DNA delivery and DNA Vaccines

Last Time: intracellular drug delivery: enhancing cross priming for vaccines

Today: DNA vaccination


Supplementary Reading:

ANNOUNCEMENTS:
Models of membrane-penetrating peptide function

**Penetratin:**
Short peptide sequence from drosophila transcription factor protein Antennapedia

**RQIKIWFQNRRMKWKK**

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ACTIVATION ON ENTRY TO THE CYTOSOL
Selective bond dissociation using reversible disulfide linkages

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Pore-forming proteins/peptides as a tool for membrane-penetrating drug carriers

Figures 1A, 1B, and 1C removed due to copyright restrictions. Please see: Bhakdi. *Arch Microbiol* 165 (1996): 73.
fusogenic peptides: using viral entry strategies for drug delivery

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DNA DELIVERY AND DNA VACCINES
Motivation for DNA vaccines
Why are synthetic vectors of interest?

1. **Self-replicating antigen!**
   - Compare to adenovirus: much more efficient in Ag expression $\geq 95\%$
   - Transfection efficiency
     - Anti-vector pre-existing immunity in humans to adenovirus $\leq 1\%$
   - Adenovirus expression efficiency $\geq 95\%$
   - As high as 80% expression in humans

2. Safety: Will DNA integrate into genome?

3. DNA synthetic vectors usually cheaper, easier to produce, more robust than live virus

4. Possibility to encode multiple factors ("adjuvants") in addition to antigen
idealized objectives of DNA delivery

2 classes of synthetic vectors we’ll discuss:

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Polyplex formation between polycations and plasmid DNA

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Packaging DNA for delivery and cytosolic release

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Polycation/DNA charge ratios in DNA packaging and release

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Substrate-mediated DNA delivery

Segura et al. Biomaterials 26 1575-1584 (2005)    NIH 3T3 fibroblasts
Lipid-DNA microstructures

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Please see: http://avantipolarlipids.com/
Lipid-DNA microstructures

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Please see: Figure 1 in Koltover, et al. Science 281 (1998): 78-81.
Lipid-DNA microstructures

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LIPID AND PARTICLE-BASED DNA CARRIERS

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TRANSPORT FROM THE CYTOSOL TO THE NUCLEUS

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Please see: Figure 1 in Escriou et al. *Adv Drug Deliv Rev* 55 (2003): 295.
Figure removed due to copyright restrictions. 
Please see: Figure 3 in Kircheis et al. *Adv Drug Deliv Rev* 53 (2001): 2341.
Limitations of current materials

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Built-in adjuvants: DNA vaccines encoding antigen and other factors

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Please see: Figure 1 in Sumida, et al. J Clinical Invest 114 (2004): 1334-1342.
Built-in adjuvants: DNA vaccines encoding antigen and other factors

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Engineering the function of antigen presenting cells by DNA delivery
**Further Reading**