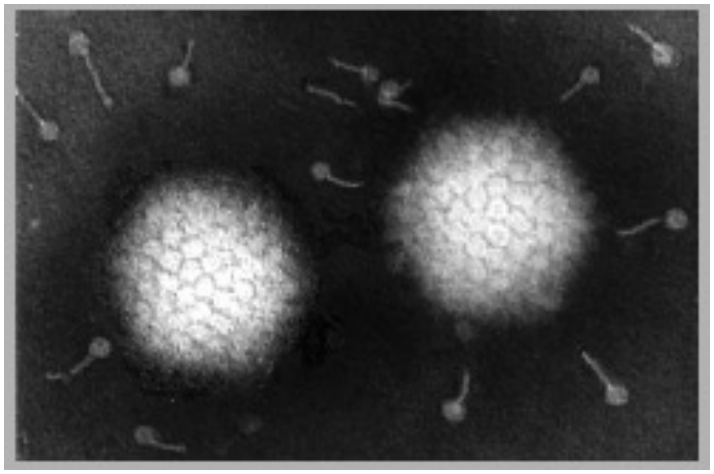
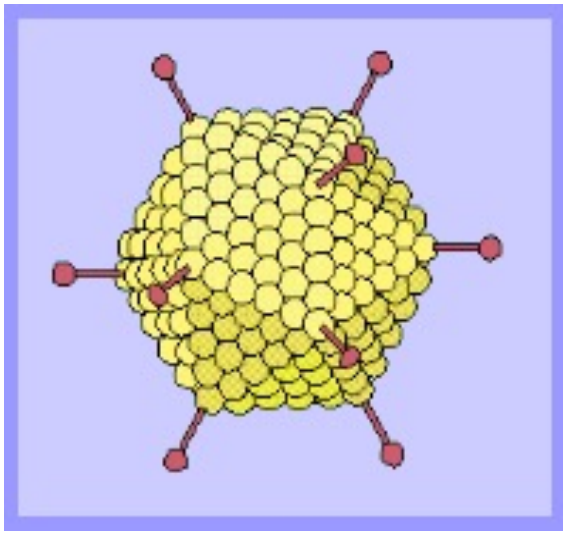
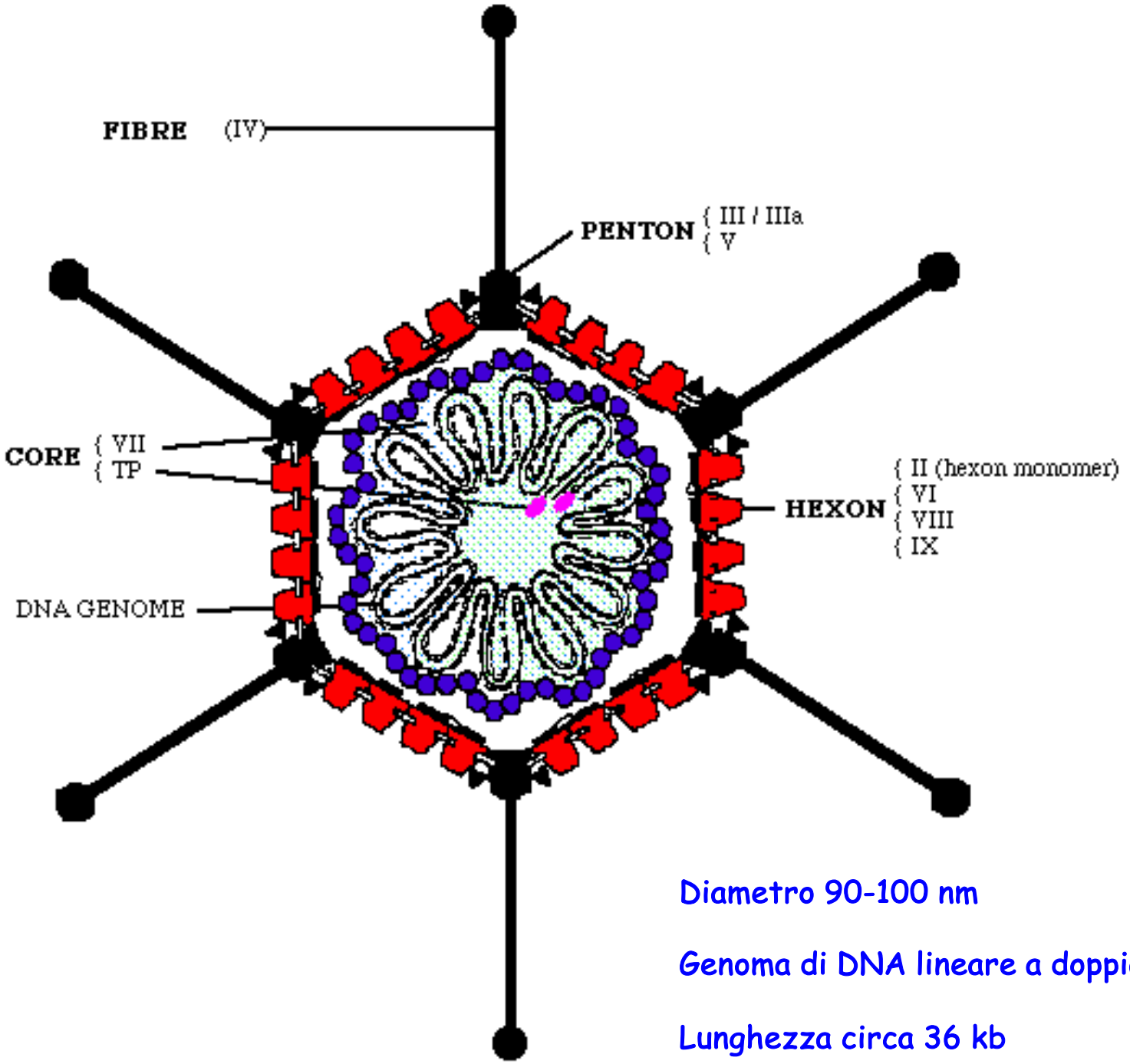
Adenovirus





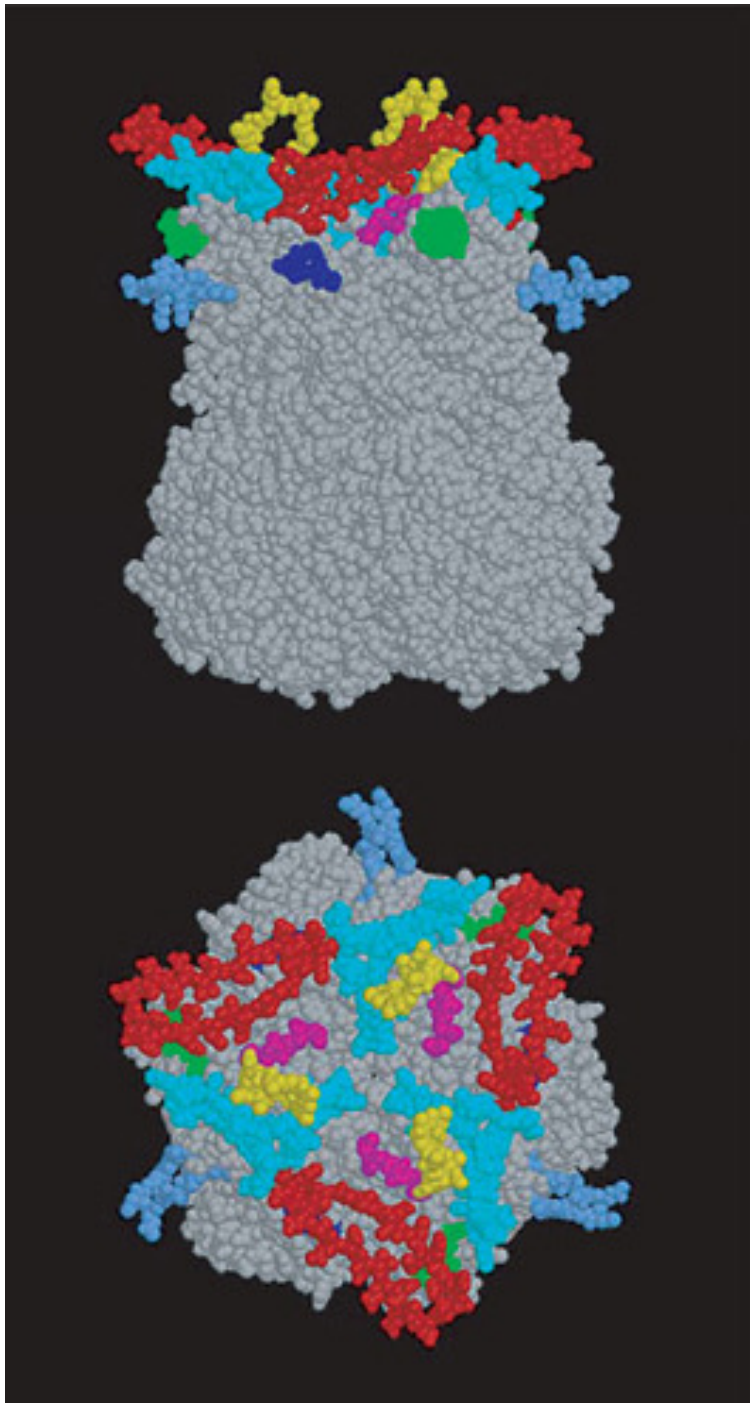


Diametro 90-100 nm

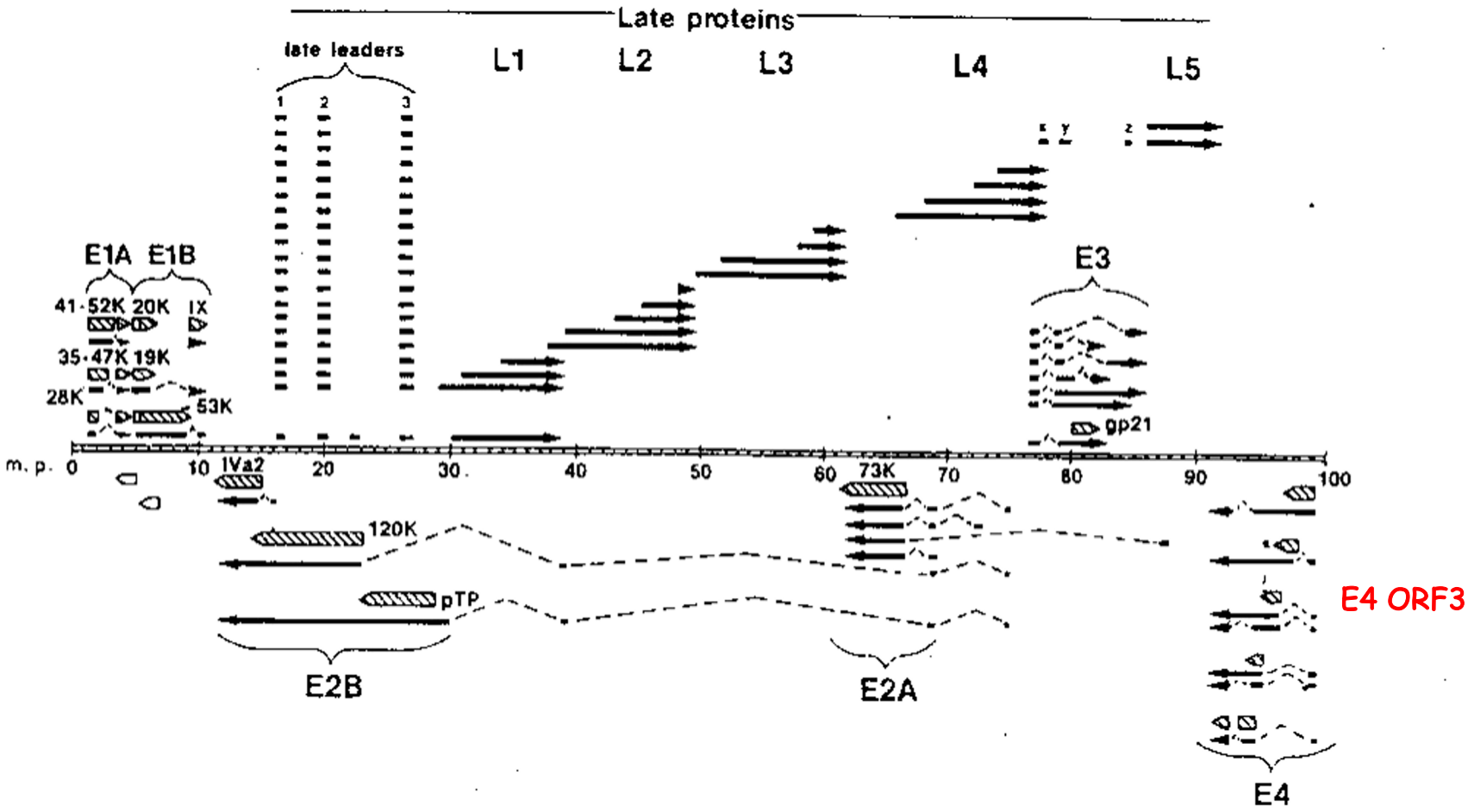
Genoma di DNA lineare a doppia elica

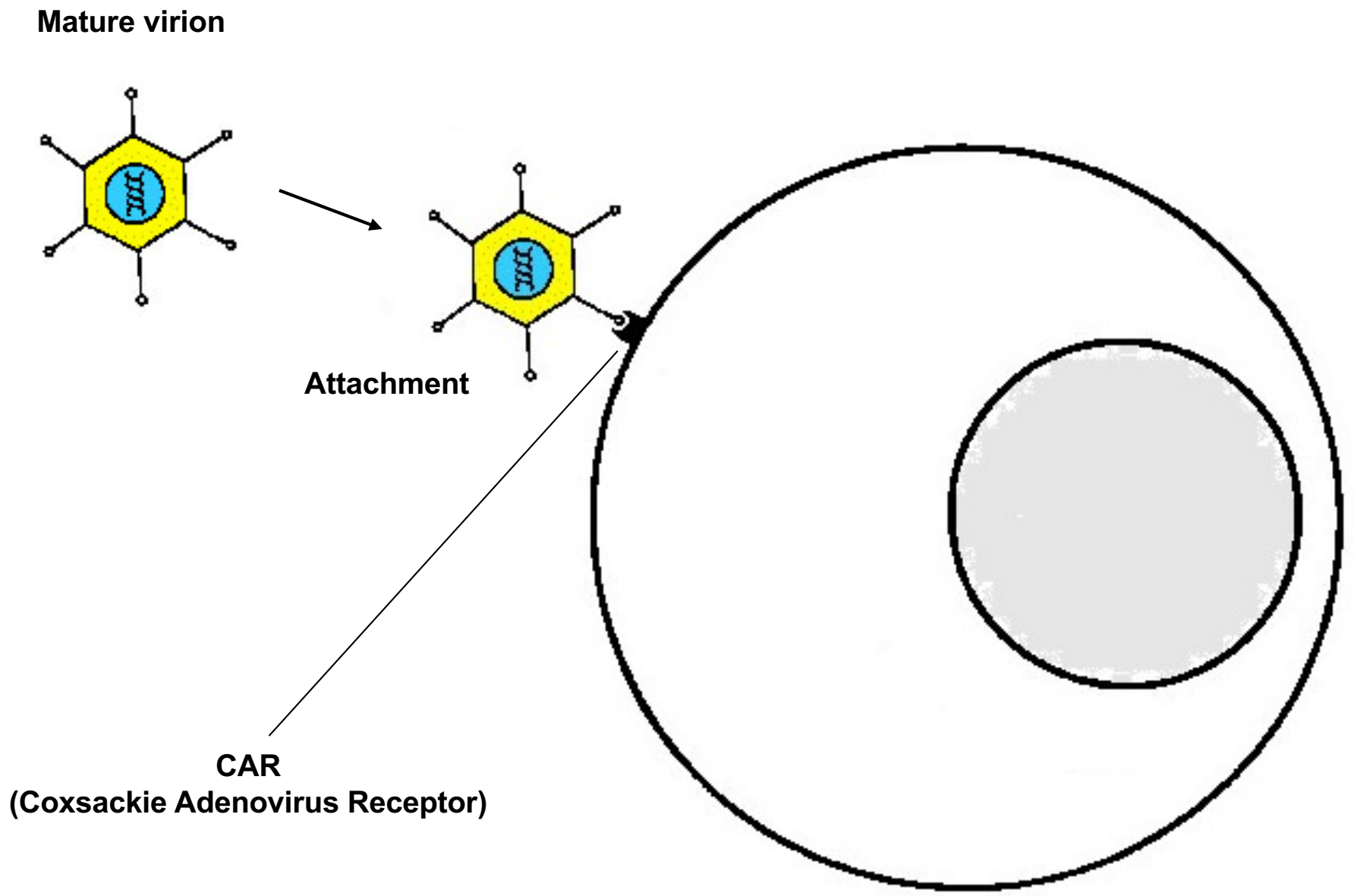
Lunghezza circa 36 kb

Le sette regioni ipervariabili dell'esone

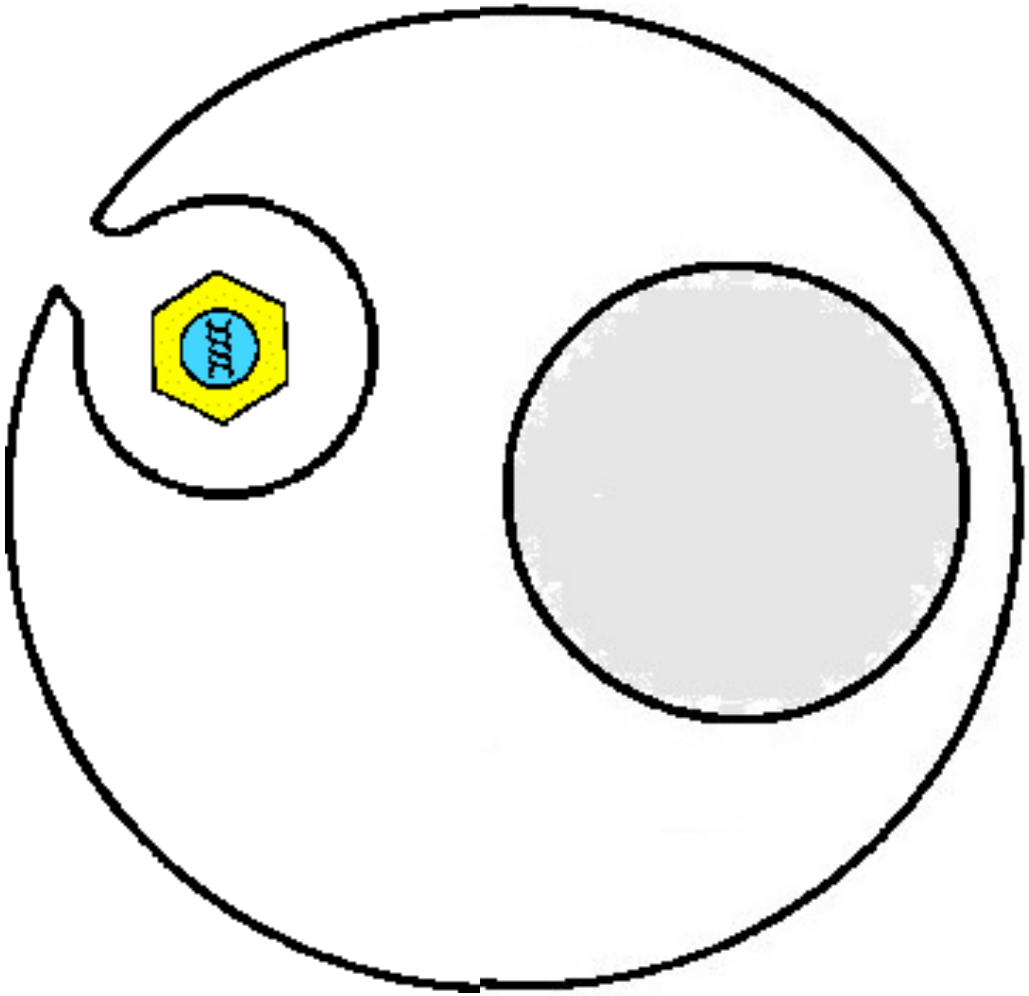


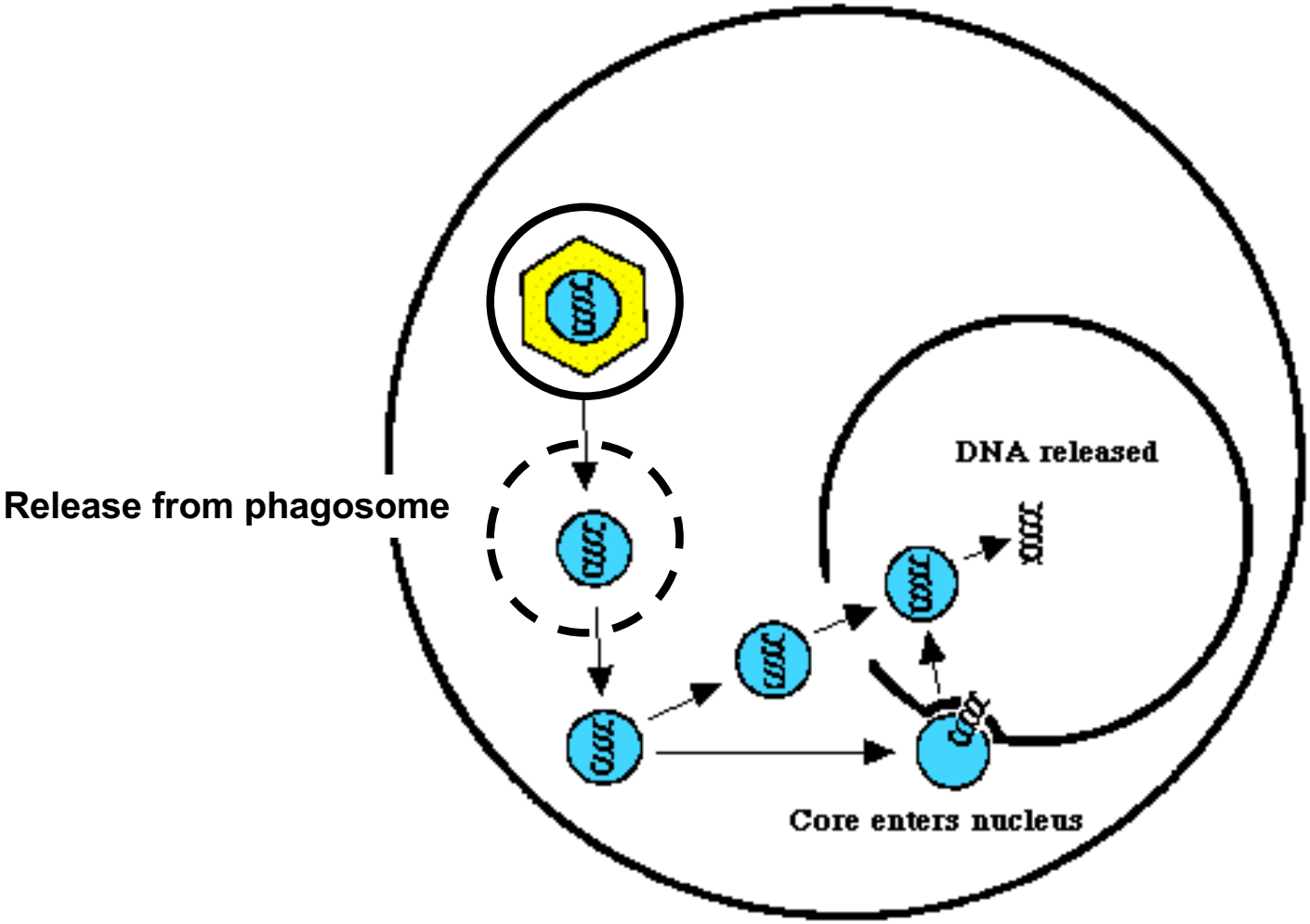
Modificata da Roberts et al.,
Nature 441:239-243, 2006

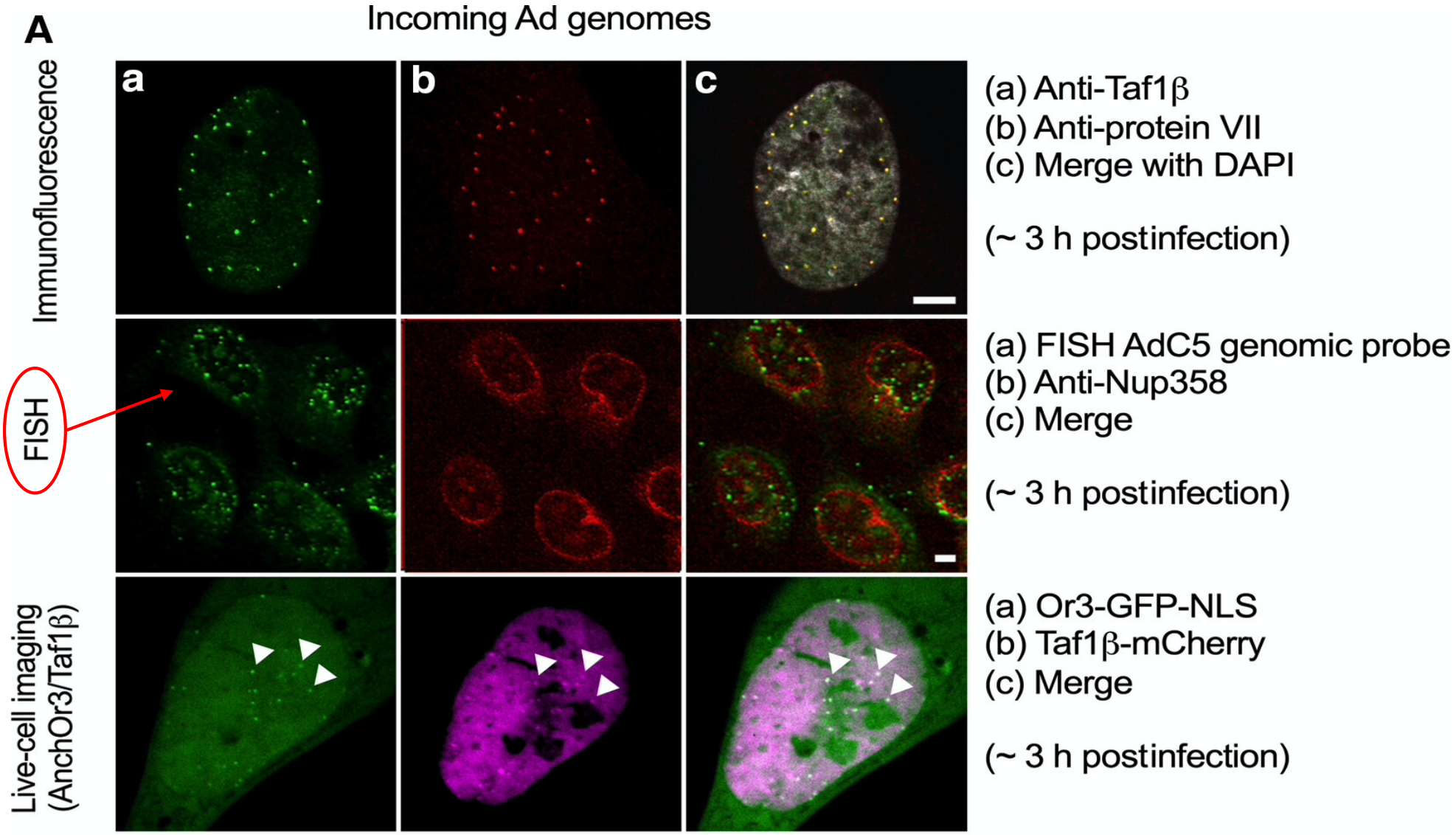

Late proteins
late leaders
L1
L2
L3
L4
L5
1
2
3
x
y
z
E1A
E1B
41·52K
20K
IX
35·47K
19K
28K
53K
E3
gp21
m.p. 0
10
IVa2
20
30
40
50
60
73K
70
80
90
100
120K
pTP
E2B
E2A
E4
E4 ORF3


Mature virion
Attachment
CAR
(Coxsackie Adenovirus Receptor)

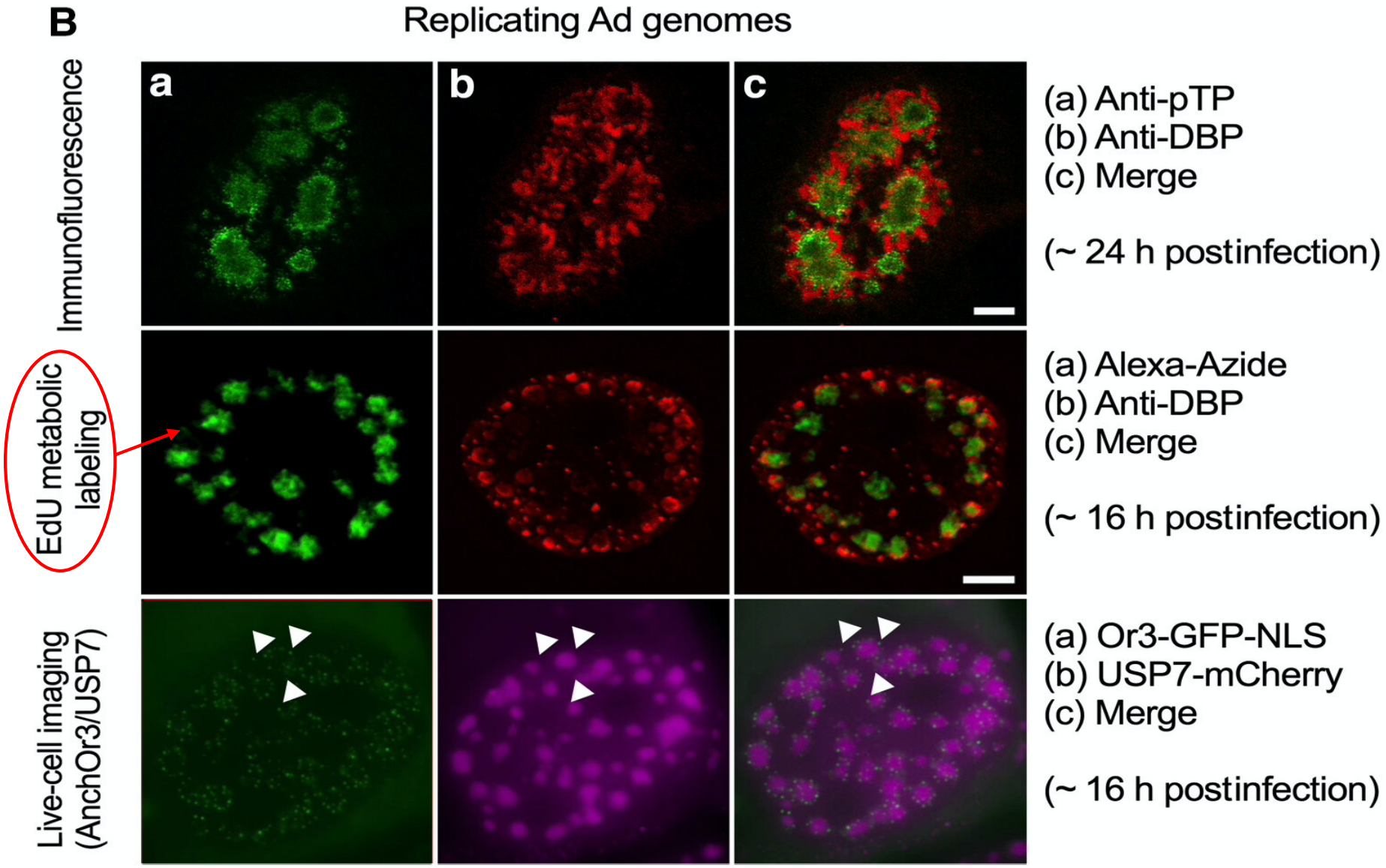
Phagocytosis



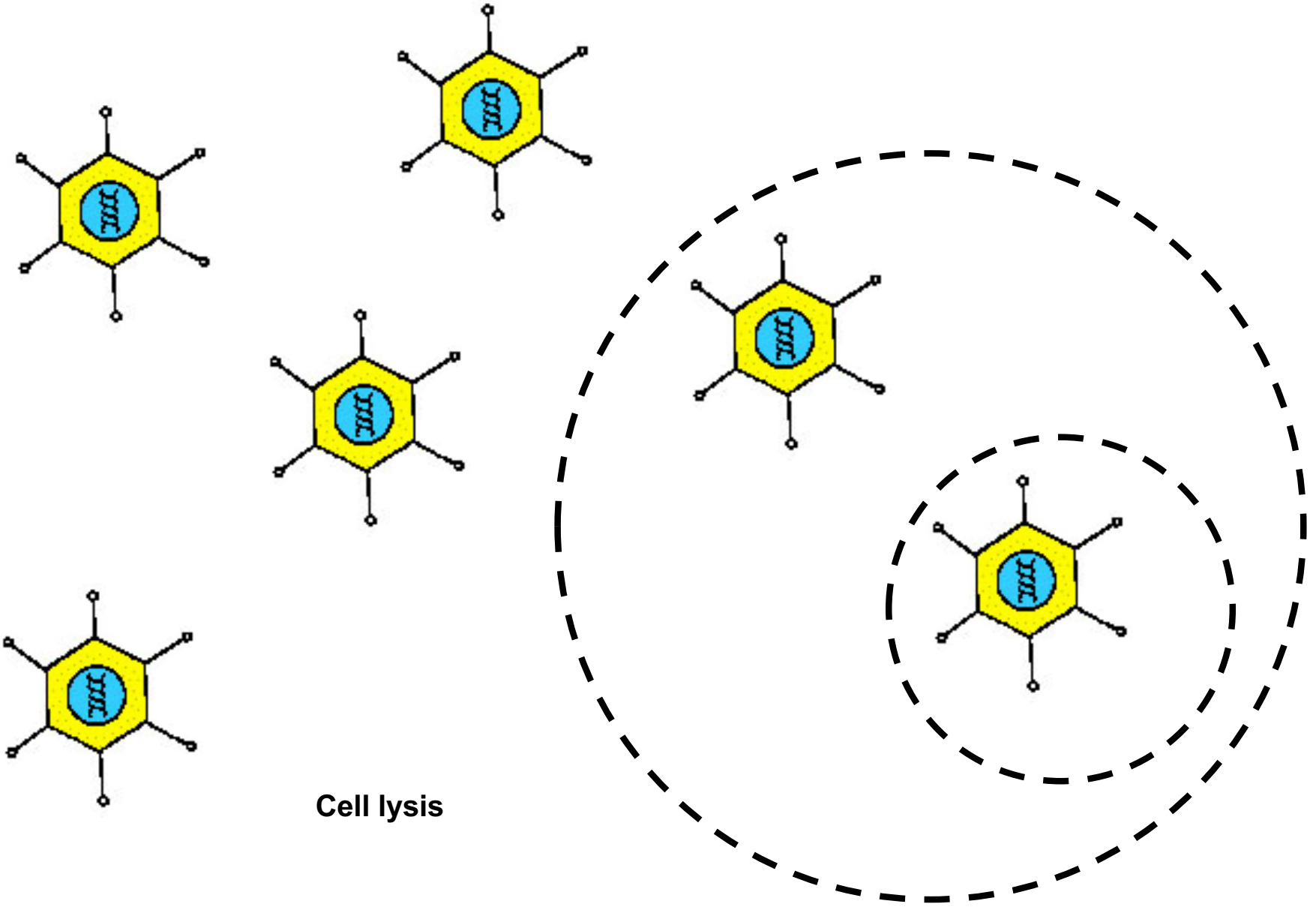

Release from phagosome
DNA released
Core enters nucleus



FEBS Letters 593: 3419–3448, 2019



FEBS Letters 593: 3419–3448, 2019


Cell lysis

Splicing dell’RNA

Proc. Natl. Acad. Sci. USA
Vol. 74, No. 8, pp. 3171–3175, August 1977
Biochemistry

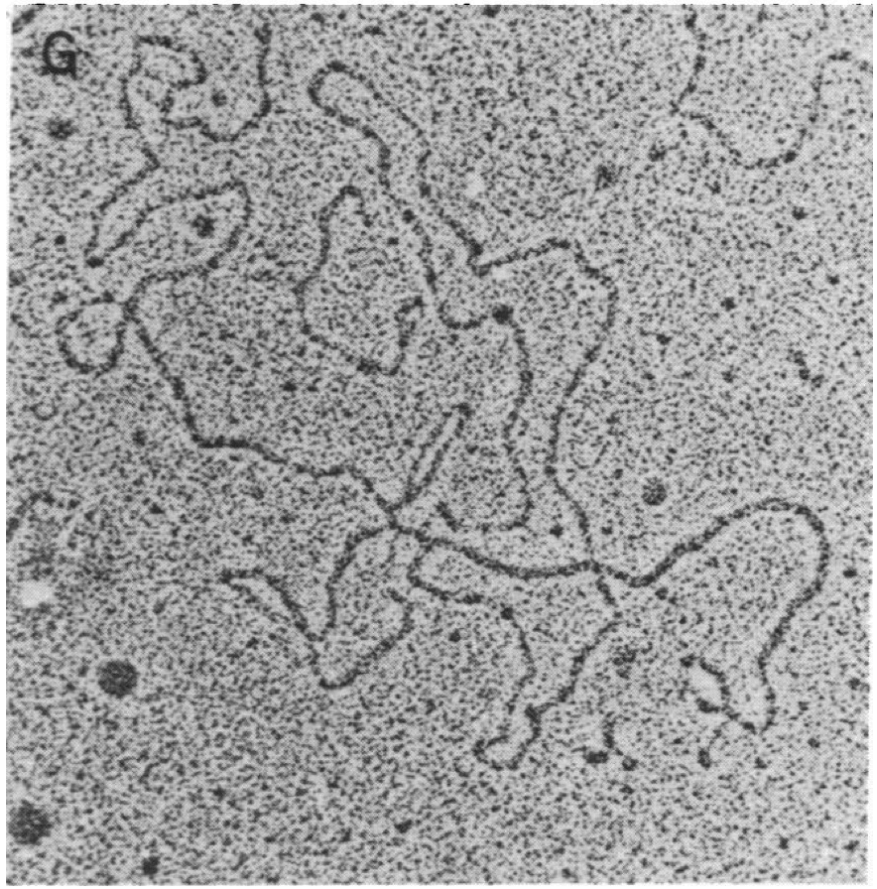
Spliced segments at the 5′ terminus of adenovirus 2 late mRNA*

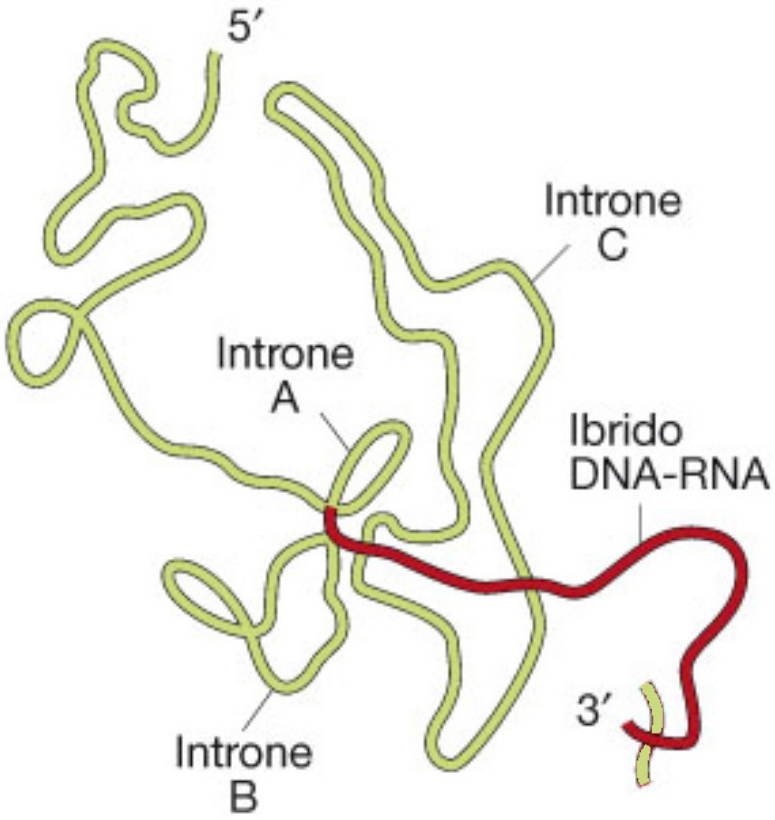
(adenovirus 2 mRNA processing/5′ tails on mRNAs/electron microscopy of mRNA·DNA hybrids)

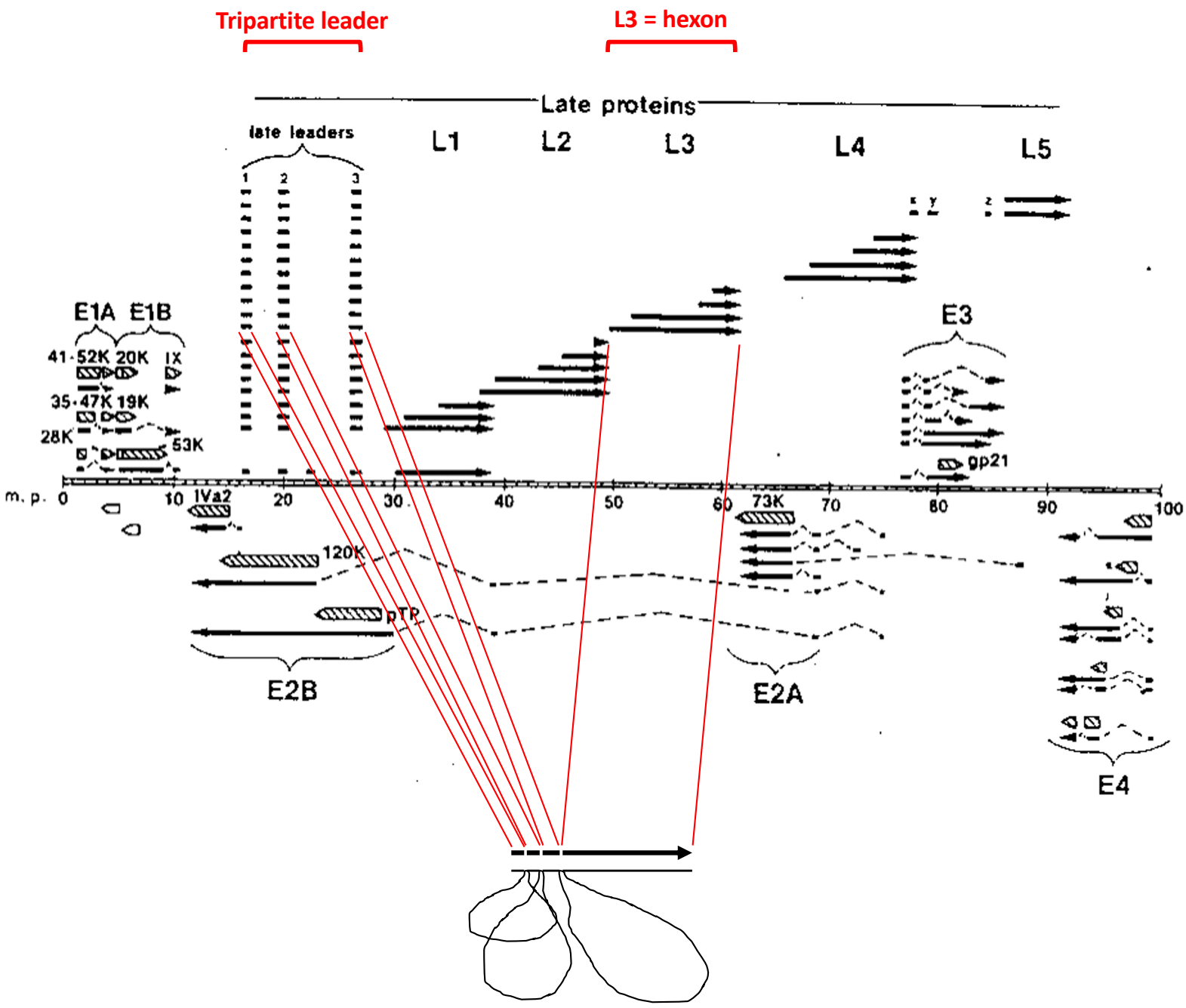
SUSAN M. BERGET, CLAIRE MOORE, AND PHILLIP A. SHARP

Center for Cancer Research and Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Communicated by David Baltimore, May 9, 1977


G

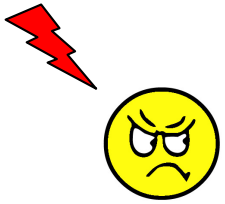

5′
Introne
C
Introne
A
Ibrido
DNA-RNA
3′
Introne
B


Tripartite leader
L3 = hexon
Late proteins
late leaders
L1
L2
L3
L4
L5
E1A
E1B
41-52K
20K
IX
35-47K
19K
28K
53K
E3
gp21
m.p. 0
10
IVa2
20
30
40
50
60
73K
70
80
90
100
120K
pTP
E2B
E2A
E4

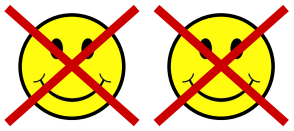
Oncogenesi

Tumorigenesi

Attivazione di
<u>oncogèni</u>



Inattivazione di
<u>oncosoppressori</u>



Esempi di oncosoppressori

p53

Arresto del ciclo cellulare
Apoptosi

Rb

Controllo del ciclo cellulare
Differenziamento

Association between an oncogene and an anti-oncogene: the adenovirus E1A proteins bind to the retinoblastoma gene product

Peter Whyte[*†], Karen J. Buchkovich[*], Jonathan M. Horowitz[‡], Stephen H. Friend[‡§], Margaret Raybuck[*†], Robert A. Weinberg[‡] & Ed Harlow[*‖]

[*] Cold Spring Harbor Laboratory, Cold Spring Harbor, New York 11724, USA
[‡] Whitehead Institute for Biomedical Research, Cambridge, Massachusetts 02142, USA and Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA
[§] Division of Hematology-Oncology, The Children's Hospital, Dana-Farber Cancer Institute, Department of Pediatrics, Harvard Medical School, Boston, Massachusetts 02115, USA

One of the cellular targets implicated in the process of transformation by the adenovirus E1A proteins is a 105K cellular protein. Previously, this protein had been shown to form stable protein/protein complexes with the E1A polypeptides but its identity was unknown. Here, we demonstrate that it is the product of the retinoblastoma gene. The interaction between E1A and the retinoblastoma gene product is the first demonstration of a physical link between an oncogene and an anti-oncogene.

REGULATION of cellular proliferation is a complex process that involves both positively and negatively acting signals. Tumourigenesis results from alterations in genes whose protein products are involved in these signalling pathways. The DNA tumour viruses encode a set of proteins that are capable of overriding and reprogramming normal regulation of cellular growth; consequently, they have been widely used as model systems for studying cellular transformation. The oncogenes—tumour-inducing genes—from polyomavirus, simian virus 40 (SV40) and adenovirus are able to induce a number of distinct changes in cell phenotype, including immortalization, secretion of growth factors, loss of contact inhibition, anchorage-independent growth and morphological transformation. Unlike the transforming retroviruses, these DNA viruses contain oncogenes that do not appear to have cellular homologues. Although functional similarities have been shown between cellular oncogenes

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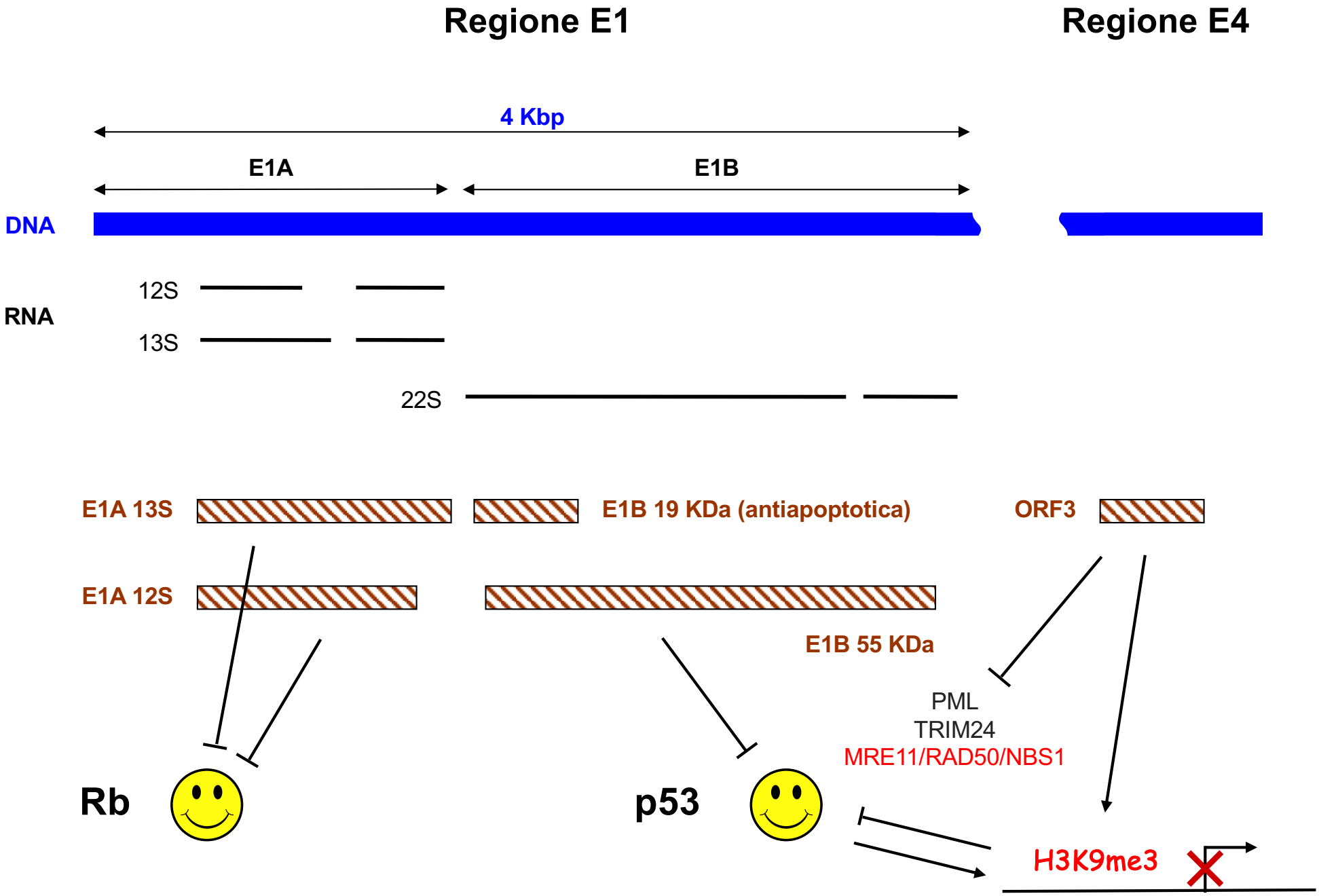
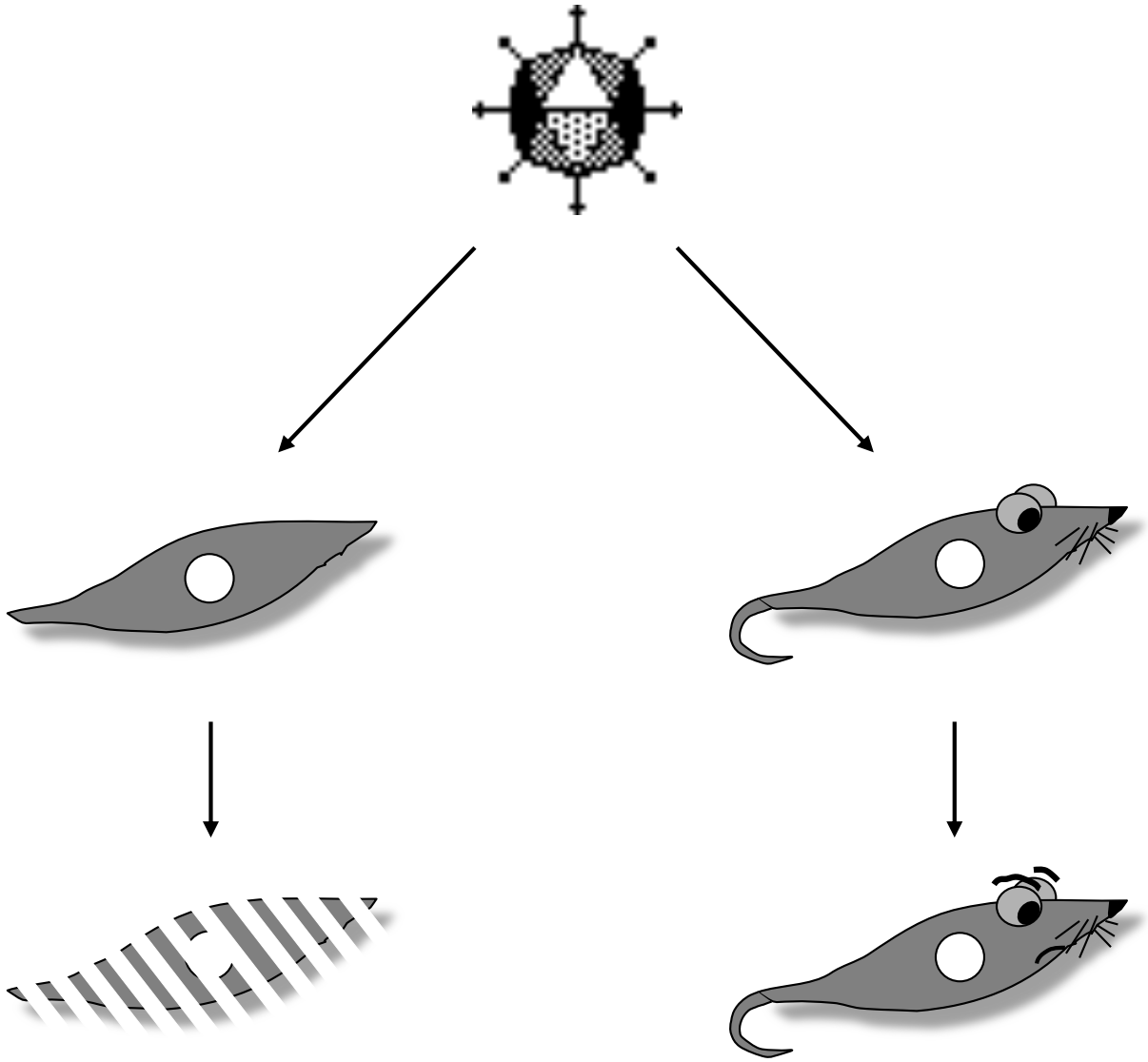
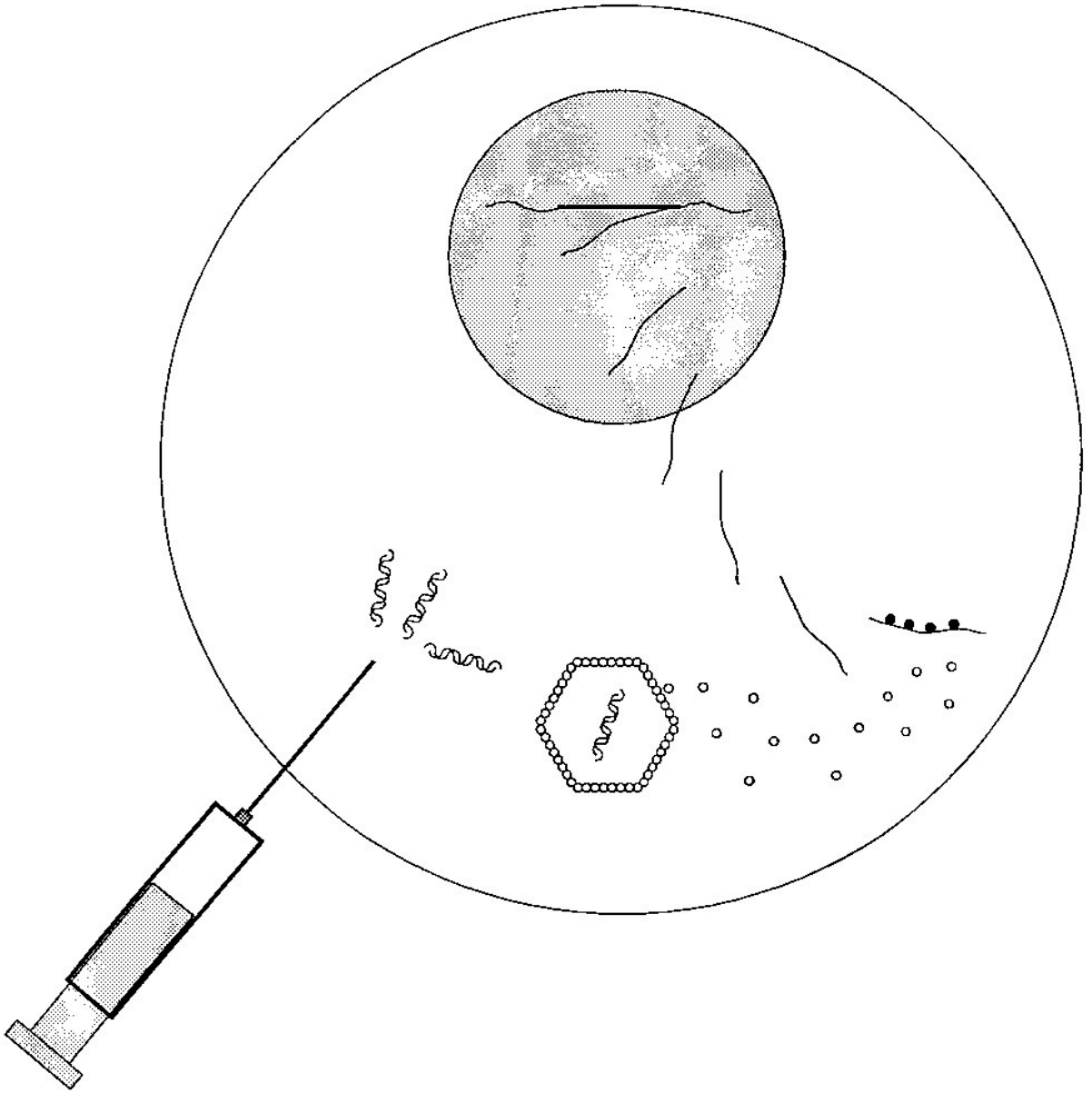
‖ To whom correspondence should be addressed.

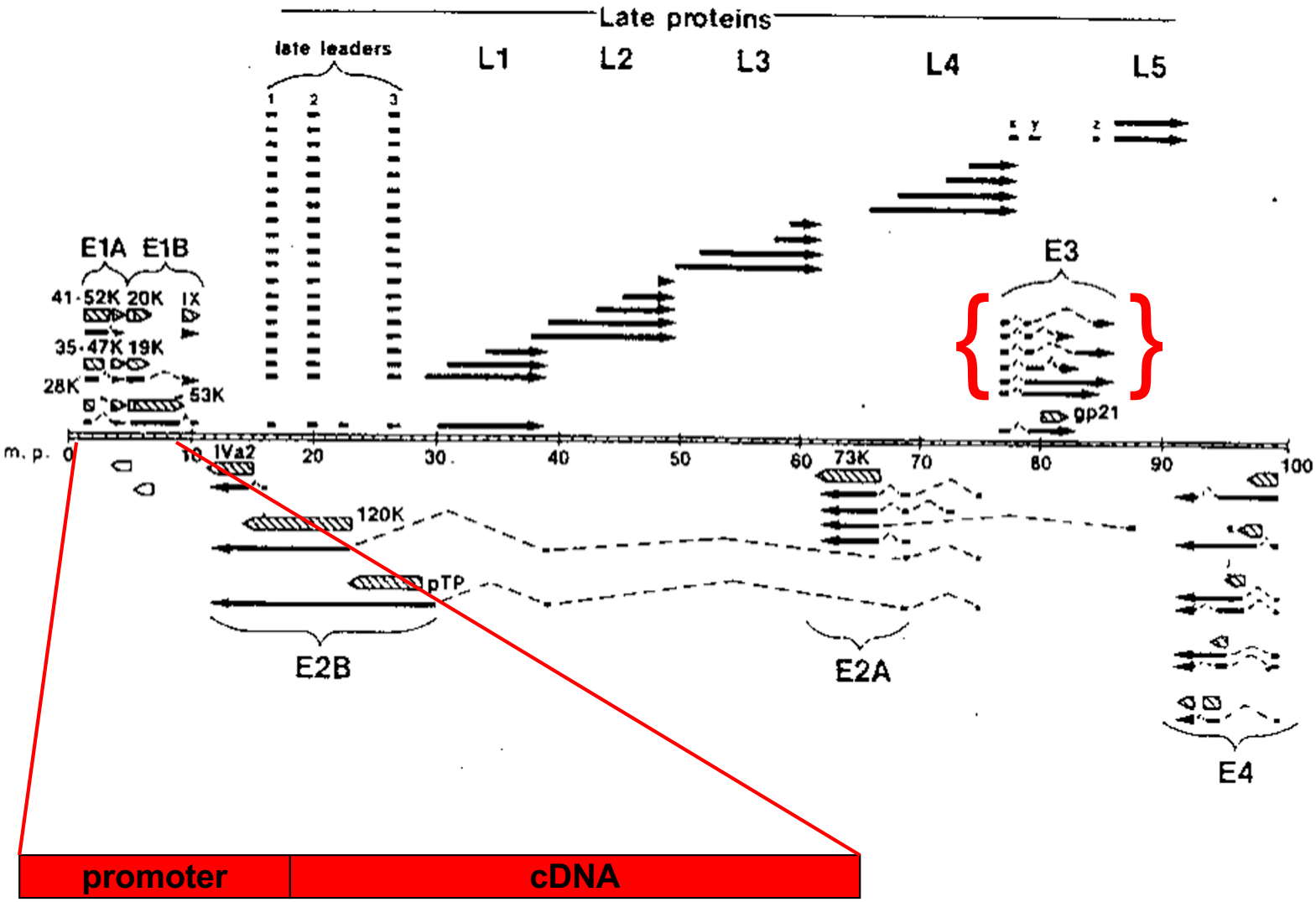
Nature 334:124-129, 1988


Regione E1
Regione E4
4 Kbp
E1A
E1B
DNA
RNA
12S
13S
22S
E1A 13S
E1B 19 KDa (antiapoptotica)
ORF3
E1A 12S
E1B 55 KDa
PML
TRIM24
MRE11/RAD50/NBS1
Rb
p53
H3K9me3

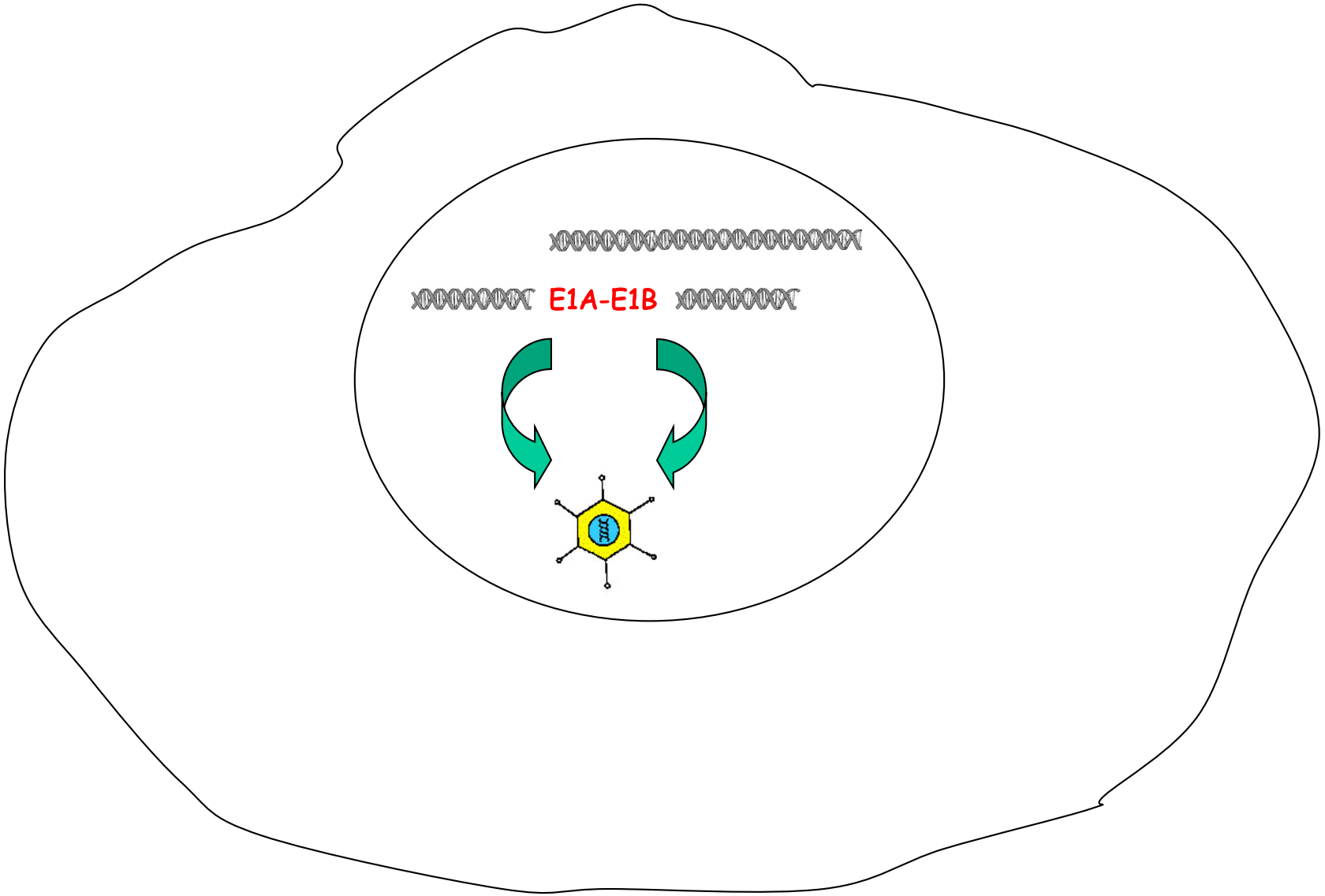


Adenovirus ricombinanti




Late proteins
late leaders
L1
L2
L3
L4
L5
E1A E1B
41·52K 20K IX
35·47K 19K
28K
53K
E3
gp21
m.p. 0
10
IVa2
20
30
40
50
60
73K
70
80
90
100
120K
pTP
E2B
E2A
E4
promoter
cDNA

HEK-293



"Gutted" adenoviruses