CD4 cells can be more efficient at tumor rejection than CD8 cells

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Anti-tumor T cells (anti-male)

Name	T cells	H-Y Antigen	Restriction element
MataHari	CD8	Uty	Class I (D^b)
Marilyn	CD4	Dby	Class II (A^b)

The tumor
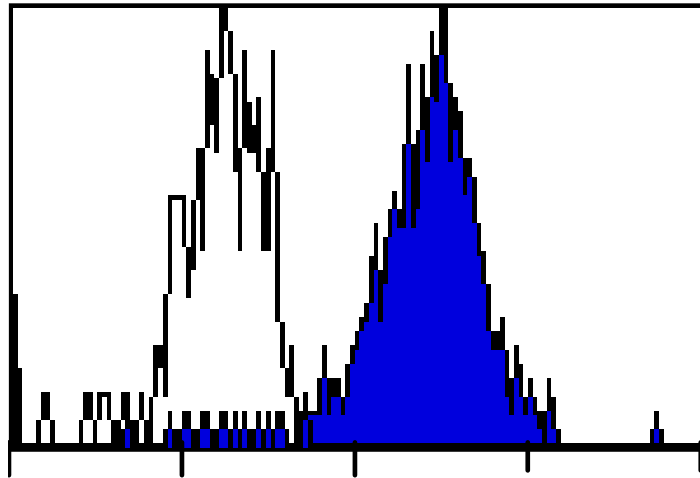
Name: MB49
Origin: Male B6 bladder carcinoma
Antigen: H-Y (Uty and Dby)
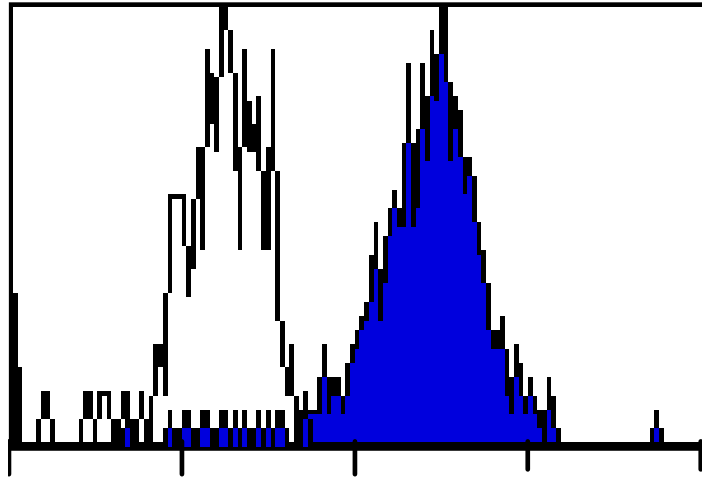
MB49 can express Class II (A^b)

D^b (Class I)   **A^b (Class II)**
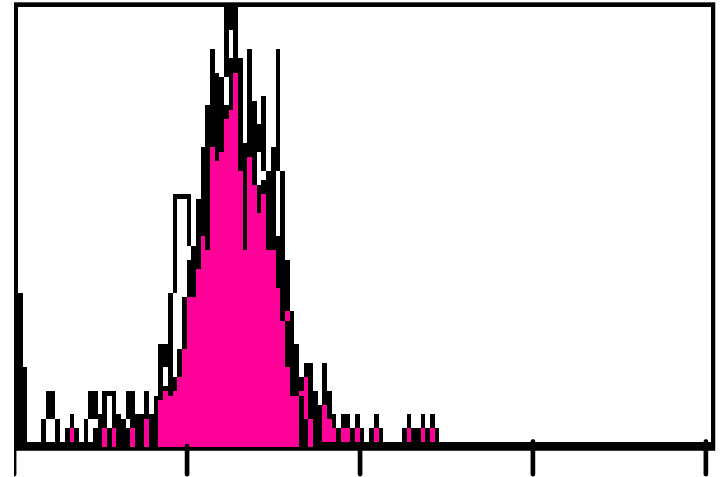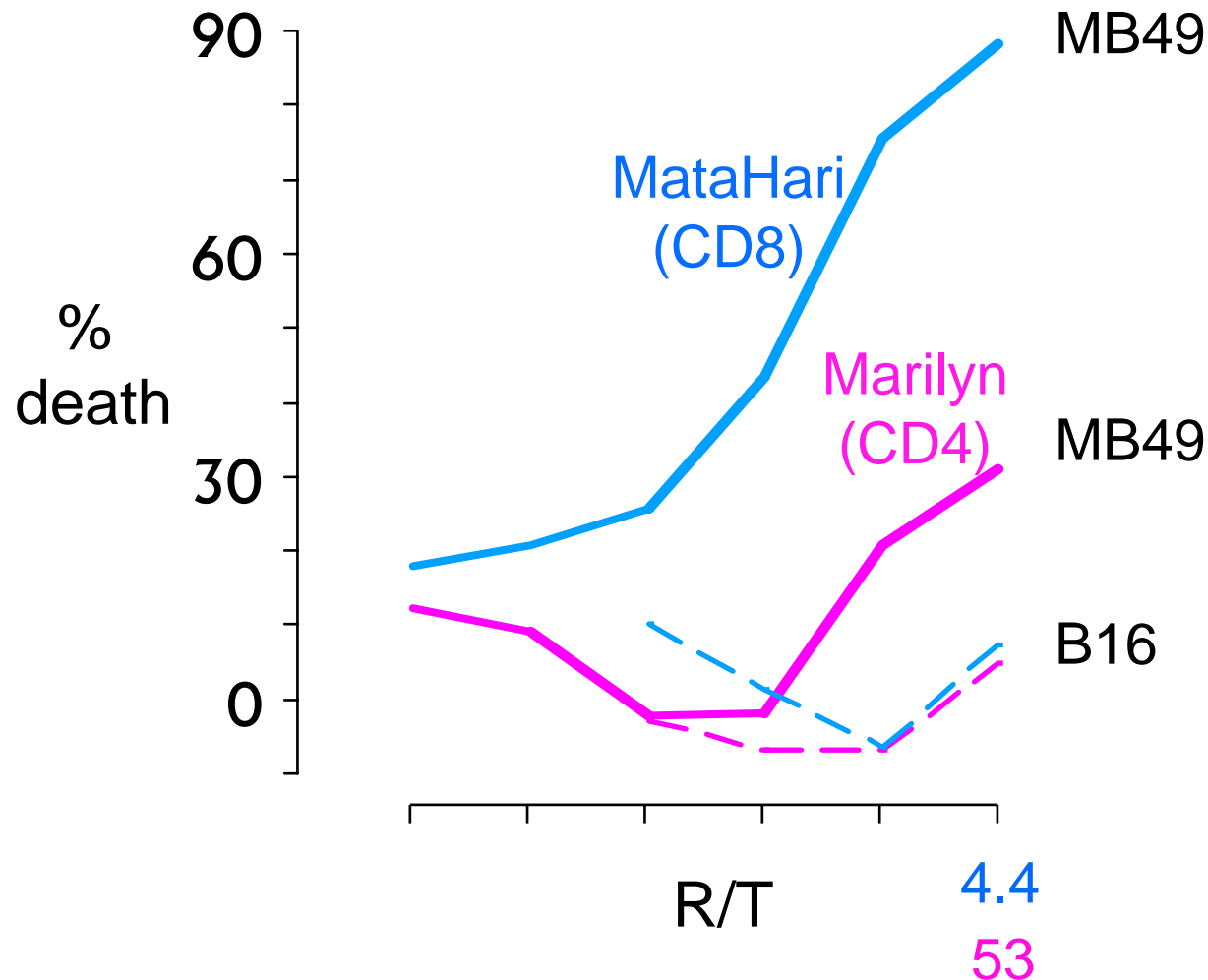
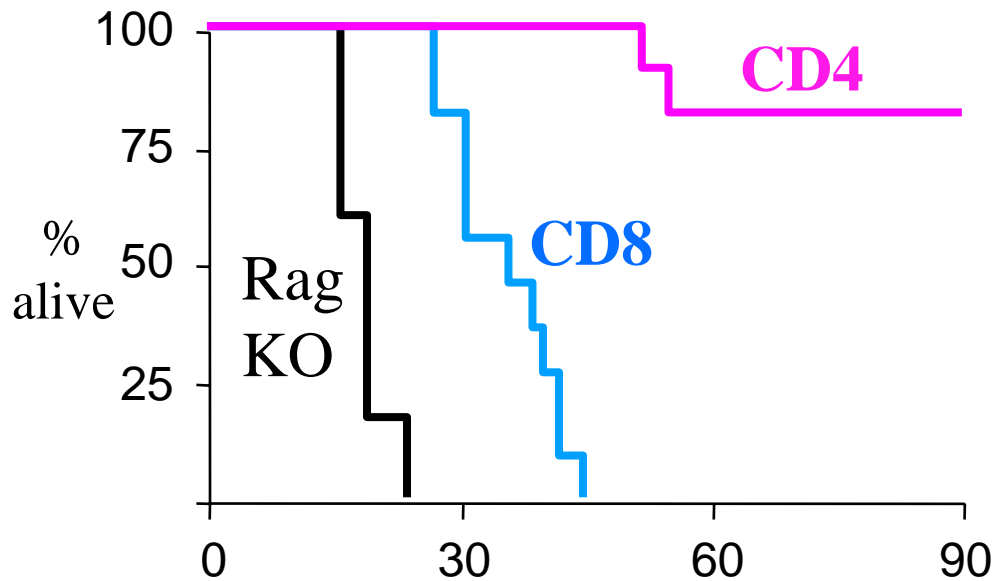# MB49 can express Class II (A^b)
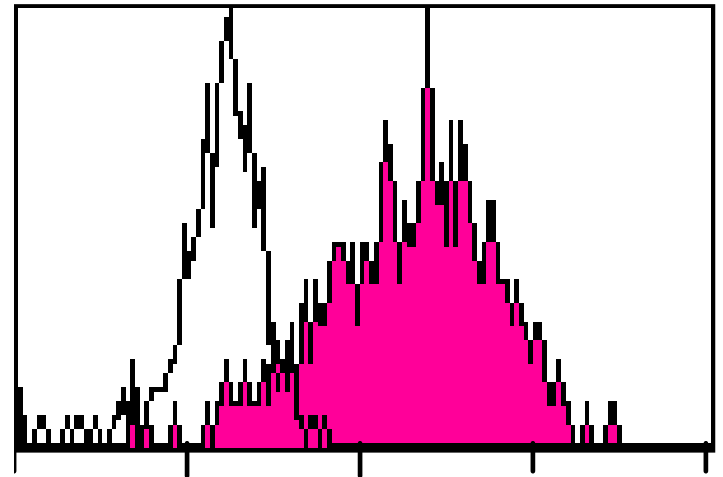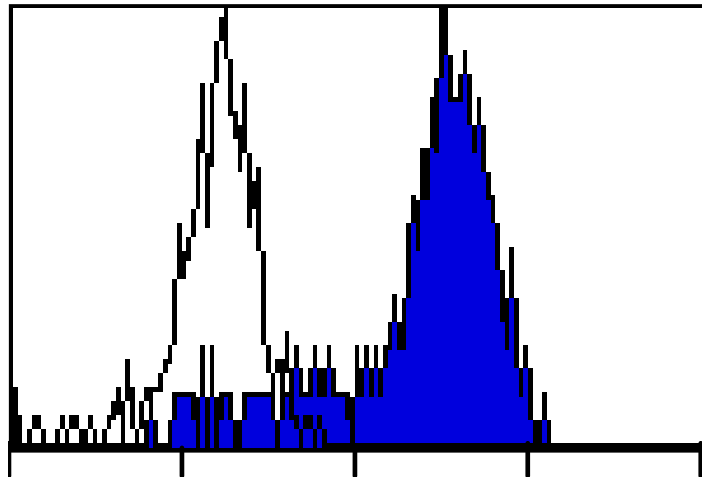
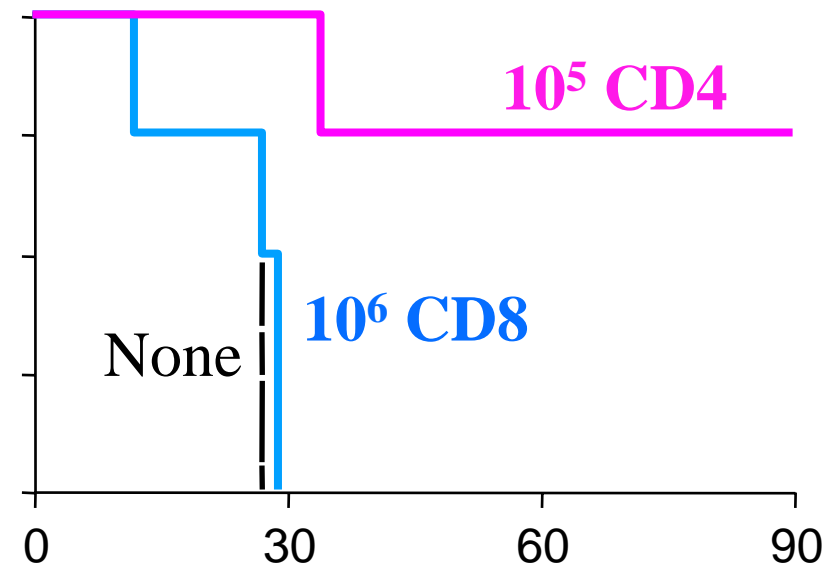# **MataHari** but not **Marilyn** cells are good killers
in vitro

Marilyn but not MataHari cells reject the tumor

Direct tumor challenge

Adoptive transfer

Why does MataHari fail?

Why does MataHari fail?

- Localization?

Why does MataHari fail?

- Localization?

- Tumor escape?

Why does **MataHari** fail?

- Localization?

- Tumor escape?
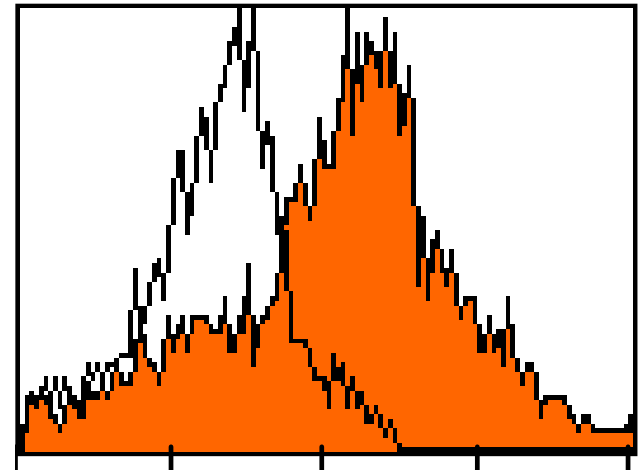
- Tumor-mediated suppression?

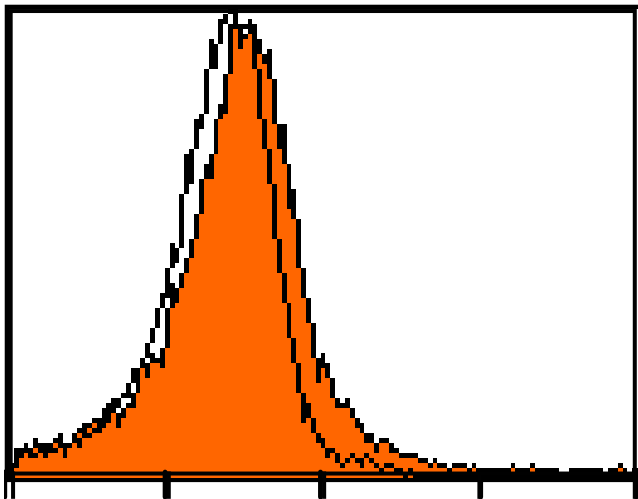# How does Marilyn succeed?
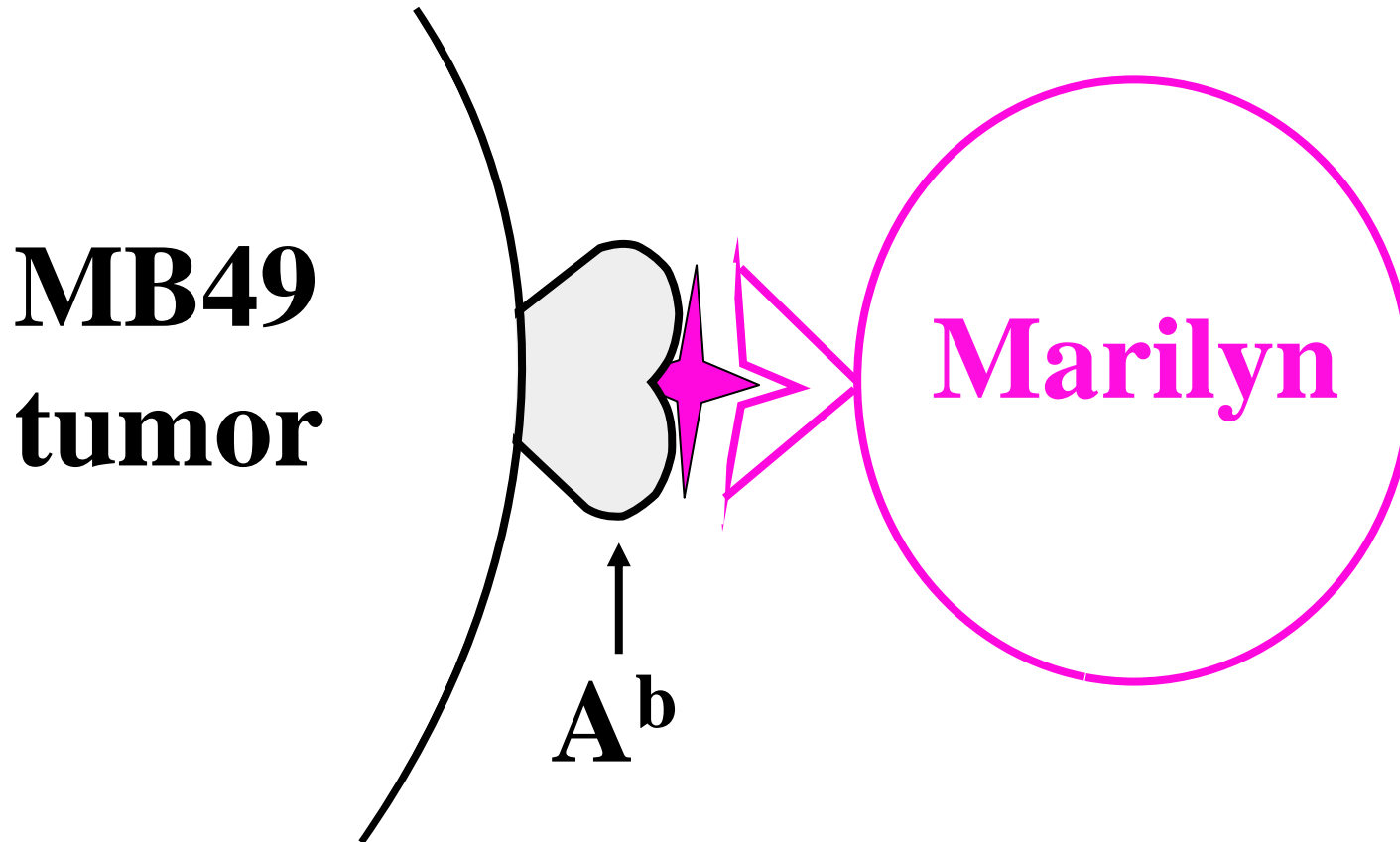
Tumor Class II expression *in vivo*
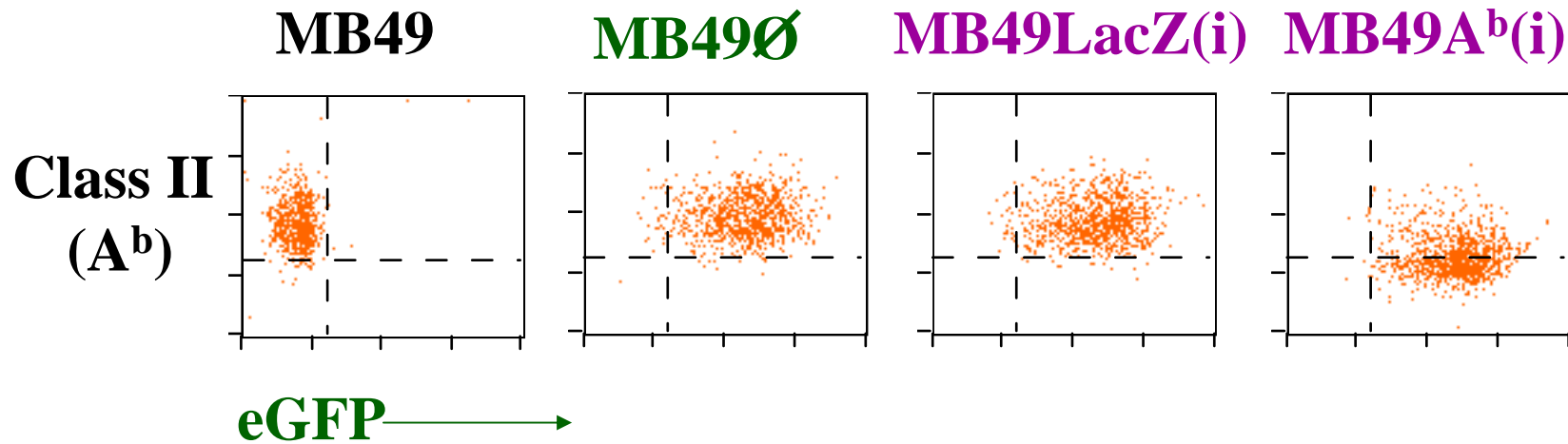
RagKO

RagKO+Marilyn

Gating on tumor cells

A^b (Class II)

Does it kill directly?

MB49 tumor

A^b

Marilyn

A^b shRNA knocks down Class II expression on MB49 cell line

MB49 **MB49Ø** **MB49LacZ(i)** **MB49A^b(i)**

Class II
(A^b)

eGFP⟶

Knocking down Class II on MB49 does not affect Marilyn effectiveness

Or indirectly?

βTC-tet tumor

A^k
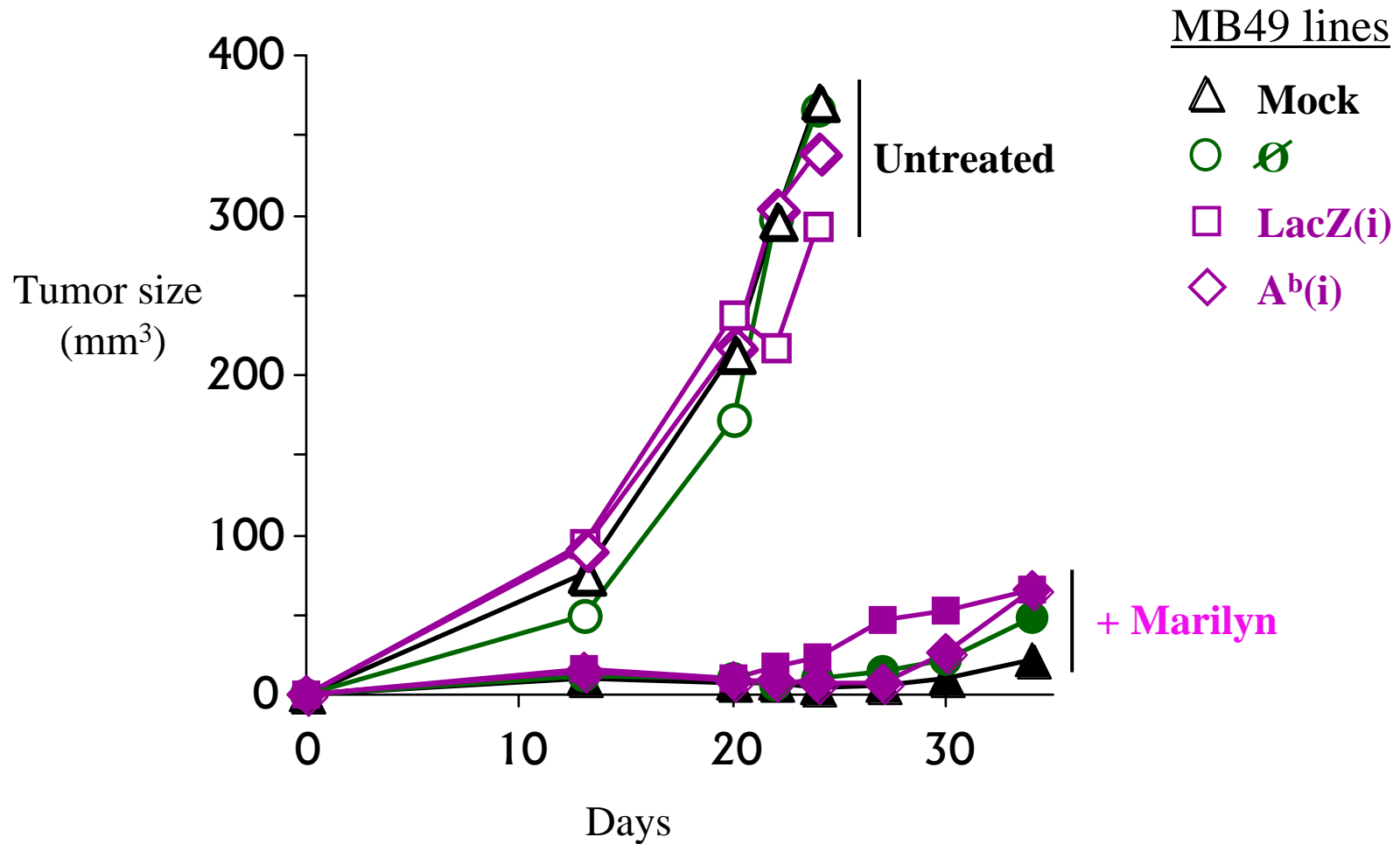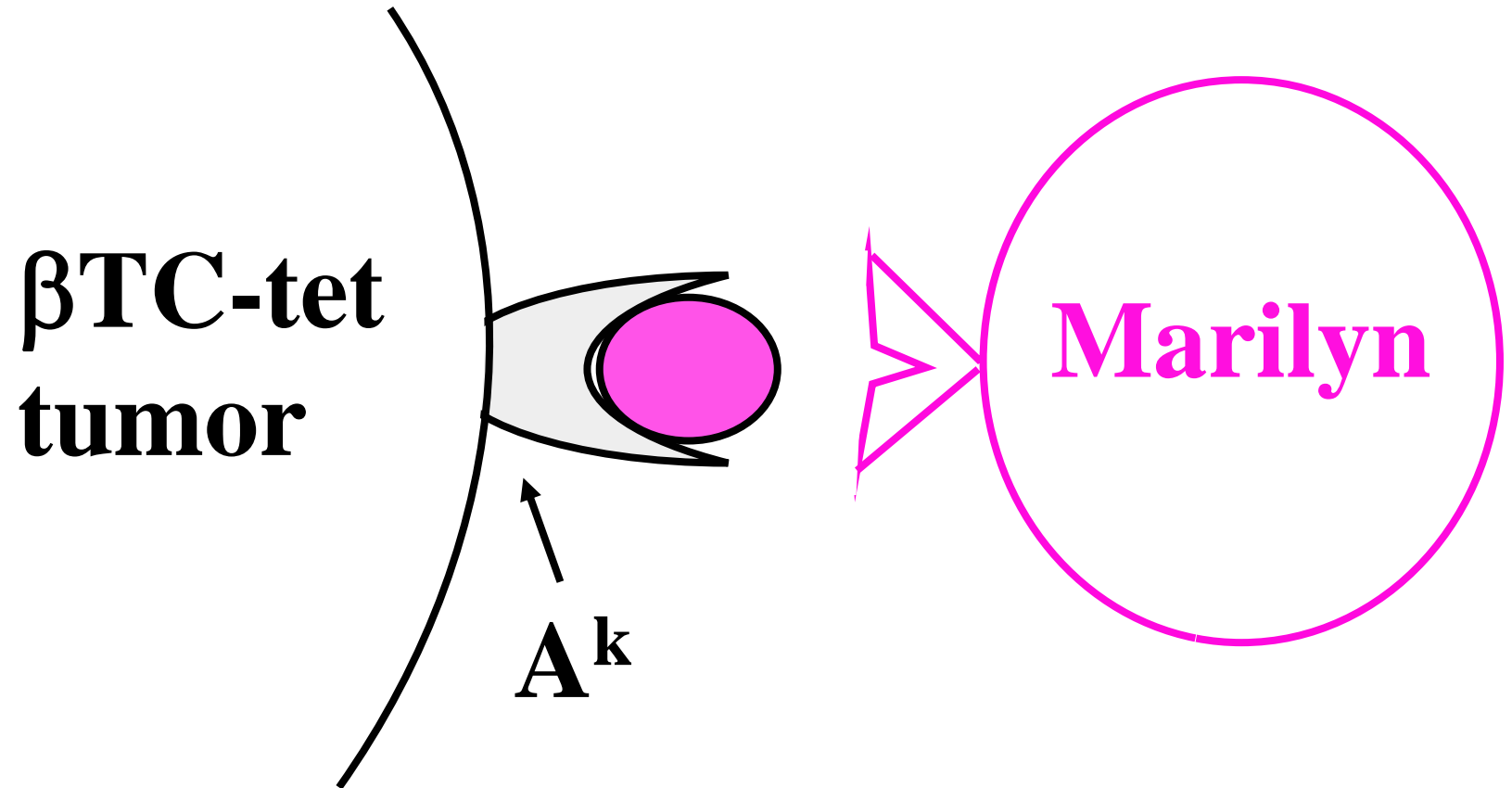
Marilyn

Marilyn can reject indirectly

βTC-tet tumor

Marilyn
(CD4)

RagKO

% alive
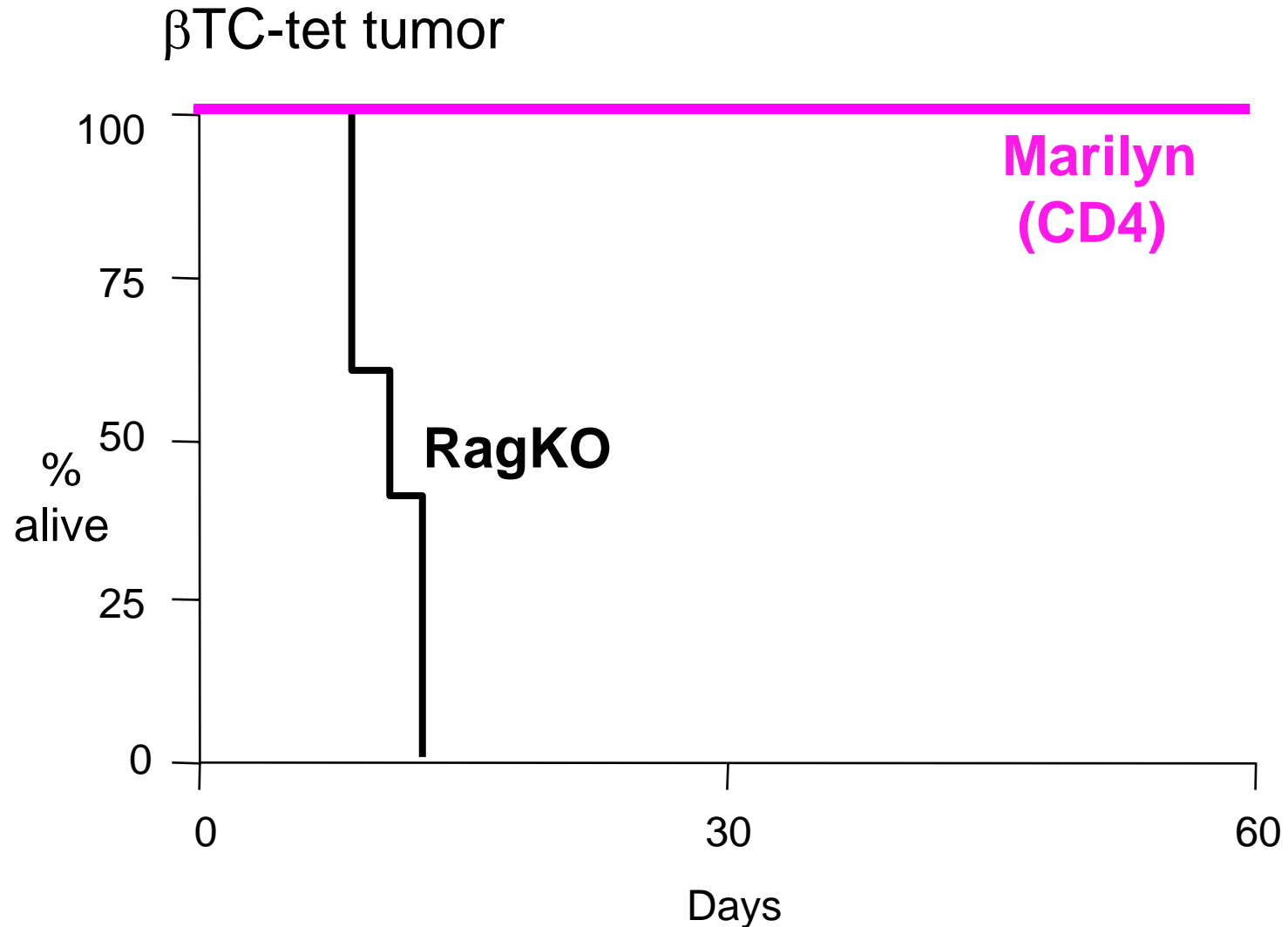
Is it generalizable?

Is it generalizable?

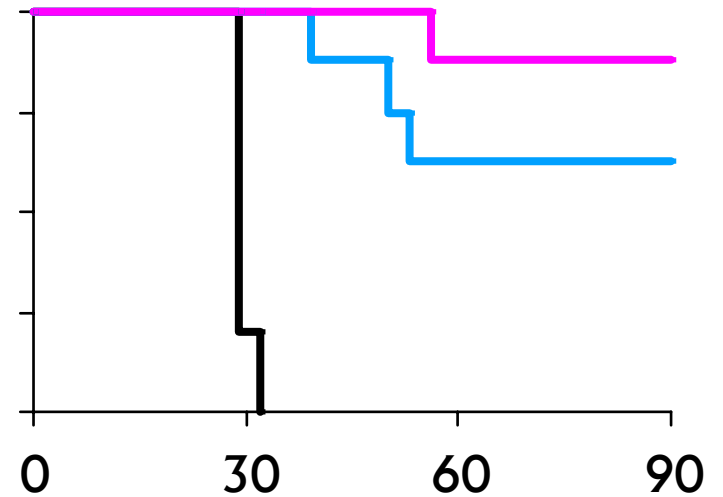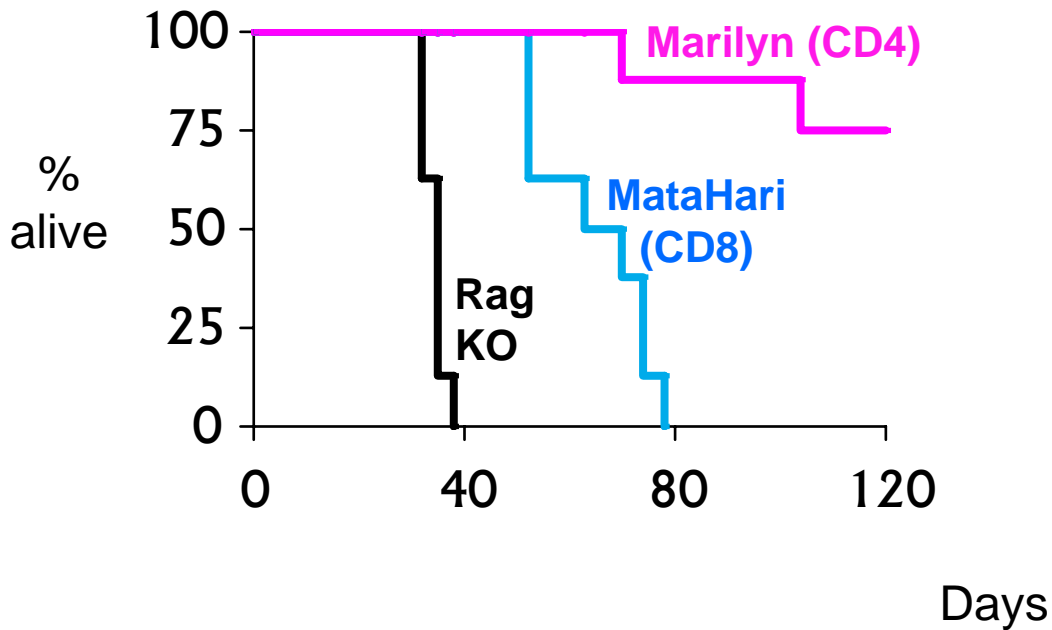- **Are Marilyn CD4 better than MataHari CD8 for other tumors?**

Is it generalizable?

- Are **Marilyn CD4** better than **MataHari CD8** for other tumors?

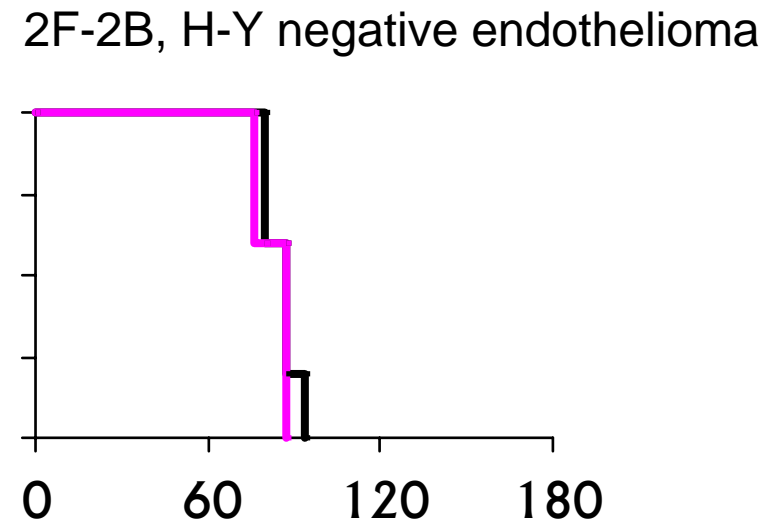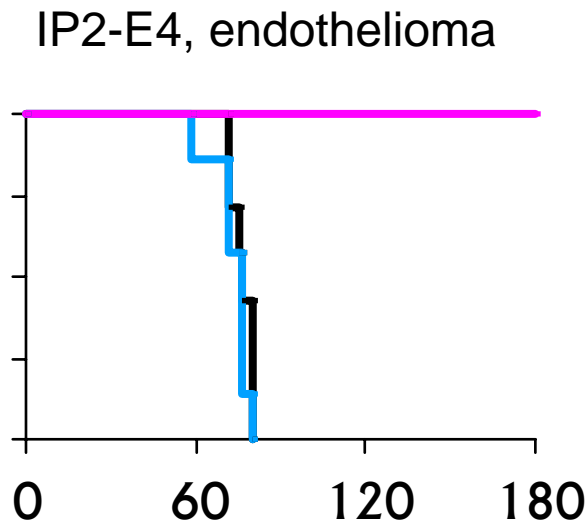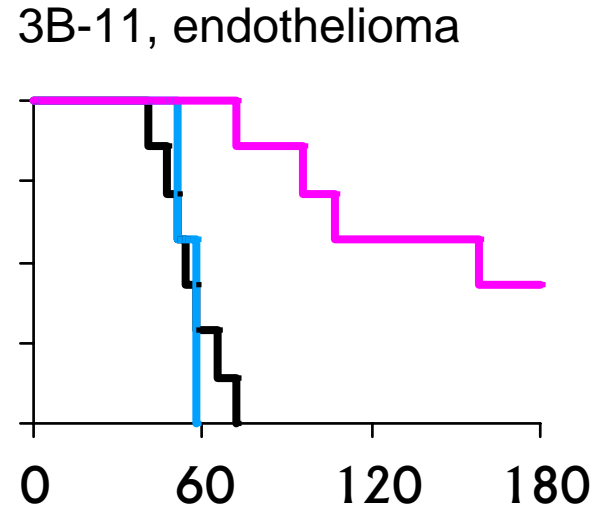- Does **Marilyn** reject other tumors that she cannot see?
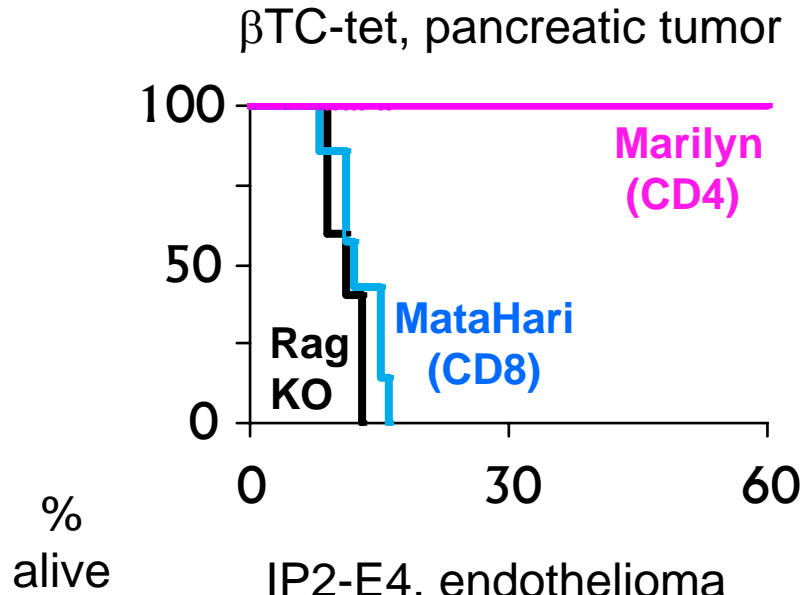
Testing other H-2^b tumors

TRAMP-C2,
a prostate carcinoma

WR21,
a salivary gland carcinoma

Testing other H-2ᵏ tumors

βTC-tet, pancreatic tumor

3B-11, endothelioma

IP2-E4, endothelioma

2F-2B, H-Y negative endothelioma

Marilyn (CD4)

MataHari (CD8)

Rag KO

% alive

Days

CONCLUSIONS

In this male antigen tumor model:

- CD4 cells reject tumors that CD8 cells can't reject

- Neither the effectiveness of CD4 cells nor the ineffectiveness of CD8 cells can be predicted from their *in vitro* activity

- Antigen presentation by the tumor cells is not required for the CD4 mediated rejection

We need to pay more attention to CD4 cells as effectors.

Thank you

Polly Matzinger

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Olivier Lantz