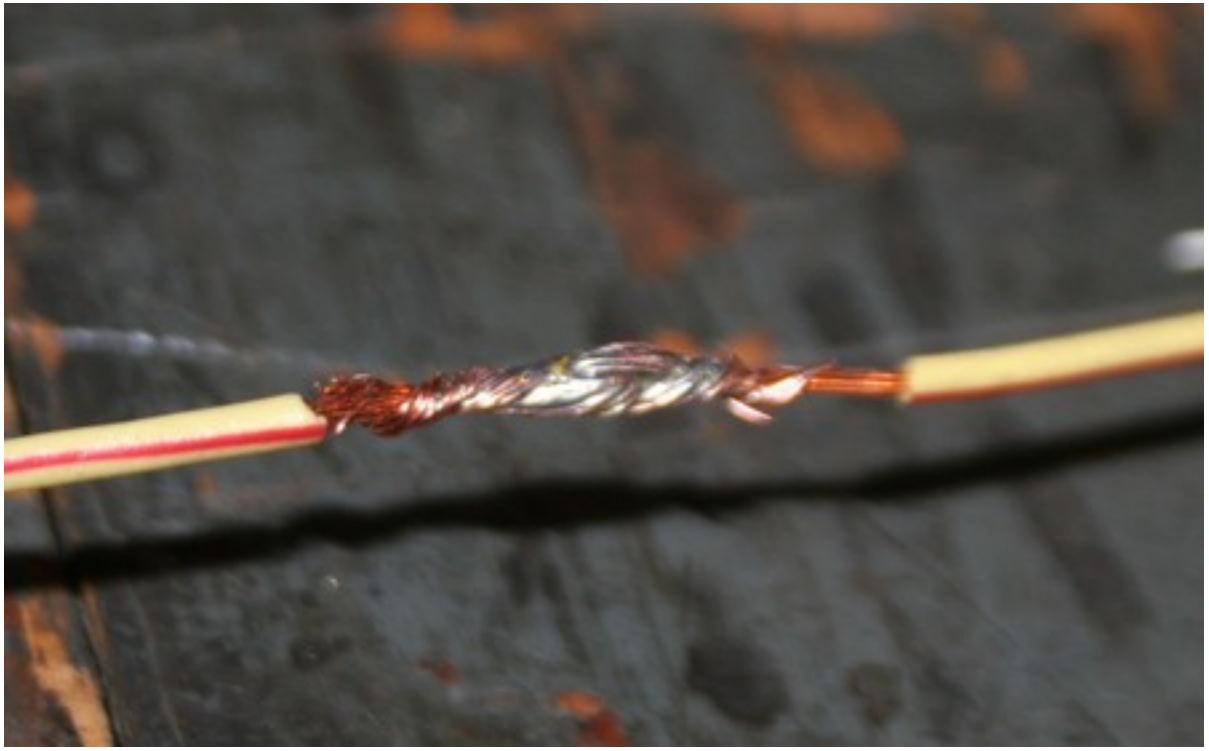
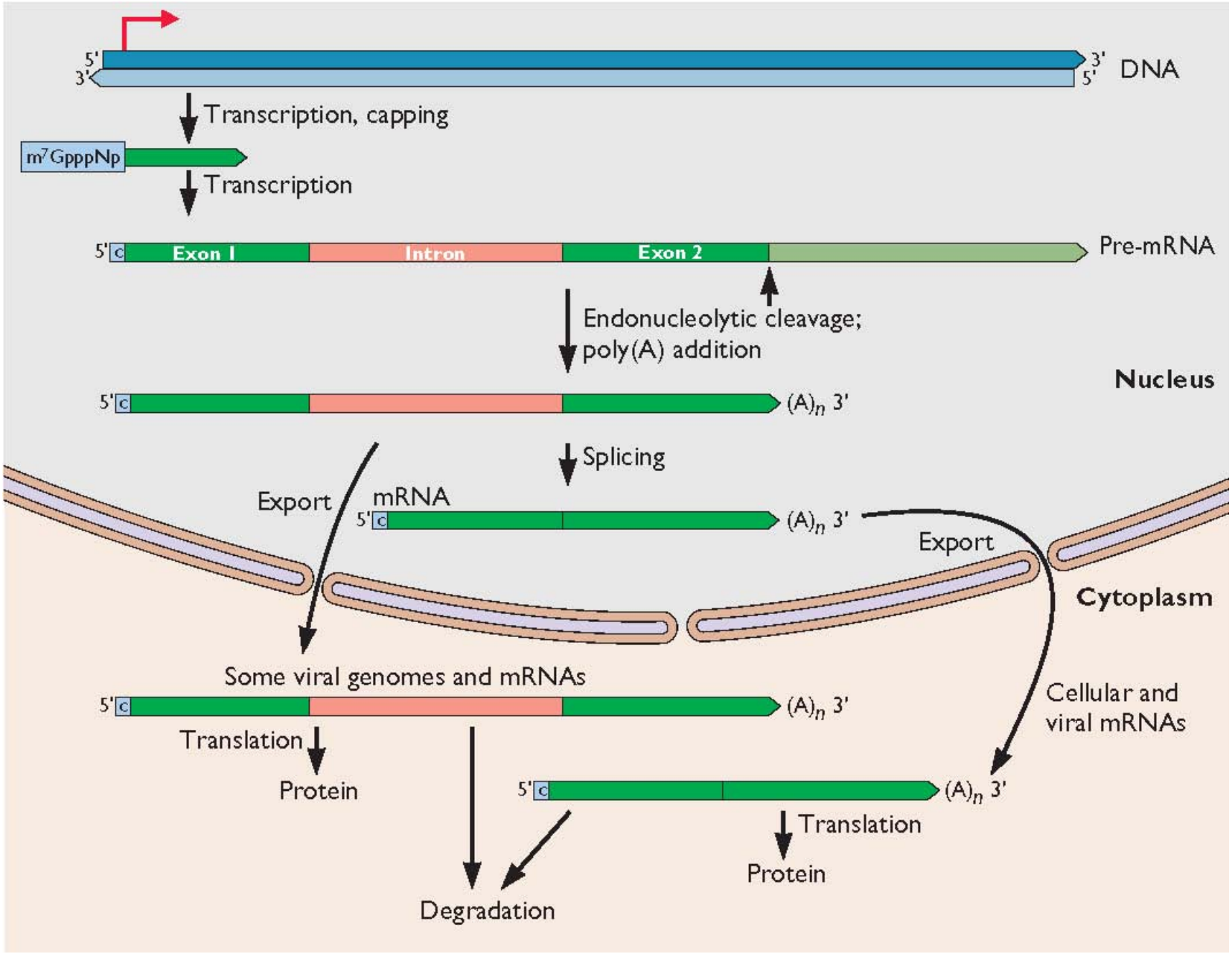
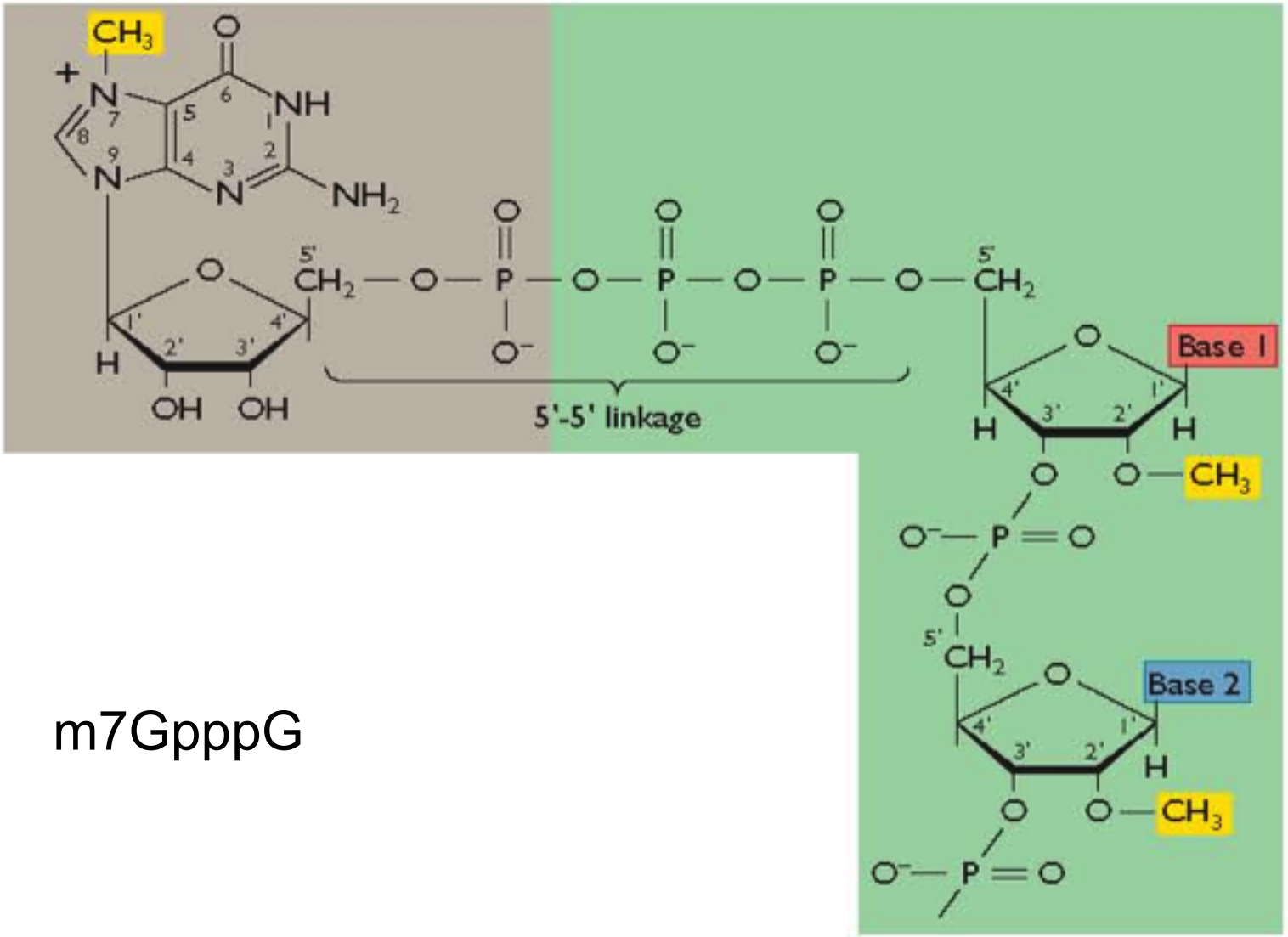
TWiV 216: Processing viral RNA

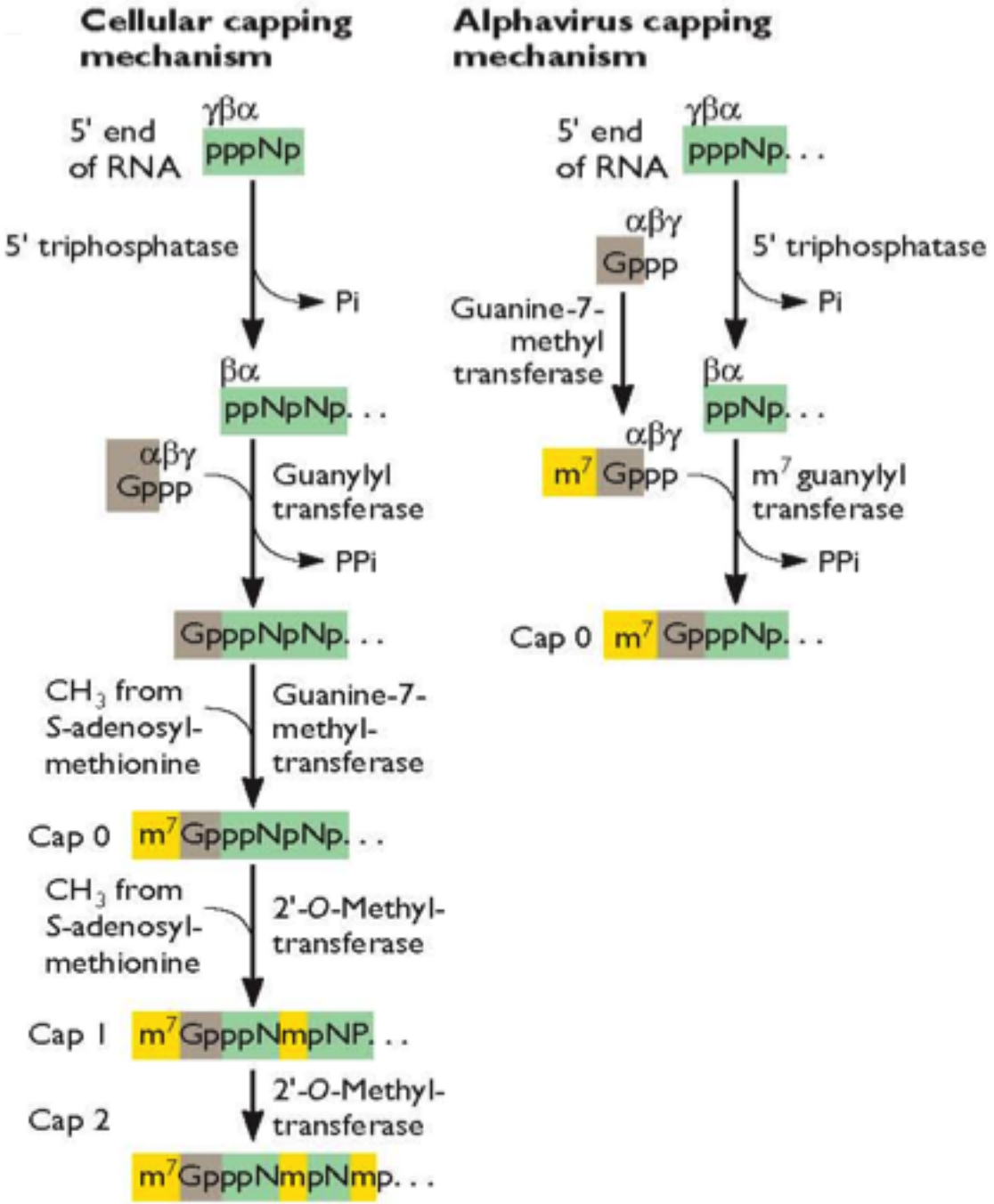
Virology 101




5'
3'
3'
5'
DNA
Transcription, capping
m7GpppNp
Transcription
5'
c
Exon 1
Intron
Exon 2
Pre-mRNA
Endonucleolytic cleavage;
poly(A) addition
Nucleus
5'
c
(A)n 3'
Splicing
Export
mRNA
5'
c
(A)n 3'
Export
Cytoplasm
Some viral genomes and mRNAs
5'
c
(A)n 3'
Translation
Protein
Degradation
Cellular and
viral mRNAs
5'
c
(A)n 3'
Translation
Protein



m7GpppG


Cellular capping mechanism
Alphavirus capping mechanism
5' end of RNA
γβα
pppNp
5' triphosphatase
Pi
βα
ppNpNp. . .
αβγ
Gppp
Guanylyl transferase
PPi
GpppNpNp. . .
CH3 from S-adenosyl-methionine
Guanine-7-methyl-transferase
Cap 0
m7GpppNpNp. . .
CH3 from S-adenosyl-methionine
2'-O-Methyl-transferase
Cap 1
m7GpppNmpNP. . .
Cap 2
2'-O-Methyl-transferase
m7GpppNmpNmp. . .
5' end of RNA
γβα
pppNp. . .
αβγ
Gppp
Guanine-7-methyl transferase
5' triphosphatase
Pi
βα
ppNp. . .
αβγ
m7Gppp
m7 guanylyl transferase
PPi
Cap 0
m7GpppNp. . .

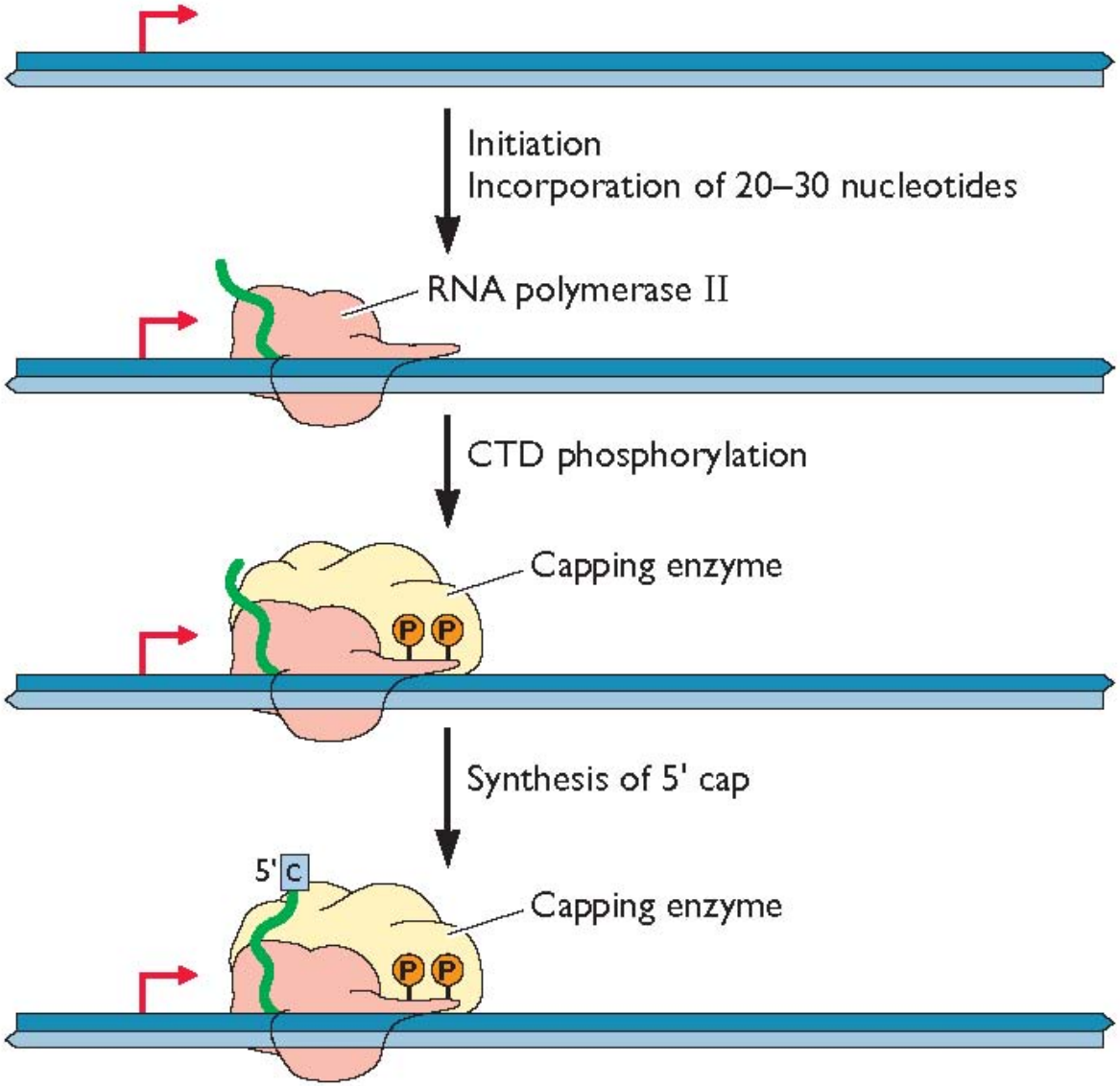
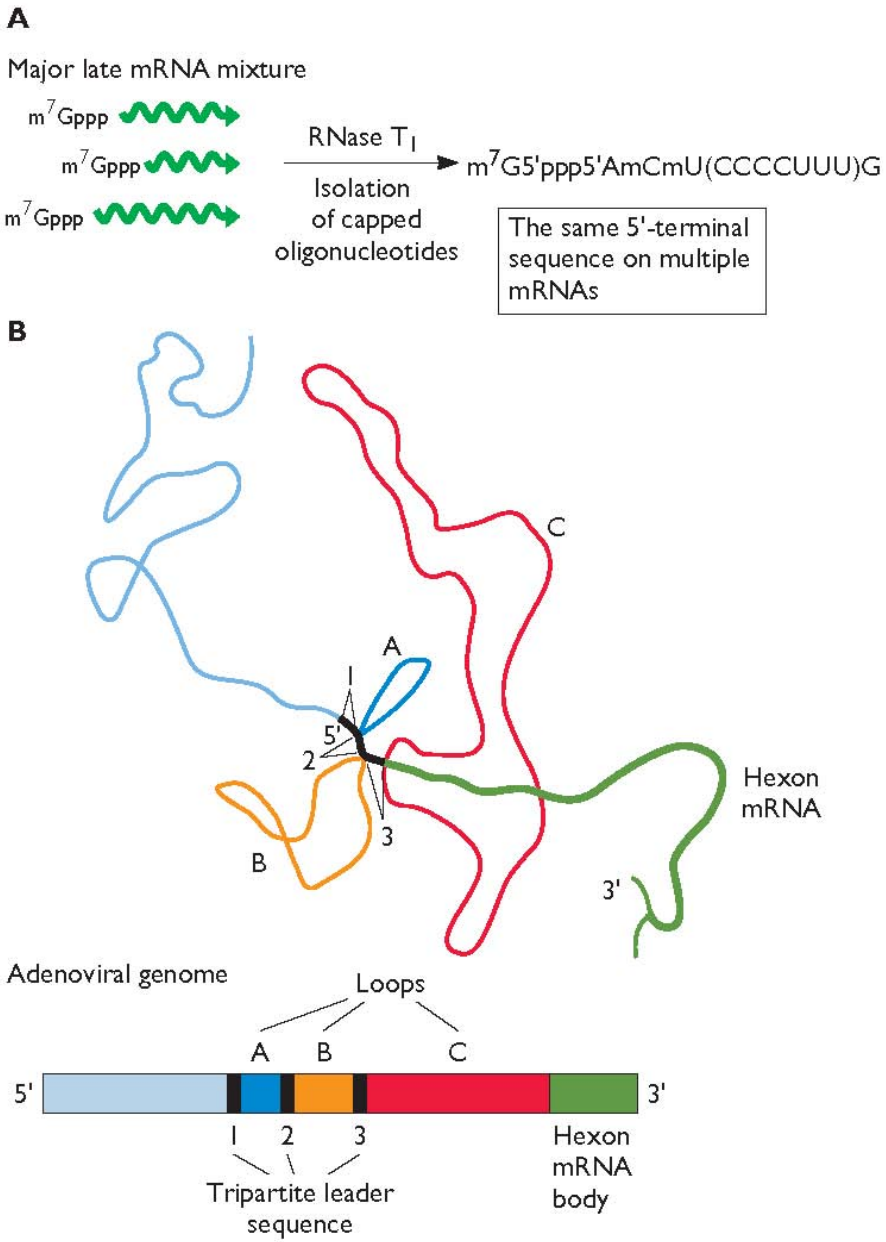

Initiation
Incorporation of 20–30 nucleotides
RNA polymerase II
CTD phosphorylation
Capping enzyme
P
P
Synthesis of 5' cap
5'
C
Capping enzyme
P
P

Table 10.1 Mechanisms of synthesis of 5′-terminal cap structures of viral mRNAs

Mechanism	Virus family	Enzyme synthesizing pre-mRNA
Synthesis by host cell enzymes	*Adenoviridae, Hepadnaviridae, Herpesviridae, Papillomaviridae, Parvoviridae, Polyomaviridae, Retroviridae*	Cellular DNA-dependent RNA polymerase II
Synthesis by viral enzymes	*Reoviridae, Rhabdoviridae, Togaviridae*	Viral RNA-dependent RNA polymerase
	Poxviridae	Viral DNA-dependent RNA polymerase
Acquisition from cellular pre-mRNA or mRNA	*Bunyaviridae, Orthomyxoviridae*	Viral RNA-dependent RNA polymerase

mRNA splicing discovered in adenovirus infected cells



Richard J. Roberts

Born: 6 September 1943, Derby, United Kingdom

Affiliation at the time of the award: New England Biolabs, Beverly, MA, USA

Prize motivation: "for their discoveries of split genes"

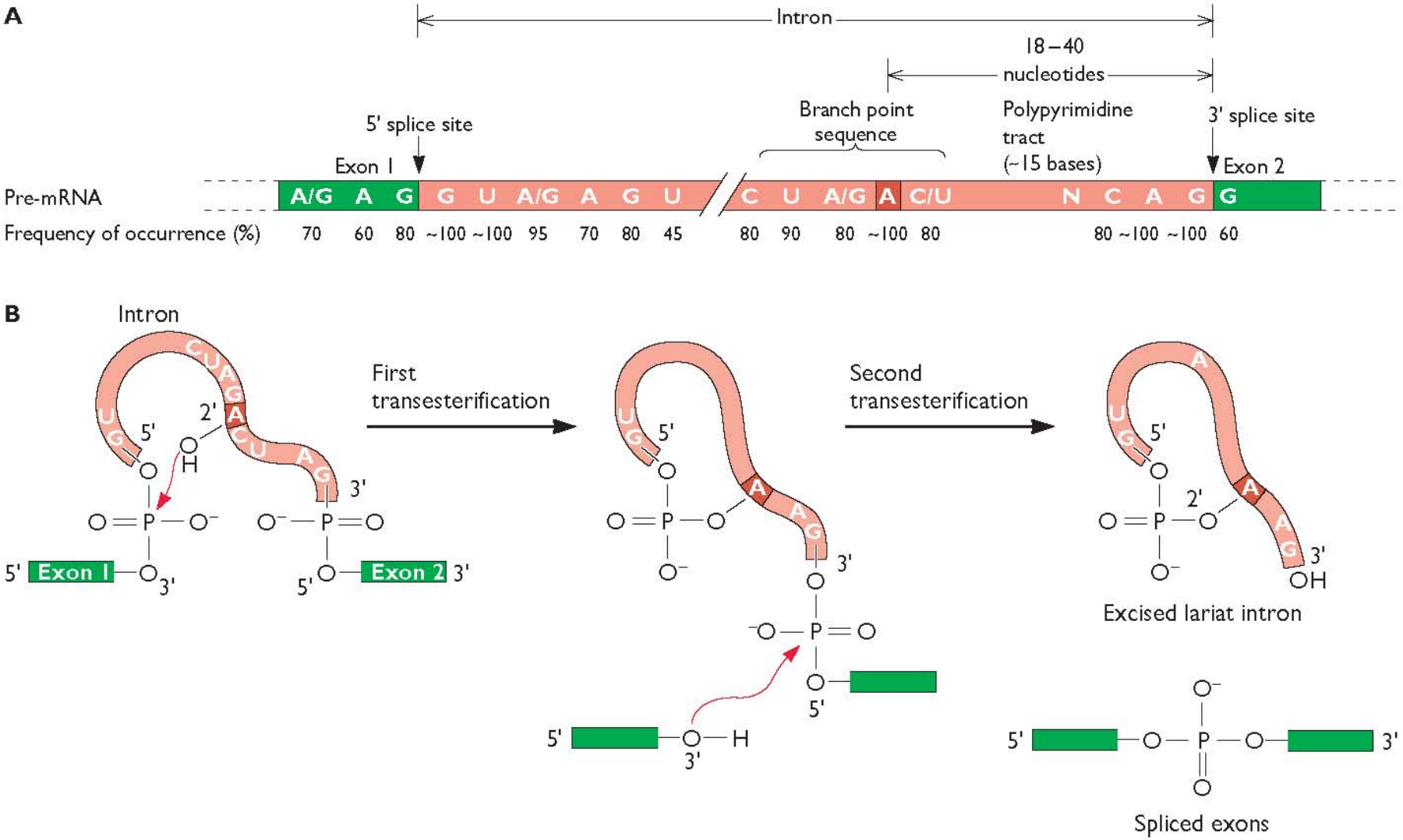
Phillip A. Sharp

Born: 6 June 1944, Falmouth, KY, USA

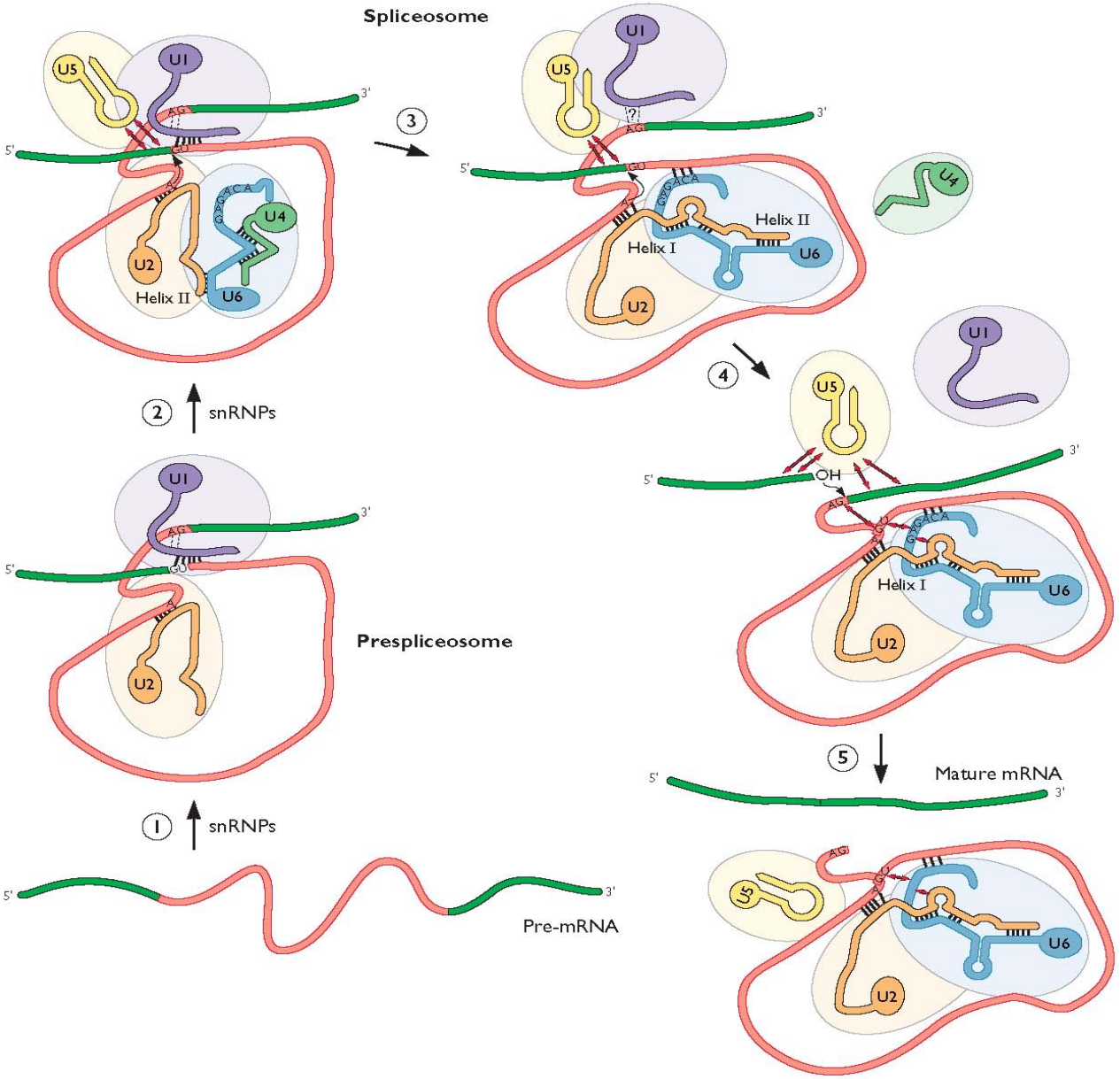
Affiliation at the time of the award: Massachusetts Institute of Technology (MIT), Center for Cancer Research, Cambridge, MA, USA

Prize motivation: "for their discoveries of split genes"

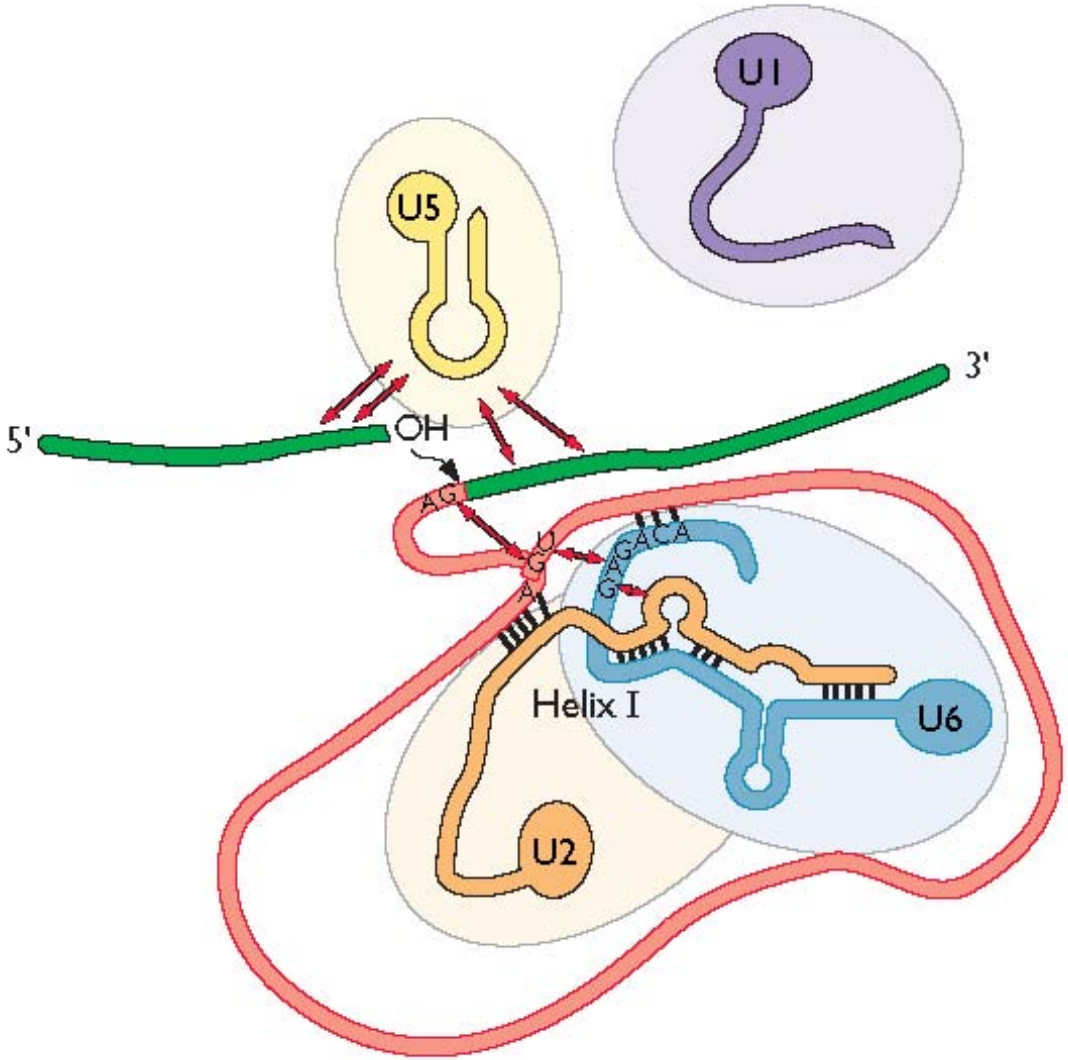
Splicing of pre-mRNA



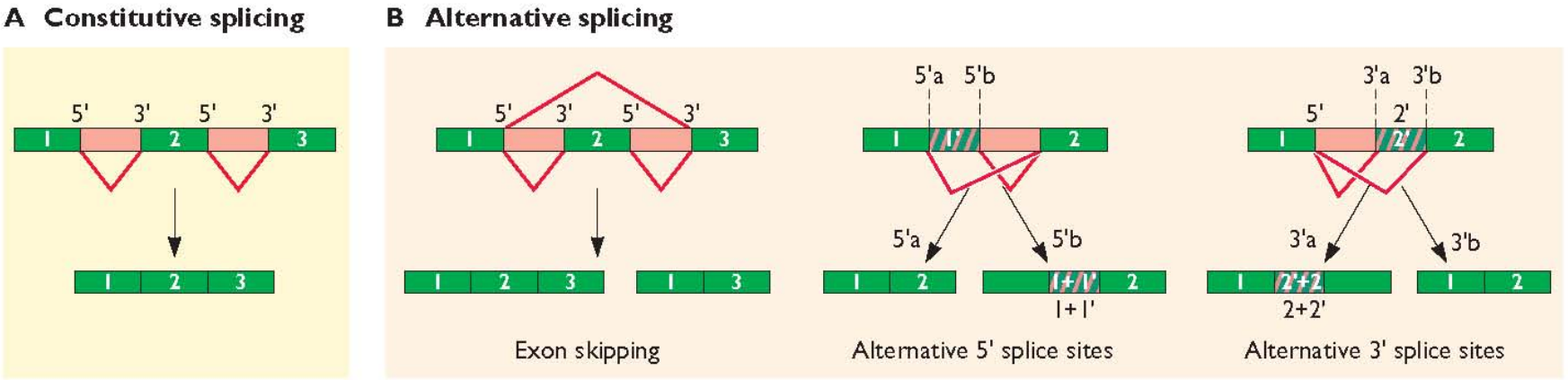
RNA-RNA interactions during splicing



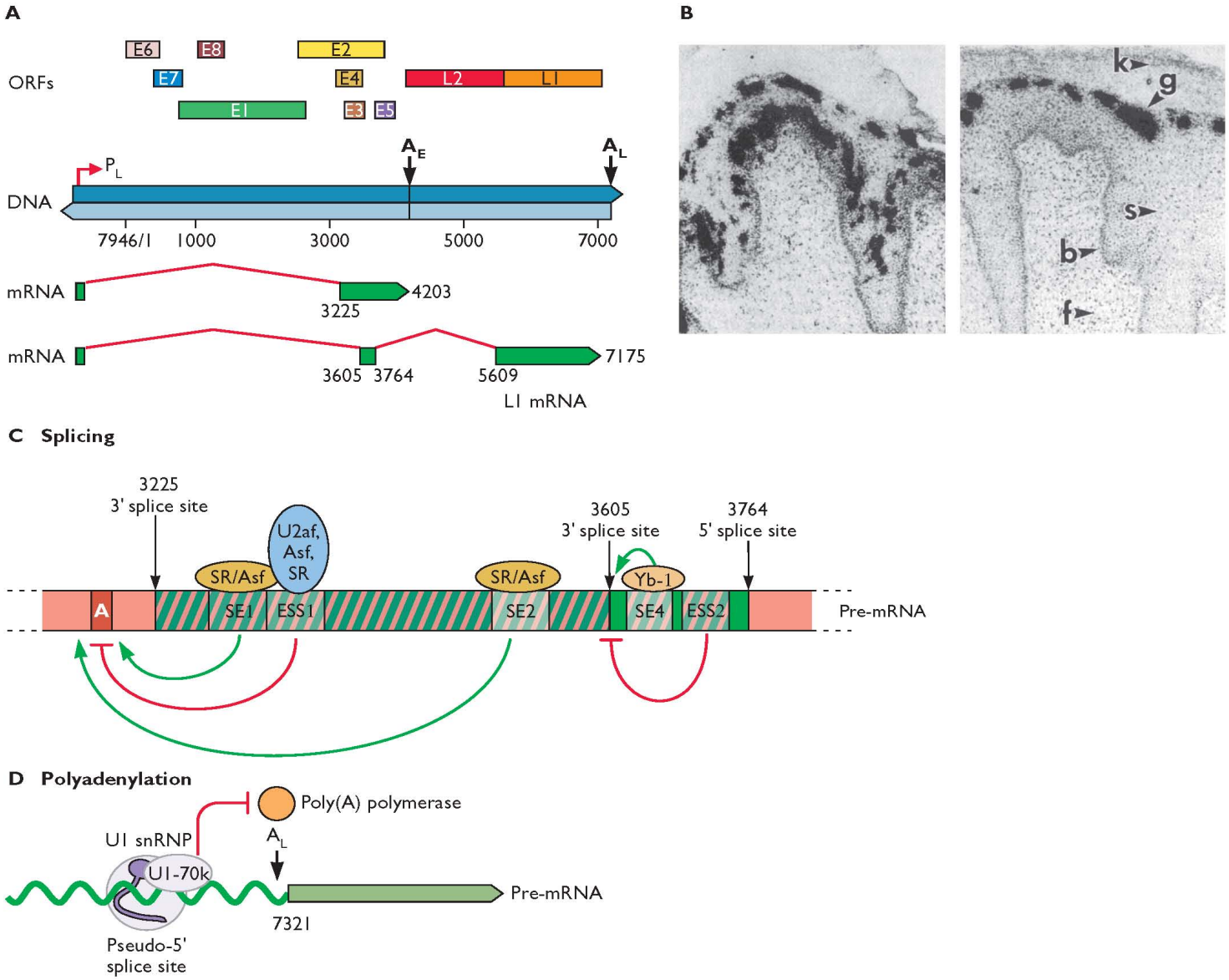
RNA catalysis without protein



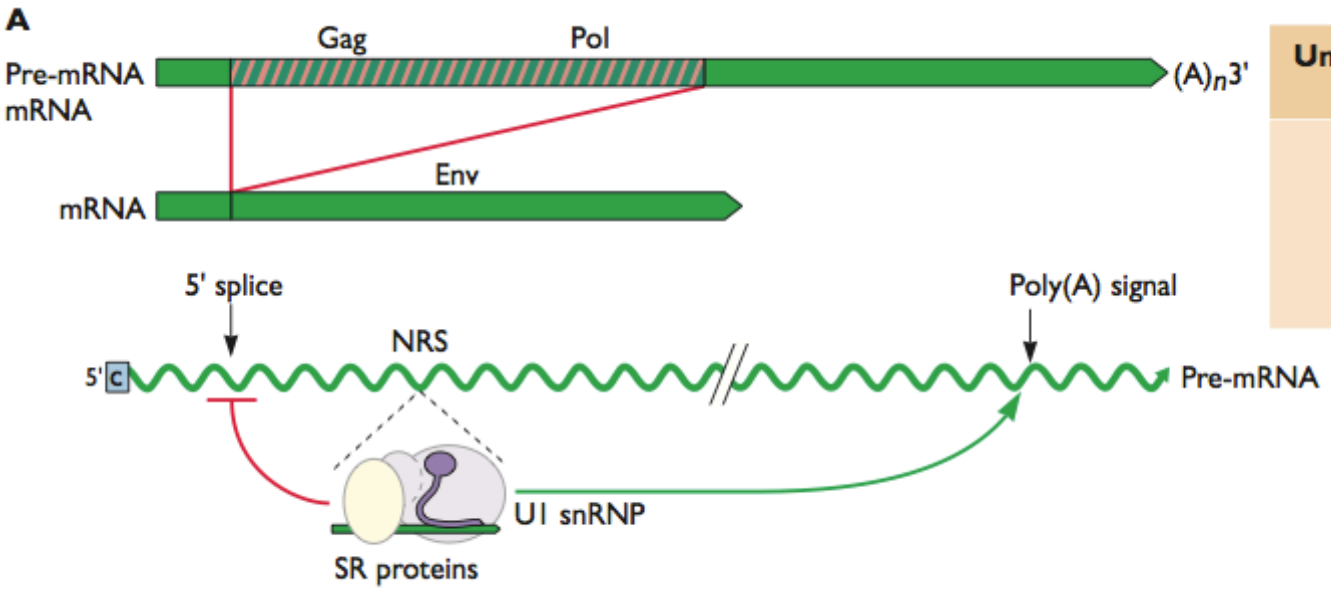
Alternative splicing



Alternative polyadenylation and splicing

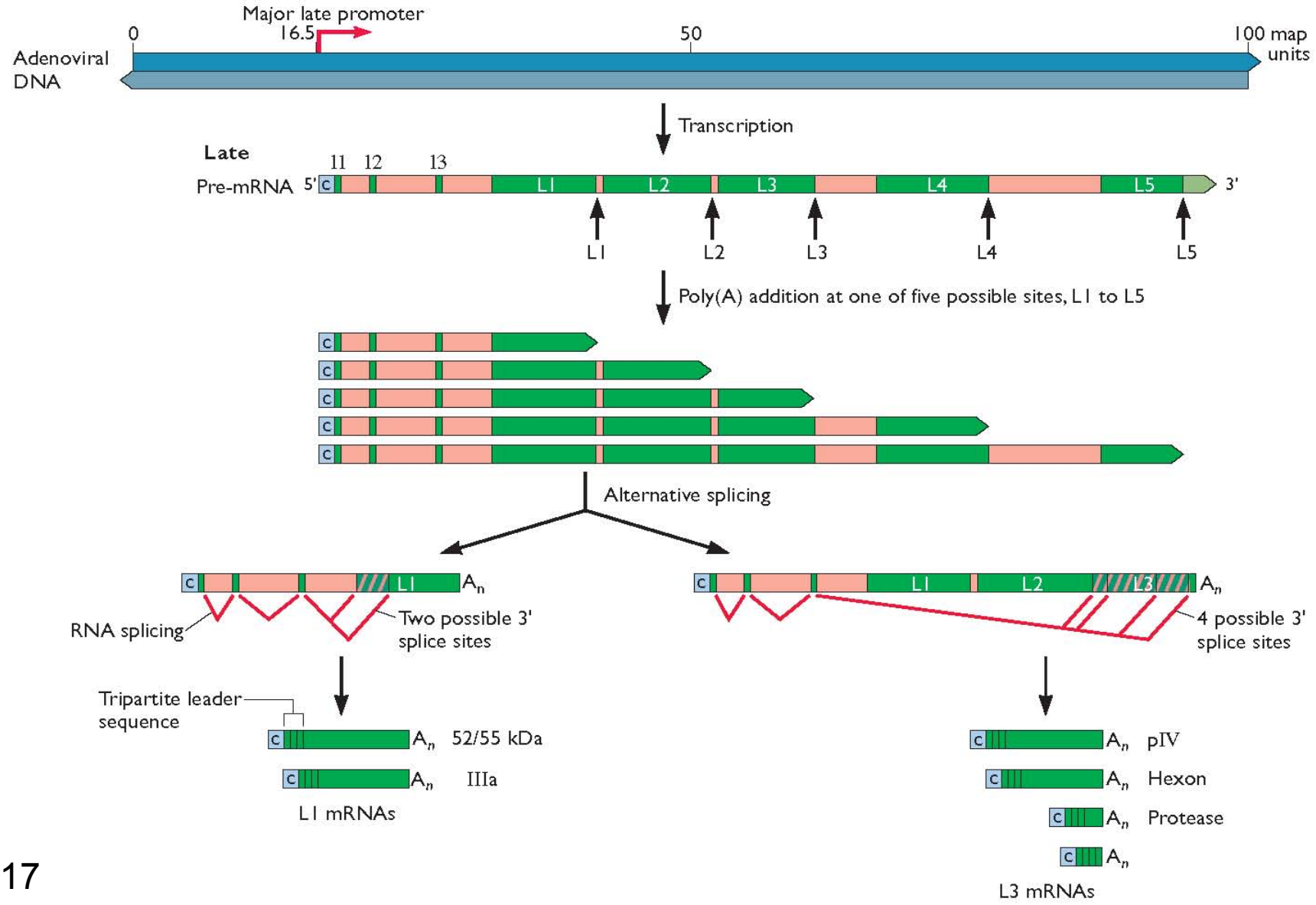


Control of RNA processing during retrovirus infection

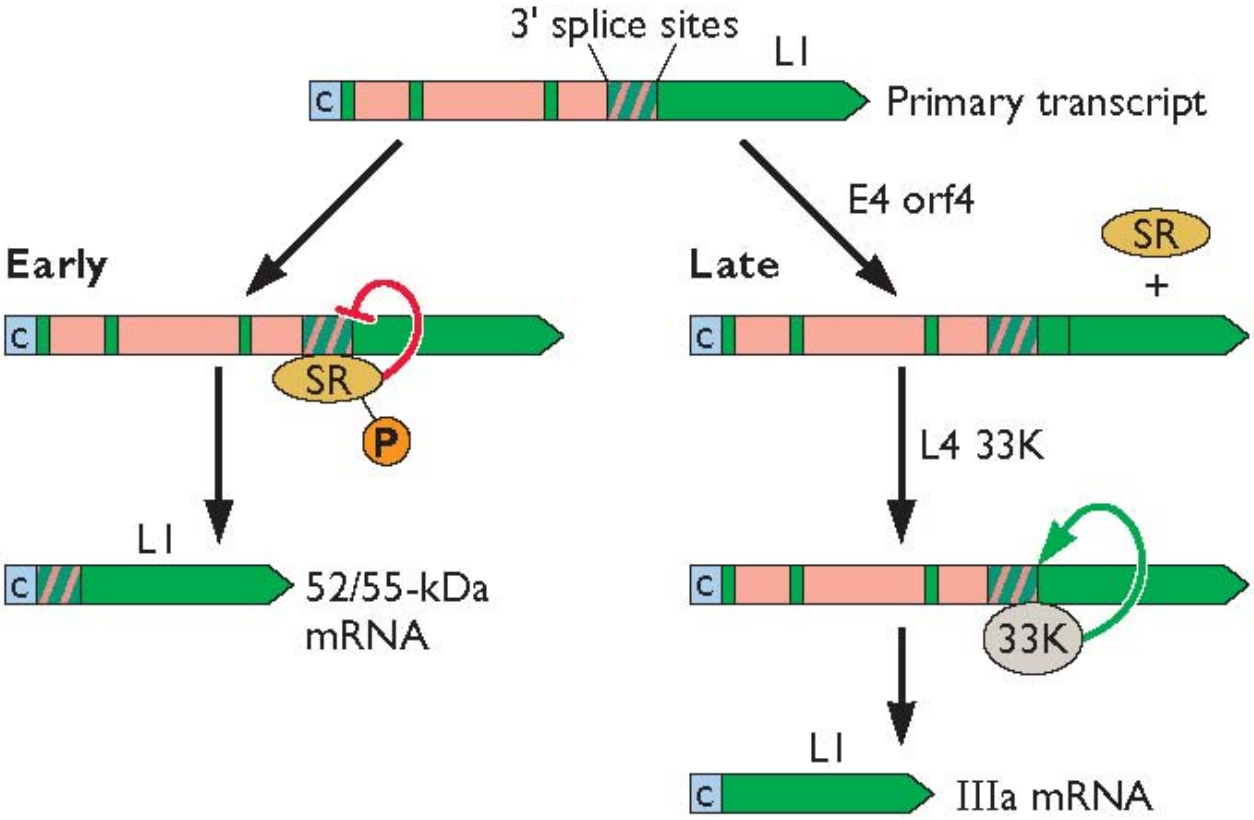


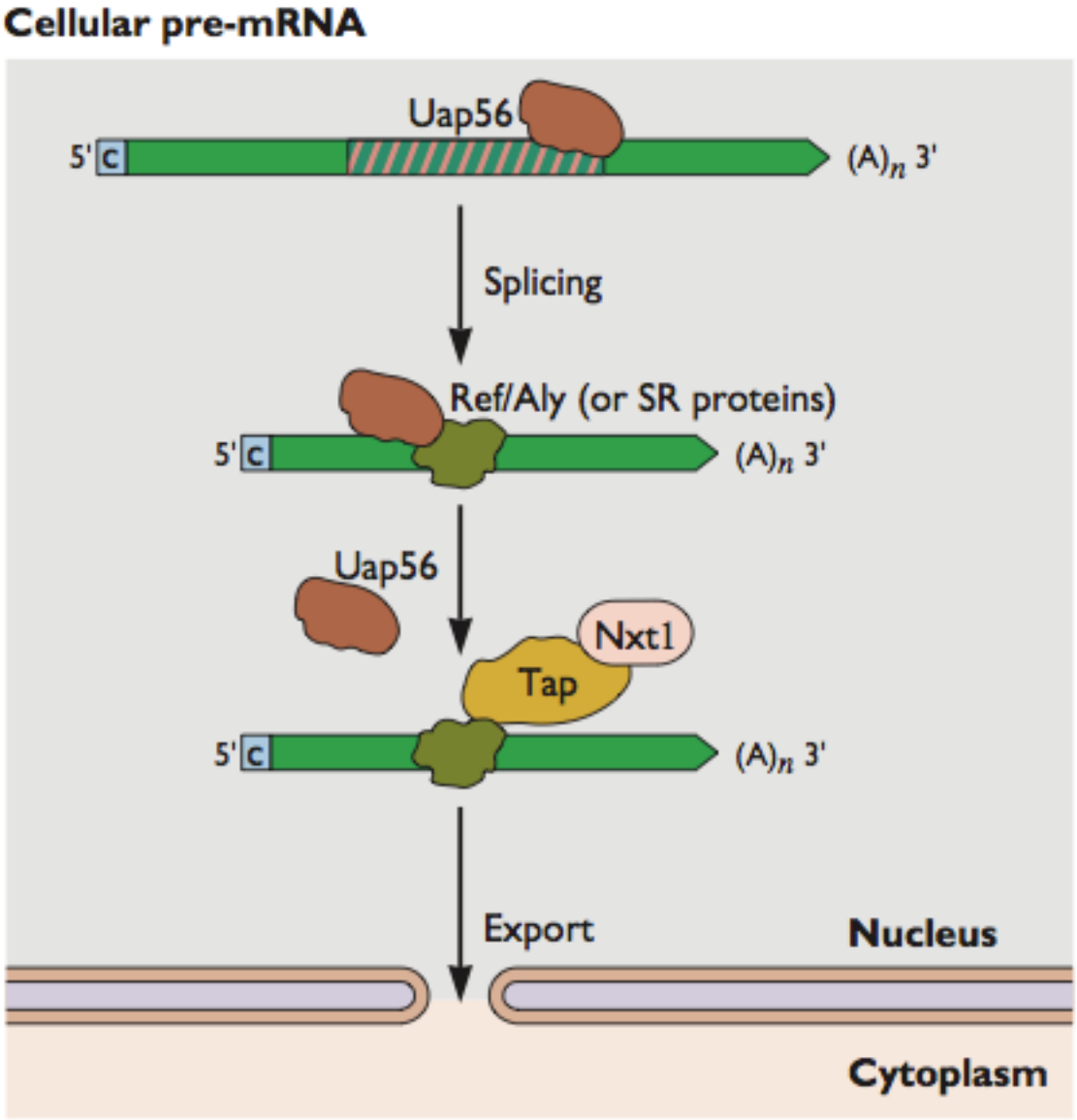
Unspliced:spliced RNA	Viral propagation
2:1	Wild type
1:1	Reduced
1:2	Undetectable

Alternative polyadenylation and splicing during adenovirus infection

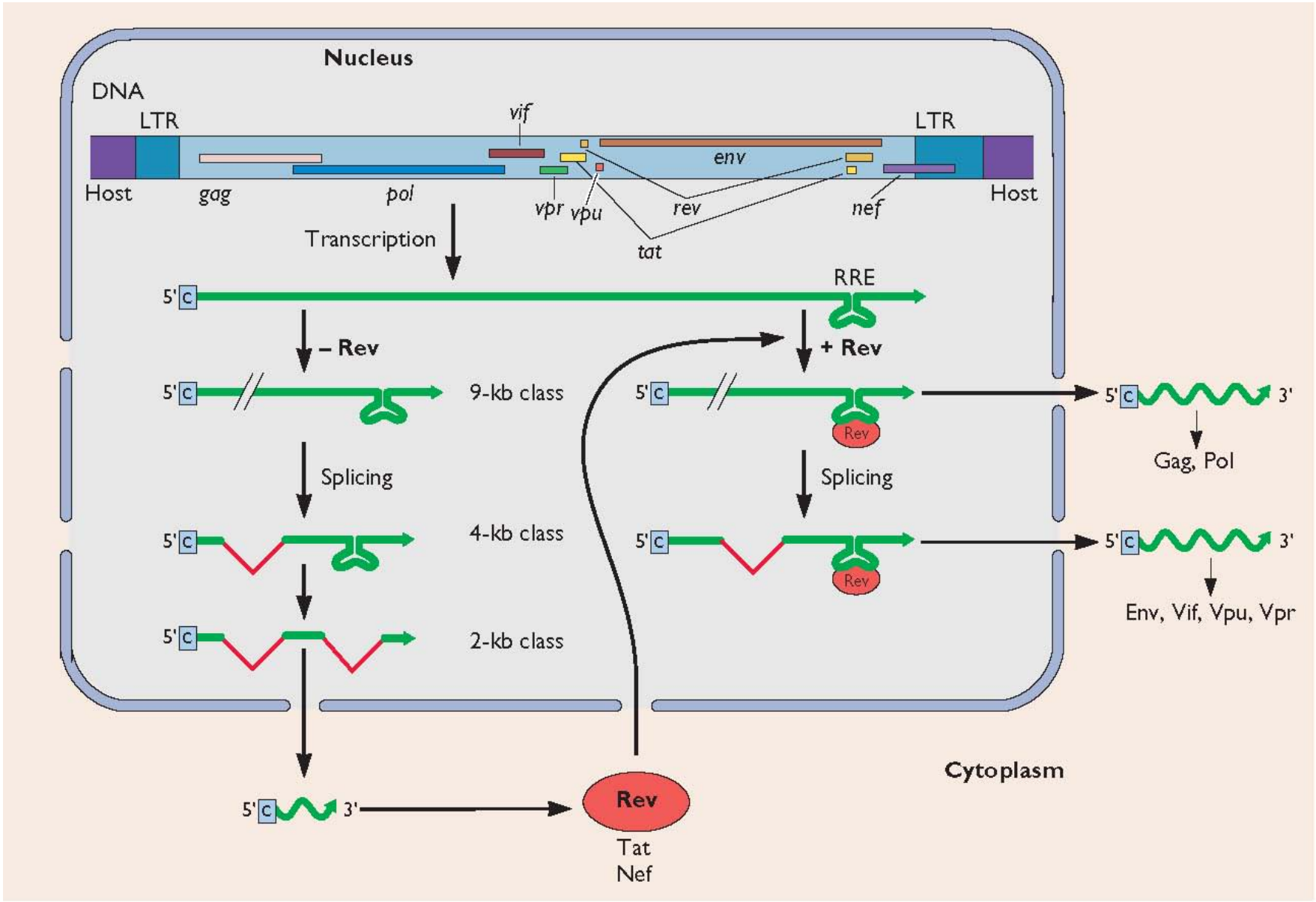


Viral proteins can regulate alternative splicing

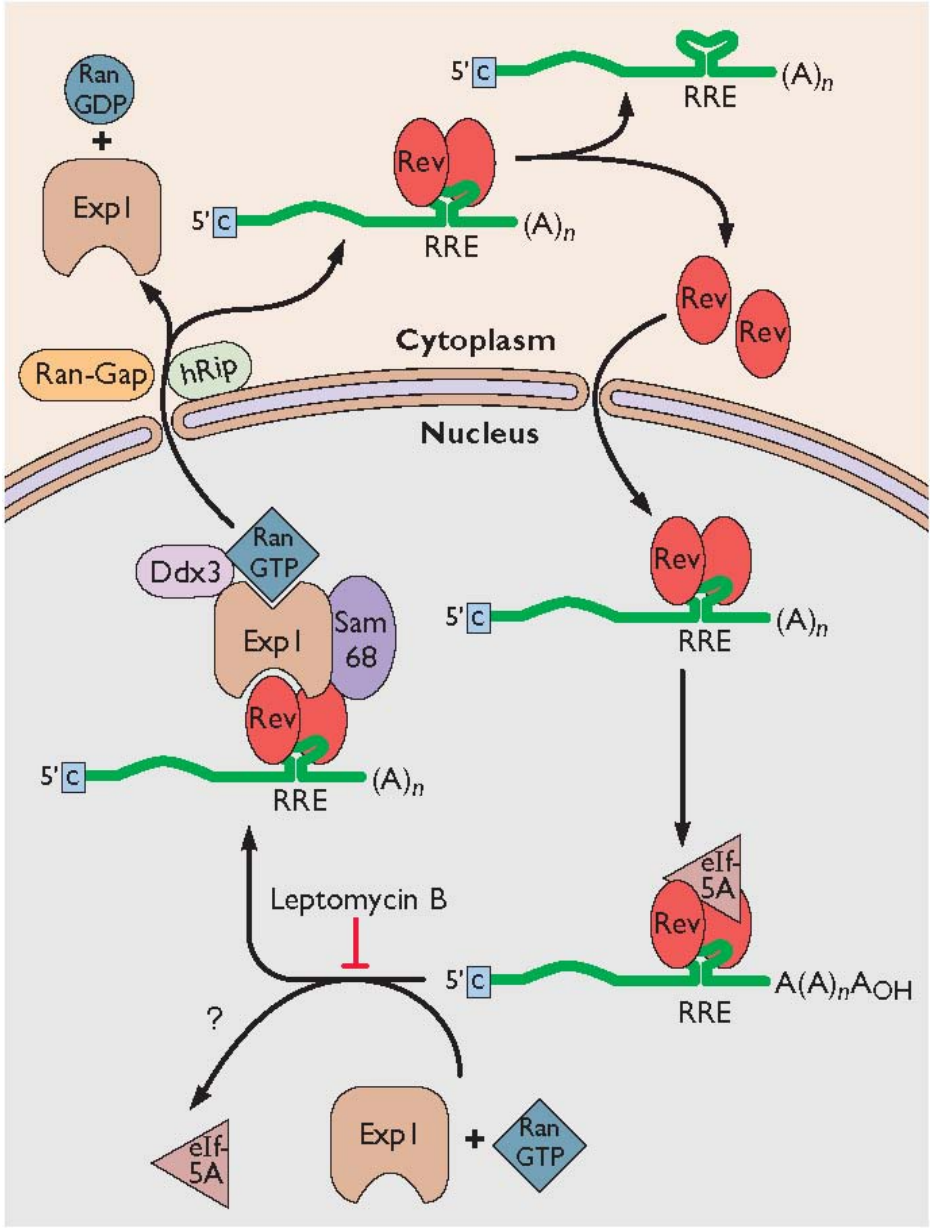



Cellular pre-mRNA
Uap56
5'
C
(A)n 3'
Splicing
Ref/Aly (or SR proteins)
5'
C
(A)n 3'
Uap56
Nxt1
Tap
5'
C
(A)n 3'
Export
Nucleus
Cytoplasm

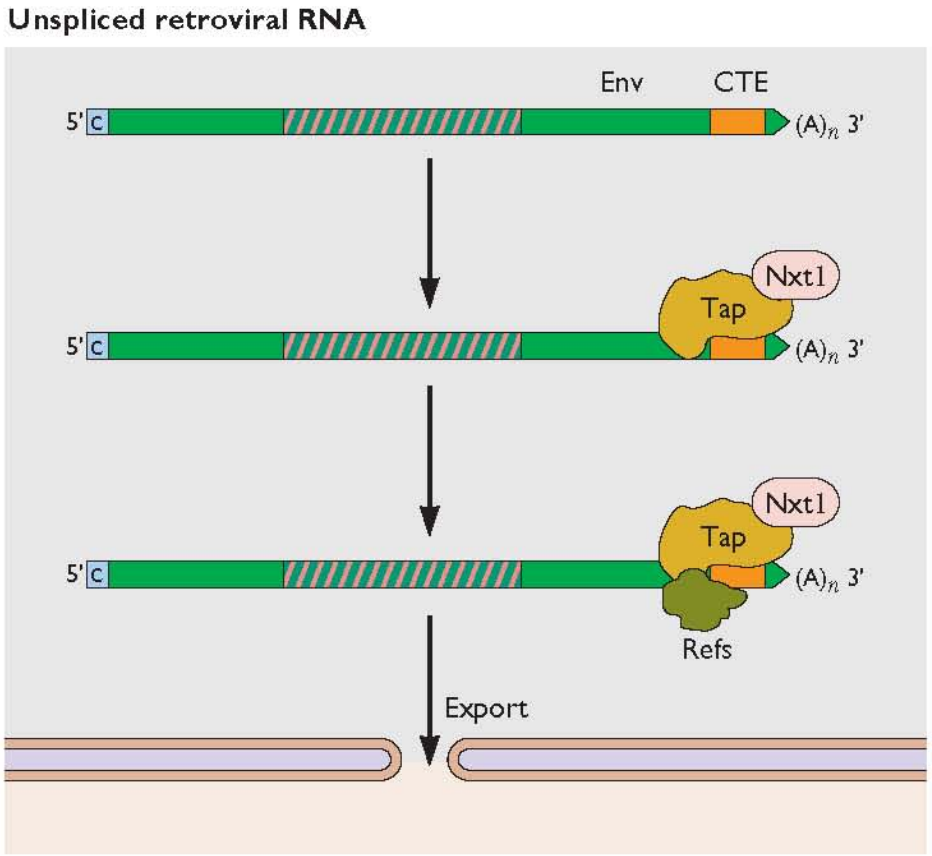
Rev protein regulates export of HIV mRNAs



Mechanism of Rev protein mediated RNA export



Retroviral mRNA export without Rev protein



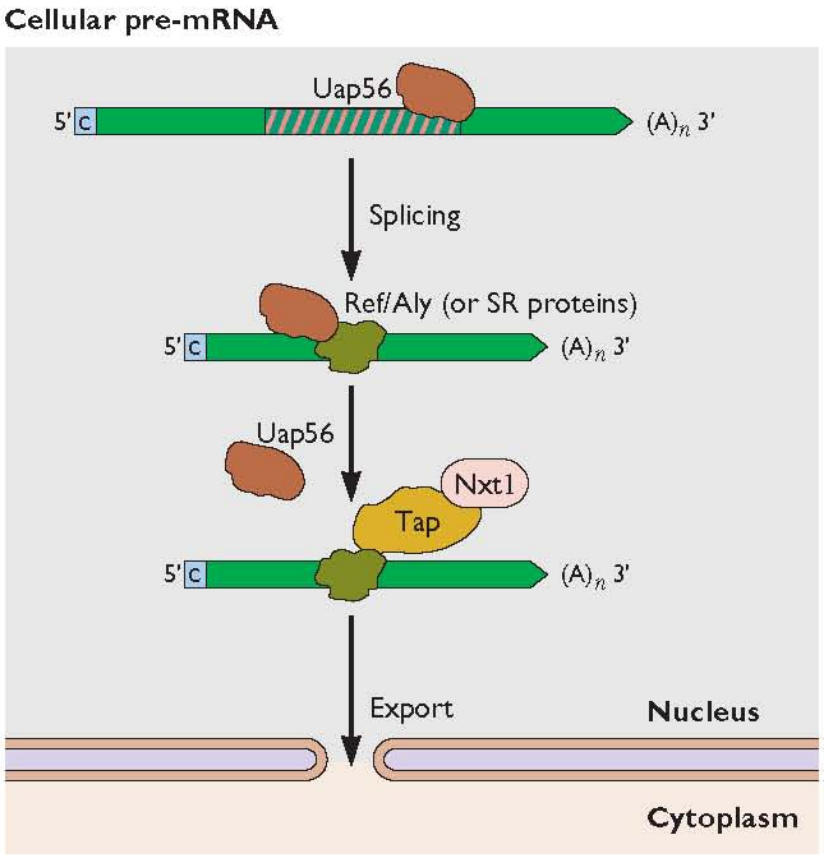
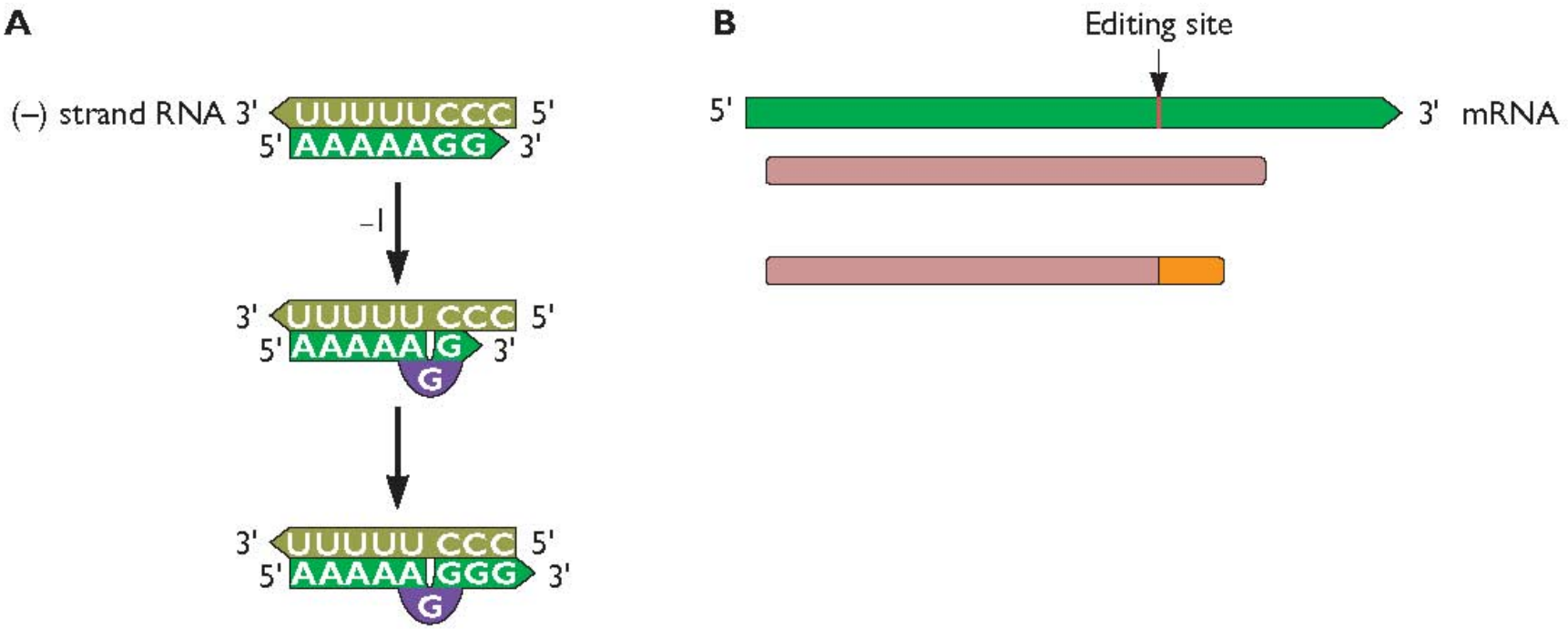


Table 10.3 Viral proteins that regulate RNA-processing reactions

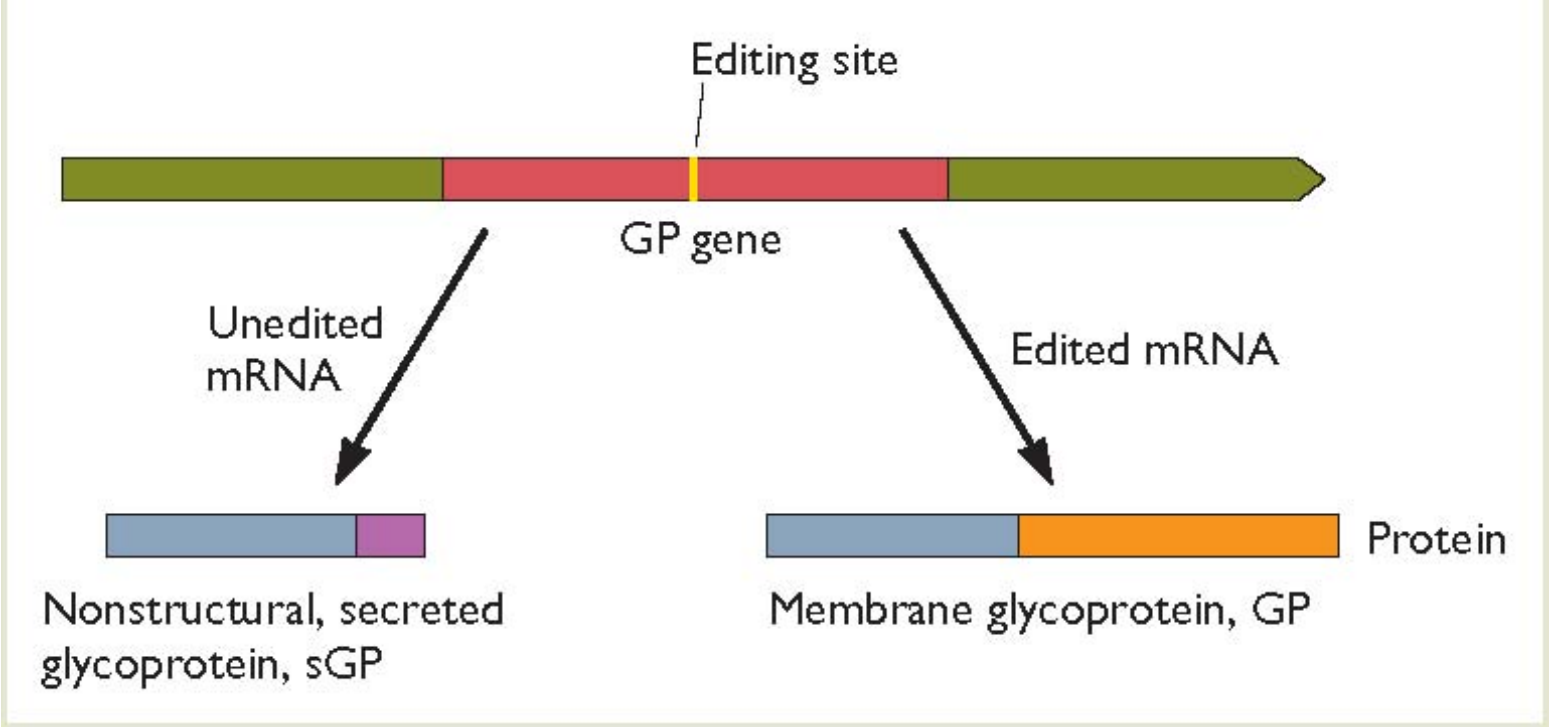
Virus	Protein(s)	Functions
Adenovirus		
Human adenovirus type 2	E4 ORF4	Induces dephosphorylation of cellular SR proteins by protein phosphatase 2A; relieves inhibition of L1 pre-mRNA splicing at the IIIa 3′ splice site by phosphorylated SR proteins present early in infection
	E1B 55-kDa–E4 ORF6	The complex inhibits export of fully processed cellular mRNAs and induces selective export of viral late mRNAs
	L4 33 kDa	Promotes alternative splicing to produce L1 IIIa mRNA
Herpesvirus		
Herpes simplex virus type 1	ICP27	Stimulates polyadenylation of viral late mRNAs with suboptimal sequences at their polyadenylation sites; inhibits splicing of intron-containing cellular and probably viral mRNAs; promotes export of viral single-exon mRNAs
Retrovirus		
Human immunodeficiency virus type 1	Rev	Mediates export of unspliced and incompletely spliced viral mRNAs

For temporal regulation of viral gene expression, or inhibition of the production of cell mRNAs

Editing of viral mRNAs



RNA editing produces mRNA for Ebola virus glycoprotein



Editing of hepatitis delta satellite virus RNA