Dendritic Cell Vaccines: Have we reached consensus?

SBT 2004
San Francisco, CA
Dendritic Cells as Vaccines

Peptides
Tumor lysate

Adjuvants
GM-CSF
KLH
CpG-ODN
HCC
Prostate
Melanoma
RCC

Maturation status

NK “help”
Type 1 polarization

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?

- 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?

- 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

Benefits:
- T-cell homeostasis
- prevents autoimmune disease
- tolerance after transplantation
- prevents GVHD
- prevents allergy
- prevents hypersensitivity

Detrimental effects:
- down-regulation of tumour immunity
- down-regulation of immunity to infection
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?