Please take the listener survey:

http://triplemojo.com/twiv

DNA-dependent RNA synthesis (transcription)

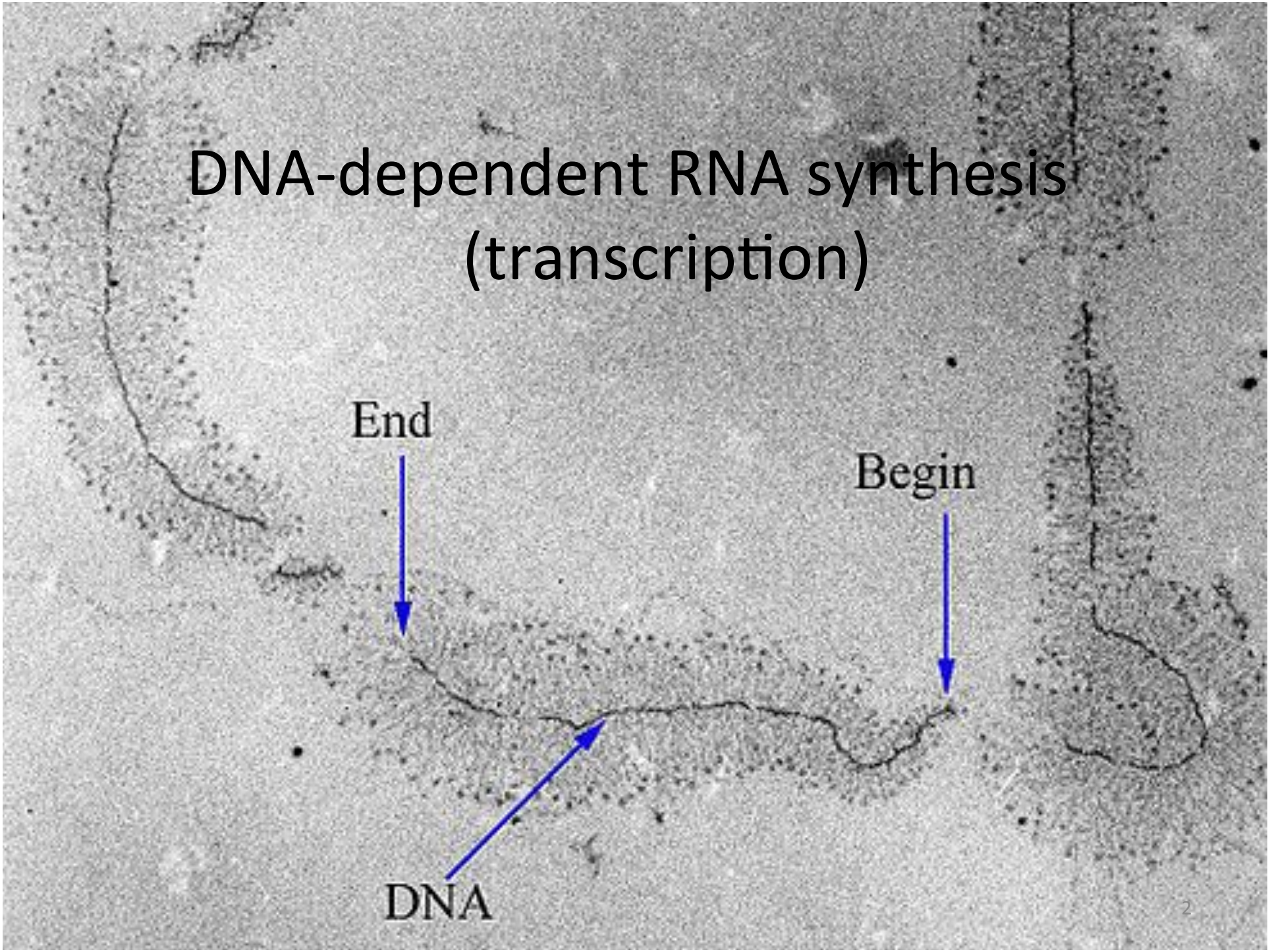


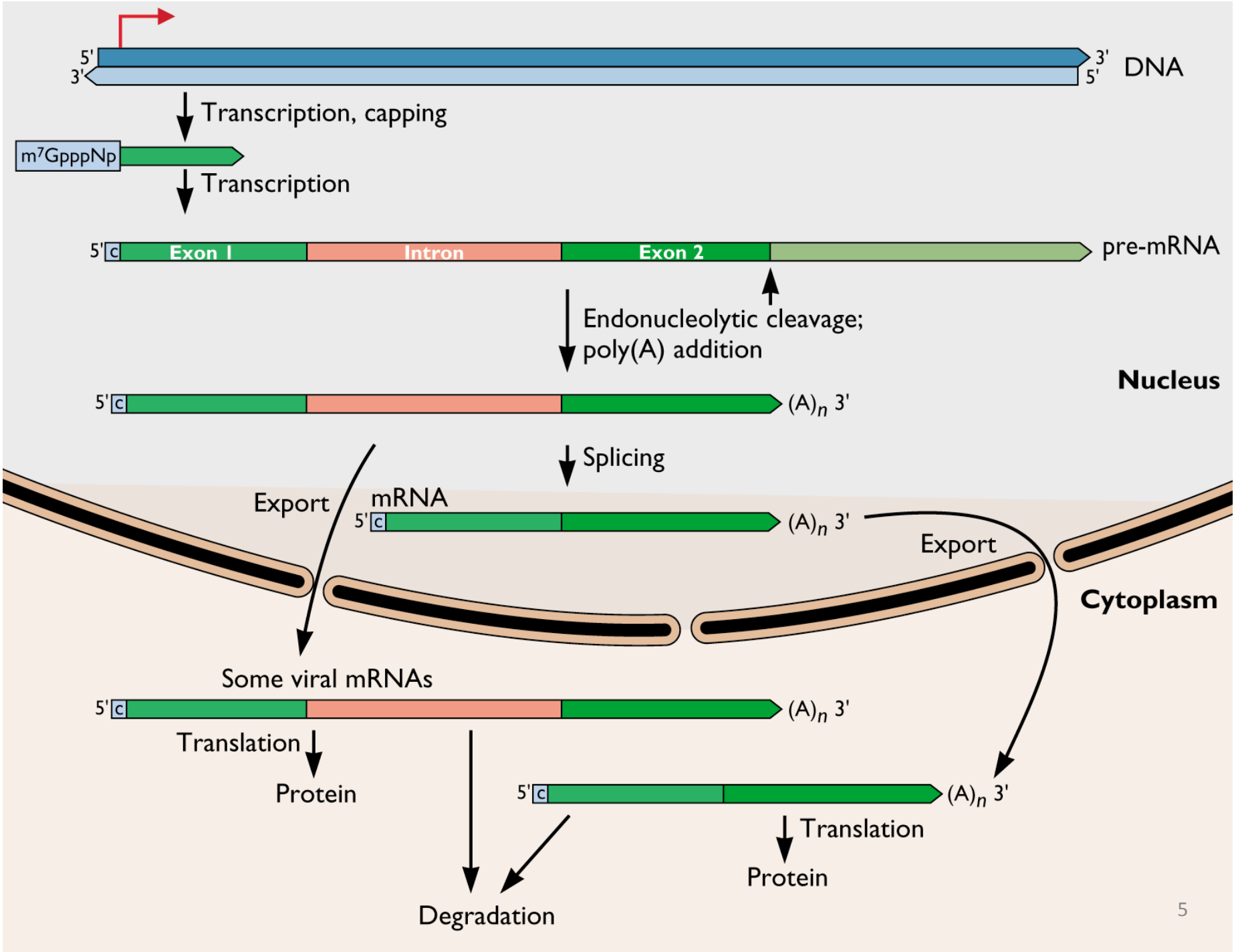
Table 8.2 Eukaryotic RNA polymerases synthesize different classes of cellular and viral RNA

Enzyme	RNAs synthesized[a]	
	Cellular	Viral
RNA polymerase I	Pre-rRNA	None known
RNA polymerase II	Pre-mRNA, pre-miRNA, snRNAs	Pre-mRNA, mRNA, pre-miRNA, HDV genome RNA
RNA polymerase III	Pre-tRNAs, 5S rRNA, U6 snRNA	Ad2 VA-RNAs, EBV EBER RNAs

[a]snRNA, small nuclear RNA; miRNA, micro-RNA; Ad2, adenovirus type 2; EBV, Epstein-Barr virus; HDV, hepatitis delta virus.

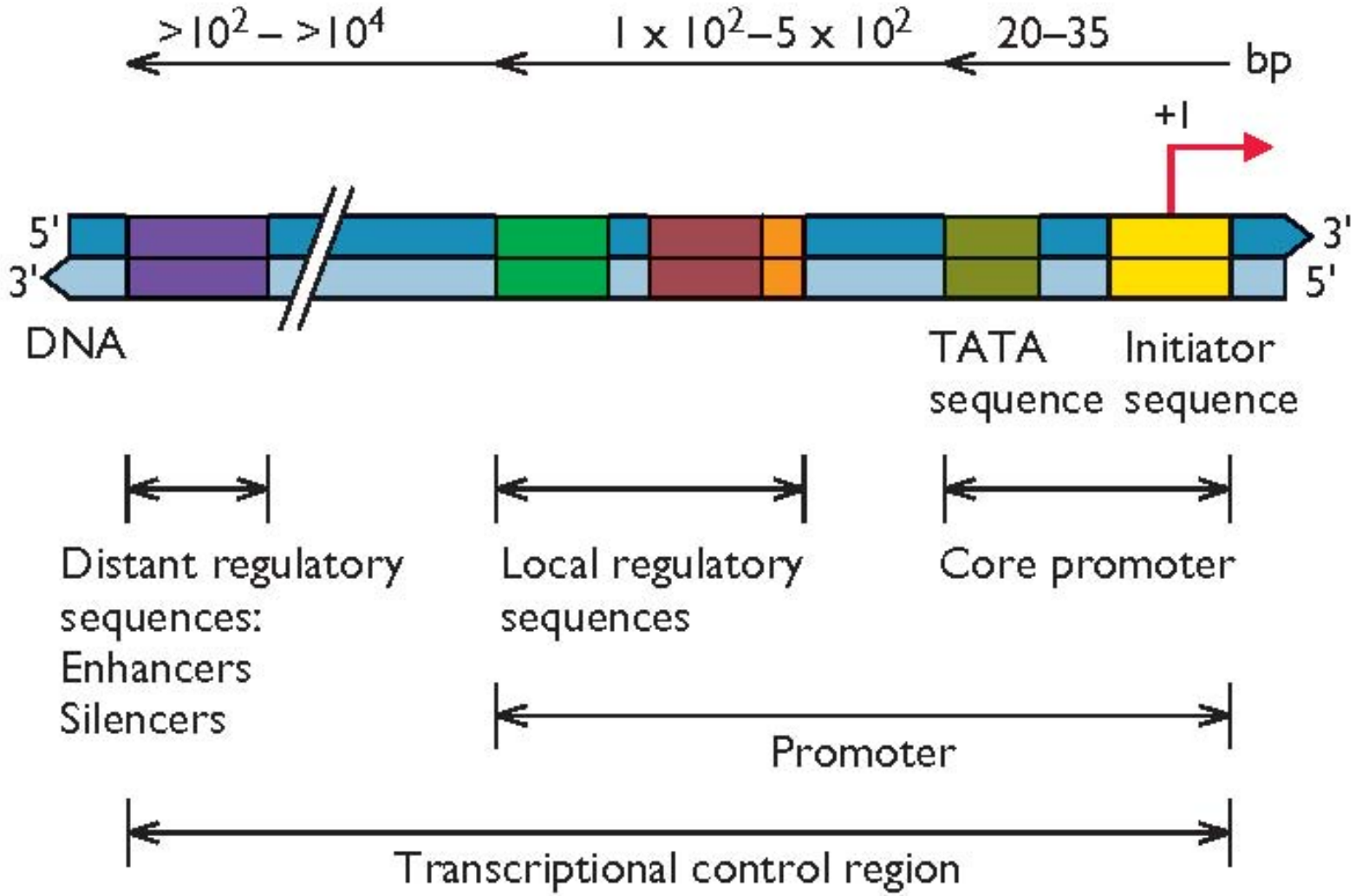
Table 8.1 Strategies of transcription of viral DNA templates

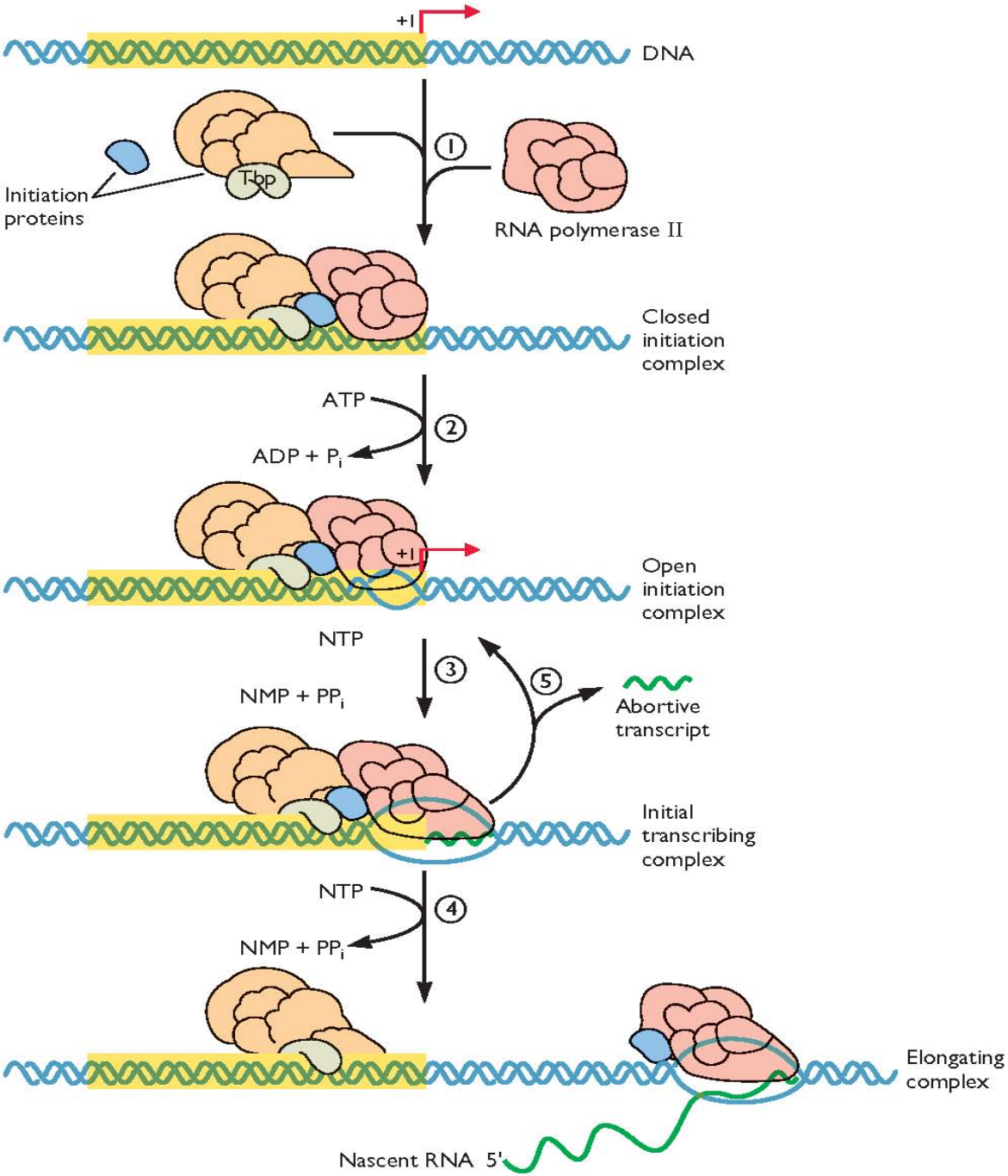
Origin of transcriptional components	Virus
Host only	Simple retroviruses
Host plus one viral protein	
The viral protein transcribes late genes	Bacteriophages T3 and T7
The viral protein regulates transcription	Complex retroviruses, parvoviruses, papillomaviruses, polyomaviruses
Host plus several viral proteins that act sequentially to stimulate transcription of particular sets of viral genes.	Adenoviruses, bacteriophage T4, herpesviruses
Viral	Poxviruses

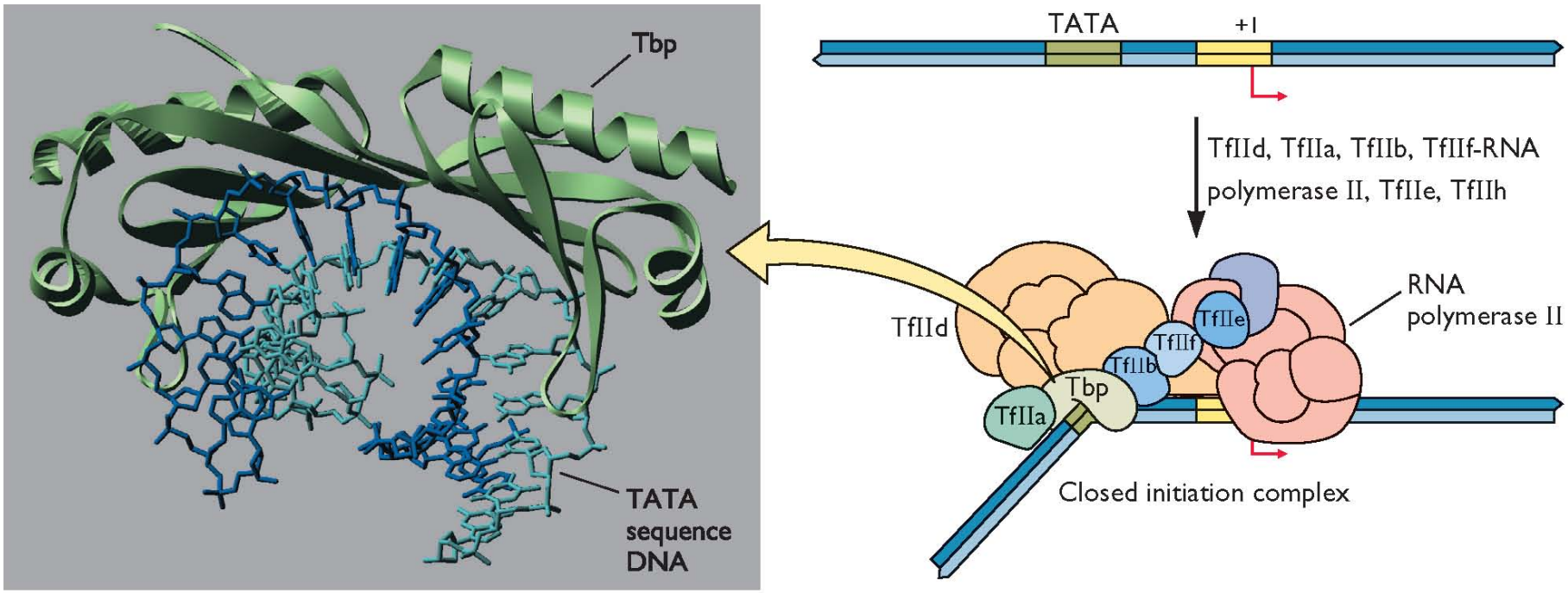

5'
3'
DNA
3'
5'
Transcription, capping
m7GpppNp
Transcription
5'
c
Exon 1
Intron
Exon 2
pre-mRNA
Endonucleolytic cleavage;
poly(A) addition
Nucleus
5'
c
(A)n 3'
Splicing
Export
mRNA
5'
c
(A)n 3'
Export
Cytoplasm
Some viral mRNAs
5'
c
(A)n 3'
Translation
Protein
5'
c
(A)n 3'
Translation
Protein
Degradation

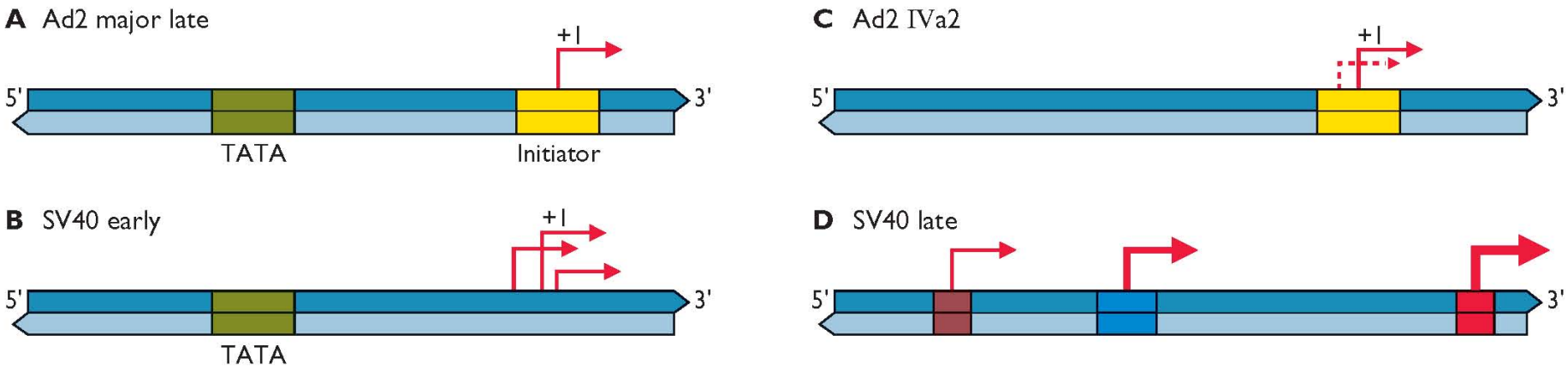
Steps in transcription

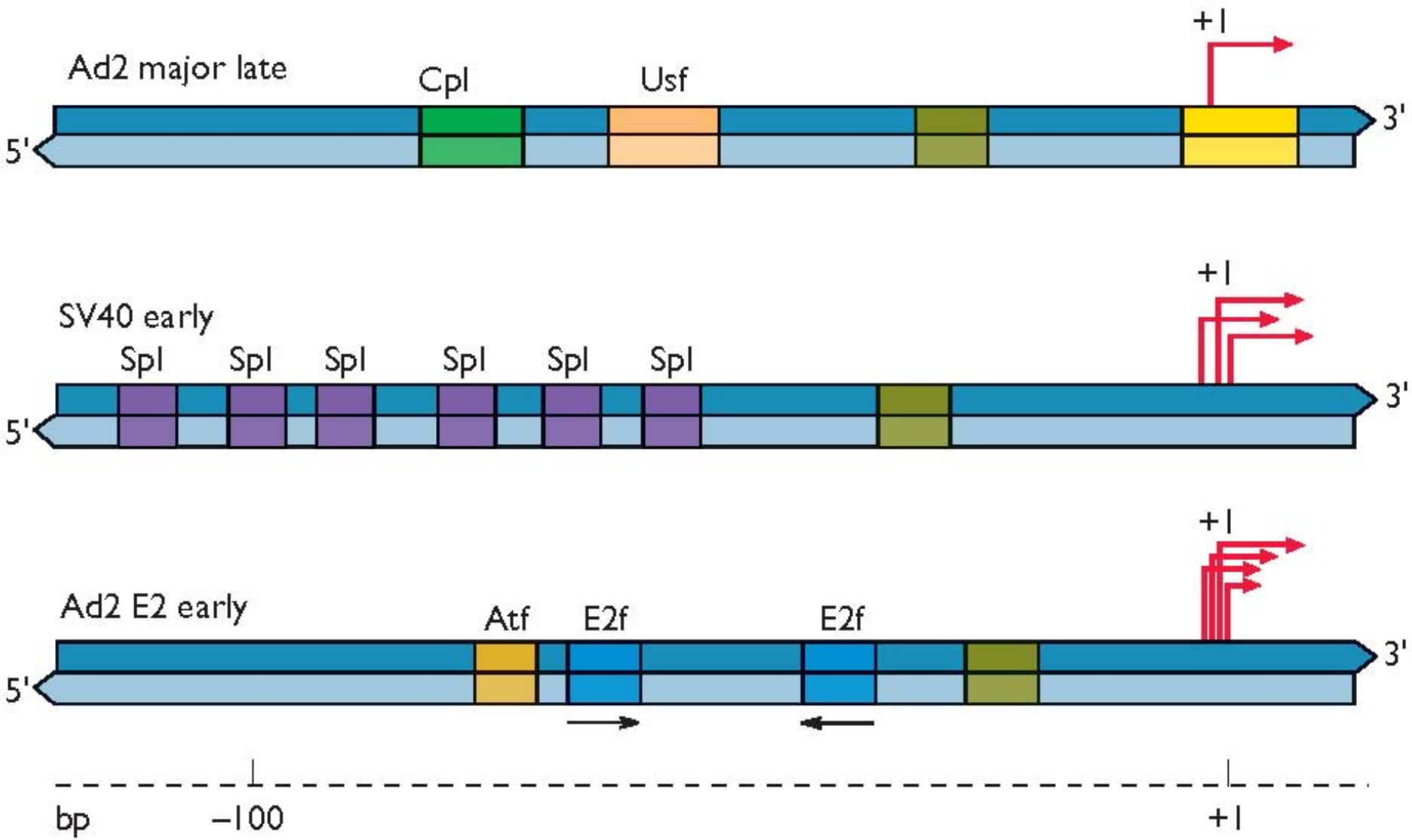
- Promoter recognition
- Preinitiation complex formation
- Initiation
- Elongation
- Termination

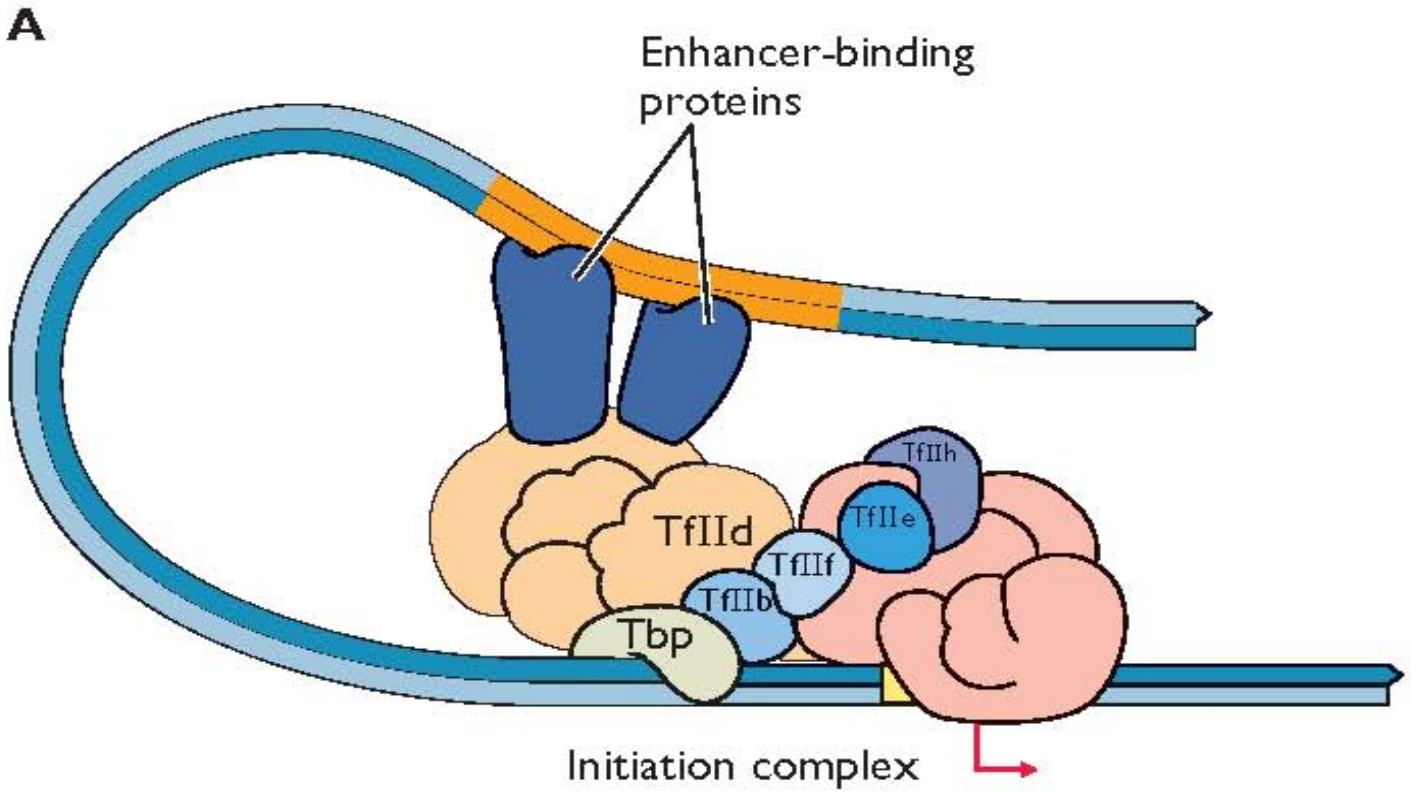

>10² – >10⁴
1 x 10²–5 x 10²
20–35
bp
+1
5'
3'
3'
5'
DNA
TATA sequence
Initiator sequence
Distant regulatory sequences: Enhancers Silencers
Local regulatory sequences
Core promoter
Promoter
Transcriptional control region

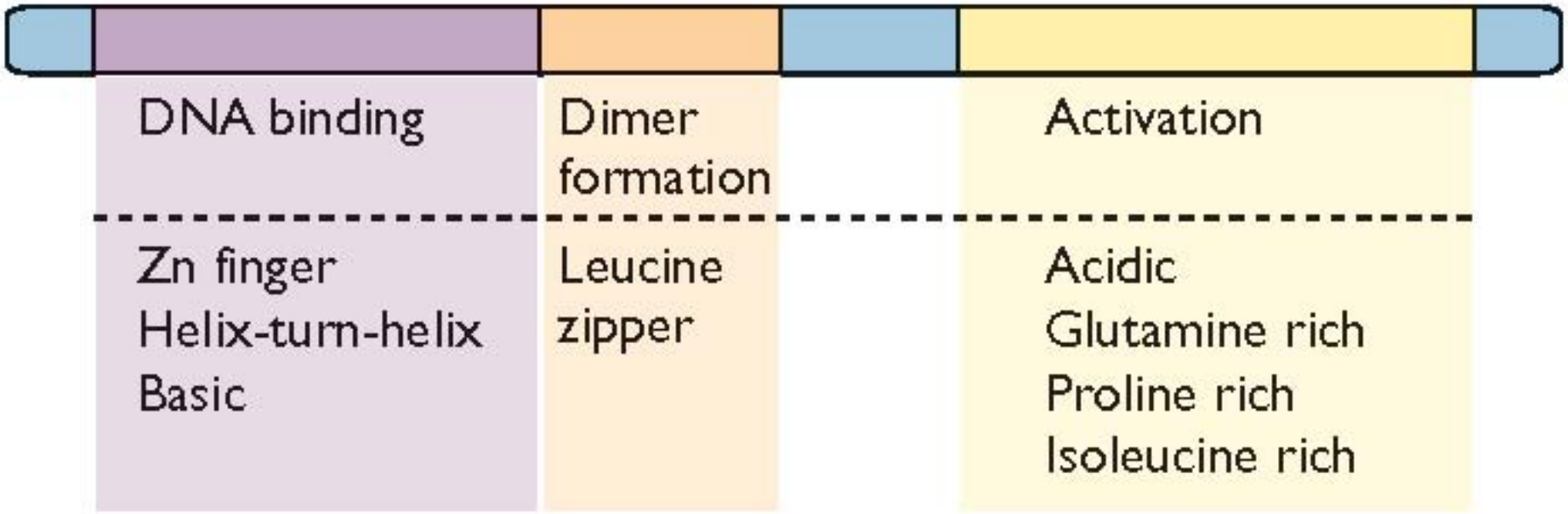

+1
DNA
Initiation proteins
TBP
1
RNA polymerase II
Closed initiation complex
ATP
2
ADP + Pi
+1
Open initiation complex
NTP
3
5
NMP + PPi
Abortive transcript
Initial transcribing complex
NTP
4
NMP + PPi
Elongating complex
Nascent RNA 5'

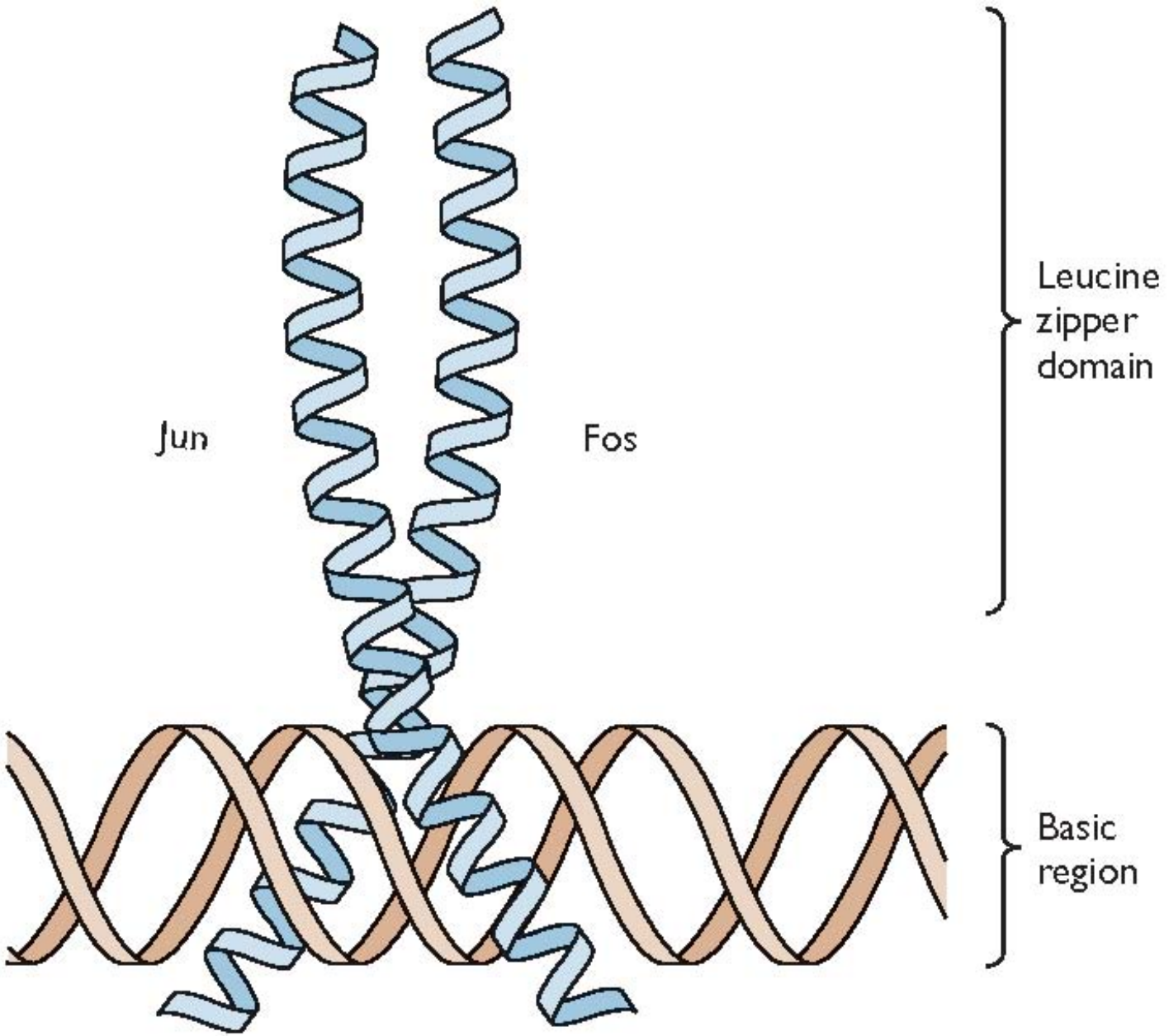

Tbp
TATA
sequence
DNA
TATA
+1
TfIId, TfIIa, TfIIb, TfIIf-RNA
polymerase II, TfIIe, TfIIh
TfIId
TfIIe
TfIIf
TfIIb
Tbp
TfIIa
RNA
polymerase II
Closed initiation complex


A Ad2 major late
+1
5'
3'
TATA
Initiator
B SV40 early
+1
5'
3'
TATA
C Ad2 IVa2
+1
5'
3'
D SV40 late
5'
3'


Ad2 major late
Cpl
Usf
+1
5'
3'
SV40 early
Spl
Spl
Spl
Spl
Spl
Spl
+1
5'
3'
Ad2 E2 early
Atf
E2f
E2f
+1
5'
3'
bp
−100
+1


A
Enhancer-binding
proteins
TfIIh
TfIIe
TfIIf
TfIIb
TfIId
Tbp
Initiation complex


DNA binding
Dimer formation
Activation
Zn finger
Helix-turn-helix
Basic
Leucine zipper
Acidic
Glutamine rich
Proline rich
Isoleucine rich


Jun
Fos
Leucine
zipper
domain
Basic
region

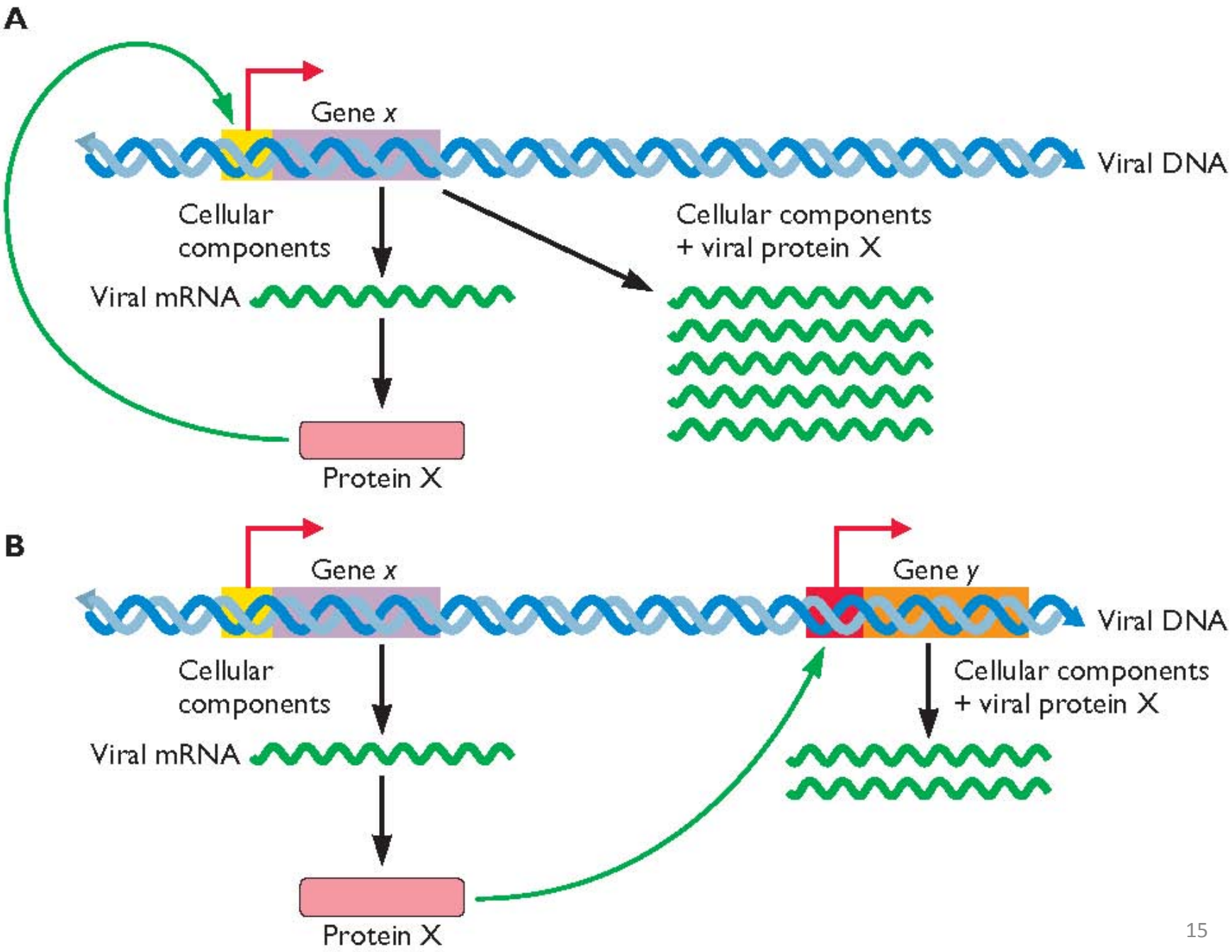
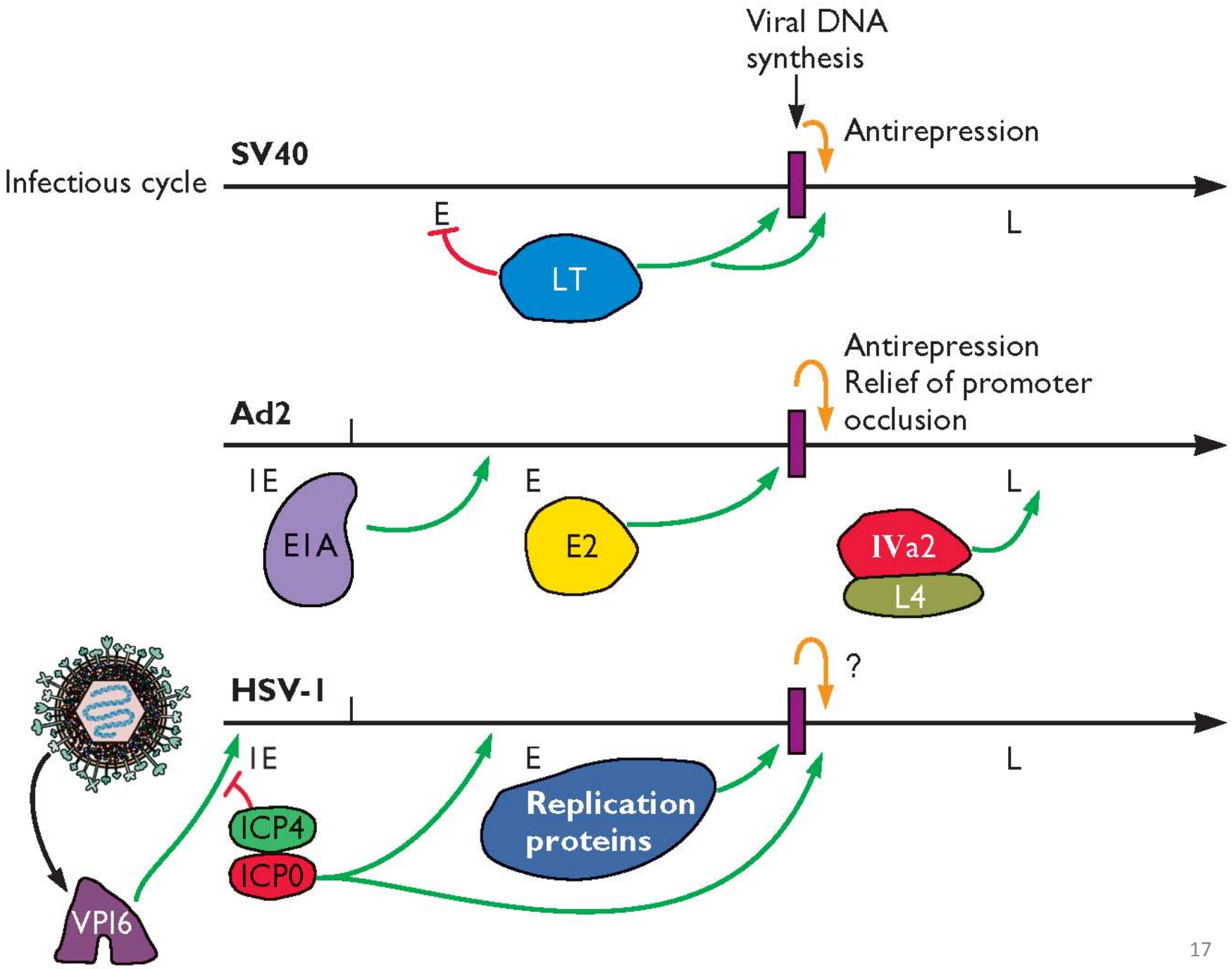
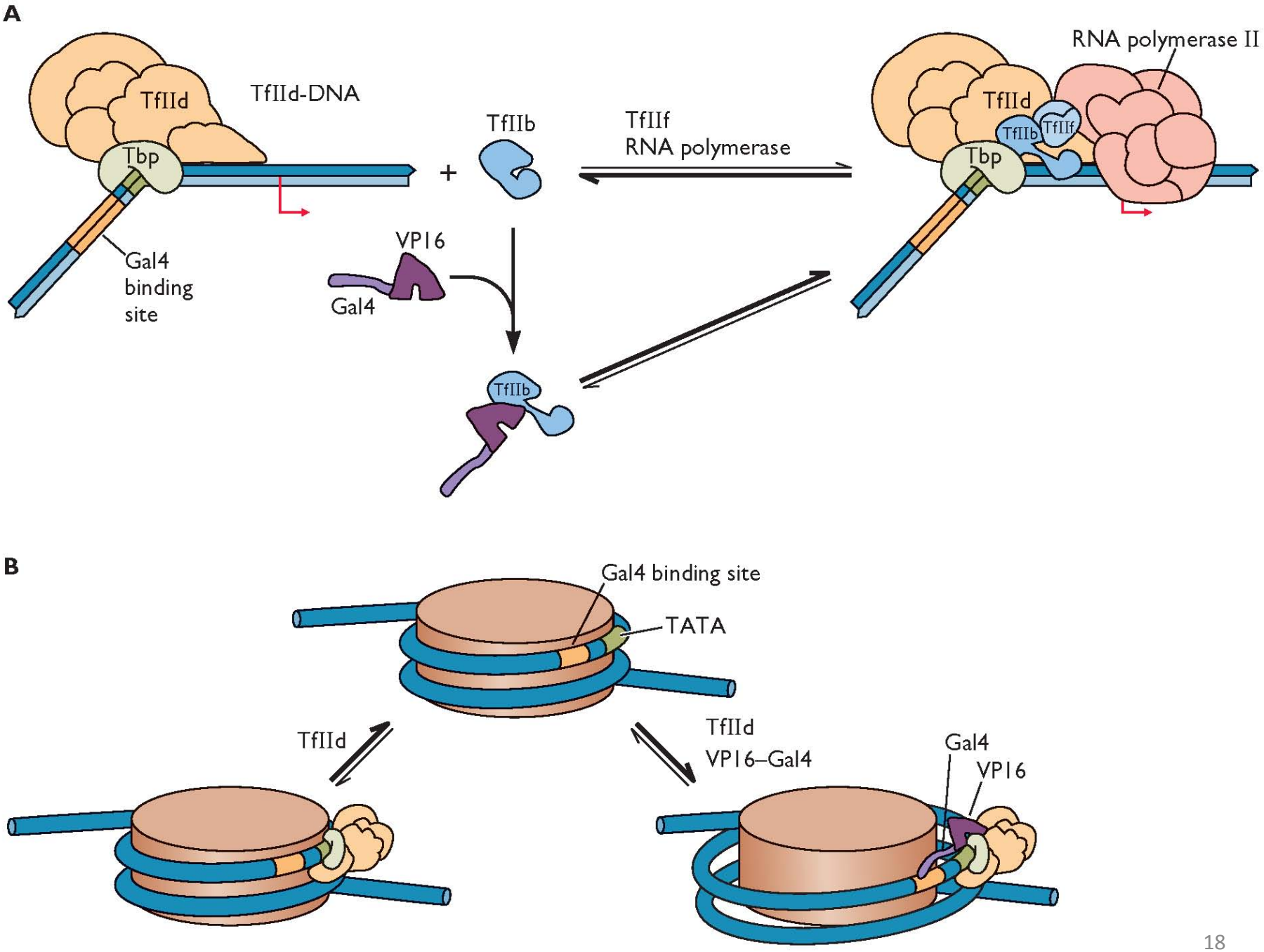
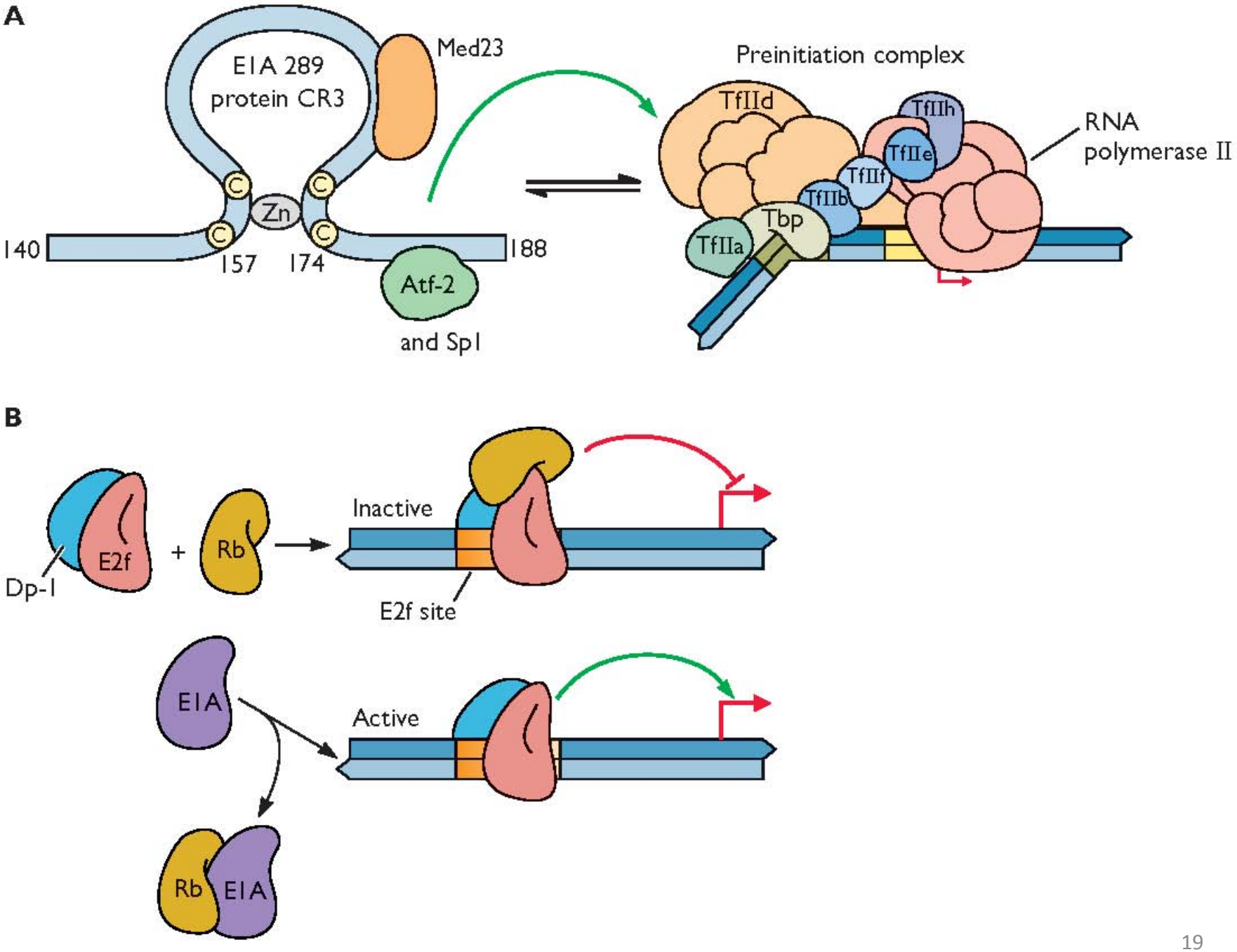

A
Gene x
Viral DNA
Cellular components
Viral mRNA
Protein X
Cellular components + viral protein X
B
Gene x
Gene y
Viral DNA
Cellular components
Viral mRNA
Protein X
Cellular components + viral protein X

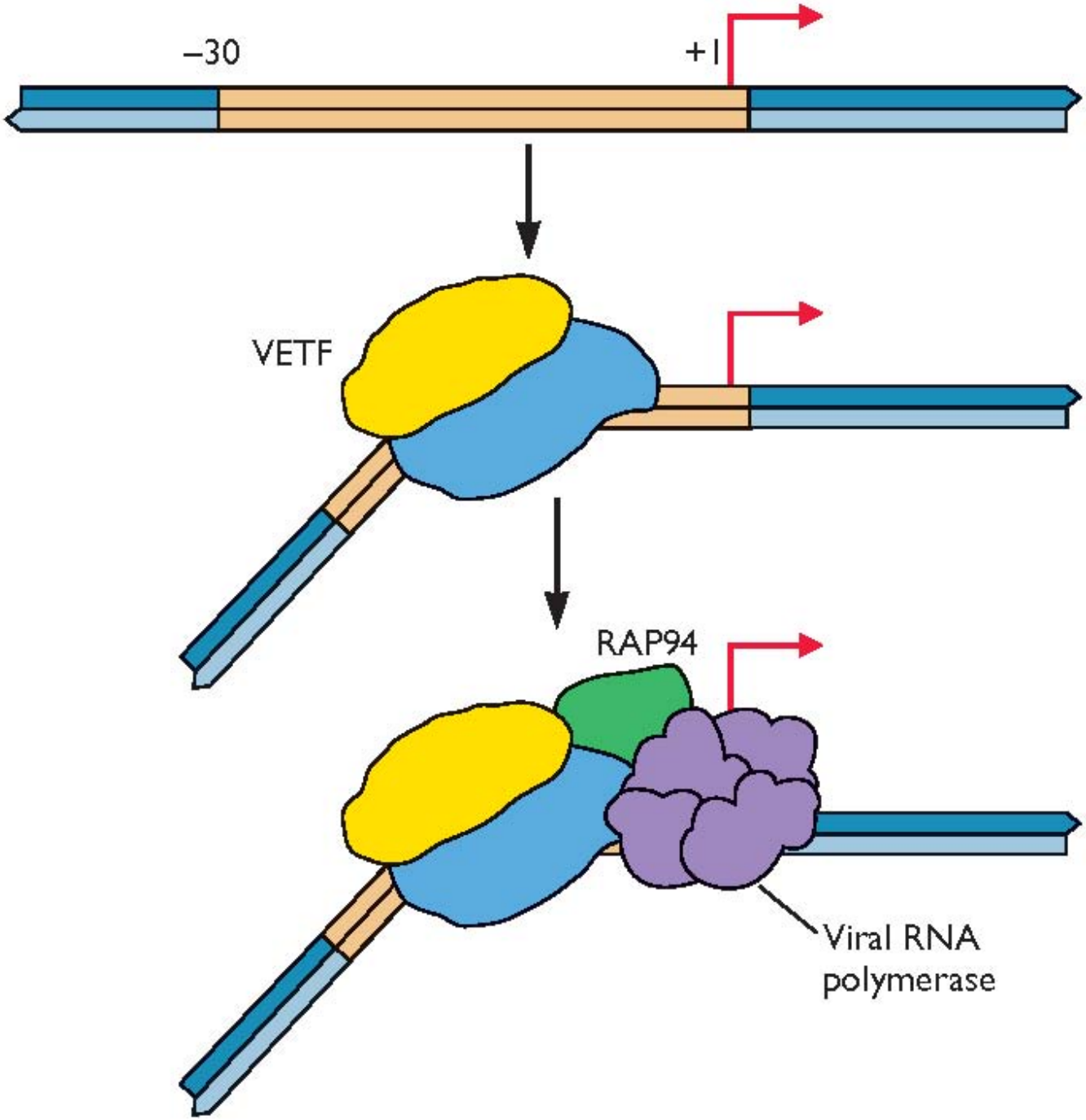
Table 8.6 Some viral transcriptional regulators that bind to specific DNA sequences

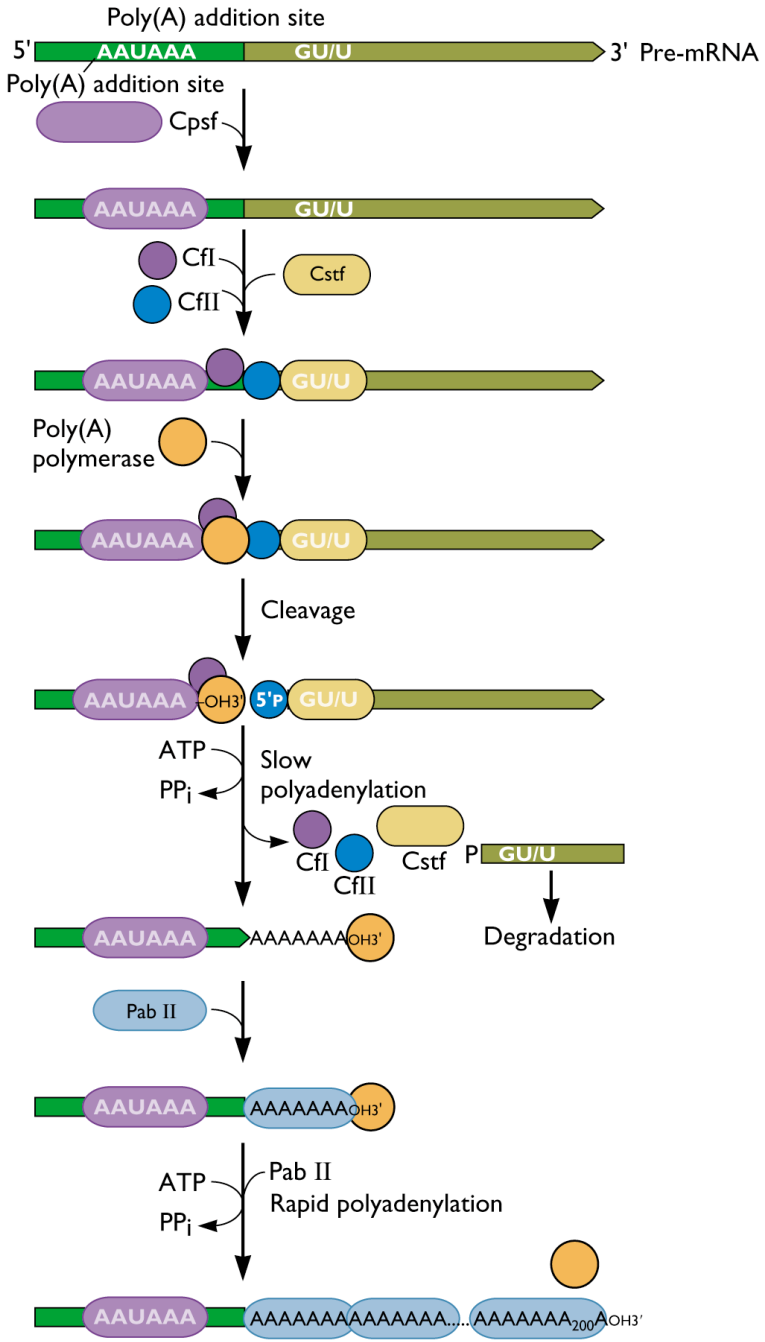
Virus	Protein	Properties	Functions
Adenovirus			
Human adenovirus type 2	IVa_2	Binds to intragenic sequence in the major late promoter; late-phase specific	In conjunction with a viral L4 protein, stimulates transcription from major late promoter
Herpesviruses			
Herpes simplex virus type 1	ICP_4	Typical domain organization; one domain binds to a degenerate consensus sequence	Stimulates transcription from early and late promoters; represses transcription from all IE promoters by binding to promoter sequences
Epstein-Barr virus	Zta	bZIP protein; synthesis and activity regulated by multiple mechanisms (see the text)	Essential activator of early gene transcription; commits to lytic infection (see the text)
Papillomavirus			
Bovine papillomavirus type 1	E2	Typical domain organization; binds as dimers; can bind TfIIb and TfIId	Stimulates transcription from several promoters as enhancer-binding protein; necessary for replication of viral DNA *in vivo*
Poxvirus			
Vaccinia virus	VETF	Binds to TA-rich early promoter sequences as heterodimer; DNA-dependent ATPase	Essential for recognition of early promoters by the viral RNA polymerase


Viral DNA synthesis
Antirepression
SV40
Infectious cycle
E
L
LT
Antirepression
Relief of promoter occlusion
Ad2
IE
E
L
EIA
E2
IVa2
L4
?
HSV-1
IE
E
L
ICP4
ICP0
Replication proteins
VP16


A
TfIId
TfIId-DNA
Tbp
Gal4
binding
site
+
TfIIb
TfIIf
RNA polymerase
RNA polymerase II
TfIId
TfIIb
TfIIf
Tbp
VP16
Gal4
TfIIb
B
Gal4 binding site
TATA
TfIId
TfIId
VP16–Gal4
Gal4
VP16


A
E1A 289
protein CR3
Med23
Zn
140
157
174
188
Atf-2
and Sp1
Preinitiation complex
TfIId
TfIIh
TfIIe
TfIIf
TfIIb
Tbp
TfIIa
RNA
polymerase II
B
Dp-1
E2f
+
Rb
Inactive
E2f site
E1A
Active
Rb
E1A


–30
+1
VETF
RAP94
Viral RNA
polymerase


Poly(A) addition site
5'
AAUAAA
GU/U
3' Pre-mRNA
Poly(A) addition site
Cpsf
AAUAAA
GU/U
CfI
CfII
Cstf
AAUAAA
GU/U
Poly(A)
polymerase
AAUAAA
GU/U
Cleavage
AAUAAA
OH3'
5'P
GU/U
ATP
PPi
Slow
polyadenylation
CfI
CfII
Cstf
P
GU/U
Degradation
AAUAAA
AAAAAAAOH3'
Pab II
AAUAAA
AAAAAAAOH3'
ATP
PPi
Pab II
Rapid polyadenylation
AAUAAA
AAAAAAAAAAAAAAA.....AAAAAAA200AOH3'

From justanotherkinase on twitter:

Dear TWiVatrons: FYI "mock" is a UK term for a practice exam. Loving the virology on TWiV 161. Please keep it up.

Gary writes:

Dear Wonderful TWiV People,

I just finished listening to your 161'st episode, well named "Concerto in B." Really well done! I've felt guilty that as a 30+ year practicing pediatrician, receiving my undergraduate and medical school education when most of this was necessarily only vaguely guessed at, I've not had the time and energy to explore the literature and bring myself up to date. This last podcast along with your previous work has provided a truckload of information that has made what would have been a K2 climb into an easy and fun one. Please consider dedicating a few of your future programs to more exploration of immune function basic science. In any case, I love listening to you guys!

All the best,

Gary, MD
Sebastopol, California

Thomas writes:

Dear TWIVers,

Firstly, my sincere gratitude for all the work you put in to making TWIV an absolute gem of a Podcast and a medium through which I can still feel involved in basic science and virology even though my studies currently have me memorizing the various proteins and associations of the coagulation cascade in medical school.

With that run-on sentence out of the way, I would like to comment on last week's TWIV regarding the CIDRAP release by saying I think you all handled it very well. Perhaps I make this conclusion due to my opinion being that which is shared by you all. Nonetheless, to suggest that science has a role in the progression of bioterrorism is probably not an incorrect statement, however, to suggest that scientists should refrain from certain works as a result of fear that knowledge and advancements may fall into the wrongs scientists' hands is ludicrous and I am glad you addressed this release.

This brings me to the reason I write you all today. I recently came across a video that shows a 1-on-1 discussion between an out-of-character Stephen Colbert and the always-fascinating Neil deGrasse Tyson. Briefly, the two discuss various issues regarding science, society, the universe, and knowledge. The entire discussion is well worth the 1 hour and 24 minutes, however there is a short section which I hope for you and all TWIV fans to watch which I think best portrays what my feelings (and I'm sure many others' feelings) regarding the issue that you discussed about scientific discovery in fields that are implicated in potential bio-threats. The section runs from about 16:00 to 17:40 and ends with Dr. Tyson stating that, "Everyone blames the scientists and we are collectively part of a society that is using or not using, to its benefit or its detriment, the discoveries made by science. And at the end of the day, it's not the discovery itself that is immoral, it's the application of it."

They go on to discuss many other issues I think are important regarding the scientific community and what role we take in society now, but I particularly like this one quote since it reminds us of an ever-developing collective scientific knowledge but does not blame the immoral application of this knowledge on science itself.

Either way, I hope you all enjoy the video, keep up the great work, and again thank you all for the weekly edu-tainment!

Sincerely,
Thomas

http://www.youtube.com/watch?feature=player_embedded&v=YXh9RQCvxmg

Kathy writes:
Hi Vincent, Rich, Alan, and Dick,

In TWiV 145, the inVinceable TWiV, a listener (David) wrote in to get suggestions of viruses that alter host behavior, resulting in increased transmission of the disease. He cited some parasitology examples and the classic rabies story, where rabies induces aggression that causes the infected animal to bite and transmit the virus. In TWiV 150, you read a suggestion from another listener (Kimberley), who described how baculovirus-infected caterpillars climb as high as possible, and then when the caterpillar melts from the infection, all the virus goo can fall down onto lower leaves. I have another suggestion, and that is viruses that cause pocks (P-O-C-K-S), including both varicella zoster virus, a virus in the herpesvirus family that causes chicken pox, and Rich's own vaccinia virus. In both of these cases, the pocks or pustules that form are full of virus. The host response to infection causes these to itch, and scratching of the pocks then can release and spread the virus. I haven't been able to find a good explanation of why mast cells or basophils might release histamine in the vicinity of pocks -- maybe there's another explanation for the itchiness.

Another case might be any of the respiratory viruses that result in coughing or sneezing (think of the famous sneezing images, such as the top hits in a Google image search for "sneeze")...

Cheers,
Kathy

Ayesha writes:

A few questions on on HPV
Maybe you would be so kind as to pose a few questions to the next HPV expert you have as a guest. There are menstral tampon alternatives that women can reuse called the Keeper TM and the Mooncup (http://www.keeper.com/index.html). I was just wondering whether women using these products who are infected with the high risk HPVs could or would shed virus and if the virus could persist in these reusable cups (and act as a place where the virus can persist and reinfect cells on the cervix, leading to more risk for transformation). I can't find studies addressing this question in pubmed. I wonder what kills HPV: boiling, detergents, vineagar? How well does it persist in water? Maybe a cleaner could be devised to make these eco products safer if in fact HPV does persist in them. Maybe I should just send off an email to the HPV researcher you had on recently.

I work on HIV-1, epithelium and *Candida albicans.* I was really tantilized by the idea that retroviruses use the immune tolerace caused by gut flora as an opportunity to evade the immnue system. David Moyes a postdoc in the same group has described a mechanism by which oral epithelium tolorates resident yeast but sets off a defensive signalling cascade when hyphae become invasive.

Many thanks for your awesome podcast. It inspires me every time I listen and recommend it to anyone who will listen!

Michelle Ozbun replies:

Really good question. HPVs as non-enveloped viruses are much more resistant to desiccation and environmental assaults compared to enveloped viruses like (e.g.) HIV or flu or herpes. My friend and colleague Richard Roden showed some time ago that HPVs are sensitive to 70% EtOH. This is what we use to disinfect in my lab when working with papillomaviruses. Richard's work also suggested that boiling for 1 hr would reduce infectivity to near baseline. My lab reported that the particles are sensitive to acid and probably will fall apart in undiluted apple cider vinegar (pH typically between pH 4.25 - 5.00).

I recommend that the products be soaked in ethanol or 70% isopropanol for 1 hour or boiled for 1 hr (depending upon the nature of the product) before thorough rinsing in water.

Roden RBS, Lowy DR, Schiller JT (1997) Papillomavirus is resistant to desiccation. J Infect Dis 176: 1076-1079.

Smith JL, Campos SK, Wandinger-Ness A, Ozbun MA (2008) Caveolin-1 dependent infectious entry of human papillomavirus type 31 in human keratinocytes proceeds to the endosomal pathway for pH-dependent uncoating. J Virol 82: 9505-9512.

I'm sure that both women and men shed virus as a route of transmission. However, I don't think anyone has investigated the reinfection issues posed, and little is understood about re-infection or infection of adjacent tissues in an infected individual... though I suspect this occurs.

PoTW

- Alan – Happy Holidays from the National Oceanic and Atmospheric Administration (NOAA): http://www.youtube.com/watch?v=-yGJbkQulQw
- Rich – http://www.vacciniamodel.com/
- Vincent – 17 year old wins $100,000 Siemens prize for anti-tumor nanoparticles

http://www.gwu.edu/explore/mediaroom/newsreleases/teensclaimtopprizesin2011siemenscompetitioninmathsciencetechnology

Sarah writes:
Hello to the TWiV crew,

Here are a couple of picks I thought would be good for provoking thought and generating discussion...

While working on a project, I came across some papers attempting to define what "critical thinking" means. I appreciated the following quote and it reminded me of the many instances in TWiV where you hosts have discussed the scientific method and thinking critically about research findings. It came from a consensus statement on defining and promoting critical thinking, published in 1990 by a university Dean.

"The ideal critical thinker is habitually inquisitive, well-informed, trustful of reason, open-minded, flexible, fairminded in evaluation, honest in facing personal biases, prudent in making judgments, willing to reconsider, clear about issues, orderly in complex matters, diligent in seeking relevant information, reasonable in the selection of criteria, focused in inquiry, and persistent in seeking results which are as precise as the subject and the circumstances of inquiry permit."

(Quote is from Table 1)
Facione, P. (1990). Critical Thinking: A Statement of Expert Consensus for Purposes of Educational Assessment and Instruction. Retrieved from http://assessment.aas.duke.edu/documents/Delphi_Report.pdf

Next, perhaps less of a pick and more to stimulate episode topic ideas for those of us who are "into" the medical side of virology, here is a paper about diagnosing viral acute respiratory infections using peripheral blood gene expression signatures. If this seems interesting to y'all, Dr. Zaas and/or Dr. Woods would be great guests on the podcast; they're both infectious disease physician-researchers.

Zaas, A. K. et al. (2009). Gene Expression Signatures Diagnose Influenza and Other Symptomatic Respiratory Viral Infection in Humans.*Cell Host & Microbe 17*, 207-217. doi:10.1016/j.chom.2009.07.006
(attached)

Last, Dr. Woods would be an interesting guest for another reason - his interest and teaching activities in a movement called One Health, which looks at human health from a human, animal, and environmental perspective. I'm still wrapping my head around exactly what One Health *is*, but apparently it's even caught on at the CDC.

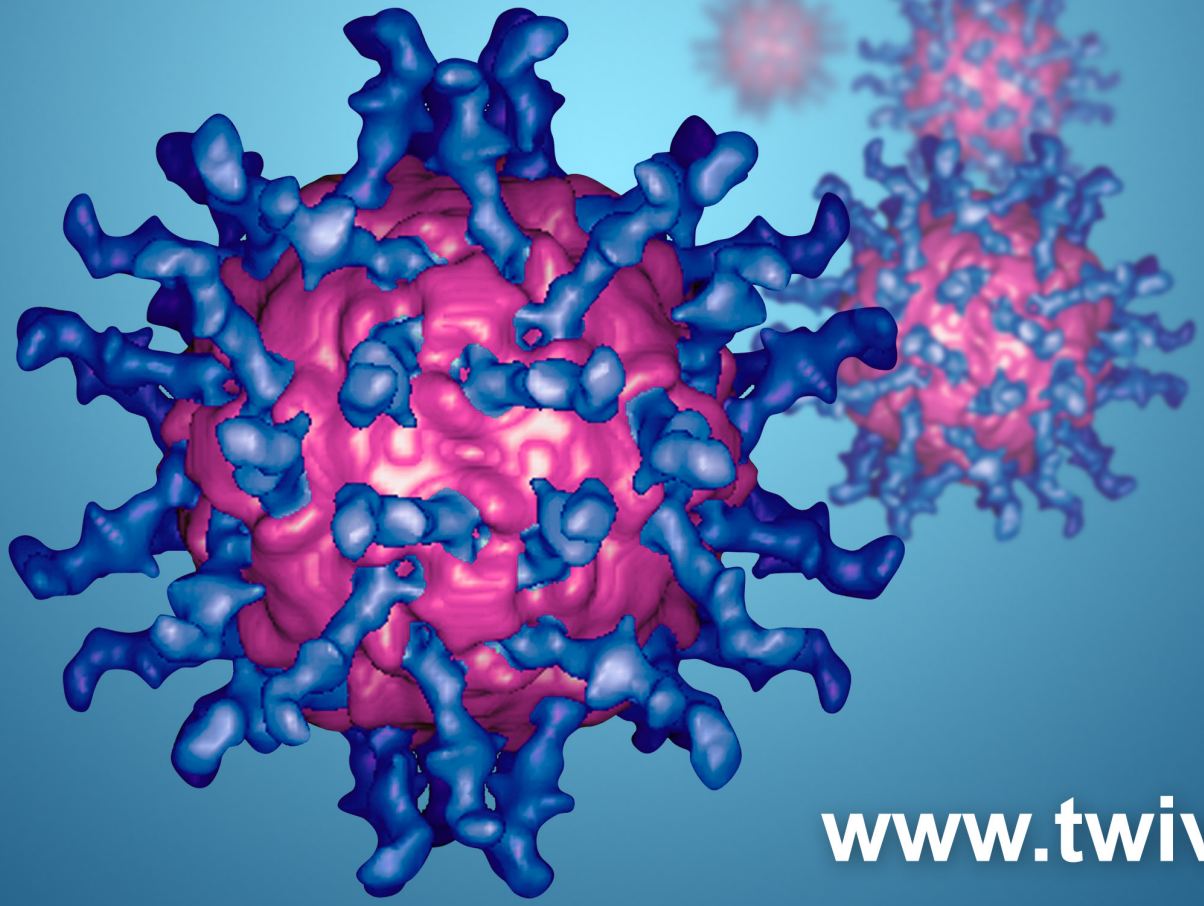
http://www.onehealthinitiative.com/
http://www.cdc.gov/onehealth/

Keep up the great work - and keep having fun!

- Alan Dove: http://www.alandove.com
- Rich Condit: http://bit.ly/poxdoc
- Vincent Racaniello: http://www.virology.ws

TWiV

THIS WEEK IN VIROLOGY



www.twiv.tv