



14 septembre 2017 – LAAS, Toulouse

# ElectroImmunoGeno therapy IL-12: Proof of concept on metastatic murine melanoma

## Vaccination antitumorale par pIRE amplifiée par expression d'IL12 par électrotransfert cutané

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# Techno



# Aims

## Cancer

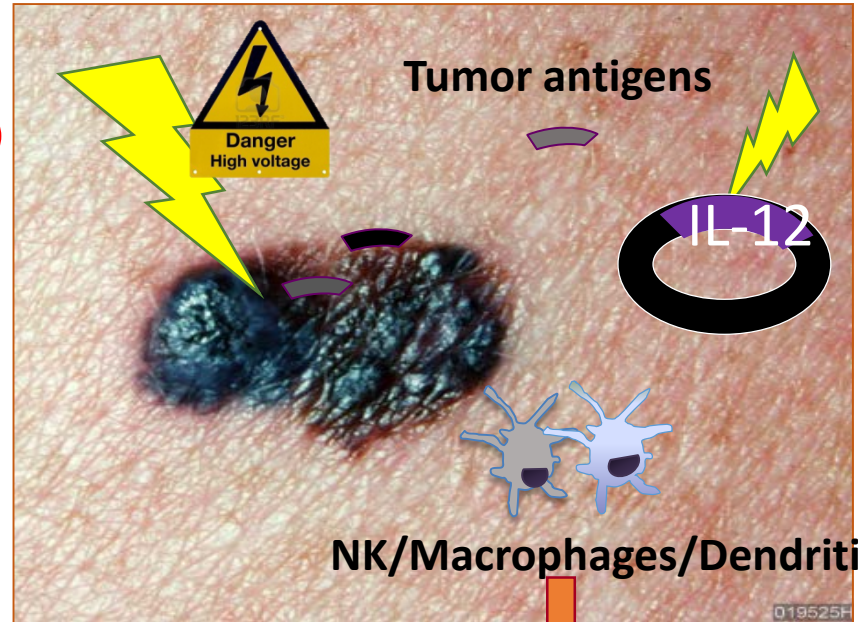
1



**PIRE:** Partial IRreversible  
Electroporation  
of the tumor

Tumor antigen exposure  
and release

**Weak** activation dendritic cells:  
**Low** impact on the immune system



**Anti-tumoral immunogenic response**

2

## Cancer

Controlled expression  
of an immunogenic  
adjuvant in the  
peritumoral skin.

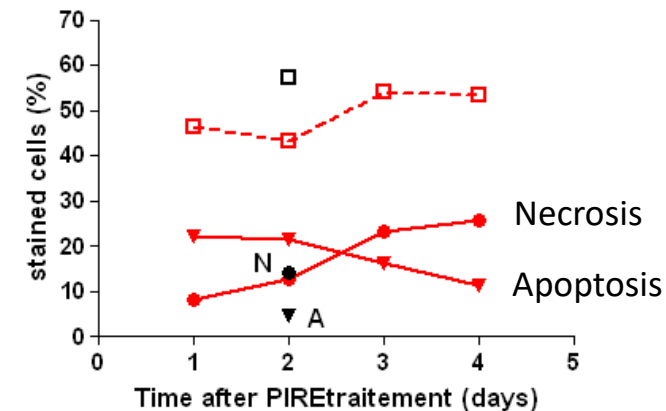
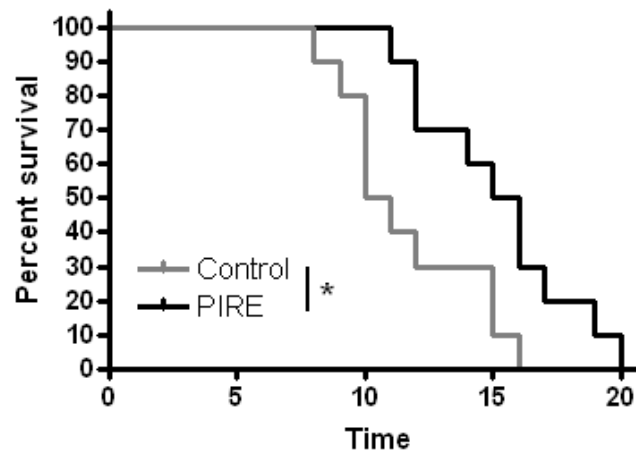
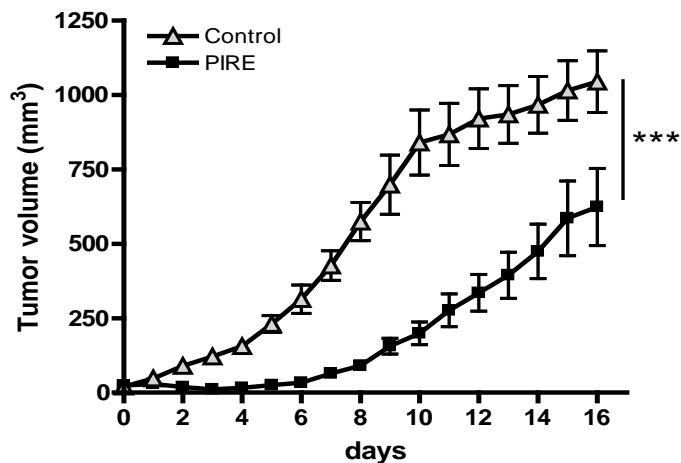
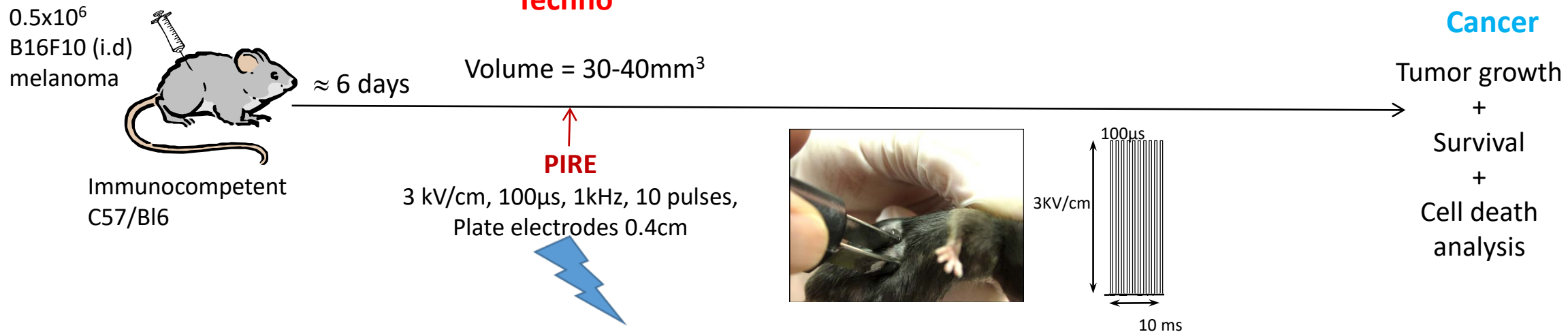


3

## Cancer

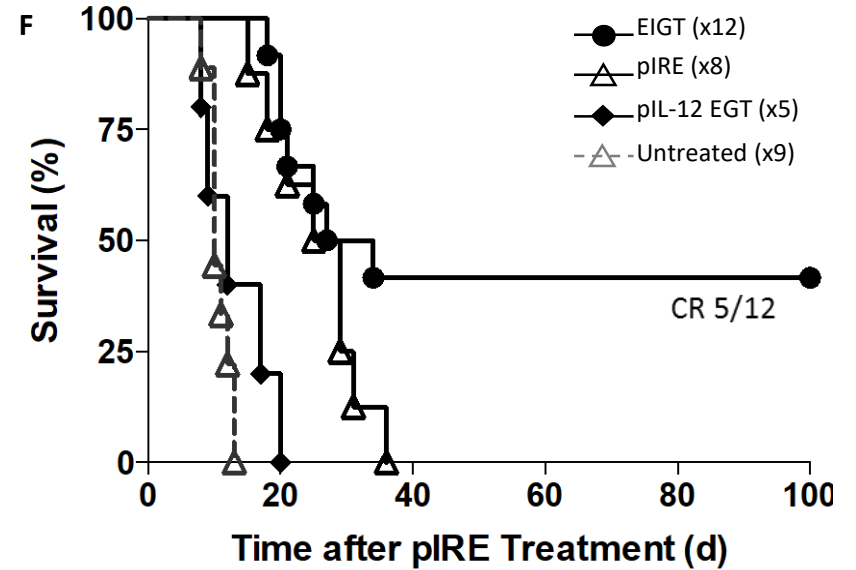
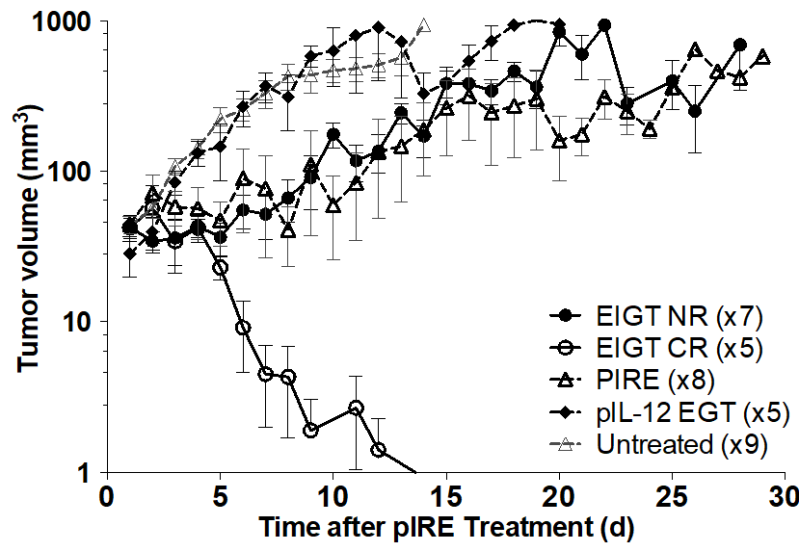
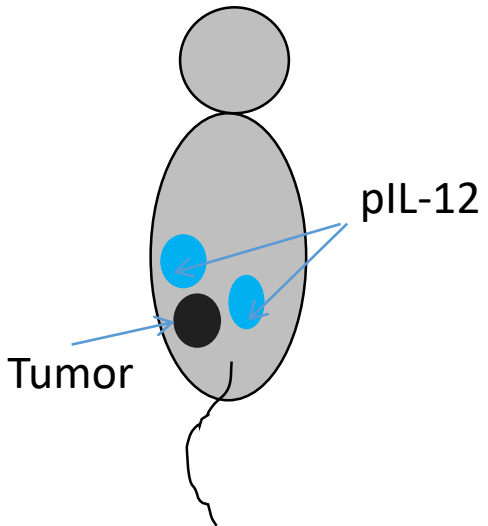
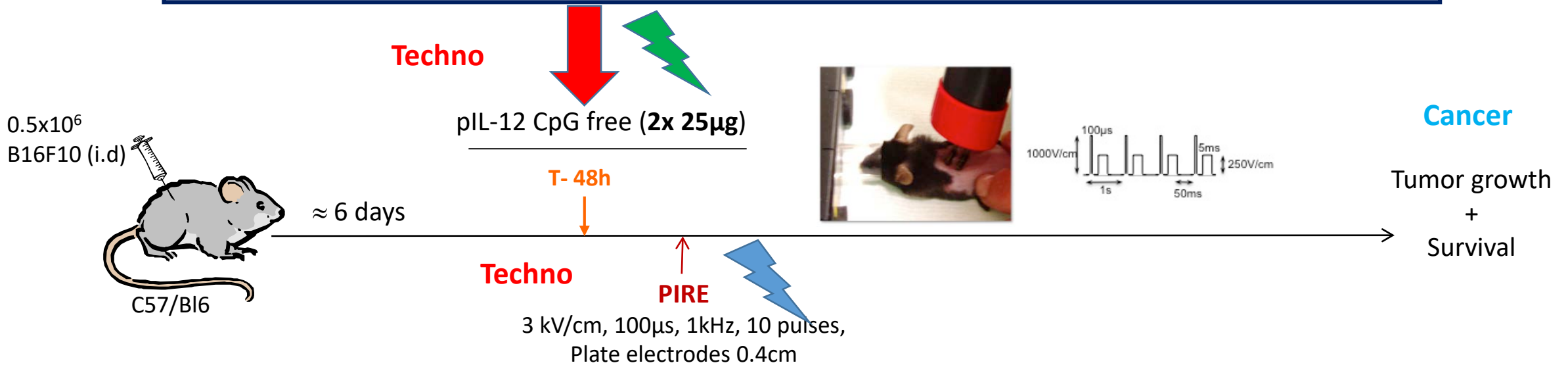
Amplified activation of  
dendritic cells:  
**Strong immune response**

# PIRE



→ Reduction of the tumor volume by PIRE treatment → Apoptosis then necrosis

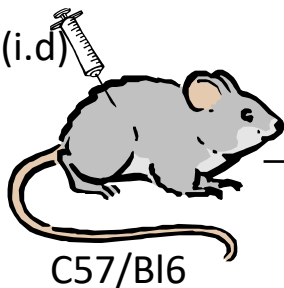
# PIRE + pIL-12 GET



**EIGT treatments induce partial B16F10 tumor regression and 5/12 complete regression (CR)**

# PIRE + pIL-12 GET

0.5x10<sup>6</sup>  
B16F10 (i.d)



**Techno** pIL-12 CpG free (2x 25µg)

≈ 6 days

T- 48h

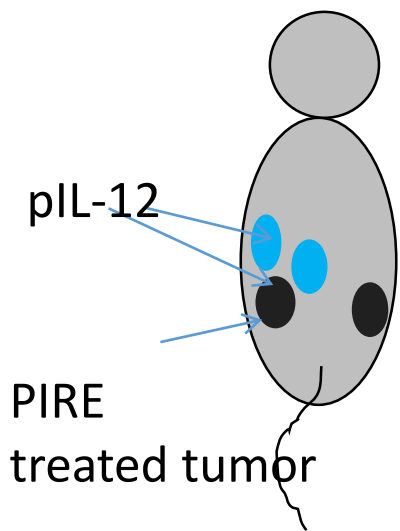
**Techno**

**PIRE**

3 kV/cm, 100µs, 1kHz, 10 pulses,  
Plate electrodes 0.4cm

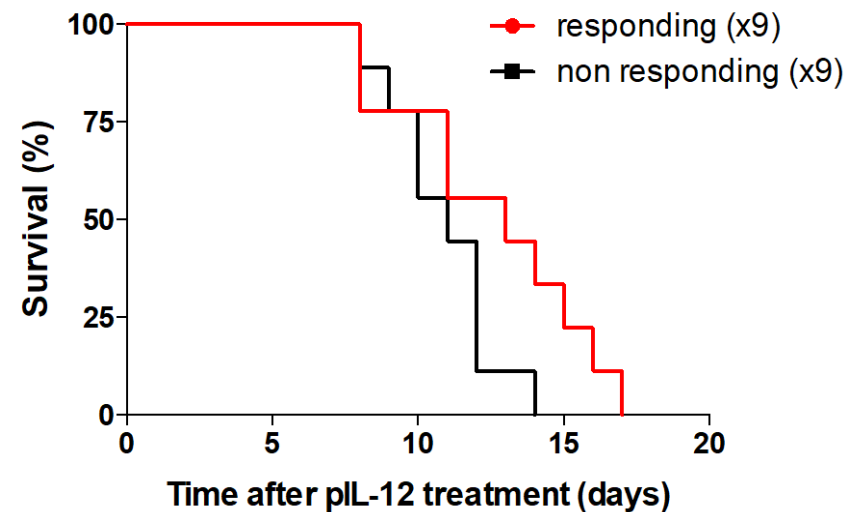
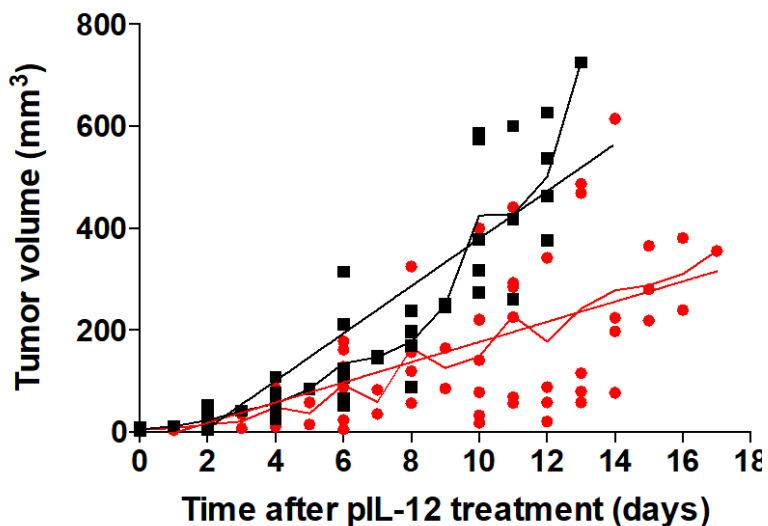
**Cancer**

Tumor  
growth +  
Survival



Non-treated  
tumor

PIRE  
treated tumor



— Regression curve of Contralateral untreated tumors growth from non-responding mice (9/18)      — Regression curve of Contralateral Untreated tumors growth from responding mice (9/18)

**EIGT treatment slows down distant tumor growth.**

# PIRE + pIL-12 GET

0.5x10<sup>6</sup>  
B16F10 (i.d)



**Techno** pIL-12 CpG free(2x25μg)

≈ 6 days

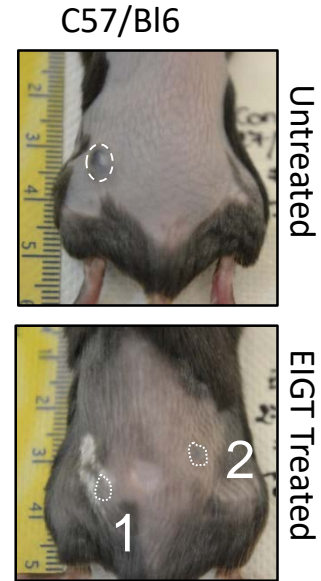
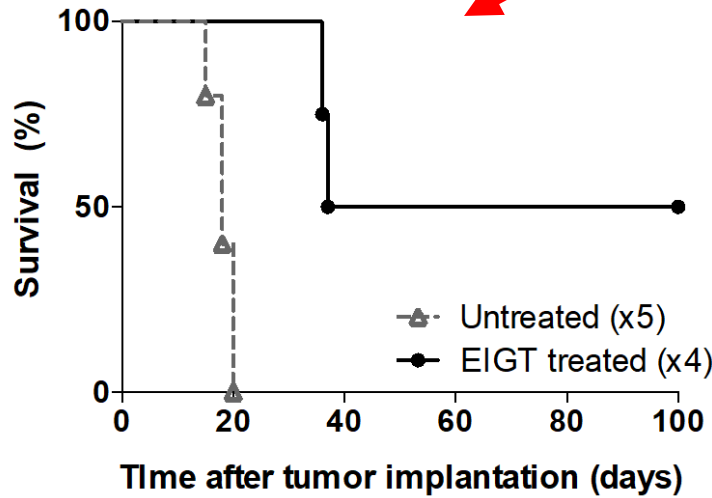
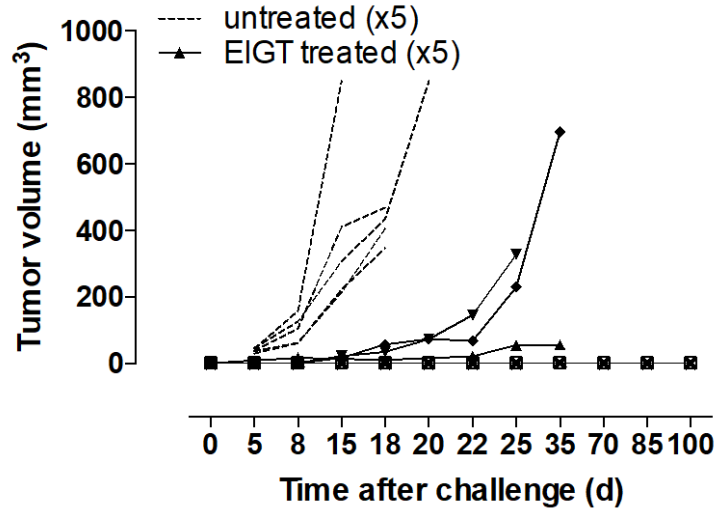
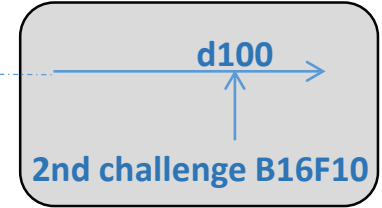
T- 48h

**Techno**

**PIRE**

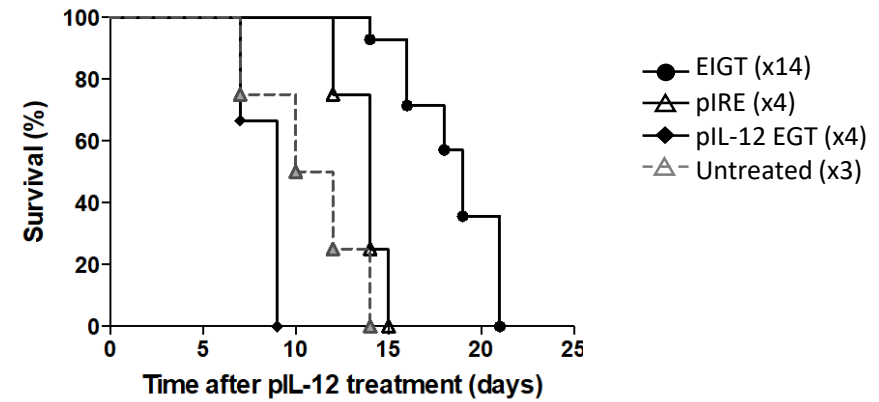
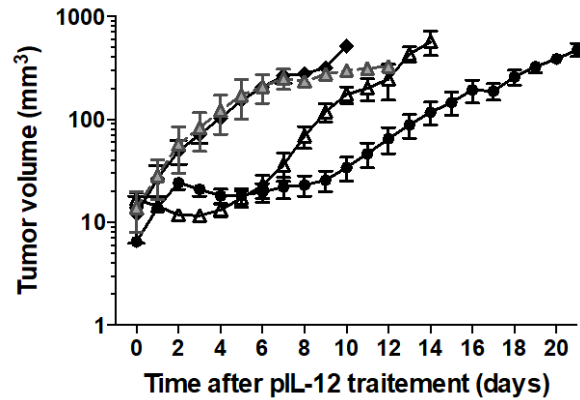
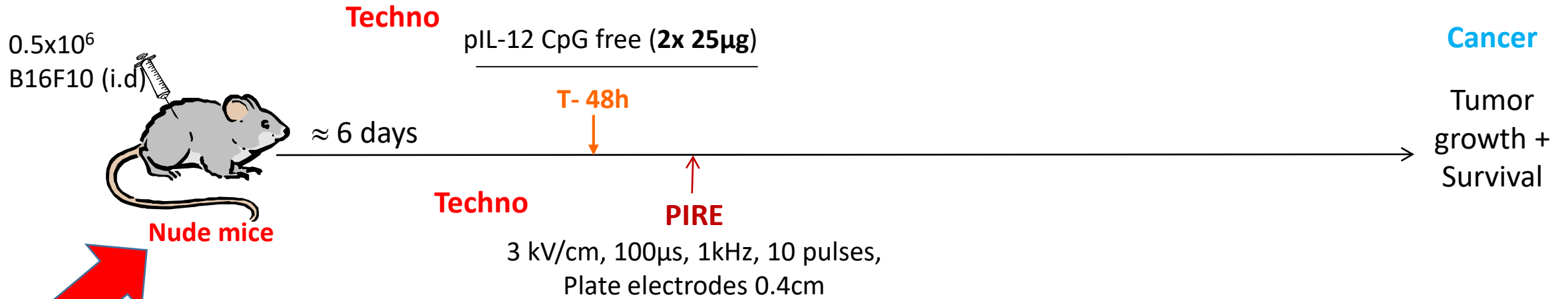
3 kV/cm, 100μs, 1kHz, 10 pulses,  
Plate electrodes 0.4cm

**Cancer**



**EIGT induces a memory immune response**

# PIRE + pIL-12 GET



**Tumor regression induced by EIGT depends on adaptive immune response**

# Biodistribution - GMO Safety

group control

Organs Days after IL12 injection	lungs	liver	spleen	kidneys	lymph nodes	skin	gonads
D15	no	no	no	no	no	no	no
D49	no	no	no	no	no	no	no



group GET

Organs Days after IL12 GET	lungs	liver	spleen	kidneys	lymph nodes	Skin pg/ $\mu$ g of tissue DNA	gonads
D15	no	no	no	no	no	0.8	no
D49	no	no	no	no	no	0.045	no

**Plasmids were transiently present specifically at the site of the treatment**



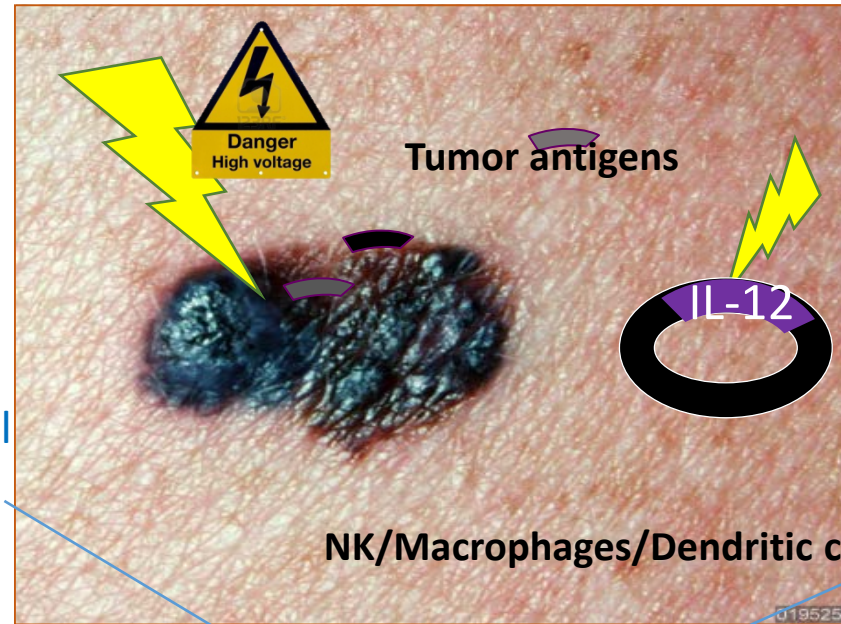
# Conclusions and Perspectives

1

**PIRE:** Partial Irreversible  
Electropermeabilisation  
of the tumor

Tumor antigen exposure  
and release

PIRE alone → ↑ survival  
But no cure



2

Controlled expression of  
an immunogenic adjuvant  
in the peritumoral skin.

EGT pIL-12 alone → ∅

PIRE + pIL-12

**Anti-tumoral immunogenic response  
- after one single treatment**

**Nous disposons de la technologie biophysique, des protocoles, de la fabrication des plasmides et avons établi la courte durée de vie du plasmide spécifiquement au site d'injection.**



**L'objectif est d'établir un partenariat avec des cliniciens pour mener un essai clinique chez l'homme.**