



DEPARTAMENTO DE  
**MICroBiologia**  
UNIVERSIDADE DE SÃO PAULO



# Antivirais

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# Desenvolvimento de antivirais

Existem relativamente poucas doenças para as quais tem sido desenvolvidas drogas antivirais eficientes.

- Existem menos alvos “óbvios” para vírus do que para bactérias.
- Os diferentes tipos de vírus apresentam um conjunto próprio de proteínas e estratégias de replicação variadas.
- Alguns vírus estabelecem latência e tratamento da infecção produtiva não cura a doença.
- Diferentes vírus podem causar sintomas semelhantes, dificultando o diagnóstico.
- Para muitos vírus o tratamento só é eficiente se aplicado na fase inicial da infecção (quando muitas vezes não há sintomas...)

# Desenvolvimento de antivirais

Uma molécula pode agir como antiviral se inibe alguma etapa da replicação viral sem ser tóxica demais para o hospedeiro.

Os possíveis mecanismos de ação incluem:

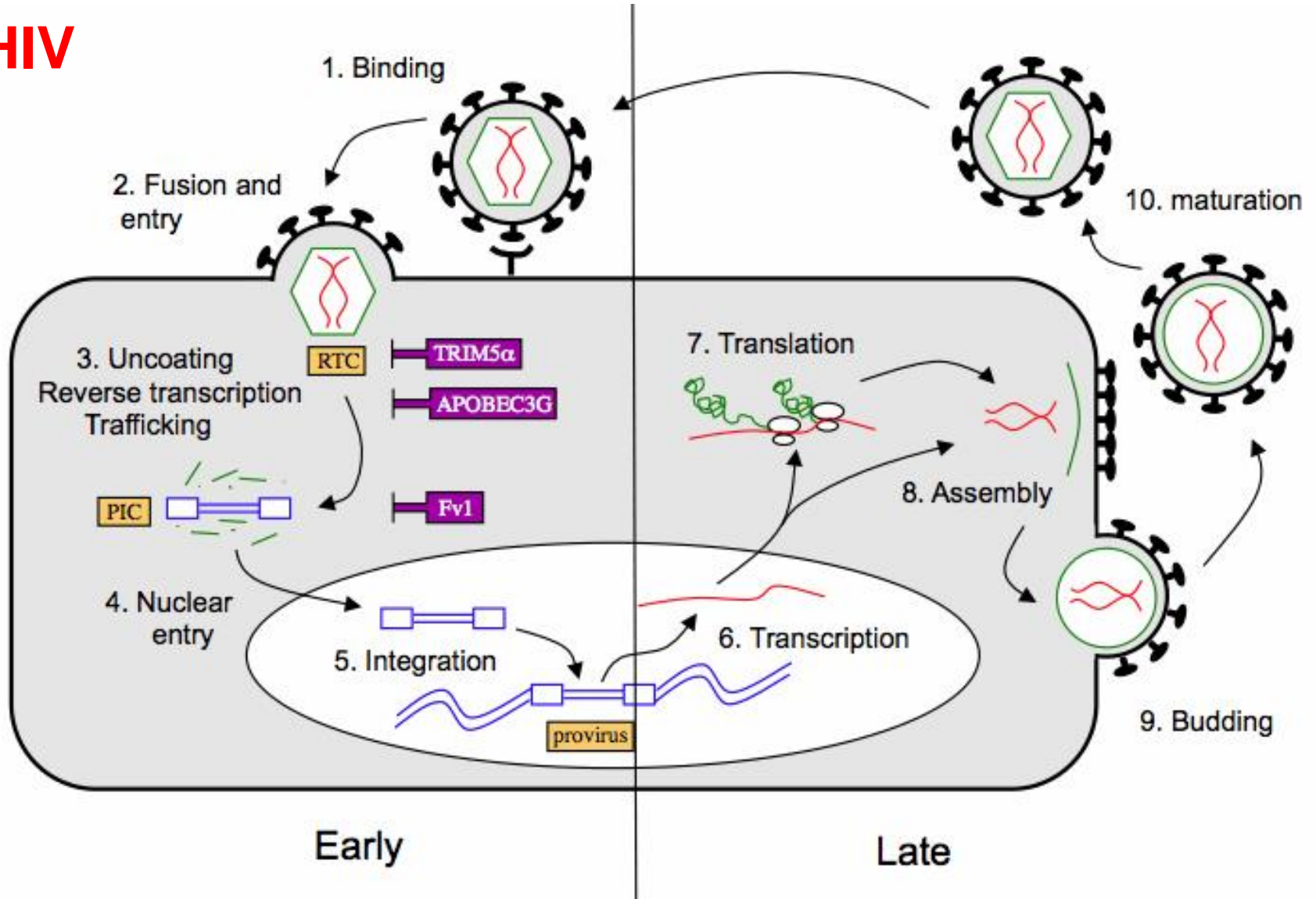
- A capacidade de inativar partículas virais extracelulares.
- Prevenir a união do vírus à célula e/ou sua entrada.
- Prevenir a replicação do genoma viral.
- Prevenir a síntese/função de proteínas virais específicas.
- Prevenir a montagem e/ou liberação de novos vírions.

# O ciclo dos diferentes vírus apresenta etapas comuns

- Adsorção
- Penetração
- Desnudamento
- Síntese dos componentes virais:
  - Proteínas
  - Ácido nucléico
- Montagem
- Maturação
- Liberação

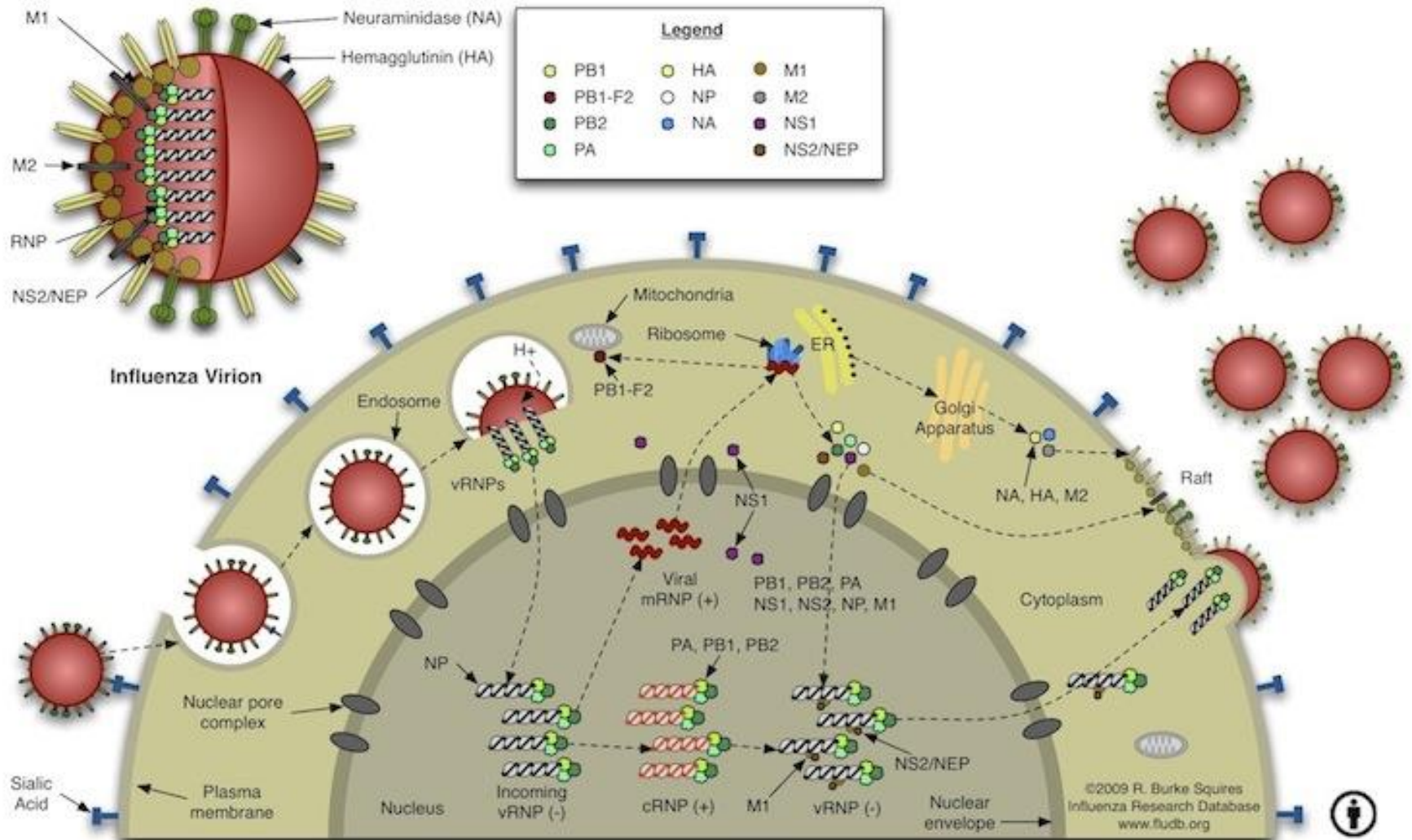
# O ciclo de cada tipo viral apresenta características próprias

HIV

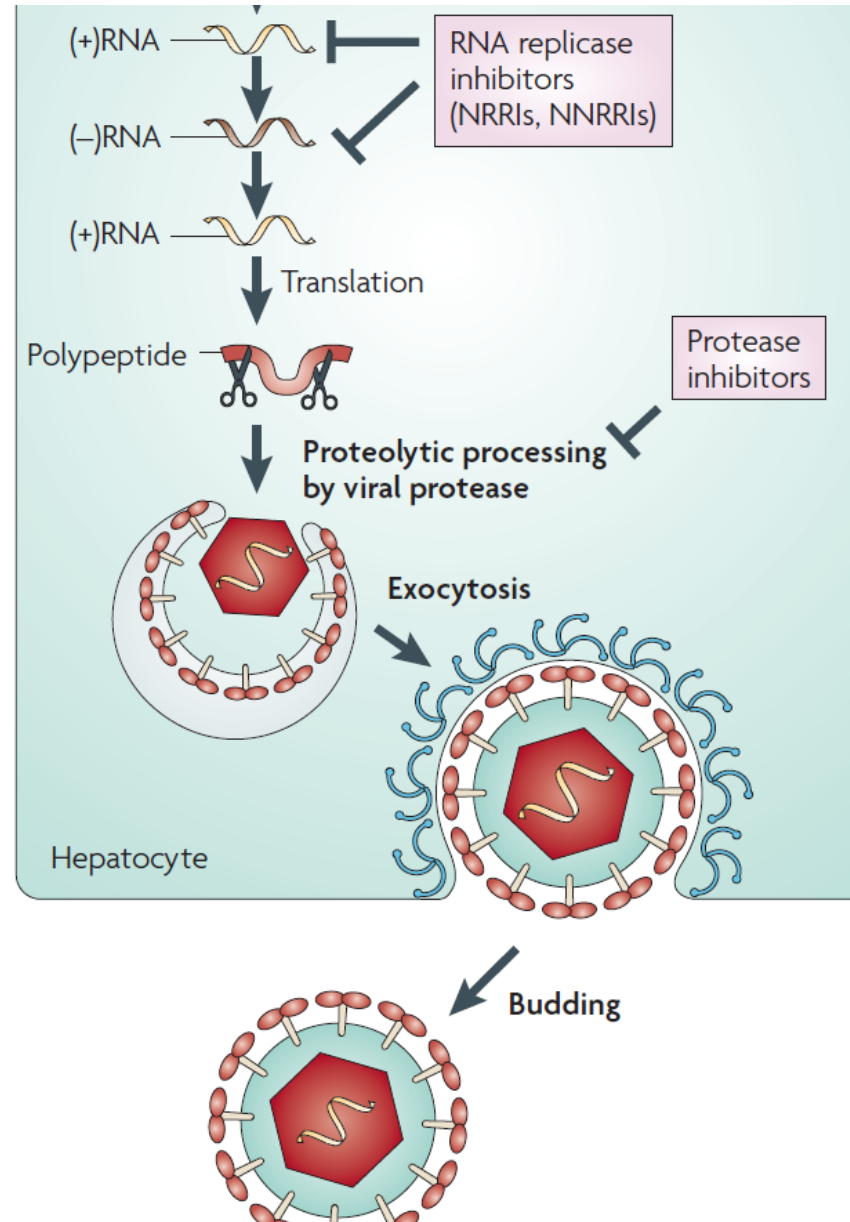
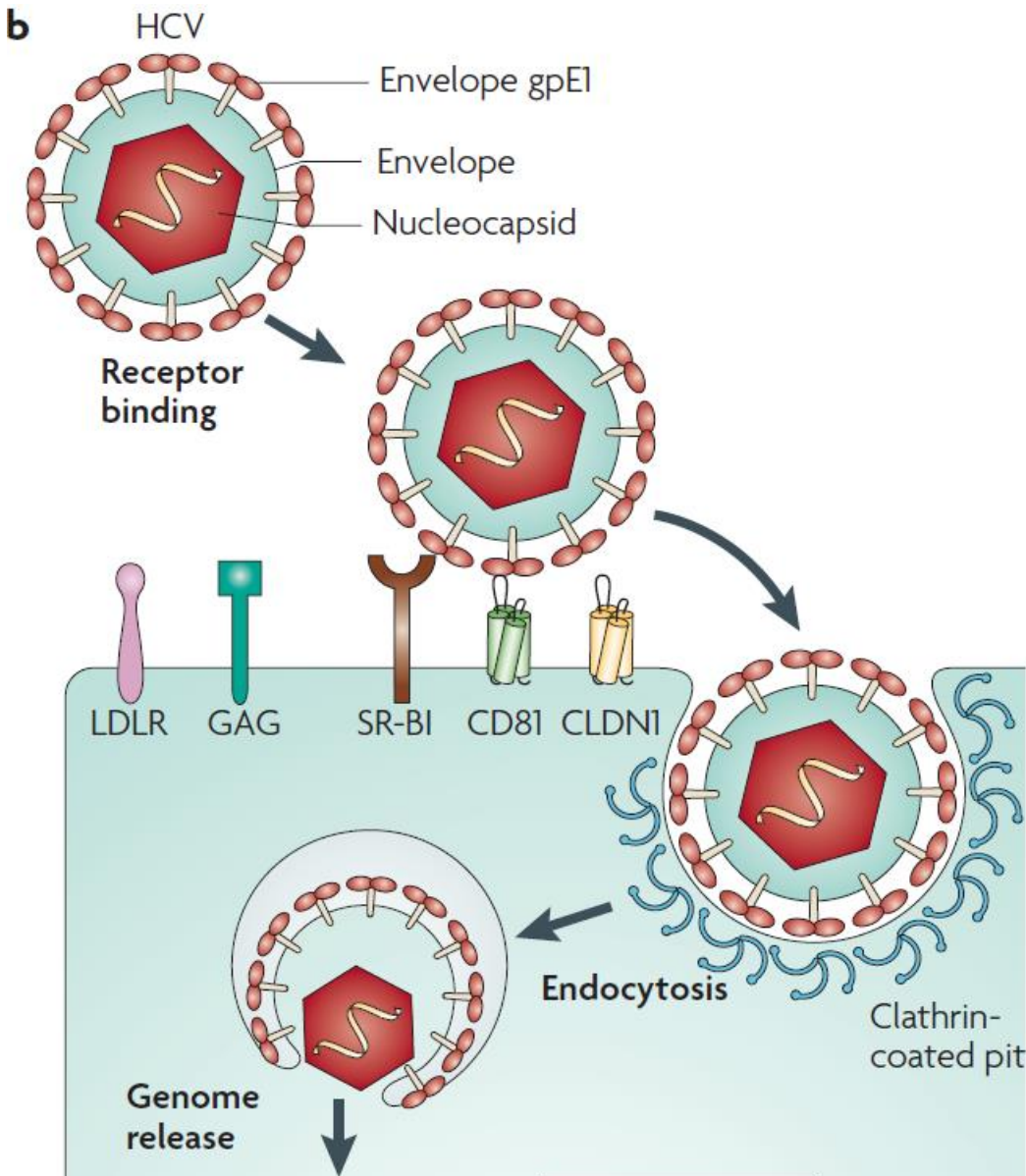


# O ciclo de cada tipo viral apresenta características próprias

## Influenza



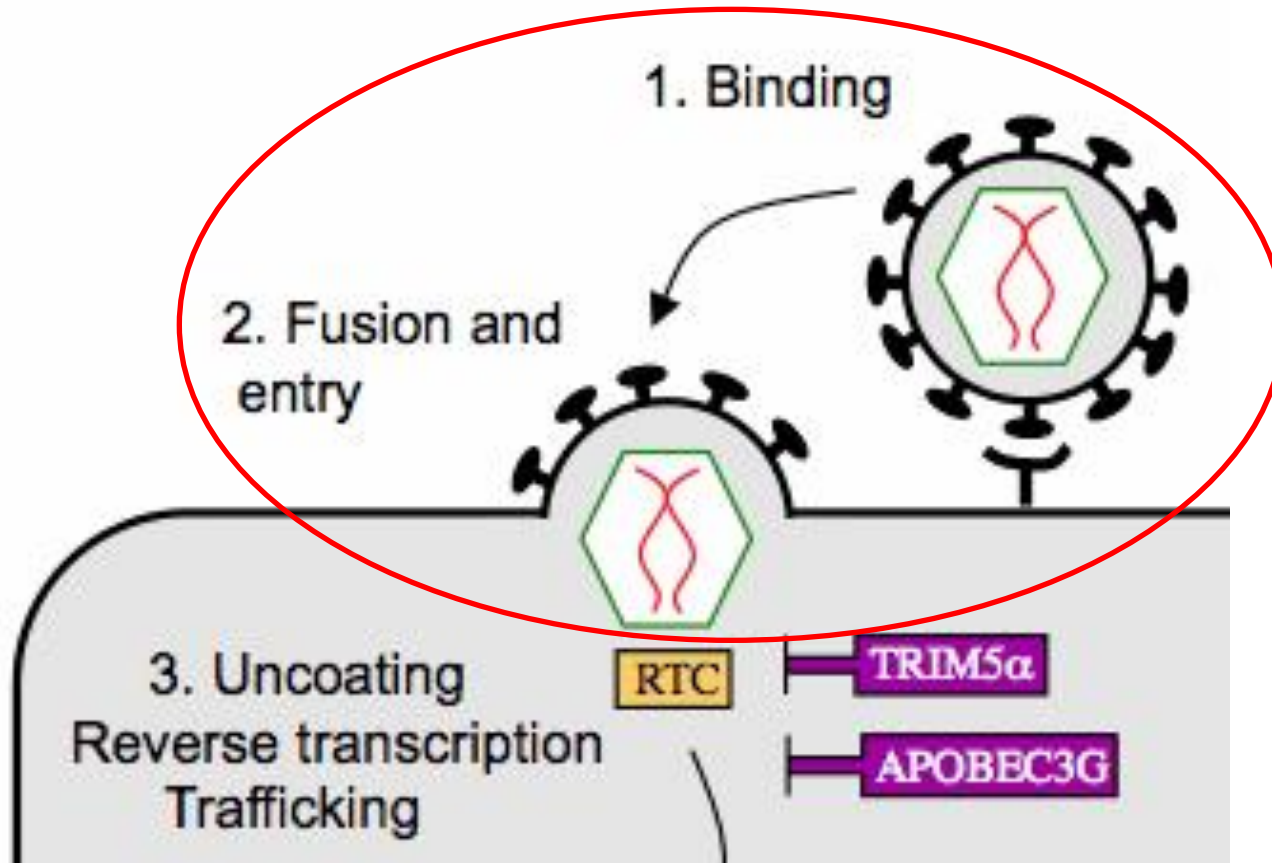
# O ciclo de cada tipo viral apresenta características próprias



# **Inibidores de adsorção e fusão**



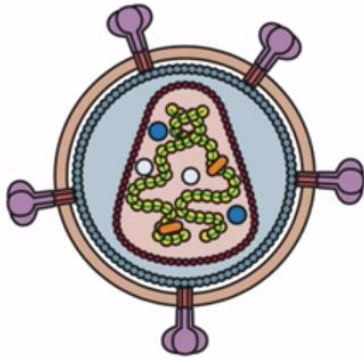
# Inibidores de fusão



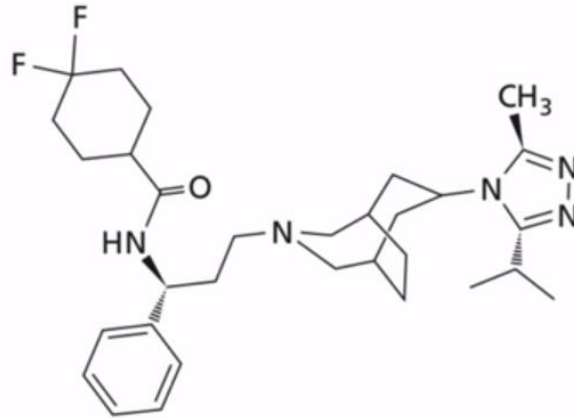


# Inibidor de entrada

## Maraviroc: inibidor de CCR5



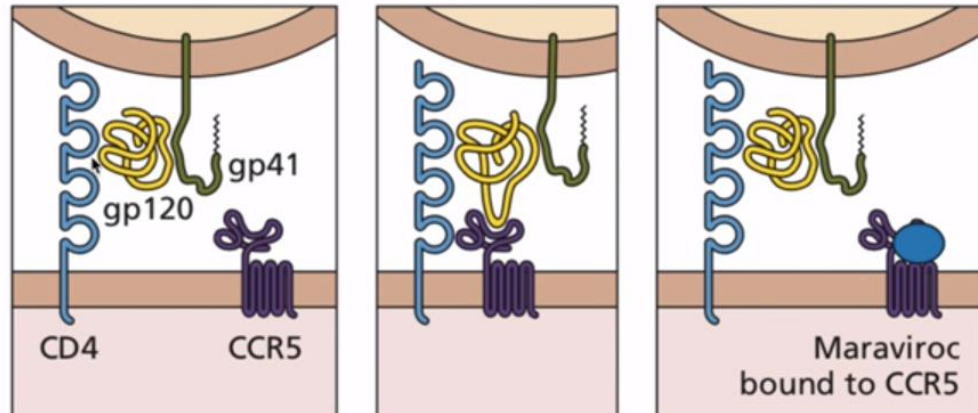
A



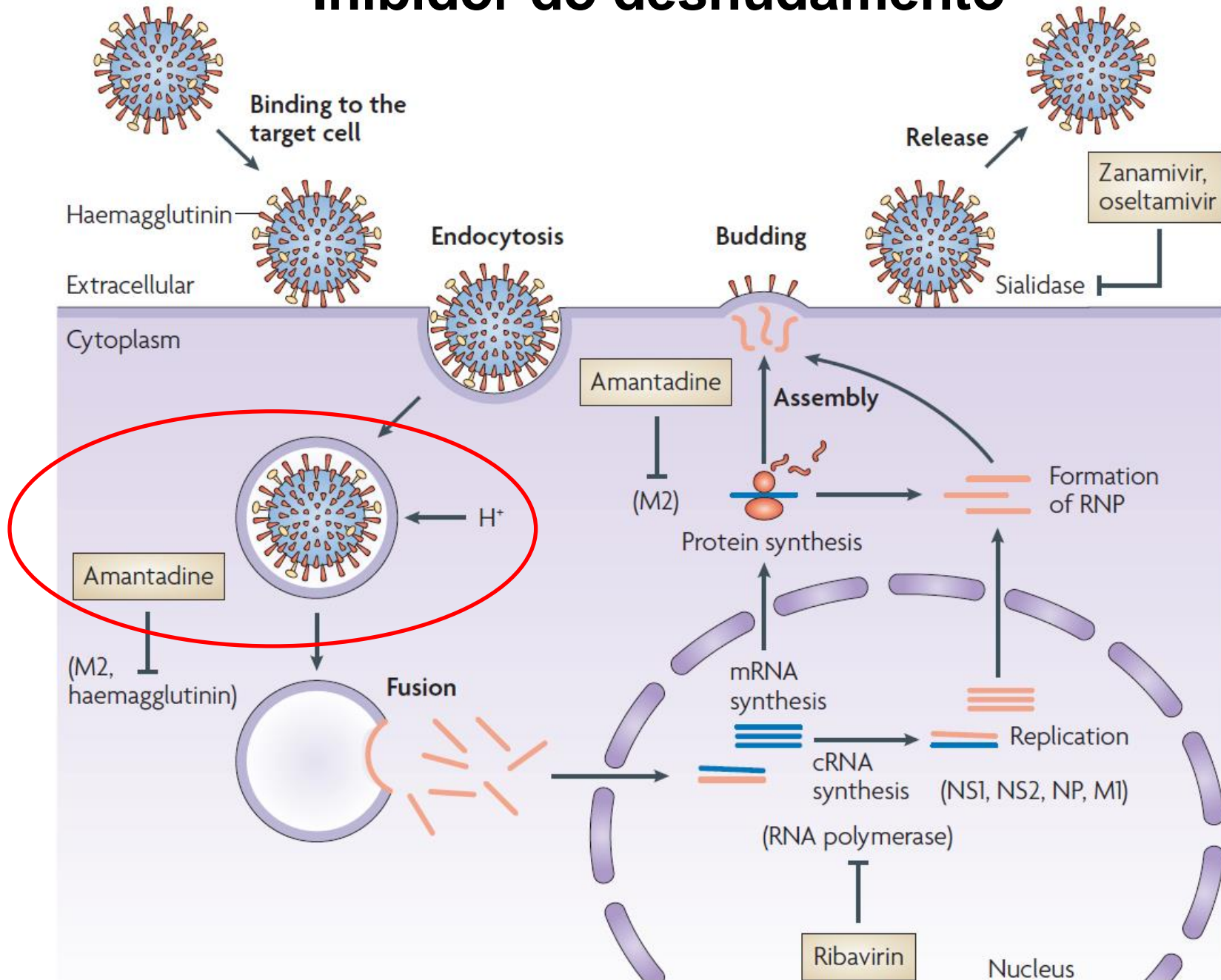
B



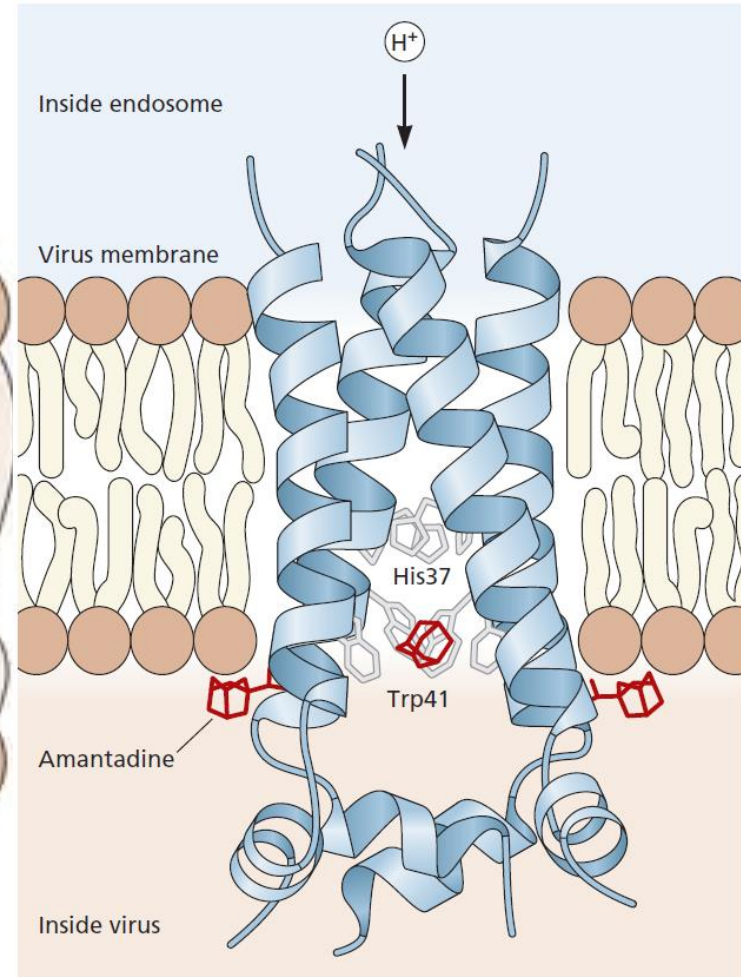
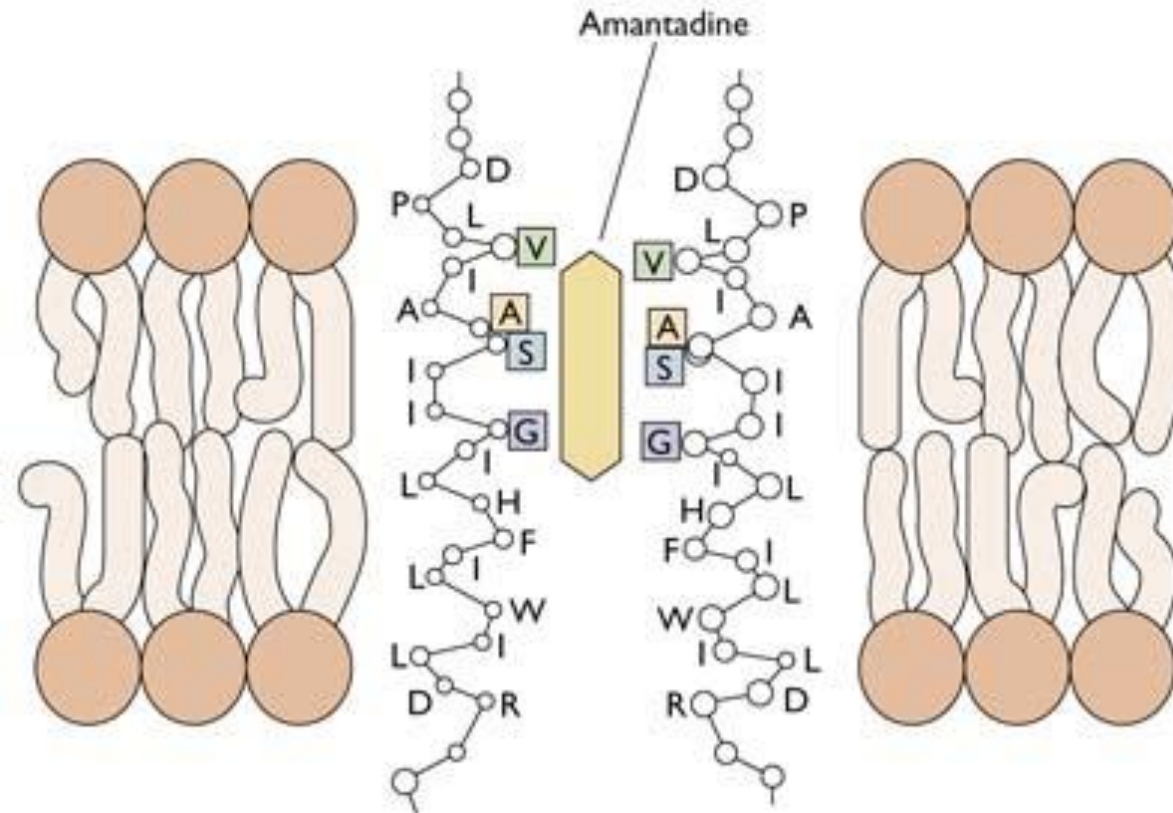
C



# Inibidor do desnudamento

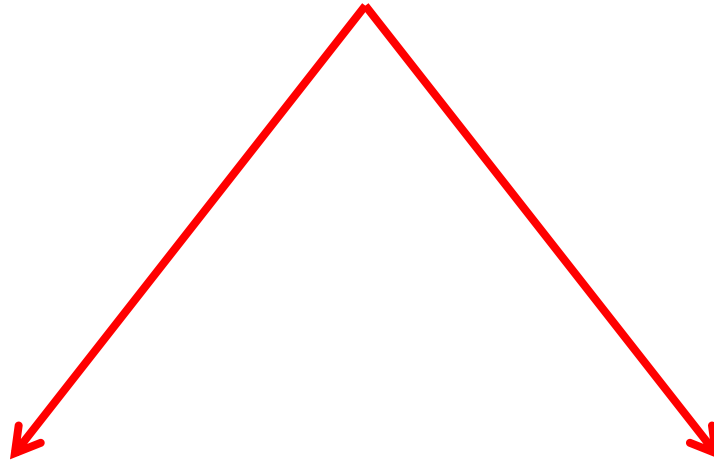


# Inibidor do desnudamento



# **Inibidores das polimerases virais**

# Inibidores das polimerases virais



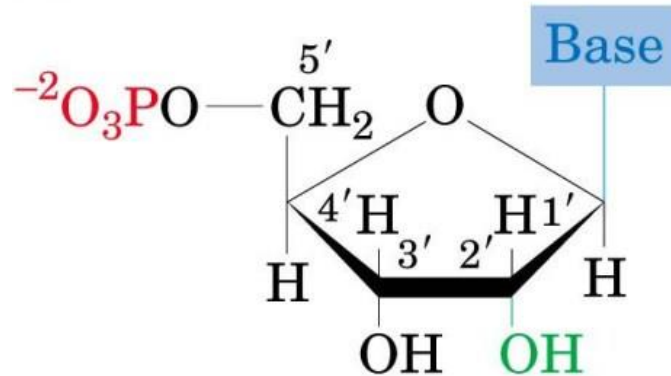
Análogos de nucleotídeos  
o de nucleosídeos.

Não análogos de nucleotídeos  
o de nucleosídeos.

- Servem, exclusivamente, para tipos virais que codificam polimerases próprias.

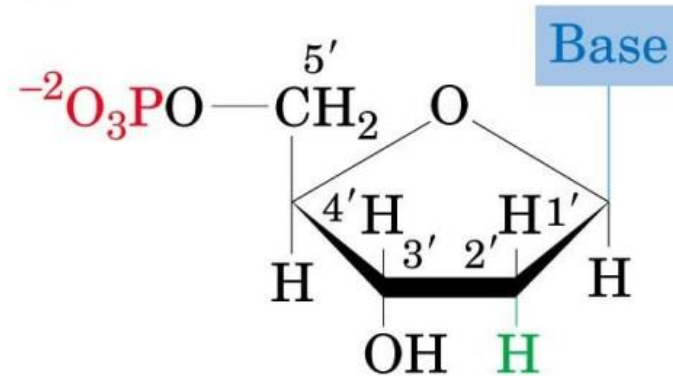
# Inibidores das polimerases virais

(a)

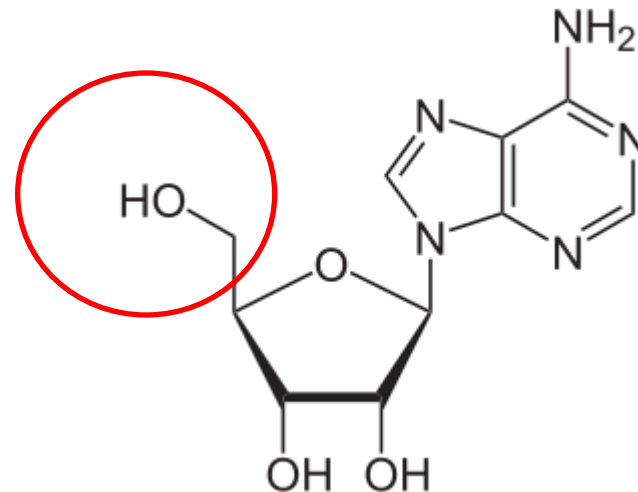


**Ribonucleotides**

(b)



**Deoxyribonucleotides**

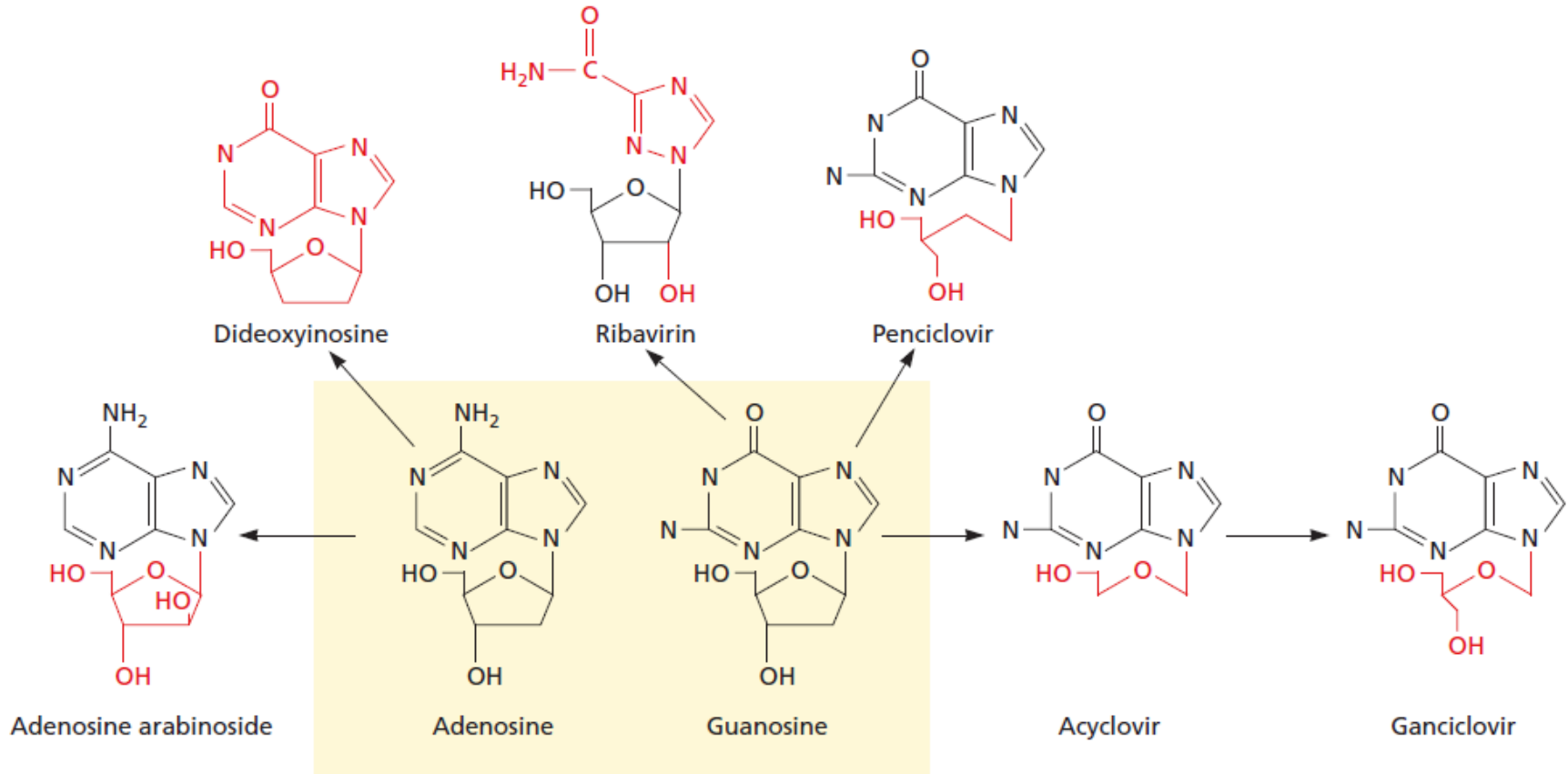


**Nucleosídeo**



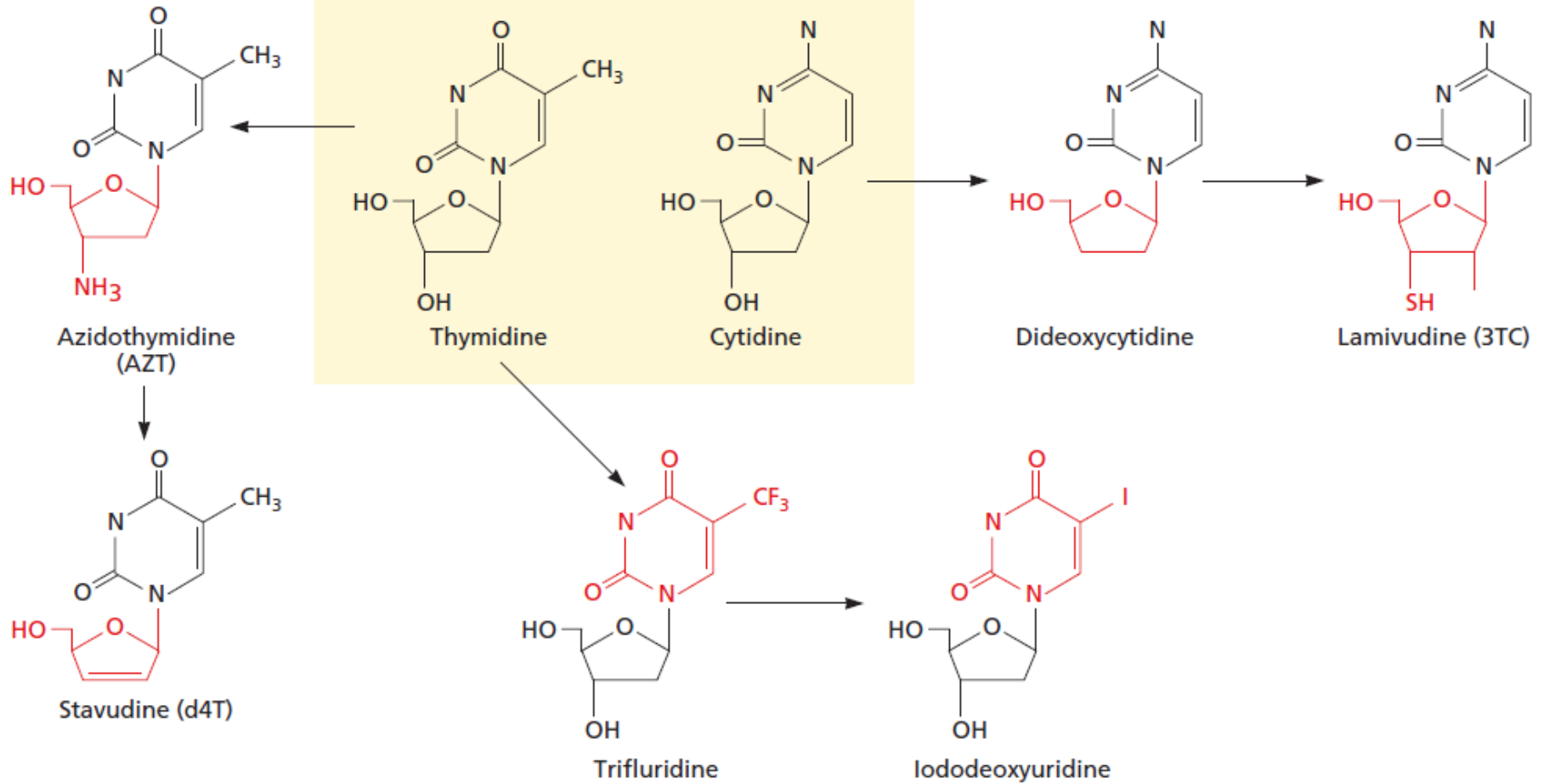
# Inibidores das polimerases virais

## Análogos de Nucleosídeos



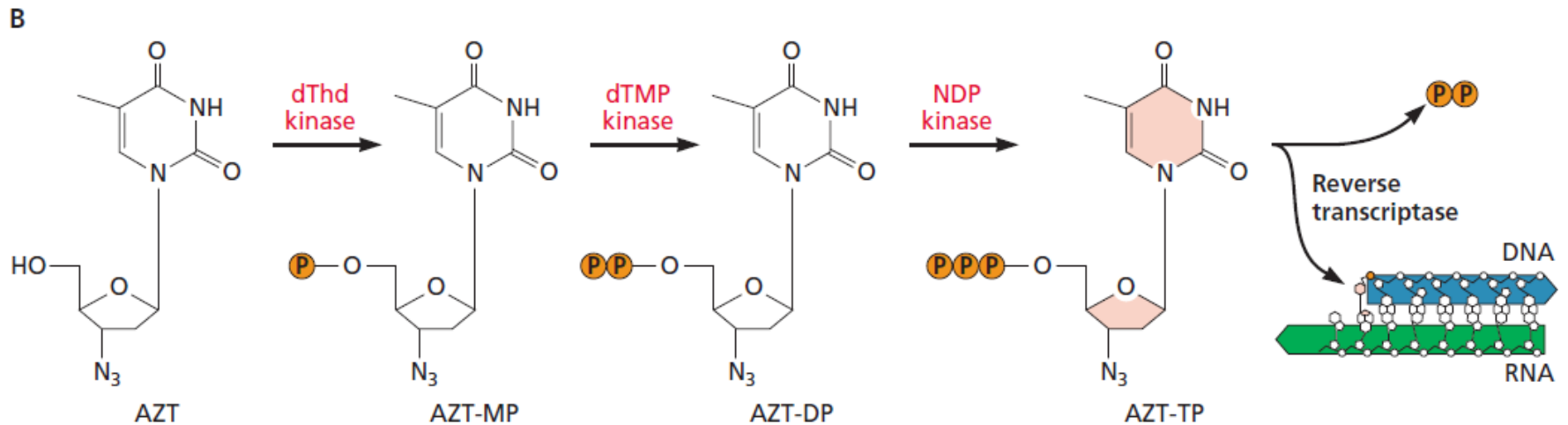
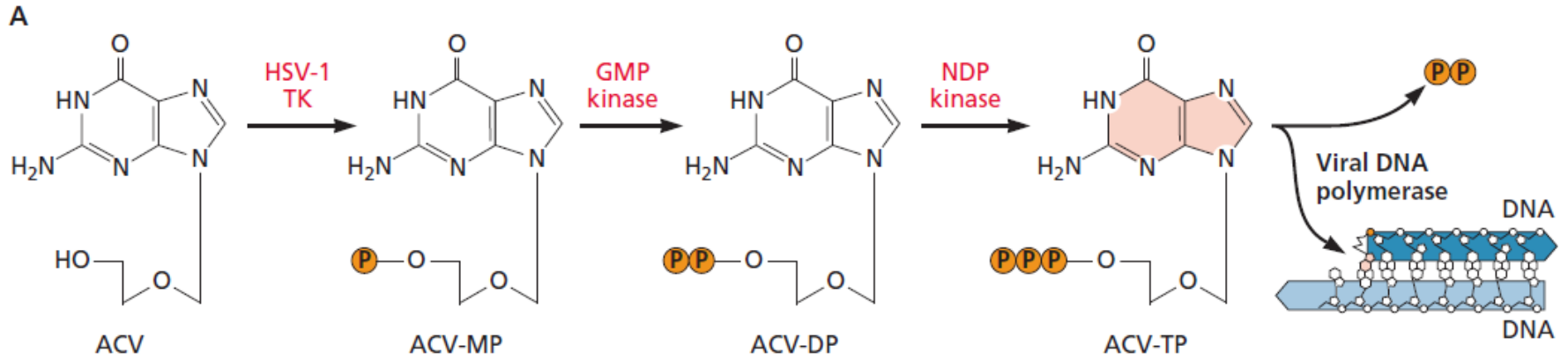
# Inibidores das polimerases virais

## Análogos de Nucleosídeos



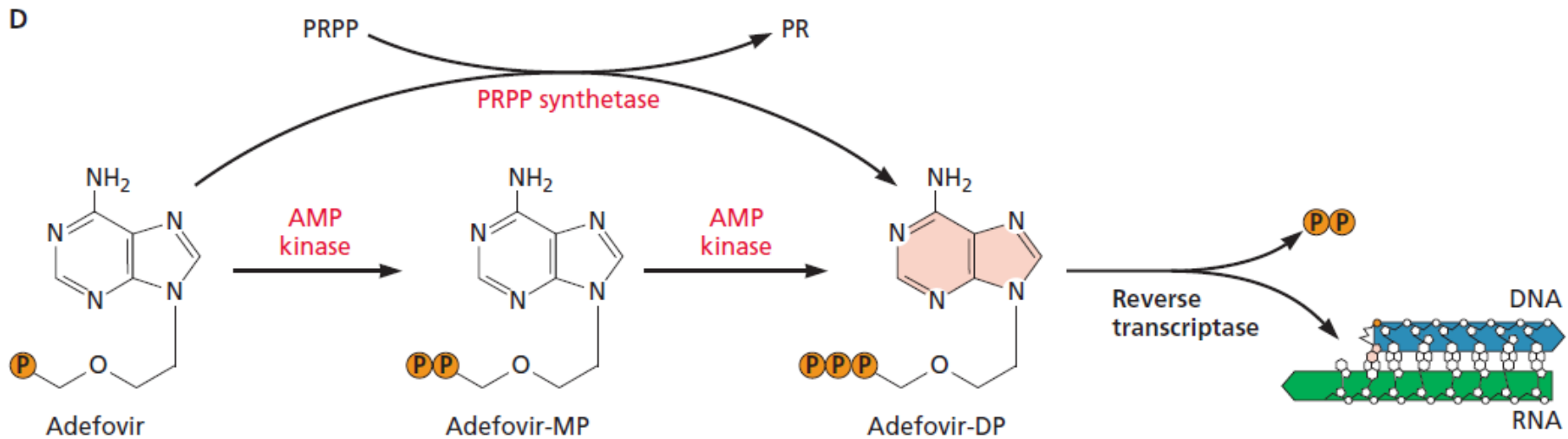
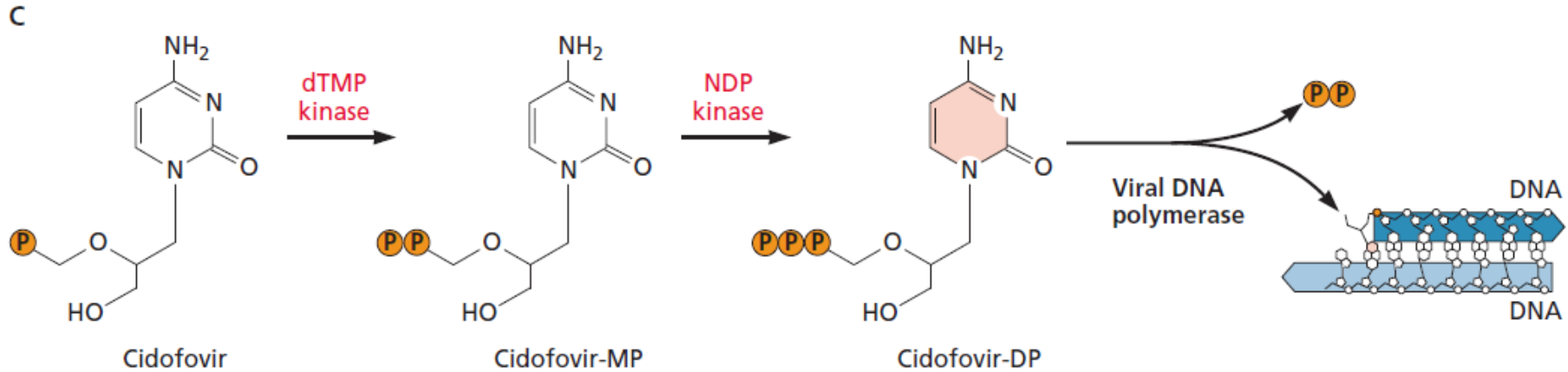
# Inibidores das polimerases virais

## Análogos de Nucleosídeos



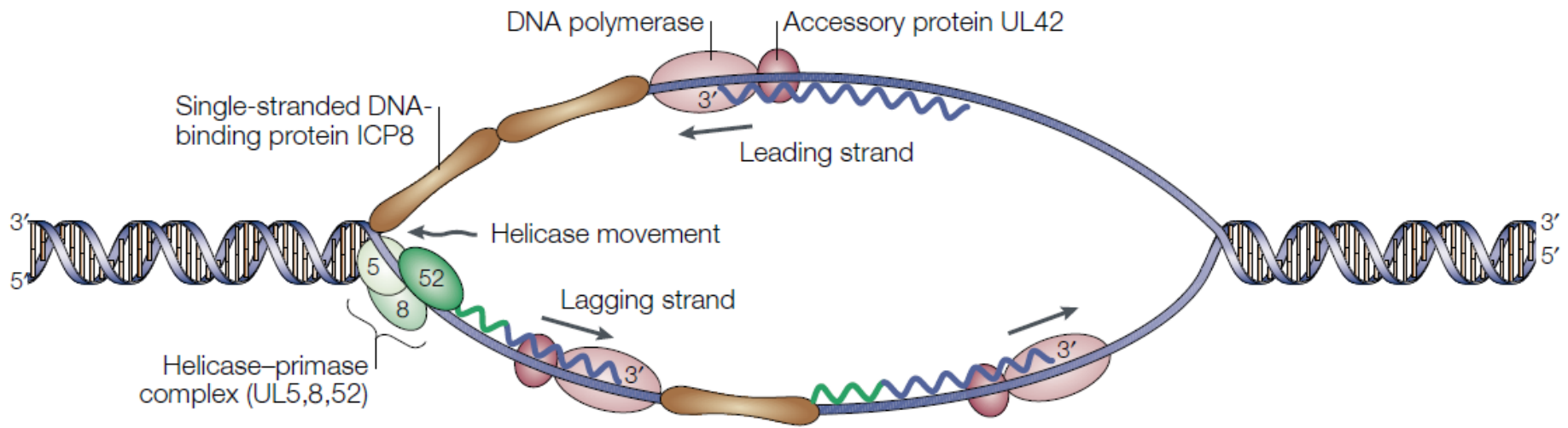
# Inibidores das polimerases virais

## Análogos de Nucleosídeos



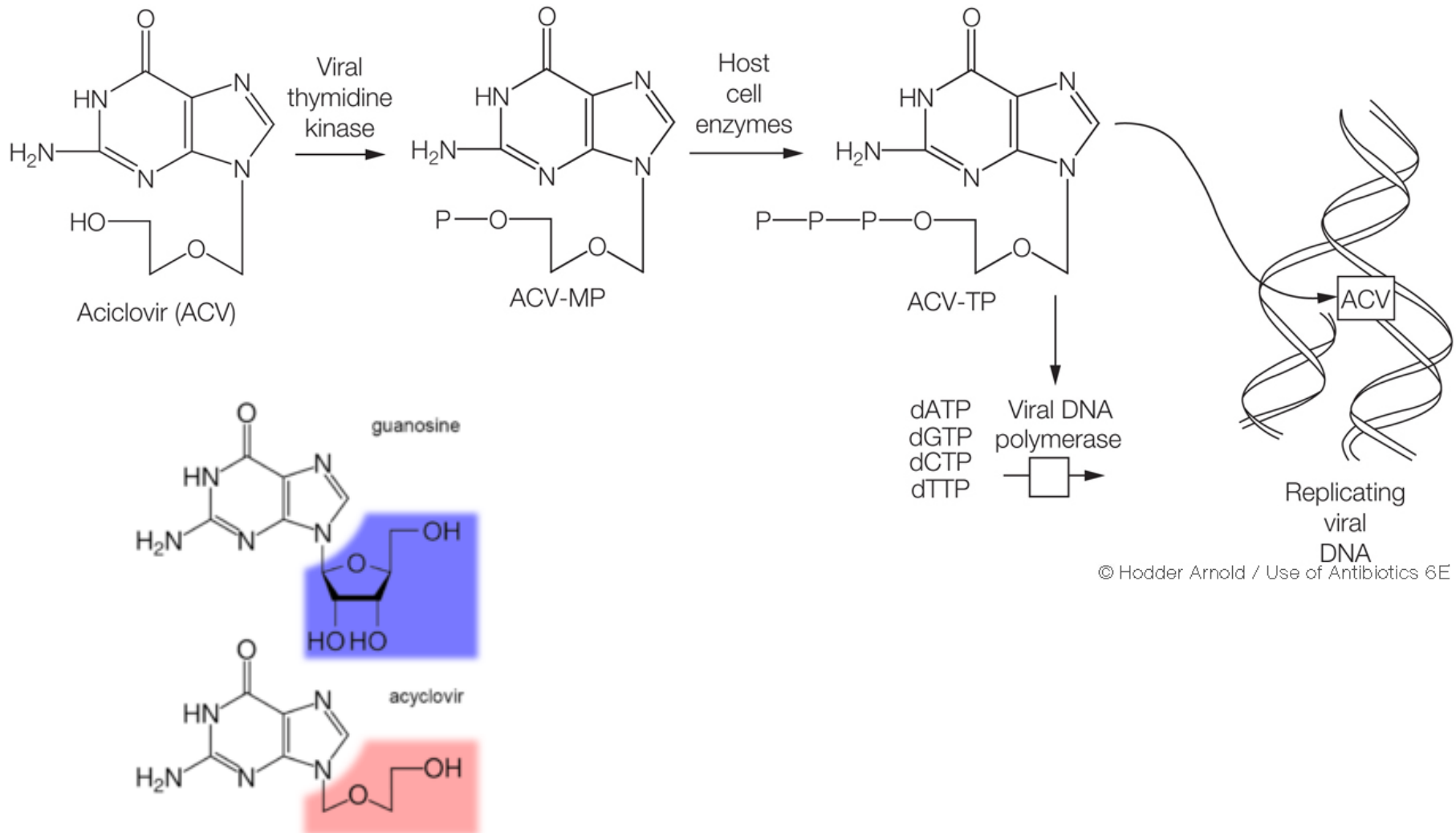
# **Inibidores da DNA polimerase de Herpesvírus**

# Inibidores da replicação de Herpesvírus



# Inibidores da replicação de Herpesvírus

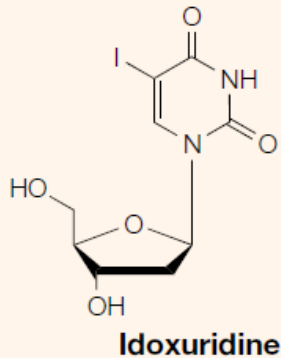
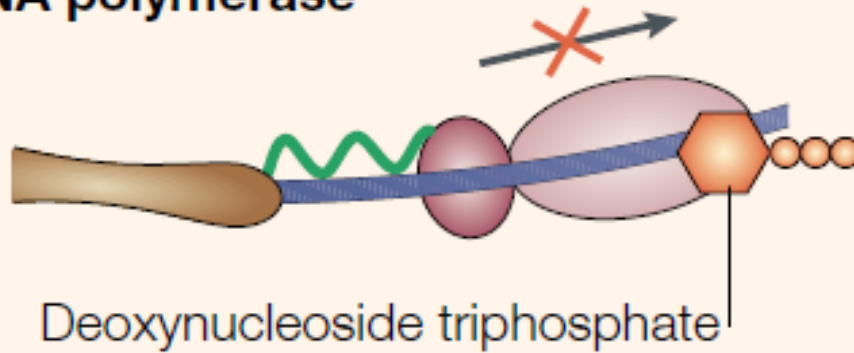
## Inibidores das polimerases virais



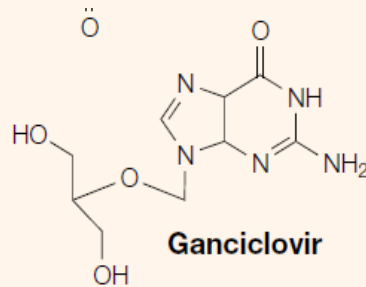
# Inibidores da replicação de Herpesvírus

## Inibidores das polimerases virais

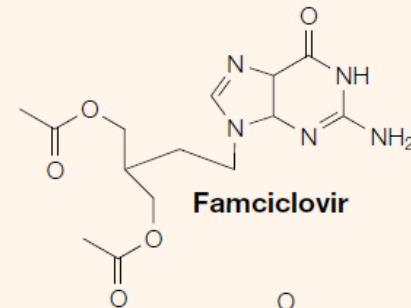
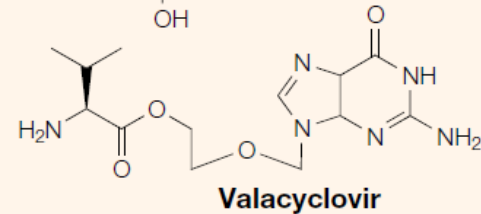
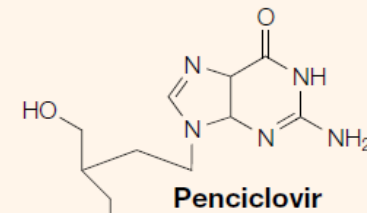
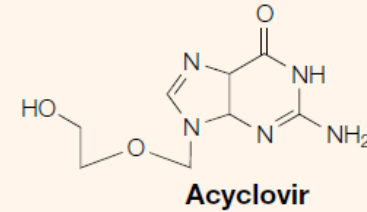
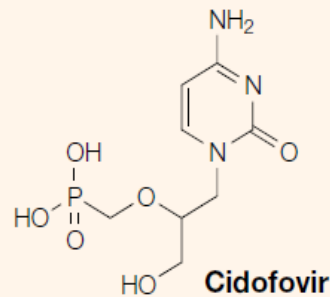
**a** Nucleoside analogues target viral DNA polymerase



HSV-1,  
HSV-2



HCMV



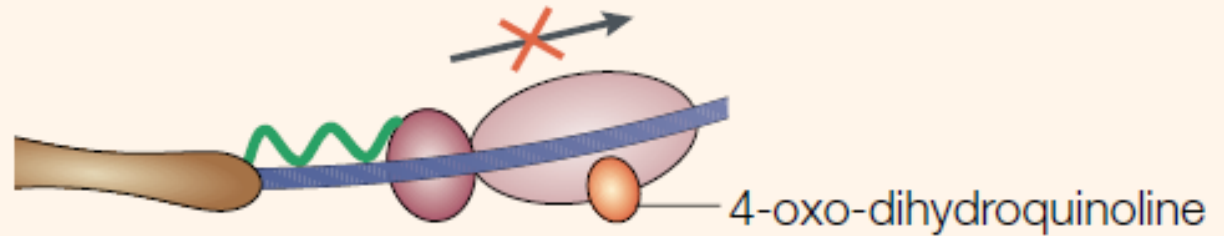
HSV-1,  
HSV-2,  
VZV



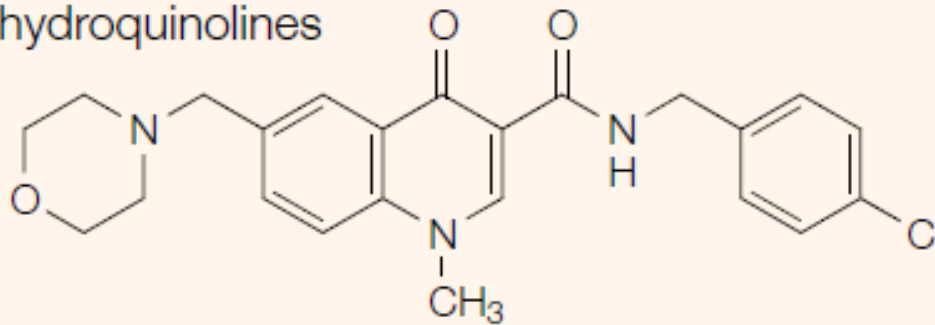
# Inibidores da replicação de Herpesvírus

## Inibidores das polimerases virais

### **b** Non-nucleoside drugs that target viral DNA polymerase

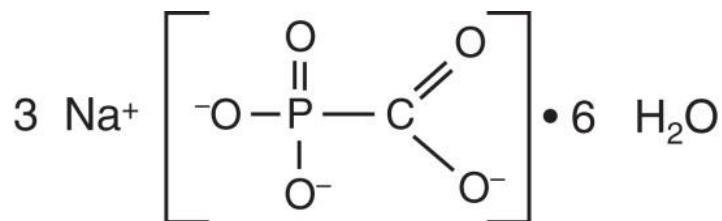


4-oxo-dihydroquinolines



**PNU-183792**

Multiple  
herpesviruses



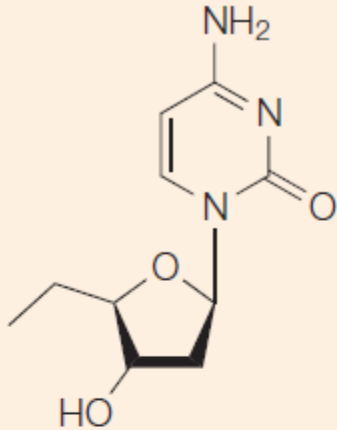
Foscarnet

# **Inibidores da DNA polimerase de Retrovírus**

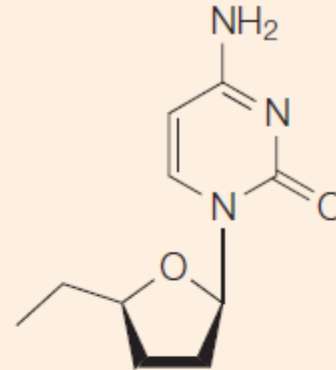
# Inibidores da replicação de Retrovírus

## Inibidores da transcriptase reversa

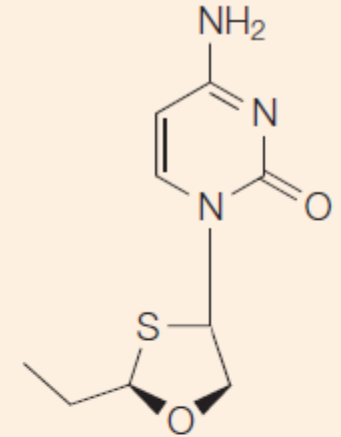
**a**



**dC**

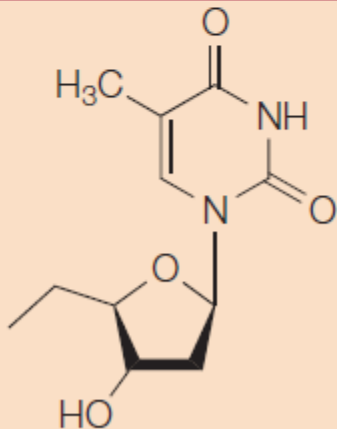


**ddCTP (zalcitabine)**

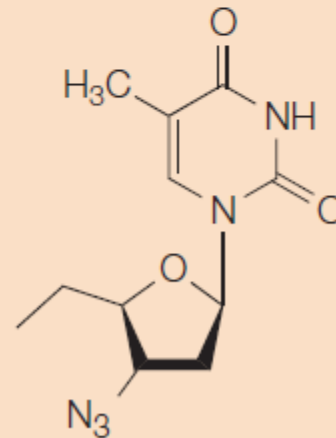


**3TC (lamivudine)**

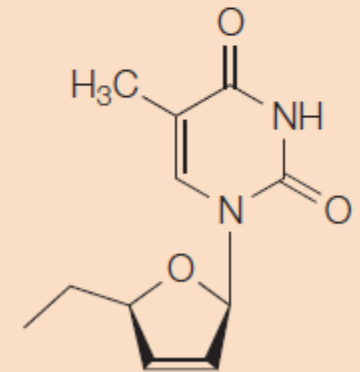
Análogos de nucleosídeos.



**dT**



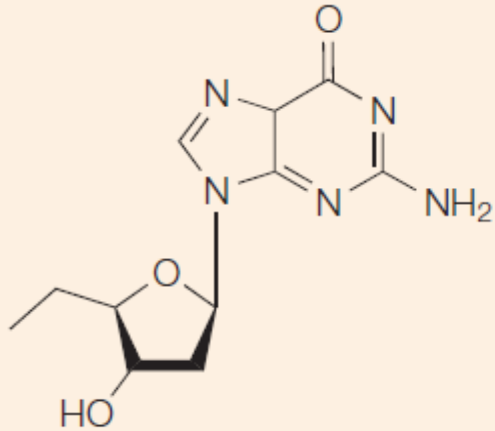
**AZT (zidovudine)**



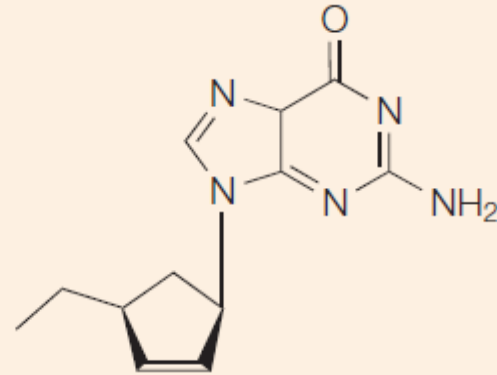
**D4T (stavudine)**

# Inibidores da replicação de Retrovírus

## Inibidores da transcriptase reversa

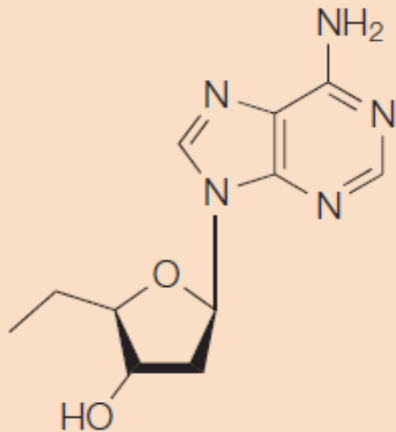


**dG**

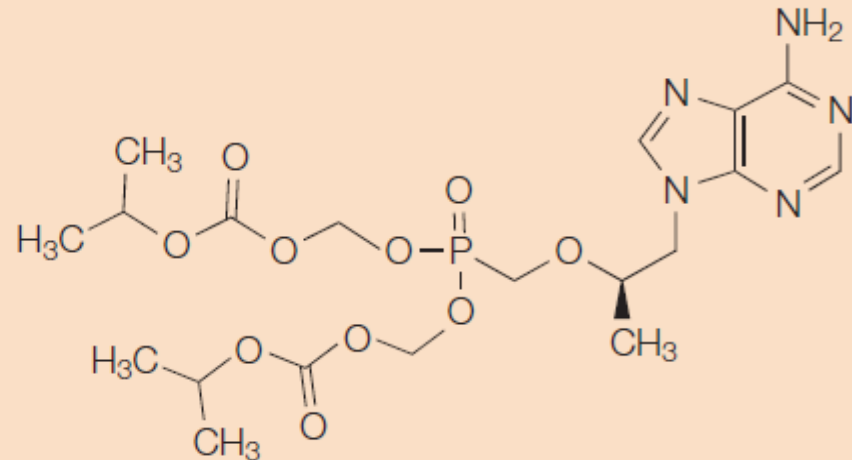


**CBV (carbovir, active form of abacavir)**

Análogos de nucleosídeos.



**dA**



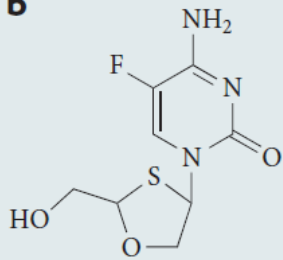
**PMPA (tenofovir)**

# Inibidores da replicação de Retrovírus

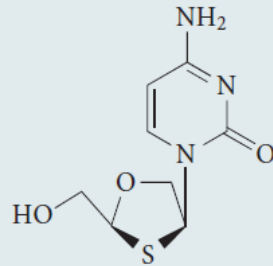
## Inibidores da transcriptase reversa

### Análogos de nucleosídeos.

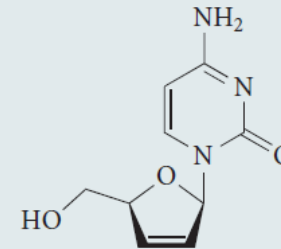
**b**



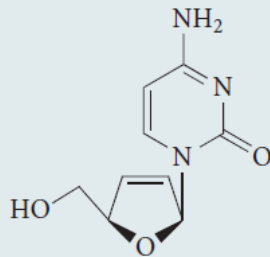
Racemic  
(±)FTC (FdOTC)  
Racivir



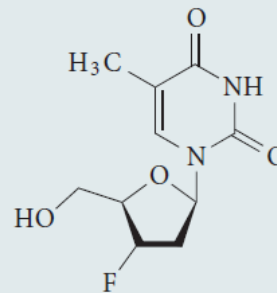
AVX-754 ((-)-dOTC)  
SPD-754  
Apricitabine



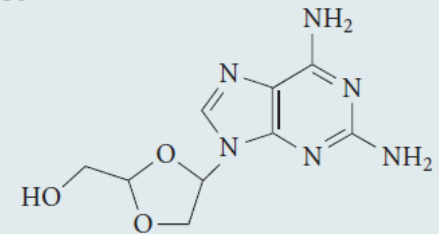
DPC-817 (β-D-Fd4C)  
Dexelvucitabine  
Reverset



ACH-126443 (β-L-Fd4C)  
Elvucitabine



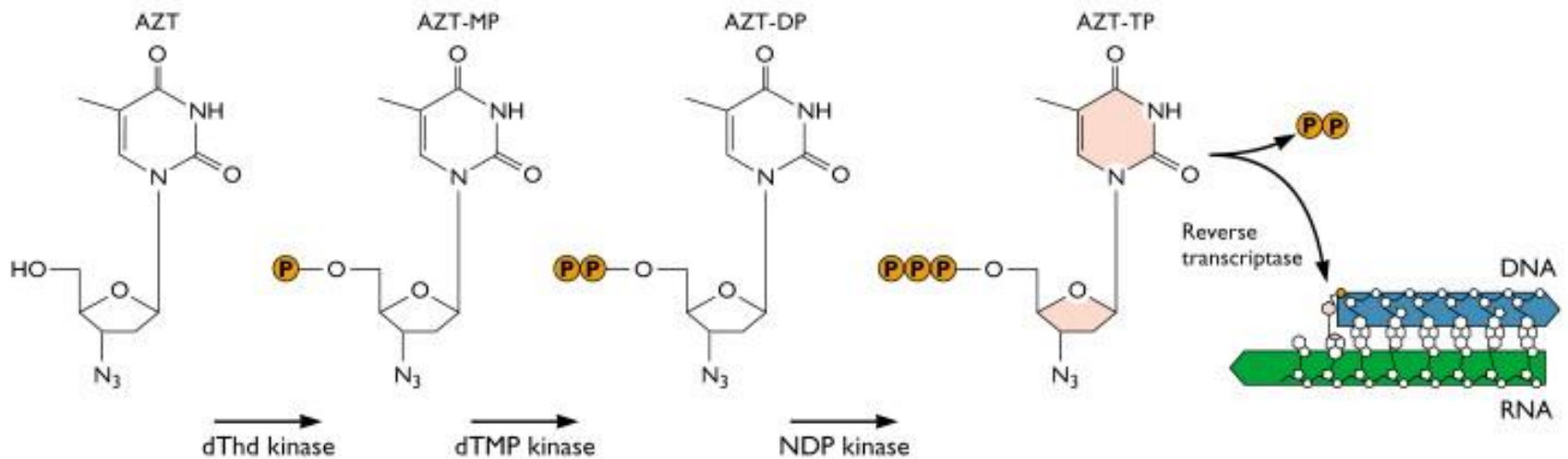
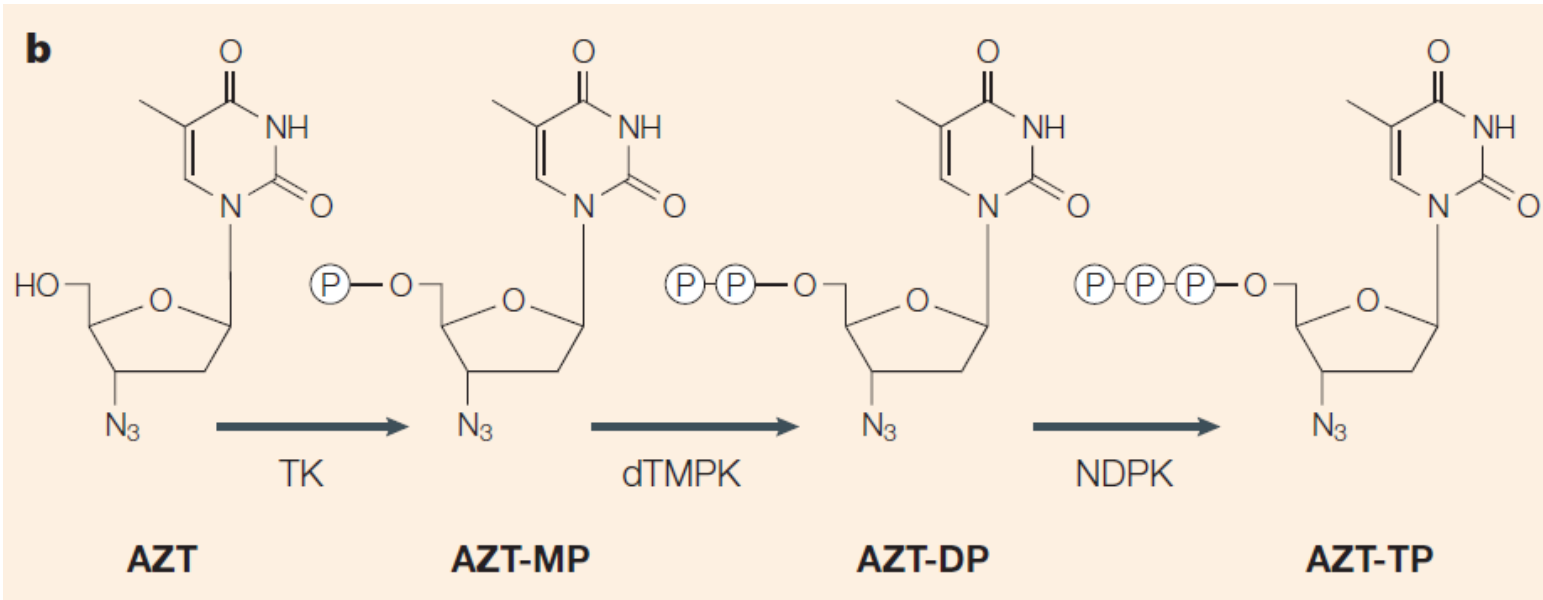
MIV-310 (FddThd, FLT)  
Alovudine



Diaminopurine  
dioxolane (DAPD)  
Amdoxovir

# Inibidores da replicação de Retrovírus

## Inibidores da transcriptase reversa

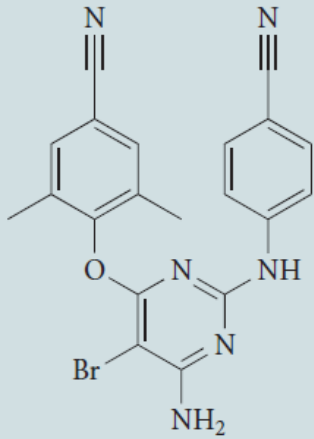


# Inibidores da replicação de Retrovírus

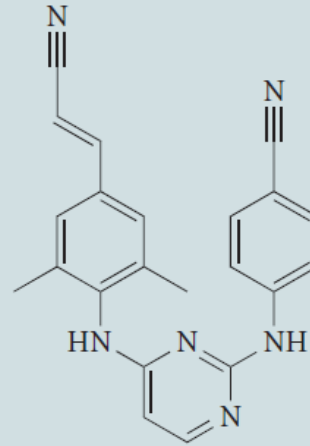
## Inibidores da transcriptase reversa

Não análogos de nucleosídeos.

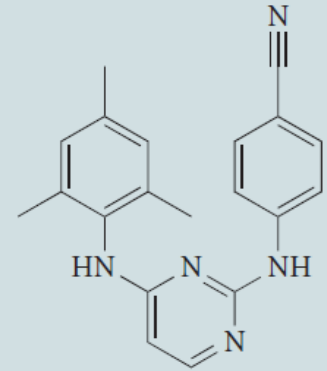
c



**Etravirine**  
(TMC125, R165335)



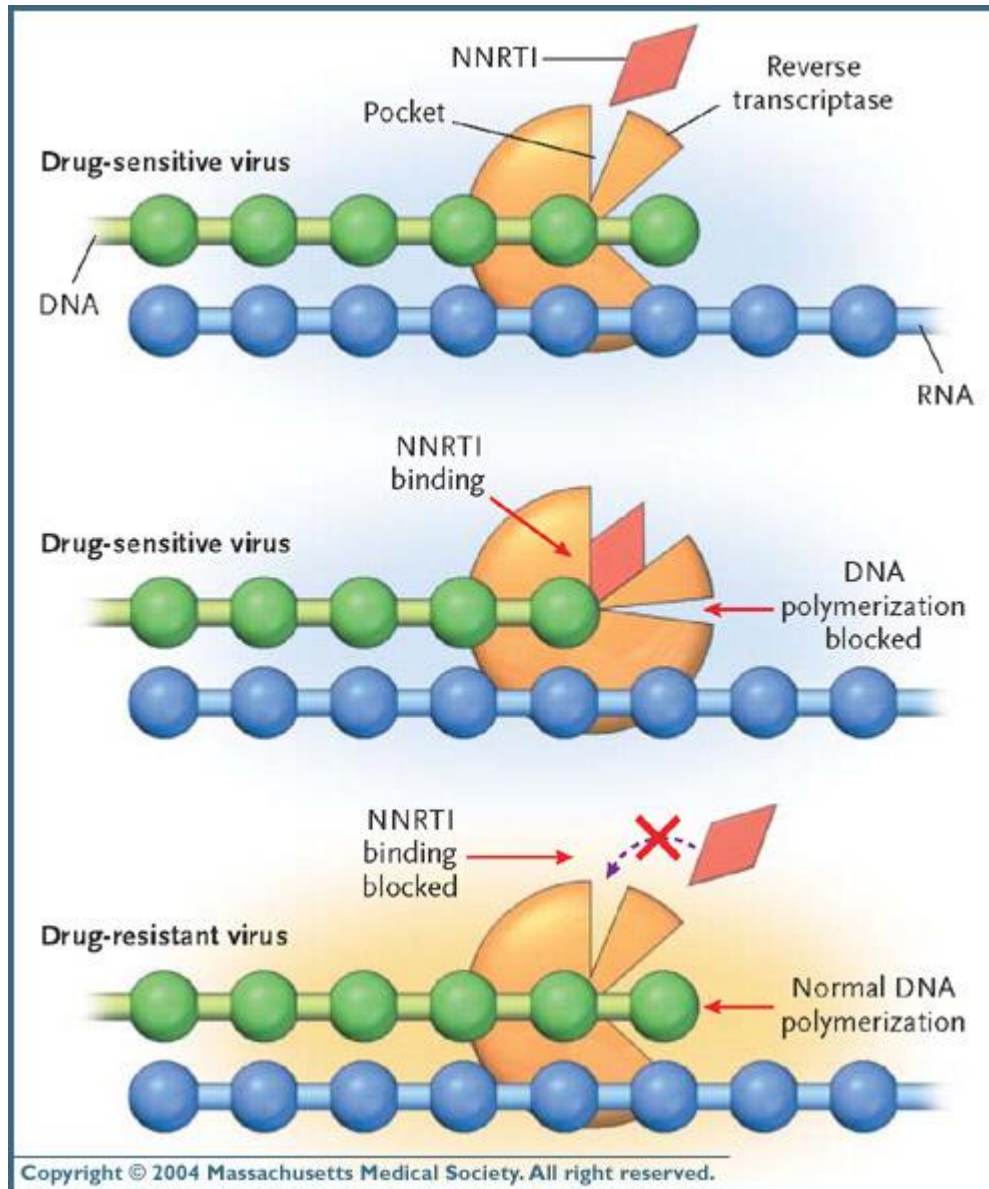
**Rilpivirine**  
(TMC278, R278474)



**Dapivirine**  
(TMC120, R147681)

# Inibidores da replicação de Retrovírus

## Inibidores da transcriptase reversa

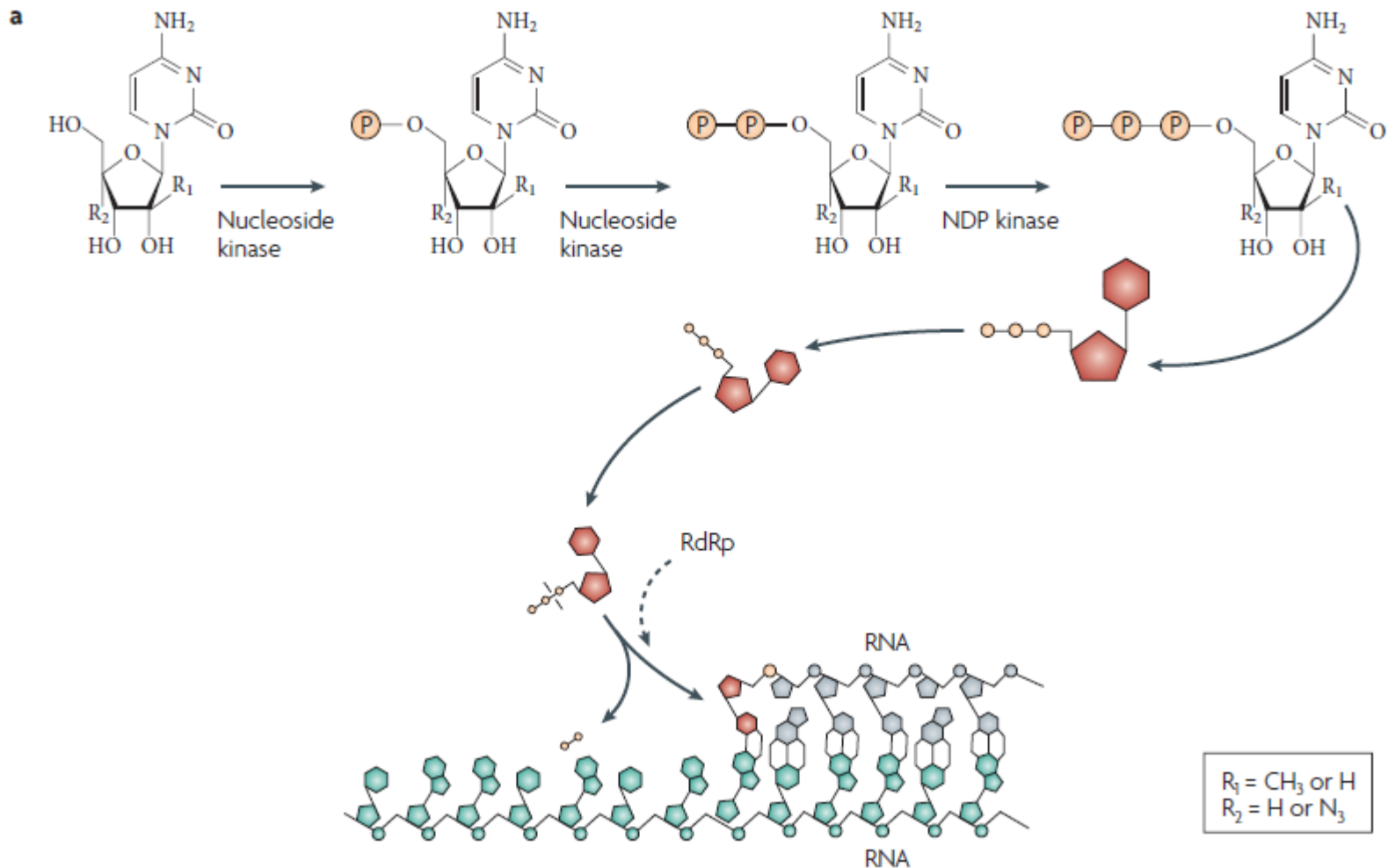




# **Inibidores da RNA polimerase de flavivírus**

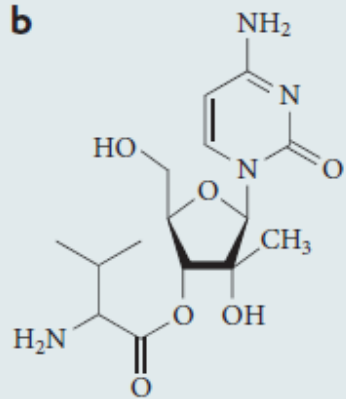
# Inibidores da RNA polimerase dependente de RNA (*replicase inhibitors*)

Inibidores da NS5B de HCV

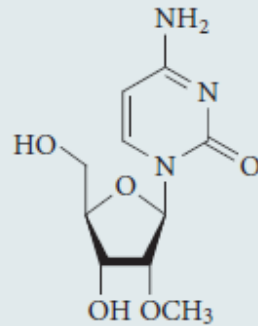


# Inibidores da RNA polimerase dependente de RNA (*replicase inhibitors*)

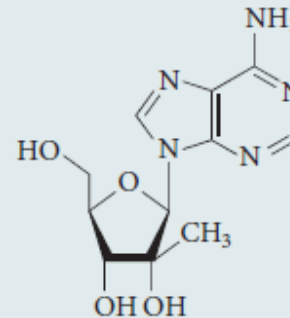
Inibidores da NS5B de HCV análogos de nucleosídeos



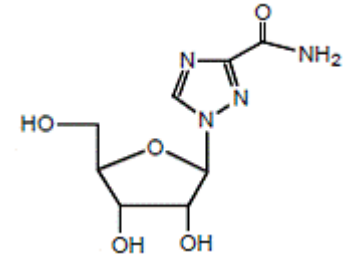
3'-valine ester of  
2'-C-methylcytidine  
Valopicitabine (NM283)



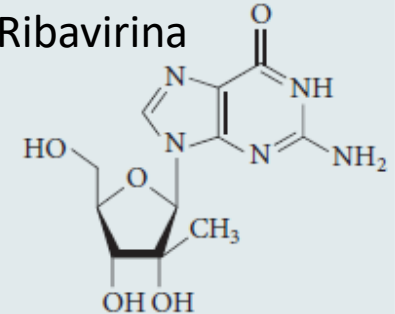
2'-O-methylcytidine



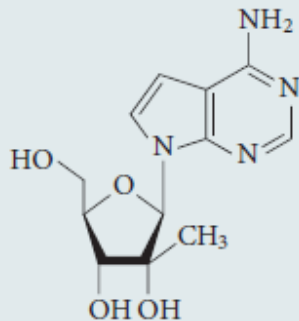
2'-C-methyladenosine



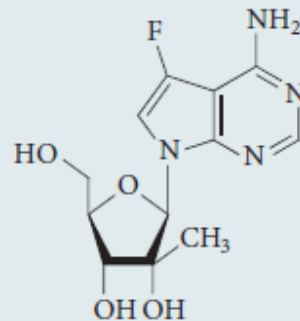
Ribavirina



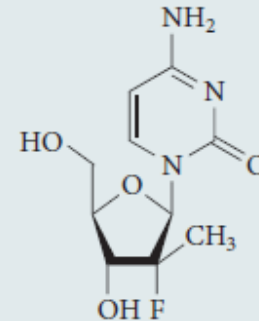
2'-C-methylguanosine



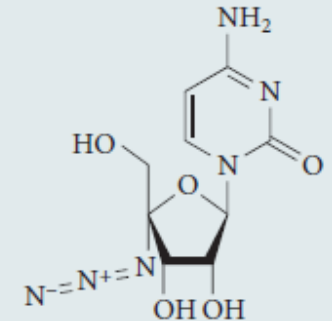
7-deaza-2'-C-methyladenosine



7-Deaza-7-fluoro-  
2'-C-methyladenosine



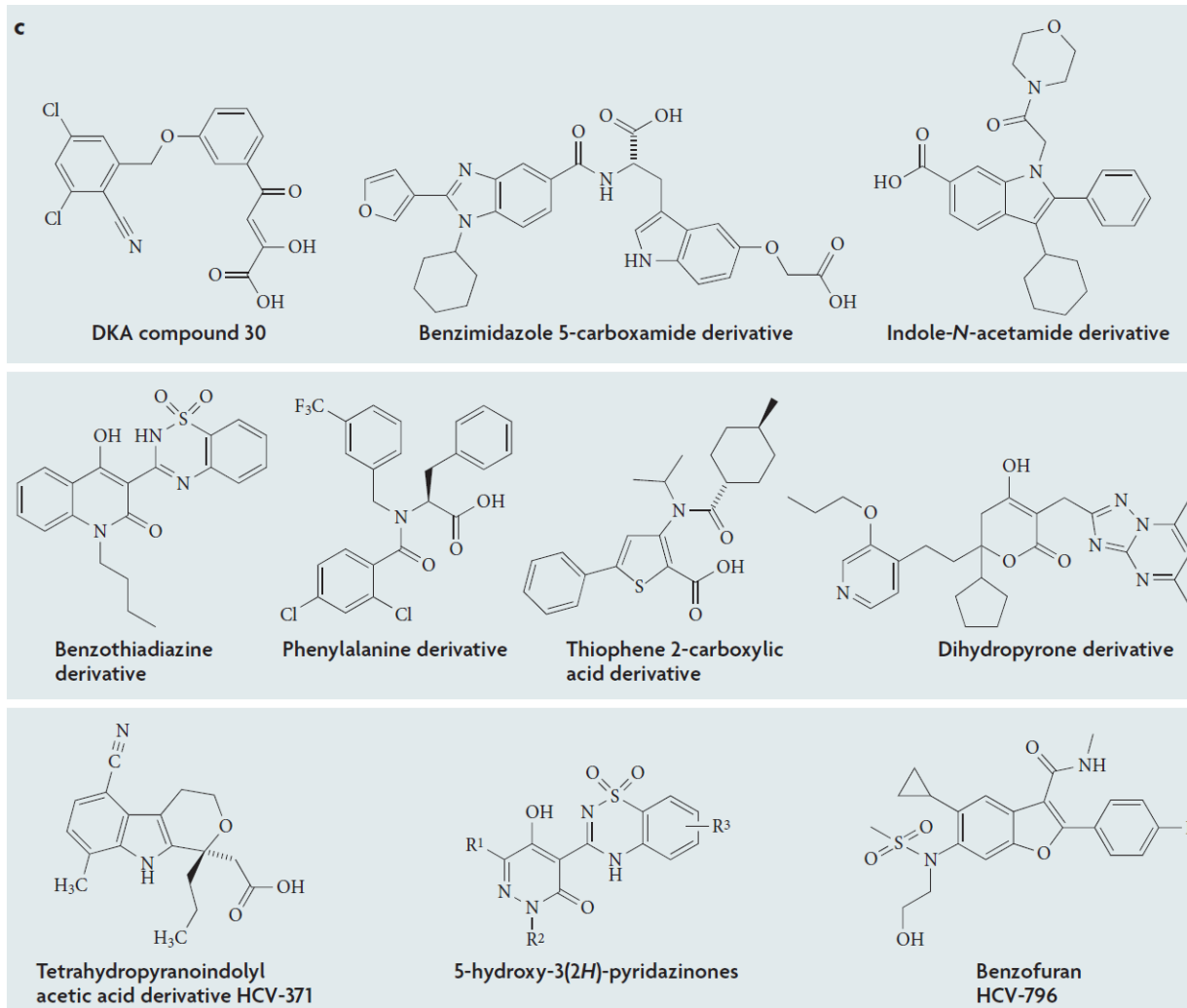
2'-Deoxy-2'-fluoro-  
2'-C-methylcytidine  
(PSI-6130)



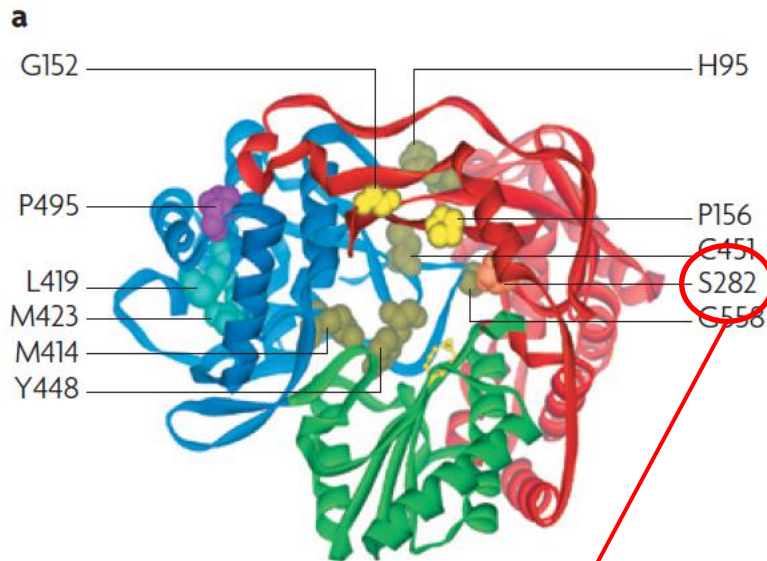
4'-Azidocytidine  
(R1479)

# Inibidores da RNA polimerase dependente de RNA (*replicase inhibitors*)

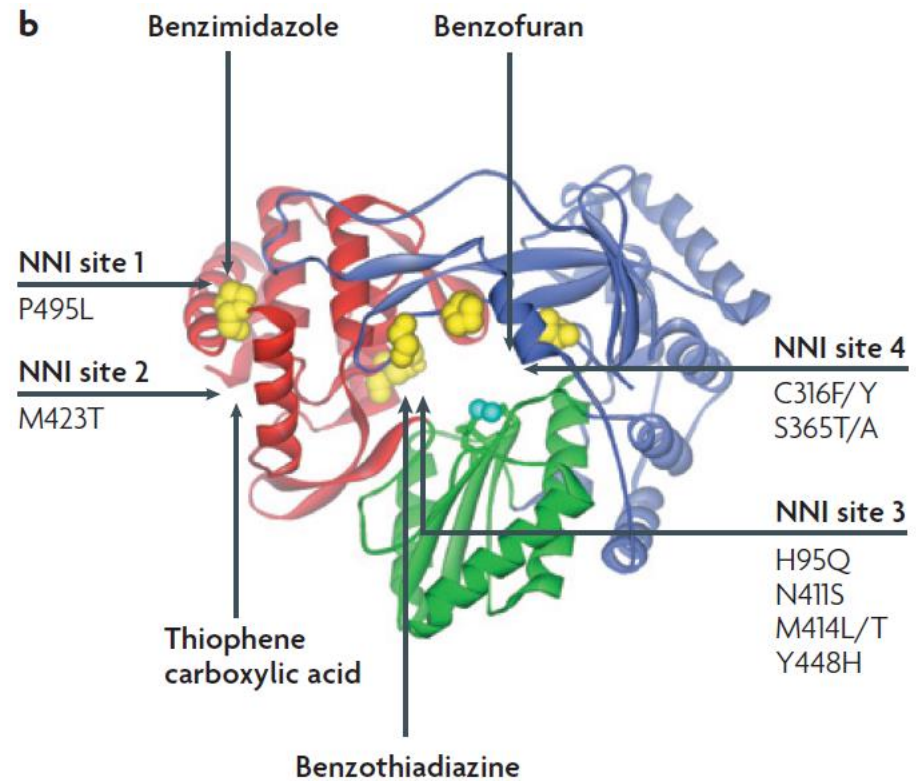
Inibidores da NS5B de HCV NÃO análogos de nucleosídeos



# Inibidores da RNA polimerase dependente de RNA (*replicase inhibitors*)



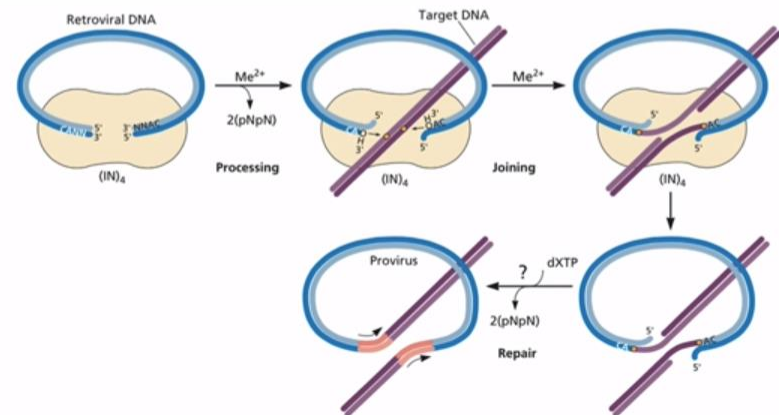
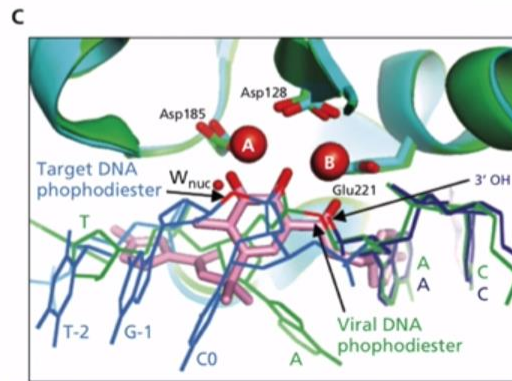
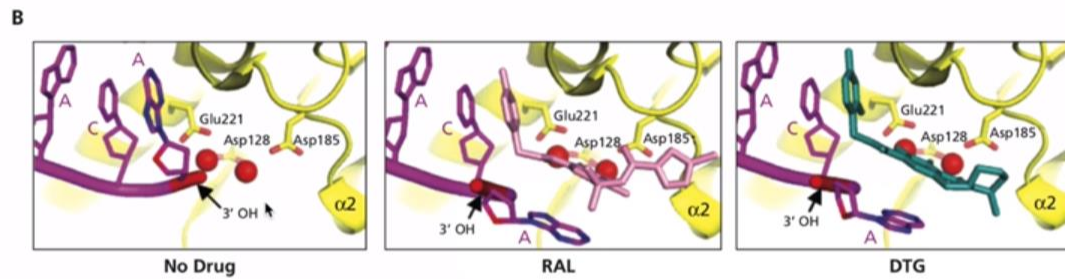
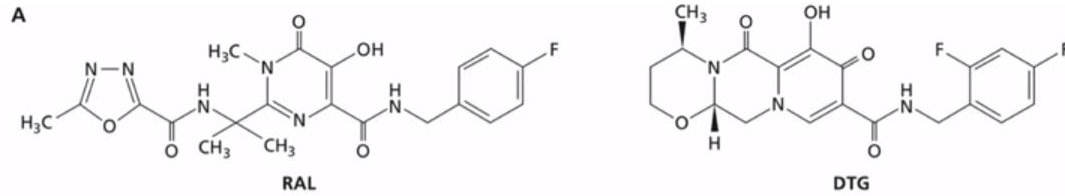
Único sítio de ligação de  
inibidores da replicase  
análogos de nucleosídeos



Existem 4 sítios de ligação de  
inibidores da replicase NÃO  
análogos de nucleosídeos

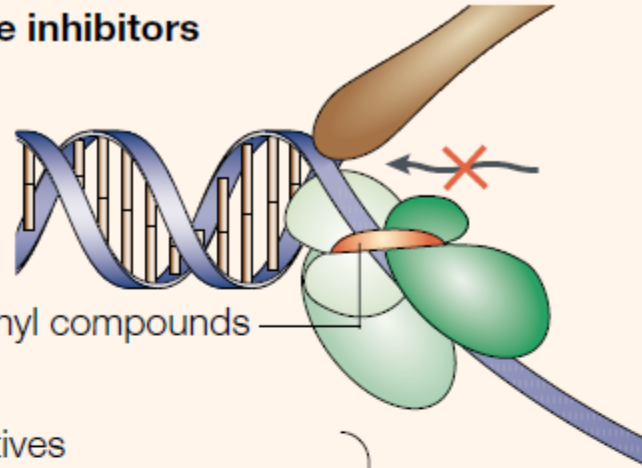
# **Inibidores de outras enzimas virais**

# Inibidores da integrase de HIV

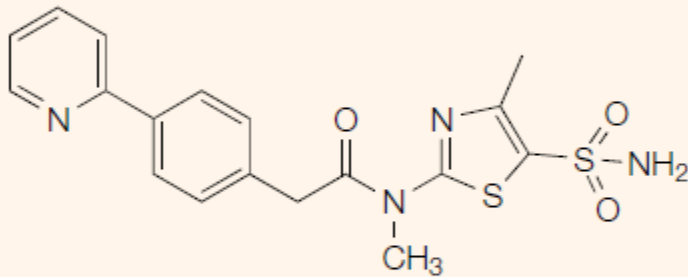


# Inibidores da replicação de Herpesvírus

## c Helicase-primase inhibitors

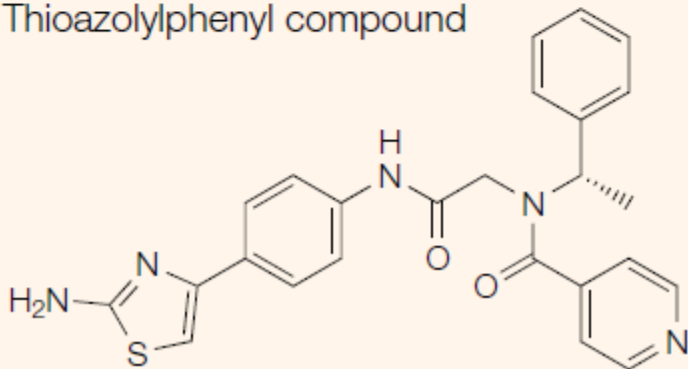


### Thioazole urea derivatives



**BAY 57-1293**

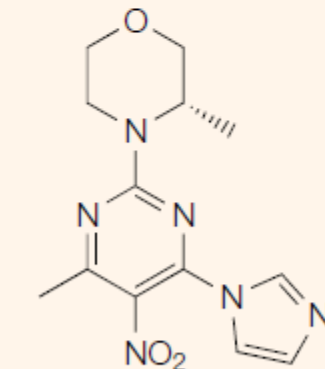
### Thioazolyphenyl compound



**BILS 179 BS**

HSV-1,  
HSV-2

### Nitropyrimidine



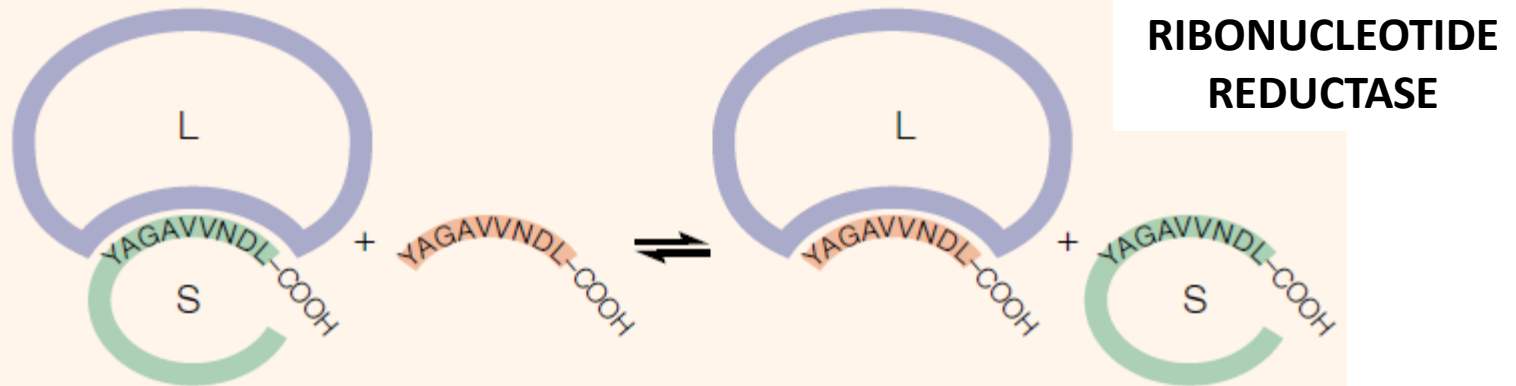
**T-0902611**

HCMV



# Inibidores da replicação de Herpesvírus

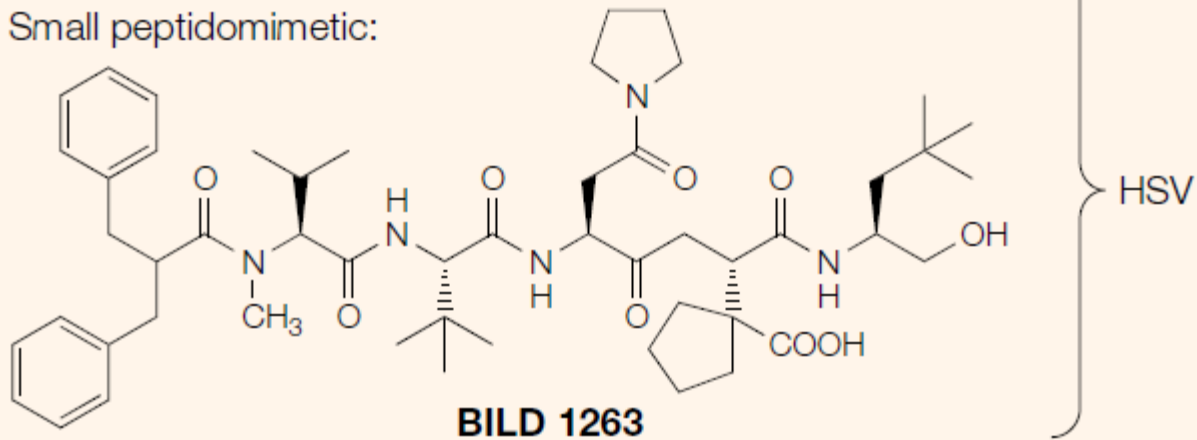
## d Inhibitors that block protein-protein interactions



Nonapeptide:

YAGAVVNDL-COOH

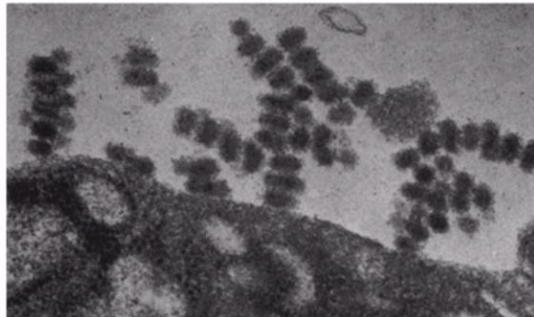
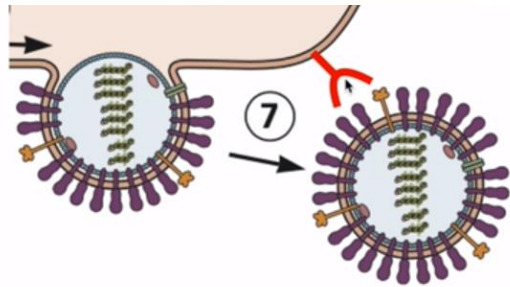
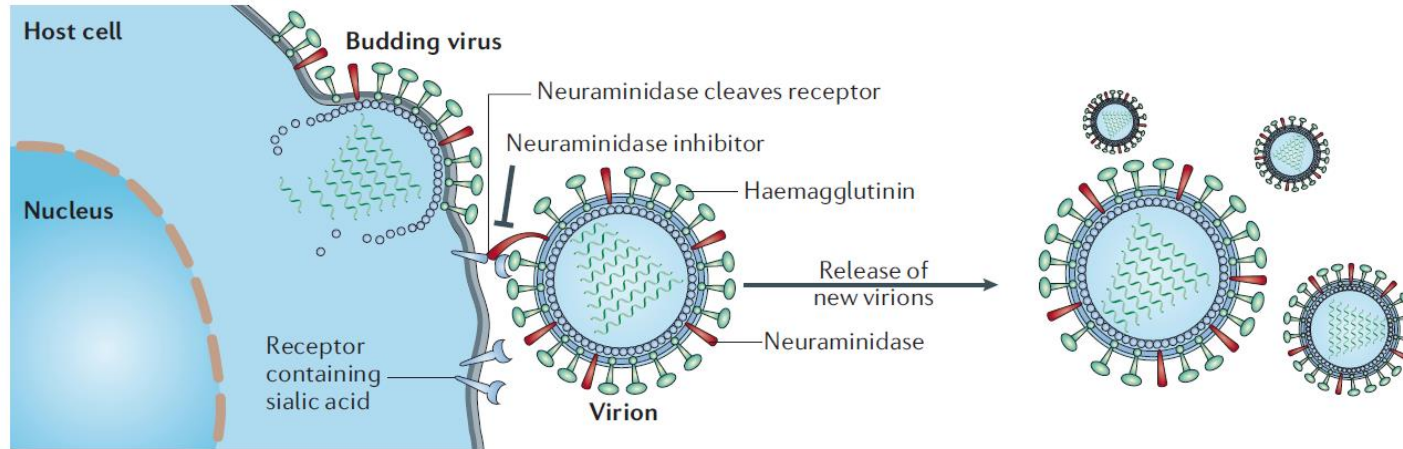
Small peptidomimetic:



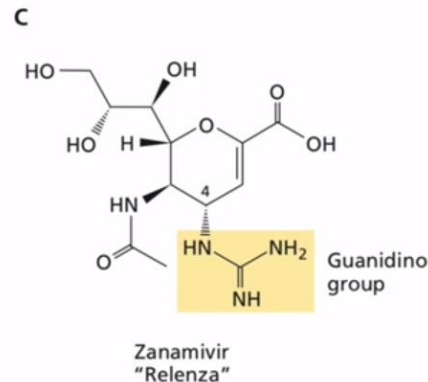
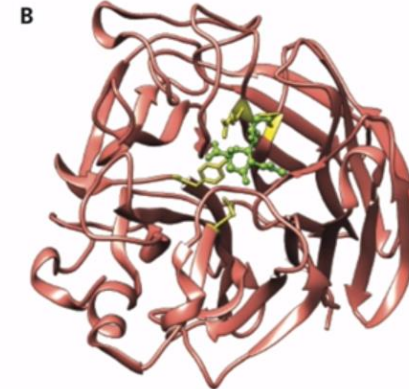
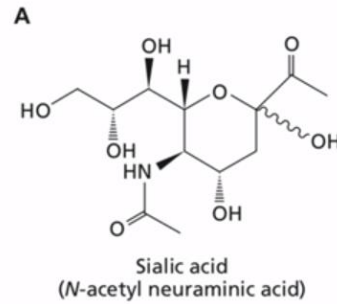
# Inibidores do brotamento

## Influenza

a Neuraminidase activity

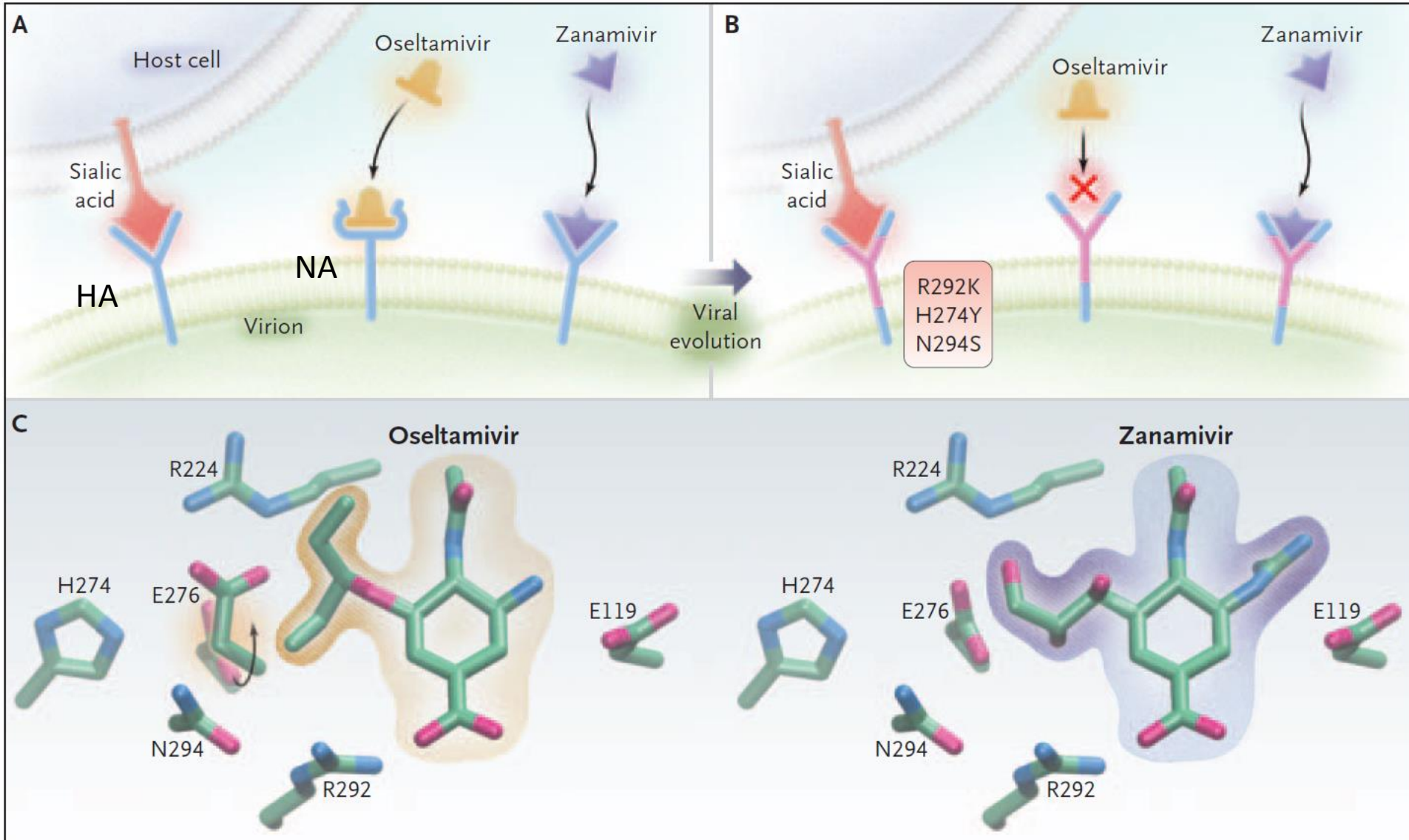


J. Gen. Virol. 1976 Oct;33(1):159-63.



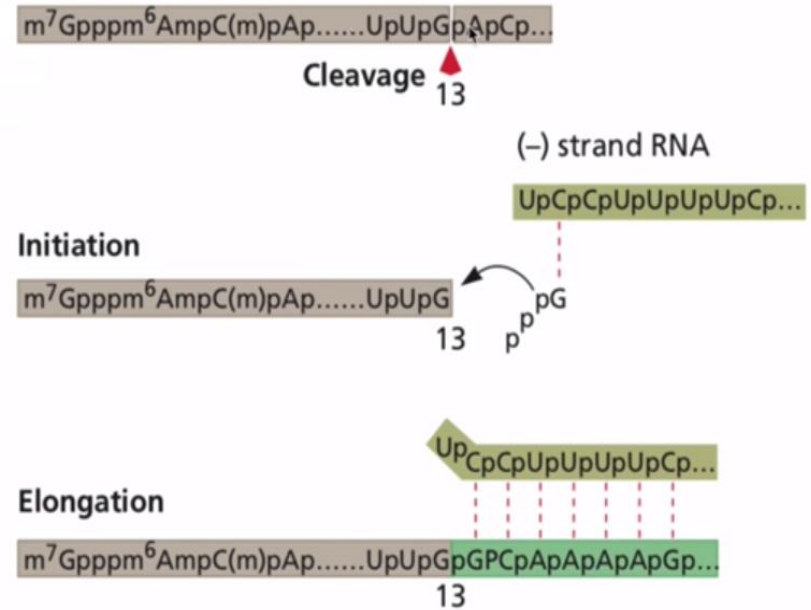
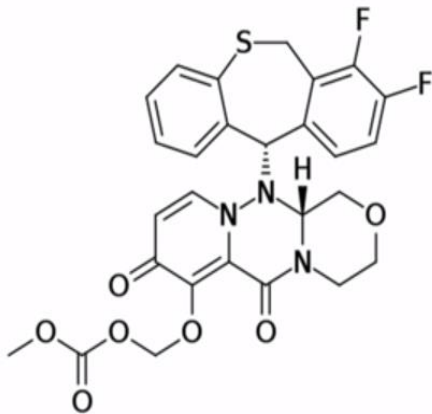
# Inibidores do brotamento

# Influenza



# Inibidores da endonuclease de influenza

- Baloxavir (aprovado em 2018)

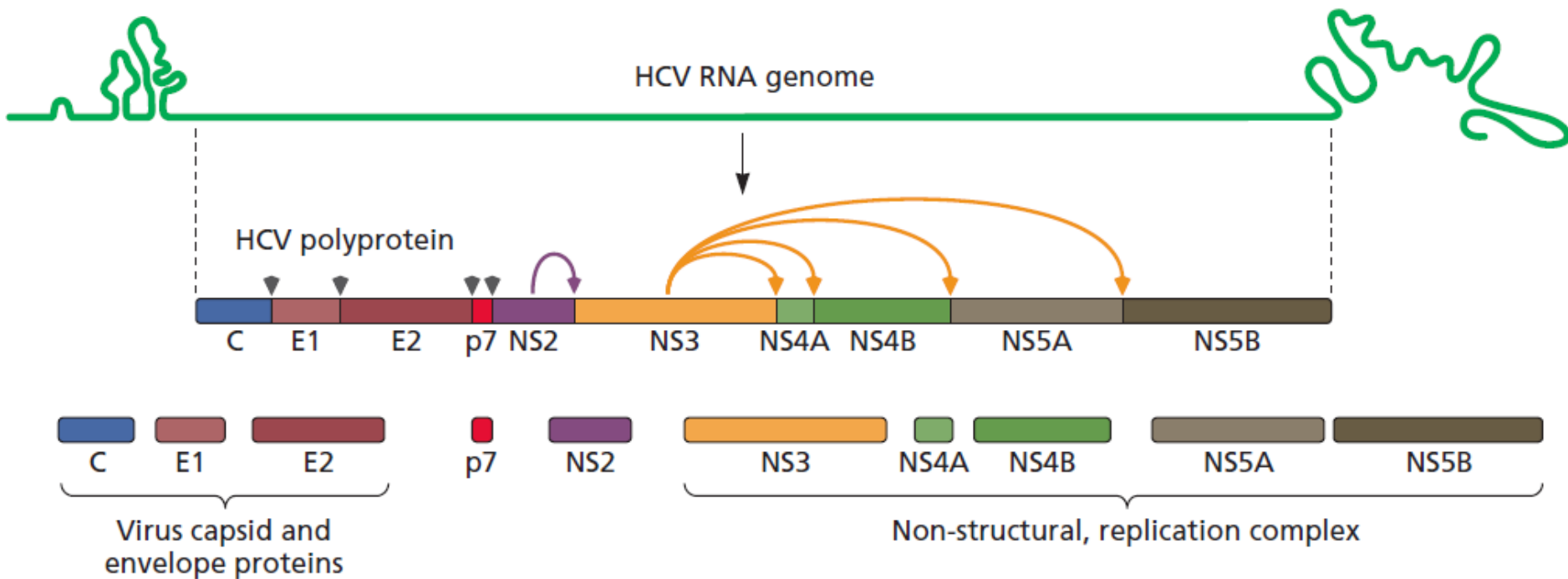


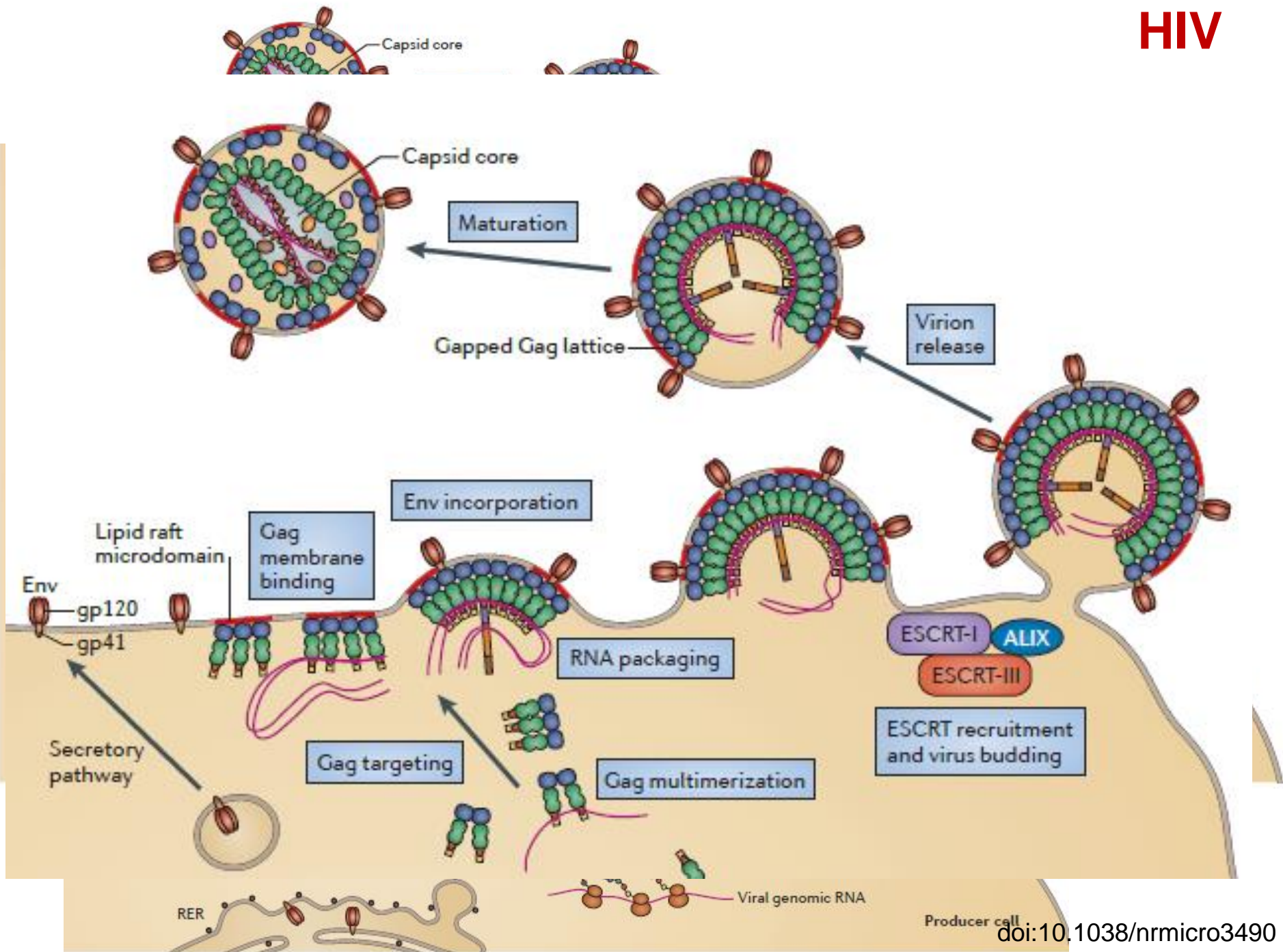
# Inibidores de proteases

# Inibidores de Protease

HCV

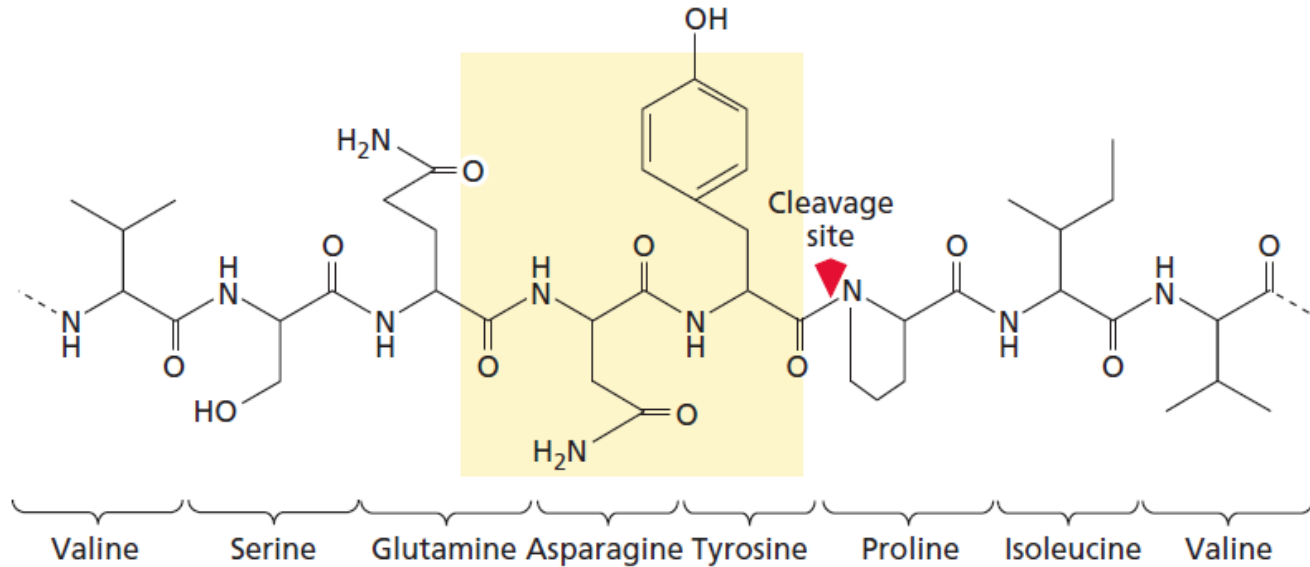
- Alguns vírus, por exemplo Retrovírus e Flavivírus produzem poliproteínas que precisam ser processadas.



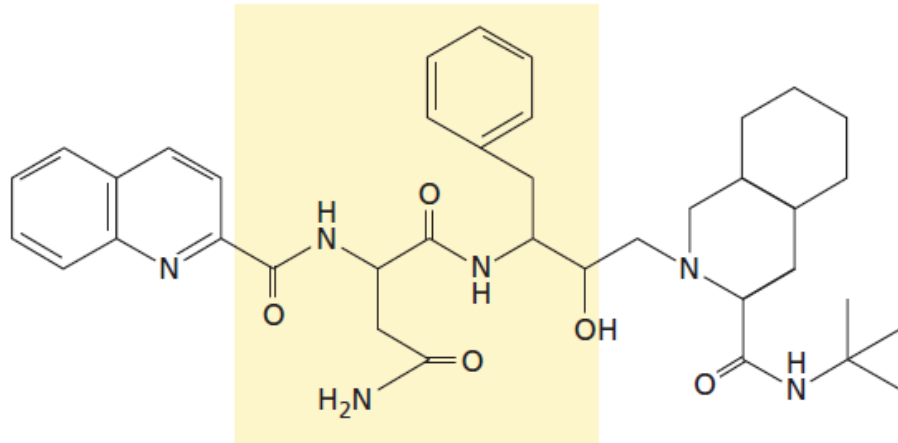


# Inibidores de Protease

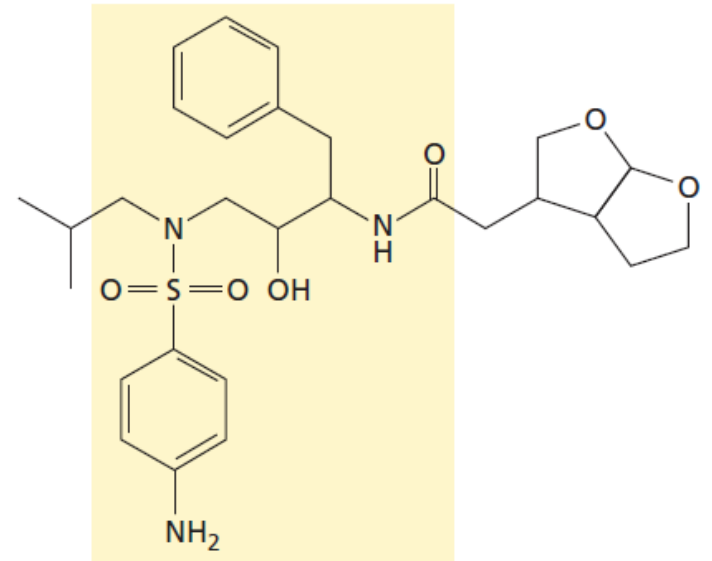
## A Natural substrate of the HIV-1 protease



## B Saquinavir

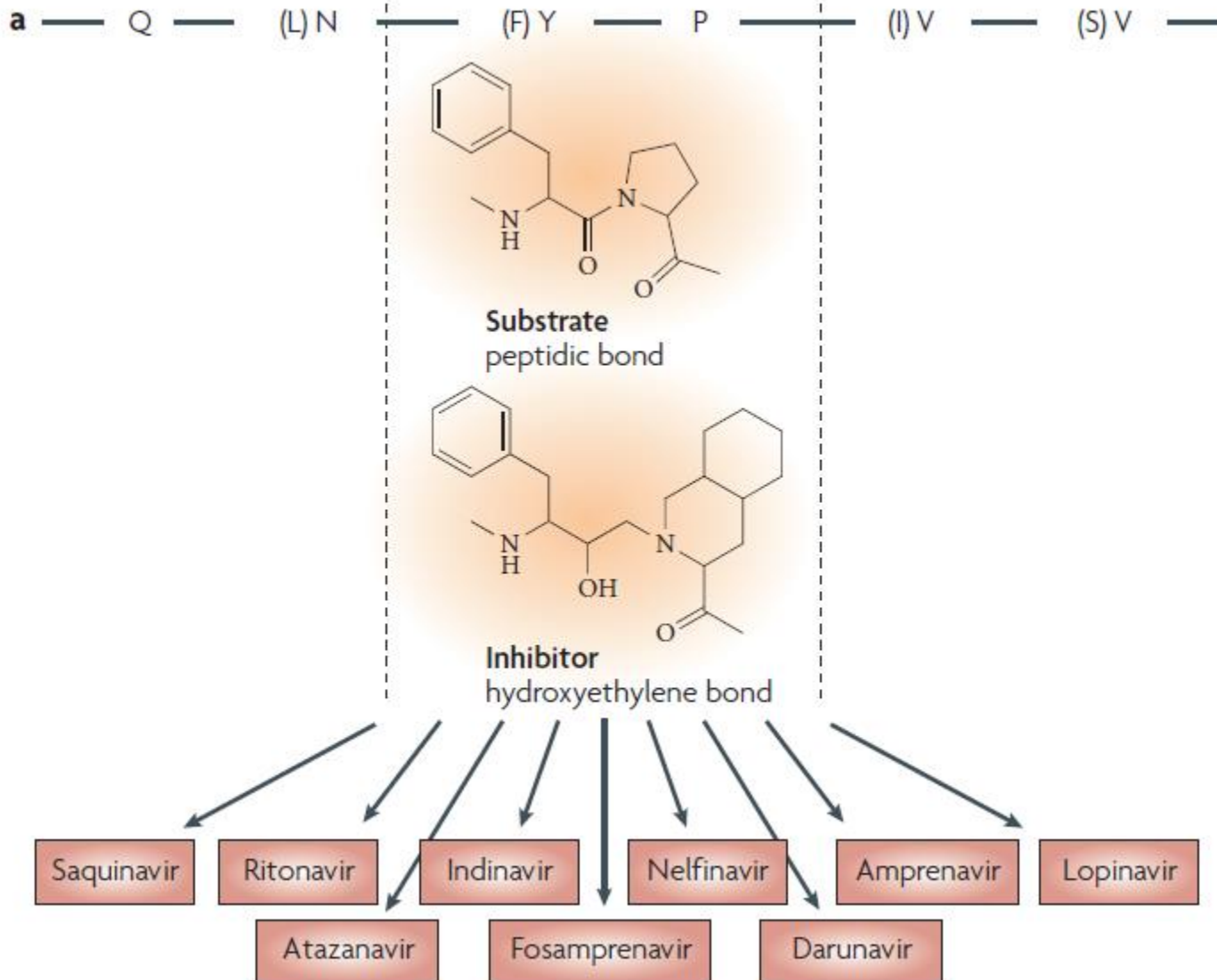


## C Darunavir

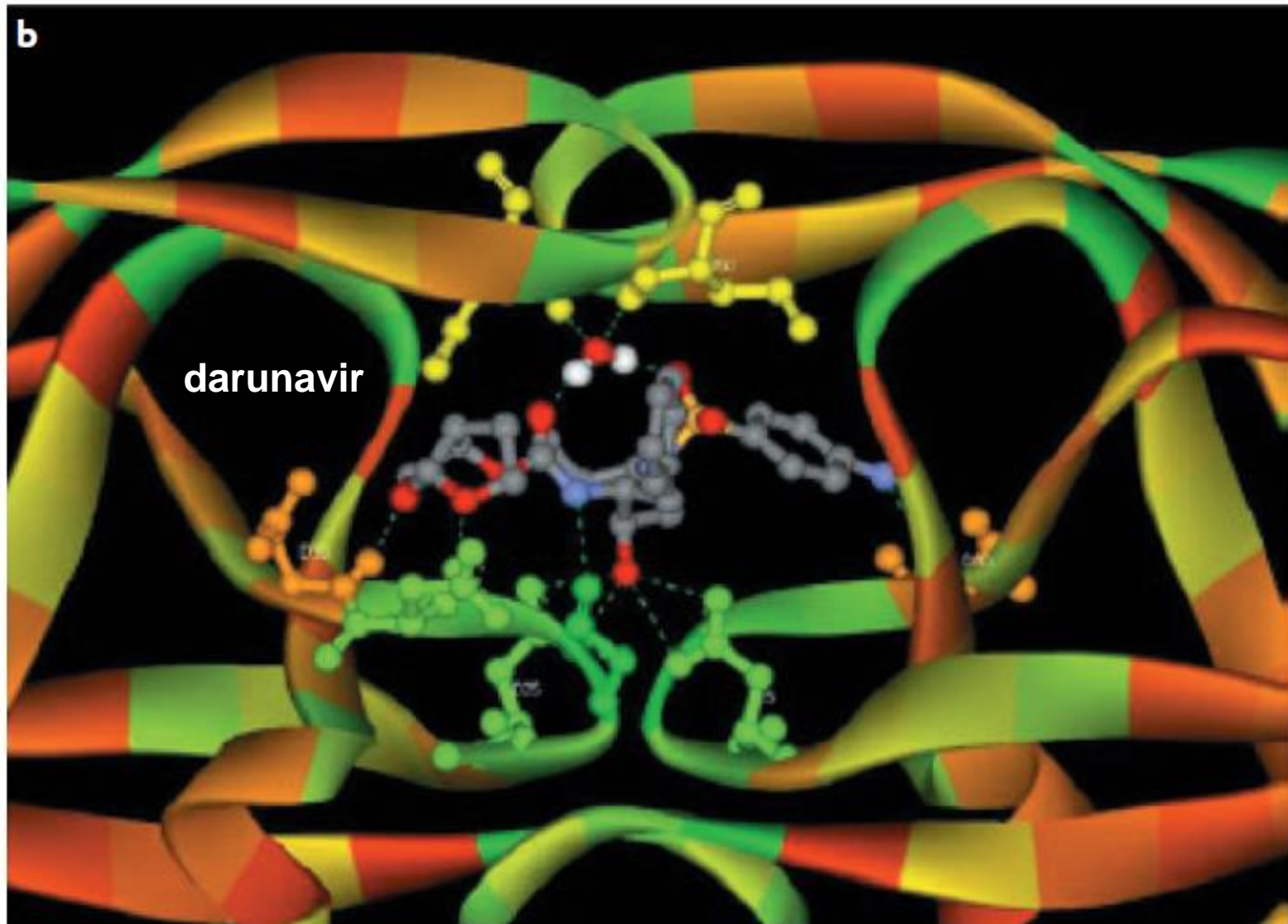




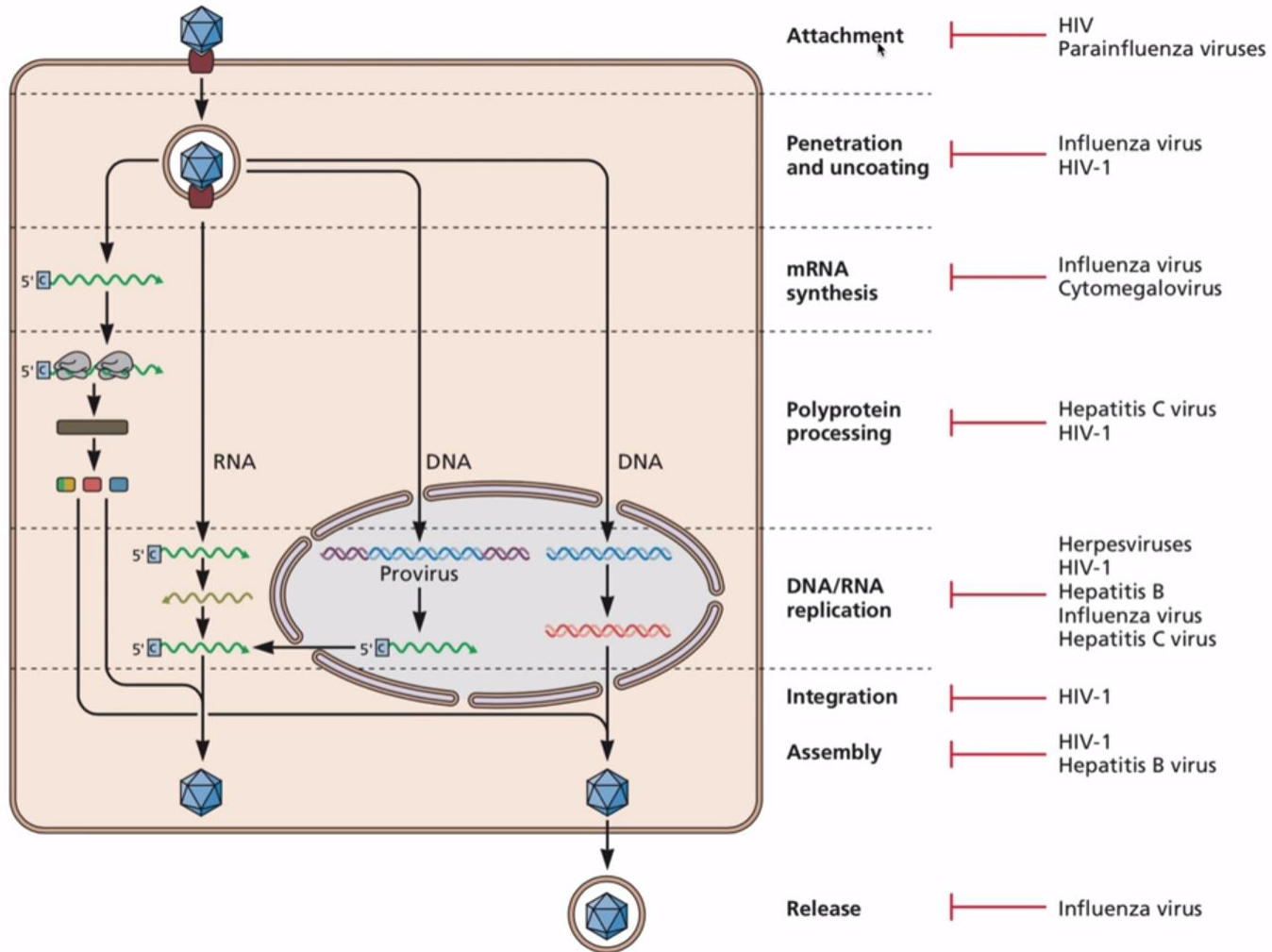
# Inibidores de Protease



# Inibidores de Protease



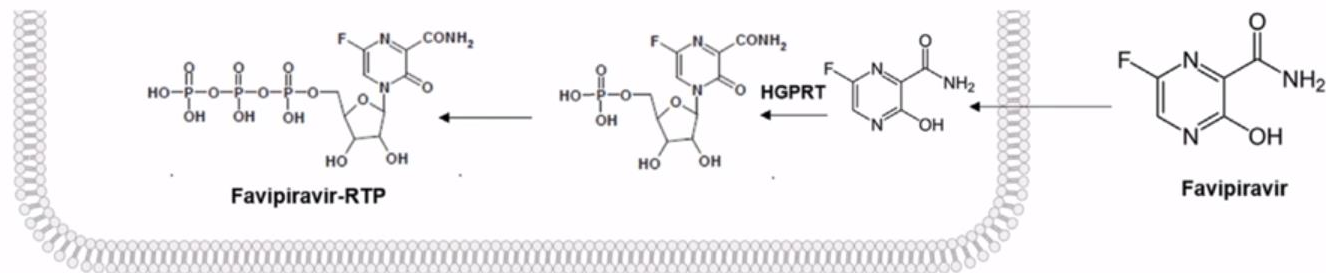
# Resumindo...



**Outros inibidores...**

# É possível criar um antiviral de amplo espectro?

## Favipiravir (Avigan)



- Broad-spectrum inhibitor of RNA viruses
- Target: RdRp, a nucleoside analog
- (+) RNA: WNV, YFV, ZIKV, WEEV, CHIKV, picornaviruses, norovirus
- (-) RNA: Lassa virus, EBOV, Rabies virus, measles virus, Pichinde, Junin, Rift Valley fever virus, Hantaviruses, Respiratory syncytial virus, parainfluenza virus
- Licensed in Japan to treat influenza

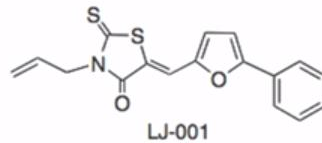
# É possível criar um antiviral de amplo espectro?

LJ001

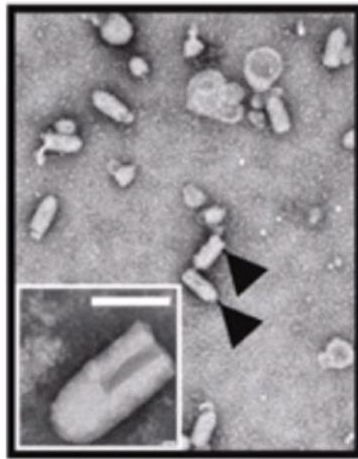
Virus	Family	Genome type	Envelope (yes/no)	Activity
Ebola <sup>L</sup> (cat A)	Filoviridae	ssRNA(-)	Y	++
Marburg <sup>L</sup> (cat A)	Filoviridae	ssRNA(-)	Y	++
Influenza A <sup>L</sup> (cat A)	Orthomyxoviridae	ssRNA(-)	Y	+++
Junin <sup>L</sup> (cat A)	Arenaviridae	ssRNA(-)	Y	++
Rift Valley fever <sup>L</sup> (cat A)	Bunyaviridae	ssRNA(-)	Y	+++
LaCrosse <sup>L</sup> (cat B)	Bunyaviridae	ssRNA(-)	Y	+++
Nipah <sup>L, P</sup> (cat C)	Paramyxoviridae	ssRNA(-)	Y	++
Omsk hemorrhagic fever <sup>L</sup> (cat C)	Flaviviridae	ssRNA(+)	Y	++
RSSE <sup>L</sup> (cat C)	Flaviviridae	ssRNA(+)	Y	++
PIV-5 <sup>L</sup>	Paramyxoviridae	ssRNA(-)	Y	++
HPIV-3 <sup>L</sup>	Paramyxoviridae	ssRNA(-)	Y	++
Newcastle disease <sup>L *</sup>	Paramyxoviridae	ssRNA(-)	Y	++
HIV-1 <sup>L, P *</sup>	Retroviridae	ssRNA(-)RT	Y	++
Murine leukemia <sup>L</sup>	Retroviridae	ssRNA(-)RT	Y	++
Yellow fever <sup>L</sup>	Flaviviridae	ssRNA(+)	Y	+++
Hepatitis C <sup>L</sup>	Flaviviridae	ssRNA(+)	Y	+++
West Nile <sup>L</sup>	Flaviviridae	ssRNA(+)	Y	+++
Vesicular stomatitis <sup>L, P</sup>	Rhabdoviridae	ssRNA(-)	Y	++
Cowpox <sup>L</sup>	Poxviridae	dsDNA	Y	+
Vaccinia <sup>L</sup>	Poxviridae	dsDNA	Y	++
Adenovirus <sup>L **</sup>	Adenoviridae	dsDNA	N	-
Coxsackie B <sup>L **</sup>	Picornaviridae	ssRNA(+)	N	-
Reovirus <sup>L</sup>	Reoviridae	dsRNA	N	-

# É possível criar um antiviral de amplo espectro?

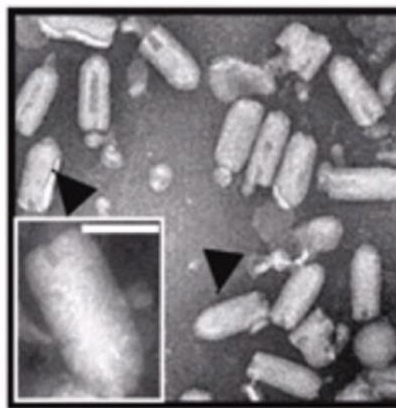
## LJ001



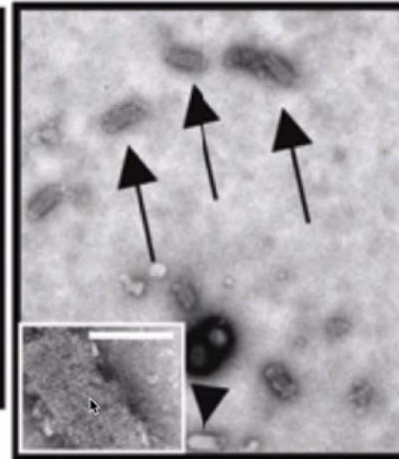
**DMSO**



**LJ025**

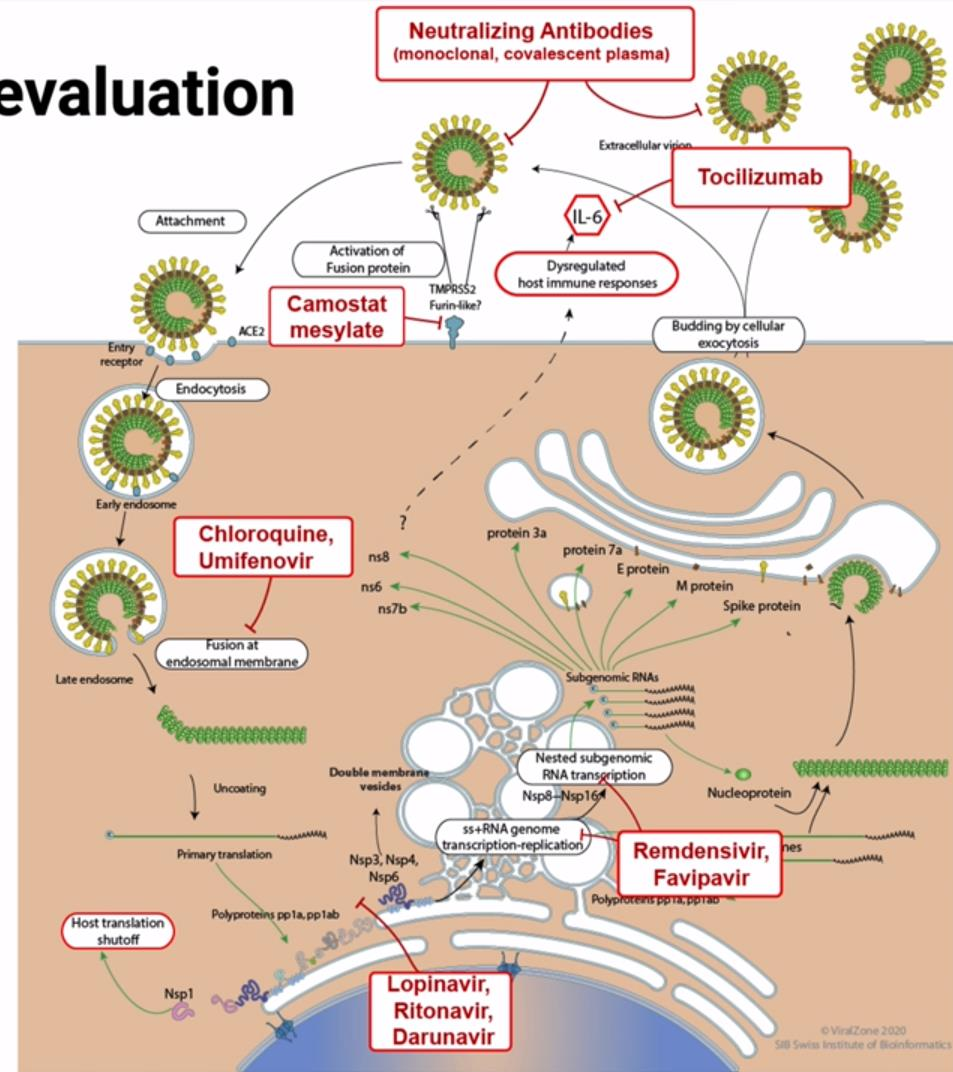


**LJ001**



# SARS-CoV-2 antivirals under evaluation

- Camostat mesylate - inhibitor of TMPRSS2 protease
- Chloroquine - raises endosomal pH
- Remdesivir, Favipiravir - nucleot/side analogs
- Lopinavir, Ritonavir, Darunavir - HIV-1 protease inhibitors
- 79 trials at [clinicaltrials.gov](https://clinicaltrials.gov)



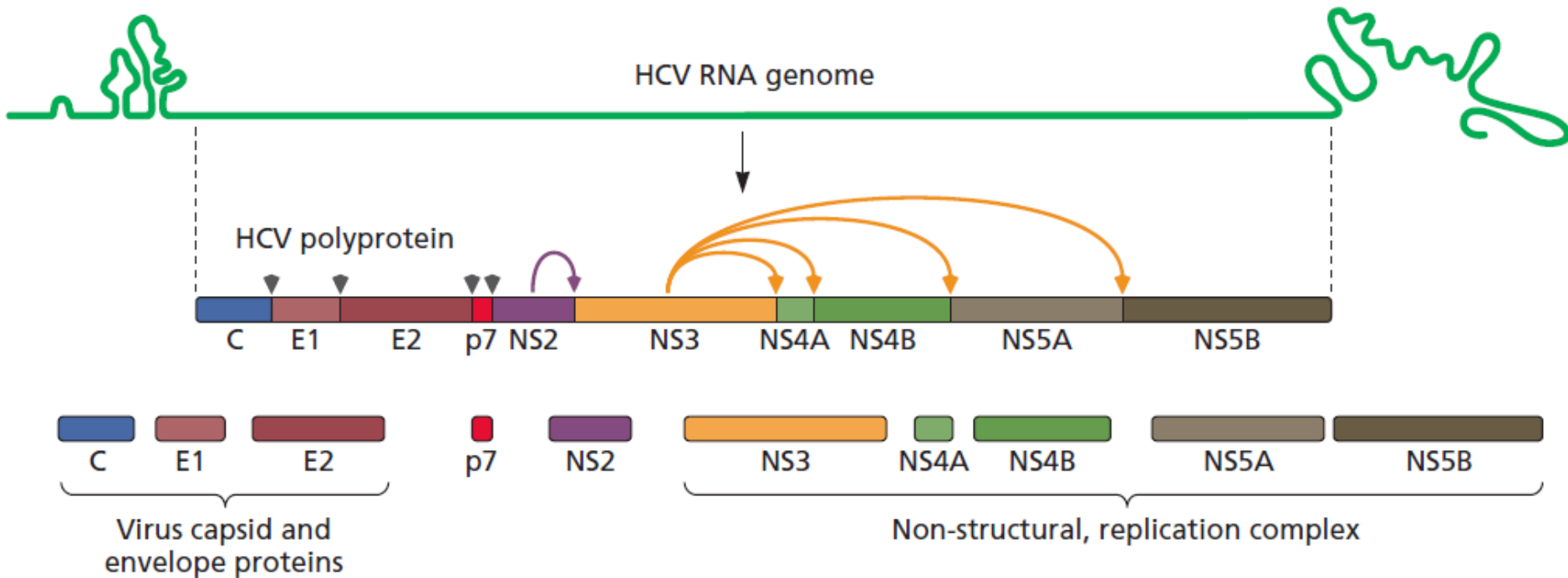
26/09/2022 --- **8269** clinical trials em andamento.



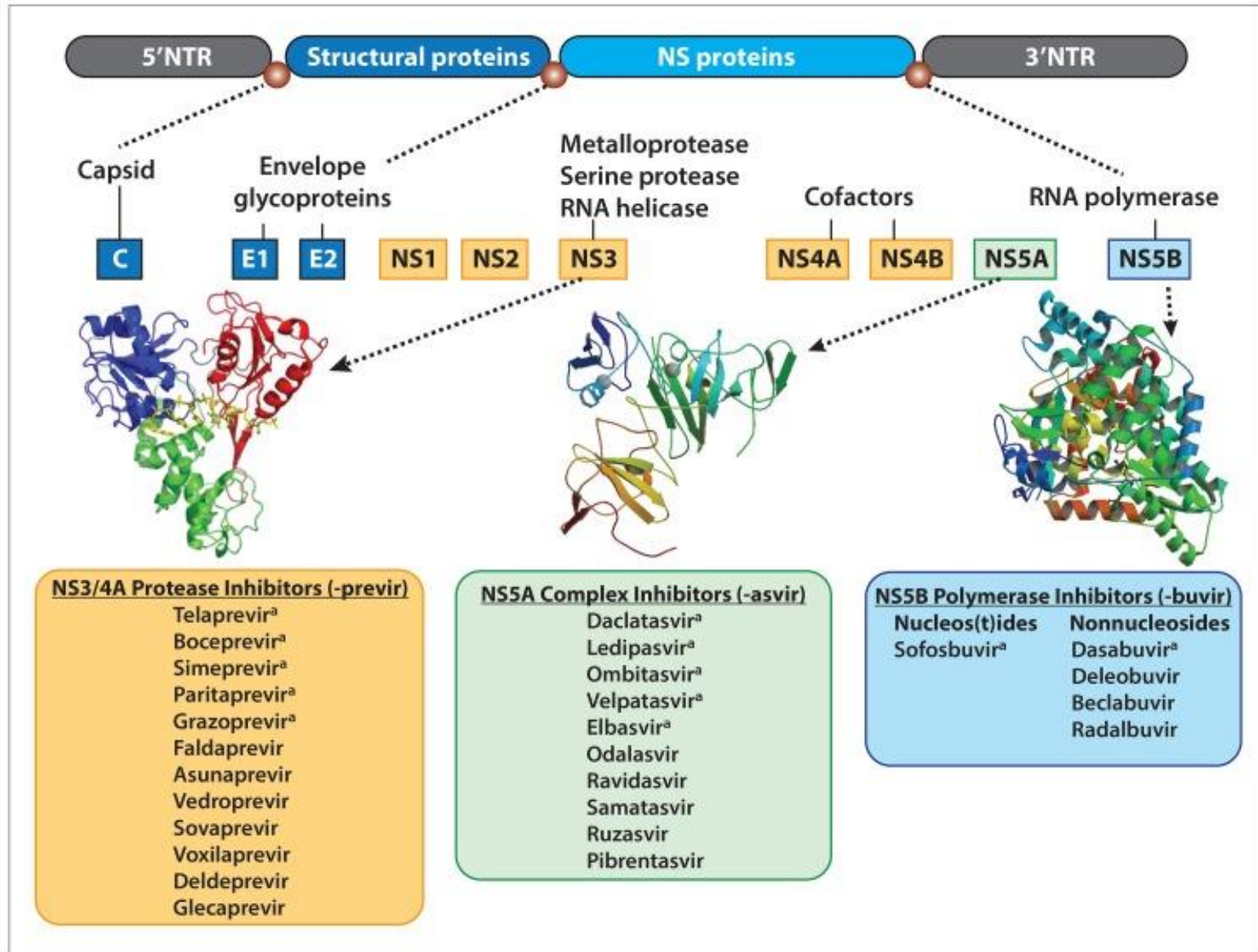
**Duas histórias de  
sucesso.**

# Vírus da Hepatite C

- Várias atividades enzimáticas.



# Vírus da Hepatite C



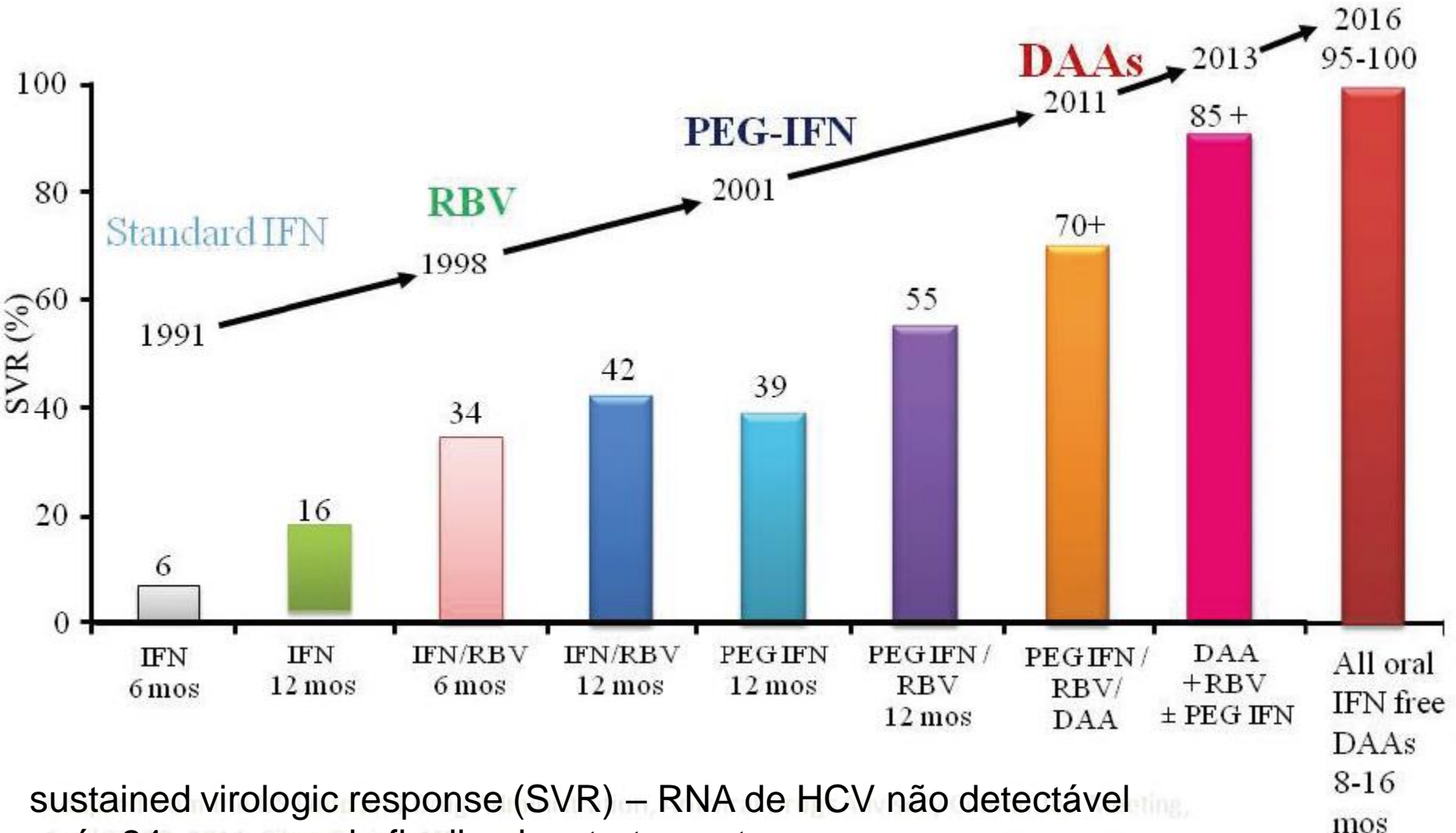
# Vírus da Hepatite C

**Table 9.2** Examples of drugs targeted against HCV proteins

Target	Generic name	Brand name	Developer	Date approved/ Trial phase
Polymerase (NS5B)	Sofosbuvir	Sovaldi	Gilead Sciences	2013
Nucleoside	Mericitabine		Roche	II
Nonnucleoside	Deleobuvir		Boehringer Ingelheim	III
	ABT-333		Abbott	III
RNA binding (NS5A)	Ledipasvir		Gilead Sciences	III (filed)
	Daclatasvir		Bristol-Myers Squibb	III
	ABT-267		Abbott	III
Protease (NS3/4A)	Telaprevir	Incivek	Vertex/Johnson & Johnson	2011
	Boceprevir	Victrelis	Merck	2011
	Simeprevir	Olysio	Janssen/Tibotec/Medivir	2013
	Faldaprevir		Boehringer Ingelheim	III
	Vaniprevir		Merck	III
	Samatasvir		Idenix	II
Combinations	Sofosbuvir + ledipasvir		Gilead Sciences	III
	Faldaprevir + deleobuvir		Boehringer Ingelheim	III
	Simeprevir + samatasvir + TMC647055/r		Janssen	II
	ABT-450/r + ABT-267 and ABT-333		Abbott	II
	MK-8742 + MK-5172		Merck	II

# Vírus da Hepatite C

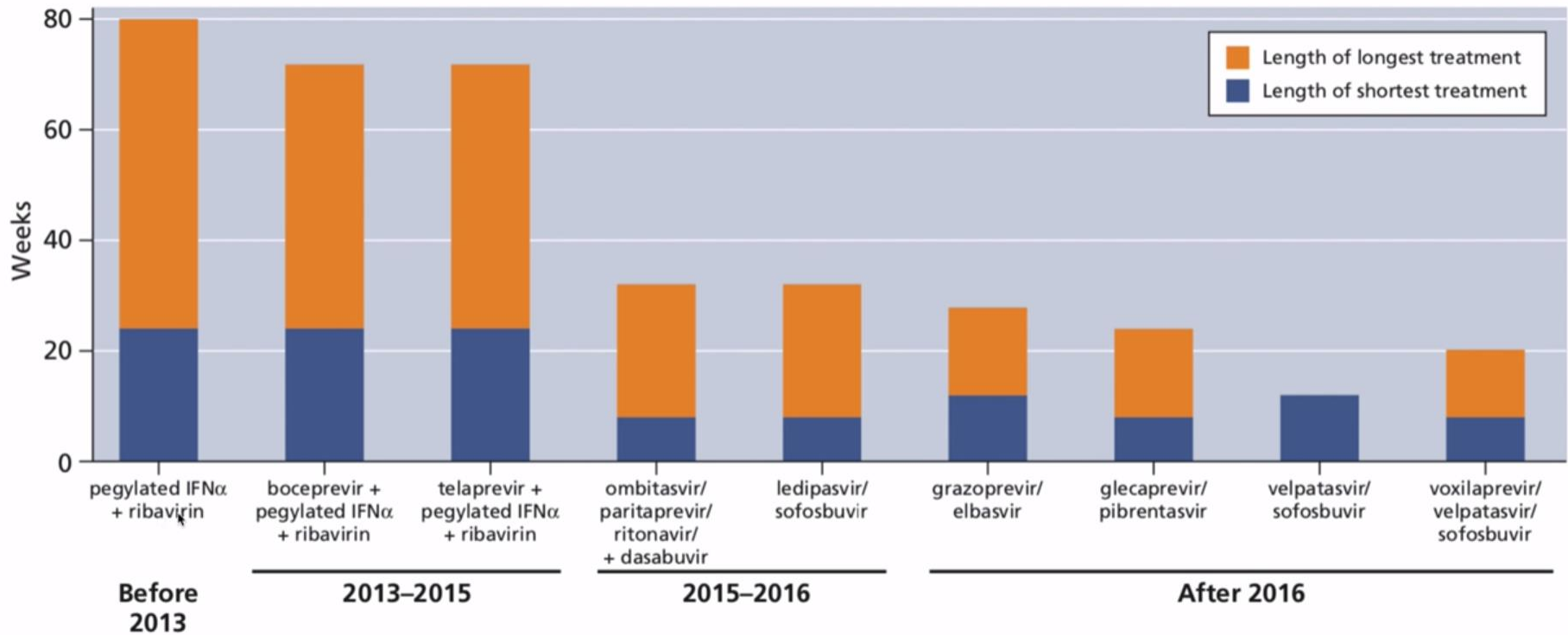
## Evolução das terapias: Maior eficácia.



sustained virologic response (SVR) – RNA de HCV não detectável após 24 semanas de finalizado o tratamento.

# Vírus da Hepatite C

Evolução das terapias: menor tempo.



# HIV

**HAART *Highly active antiretroviral therapy***

# HAART Highly active antiretroviral therapy

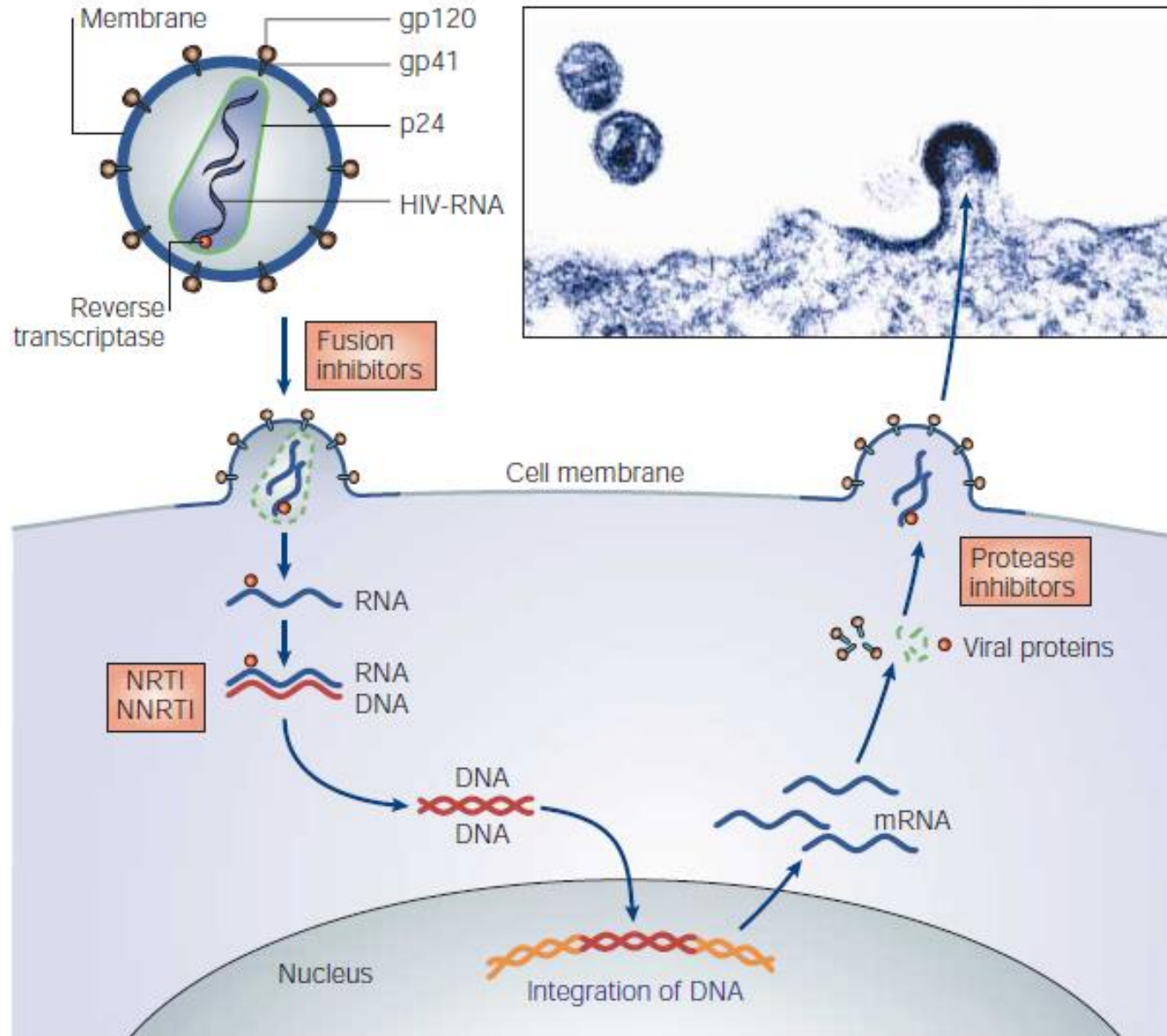
- Drogas anti-retrovirais que inibem a reprodução do HIV no sangue;
- Terapia anti-retroviral, também chamada de coquetel;
- Atualmente, são dezenas de medicamentos divididos em cinco classes.



# HAART Highly active antiretroviral therapy

- inibidores de transcriptase reversa análogos de nucleosídeos
- inibidores de transcriptase reversa não análogos de nucleosídeos
- Inibidores de protease
- Inibidores de fusão
- Inibidores da integrase

# HAART Highly active antiretroviral therapy



# HAART Highly active antiretroviral therapy

Target	Generic name	Brand name	Manufacturer	Year	
Reverse transcriptase	Zidovudine (AZT)	Retrovir	GlaxoSmithKline	1987	
Nucleos(t)ide inhibitors	Didanosine (ddI)	Videx	Bristol-Myers Squibb	1991	
	Zalcitabine (ddC)	Hivid	Hoffmann-La Roche	1992	
	Stavudine (d4T)	Zerit	Bristol-Myers Squibb	1994	
	Lamivudine (3TC)	Epivir	GlaxoSmithKline	1995	
	Abacavir (ABC)	Ziagen	GlaxoSmithKline	1998	
	Tenofovir (TDF)	Viread	Gilead Sciences	2001	
	Emtricitabine (FTC)	Emtriva	Bristol-Myers Squibb	2003	
	Nonnucleoside inhibitors	Nevirapine (NVP)	Viramune	Roxane	1996
Delavirdine (DLV)		Rescriptor	Pfizer	1997	
Efavirenz (EFV)		Sustiva	DuPont	1998	
Etravirine (ETR)		Intelence	Tibotec	2008	
Rilpivirine (RPV)		Edurant	Tibotec	2011	
Protease	Saquinavir (SQV)	Invirase	Hoffmann-La Roche	1995	
	Ritonavir (RTV)	Norvir	Abbott	1996	
	Indinavir (IDV)	Crixivan	Merck	1996	
	Nelfinavir (NFV)	Viracept	Agouron	1997	
	Amprenavir (APV)	Agenerase	GlaxoSmithKline	1999	
	Lopinavir/RTV	Kaletra	Abbott	2000	
	Atazanavir (ATV)	Reyataz	Bristol-Myers Squibb	2003	
	Fosamprenavir (FPV)	Lexia	ViiV	2003	
	Tipranavir (TPV)	Aptivus	Boehringer Ingelheim	2005	
	Darunavir (DRV)	Prezista	Tibotec	2006	
	Integrase	Raltegravir (RAL)	Isentress	Merck	2007
		Elvitegravir (EVG)	Vitekta	Gilead Sciences	2012
		Dolutegravir (DTG)	Tivicay	GlaxoSmithKline	2013
Entry	Enfuvirtide (T20)	Fuzeon	Genentech	2003	
	Maraviroc (MVC)	Selzentry	Pfizer	2007	
Combinations	3TC/AZT	Combivir	ViiV	1997	
	ABC/3TC/AZT	Trizivir	ViiV	2000	
	TDF/FTC	Truvada	Gilead Sciences	2004	
	DRV/cobicistat (COBI)	Prezcobix	Janssen	2006	
	TDF/FTC/EFV	Atripla	Bristol-Myers Squibb/ Gilead Sciences	2006	
	TDF/FTC/RPV	Complera	Gilead Sciences	2011	
	TDF/FTC/EVG/COBI	Stribild	Gilead Sciences	2012	
	DTG/ABC/3TC	Triumeq	Gilead Sciences	2014	
	RAL/3TC	Dutrebis	Merck	2015	
	ATV/COBI	Evotaz	ViiV	2015	
	TAP <sup>2</sup> /COBI/FTC/EVG	Genvoya	Gilead Sciences	2015	
	TAF/RPV/FTC	Odefsey	Gilead Sciences	2016	
	TAF/FTC	Descovy	Gilead Sciences	2016	
	DTG/RPV	Juluca	ViiV	2017	
	Bictegravir/FTC/TAF	Biktarvy	Gilead Sciences	2018	

# FDA Approval of HIV Medicines

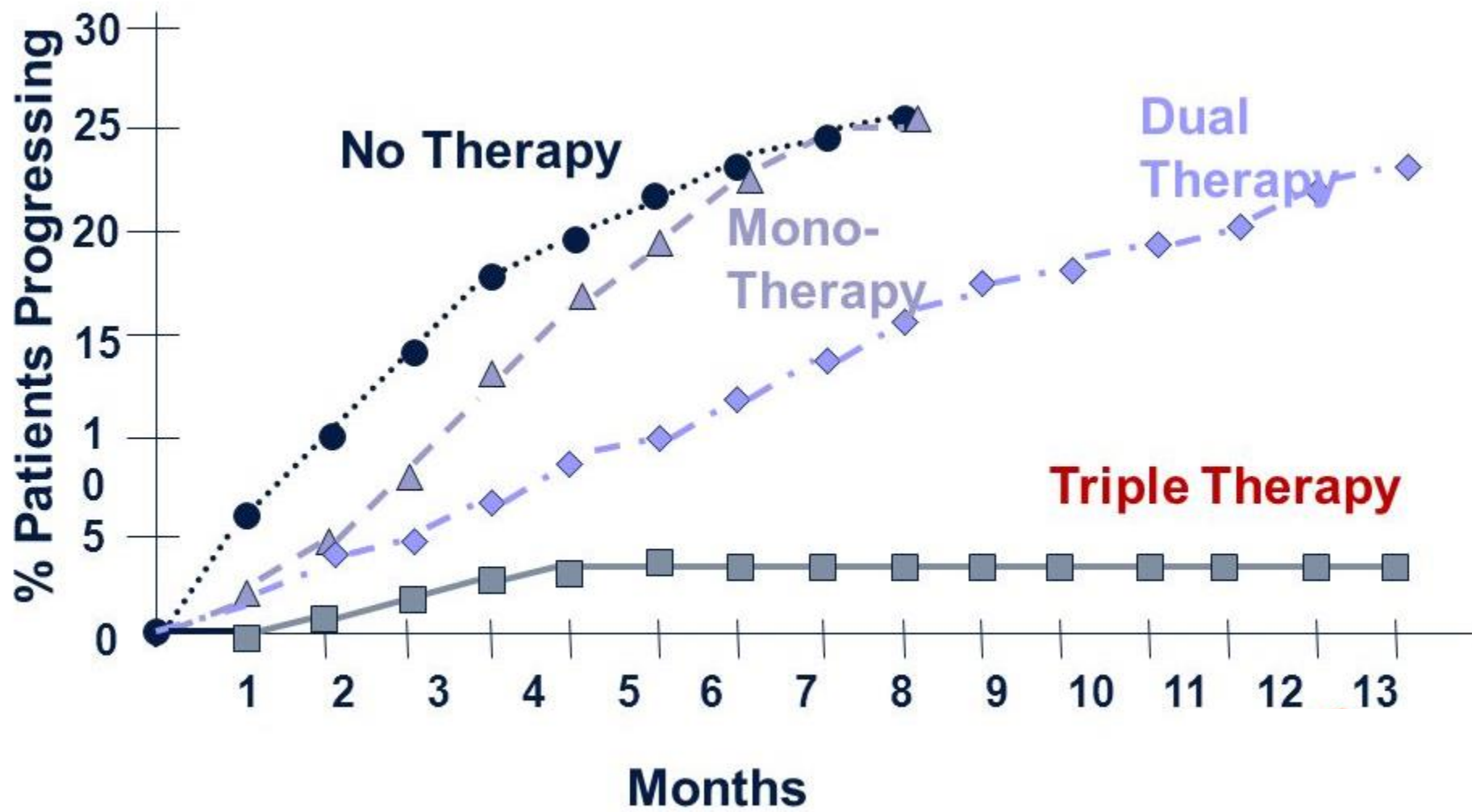
1981: First AIDS cases are reported in the United States.				
'85-'89	<b>1987</b> Zidovudine (NRTI)			
'90-'94	<b>1991</b> Didanosine (NRTI)	<b>1992</b> Zalcitabine (NRTI)	<b>1994</b> Stavudine (NRTI)	
'95-'99	<b>1995</b> Lamivudine (NRTI) Saquinavir (PI)	<b>1996</b> Indinavir (PI) Nevirapine (NNRTI) Ritonavir (PI)	<b>1997</b> Combivir (FDC) Delavirdine (NNRTI) Nelfinavir (PI)	<b>1998</b> Abacavir (NRTI) Efavirenz (NNRTI) <b>1999</b> Amprenavir (PI)
'00-'04	<b>2000</b> Didanosine EC (NRTI) Kaletra (FDC) Trizivir (FDC)	<b>2001</b> Tenofovir DF (NRTI)	<b>2003</b> Atazanavir (PI) Emtricitabine (NRTI) Enfuvirtide (FI) Fosamprenavir (PI)	<b>2004</b> Epzicom (FDC) Truvada (FDC)
'05-'09	<b>2005</b> Tipranavir (PI)	<b>2006</b> Atripla (FDC) Darunavir (PI)	<b>2007</b> Maraviroc (CA) Raltegravir (INSTI)	<b>2008</b> Etravirine (NNRTI)
'10-'14	<b>2011</b> Complera (FDC) Nevirapine XR (NNRTI) Ralpivirine (NNRTI)	<b>2012</b> Stribild (FDC)	<b>2013</b> Dolutegravir (INSTI)	<b>2014</b> Cobicistat (PE) Elvitegravir (INSTI) Triumeq (FDC)
'15-'19	<b>2015</b> Evotaz (FDC) Genvoya (FDC) Prezcobix (FDC)	<b>2016</b> Descovy (FDC) Odefsey (FDC)	<b>2017</b> Juluca (FDC) <b>2018</b> Biktarvy (FDC) Cimduo (FDC) Delstrigo (FDC) Doravirine (NNRTI) Ibalizumab-uiyk (PAI) Symfi (FDC) Symfi Lo (FDC) Symtuza (FDC) Temixys (FDC)	<b>2019</b> Dovato (FDC)

## Drug Class Abbreviations:

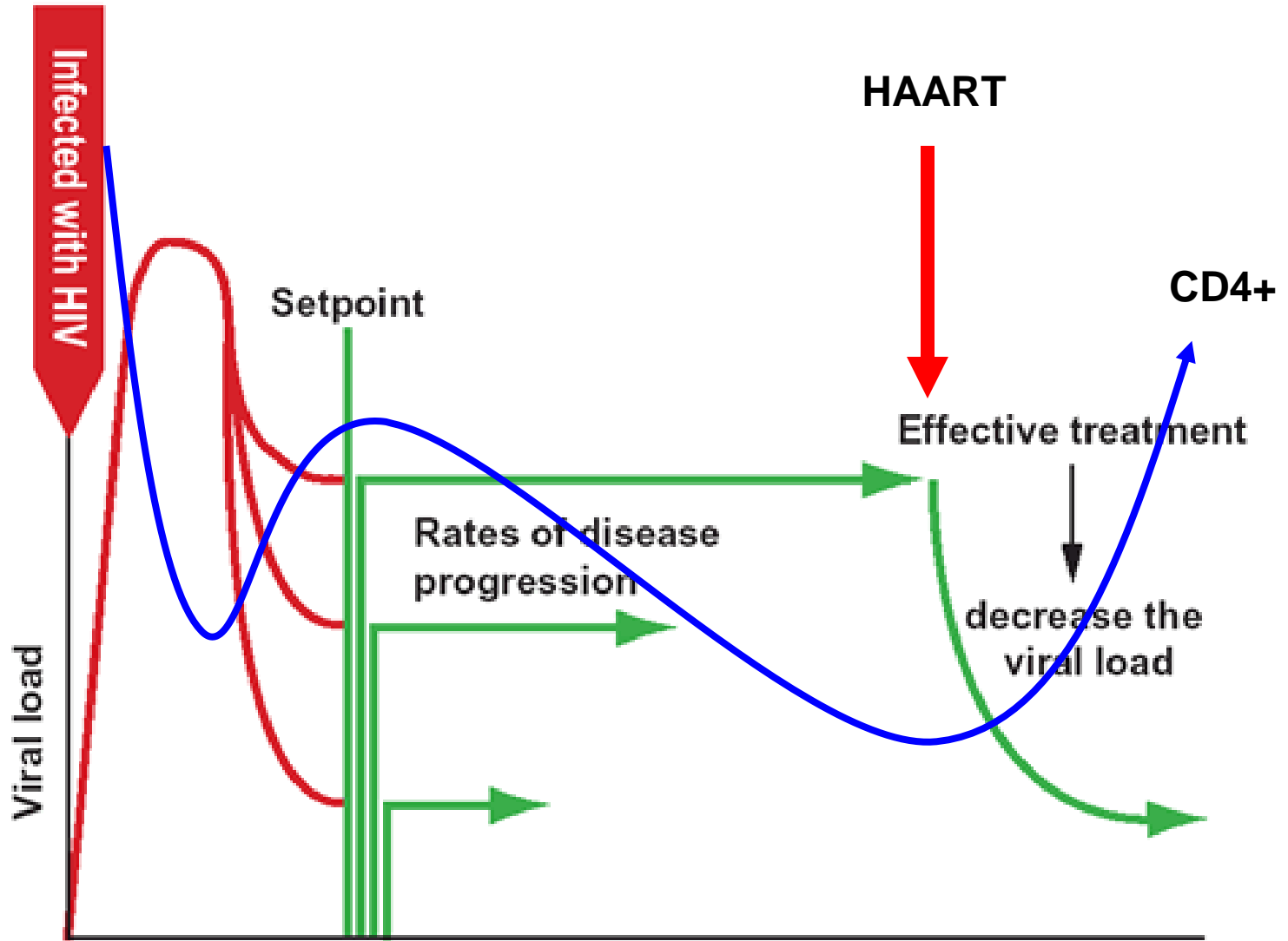
**CA:** CCR5 Antagonist; **FDC:** Fixed-Dose Combination; **FI:** Fusion Inhibitor; **INSTI:** Integrase Inhibitor; **NNRTI:** Non-Nucleoside Reverse Transcriptase Inhibitor; **NRTI:** Nucleoside Reverse Transcriptase Inhibitor; **PE:** Pharmacokinetic Enhancer; **PI:** Protease Inhibitor; **PAI:** Post-Attachment Inhibitor

**Note:** Drugs in gray are no longer available and/or are no longer recommended for use in the United States by the HHS HIV/AIDS medical practice guidelines. These drugs may still be used in fixed-dose combination formulations.

# HAART Highly active antiretroviral therapy



# HAART Highly active antiretroviral therapy



# HAART Highly active antiretroviral therapy

Terapia combinada:

- três inibidores da transcriptase reversa;
- dois inibidores da transcriptase reversa e um inibidor de protease.

Terapia combinada



PrEP e PEP

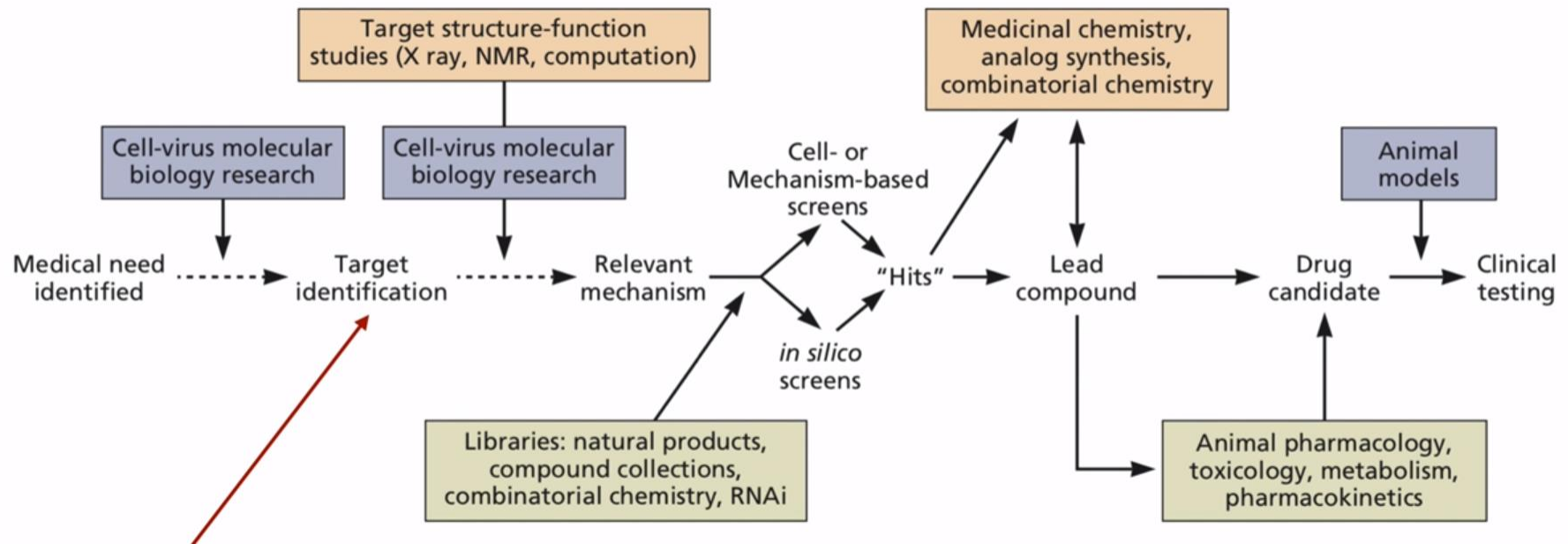


**Duas Histórias de  
sucesso...**

**Por quê apenas  
duas?**



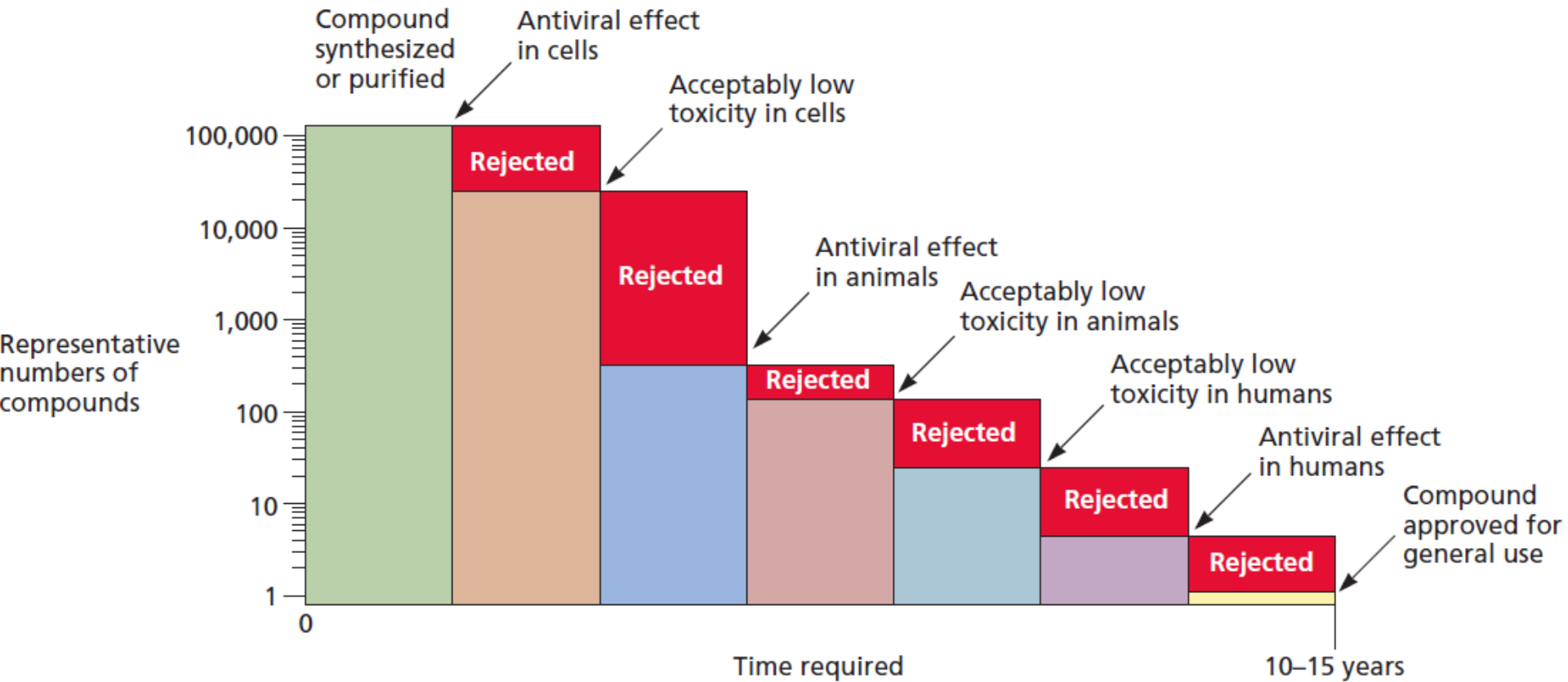
# O desenvolvimento de Antivirais é lento e caro



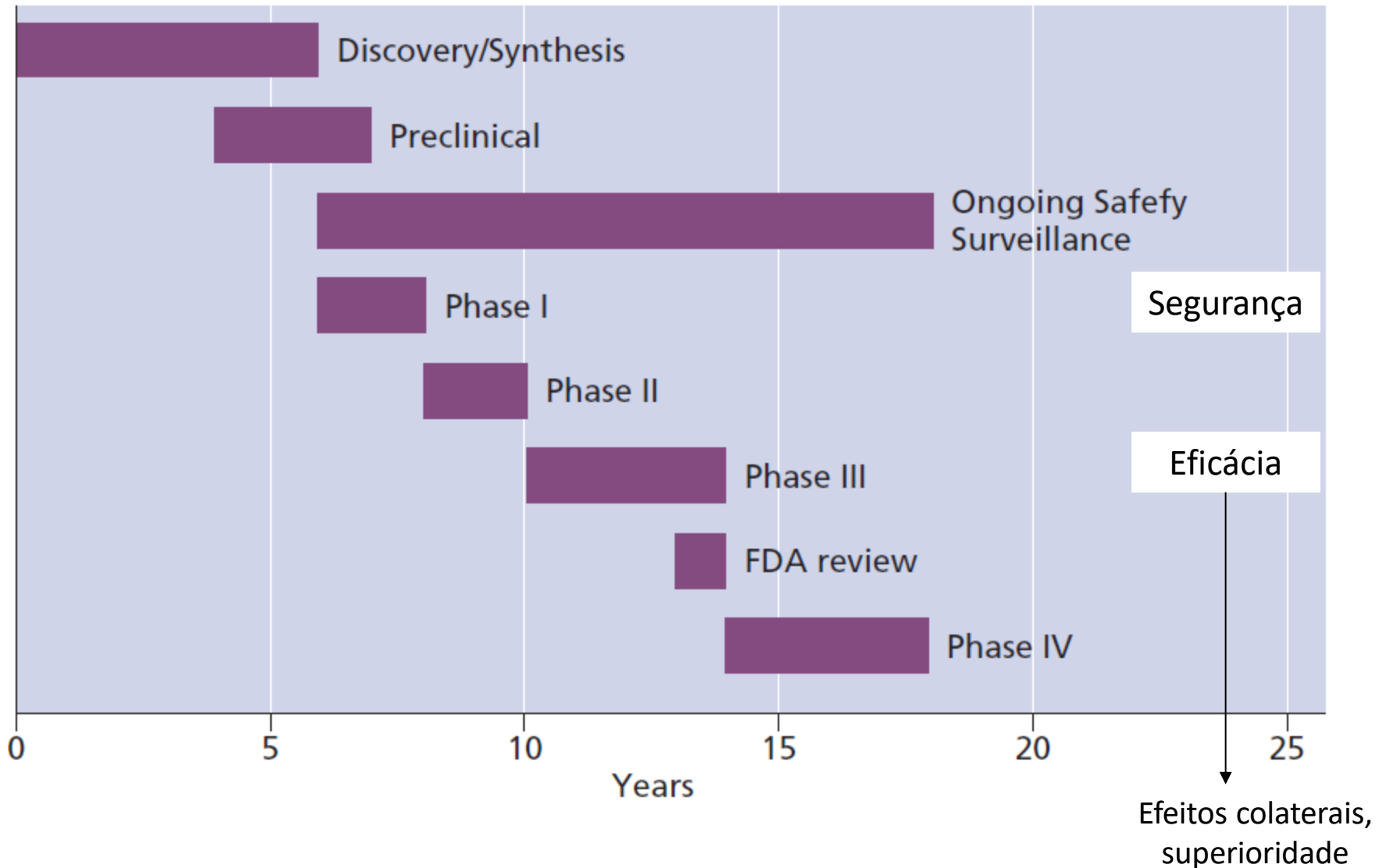
Prova de conceito

- Biodisponibilidade.
  - Farmacocinética.
  - Segurança.
- 
- Não existem modelos experimentais para alguns vírus.
  - Alguns vírus são muito perigosos para trabalhar.
  - O antiviral precisa ser potente (atividade parcial não é aceitável).

# O desenvolvimento de Antivirais é lento e caro

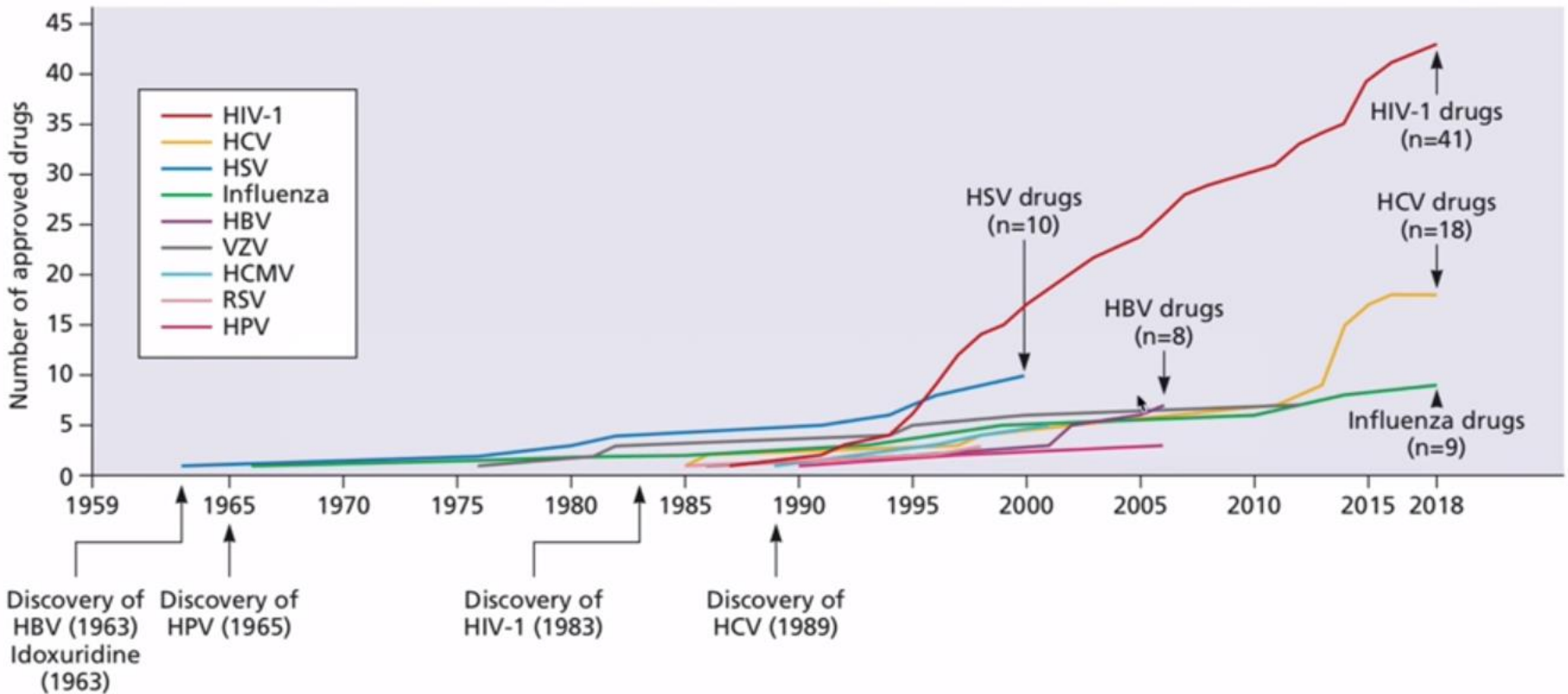


# O desenvolvimento de Antivirais é lento e caro



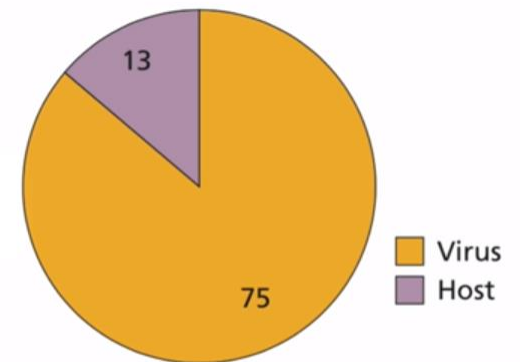
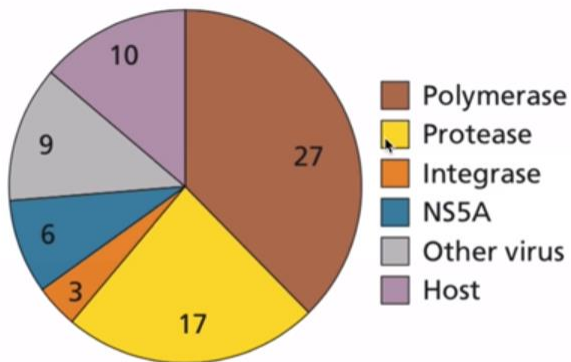
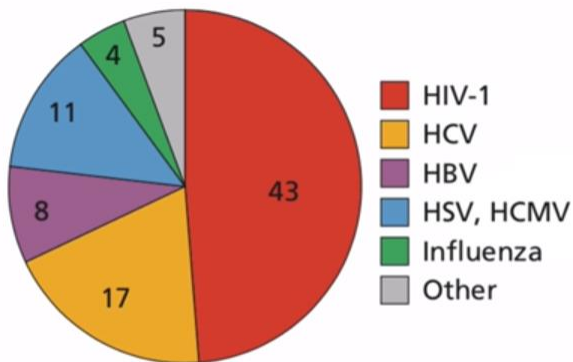
# O desenvolvimento de Antivirais é lento e caro

- Poucos fármacos antivirais disponíveis.



# O desenvolvimento de Antivirais é lento e caro

- Poucos fármacos antivirais disponíveis.

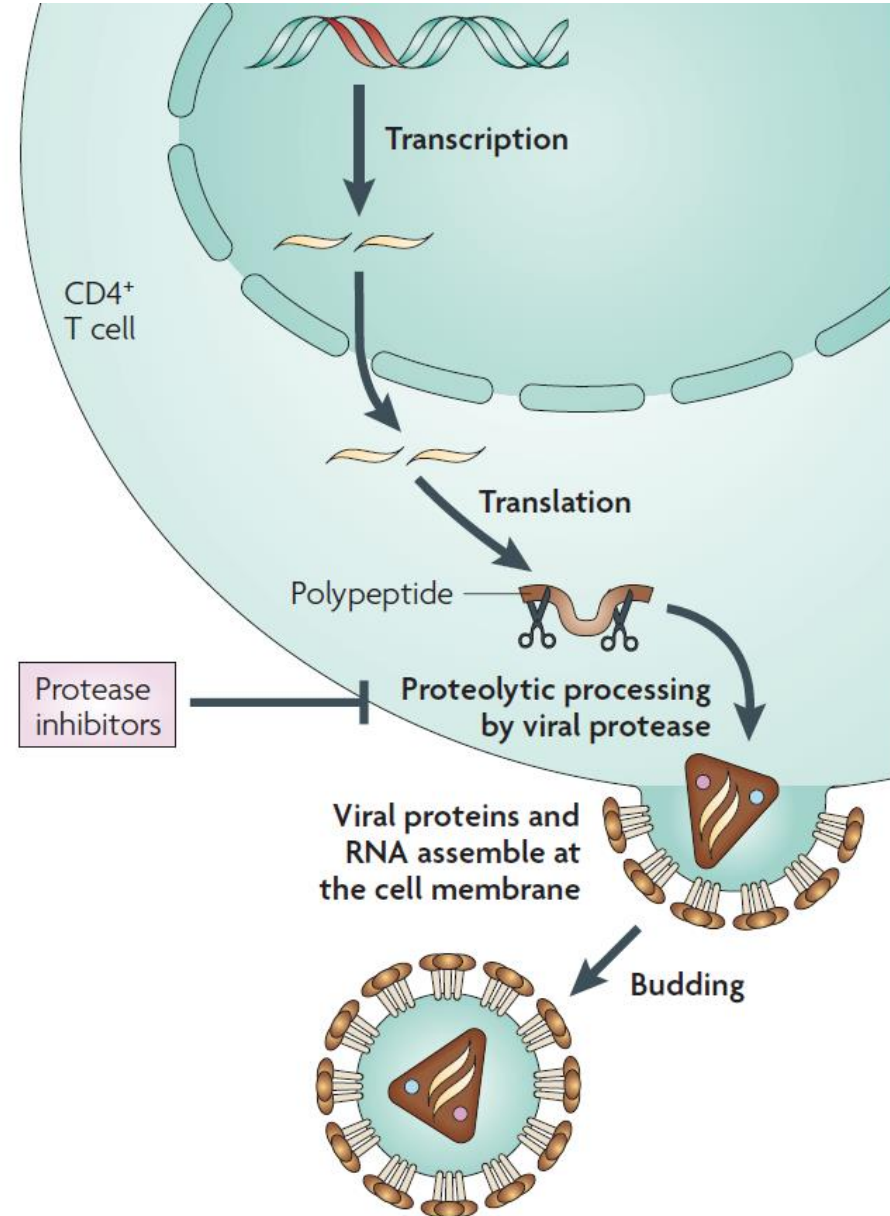
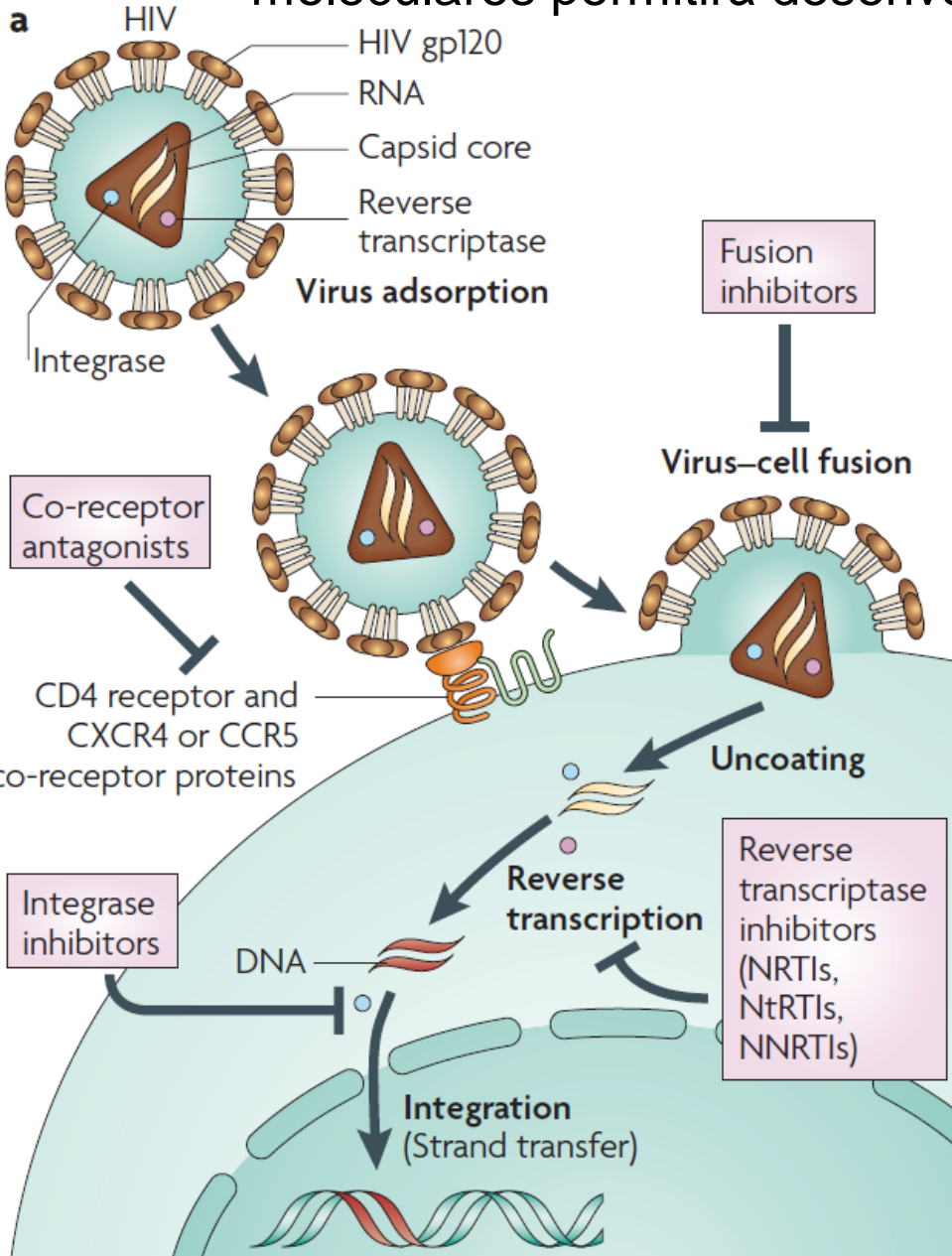


# ANTIVIRAIS

- Novas drogas devem ser desenvolvidas.
- Novas estratégias devem ser implementadas.
- Medidas “simples”, porém efetivas podem ser aplicadas.
- Imiquimod, Interferon...

# PREVENÇÃO

# Entender melhor o ciclo viral e seus componentes em termos moleculares permitirá desenvolver drogas mais eficientes



**Obrigado!!!**