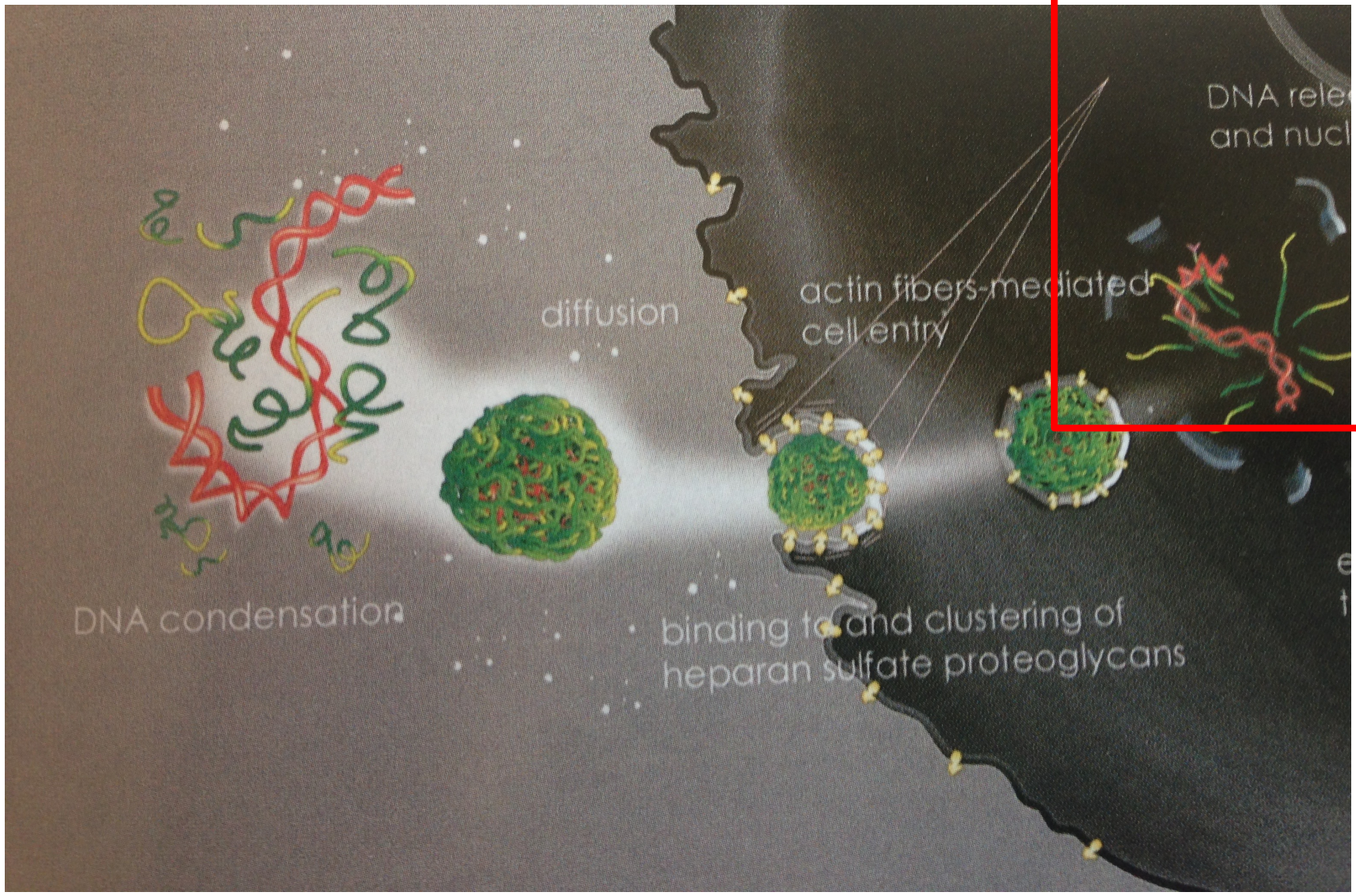
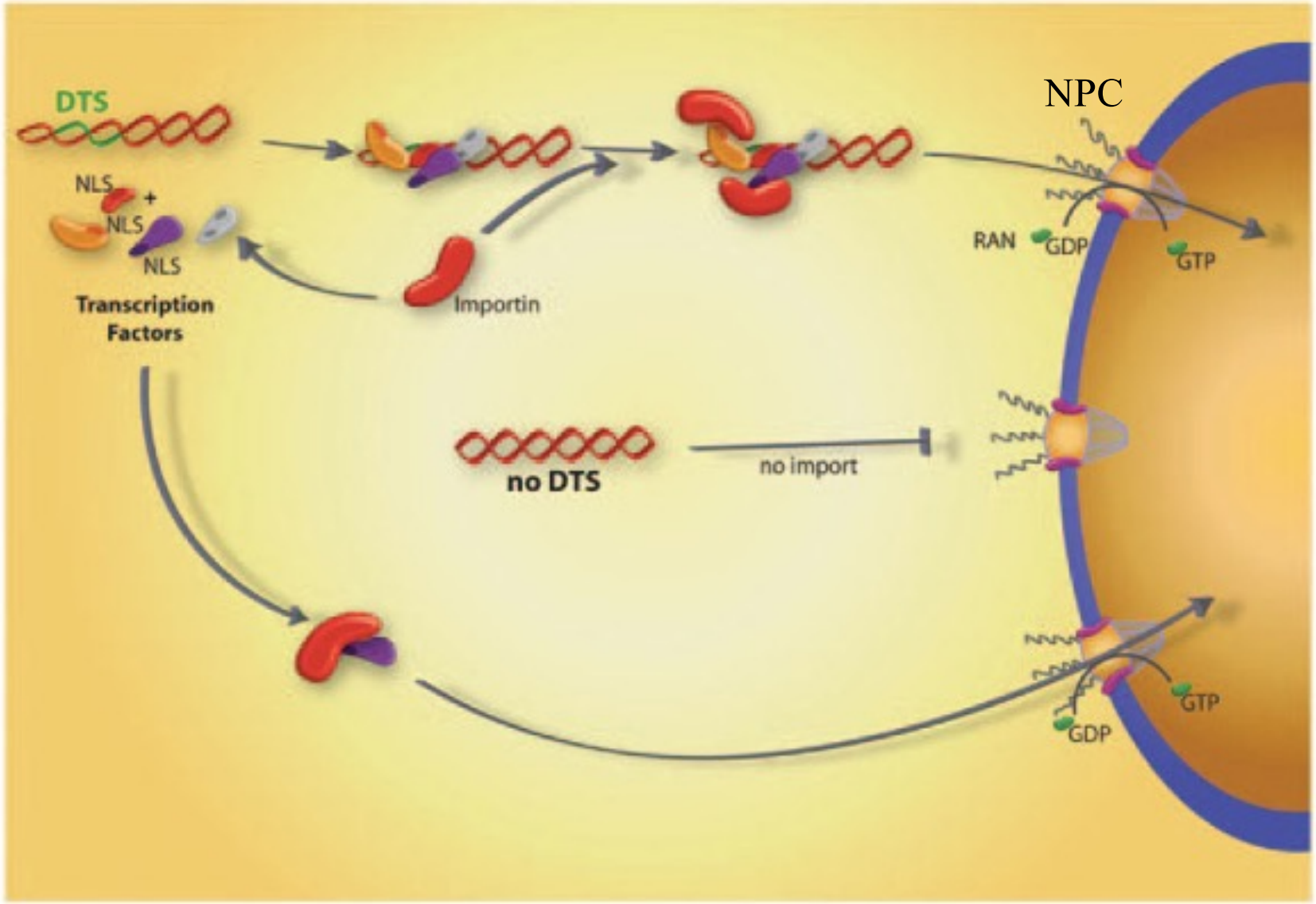
Non viral vectors: the objectives of nanotech studies applied to gene transfer

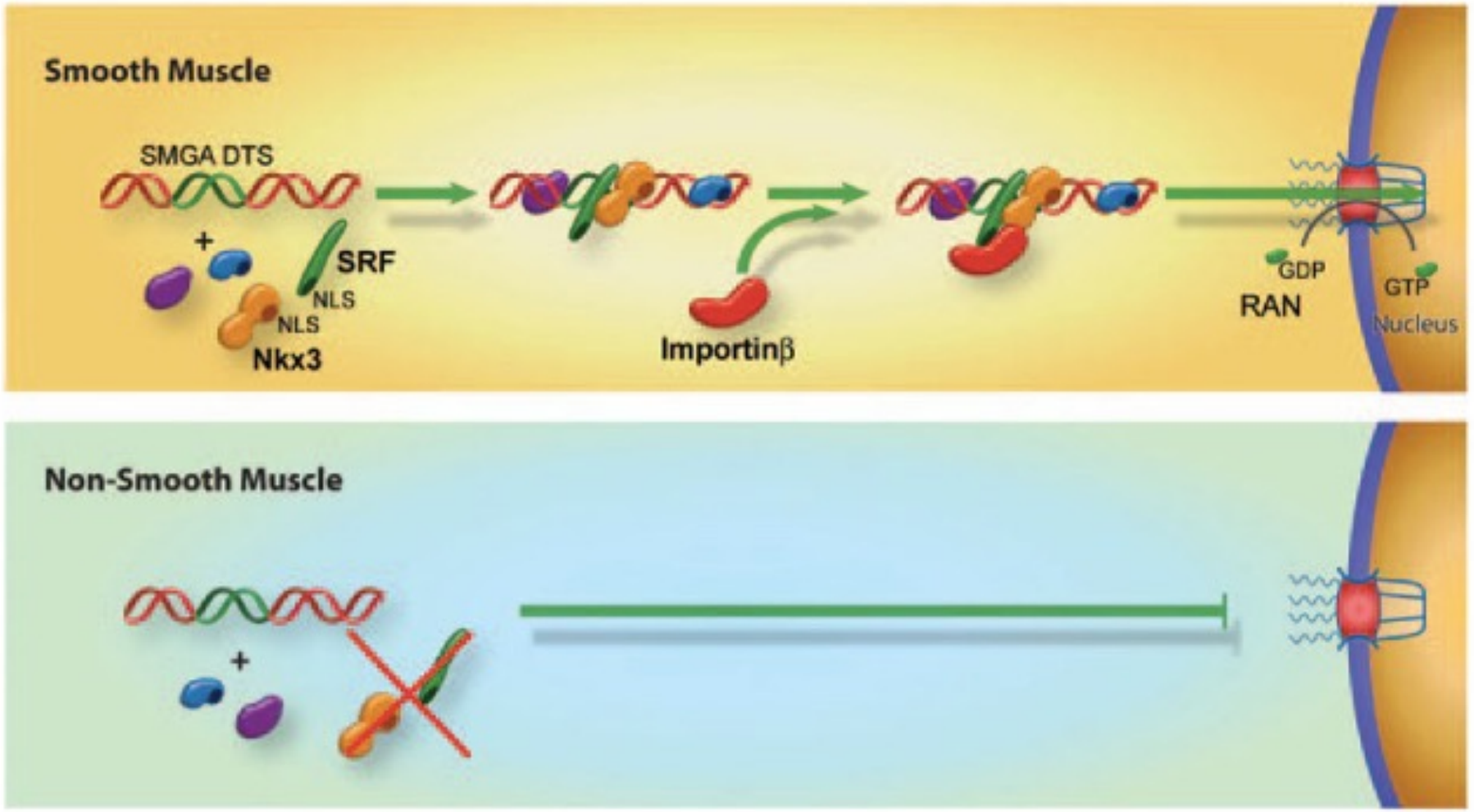


Nuclear targeting- inserting DTS in the DNA



Gene therapy 2010 Lam and Dean

Cell specific nuclear targeting: DTS of smooth muscle γ-actin promoter



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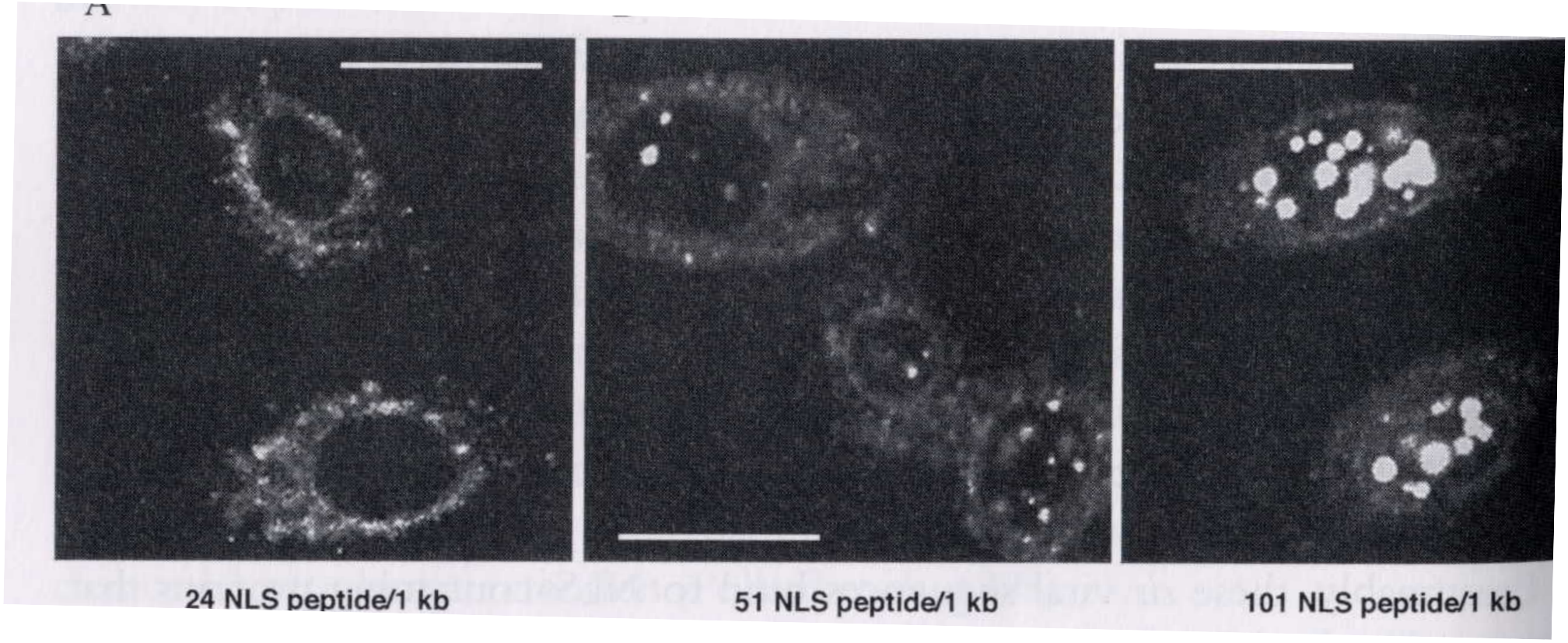
Addition of a nuclear localization signal-peptide



Bottom up

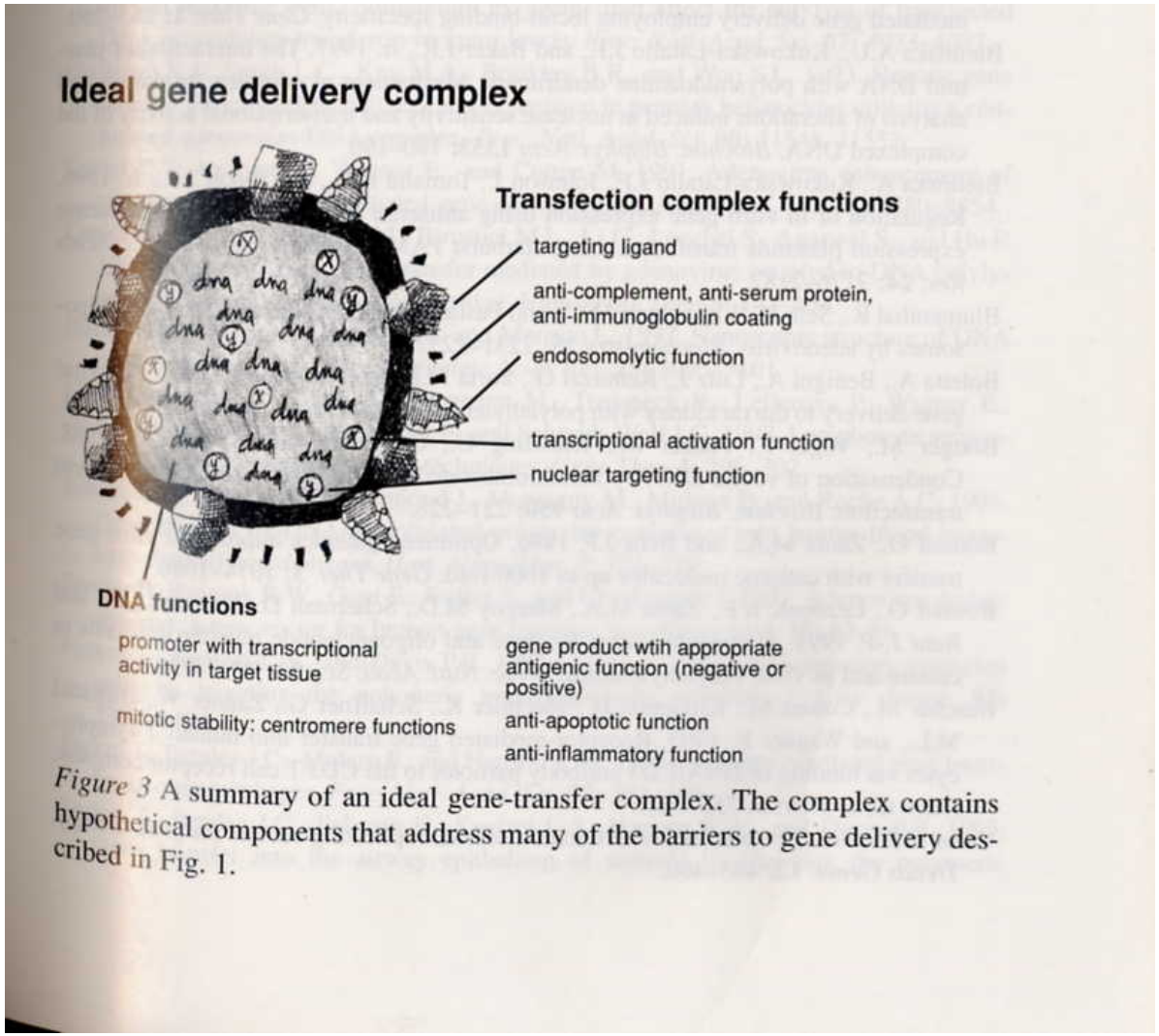


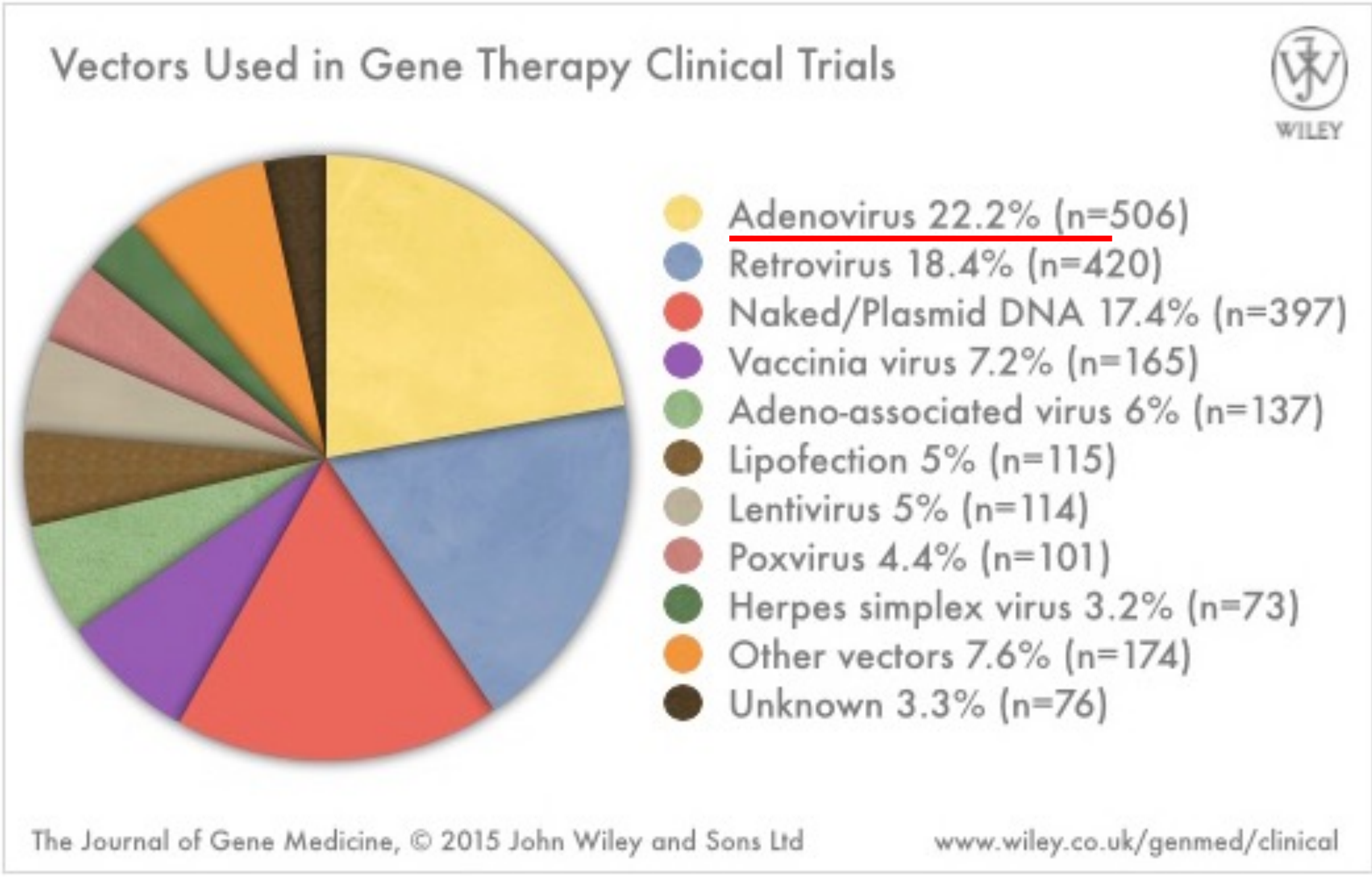
Figure 3 A summary of an ideal gene-transfer complex. The complex contains hypothetical components that address many of the barriers to gene delivery described in Fig. 1.

Viral *offer*

Table 3-2. Examples of viral entry functions

Entry function	Virus	Viral domain, mechanism
Packaging of genome	Adenovirus, Retroviruses	Mu peptide, core particle, gag proteins
Binding to cell surface	Influenza virus	HA-1, binding to sialic acid
	Rhinoviruses	major group: ICAM, minor group: LDL-receptor
	Retroviruses	MLV: gp70-phosphate transporter HIV: gp120-CD4 of T-cells;
Internalization into the cell	Adenovirus, rhinovirus, Influenza virus, SFV	endocytosis into endosomes
	Herpes viruses, HVJ	fusion at cell surface
Release into cytoplasm	Adenovirus	endosome disruption
	Rhinovirus	formation of endosomal pore; VP-1
	Influenza virus, HIV, Sendai virus, SFV	fusion; influenza HA-2, HIV gp 41, Sendai F1, SFV E1 protein
Transfer into nucleus	Adenovirus	injection of DNA through nuclear pore
	Influenza virus	transport of RNPs into nucleus
	HIV	nuclear localization of HIV core particle
Maintenance of expression	Retroviruses	integration (integrase, LTR elements)
	Adeno-associated virus	integration (rep proteins, ITR elements)
	Herpes virus, EBV	episomal persistence (e.g. oriP, EBNA-1)

Top down


Vectors Used in Gene Therapy Clinical Trials
WILEY
Adenovirus 22.2% (n=506)
Retrovirus 18.4% (n=420)
Naked/Plasmid DNA 17.4% (n=397)
Vaccinia virus 7.2% (n=165)
Adeno-associated virus 6% (n=137)
Lipofection 5% (n=115)
Lentivirus 5% (n=114)
Poxvirus 4.4% (n=101)
Herpes simplex virus 3.2% (n=73)
Other vectors 7.6% (n=174)
Unknown 3.3% (n=76)
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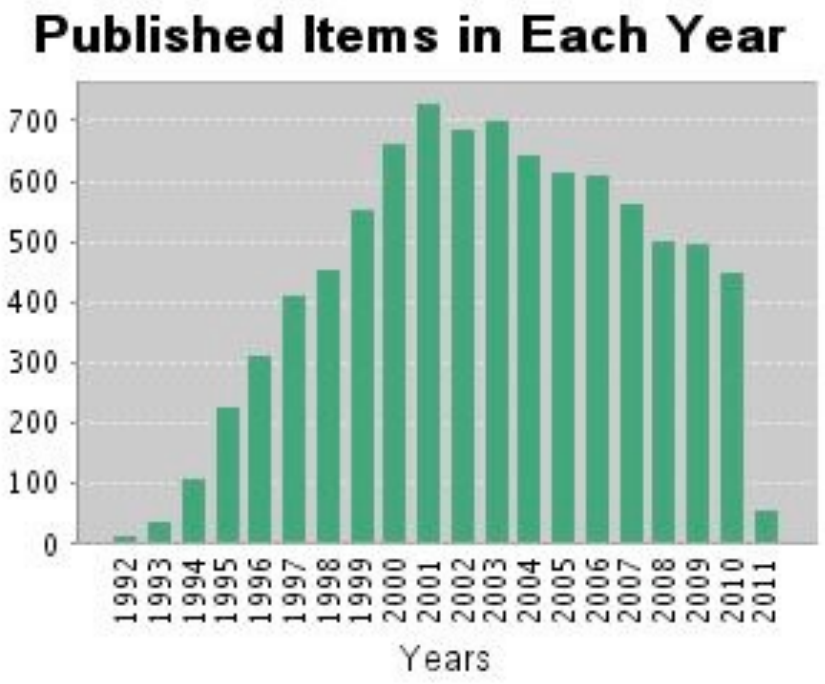
www.wiley.co.uk/genmed/clinical

ISI adenovirus and gene therapy 1985 -2011



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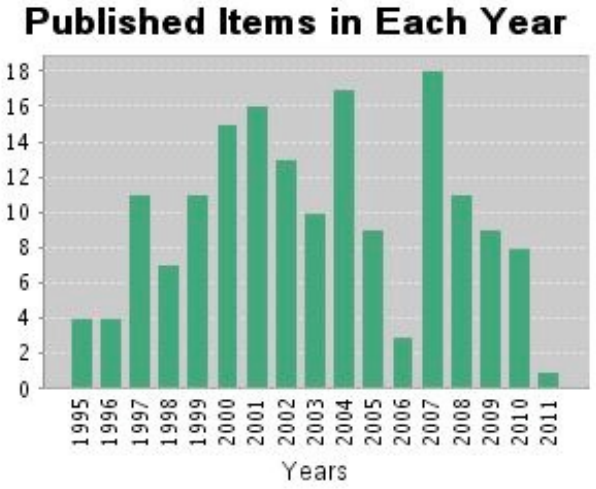

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Ad

- isolated in adenoids
- largest nonenveloped viruses
- 51 immunologically distinct human s serotypes (6 species: *A* through *F*)
- cause infections ranging from respiratory disease (mainly species HAdV-B and C), and conjunctivitis (HAdV-B and D), to gastroenteritis (HAdV-F serotypes 40 and 41)
- stable to chemical or physical agents and adverse pH conditions
- spread via respiratory droplets, fecal routes as well
- Most people recover from adenovirus infections

DOMANDE?