

Determining Potency of Immunologic Therapy:

Assessing Dendritic Cell Vaccines

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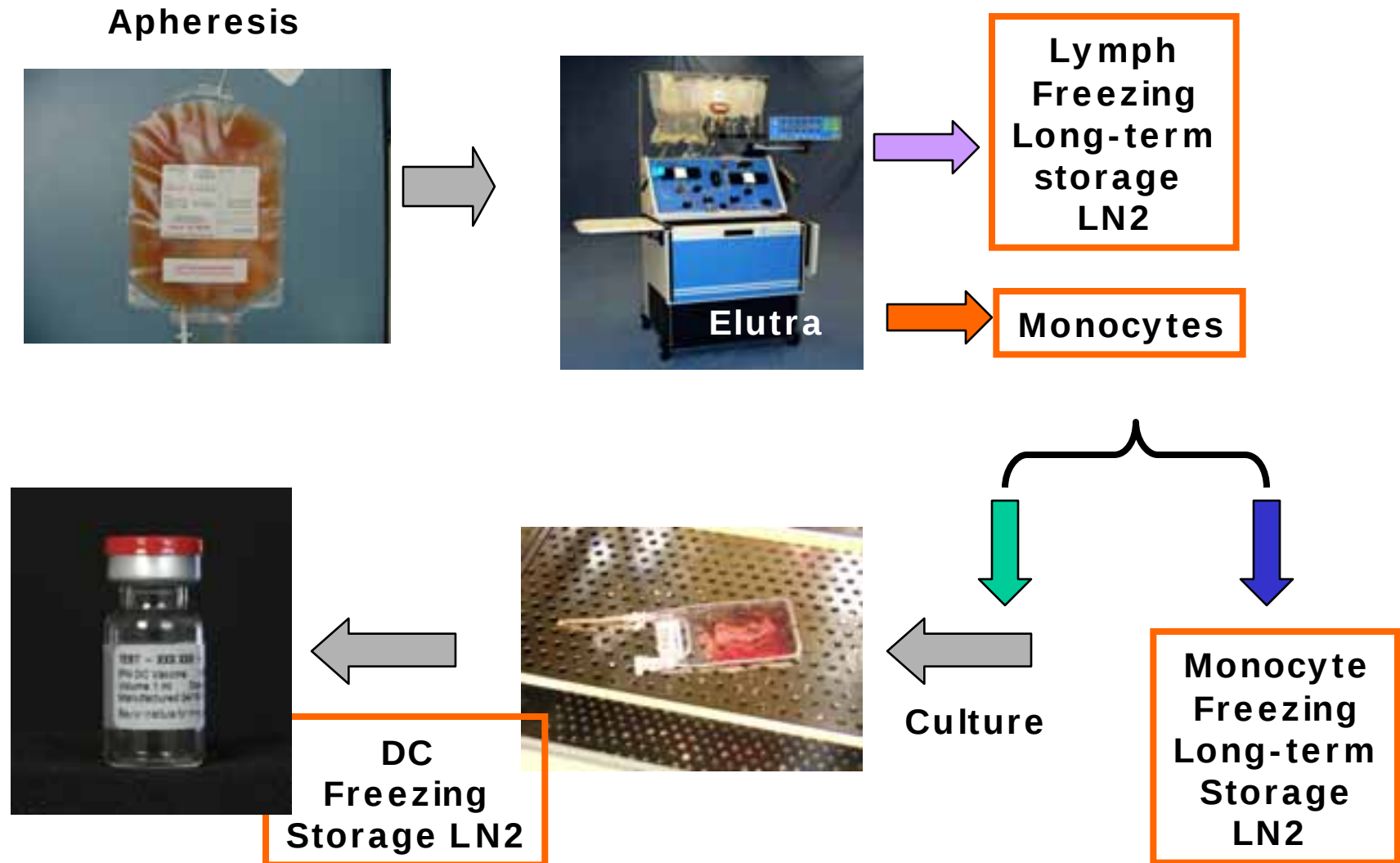
**Baylor Institute for Immunology Research, Center for Human Vaccines, Dallas
Mount Sinai School of Medicine, Dept of Cell and Gene Therapy, New York**

Assessing Dendritic Cell Vaccines:

**Ten years of experience with
ex vivo generated DC vaccines**

- **cGMP Vaccine manufacture core**
- **cGMP Cell and Tissue Procurement Core**
- **GLP Immunomonitoring Core including
polychromatic flow and genomics**

Baylor closed system for DC vaccines



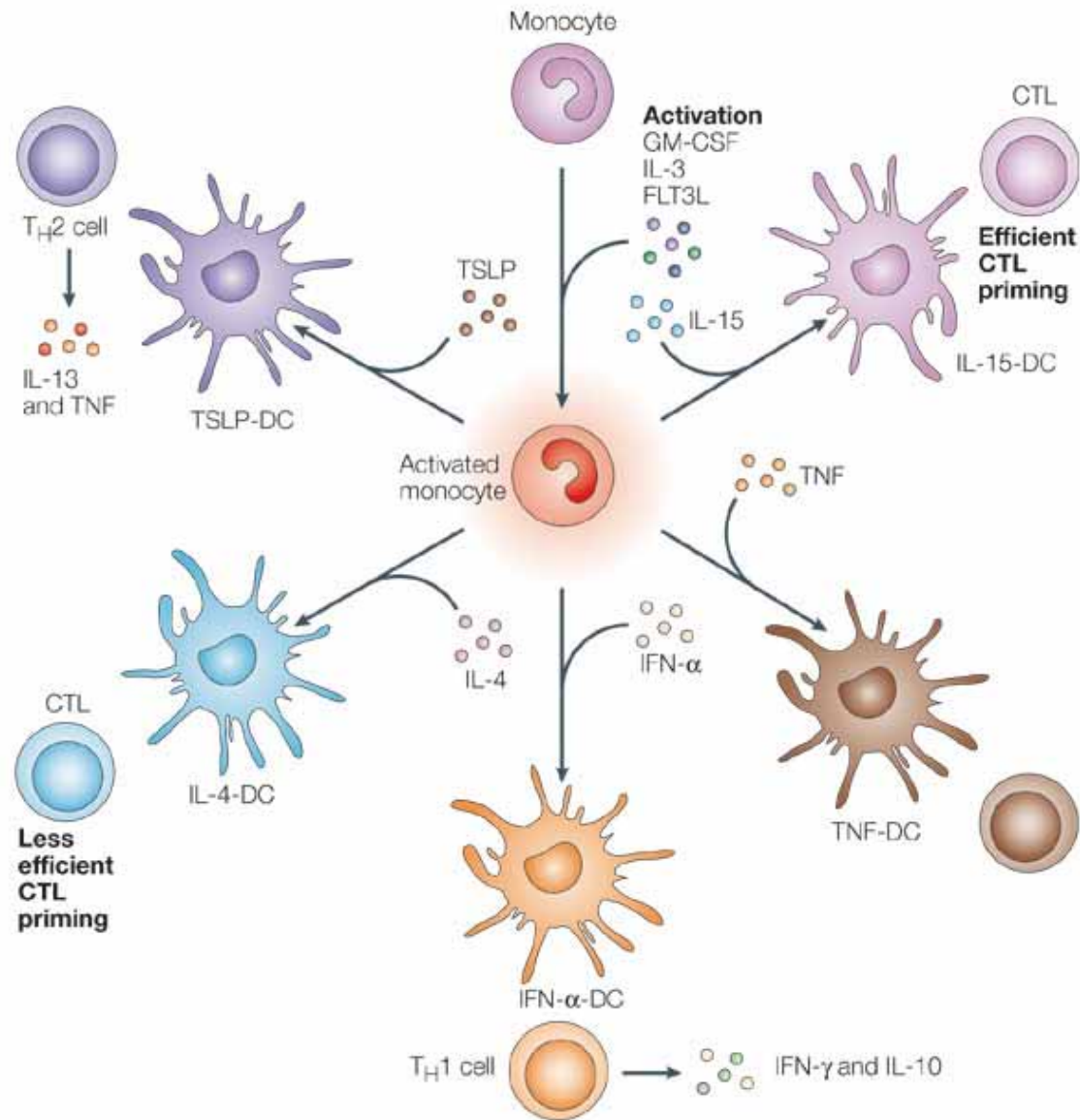
Roberts, Burkeholder, Taquet, Walters, Finholt

Assessing Dendritic Cell Vaccines:

**Ten years of experience with
ex vivo generated DC vaccines**

- **Immune and clinical outcomes**
- **Assessing potency of vaccine products**
- **Predictive biomarkers of vaccine efficacy**

Distinct DC subsets induce distinct type of immune responses



Banchereau & Palucka, 2005

DENDRITIC CELL MATURATIONS

The control point of cellular immunity

Microbial Products:

TLR, NOD and lectin ligands
LPS, DNA, RNA

Tissue damage:

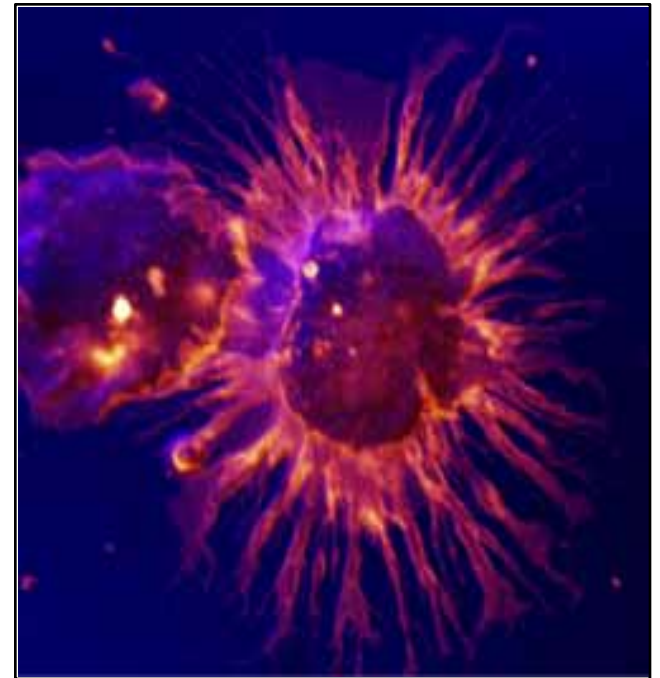
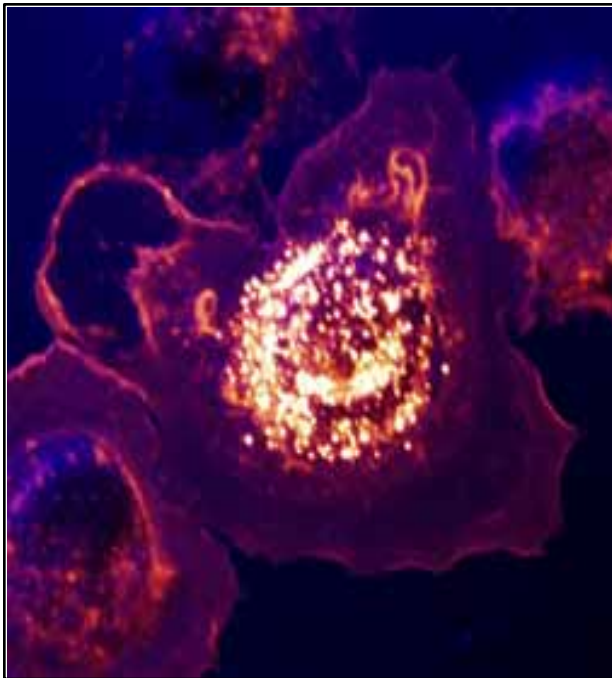
Uric acid, HSPs

Cells of innate immunity

pDC, NK, NK T,
Neutrophils
IFN, TNF, GM-CSF

Cells of adaptive immunity

T and B cells
CD40 L, RANK



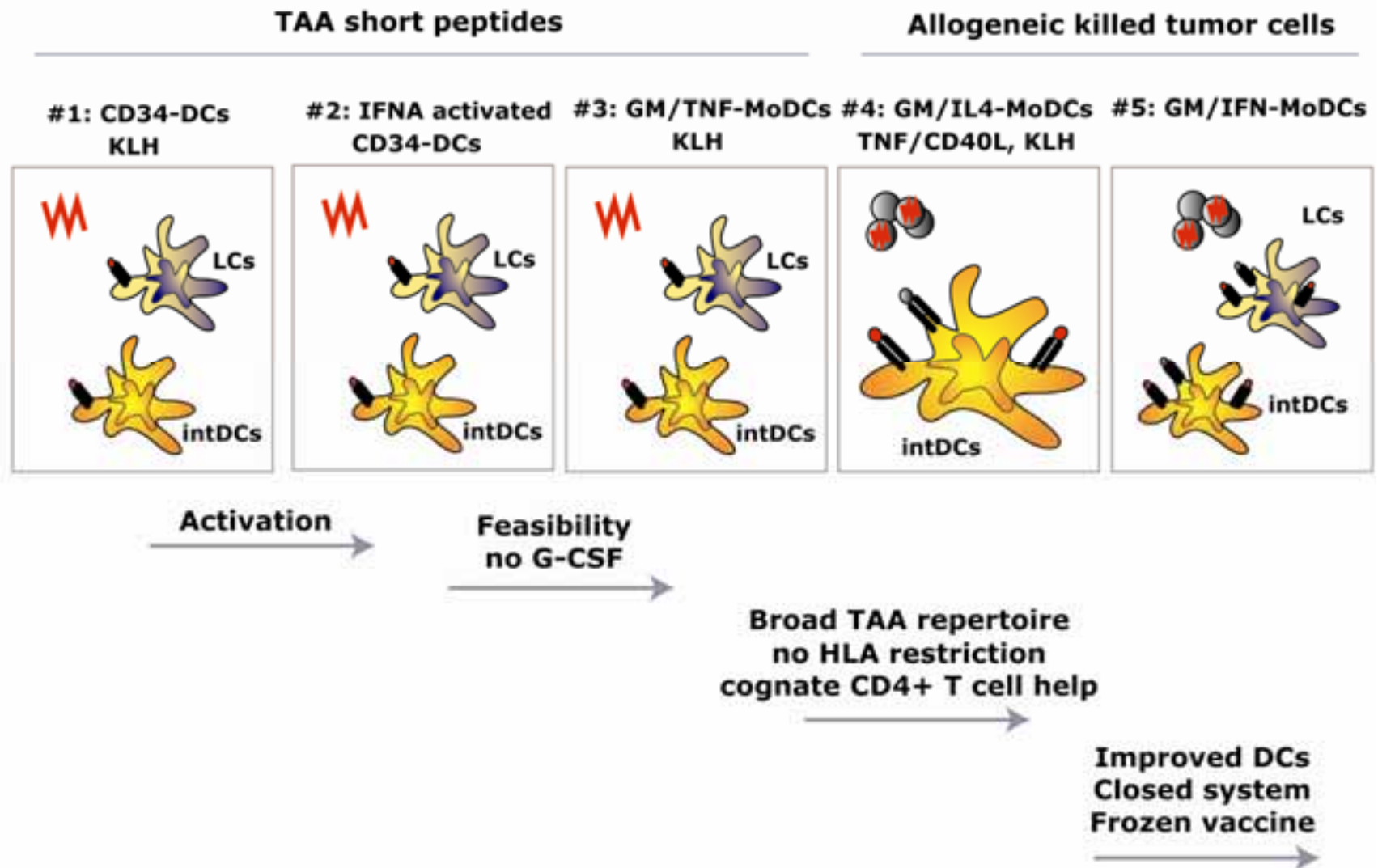
Immature DC



Mature DC

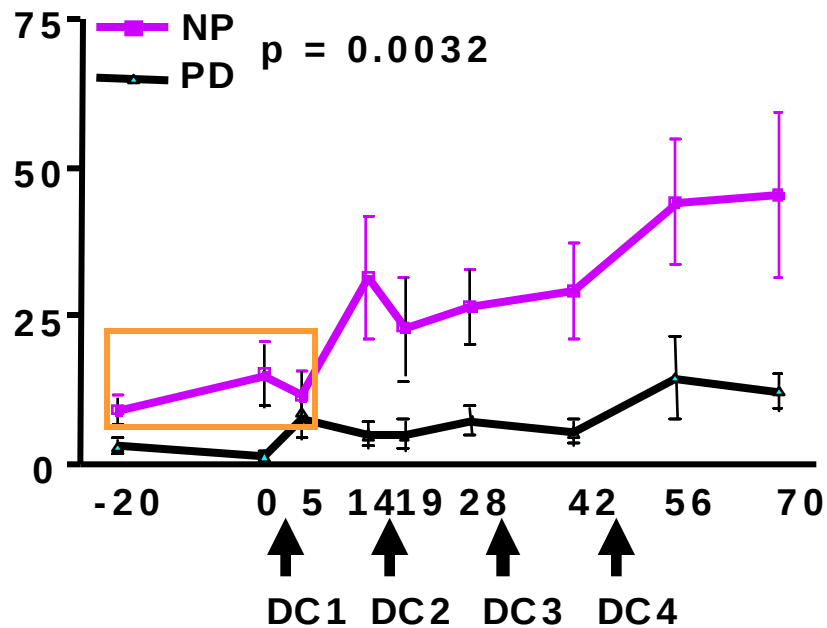
Steinman & Mellman

BIIR DENDRITIC CELL VACCINE TRIALS: FIRST GENERATION TRIALS IN METASTATIC MELANOMA



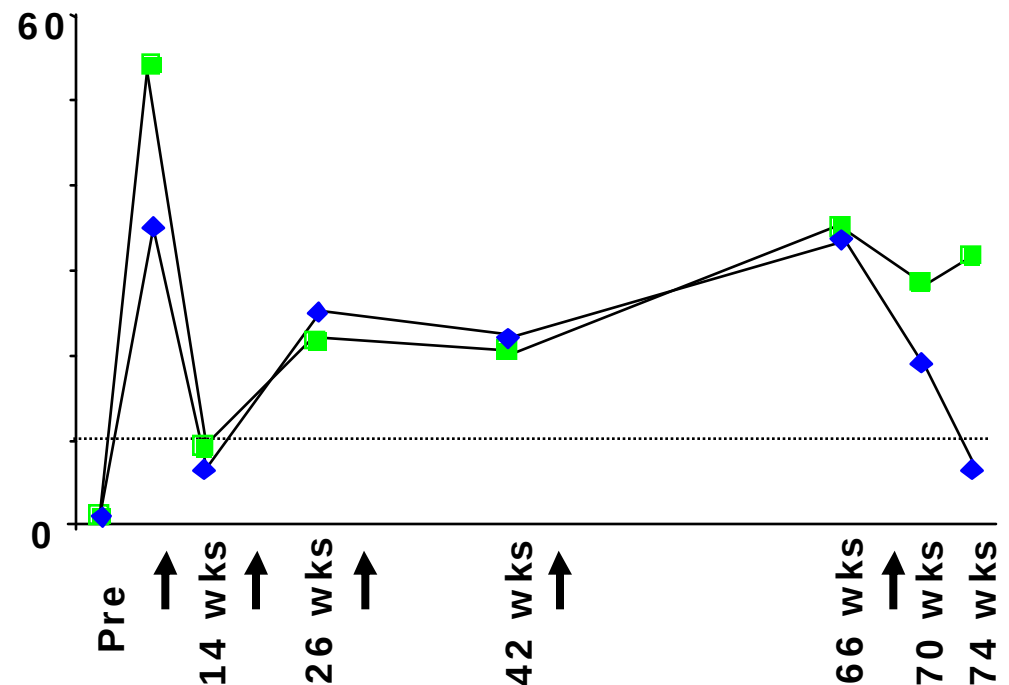
Peptide & KLH -pulsed CD34-DCs

Progressive patients do not mount TAA-specific responses



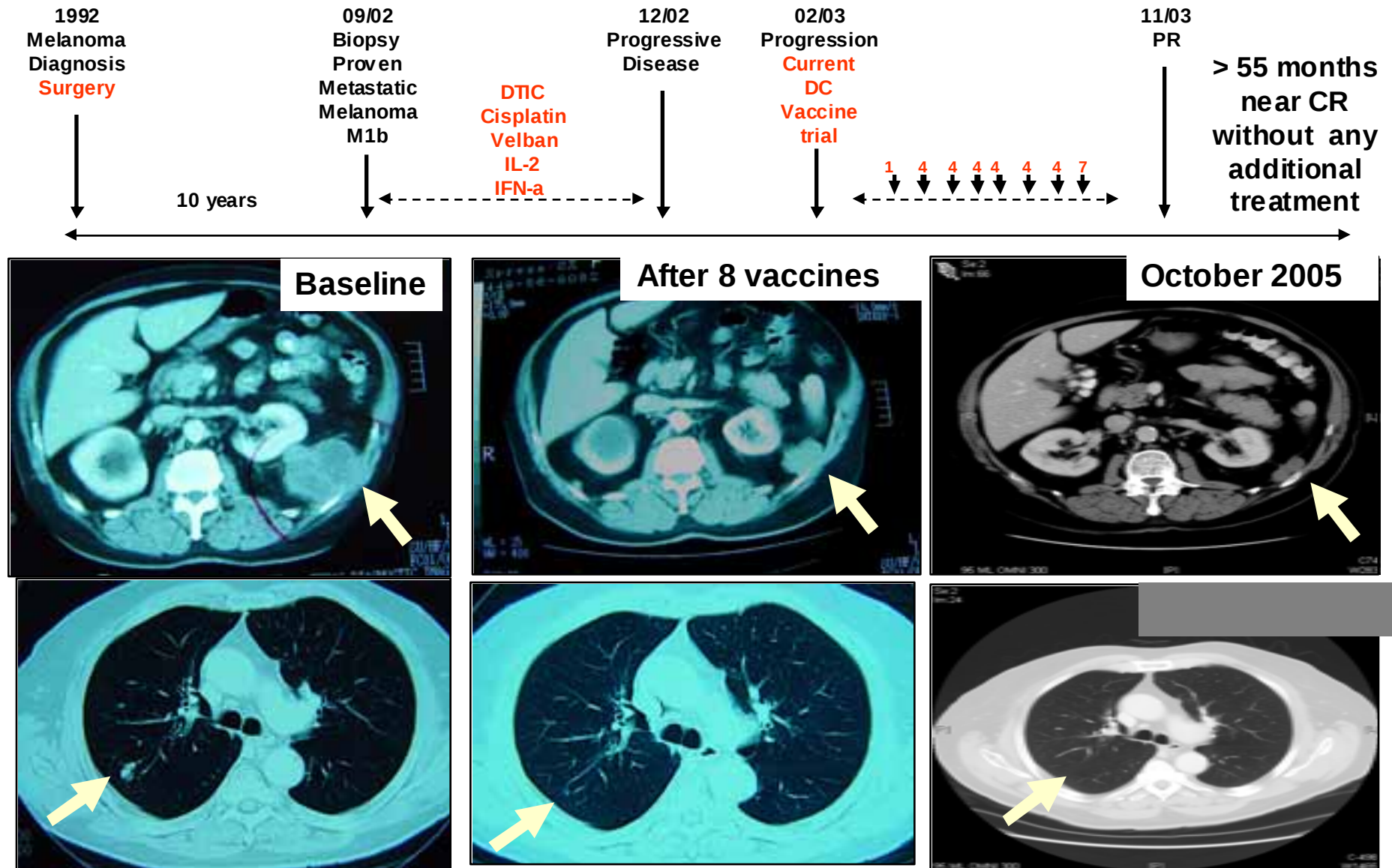
Melanoma-specific
ELISPOTS / 2×10^5 PBMC

Boosting vaccinations can maintain long-lived melanoma-specific memory T cells

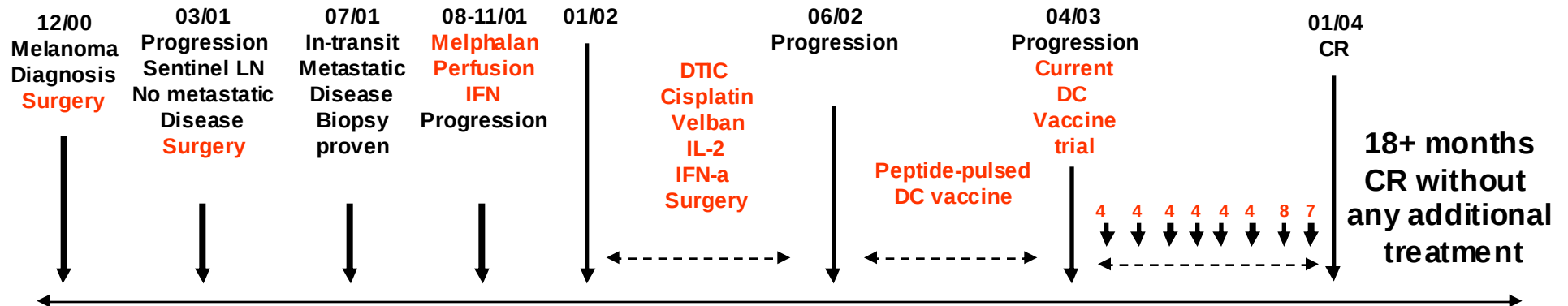


Palucka et al. J Immunother 2003
Palucka et al J Immunotherapy 2005

DC vaccine loaded with killed allogeneic melanoma cells can induce durable clinical responses (2+1/20 patients)

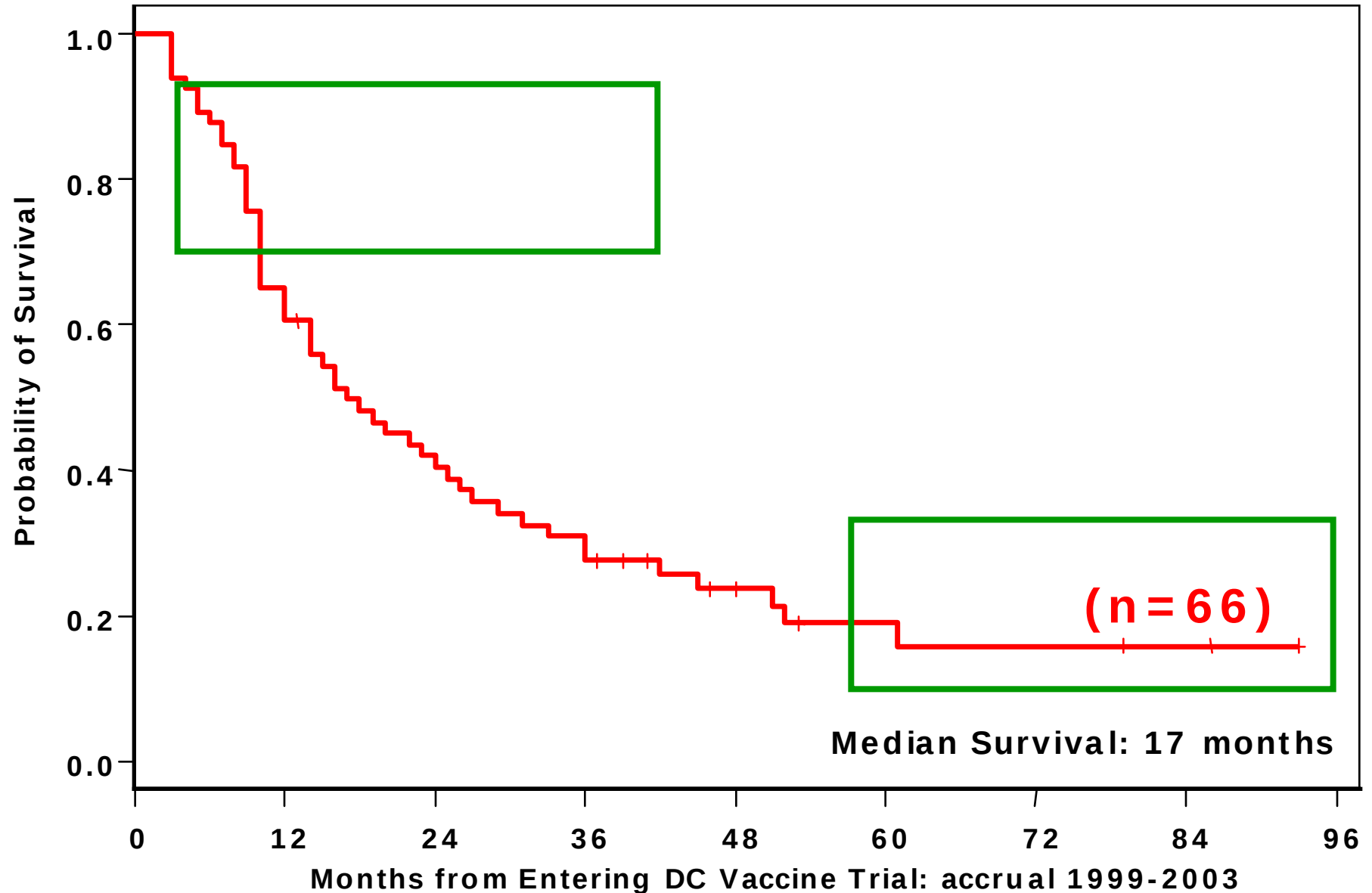


DC vaccine loaded with killed allogeneic melanoma cells can induce durable clinical responses (2+1/20 patients)

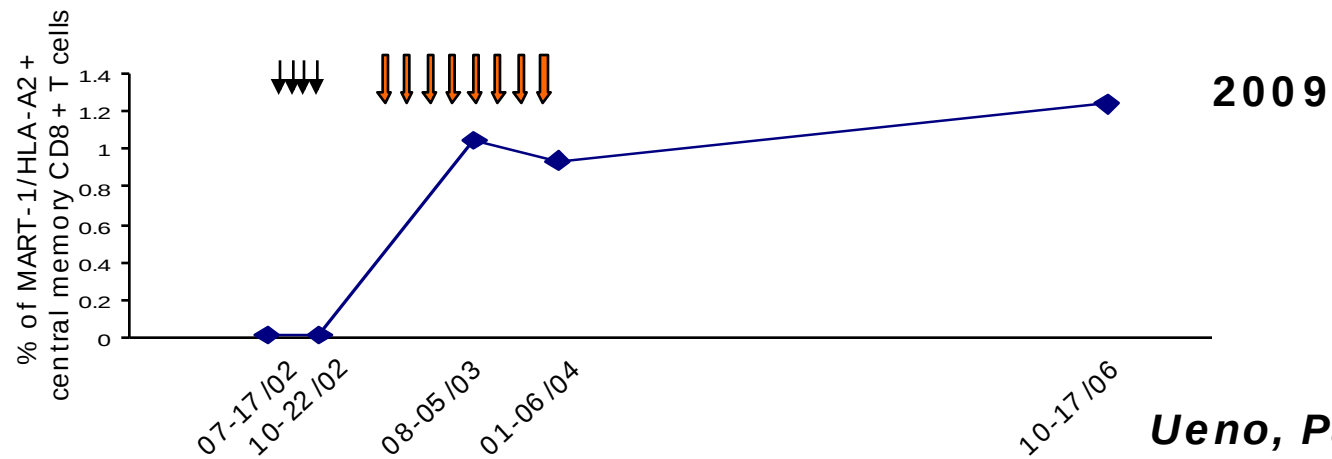
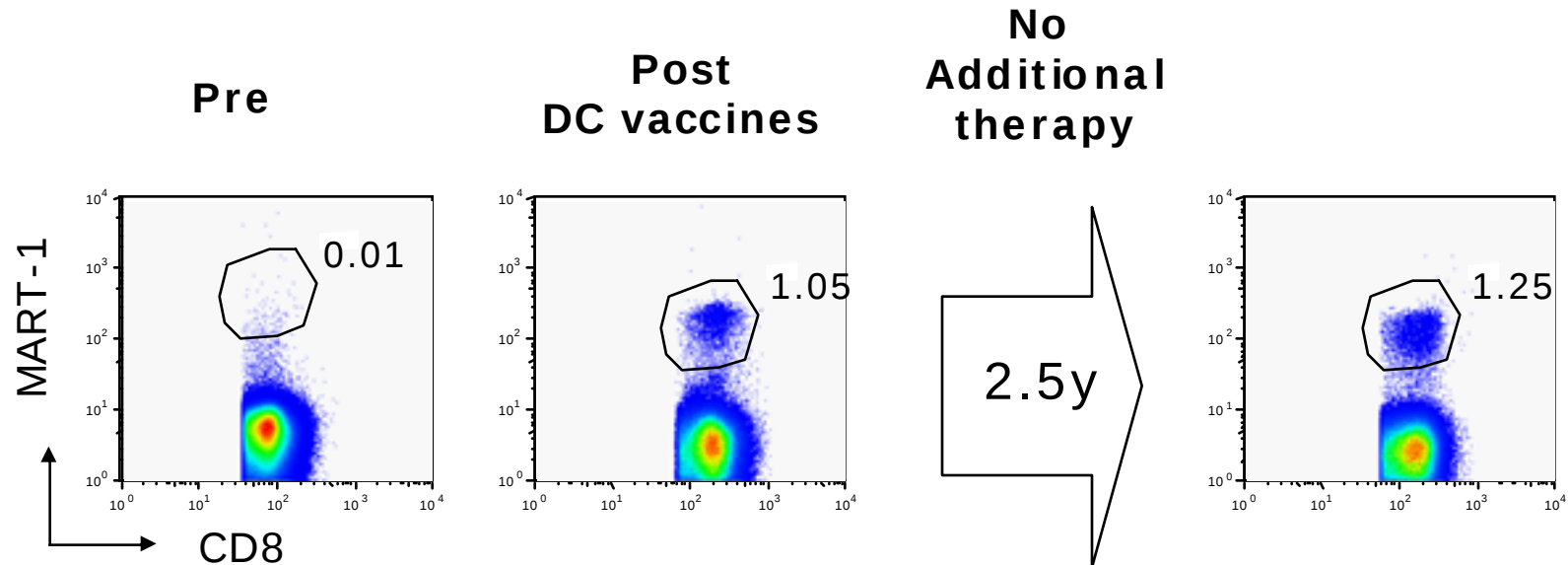


Palucka et al. J Immunotherapy 2006

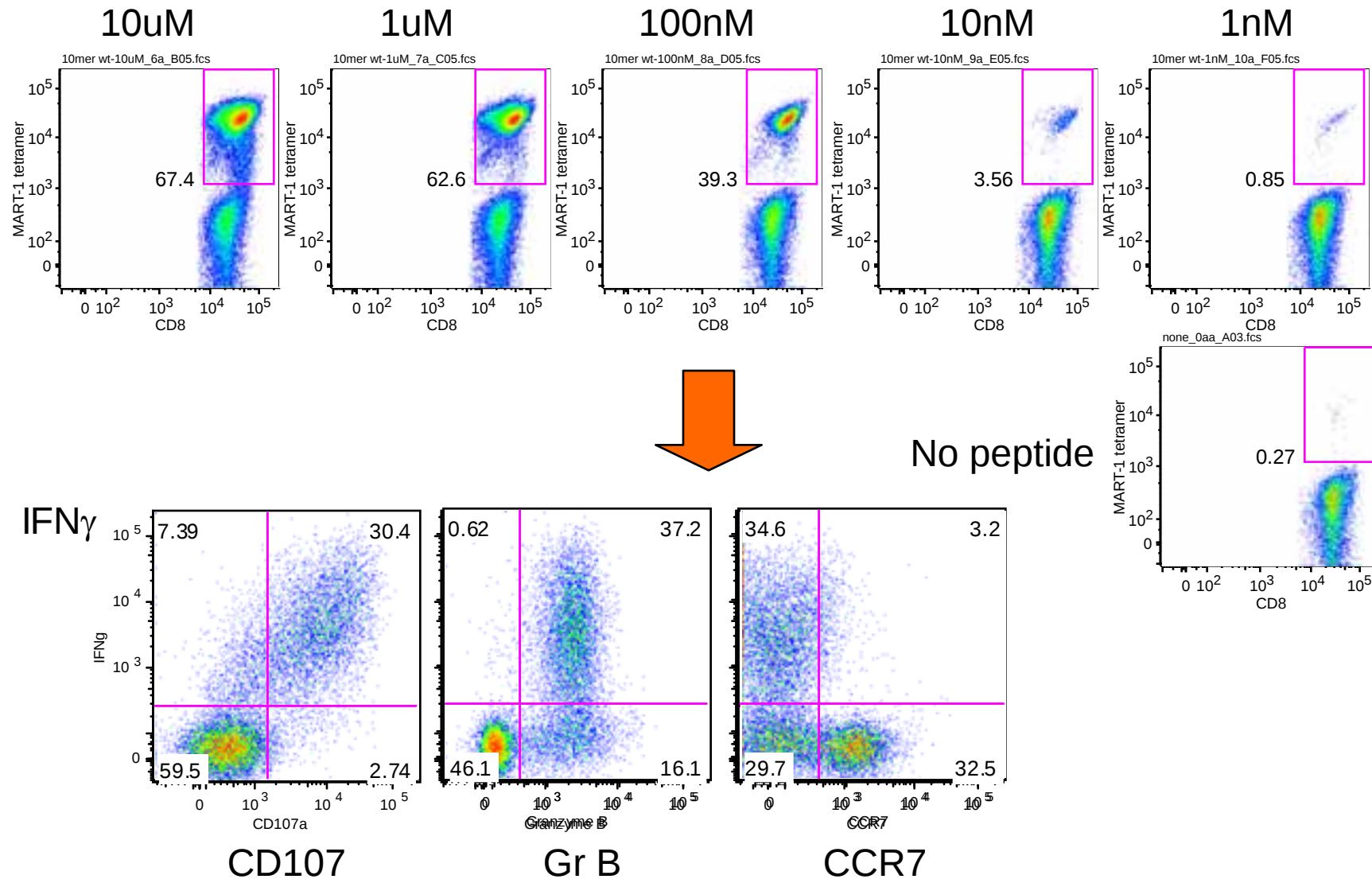
Clinical Responders and Long term survivors: the key to design of efficient therapeutic cancer vaccine



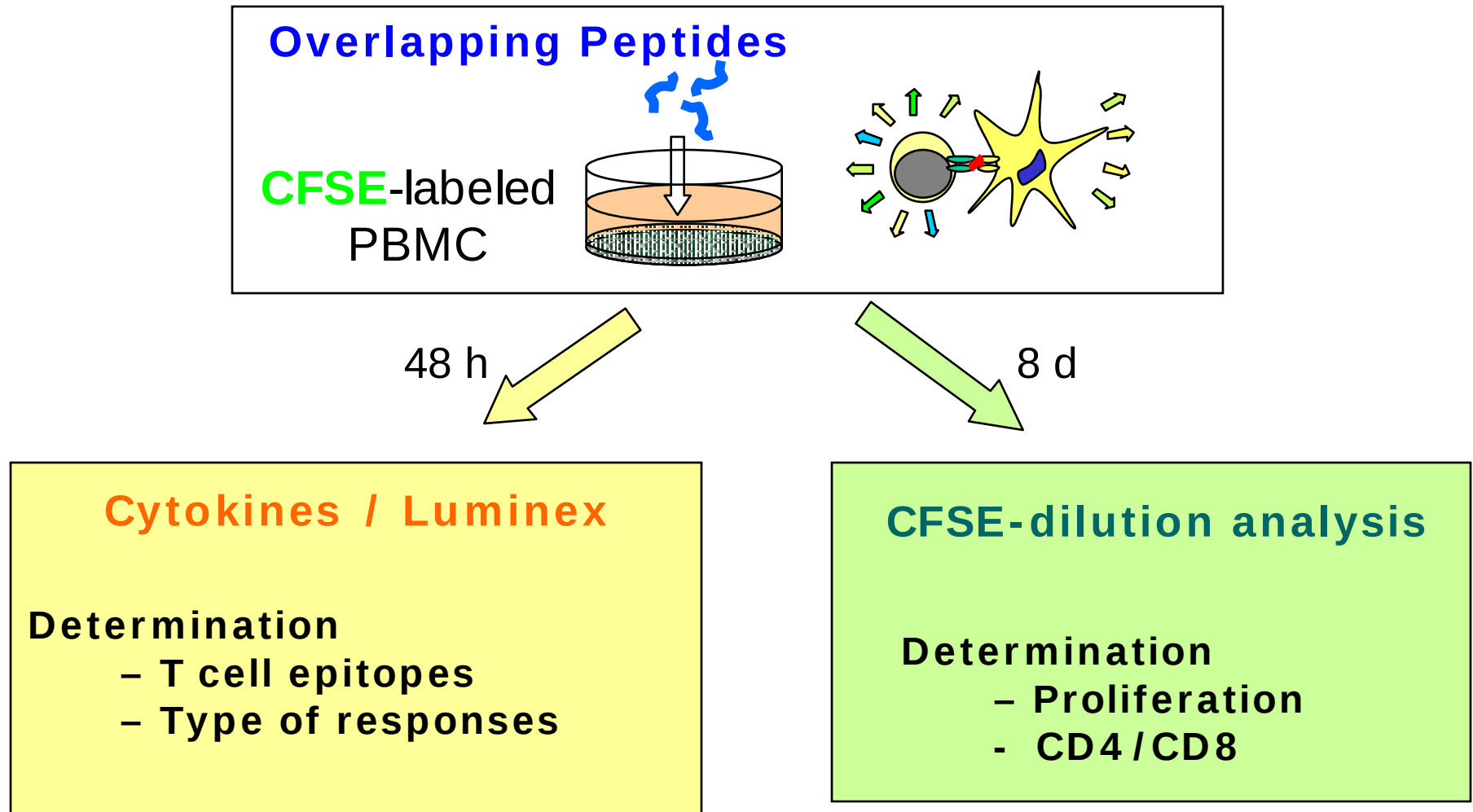
DC vaccines can expand long-lived melanoma-antigen specific CD8⁺ memory T cells



DC vaccines can expand high avidity polyfunctional MART-1 melanoma-antigen specific CD8⁺ T cells

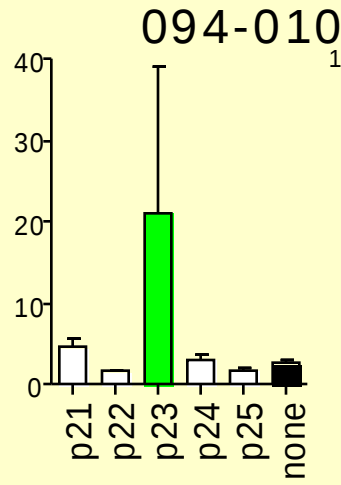
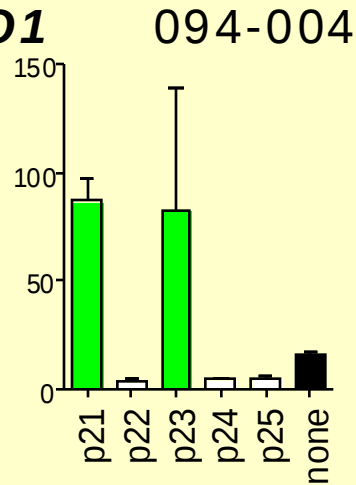


EPIMAX: Assessment of Antigen-specific T cell repertoire ex vivo

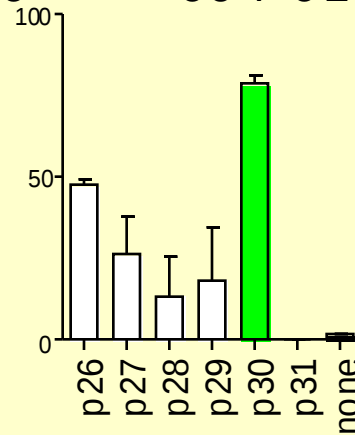


Patients with metastatic melanoma have circulating melanoma antigen-specific IL10-producing T cells at baseline

NY-ESO1

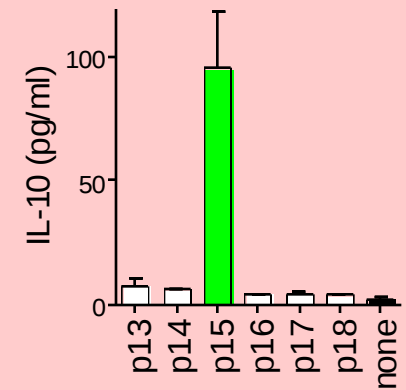


094-017

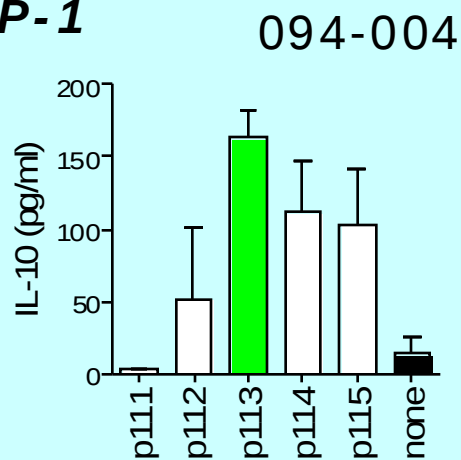


Survivin

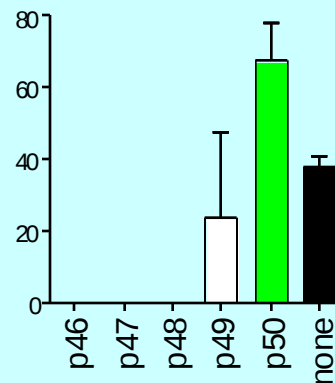
094-004



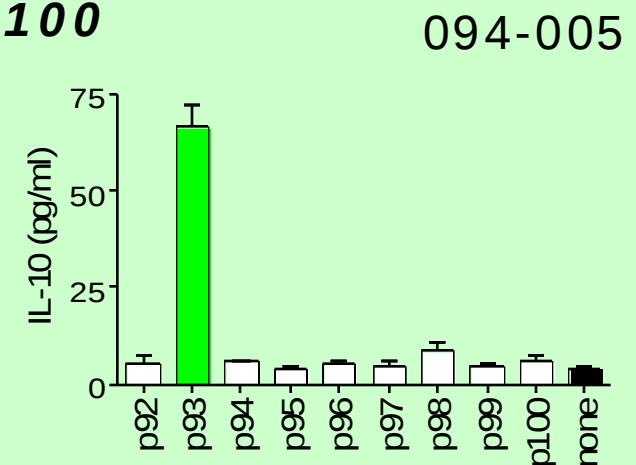
TRP-1



094-009

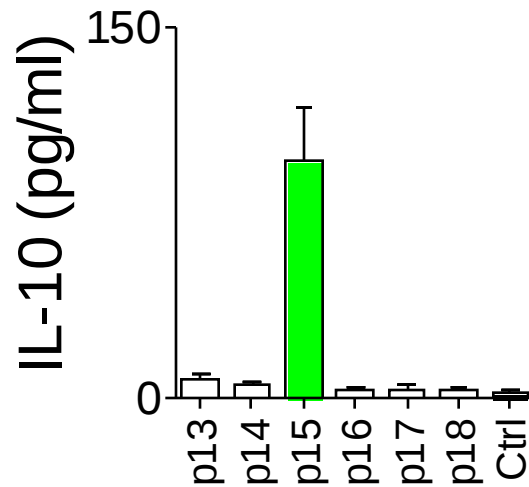


gp100

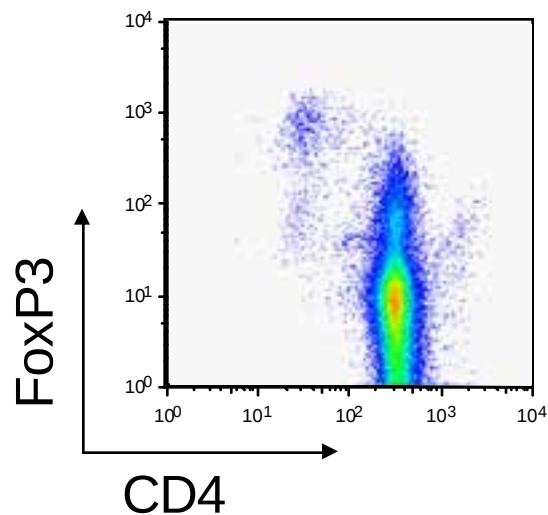


Patients with Metastatic Melanoma Display Circulating Tumor Antigen-specific T regs

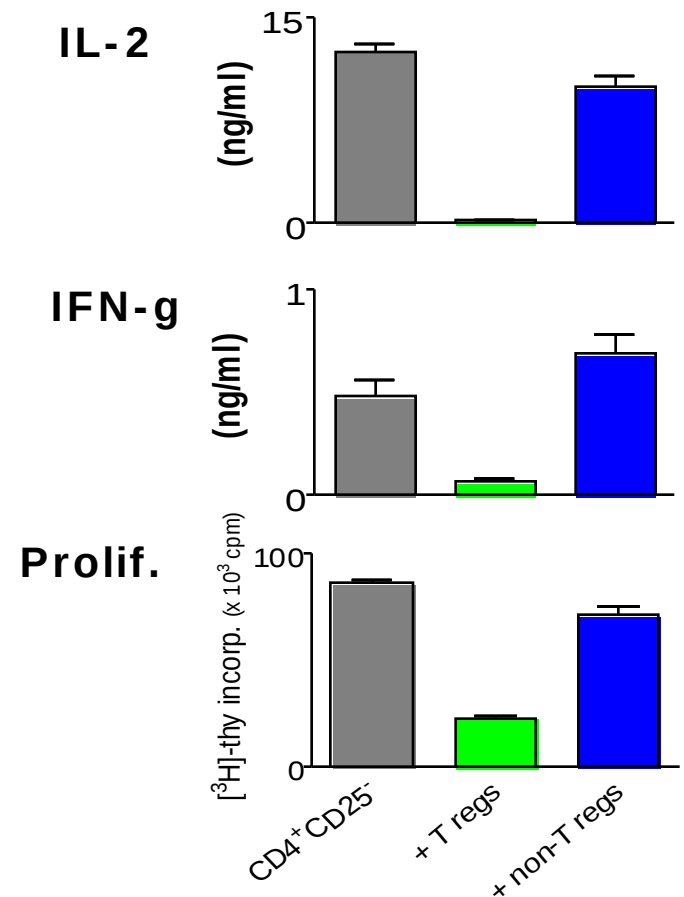
Determination of IL-10-inducing peptide



Proliferation of peptide-specific T regs



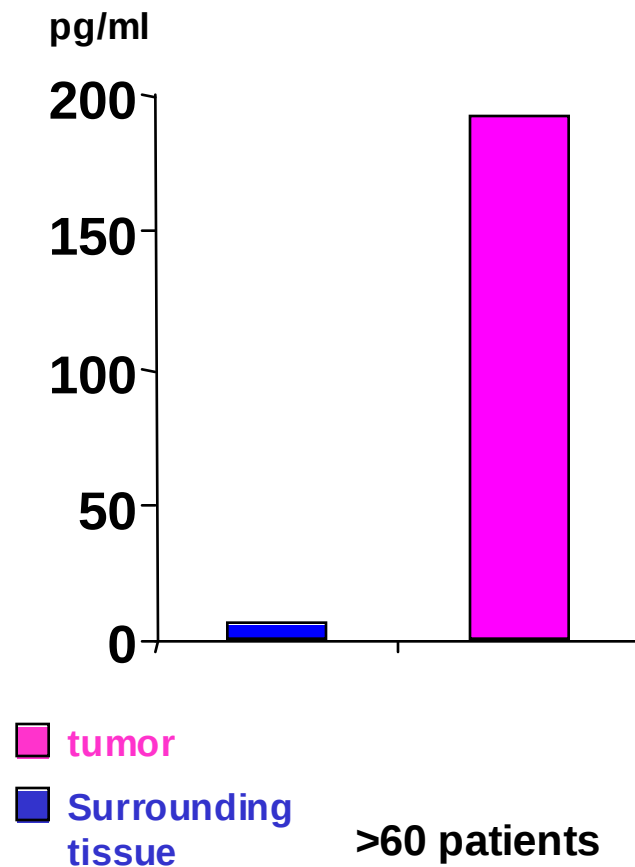
Suppressive function of specific T regs



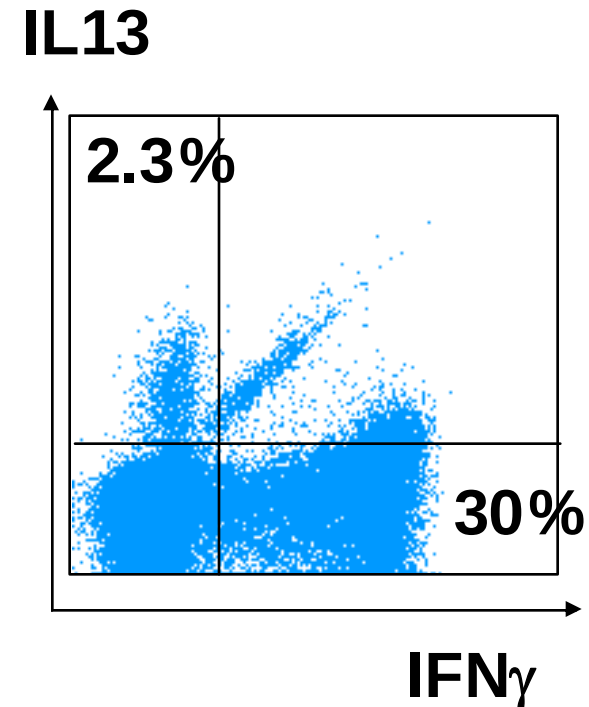
Vence et al. PNAS, 2007

Breast cancer tumors are infiltrated by CD4⁺ T cells secreting IL-13

IL-13 in tumor supernatant



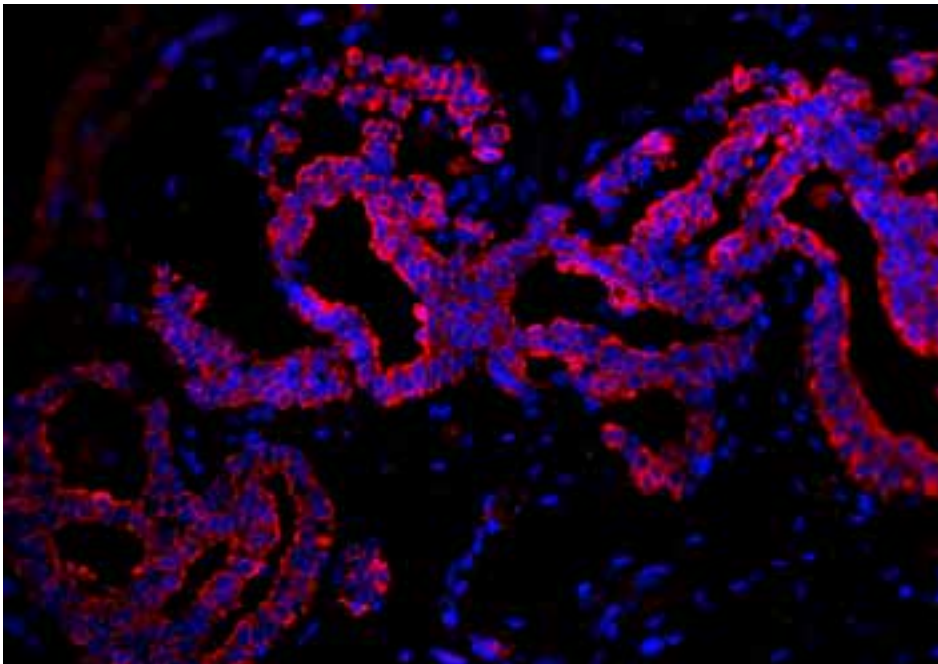
IL-13⁺ CD4⁺ T cells



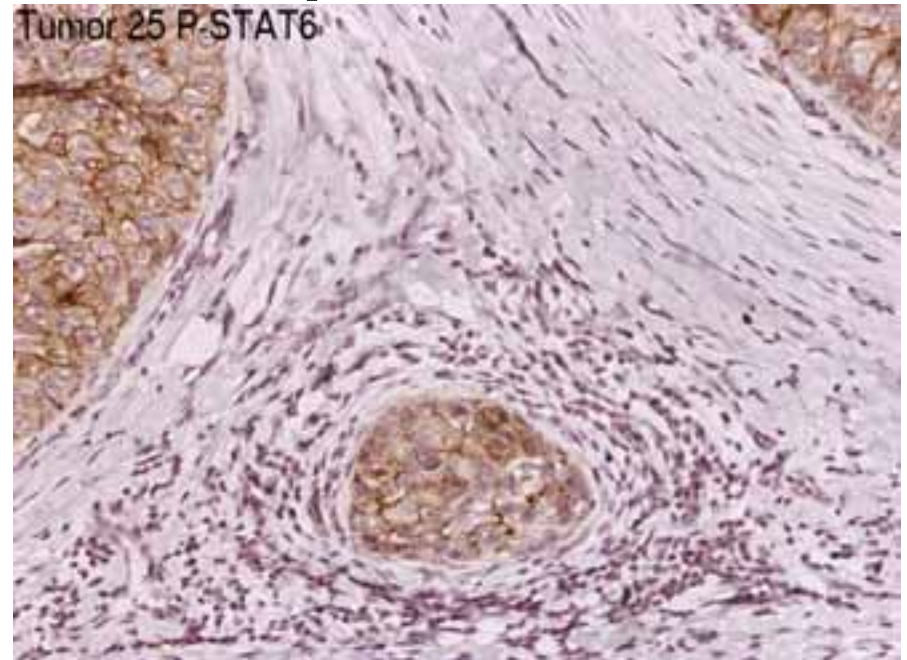
Aspord et al J Exp Med 2007

Breast cancer cells show IL-13 staining and display an IL-13 signature (pSTAT6)

IL-13



pSTAT6



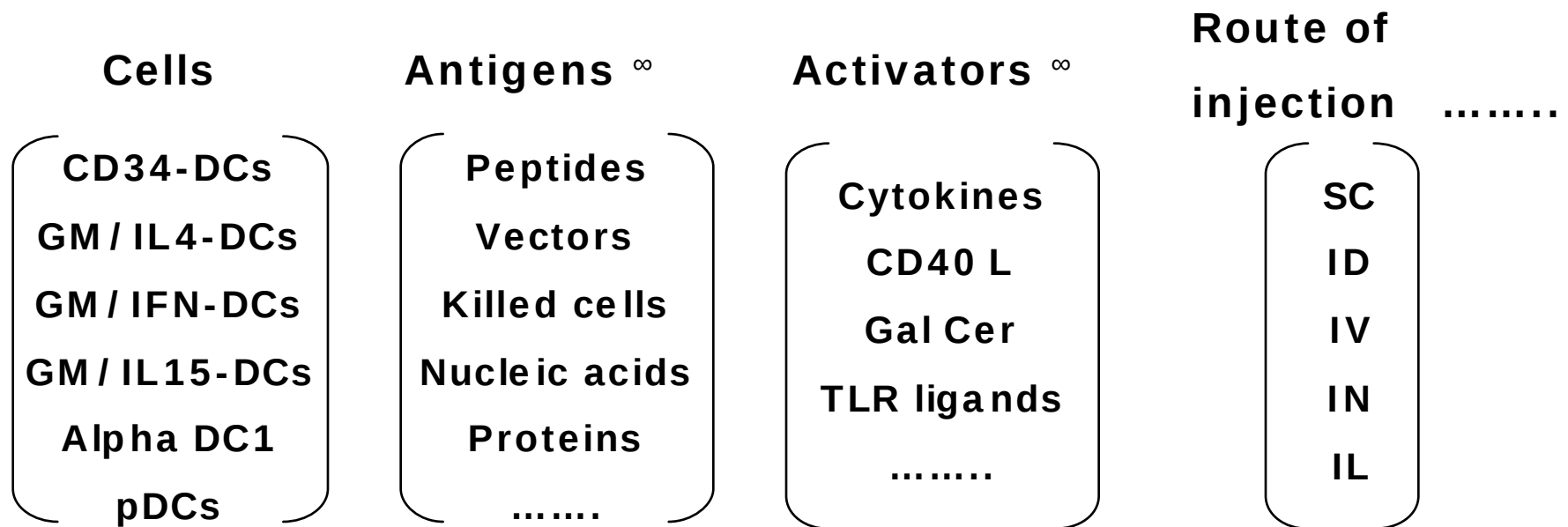
Aspord et al. J.Exp.Med. 2007 Vol.204: 1037

Assessing Dendritic Cell Vaccines:

- **Immune and clinical outcomes to define biomarkers of efficacy:**
 - **Which patient populations to assess immunogenicity:**
MRD vs metastatic disease

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Assessing Dendritic Cell Vaccines: Multivariate analysis



**Mechanism / Infrastructure
for analysis from many trials
to draw statistically meaningful conclusions**

Thanks to our patients

**SUPPORT: BUMC FOUNDATION, SAMMONS CANCER CENTER,
NCI, NIAID, INSERM, ANRS,**

Dr M. Ramsay

- **Vaccine:**

**S. Burkeholder
M. Leogier
F. Kerneis
M. Michnevitz
J. Finholt-Perry**

- **Cell and Tissue Core:**
L. Walters

- **cGMP Lab:**
**L. Roberts
N. Taquet**

- **Targeting**
**G. Zurawski
S. Zurawski
AL. Flamar
E. Klechevsky
SK. Oh**

- **Clinical Core:**

**Joe Fay
S. Hicks
B-J. Chang
D. Wood**

- **Post-docs / Students:**

**C. Aspod
F. Berard
P. Blanco
P. Dubsky
D. Frleta
E. Klechevsky
A. Pedroza
S. Paczesny
H. Saito
L. Vence
C. Yu**

- **Immunomonitoring:**

**Hide Ueno
J-P. Blanck
L. Boudery
J. Shay**

- **Microarrays**

**D. Chaussabel
N. Baldwin**

**R. Steinman
M. Dhodapkar
Y. Reiter**

**F. Marches
M. Gallegos
S. Tindle
M. Michnevitz**

JACQUES BANCHEREAU

**AND MANY
BIIR MEMBERS.....**