

Immunotransplant for Mantle Cell Lymphoma:

A phase I/II study demonstrating
amplification of tumor-reactive T cells



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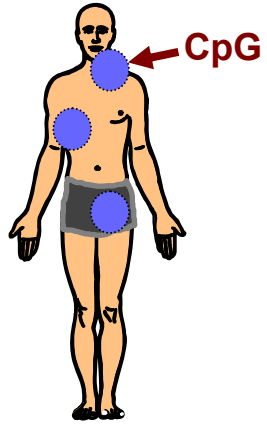
SEQUENTA

Presenter Disclosure Information

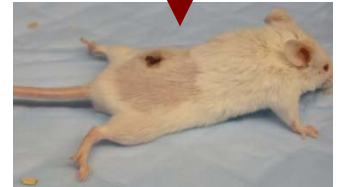
Joshua Brody M.D.

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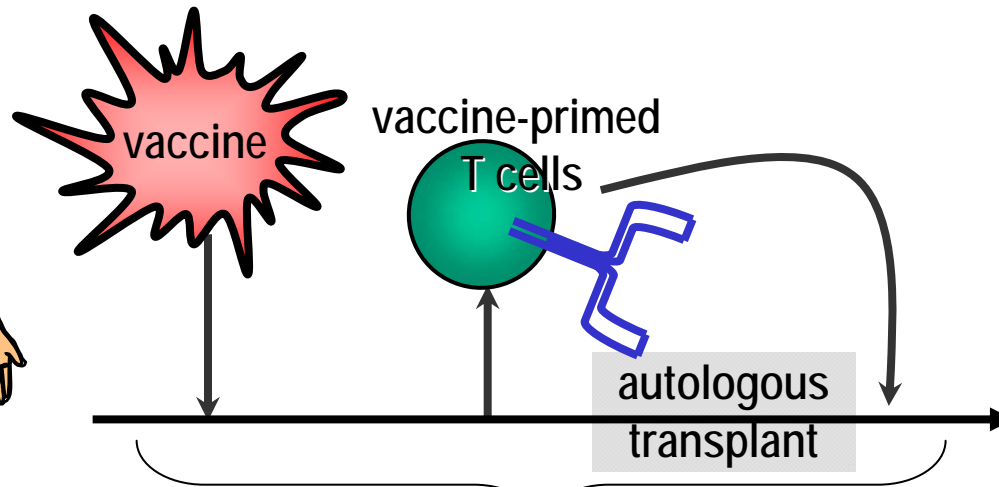
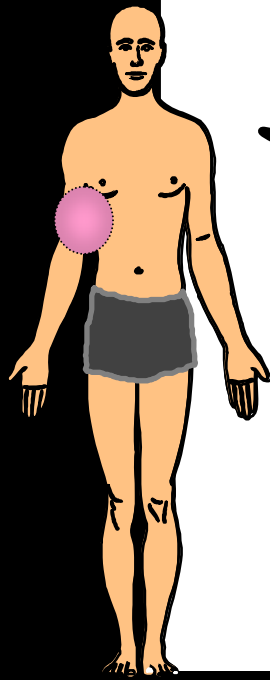
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***in situ* vaccine**
(low grade lymphoma)

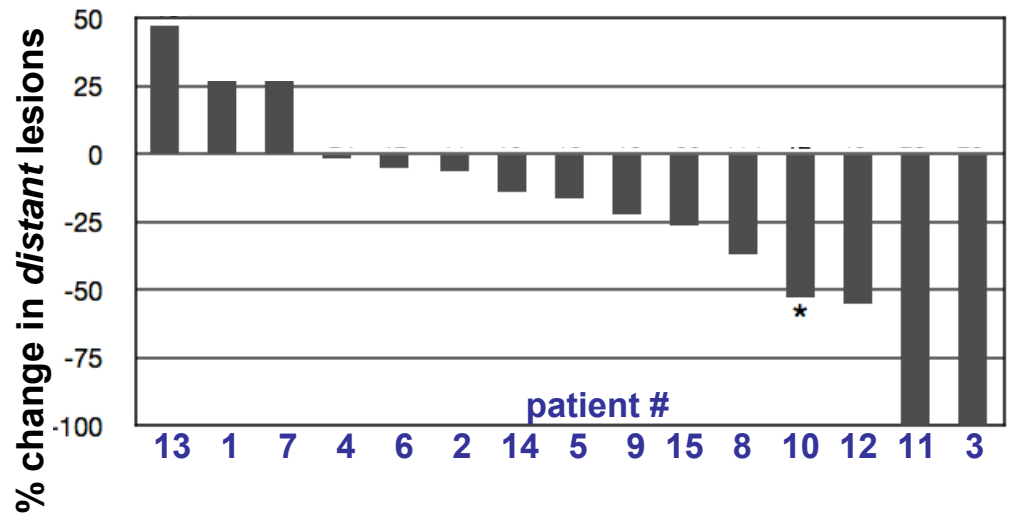
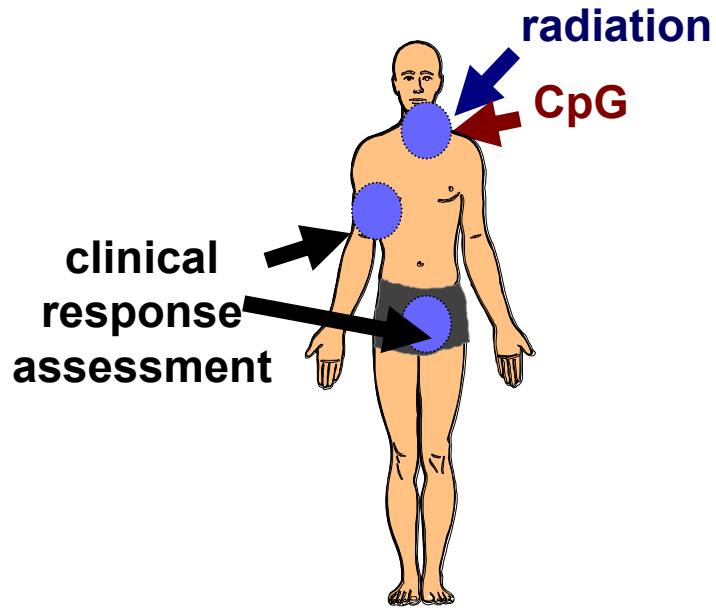
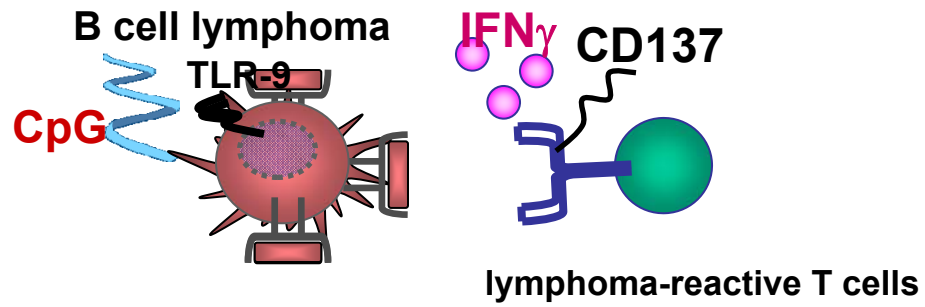


immunotransplant



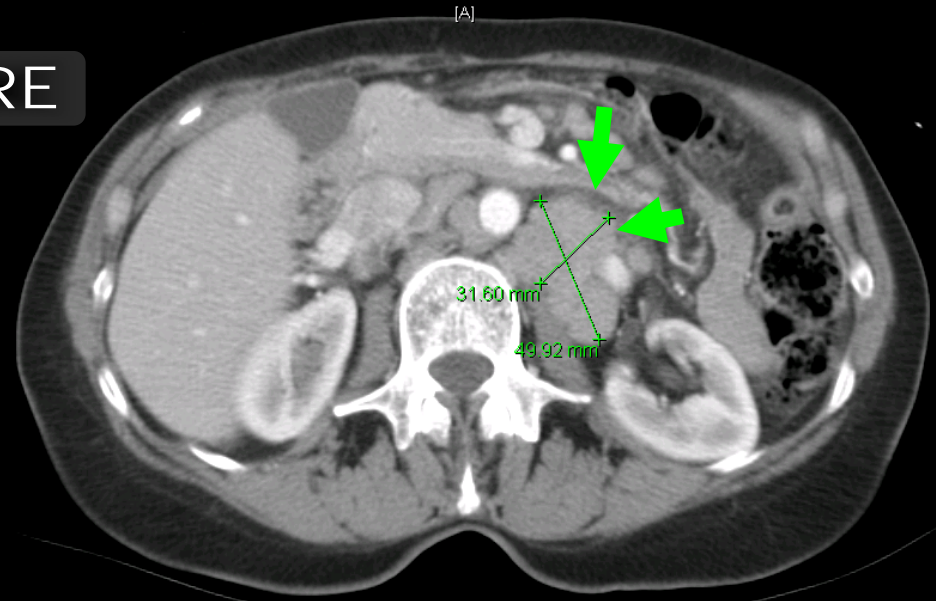
immunotransplant
(mantle cell lymphoma)

CpG-based vaccine for *low-grade* lymphoma

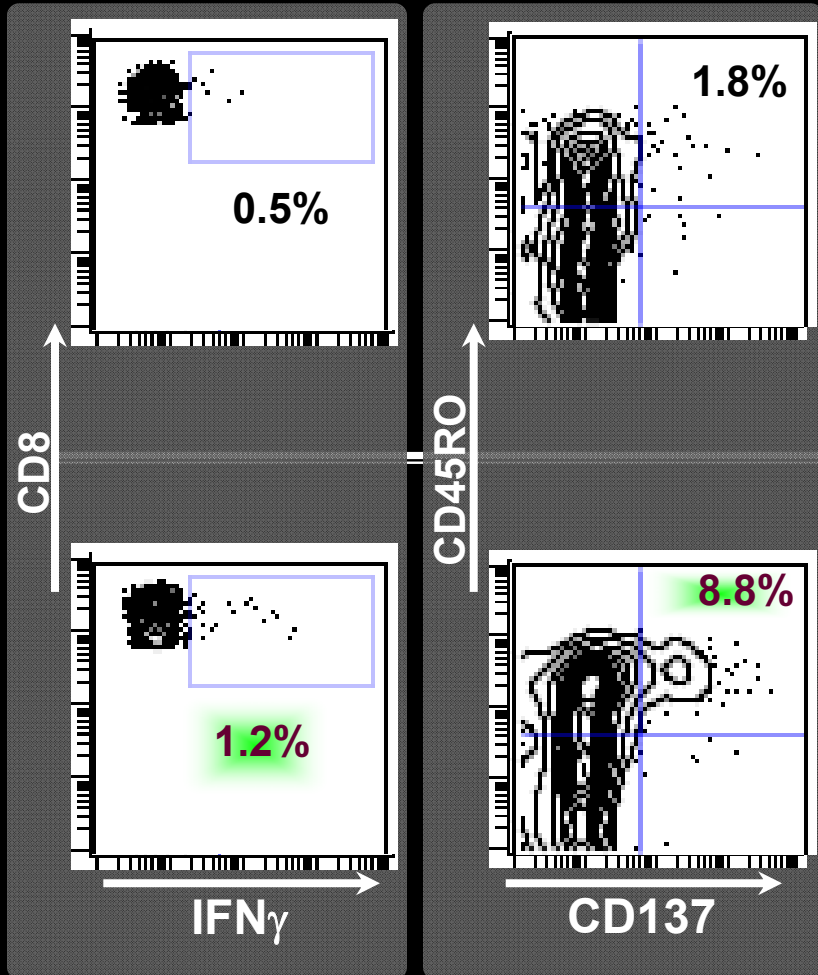
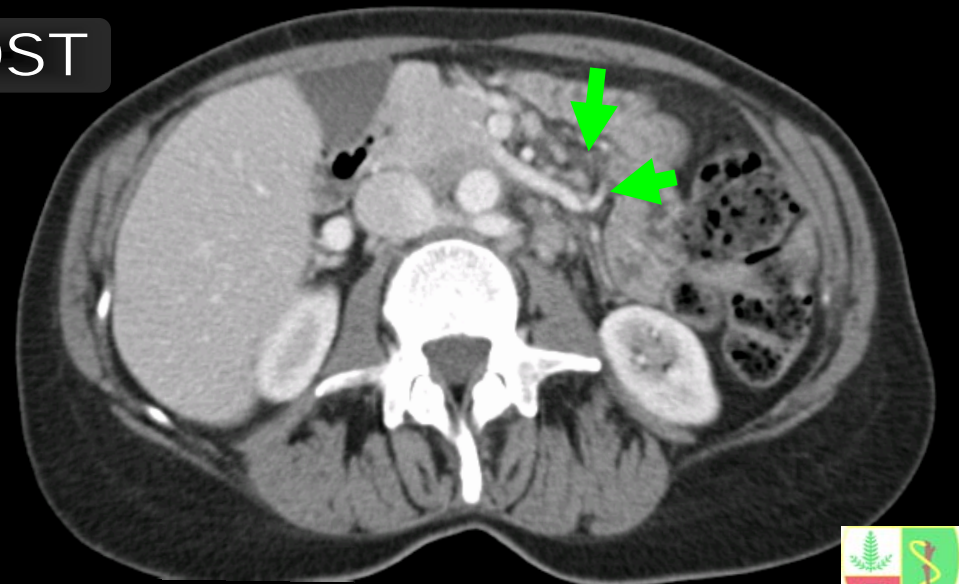


CpG-based vaccine induces anti-tumor T cells

PRE



POST

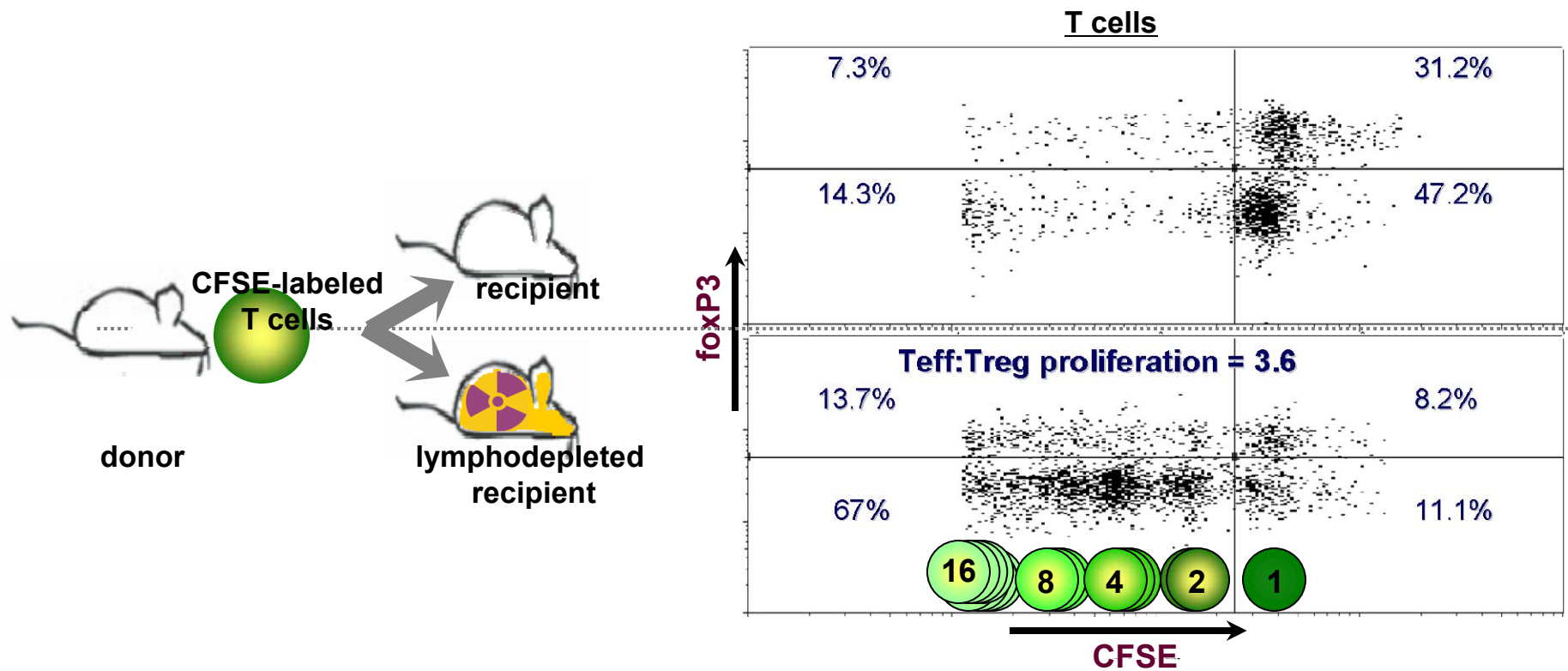


CD8 T cell gate

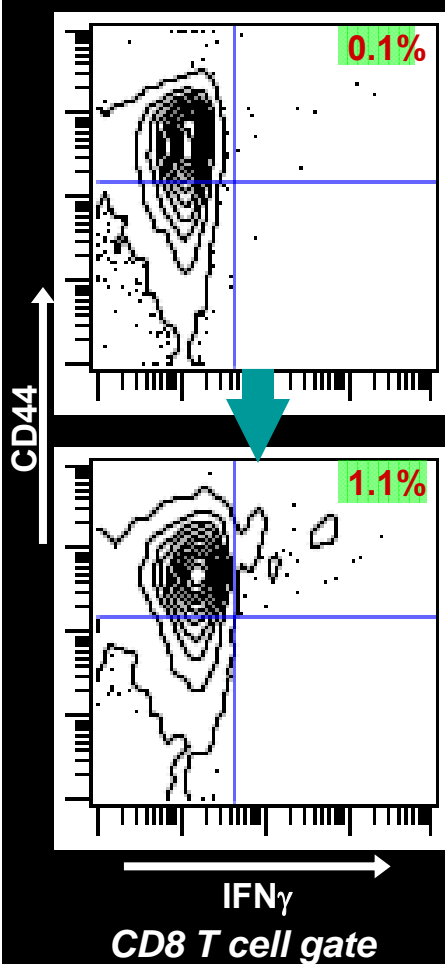
Brody JD et al., *J Clin Oncol.* 2010 Oct 1;28(28).



T-cell transfer into lymphodepleted recipients induces preferential $T_{\text{effector}} > T_{\text{reg}}$ proliferation

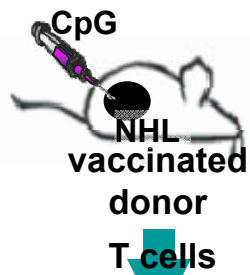


Immunotransplant amplifies anti-tumor T cells induced by CpG-based vaccines

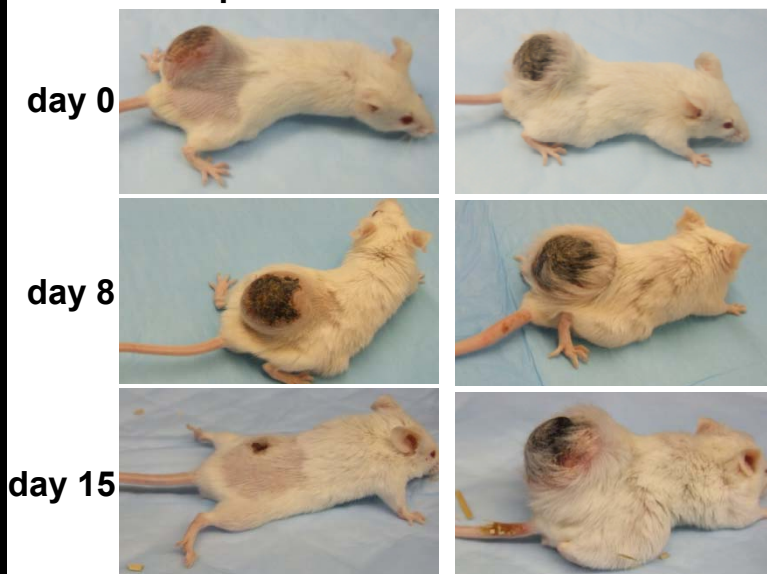


CpG *in situ* vaccine

immunotransplant

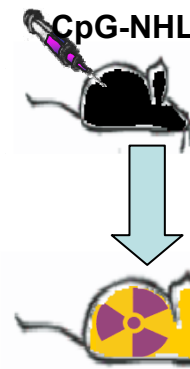


transplant

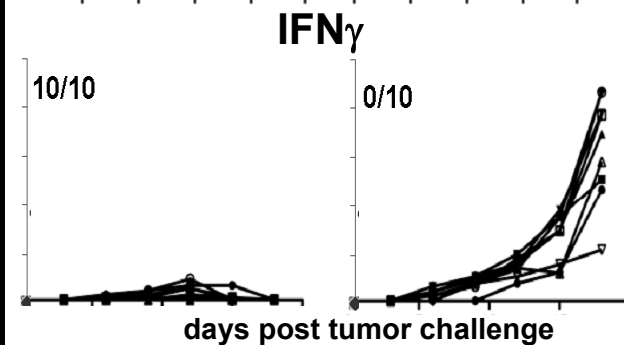
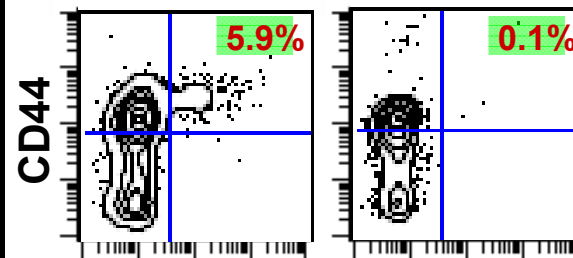


CpG *ex vivo* vaccine

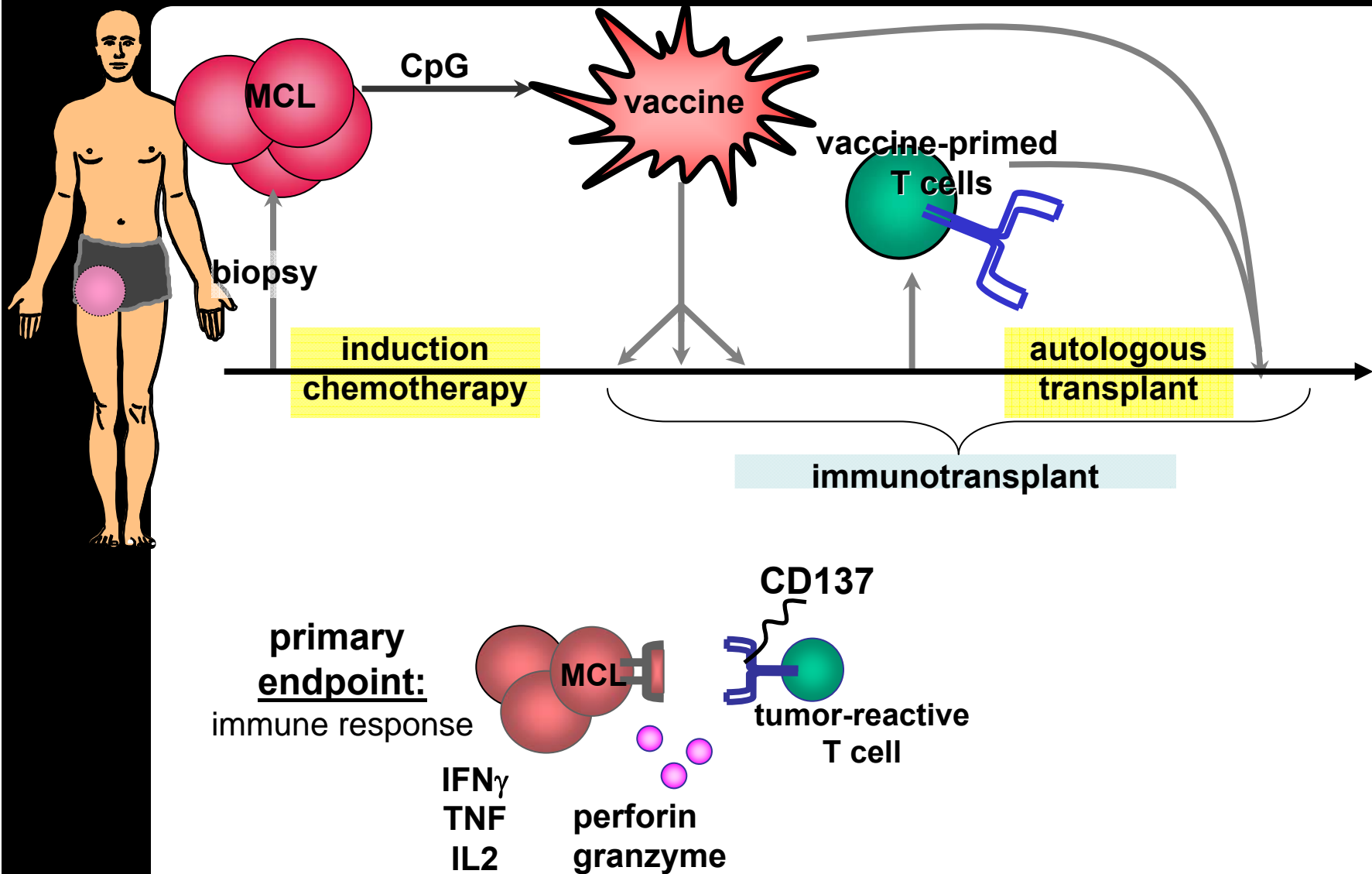
immunotransplant



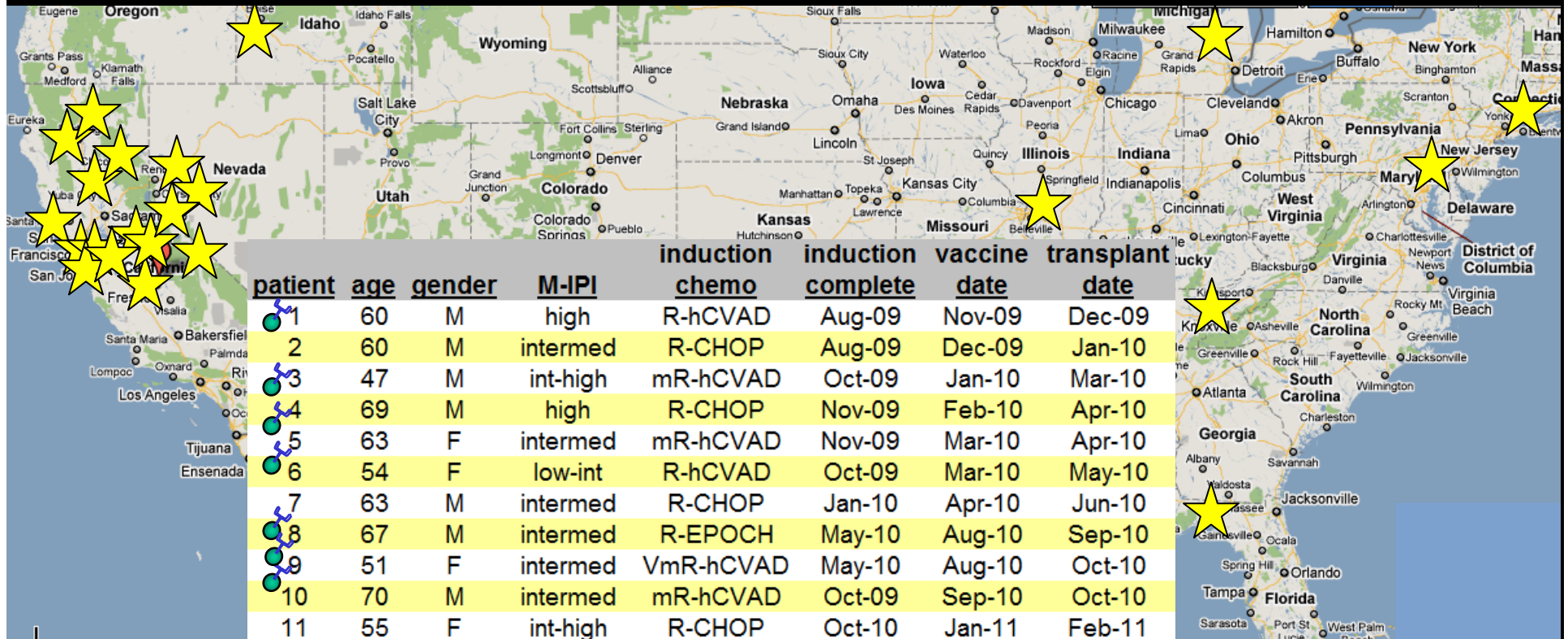
transplant



Immunotransplant for MCL: schema & endpoints



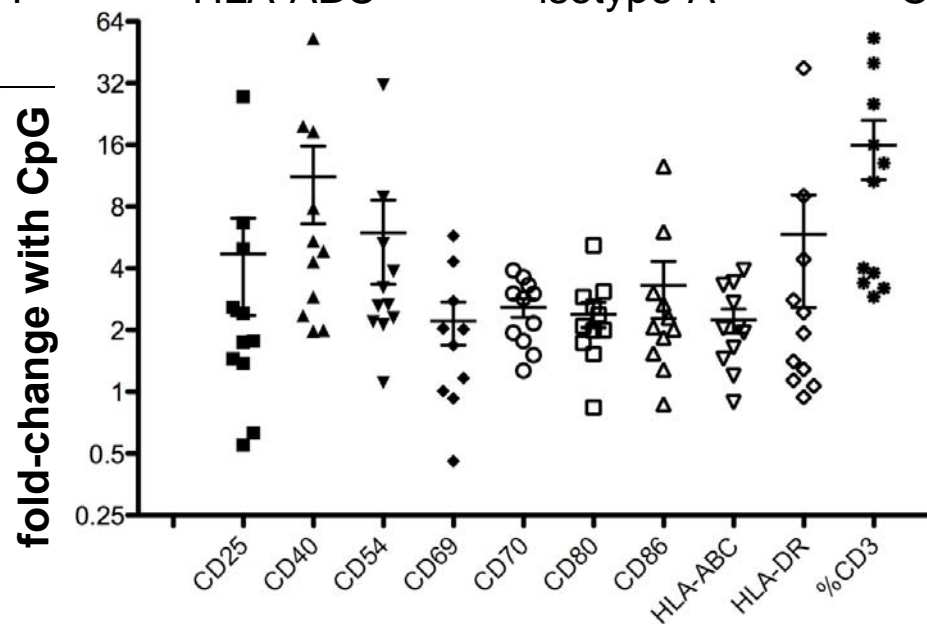
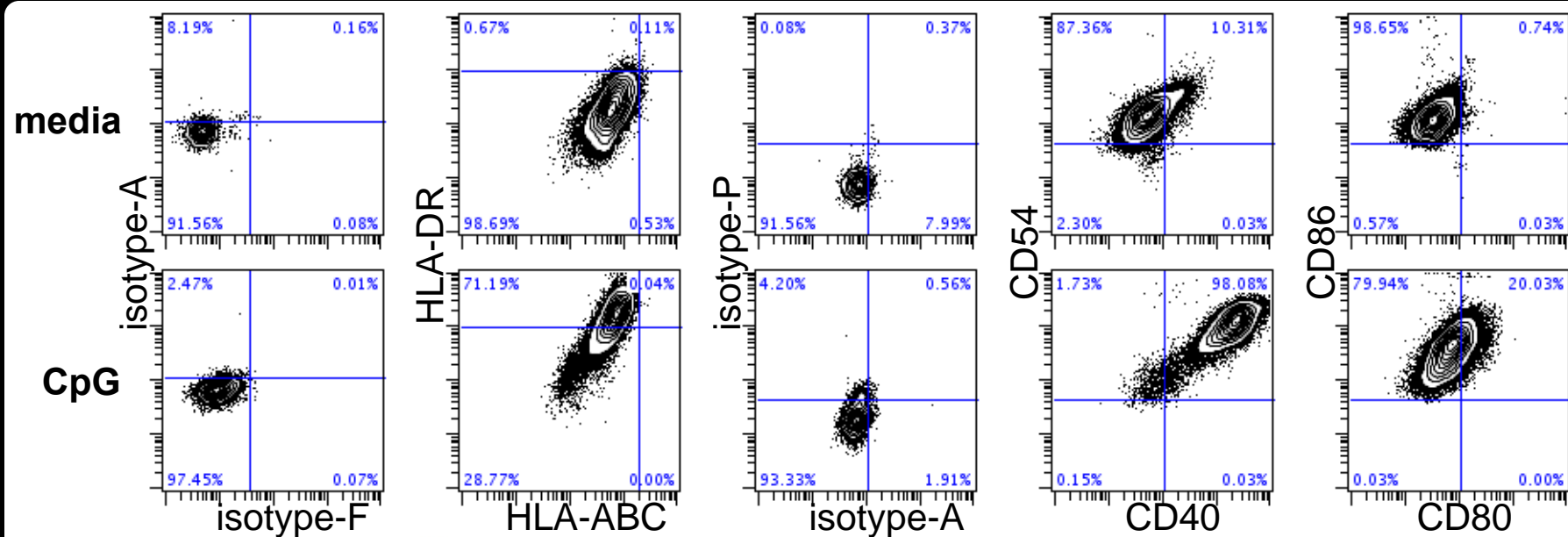
Immunotransplant for MCL: cohort



patient	age	gender	M-IPi	induction chemo	induction complete	vaccine date	transplant date
1	60	M	high	R-hCVAD	Aug-09	Nov-09	Dec-09
2	60	M	intermed	R-CHOP	Aug-09	Dec-09	Jan-10
3	47	M	int-high	mR-hCVAD	Oct-09	Jan-10	Mar-10
4	69	M	high	R-CHOP	Nov-09	Feb-10	Apr-10
5	63	F	intermed	mR-hCVAD	Nov-09	Mar-10	Apr-10
6	54	F	low-int	R-hCVAD	Oct-09	Mar-10	May-10
7	63	M	intermed	R-CHOP	Jan-10	Apr-10	Jun-10
8	67	M	intermed	R-EPOCH	May-10	Aug-10	Sep-10
9	51	F	intermed	VmR-hCVAD	May-10	Aug-10	Oct-10
10	70	M	intermed	mR-hCVAD	Oct-09	Sep-10	Oct-10
11	55	F	int-high	R-CHOP	Oct-10	Jan-11	Feb-11
12	69	F	intermed	mR-hCVAD	Oct-10	Jan-11	Feb-11
13	63	M	intermed	mR-hCVAD	Nov-10	Jan-11	Mar-11
14	44	M	low-int	mR-hCVAD	Dec-10	Feb-11	Mar-11
15	60	M	intermed	mR-hCVAD	May-11	-	-
16	62	M	intermed	mR-hCVAD	-	-	-
17	70	F	high	mR-hCVAD	-	-	-
18	60	M	intermed	mR-hCVAD	-	-	-
19	67	M	intermed	RCHOP/DHAP	-	-	-
21	70	F	intermed	mR-hCVAD	-	-	-
20	59	F	intermed	mR-hCVAD	-	-	-
22	48	M	int-high	mR-hCVAD	-	-	-
23	61	M	intermed	-	-	-	-
24	65	M	intermed	-	-	-	-

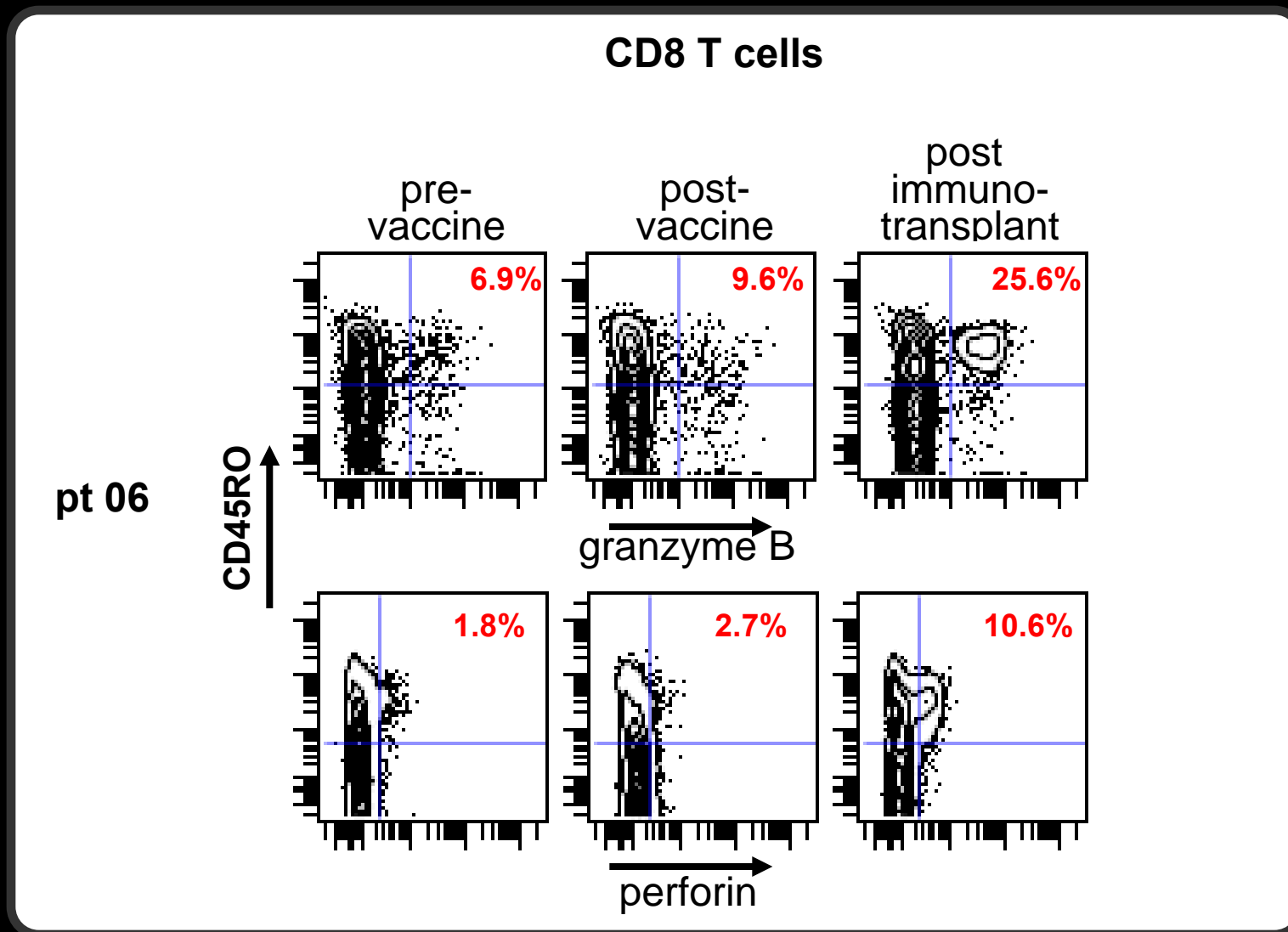


CpG-MCL vaccine: CpG differentially induces activation markers



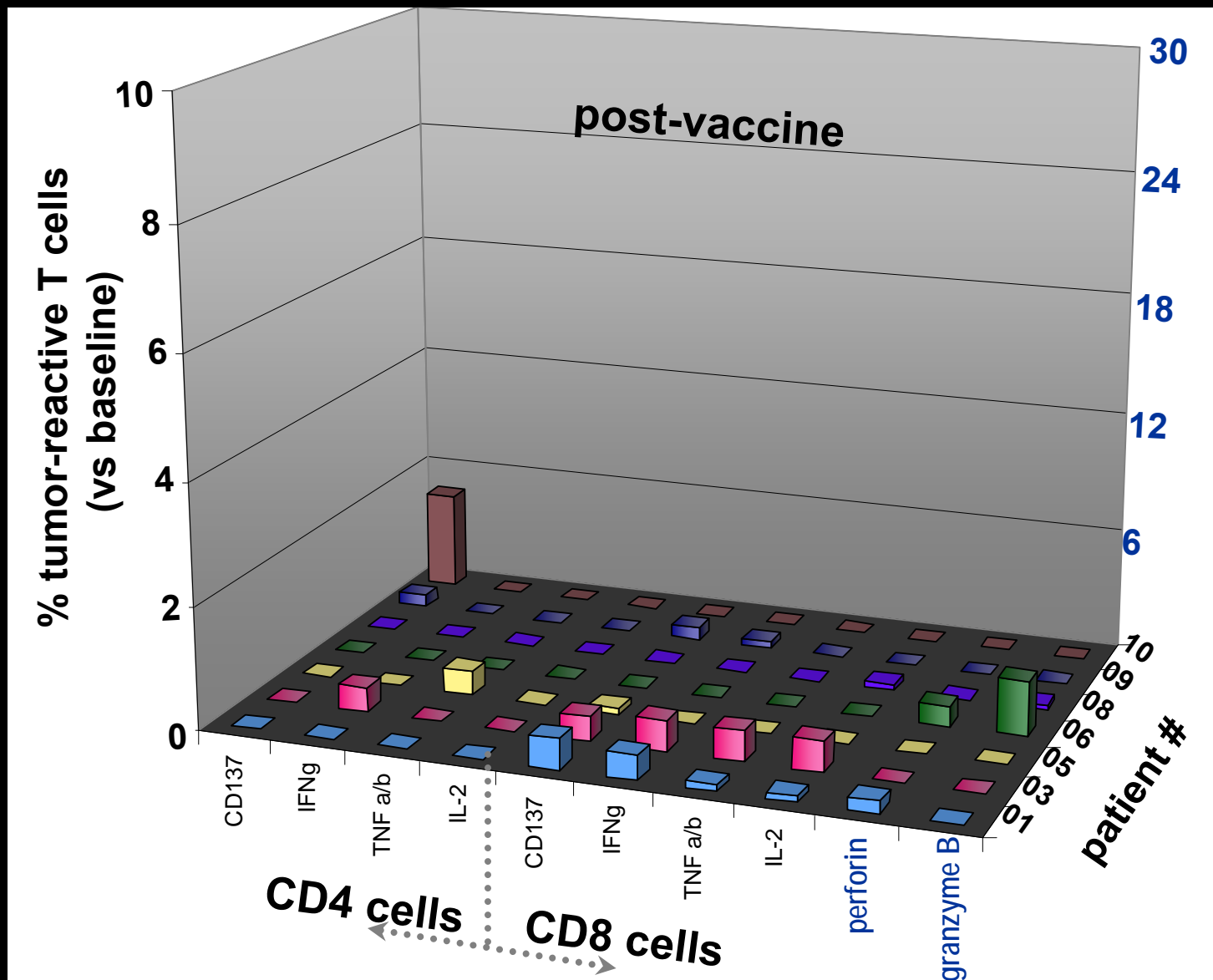
Immunotransplant for MCL: immune response

Induction of tumor-reactive T cells occurs only *after* immunotransplant



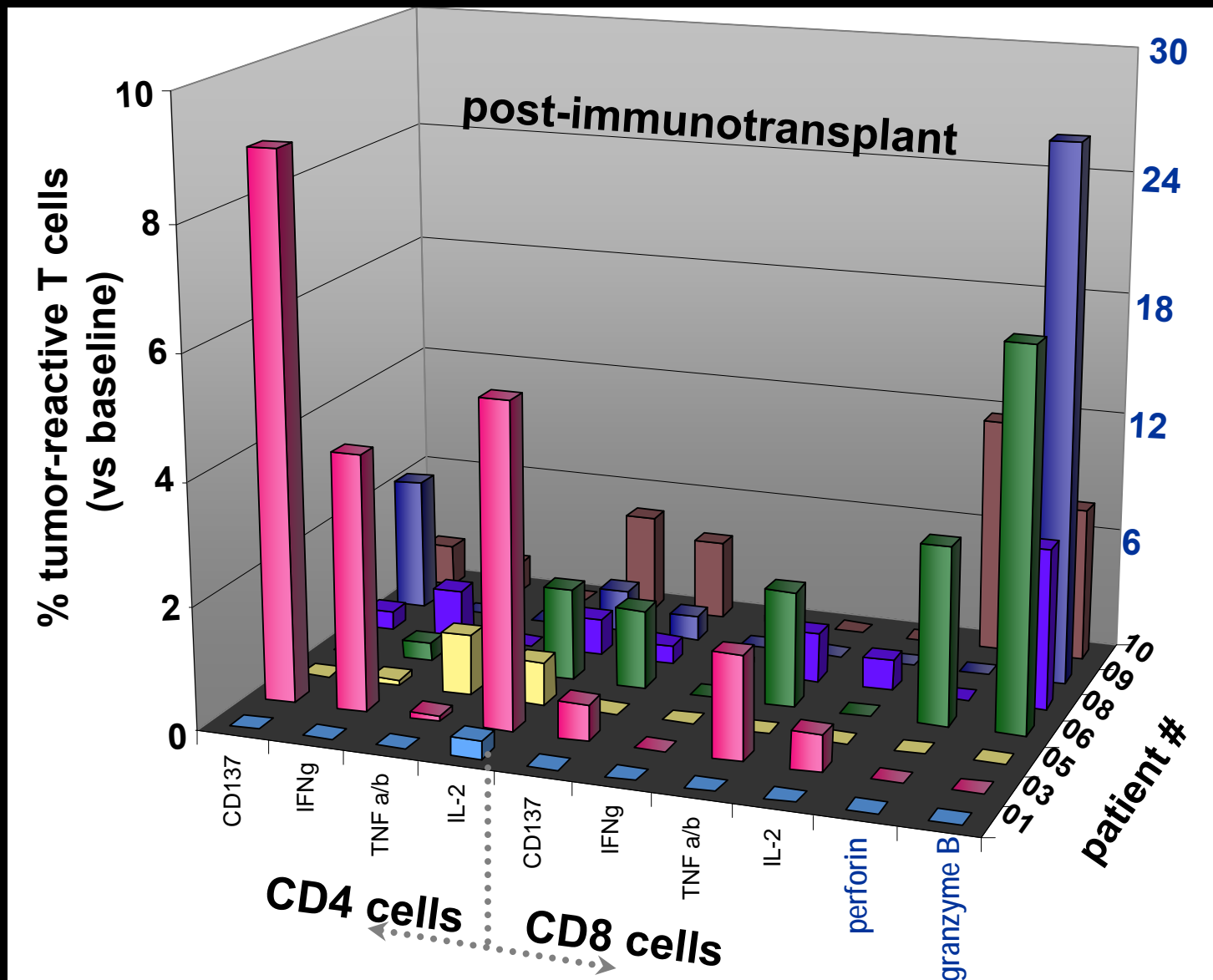
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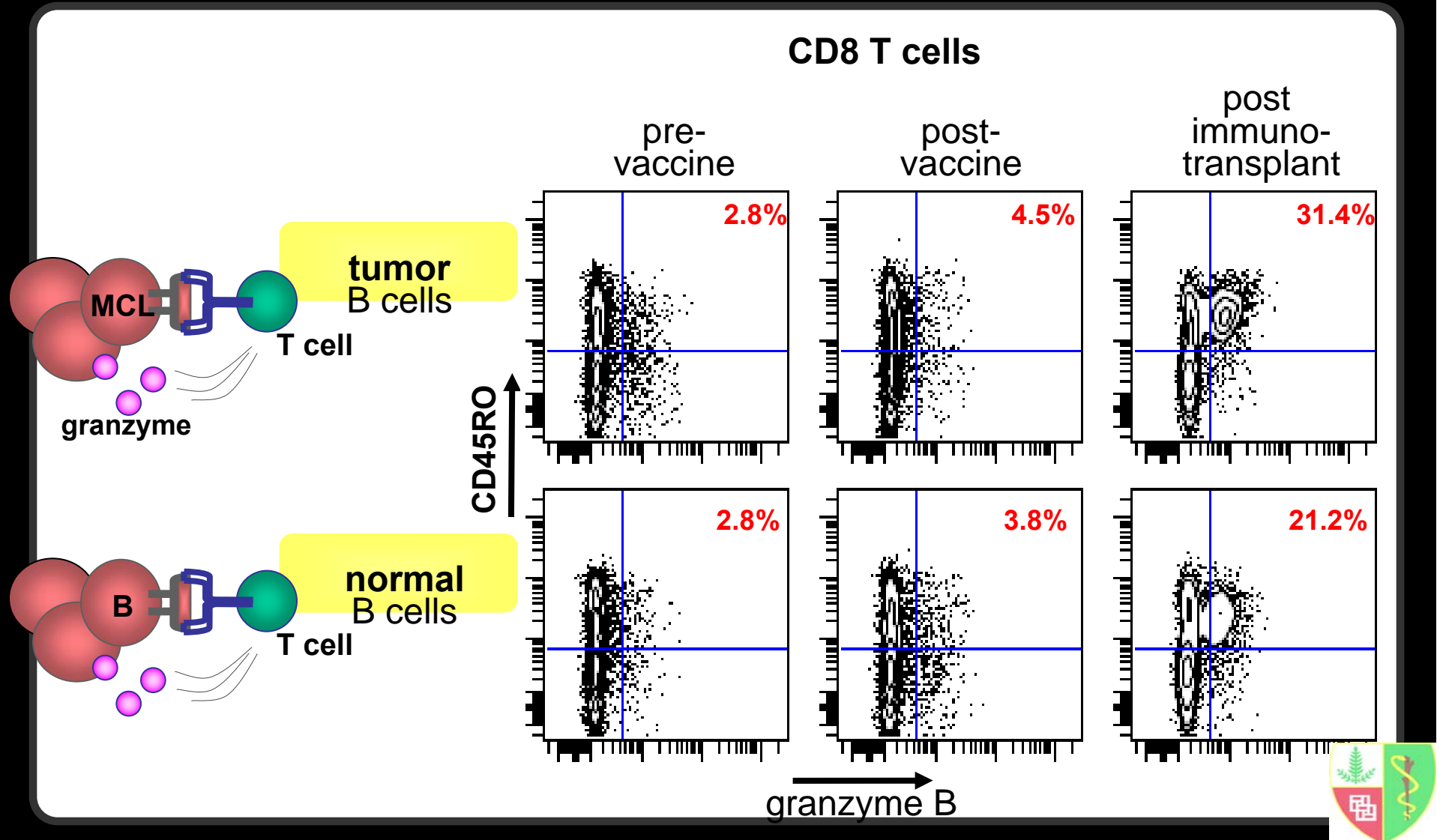
Immunotransplant for MCL: immune response

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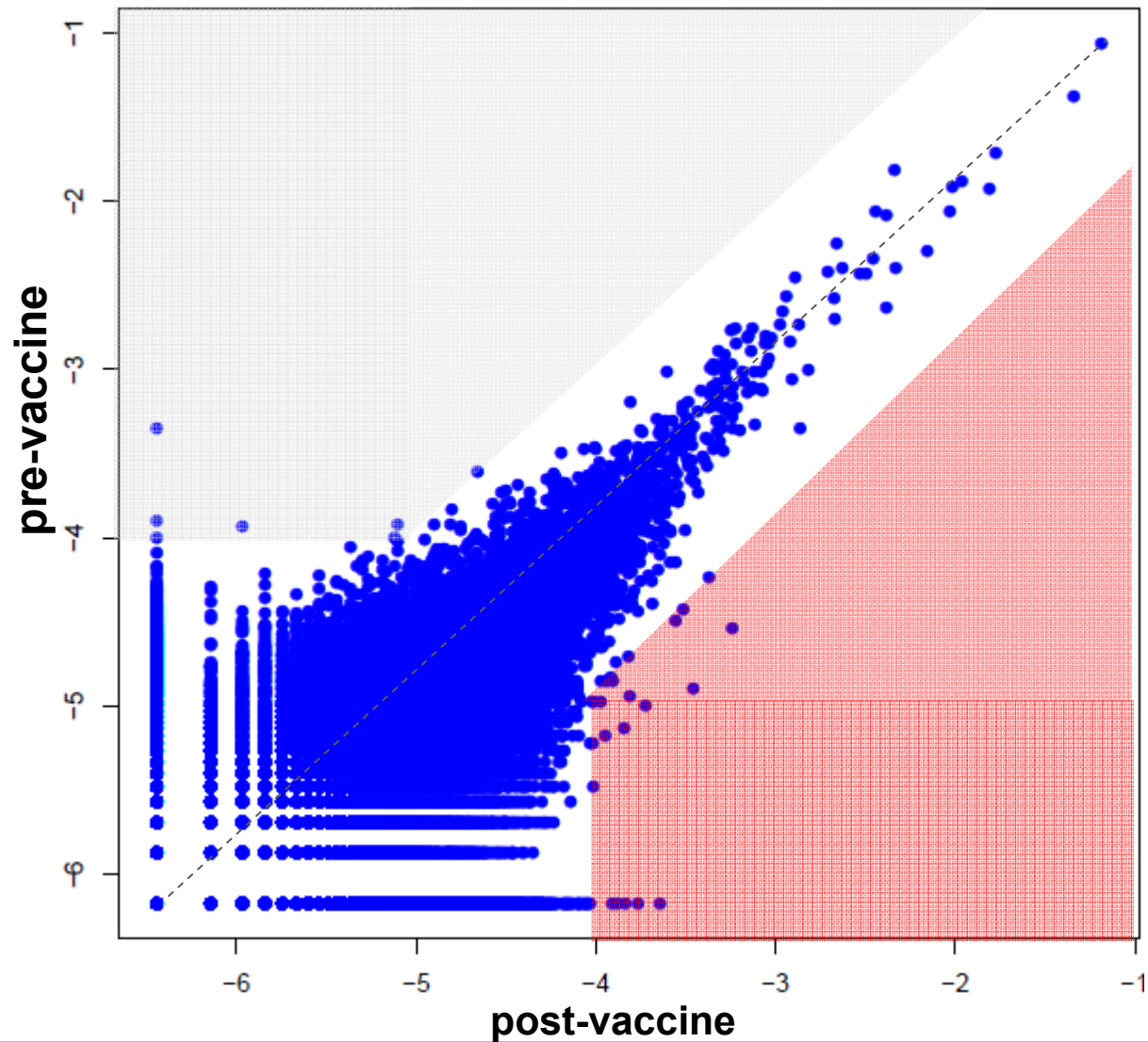


Immunotransplant for MCL: preliminary results

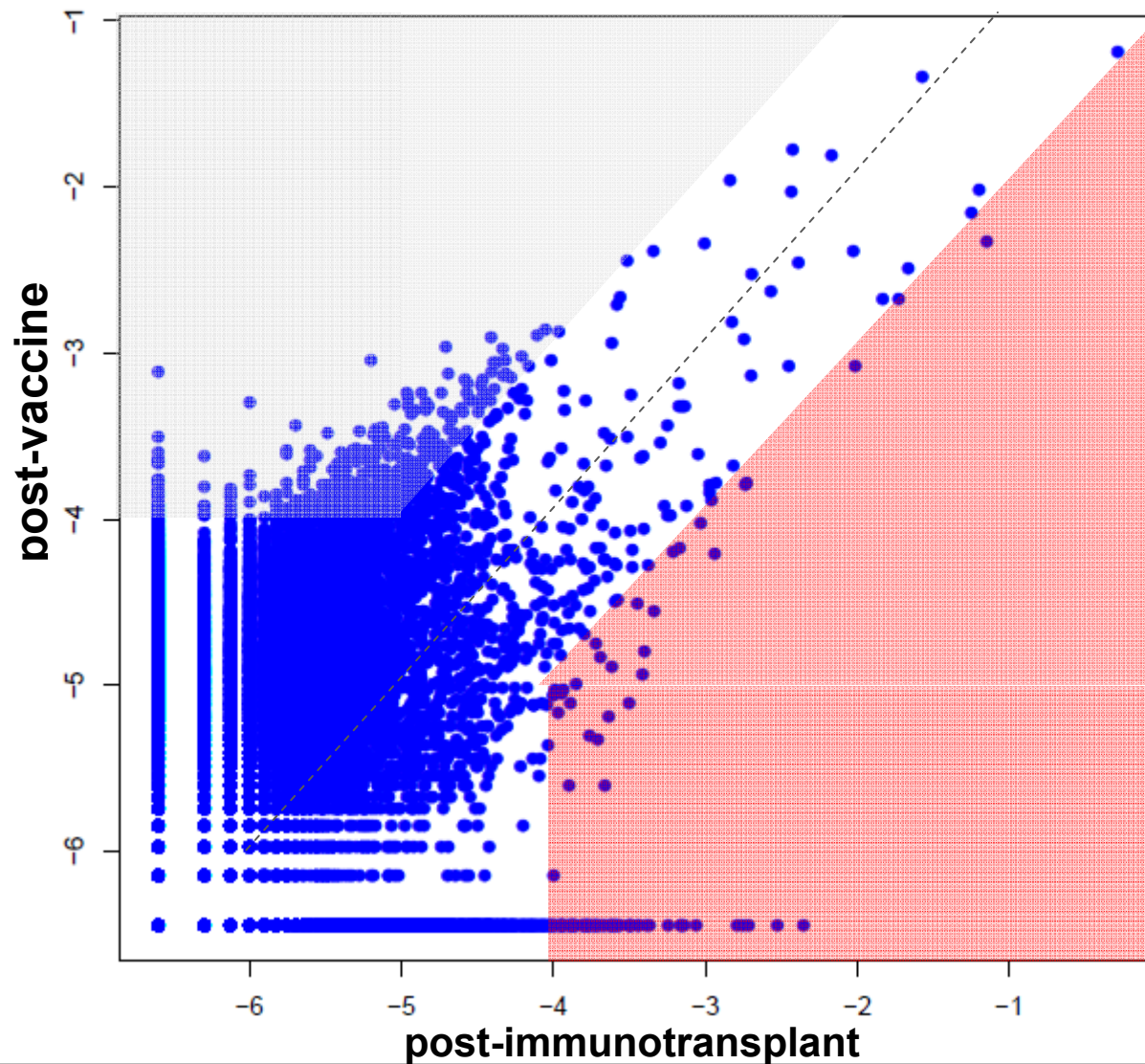
A proportion of tumor-*reactive* T cells are tumor-*specific*



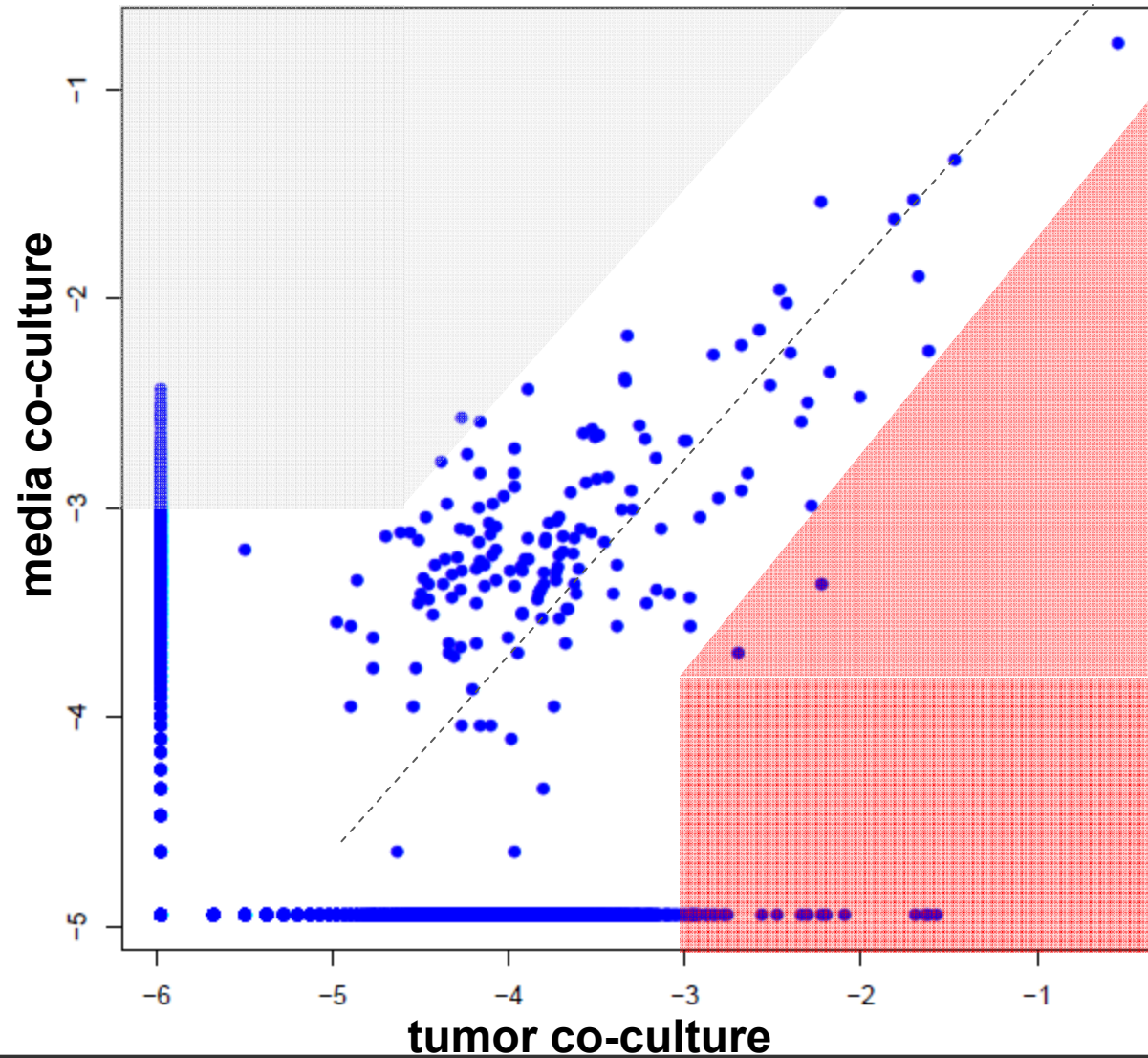
Tracking T cells with TCR β V high throughput sequencing: few T cell clones are amplified by CpG-MCL vaccine



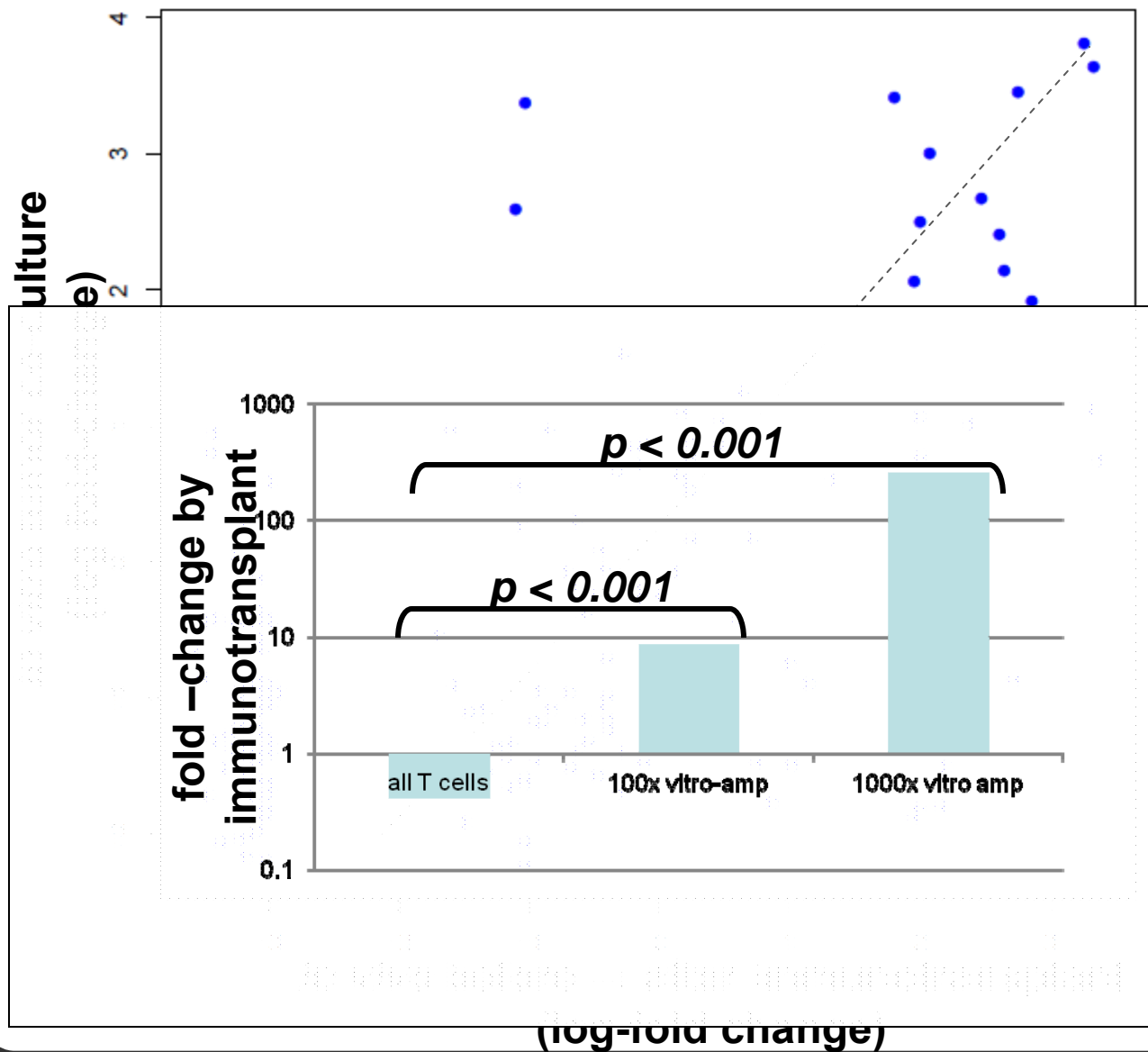
Tracking T cells with TCR β V high throughput sequencing: more T cell clones are amplified by immunotransplant



Tracking T cells with TCR β V high throughput sequencing: some T cell clones are amplified by *in vitro* tumor co-culture



TCR β V high throughput sequencing tumor-reactive T cells are amplified by immunotransplant



Future Directions:

- 1) Assess whether immunotransplant improves the molecular remission rate compared to recent large studies of standard transplant for MCL:

Pott C. et al., *Blood*. 2010 Apr 22;115(16):3215-23.

Geisler CH, et al., *Blood*. 2008 Oct 1;112(7):2687-93.

- 2) Immunotransplant for:

- aggressive NHL, PTCL, Myeloma

- 3) Non-ablative immunotransplant (e.g. fludarabine-based) for:

- Hematologic: low-grade NHL, elderly MCL

- Solid tumor: prostate CA
melanoma



Thanks:

Lymphoma Team:

Ranjana Advani
Holbrook Kohrt

Transplant Team:

Robert Negrin
Kevin Sheehan
BMT Lab

Immune Studies

Debra Czerwinski
Etelka Gabriel

High Throughput Sequencing

Malek Faham
Victoria Carlton
(Sequentia Inc.)

Biostatistics

Phil Lavori

Funding:

Lymphoma Research Foundation
NCI K99/R00 'Pathway' Award

Mentorship:

Ronald Levy
Shoshana Levy

PF-3512676

Pfizer Inc.

All of the patients on:

NCT00185965

NCT00880581

NCT00490529

SEQUENTA



extra

T_{reg}-inducing tumors: inverse correlation with outcome

