# Dendritic Cell Vaccines: Have we reached consensus?

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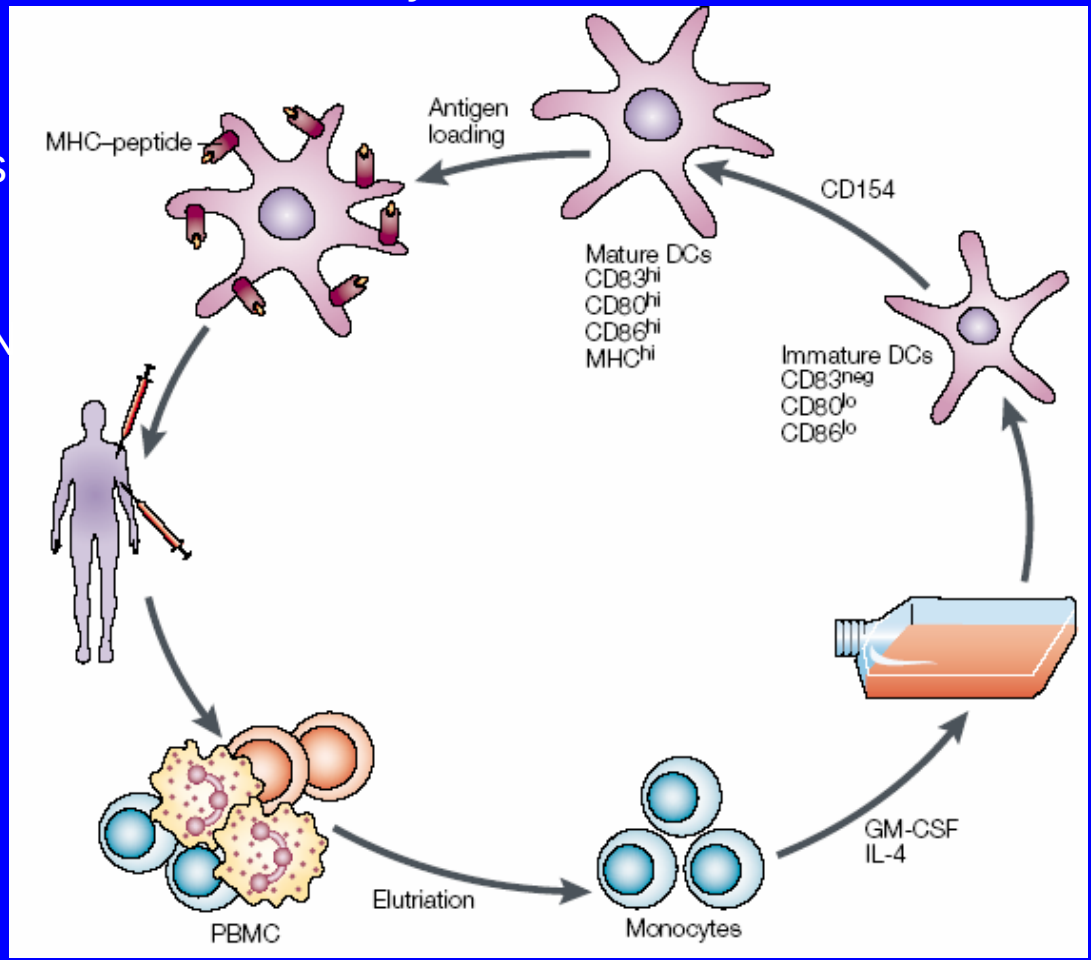
# Dendritic Cells as Vaccines

Peptides
Tumor lysate

Adjuvants
GM-CSF
KLH
CpG-ODN

HCC
Prostate
Melanoma
RCC




Maturation status

NK “help”
Type 1 polarizatio

Berzofsky et al. Nat Rev Immunol 2001

# Key Questions in DC Vaccine Strategies

- What diseases should be targeted?
- What is the best source of antigen?
- How should DC be optimized?
- How should DC vaccines be monitored?
- What are meaningful endpoints?

- Should we optimize in Phase II or proceed directly to Phase III?

# What diseases should be targeted?

| | |
|---|---|
| • HCC | Butterfield, et al. |
| • Prostate CA | Klyushnenkova, et al. |
| | Small, et al. |
| • Melanoma | Letsch, et al. |
| | Riccobon, et al. |
| • RCC | Riccobon, et al. |
| • Others? | |

# What is the best source of antigen?

- Peptides — Butterfield, et al.; Klyushnenkova, et al.; Letsch, et al.
- Tumor lysate — Riccobon, et al.
- Allogeneic tumor cells — Small, et al.

# How should DC be optimized?

| | |
|---|---|
| • Type 1 polarization | Giermasz, et al. |
| • NK cell “help” | Maillard et al. |
| • Optimizing epitopes | Klyushnenkova, et al. |
| • GM-CSF/KLH | Letsch, et al. |
| • Maturation status | Riccobon, et al. |
| • CpG-ODN | Riker, et al. |
| • GM-CSF secreting tumor cells | Small et al. |

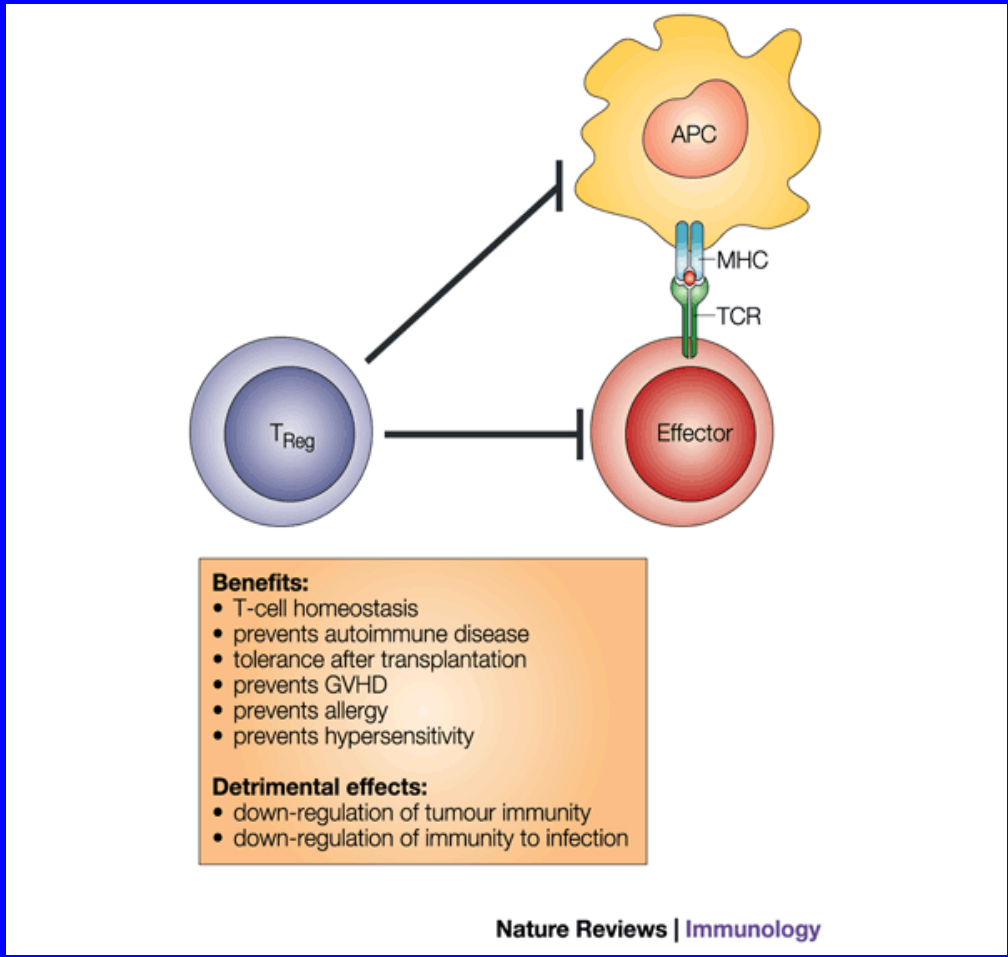
# How should DC vaccines be monitored?

| | |
|---|---|
| • ELISPOT | Butterfield, et al.<br>Maillard, et al. |
| • ICS | Letsch et al. |
| • Tetramer staining | Maillard, et al. |
| • CTL assay | Maillard, et al. |
| • DTH | Riccobon, et al. |
| • Antibody response | Small, et al. |

# What are meaningful endpoints?

- Immune response — Butterfield, et al.; Letsch, et. Al.; Maillard, et al.; Riccobon, et al.; Small, et al.
- Clinical response — Riccobon, et al.
- Tumor markers — Small, et al.

# Other Obstacles:
# Regulatory T cells inhibit immunity



# DC Vaccines: Have we reached consensus?

Little agreement on:

- type of cancer
- source of antigen
- methods for optimizing DC
- how to monitor immune responses
- which clinical endpoints to choose

Progress has been made:

- safety
- technical aspects of vaccine development
- importance of immune response
- understanding the obstacles

# Have we reached consensus?

- If yes, are we ready to proceed to Phase III clinical trials?

- If not, how should we optimize the system further?