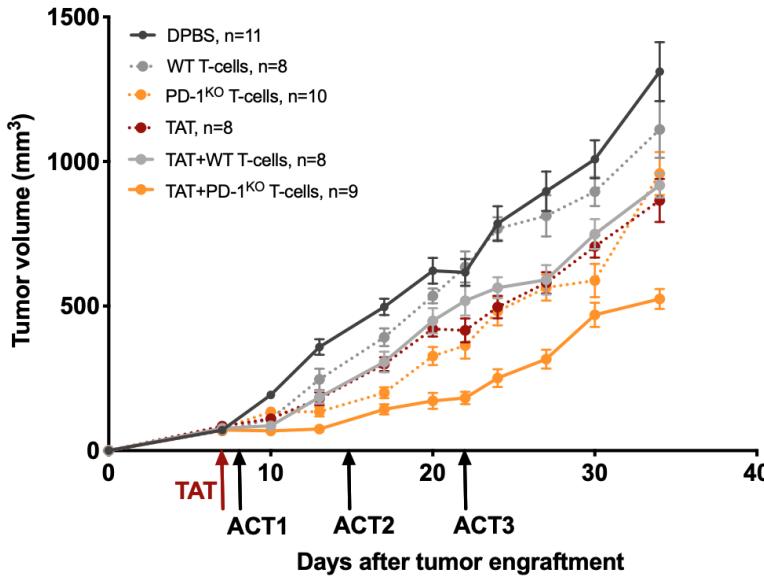
Impact of TAT on immune checkpoint expression



TAT and Adoptive Cell Transfer of Tumor Specific T-cells in Melanoma

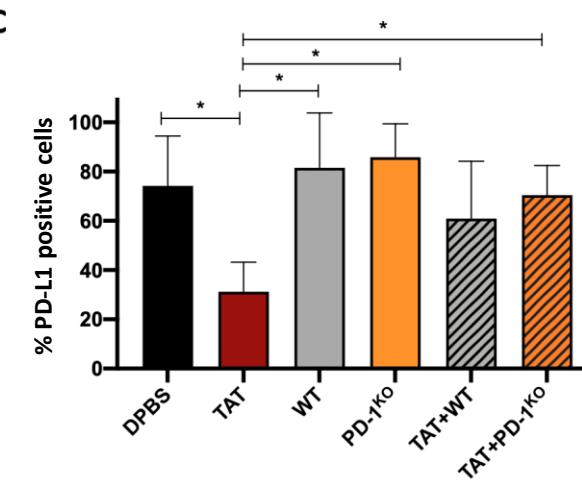
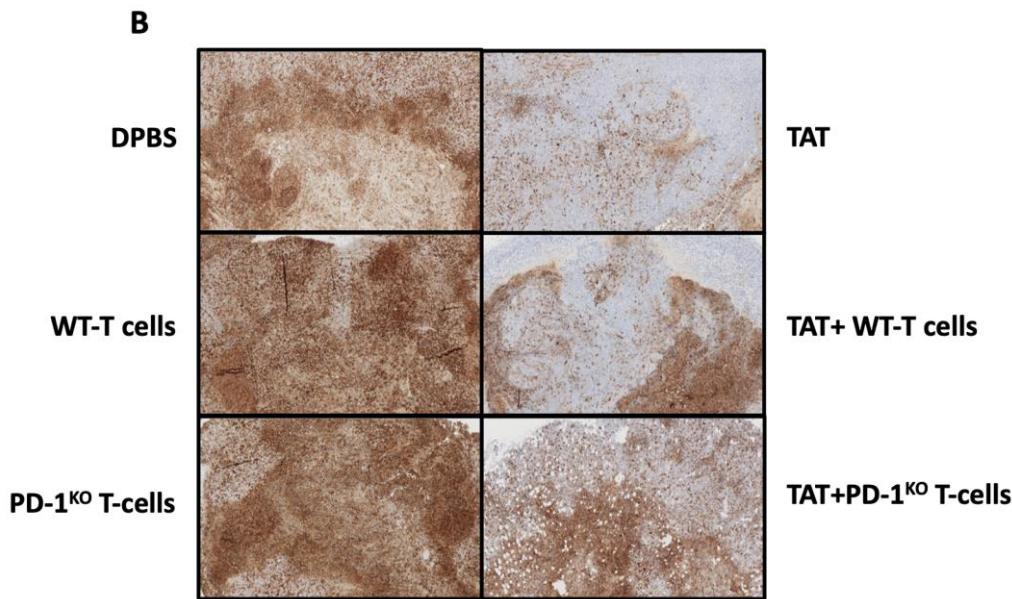
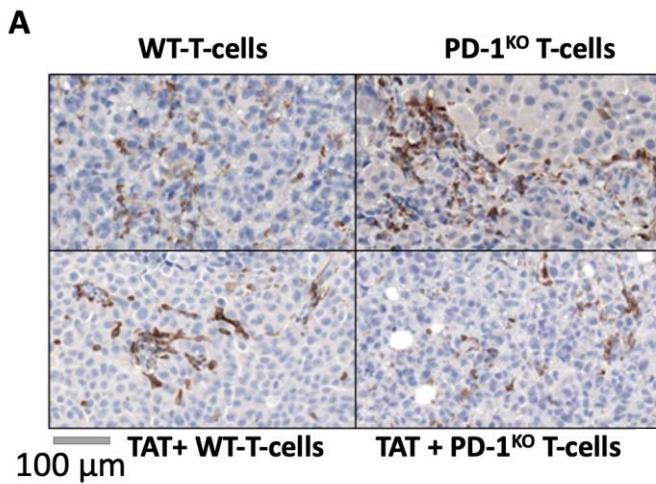


Efficacy of the combination therapy

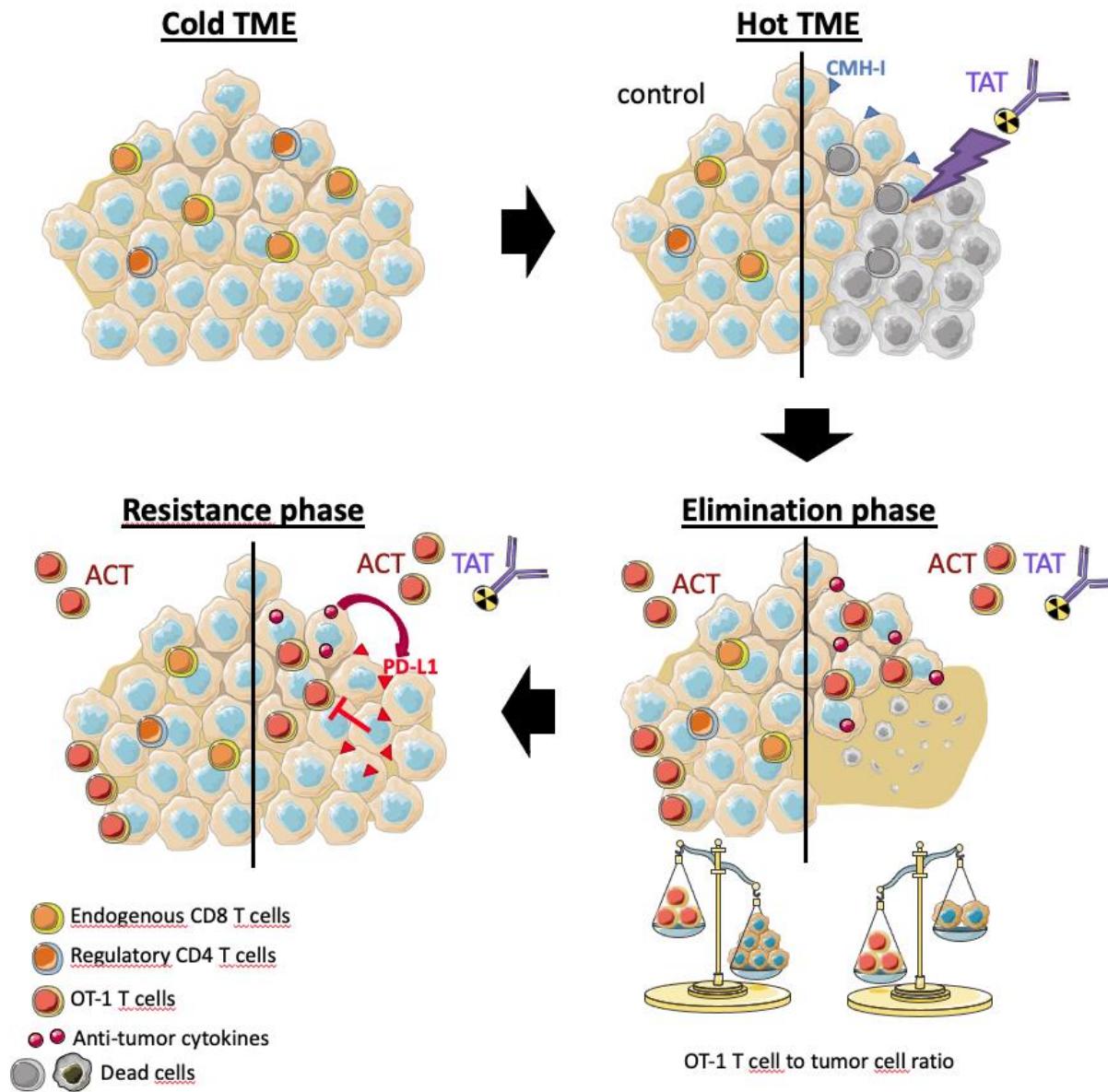


	DPBS (n=11)	ACT WT (n=8)	ACT PD-1 ^{KO} (n=10)	TAT (n=8)	TAT + ACT WT (n=9)	TAT + ACT PD-1 ^{KO} (n=9)
DPBS (n=11)		ns	**** $p<0.0001$	**** $p<0.0001$	*** $p=0.0002$	**** $p<0.0001$
ACT WT (n=8)	ns		** $p=0.003$	*	ns	**** $p<0.0001$
ACT PD-1 ^{KO} (n=10)	**** $p<0.0001$	** $p=0.003$		ns	ns	** $p=0.005$
TAT (n=8)	**** $p<0.0001$	*	ns		ns	** $p=0.0016$
TAT + ACT WT (n=8)	*** $p=0.0002$	ns	ns	ns		*** $p=0.0003$
TAT + ACT PD-1 ^{KO} (n=9)	**** $p<0.0001$	**** $p<0.0001$	** $p=0.005$	** $p=0.0016$	*** $p=0.0003$	

Impact of TAT on T-cell tumor infiltrate and PD-L1 tumor expression



Take home message



Acknowledgments

CRCI²NA Equipe 2 **Oncologie Nucléaire**

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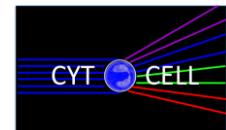
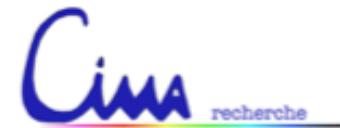
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