Rudiments of vaccine design

Last Time:	continued discussion of stealth particles basic immunobiology underlying vaccination
Today:	basics of vaccine design and vaccine immune responses
Reading:	Raychaudhuri and Rock, 'Fully mobilizing host defense: building better vaccines,' *Nat. Biotech*. **16** 1025-1031 (1998)
Supplementary Reading:	

ANNOUNCEMENTS:

Note on take-home exam: 6-page limit includes any schematics or figures from the literature (1/3 of space max)

KEY EFFECTORS OF ADAPTIVE IMMUNITY

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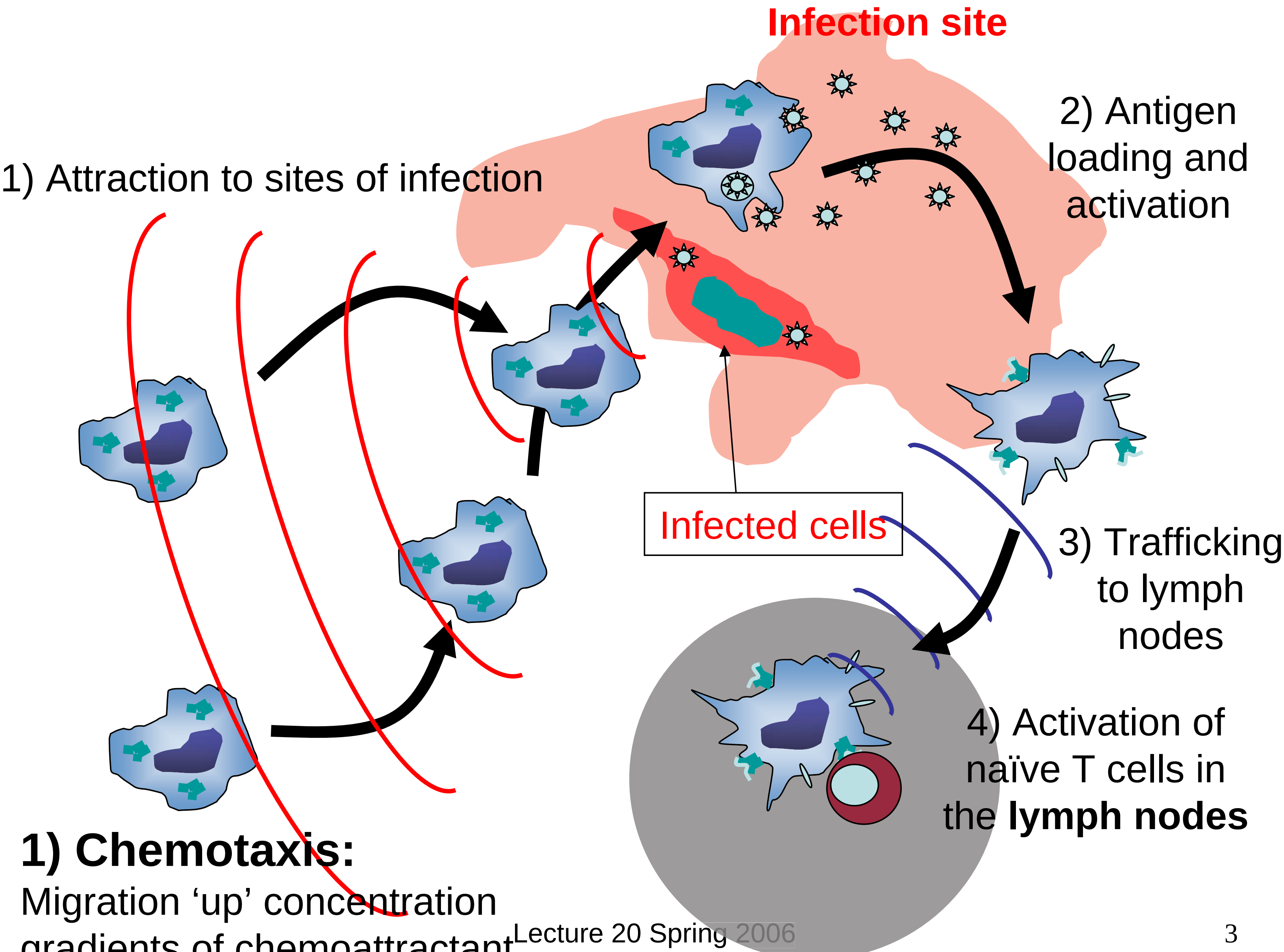
Please see: Abbas, A. K., and A. H. Lichtman. *Cellular and Molecular Immunology*. San Diego, CA: Elsevier, 2005. ISBN: 1416023895.



1) Chemotaxis:
Migration ‘up’ concentration gradients of chemoattractant

PAMP recognition of microbes by dendritic cells

Immune cells integrate many signals to 'fingerprint' pathogens:

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Please see: Huang, et al. *Science* 294 (2001): 3870.

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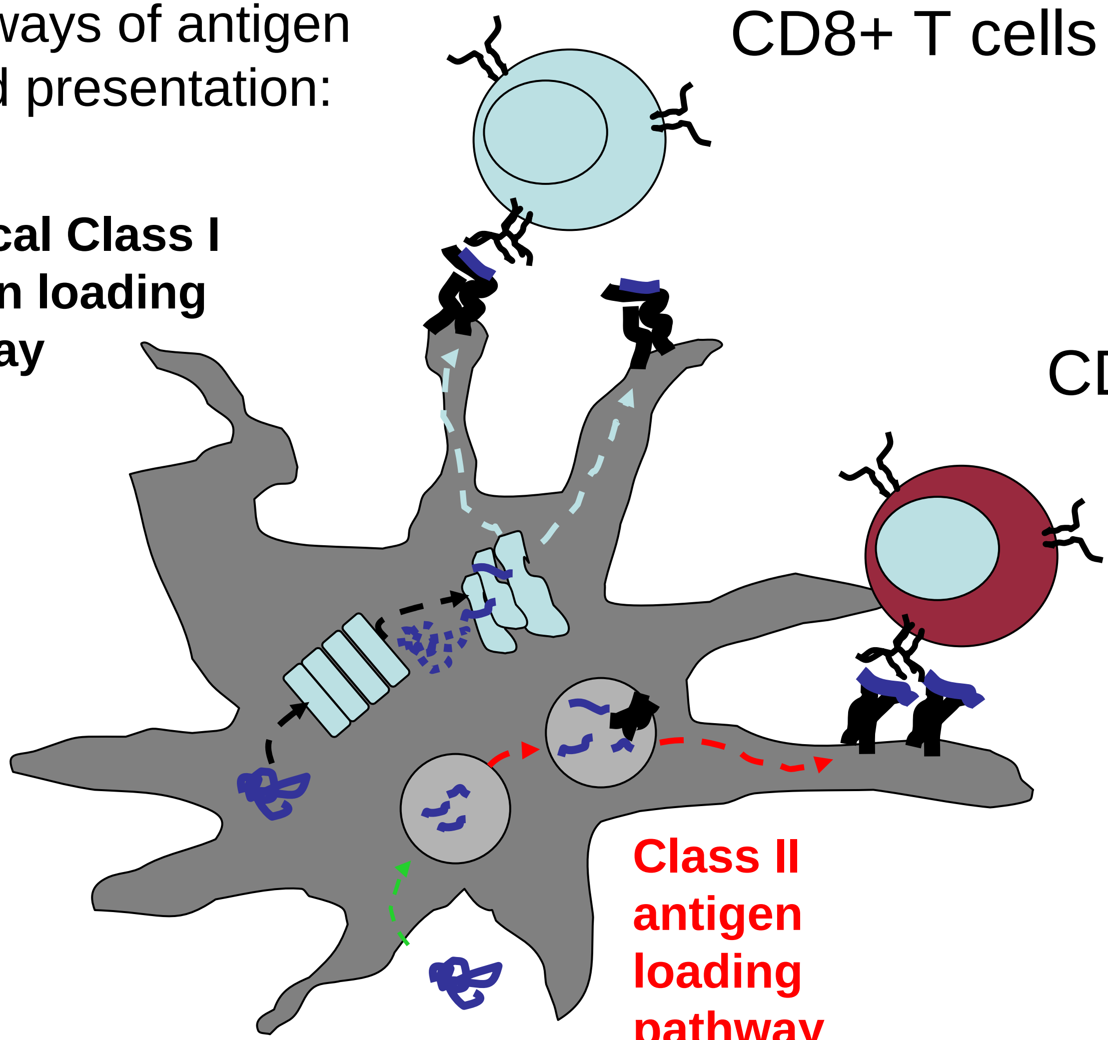
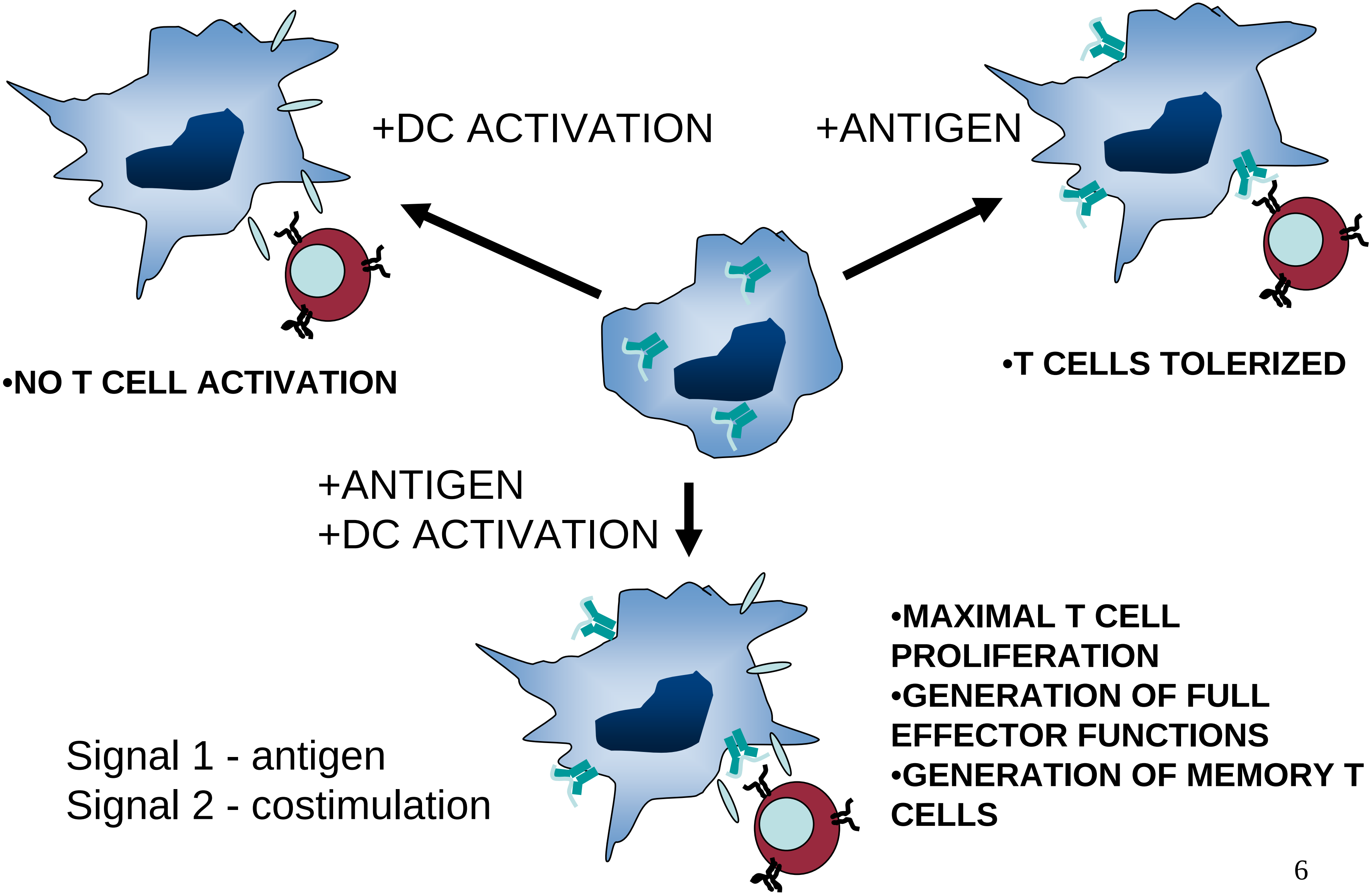
Please see: Kawai, and Akira. *Curr Opin Immunol* 17 (2005): 338-344.

Biology of dendritic cells in T cell activation

Classical pathways of antigen processing and presentation:



Antigen is *one* of (at least) *two* signals that must be delivered by a vaccine



Signal 1 - antigen
Signal 2 - costimulation

B cell activation

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Please see: Abbas, A. K., and A. H. Lichtman. *Cellular and Molecular Immunology*. San Diego, CA: Elsevier, 2005. ISBN: 1416023895.

Induction of immunological memory (the basis of vaccination)

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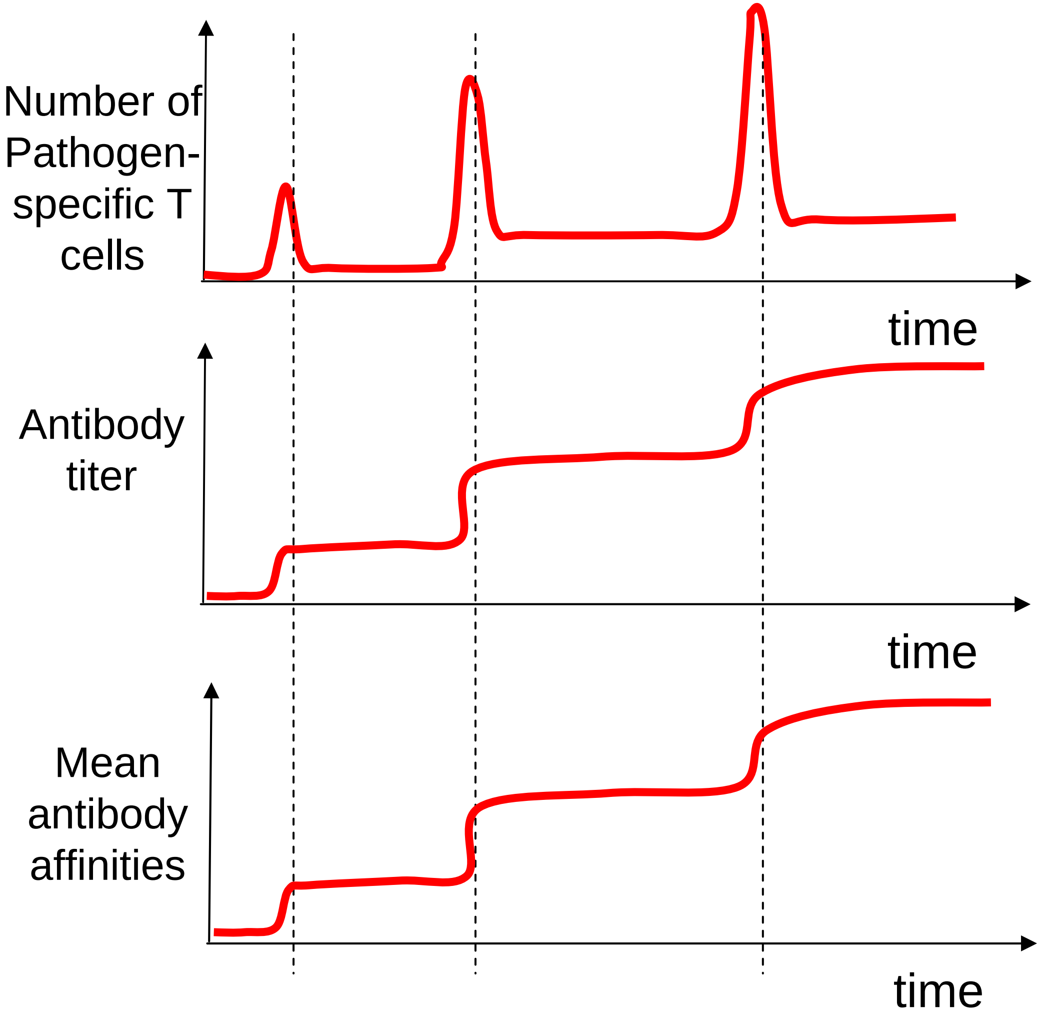
Please see: Ahmed. *Science* 300 (2003): 263-264.



OBJECTIVES OF VACCINATION

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Please see: Neutra, and Kozlowski. *Nat Rev Immunol* 6 (2006): 148-158.

Prophylactic vs. therapeutic immunization

Two situations where vaccination is of interest:

(1) Therapeutic vaccine:

(2) Prophylactic vaccine:

ROUTES OF IMMUNIZATION

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Please see: Neutra, and Kozlowski. *Nat Rev Immunol* 6 (2006): 148-158.

Rudimentary components of vaccines

- Antigen:

- Adjuvant:

Compositions of vaccines- clinical and experimental

- Live attenuated pathogen
- Killed pathogen

Compositions of vaccines- clinical and experimental

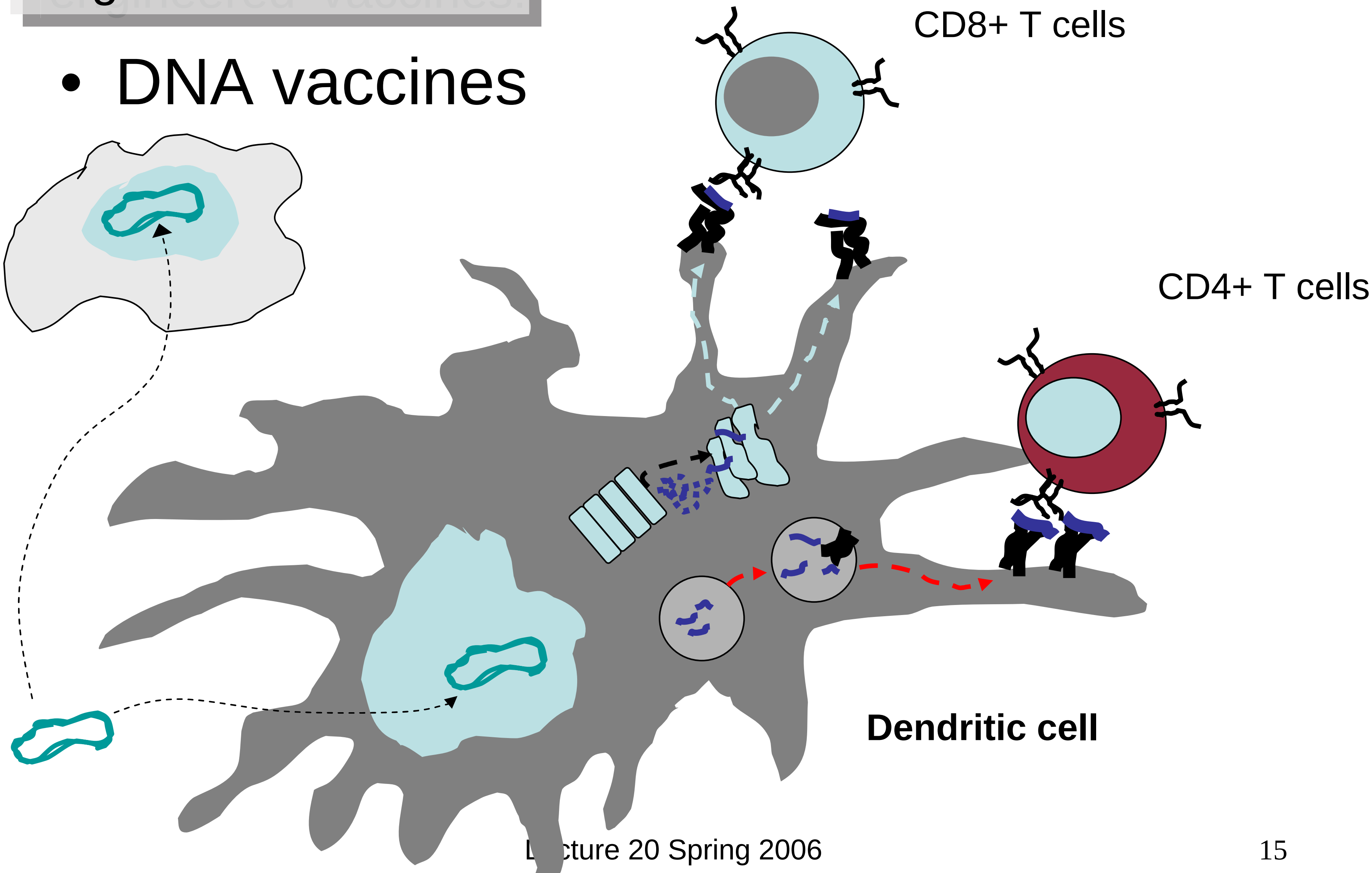
‘engineered’ vaccines:

- Subunit vaccines
  - – Whole protein
  - – Peptide vaccines
  - – Virus-like particles

Compositions of vaccines- clinical and experimental

‘engineered’ vaccines:

- DNA vaccines



Compositions of vaccines- clinical and experimental

‘engineered’ vaccines:

- DNA vaccines

Existing vaccines

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Please see: Table 1 in Ada, G. "Advances in Immunology - Vaccines and Vaccination." *New England Journal of Medicine* 345 (2001): 1042-53.

Existing vaccines

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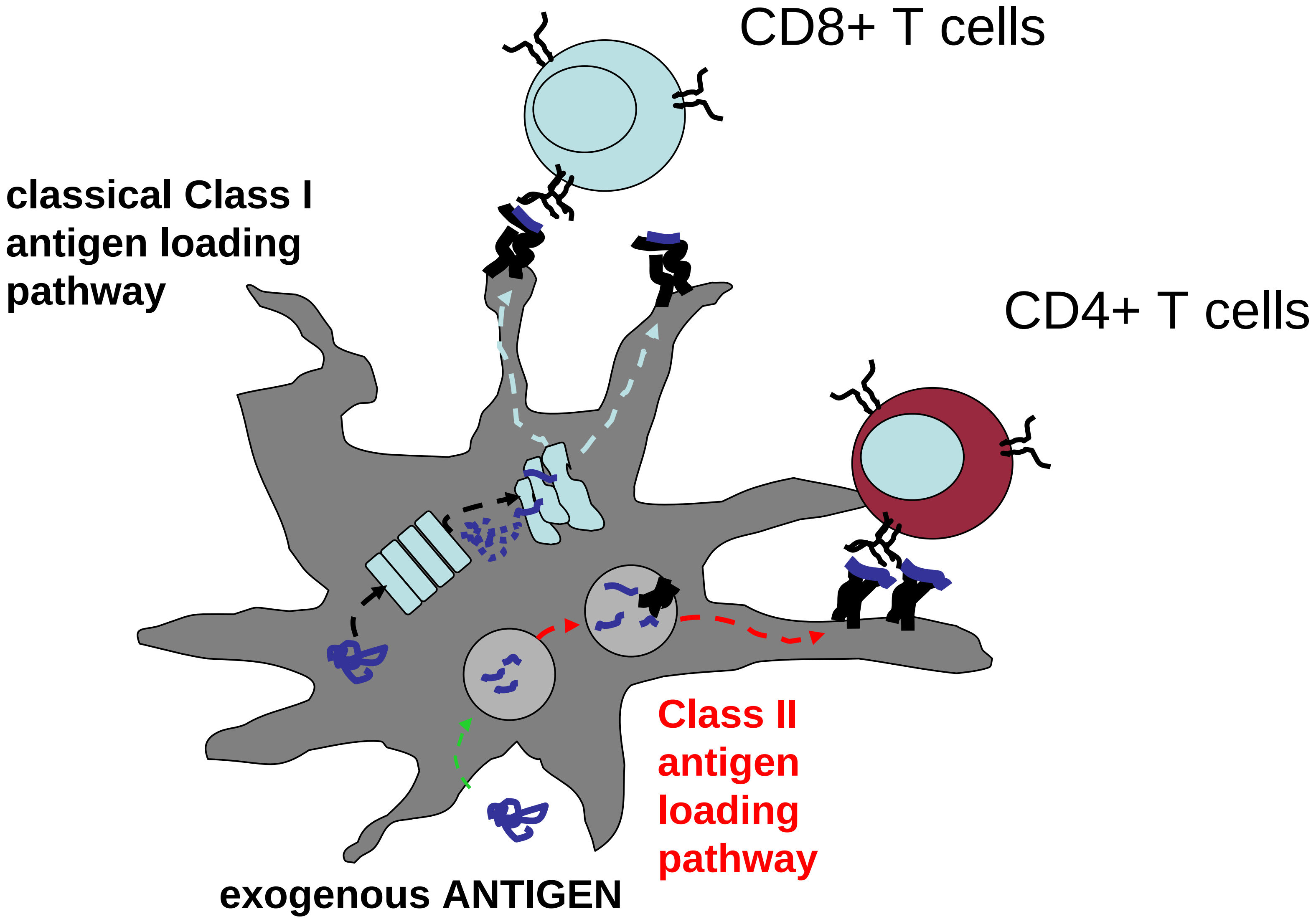
Please see: Table 1 in Ada, G. "Advances in Immunology - Vaccines and Vaccination." *New England Journal of Medicine* 345 (2001): 1042-53.

Biomaterials to adjuvant subunit vaccines:

intracellular drug delivery and the design of protein and peptide vaccines that stimulate cytotoxic T cell responses

Cross presentation and Particulate antigen delivery



Pathways of intracellular import

Endocytosis:
(nearly all cells)

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Please see: Figure 13-46 in Bruce, Alberts, et al. *Molecular Biology of the Cell.* New York, NY: Garland, 2004.

Pathways of intracellular import

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Please see: http://www.cellsalive.com

macropinocytosis:

How do exogenous antigens get presented on class I MHC?

Please see: Figure 13-46 in Bruce, Alberts, et al. *Molecular Biology of the Cell*. New York, NY: Garland, 2004.

Particle-stimulated cross presentation

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Please see: Kovacs-Bankowski, et al. *PNAS* 90 (1993): 4942-4946.

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Please see: Lehner, and Cresswell. *Curr Opin Immunol* 16, no. 82 (2004).

Particle-stimulated cross presentation

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Please see: Rodrigues, et al. *Nat Cell Biol* 1 (1999): 362.

ENDOSOMAL ESCAPE:

Enhancing cross presentation
cytosolic delivery of large macromolecules

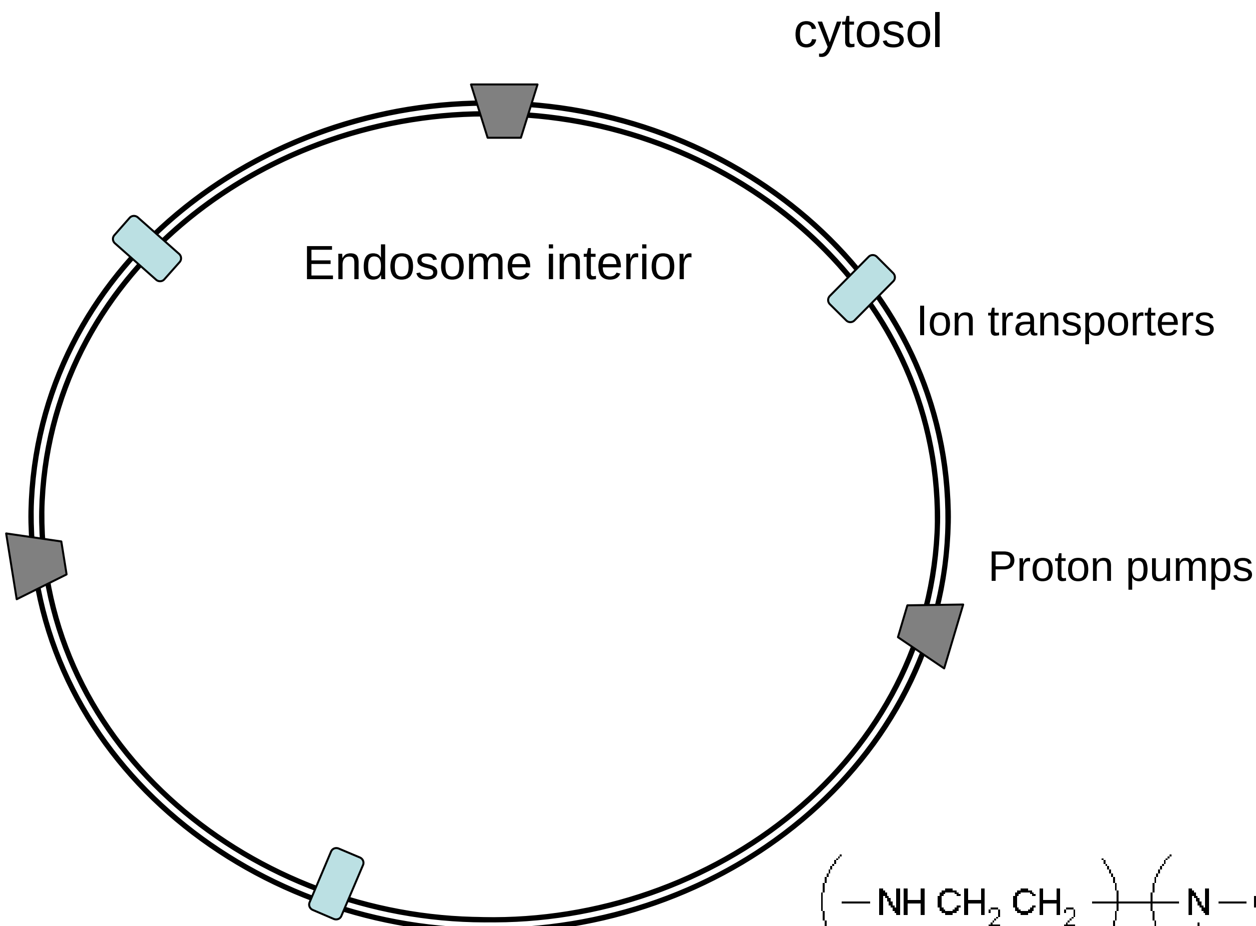
Mechanisms for endosomal escape by polymeric carriers

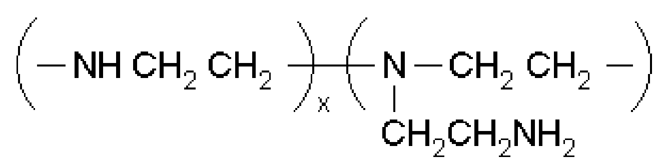
(1) 'proton sponge' effect

(2) Direct membrane interaction/destabilization

(3) pH-activated CPPs

Proton sponge effect





polyethyleneimine

Further Reading

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6. Schwarze, S. R., Ho, A., Vocero-Akbani, A. & Dowdy, S. F. In vivo protein transduction: delivery of a biologically active protein into the mouse. *Science* **285**, 1569-72 (1999).
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Further Reading

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18. Singh, M. & O'Hagan, D. Advances in vaccine adjuvants. Nat Biotechnol 17, 1075-81 (1999).
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