

Introduction to the Biology of HIV-1

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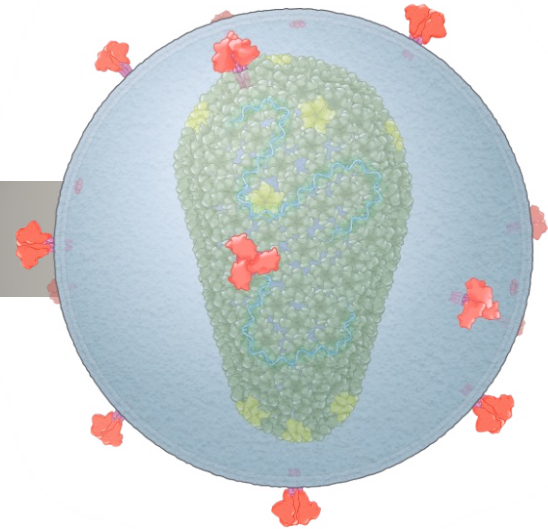
Disclosures

Dr. Spach does not have any disclosures.



Introduction to the Biology of HIV-1: Outline

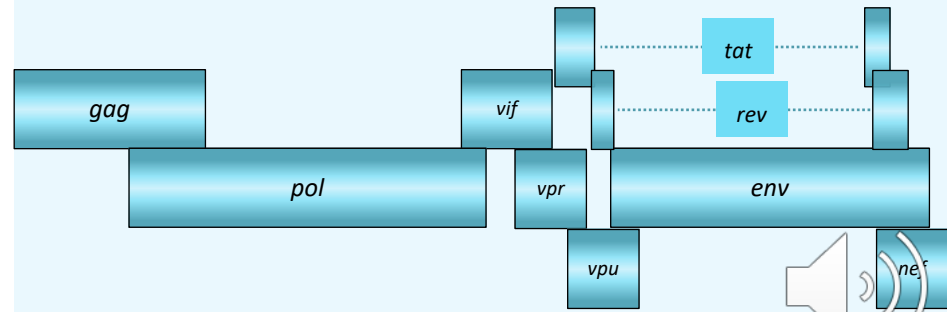
Structure



Introduction to the Biology of HIV-1: Outline

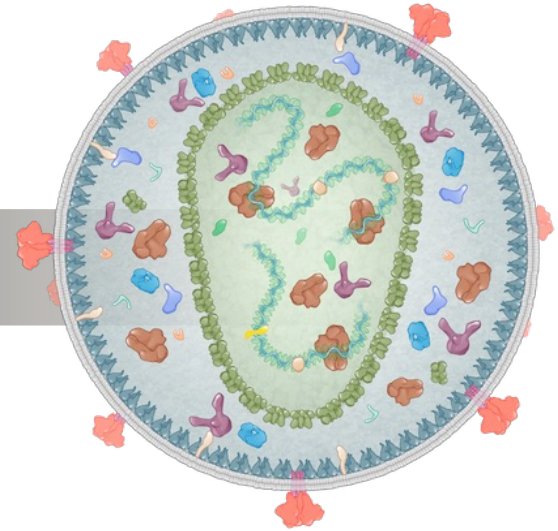
Genome

HIV-1 Genomic RNA



Introduction to the Biology of HIV-1: Outline

Structural Proteins



Envelope



Matrix



Capsid



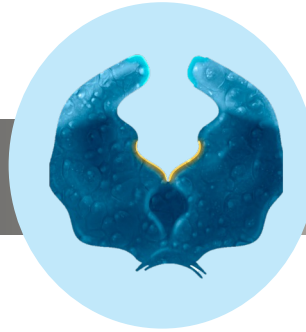
Nucleocapsid



p6

Introduction to the Biology of HIV-1: Outline

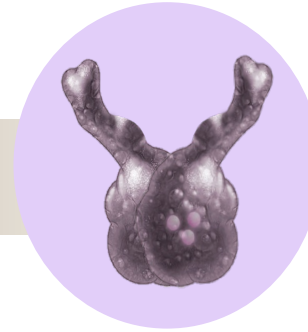
Enzymes



Protease



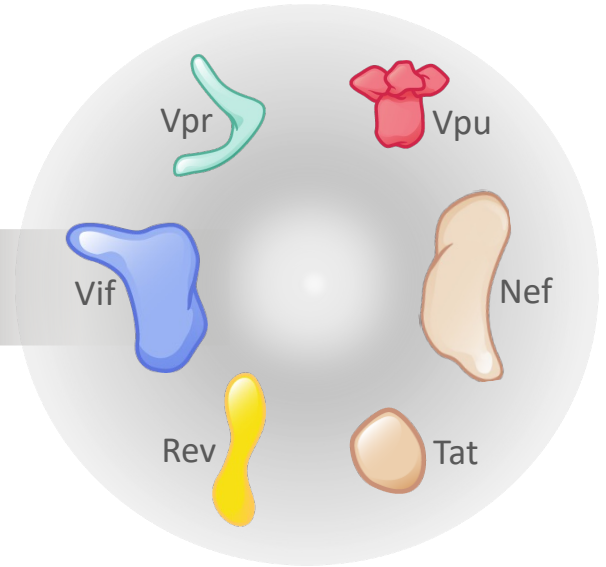
Reverse Transcriptase



Integrase

Introduction to the Biology of HIV-1: Outline

Accessory and Regulatory Proteins



Introduction to the Biology of HIV-1: Outline

Structure

Genome

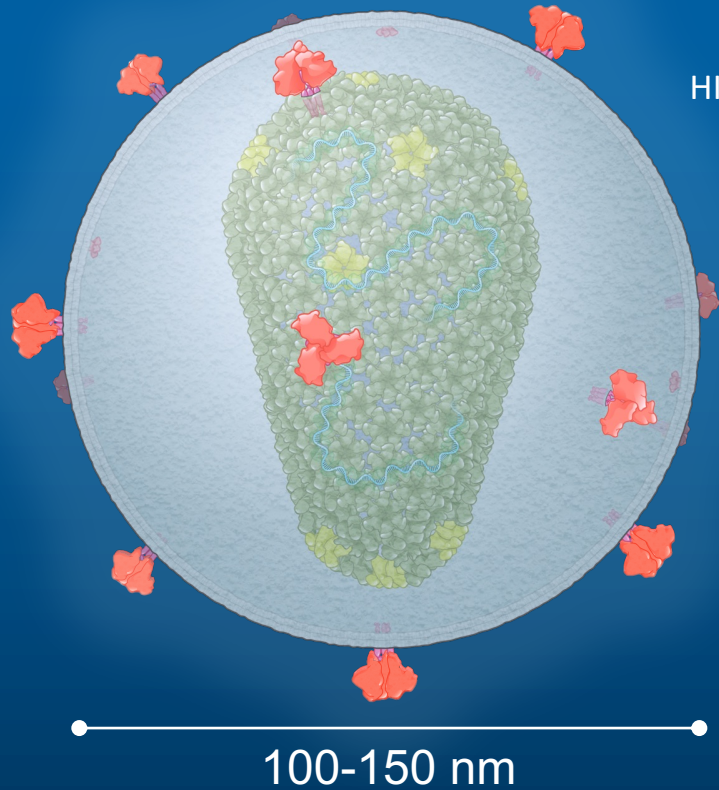
Structural Proteins

Enzymes

Accessory and Regulatory Proteins

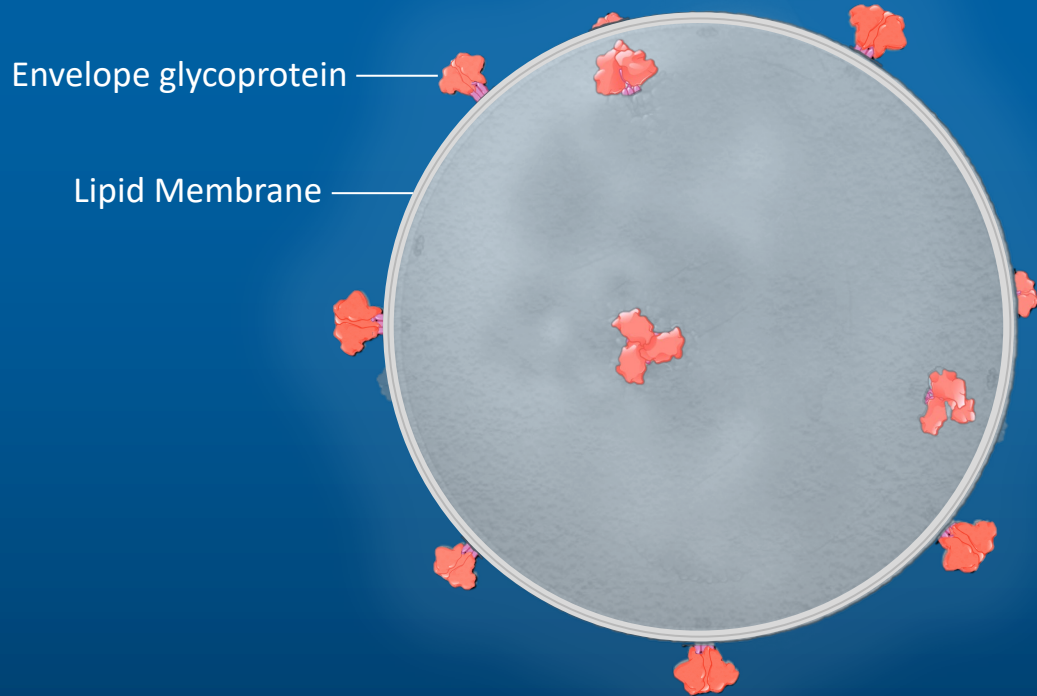
HIV Structure

HIV

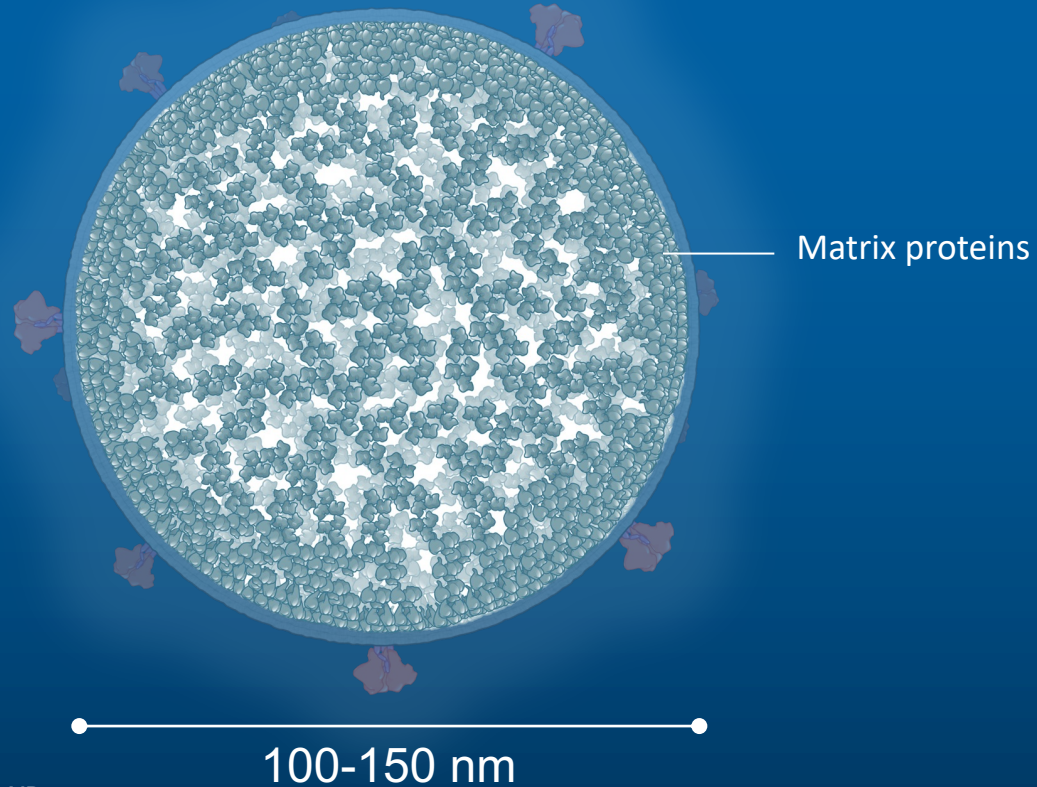


HIV = Human Immunodeficiency Virus

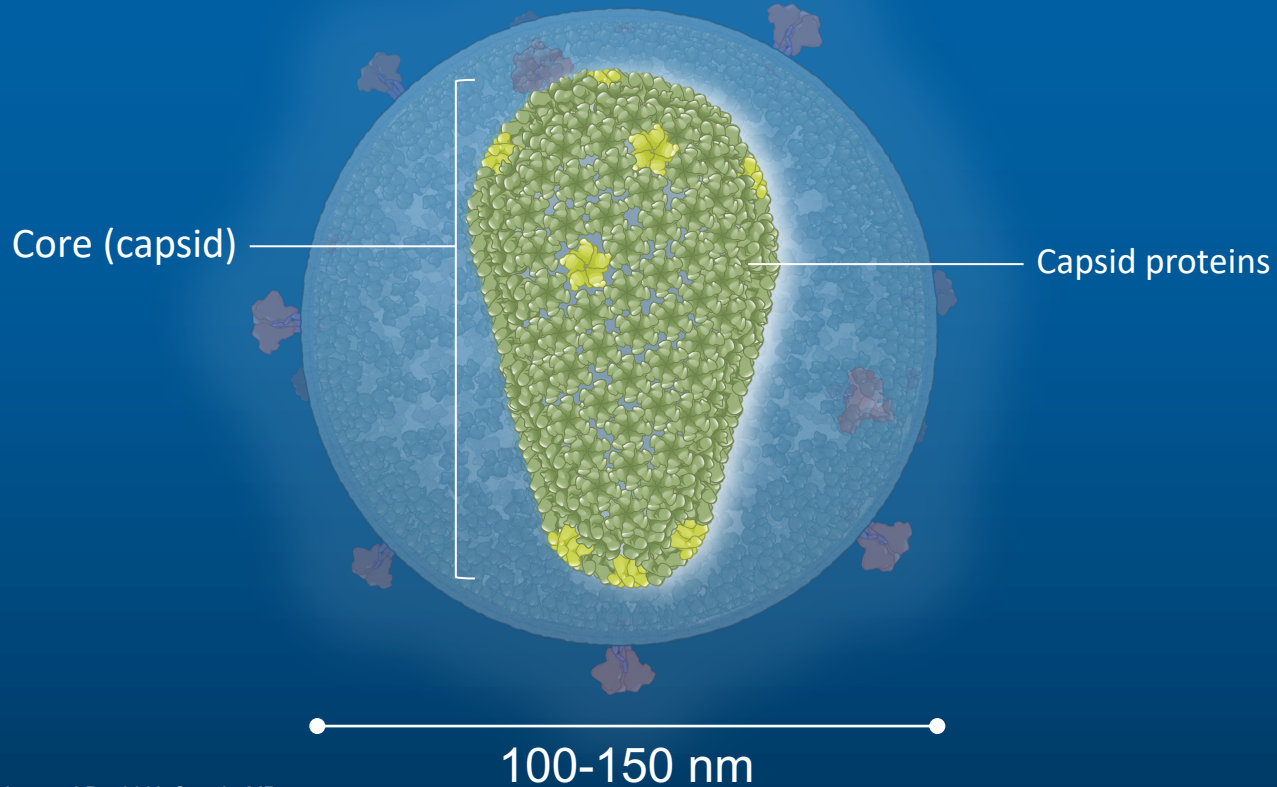
HIV Envelope



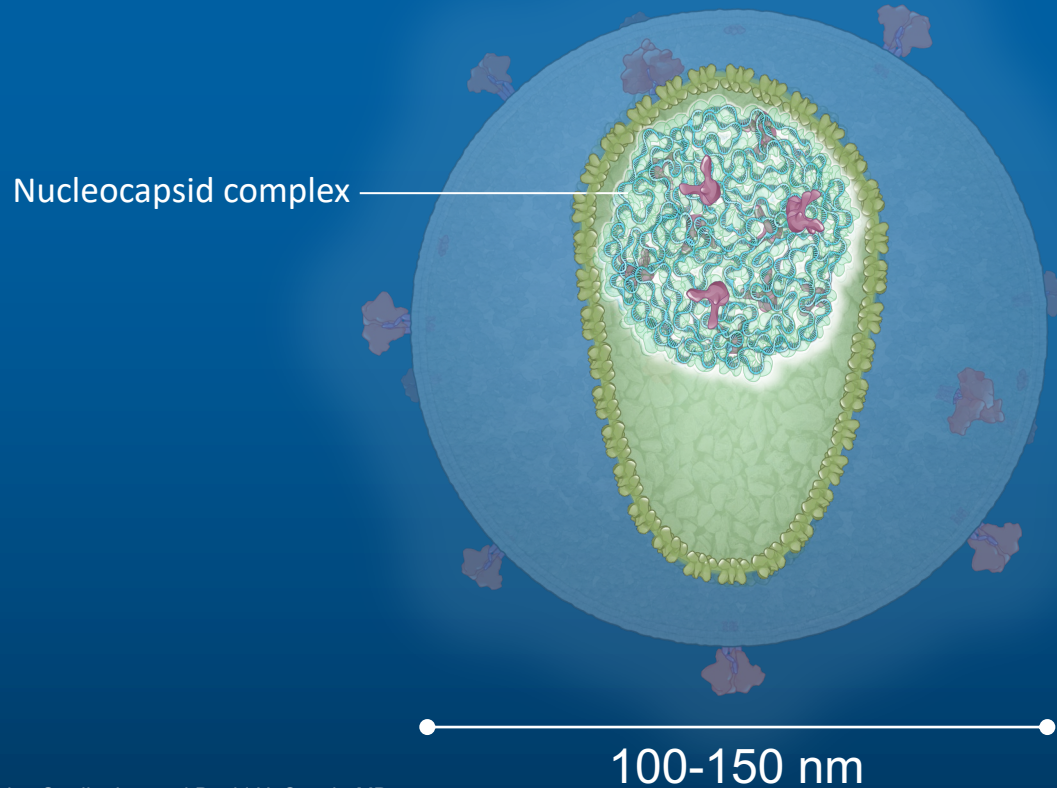
HIV Matrix Shell



HIV Core (Capsid)



HIV Nucleocapsid Complex



HIV Genome

HIV-1 Genome

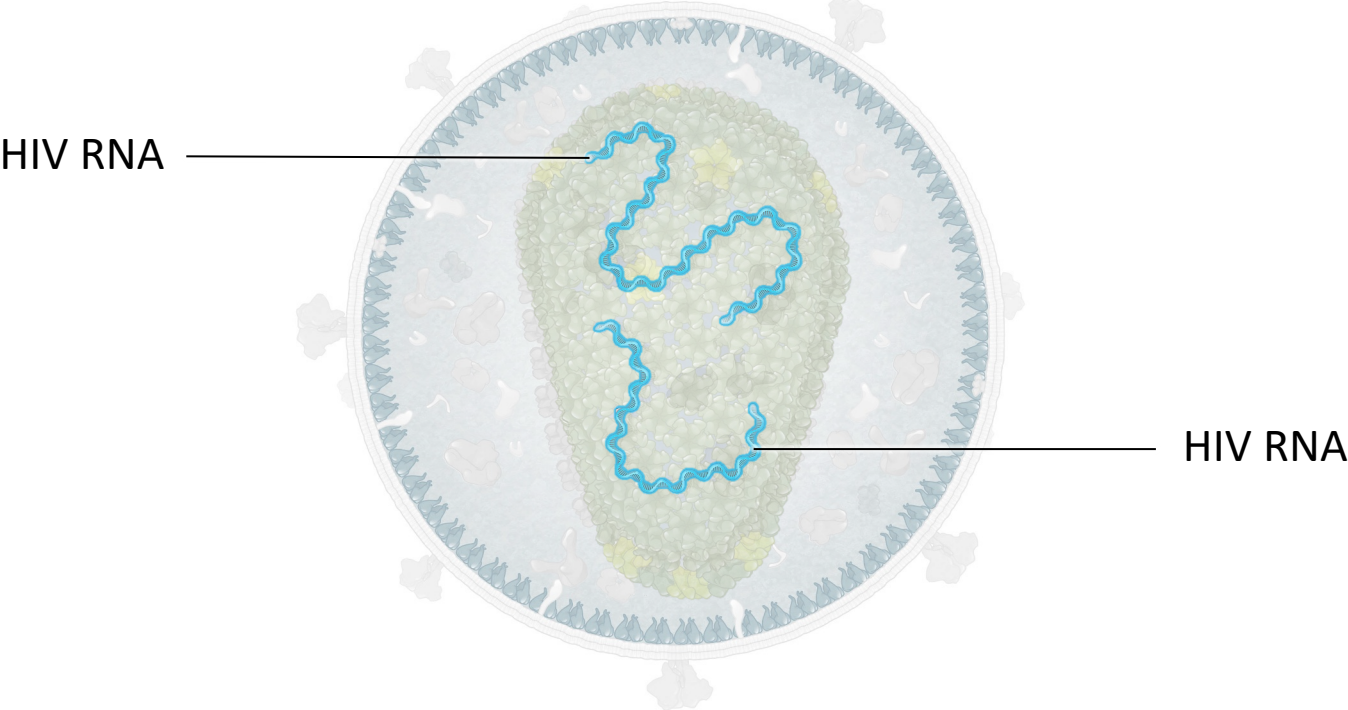


Illustration: Cognition Studio, Inc. and David H. Spach, MD

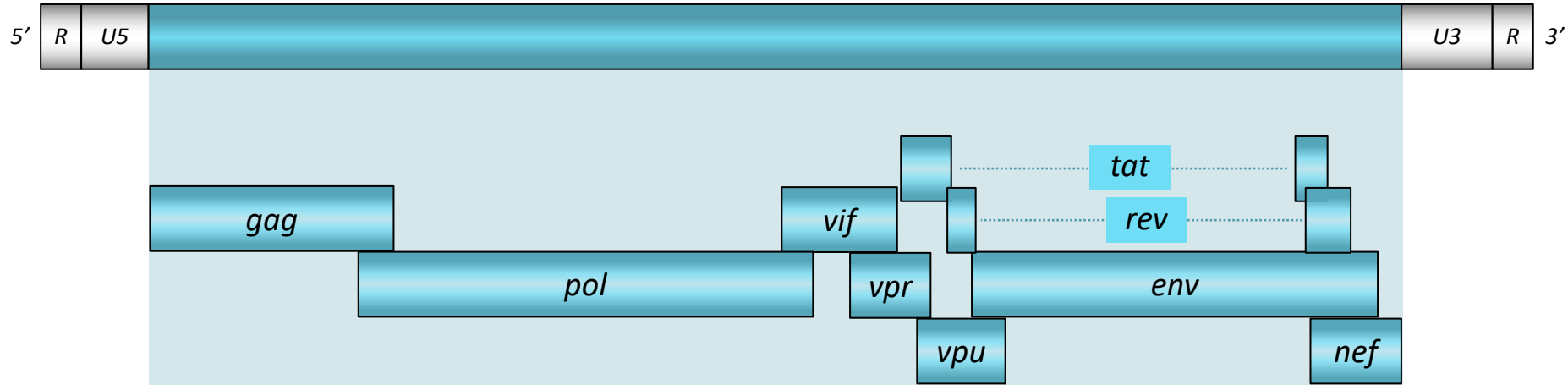
HIV-1 RNA Genome



Positive-sense, single strand RNA, \approx 9,750 base pairs

LTR = long terminal repeat; U = unique; R = Repeat

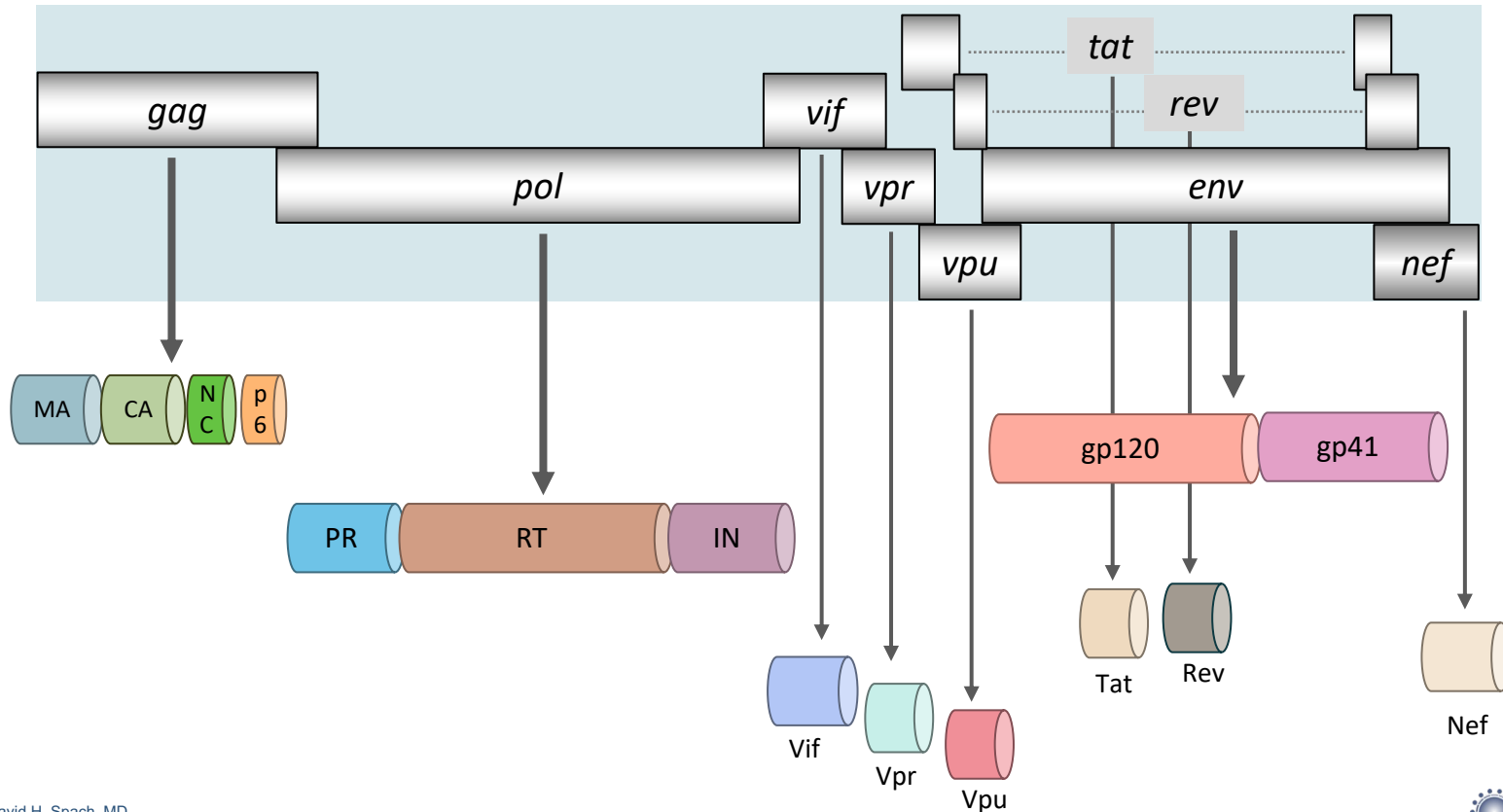
HIV-1 Genome: 9 Genes



HIV-1 Genome Contains 9 Genes that Encode 15 Viral Proteins

Genes

Proteins



HIV Proteins

HIV-1 Proteins (n =15)

Structural (6)

Enzymes (3)

Accessory (4)

Regulatory (2)

Structural Proteins

Structural (6)

gp120

gp41

Matrix (p17)

Capsid (p24)

Nucleocapsid (p7)

p6

Enzymes (3)

Accessory (4)

Regulatory (2)

Enzymes

Structural (6)

gp120

gp41

Matrix (p17)

Capsid (p24)

Nucleocapsid (p7)

p6

Enzymes (3)

Protease

Reverse Transcriptase

Integrase

Accessory (4)

Regulatory (2)

Accessory Proteins

Structural (6)

gp120

gp41

Matrix (p17)

Capsid (p24)

Nucleocapsid (p7)

p6

Enzymes (3)

Protease

Reverse Transcriptase

Integrase

Accessory (4)

Vif

Vpr

Vpu

Nef

Regulatory (2)

Regulatory Proteins

Structural (6)

gp120

gp41

Matrix (p17)

Capsid (p24)

Nucleocapsid (p7)

p6

Enzymes (3)

Protease

Reverse Transcriptase

Integrase

Accessory (4)

Vif

Vpr

Vpu

Nef

Regulatory (2)

Tat

Rev



HIV-1 Proteins (n =15)

Structural (6)

gp120

gp41

Matrix (p17)

Capsid (p24)

Nucleocapsid (p7)

p6

Enzymes (3)

Protease

Reverse Transcriptase

Integrase

Accessory (4)

Vif

Vpr

Vpu

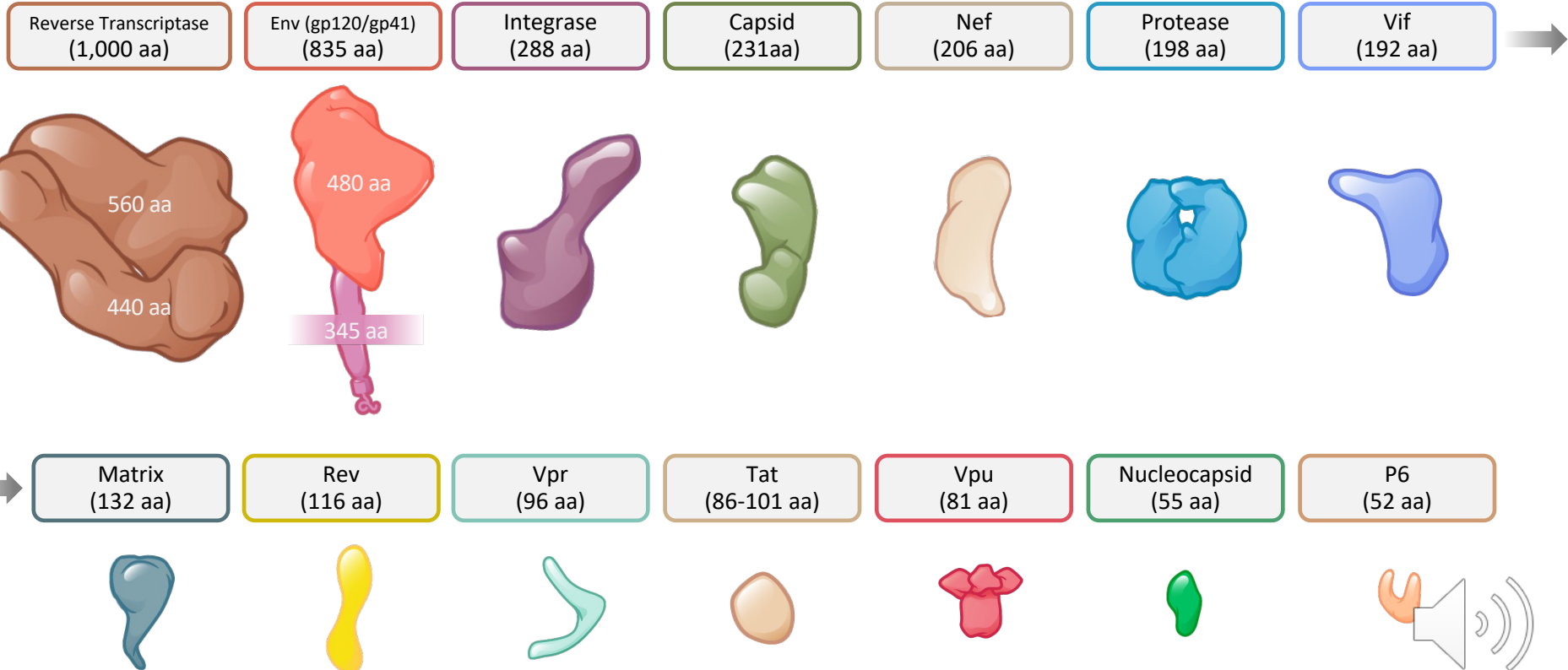
Nef

Regulatory (2)

Tat

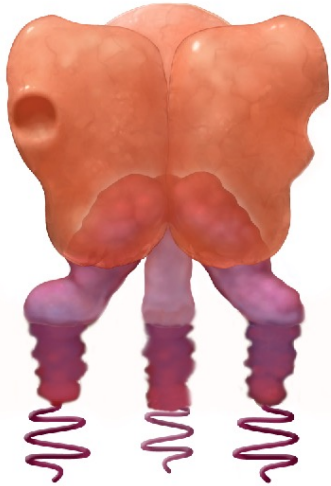
Rev

HIV-1 Proteins by Relative Size (aa = amino acid)

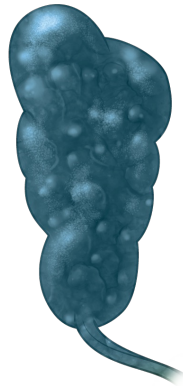


HIV Structural Proteins

HIV Structural Proteins



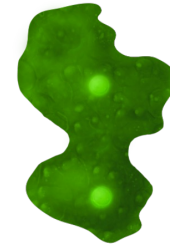
Envelope
(gp120/gp41)



Matrix
(p17)



Capsid
(p24)



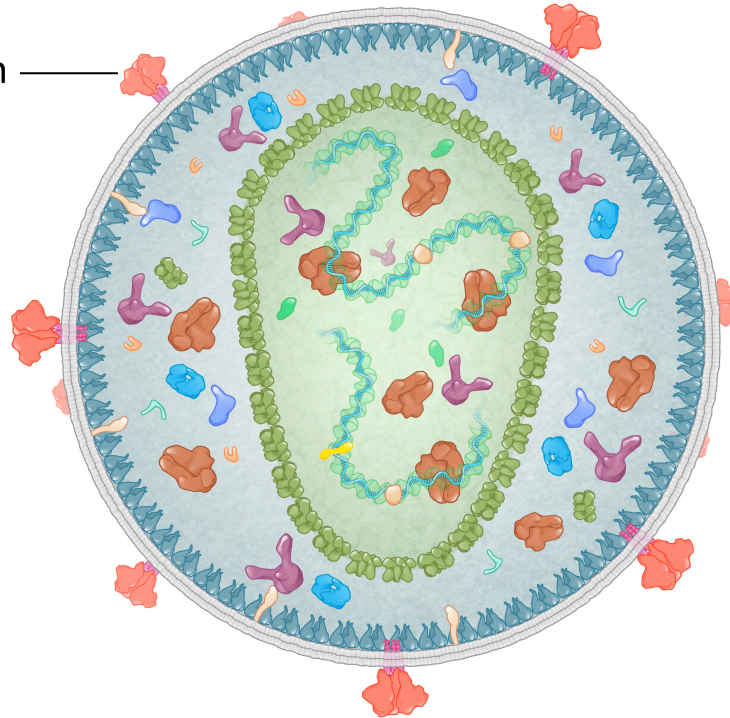
Nucleocapsid
(p7)



p6

HIV Envelope Glycoprotein

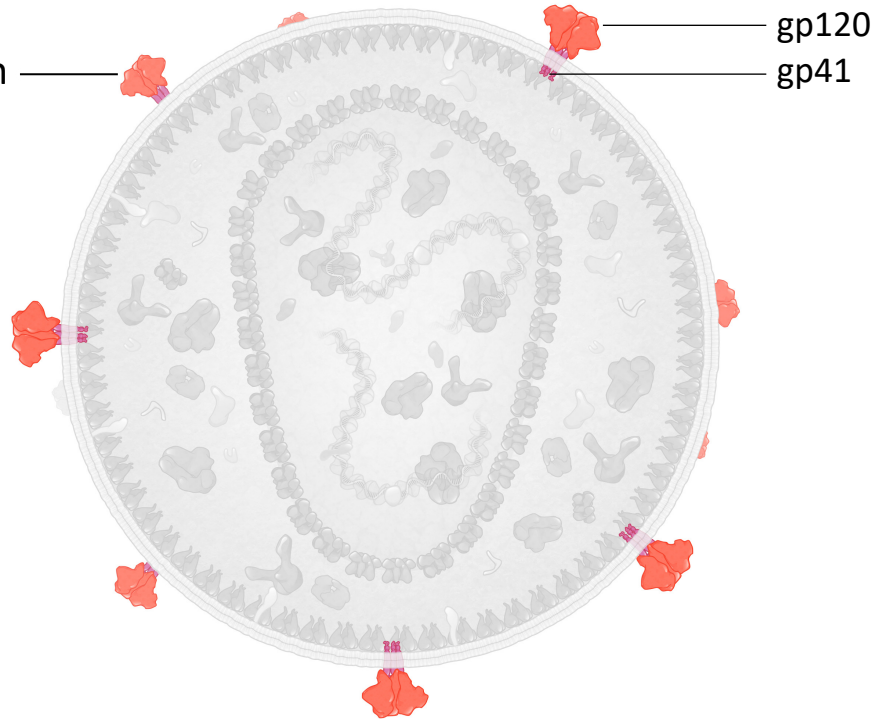
HIV Envelope Glycoprotein



HIV Envelope Glycoprotein

Structural Protein

HIV Envelope Glycoprotein

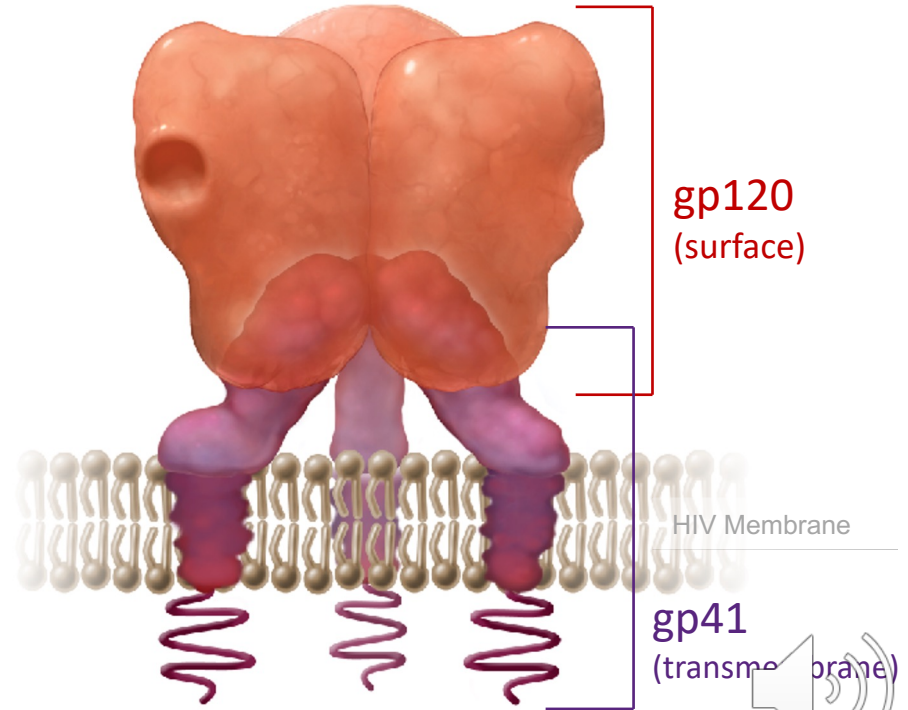


HIV Envelope Glycoproteins: gp120 and gp41 Subunits

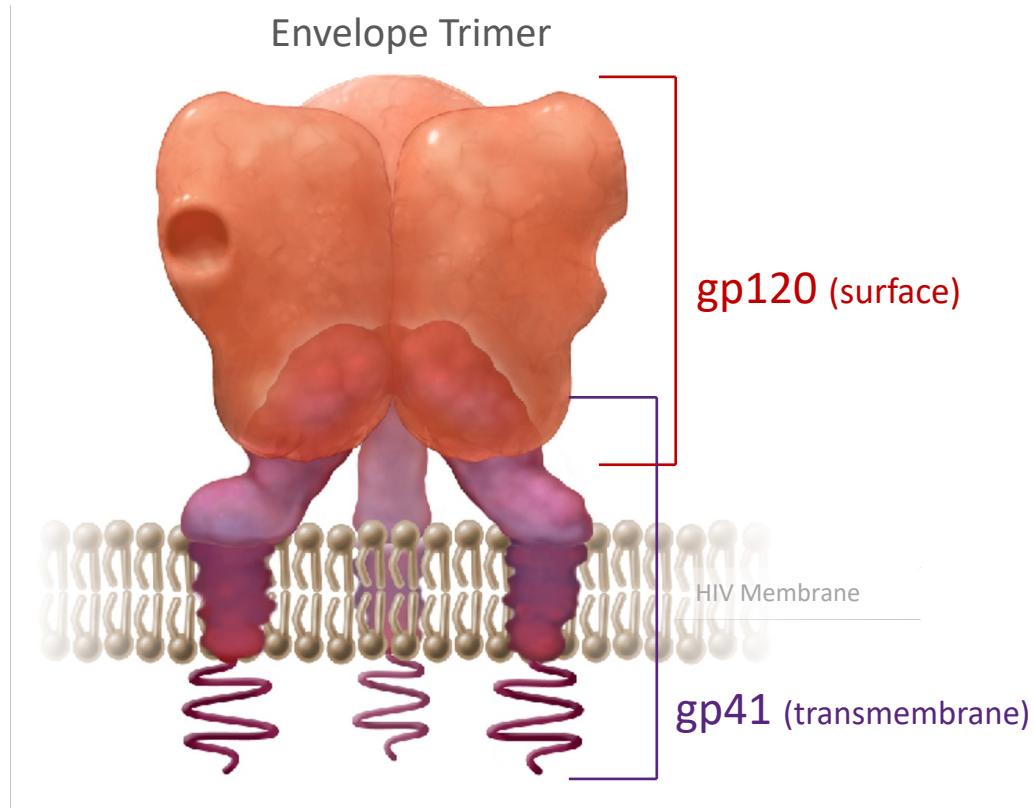


Illustration: Cognition Studio, Inc. and David H. Spach, MD

HIV Envelope Trimer

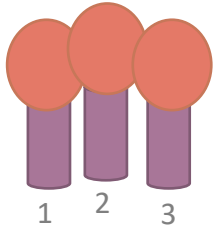


HIV Envelope Glycoprotein: Trimer Structure

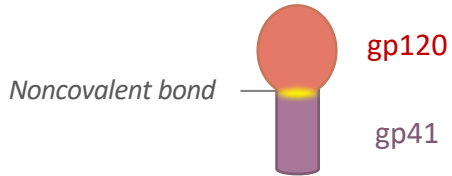


HIV Envelope Glycoprotein: Trimer Structure

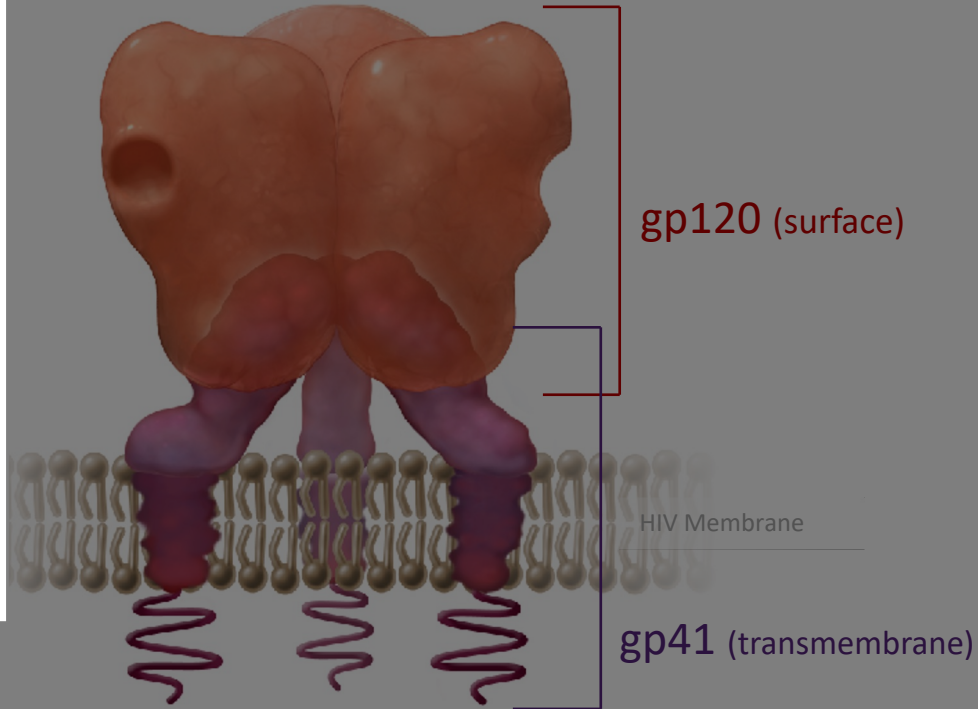
Trimer



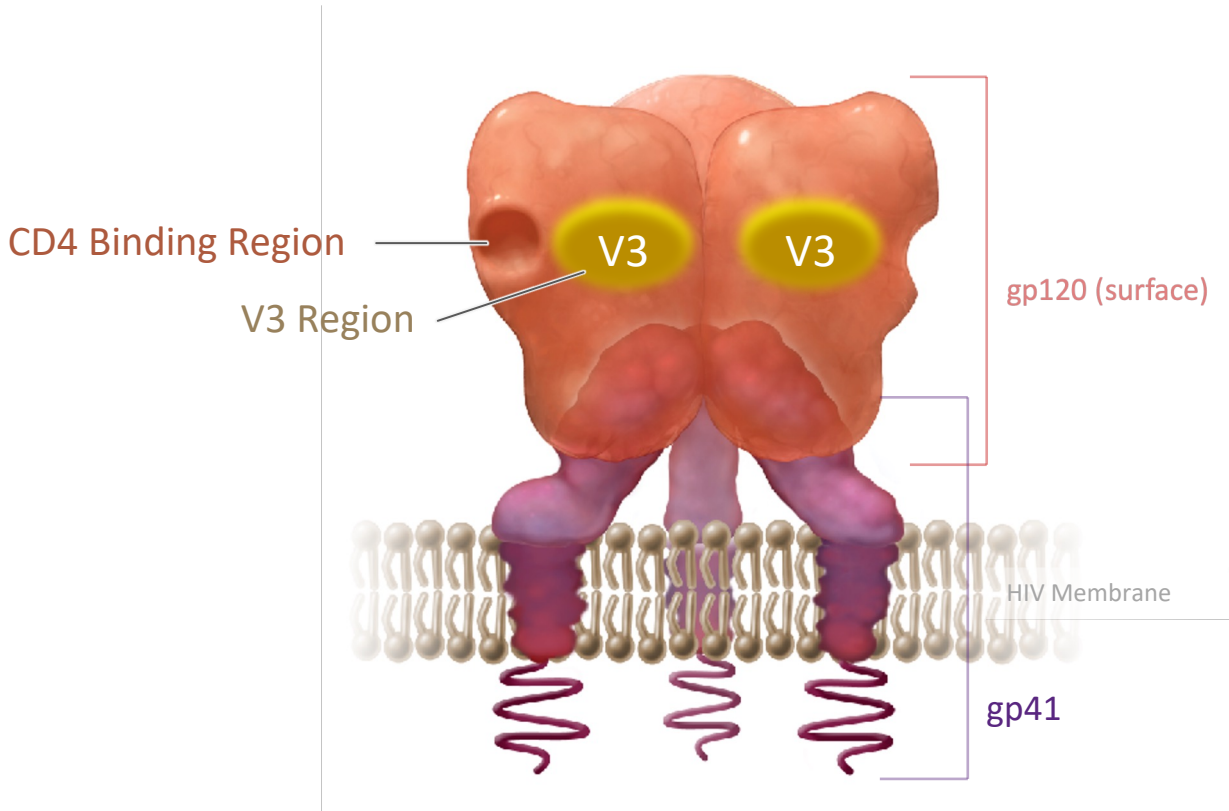
gp120-gp41 pair



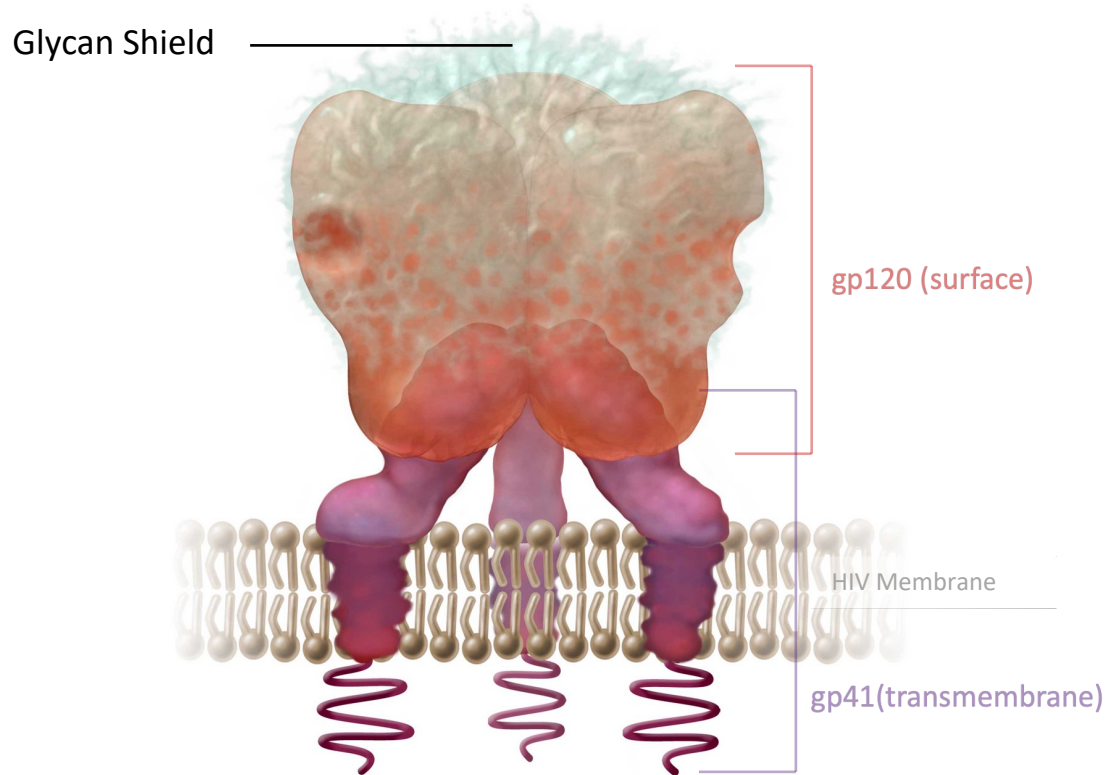
Envelope Trimer



HIV Envelope Glycoprotein: Regions Involved in Cell Entry

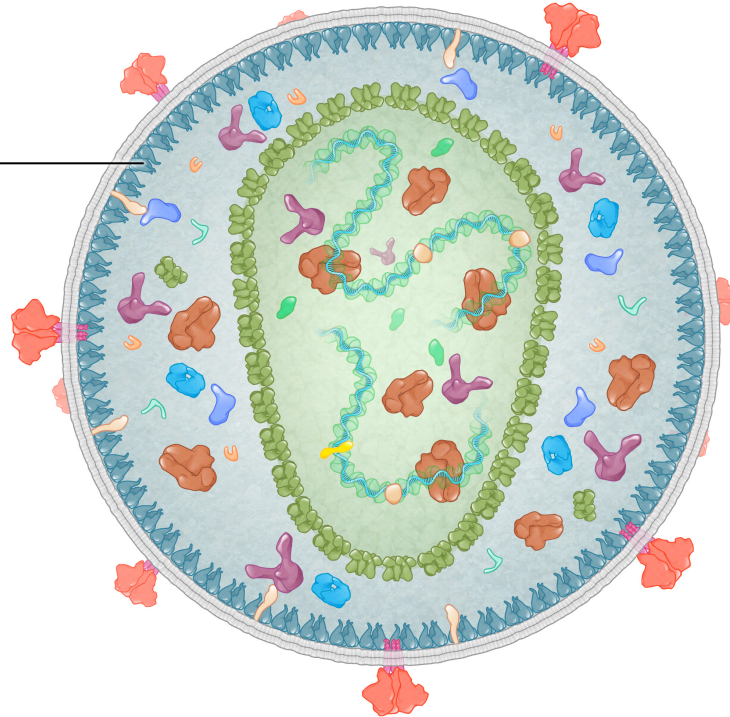


HIV Envelope Glycoprotein: Glycan Shield



HIV Matrix (p17)

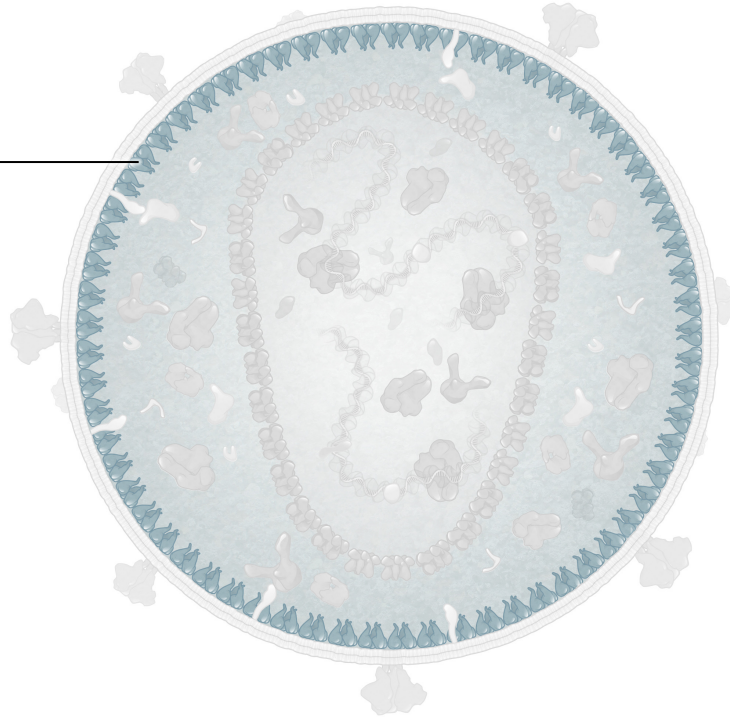
HIV Matrix (p17)



HIV Matrix

Structural Protein

HIV Matrix (p17)

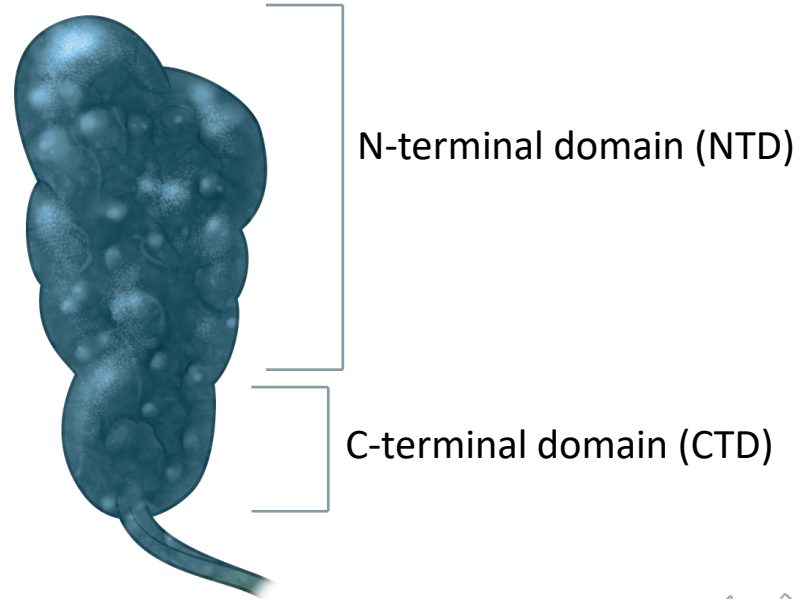


HIV Matrix: Monomer Structure



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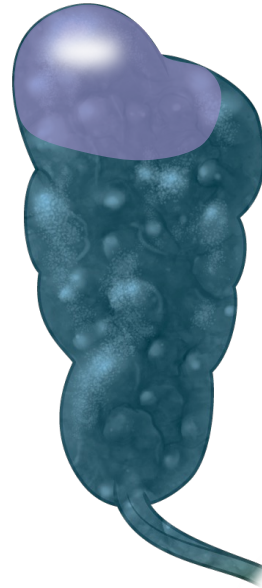
HIV Matrix Monomer



HIV Matrix: Basic Region



Basic Region

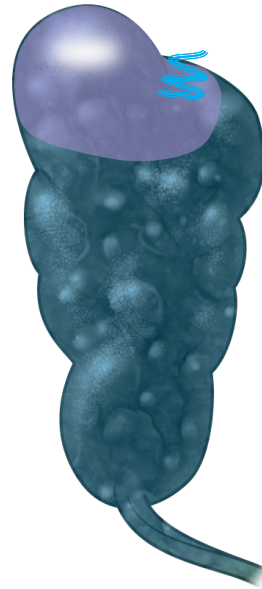



N-terminal domain (NTD)

HIV Matrix: Myristyl Group



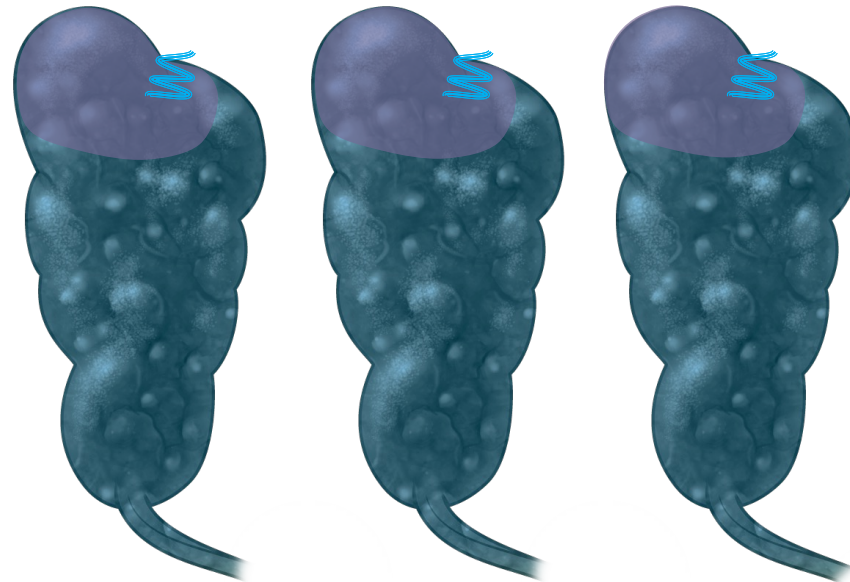
Illustration: Cognition Studio, Inc. and David H. Spach, MD



Myristyl Group 
N-terminal domain (NTD)

HIV Matrix: Myristyl Group Sequestered Conformation

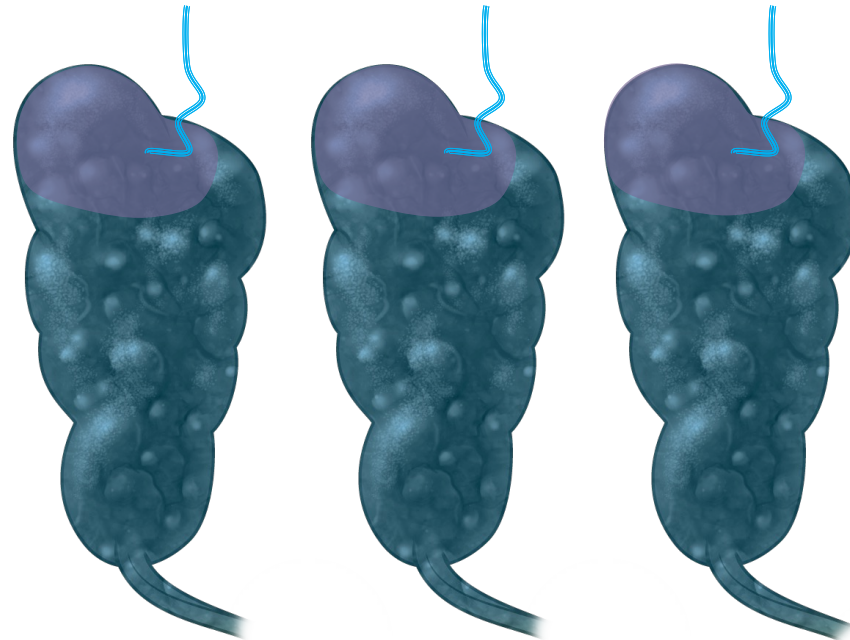
Sequestered Conformation



Myristyl Group

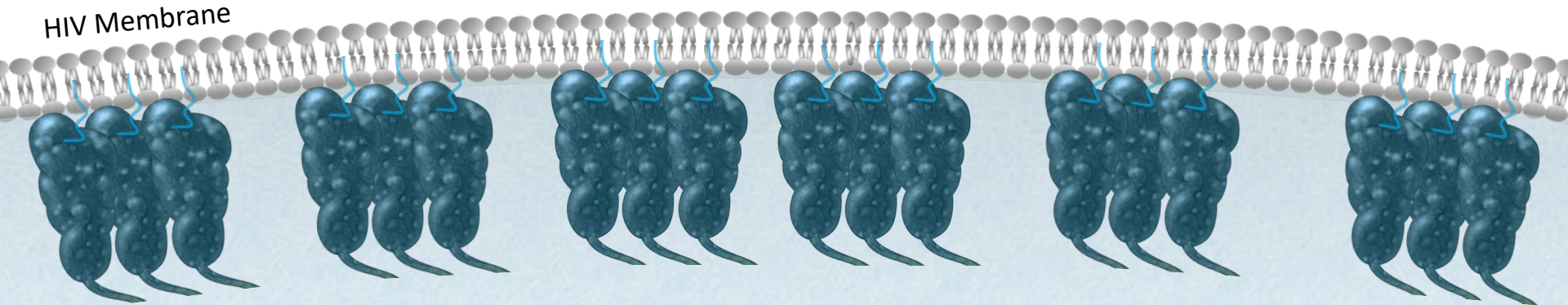
HIV Matrix: Myristyl Group Exposed Conformation

Exposed Conformation



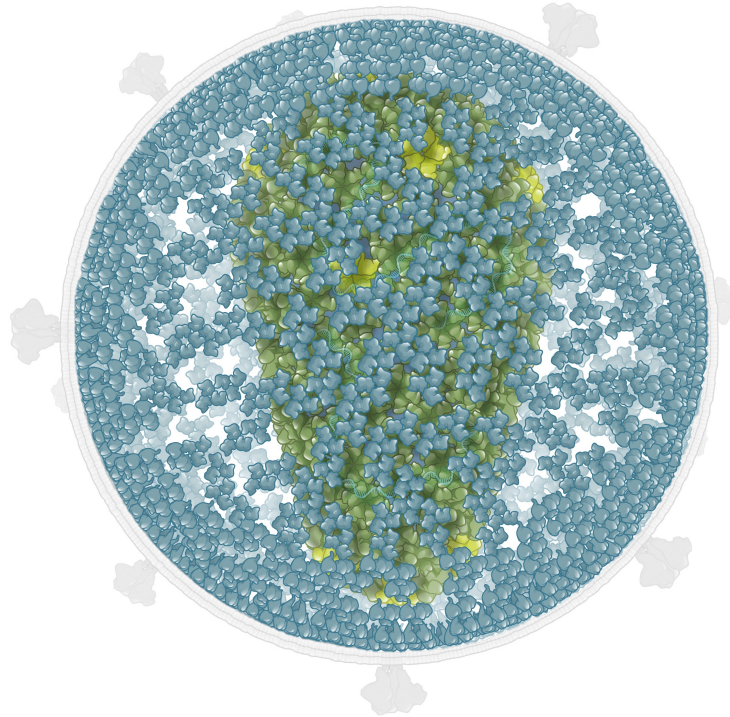
Myristyl Group

HIV Matrix: Membrane Bound Trimers

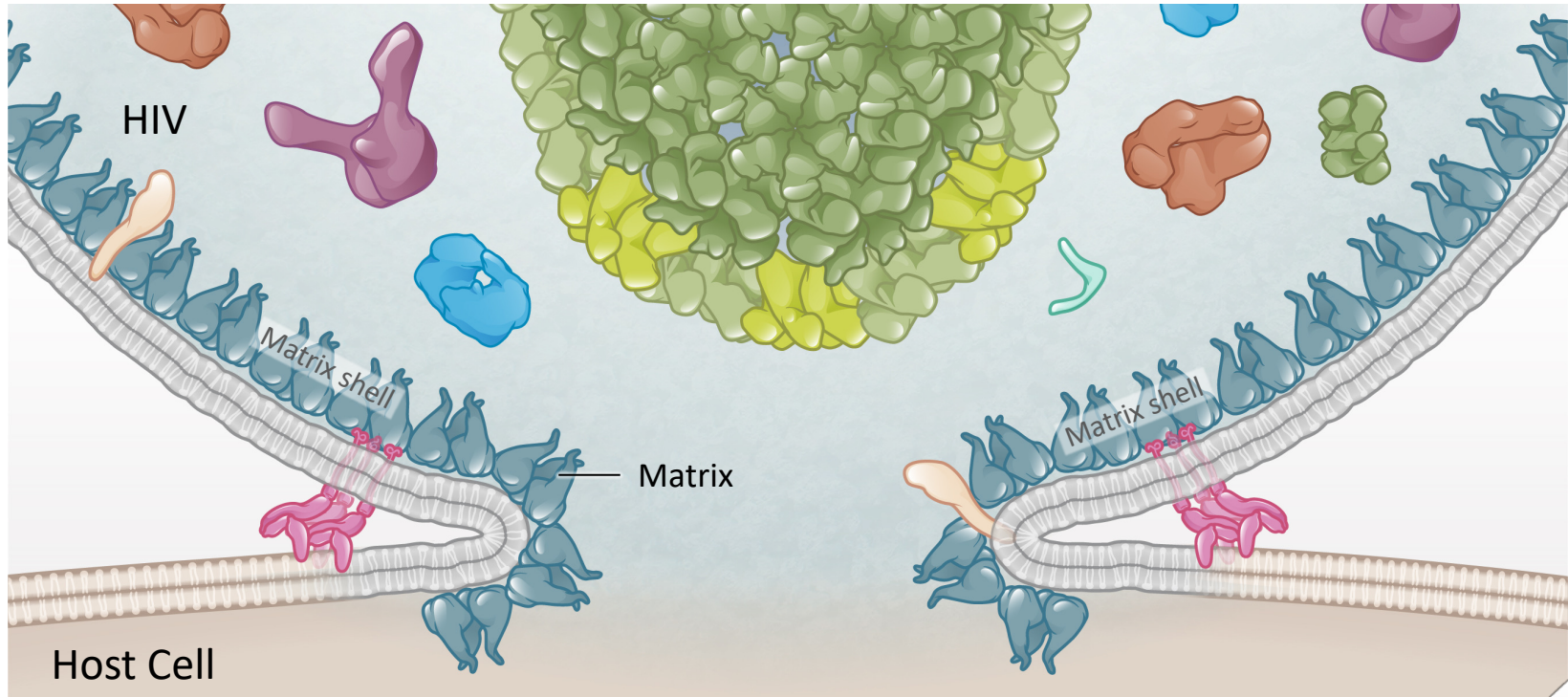


HIV Matrix Trimer

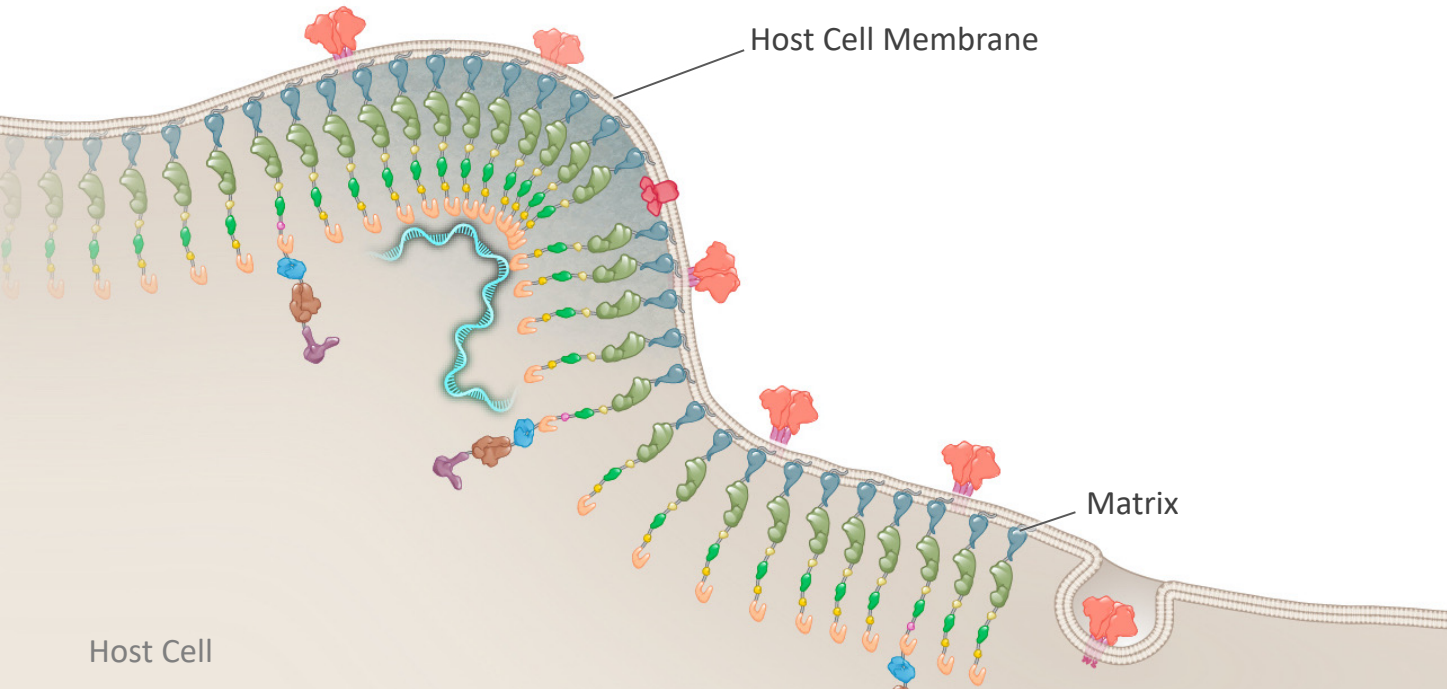
HIV Matrix: Trimers Forming Matrix Shell



HIV Matrix: Role in Cell Entry



HIV Matrix: Role Late in Viral Assembly

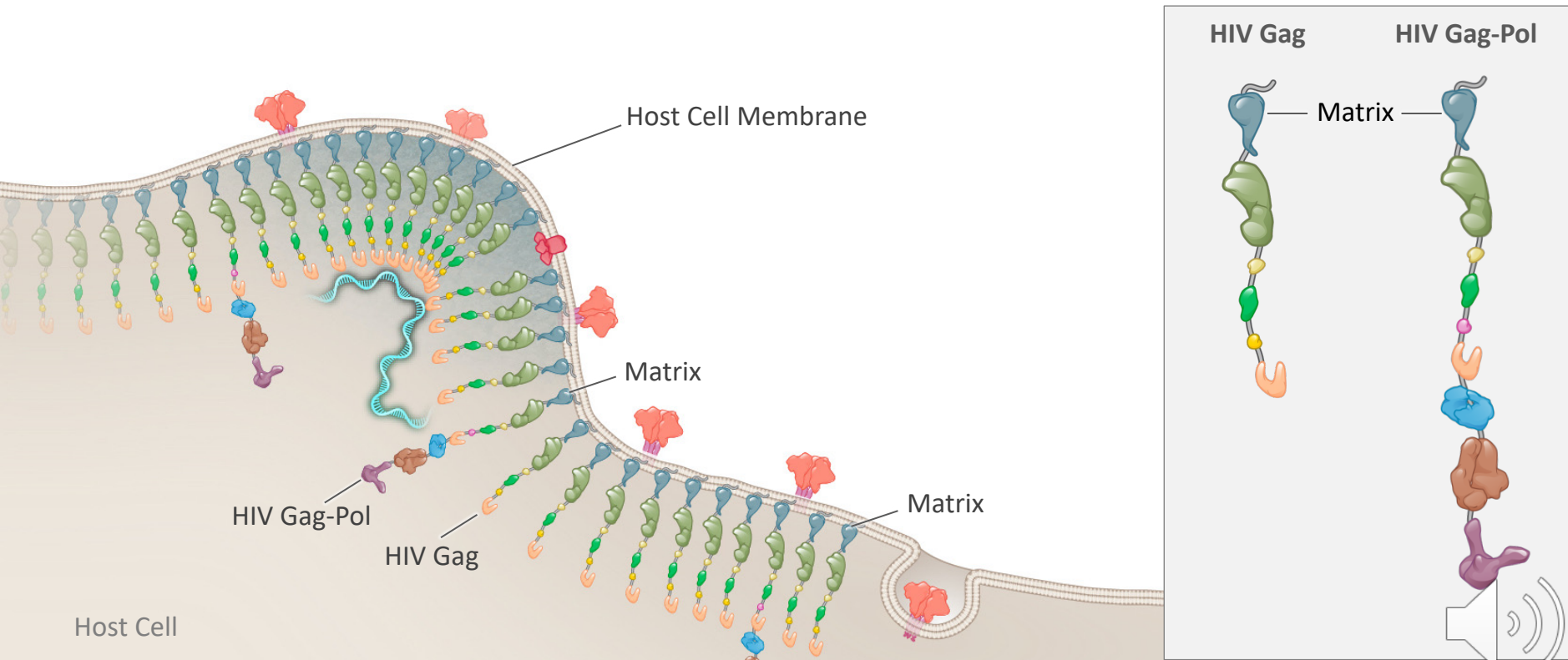


Host Cell

Host Cell Membrane

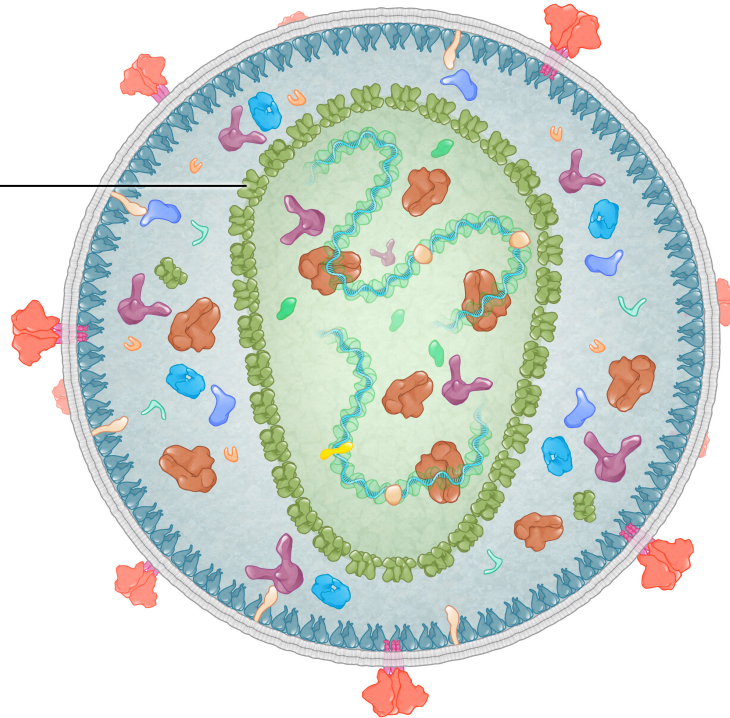
Matrix

HIV Matrix: Role Anchoring HIV Gag and Gag-Pol



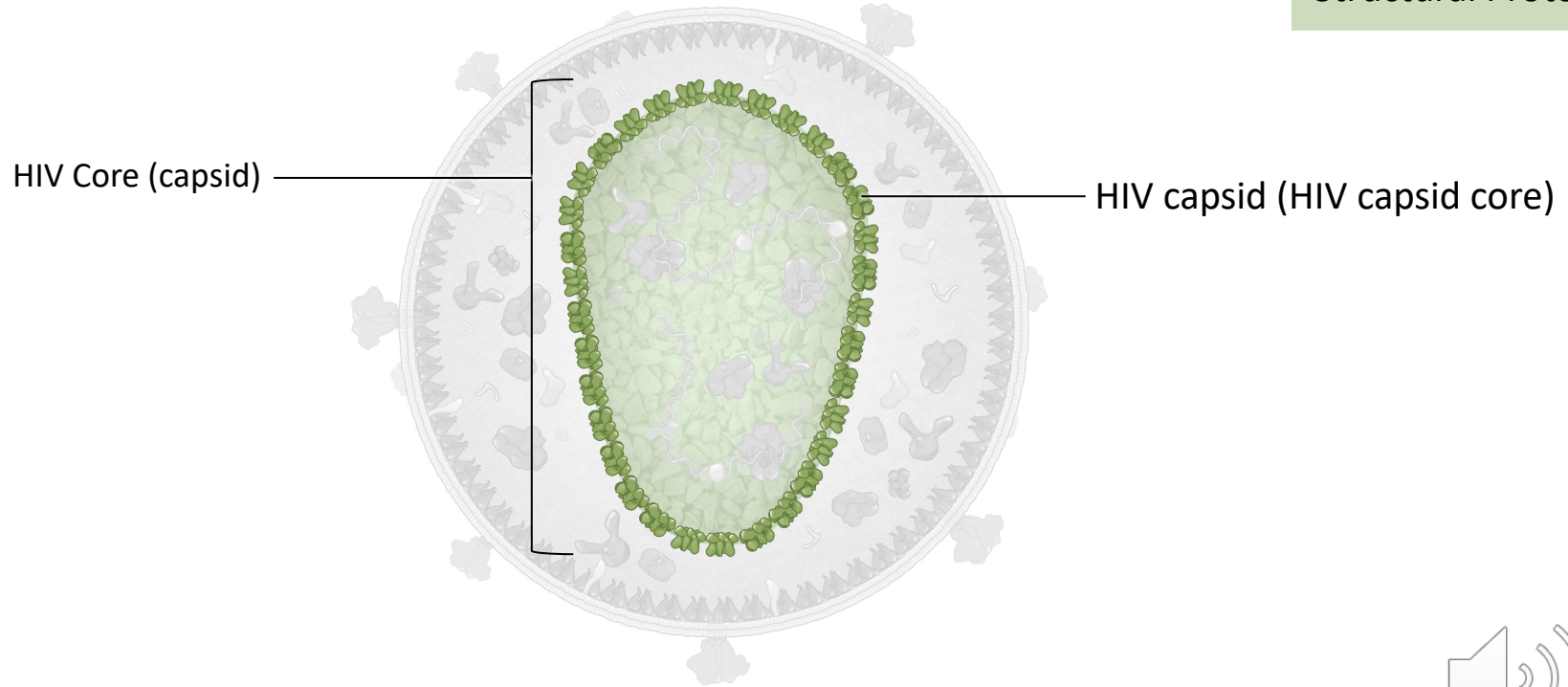
HIV Capsid (p24)

HIV capsid (p24)



HIV Capsid and HIV Core

Structural Protein



HIV Capsid: Monomer Structure

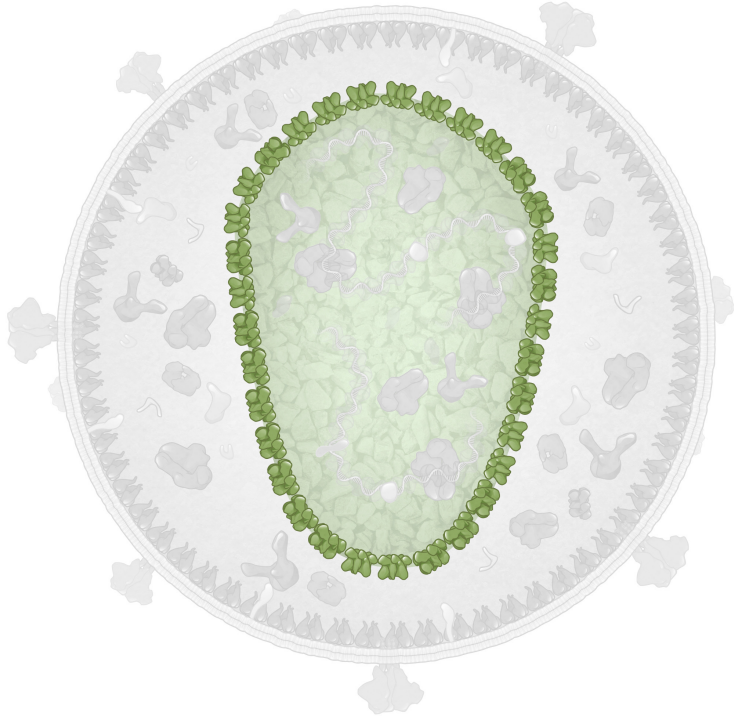
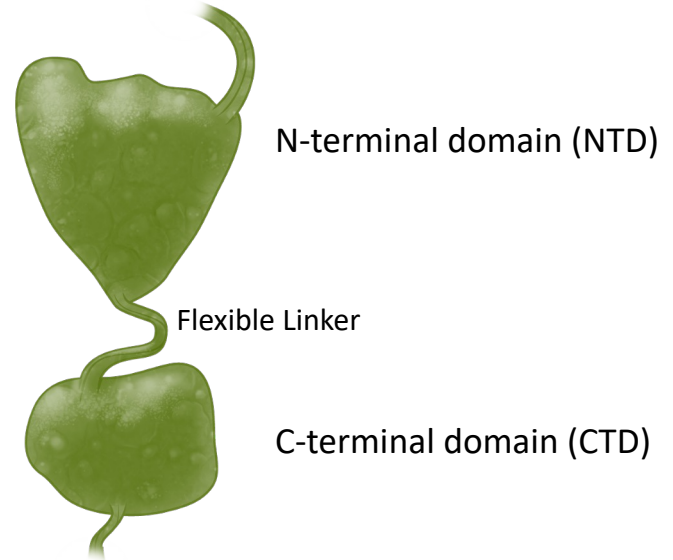
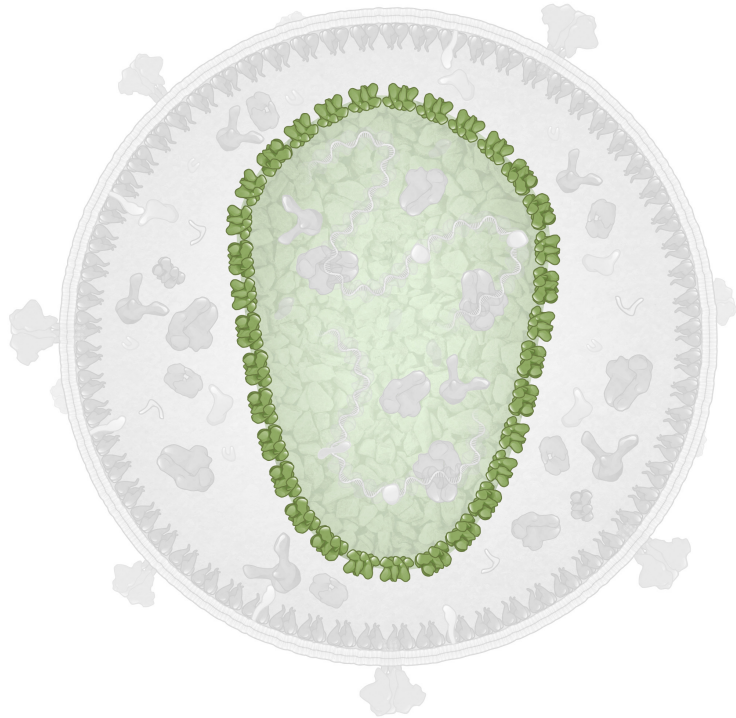


Illustration: Cognition Studio, Inc. and David H. Spach, MD

HIV Capsid Monomer



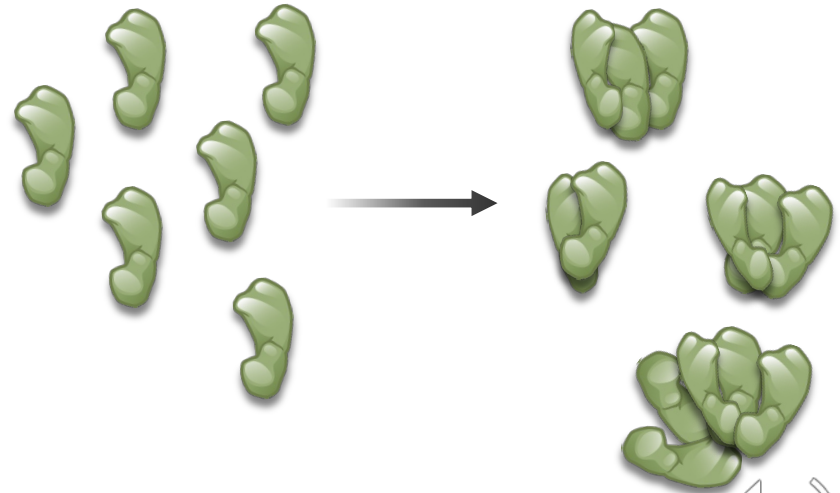
HIV Capsid: Monomers and Polymers



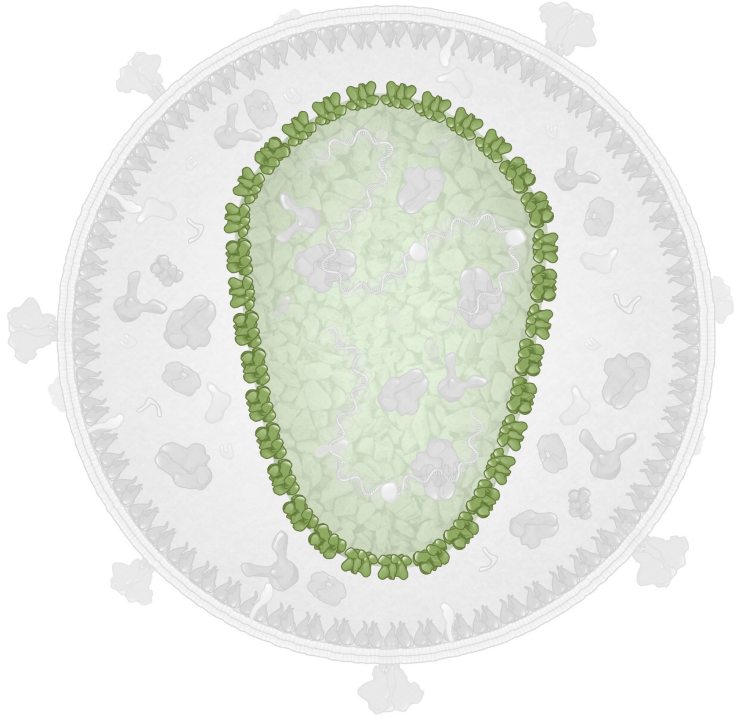
HIV Capsid

Monomers

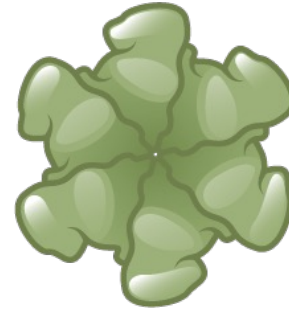
Polymers



HIV Capsid: Hexamers and Pentamers



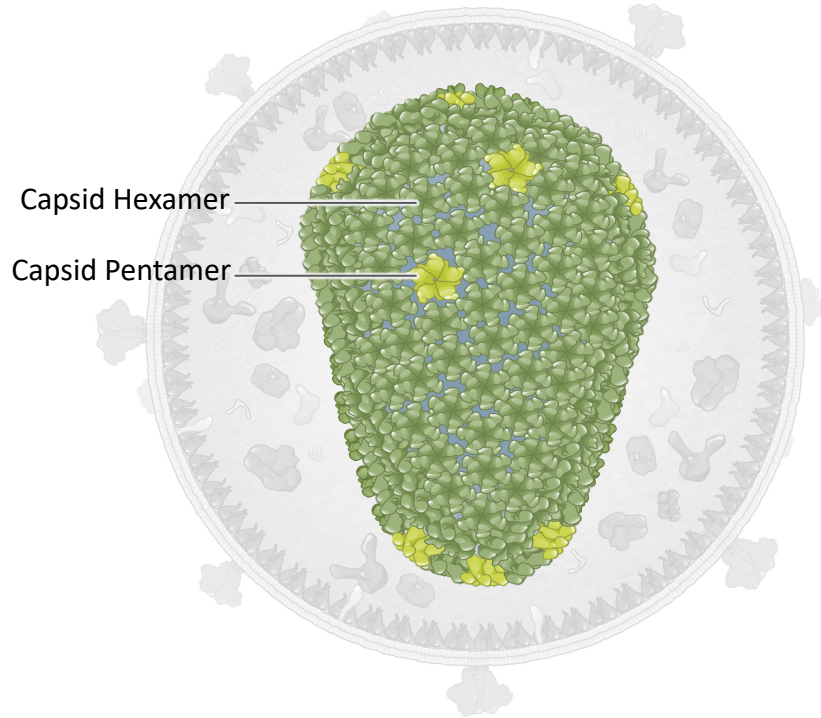
Capsid Hexamer



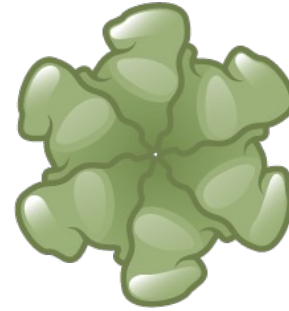
Capsid Pentamer



HIV Capsid: Hexamers and Pentamers



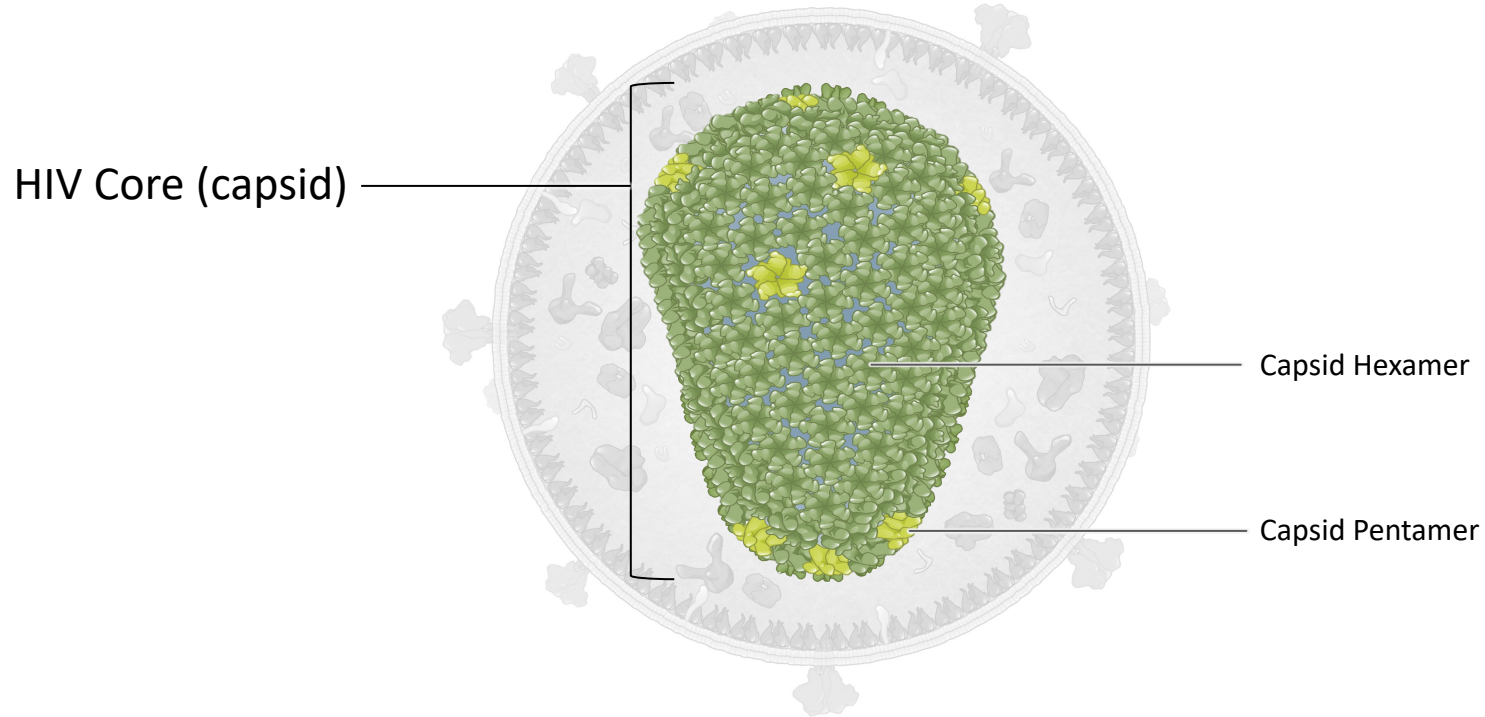
Capsid Hexamer



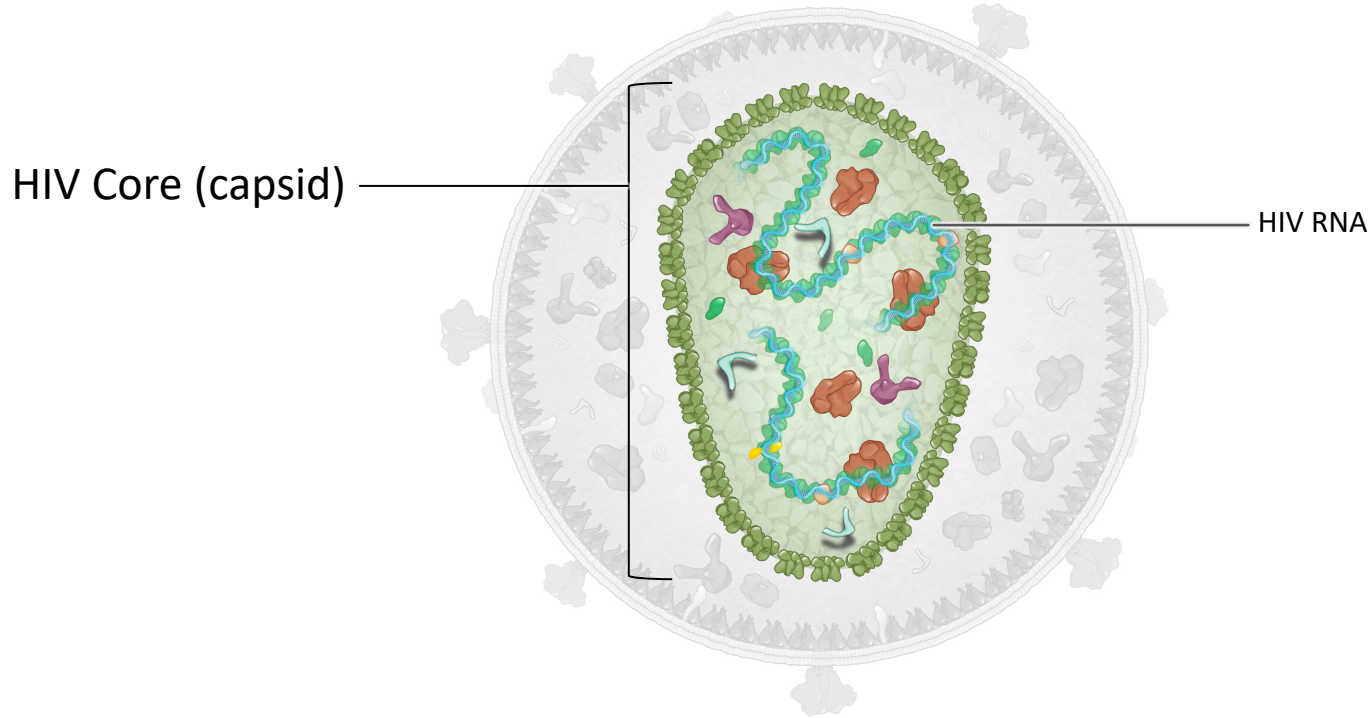
Capsid Pentamer



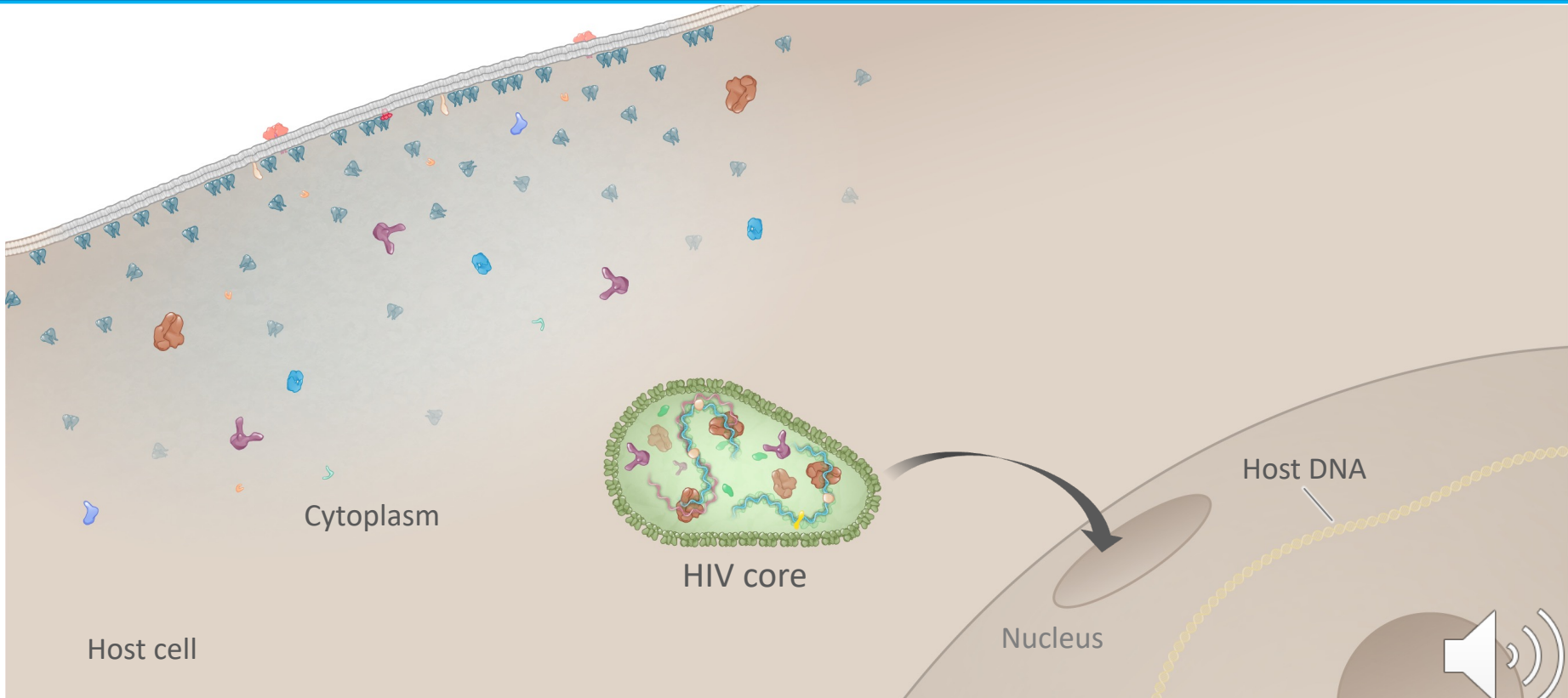
HIV Capsid: Cone-Shaped Structure of HIV Core



HIV Core: Structural Barrier

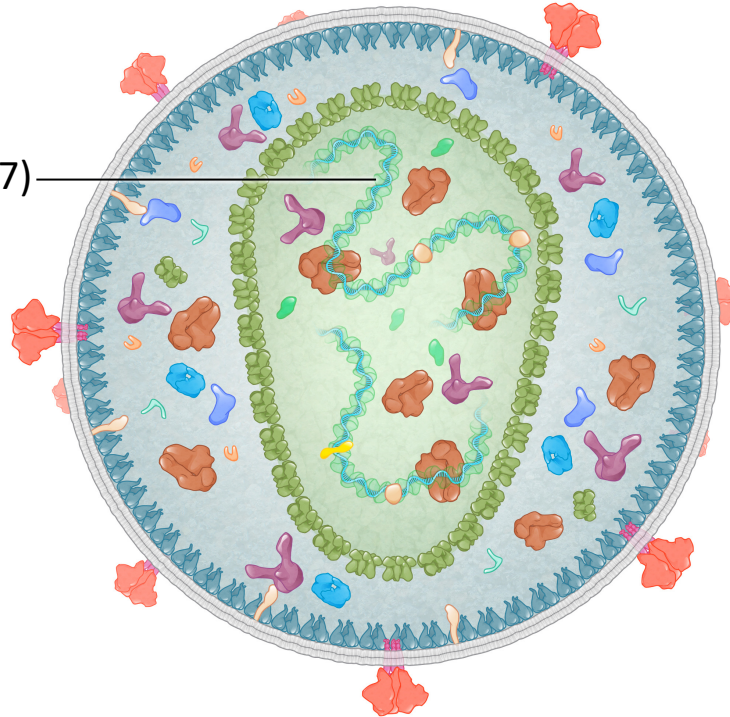


HIV Core: Role in Migration to Host Cell Nucleus



HIV Nucleocapsid (p7)

HIV Nucleocapsid (p7)

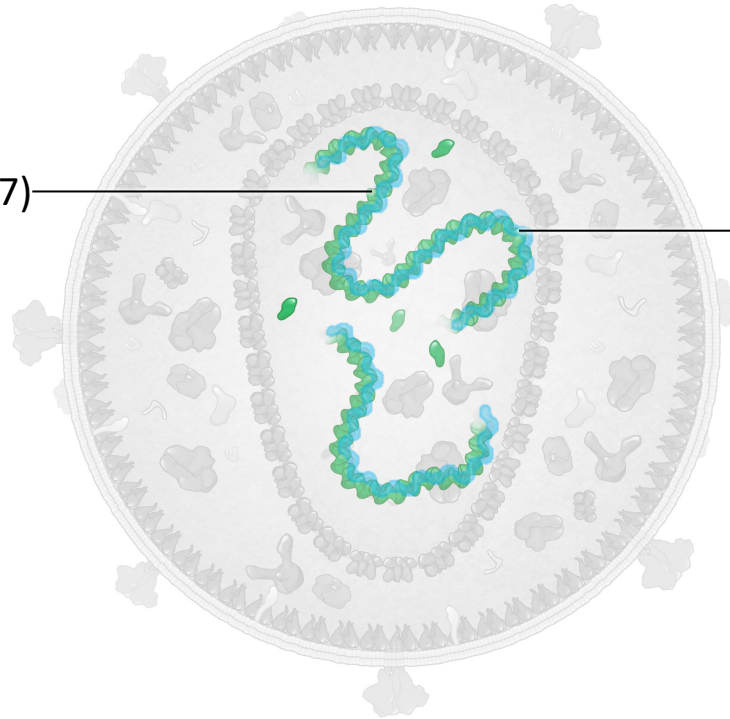


HIV Nucleocapsid (p7)

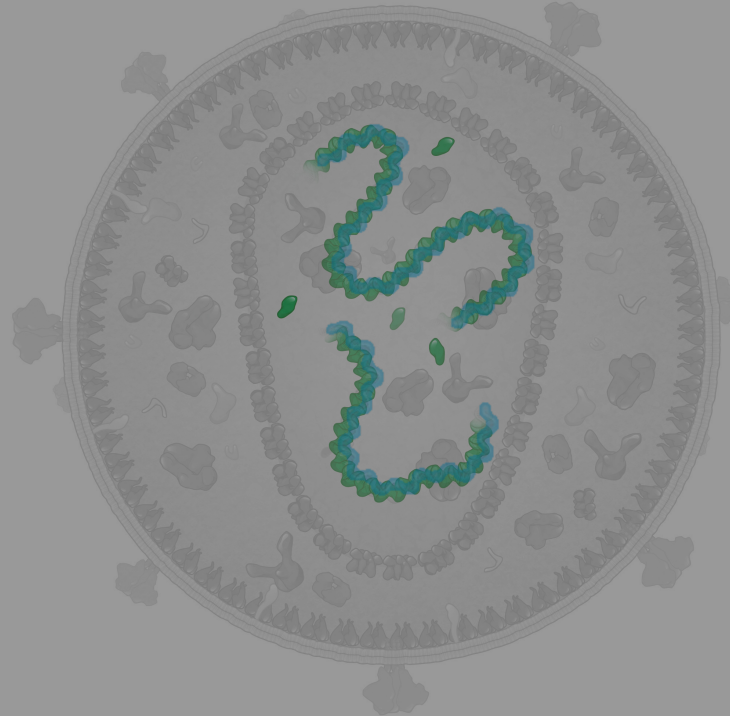
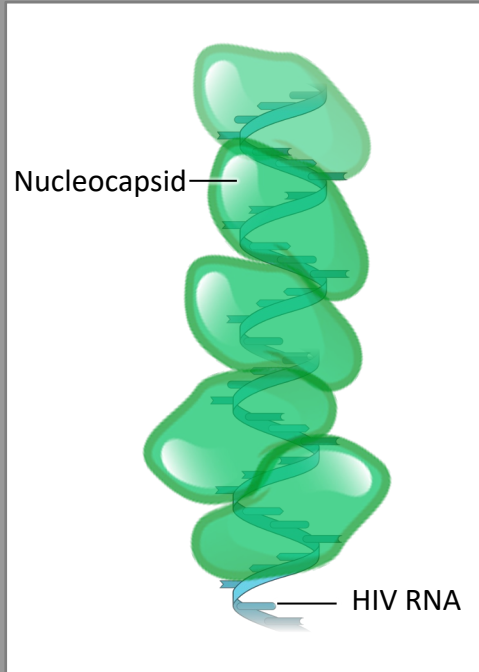
Structural Protein

HIV Nucleocapsid (p7)

HIV RNA



HIV Nucleocapsid (p7): HIV RNA Coating



HIV Nucleocapsid: Structure

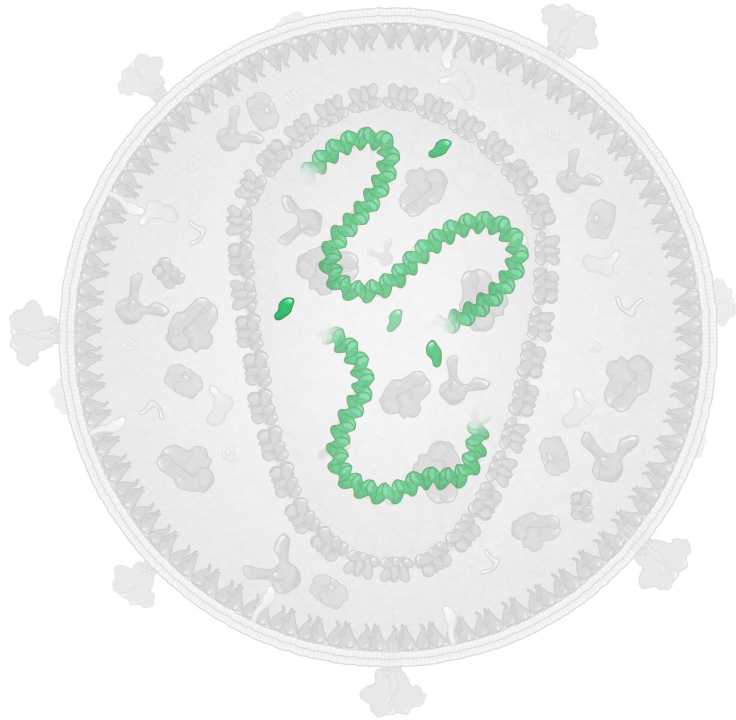
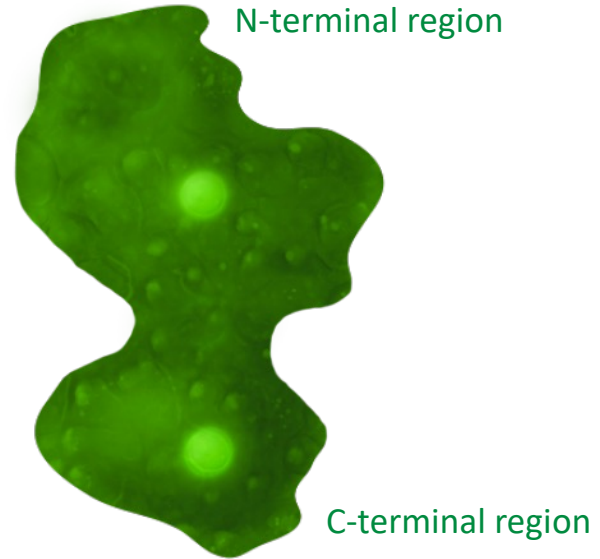


Illustration: Cognition Studio, Inc. and David H. Spach, MD

HIV Nucleocapsid Monomer



HIV Nucleocapsid: Zinc-Binding Domains

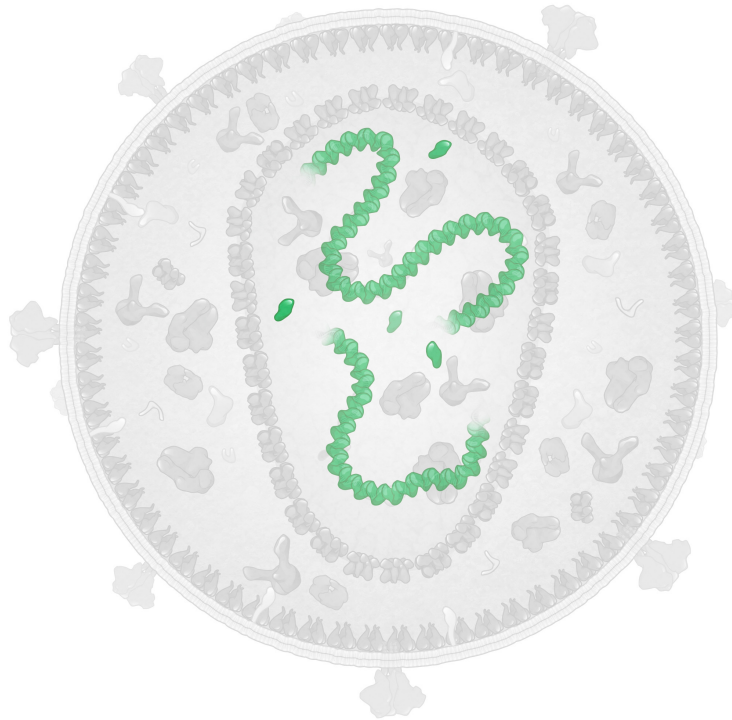
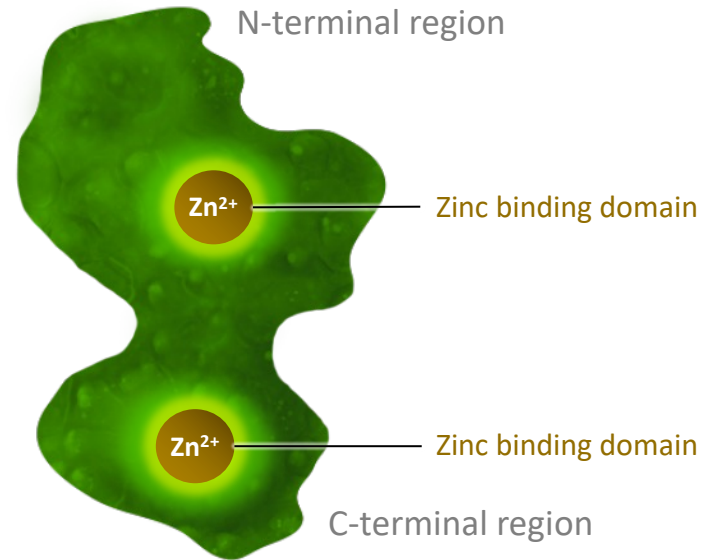
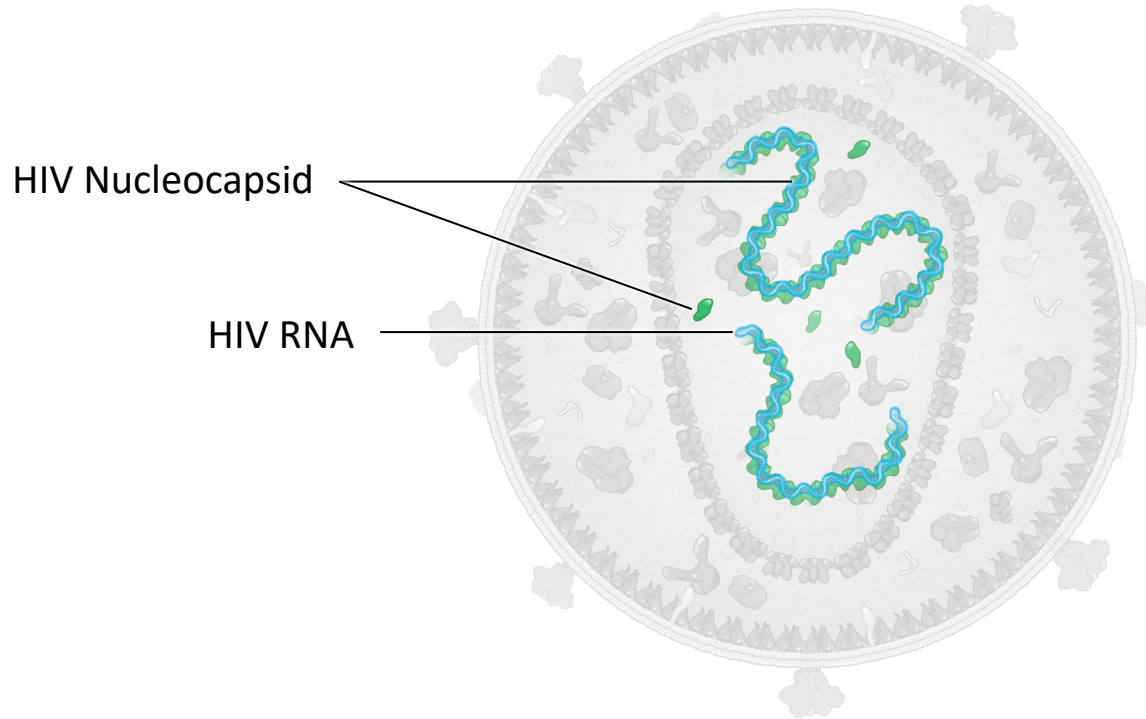


Illustration: Cognition Studio, Inc. and David H. Spach, MD

HIV Nucleocapsid Monomer

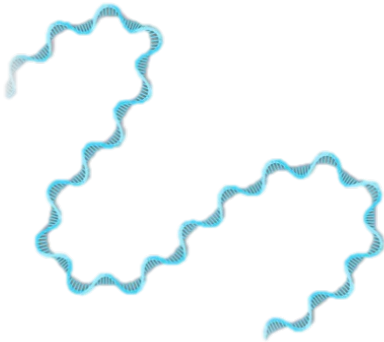


HIV Nucleocapsid: Complexed with HIV RNA



HIV Ribonucleoprotein Complex

HIV Genomic RNA



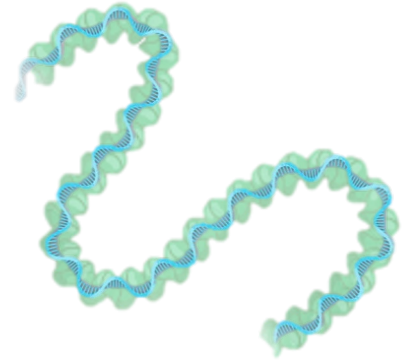
Nucleocapsid Proteins



+

=

Ribonucleoprotein Complex



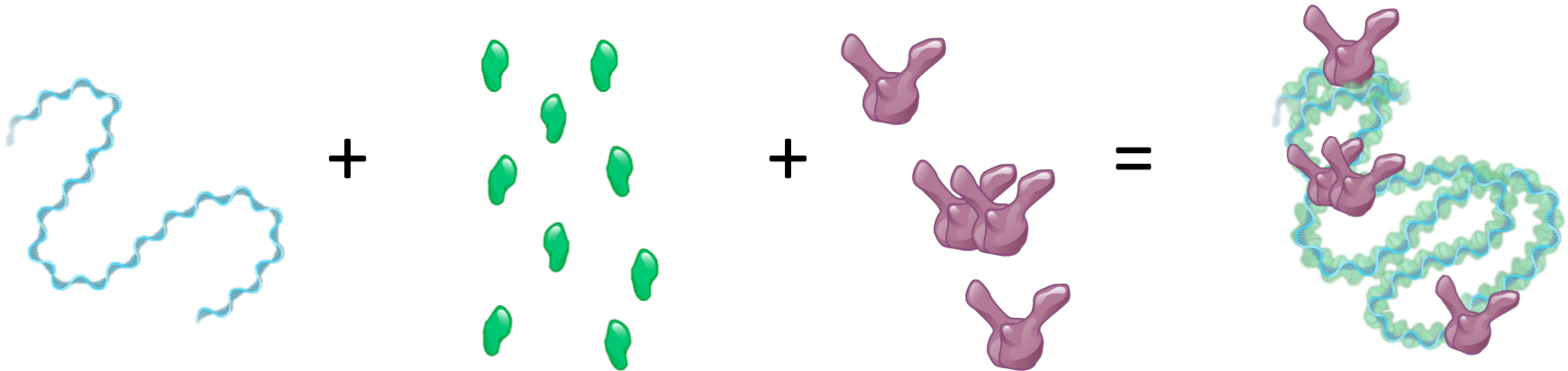
HIV Ribonucleoprotein Complex with Integrase

HIV Genomic RNA

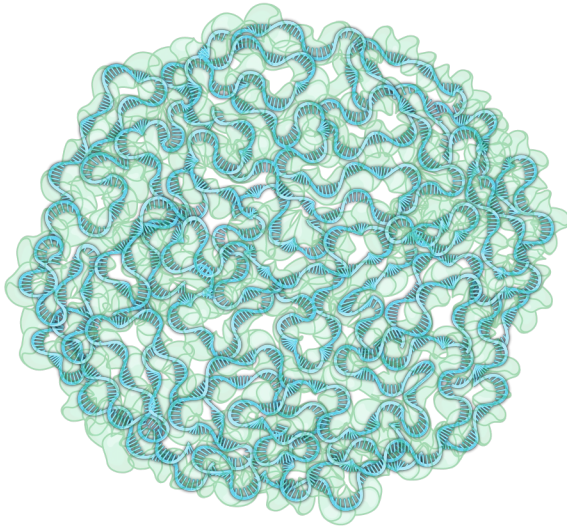
Nucleocapsid Proteins

Integrase

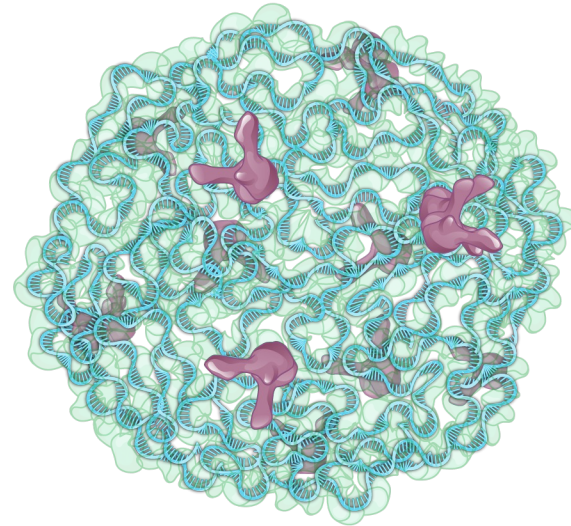
Ribonucleoprotein Complex



HIV Ribonucleoprotein Complex



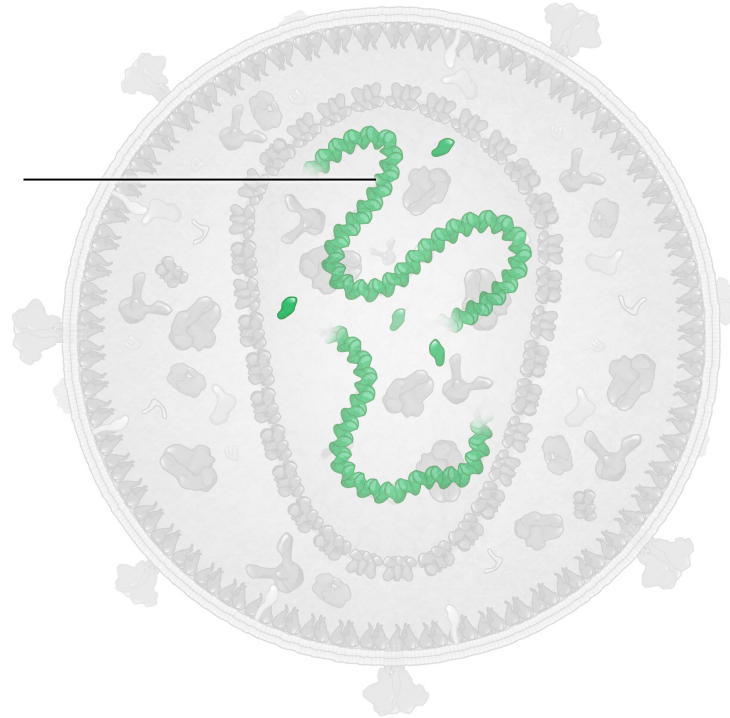
(-) Integrase



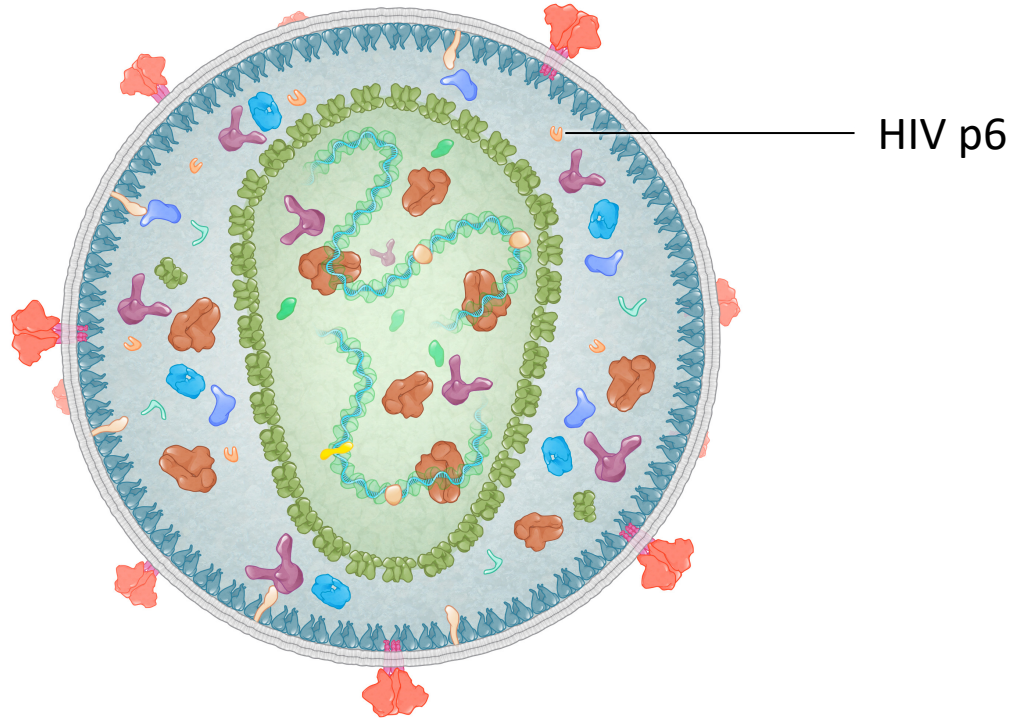
(+) Integrase

HIV Nucleocapsid Protein: Role in Reverse Transcription

HIV Nucleocapsid

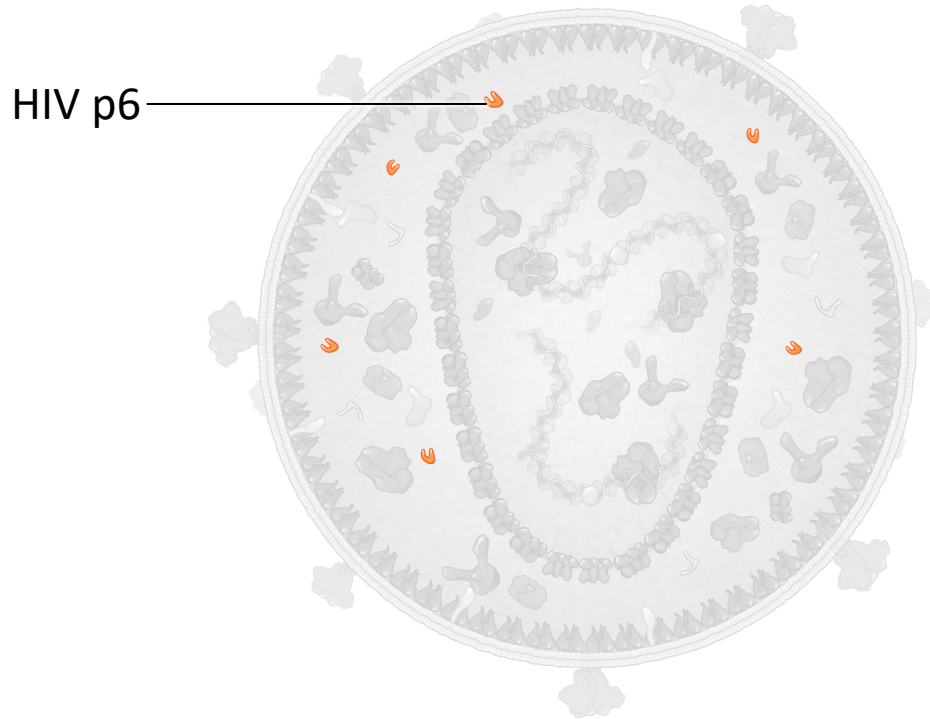


HIV p6



HIV p6

Structural Protein

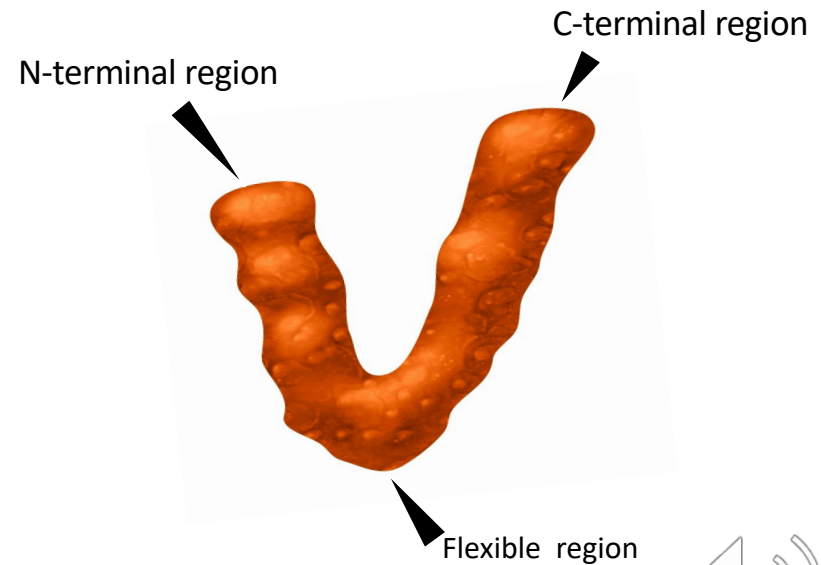


HIV p6: Structure



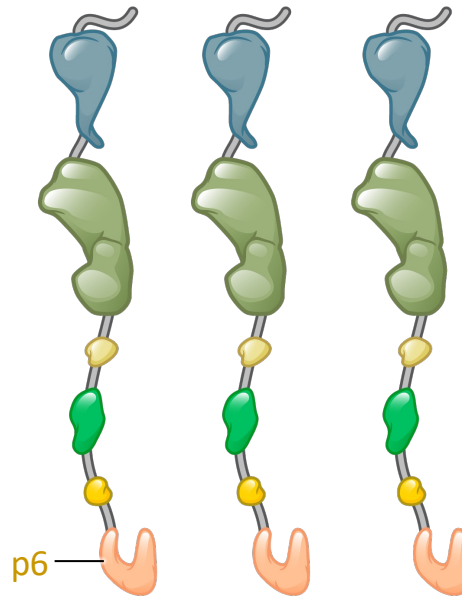
Illustration: Cognition Studio, Inc. and David H. Spach, MD

HIV p6 Monomer

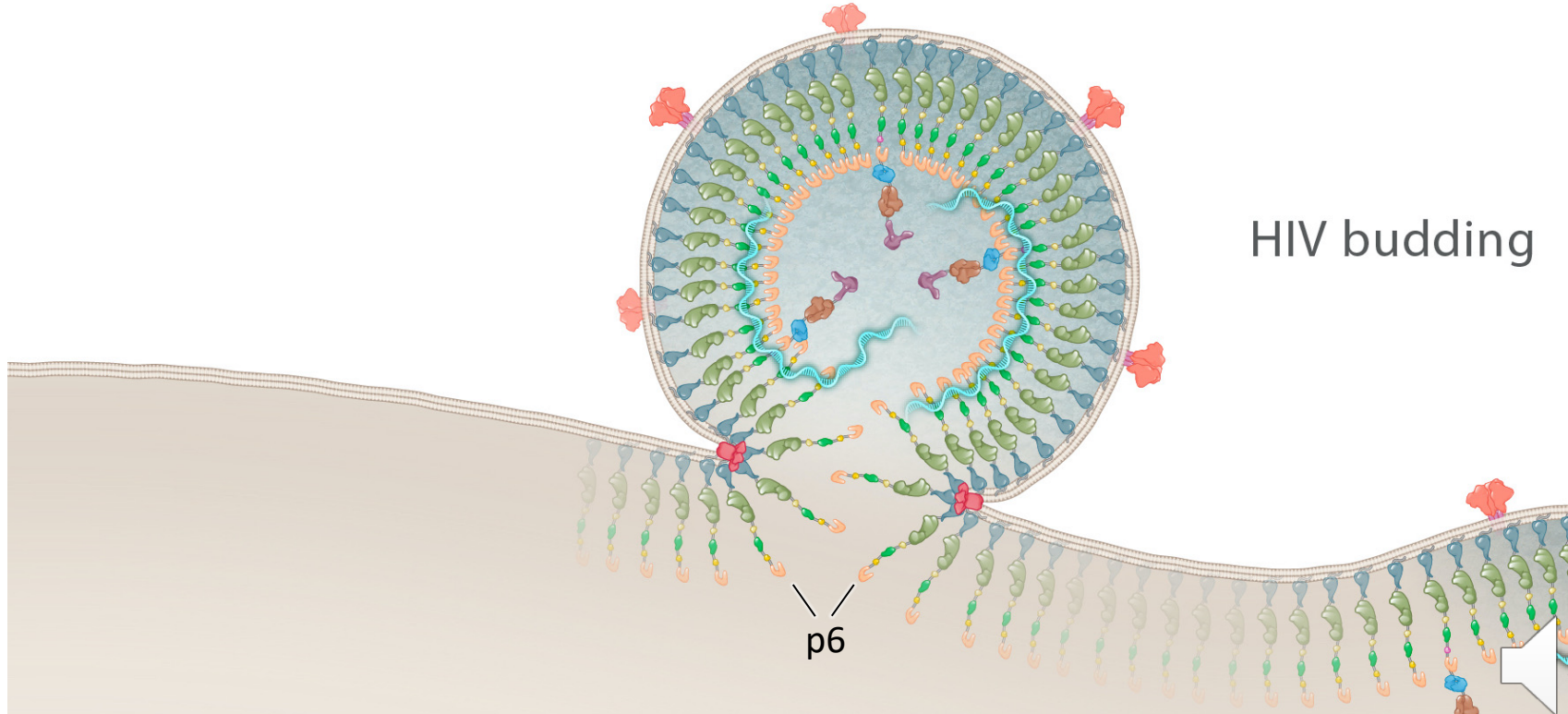


HIV p6: Role

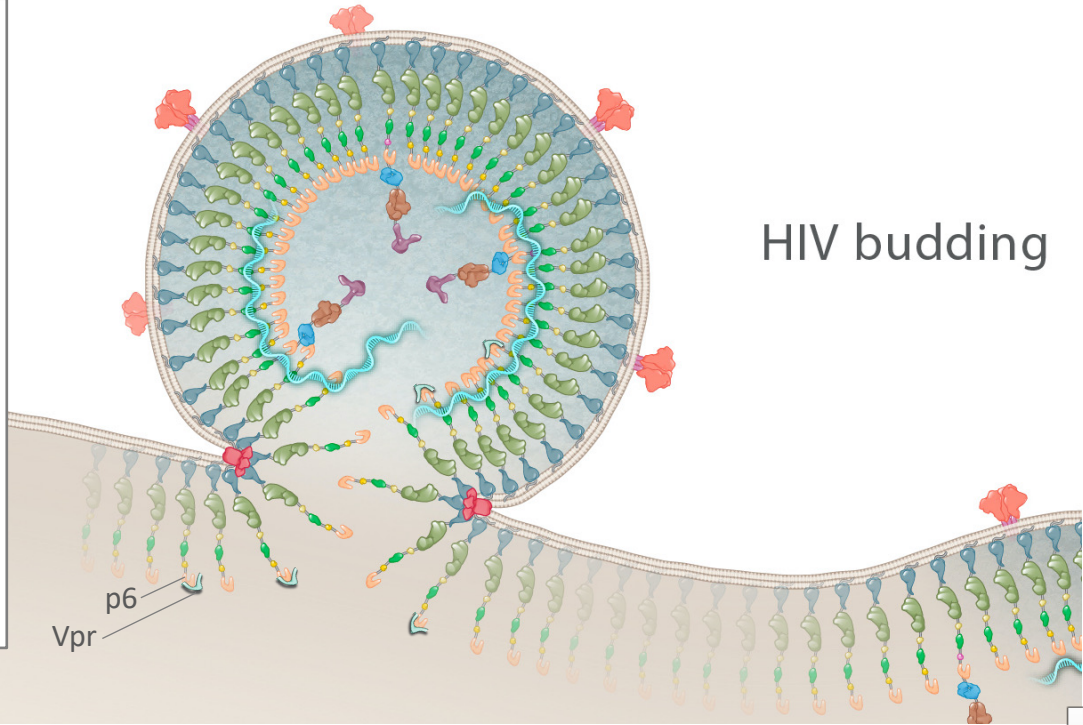
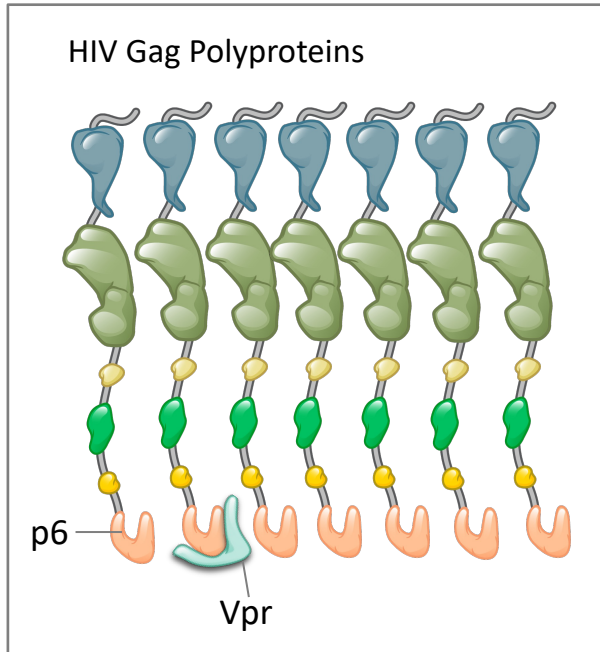
Gag Polyproteins



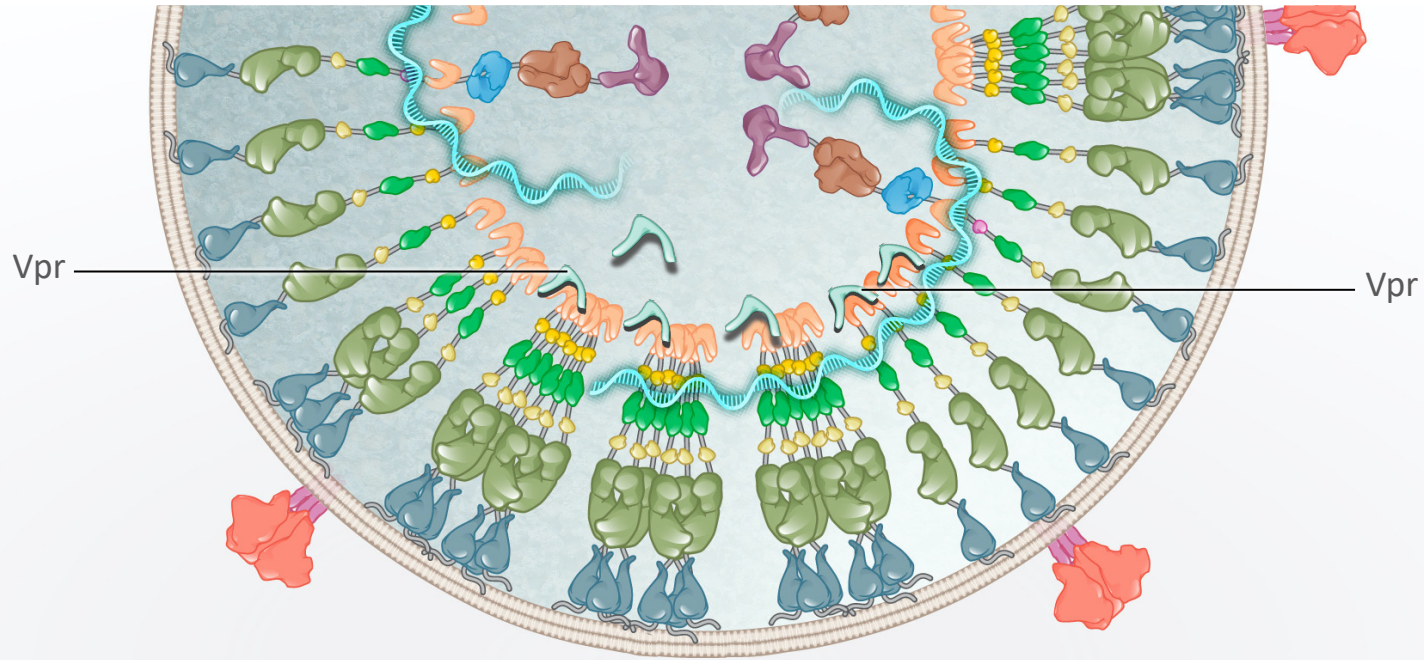
HIV p6: Role in HIV Budding



HIV p6: Role as Docking Site for Vpr

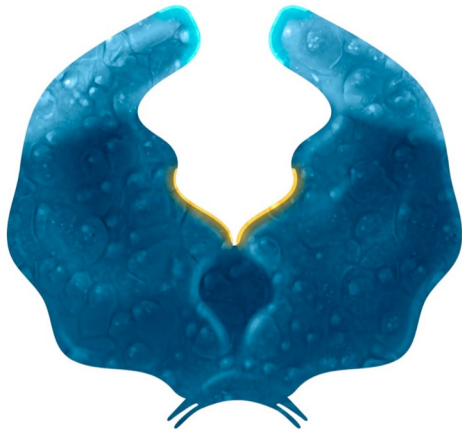


HIV p6: Facilitates Incorporation of Vpr



HIV Enzymes

HIV Enzymes



Protease



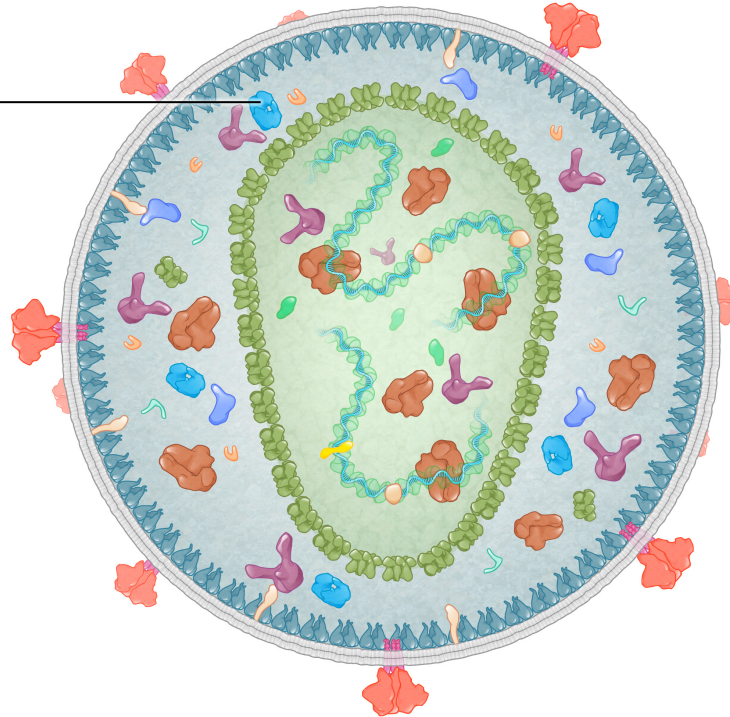
Reverse Transcriptase



Integrase

HIV Protease

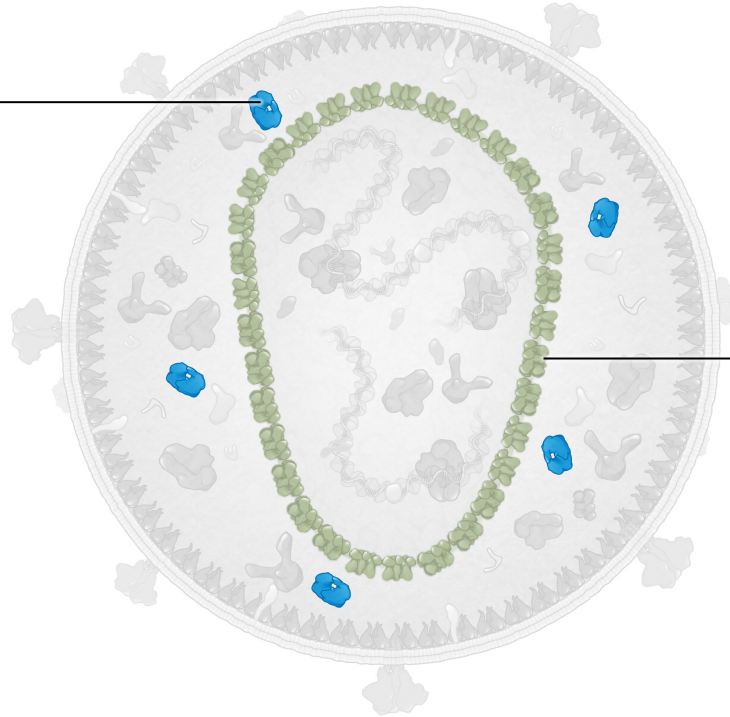
HIV Protease



HIV Protease

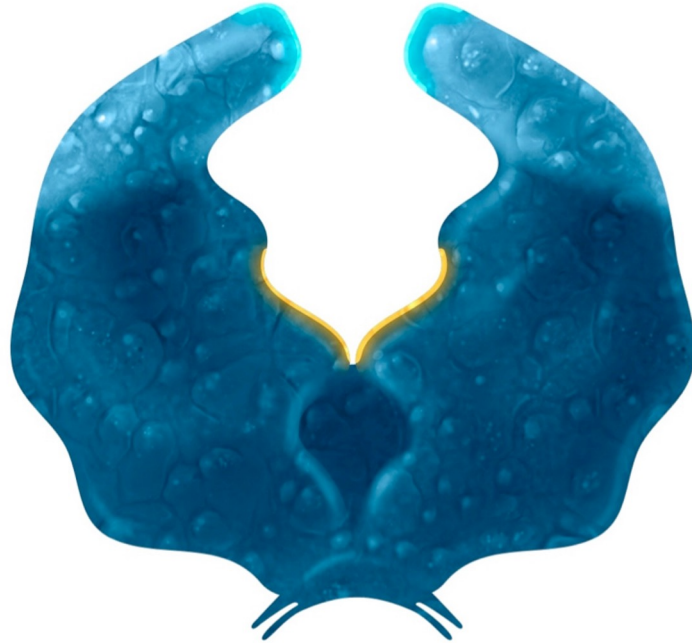
Enzyme

HIV Protease

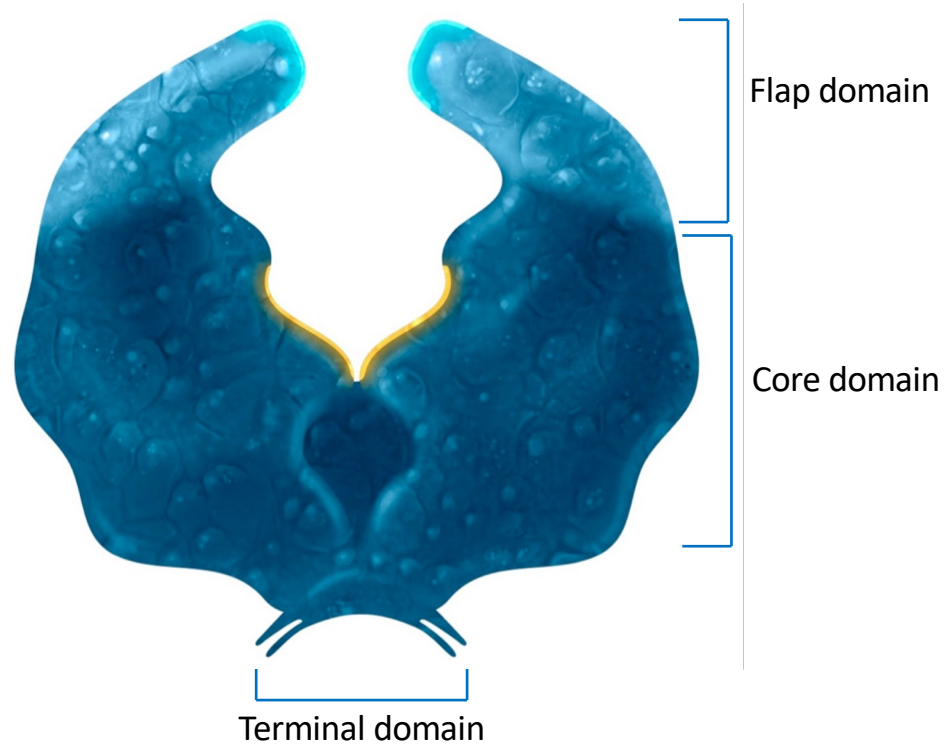


HIV Core

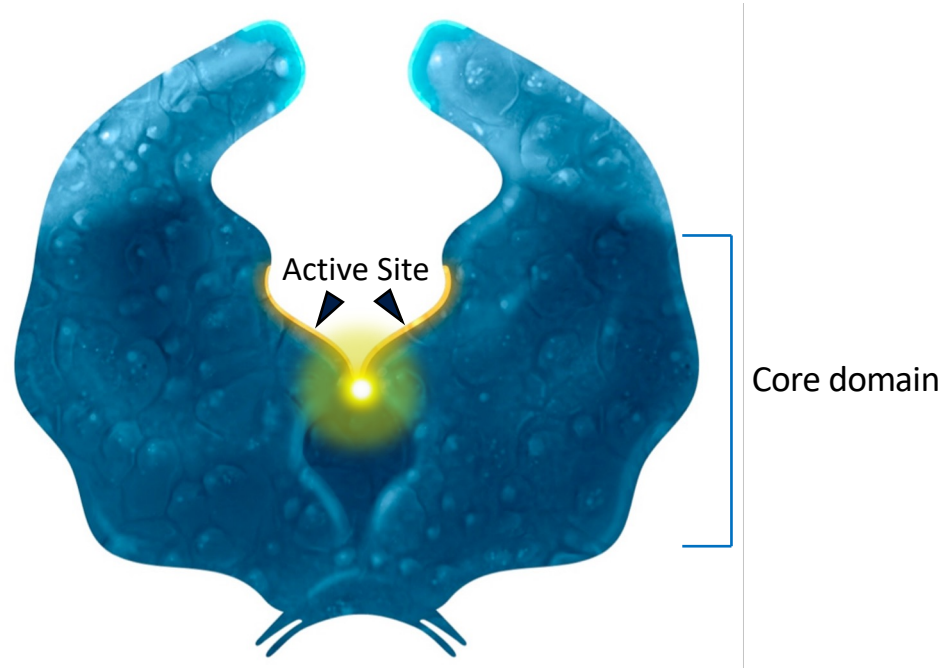
HIV Protease: Homodimer Structure



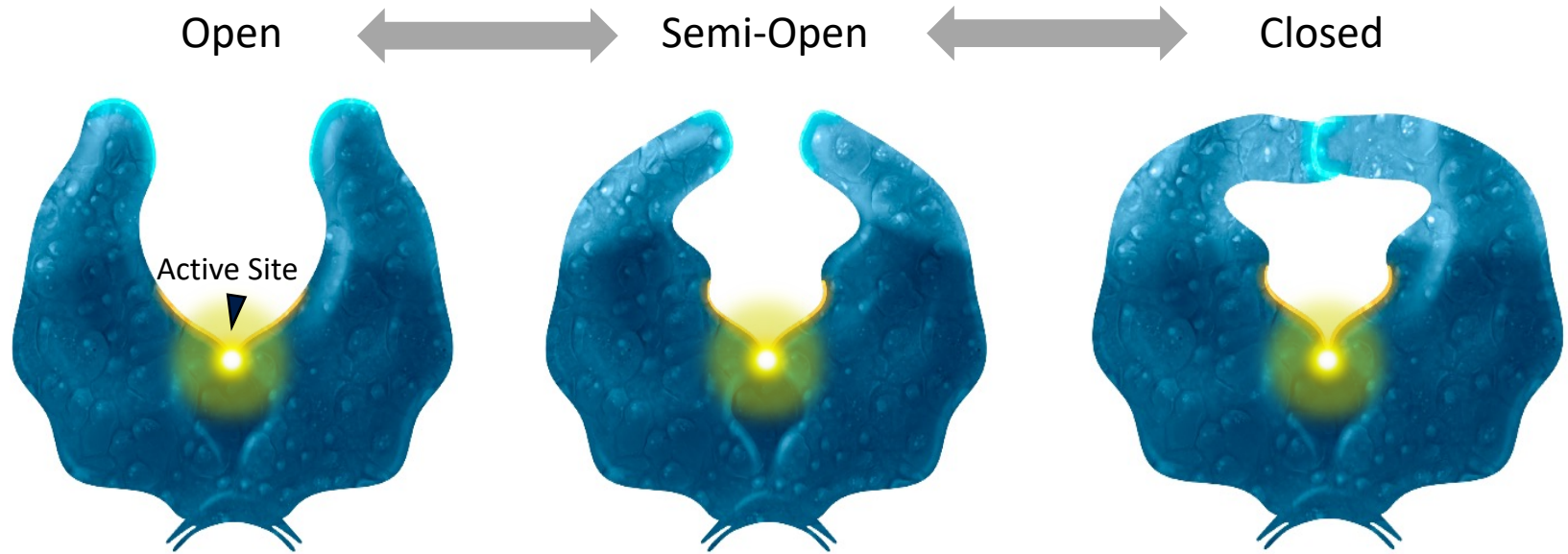
HIV Protease: Structural Domains



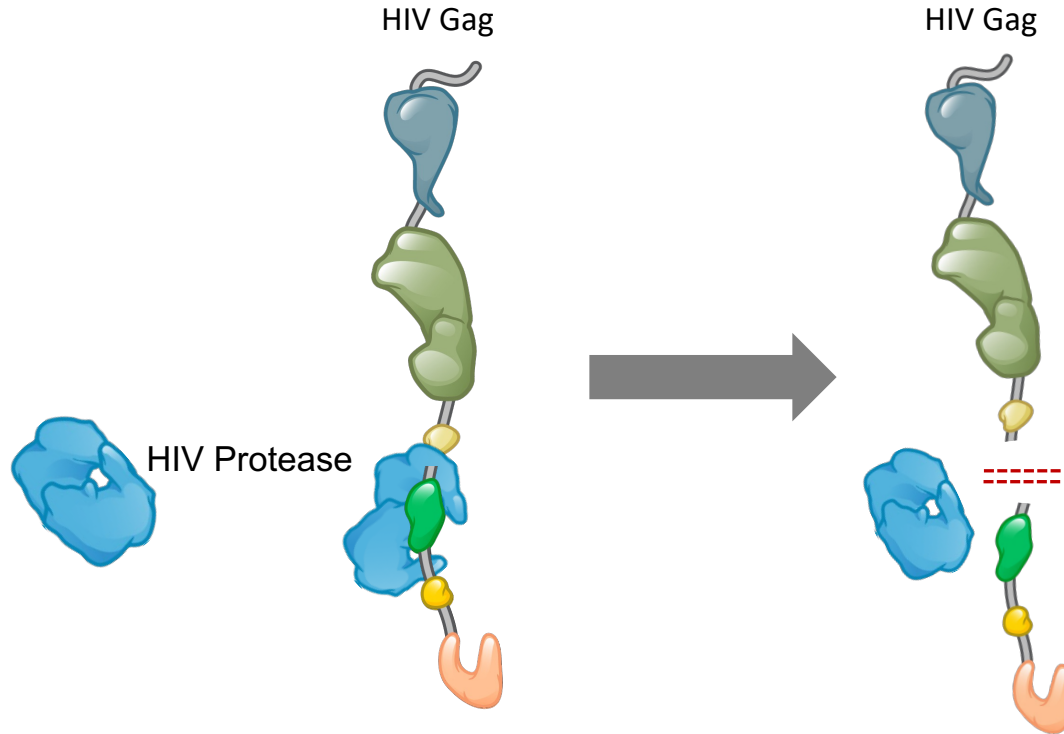
HIV Protease: Active Site



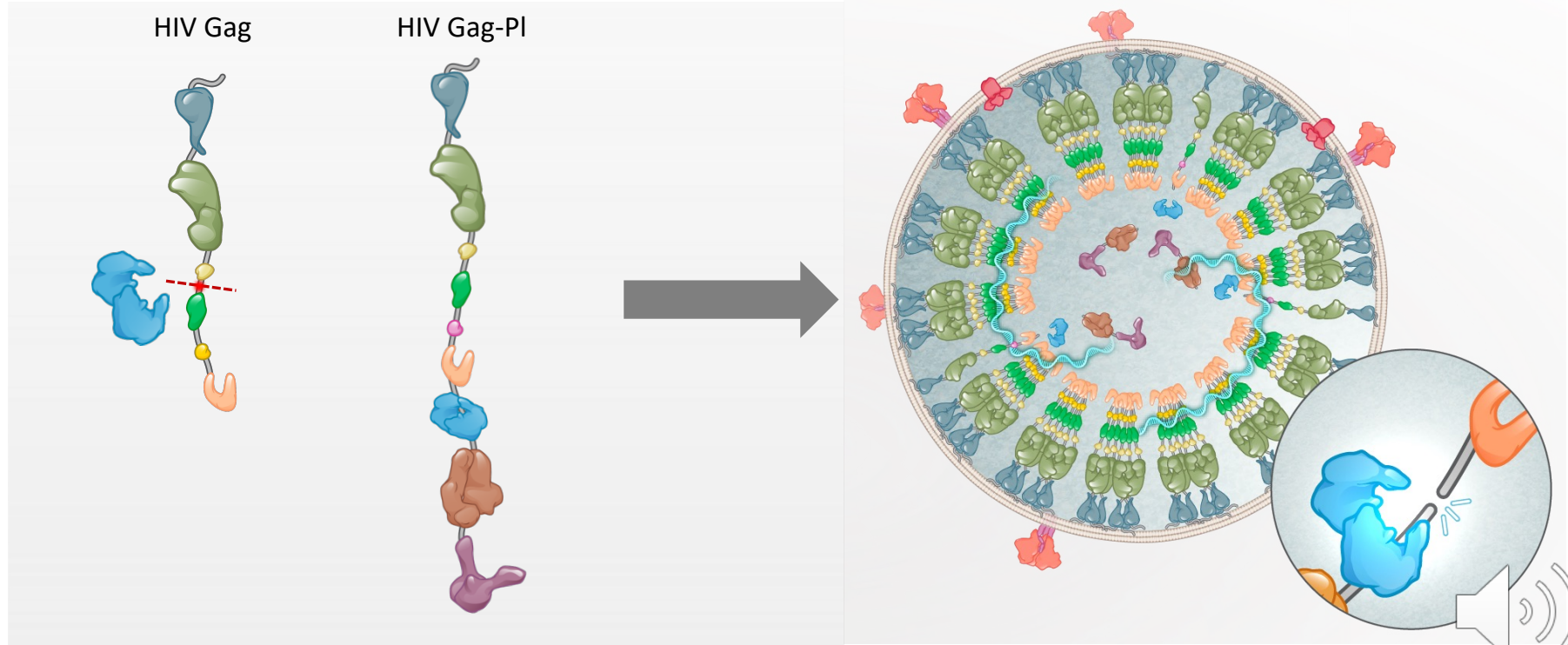
HIV Protease: Conformations



HIV Protease: Polypeptide Cleavage

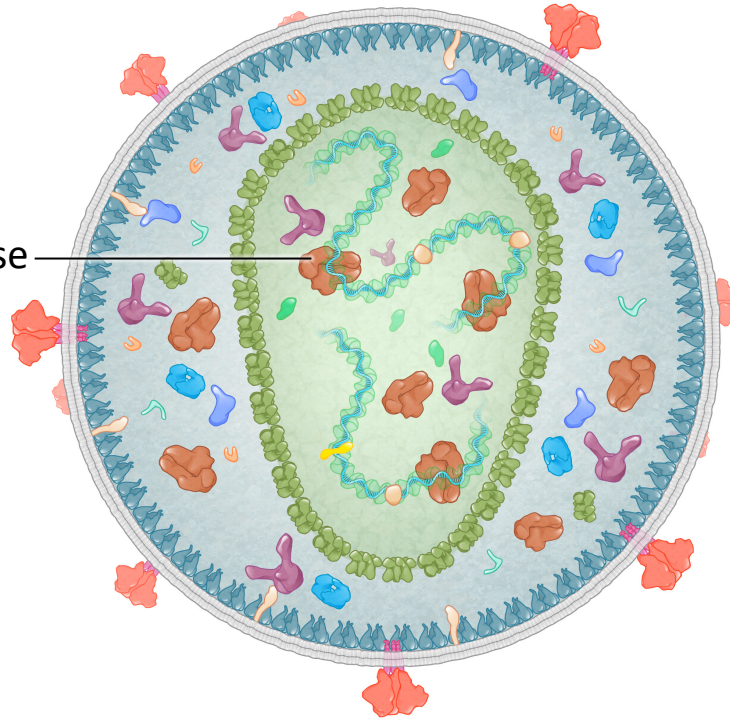


HIV Protease: Polypeptide Cleavage

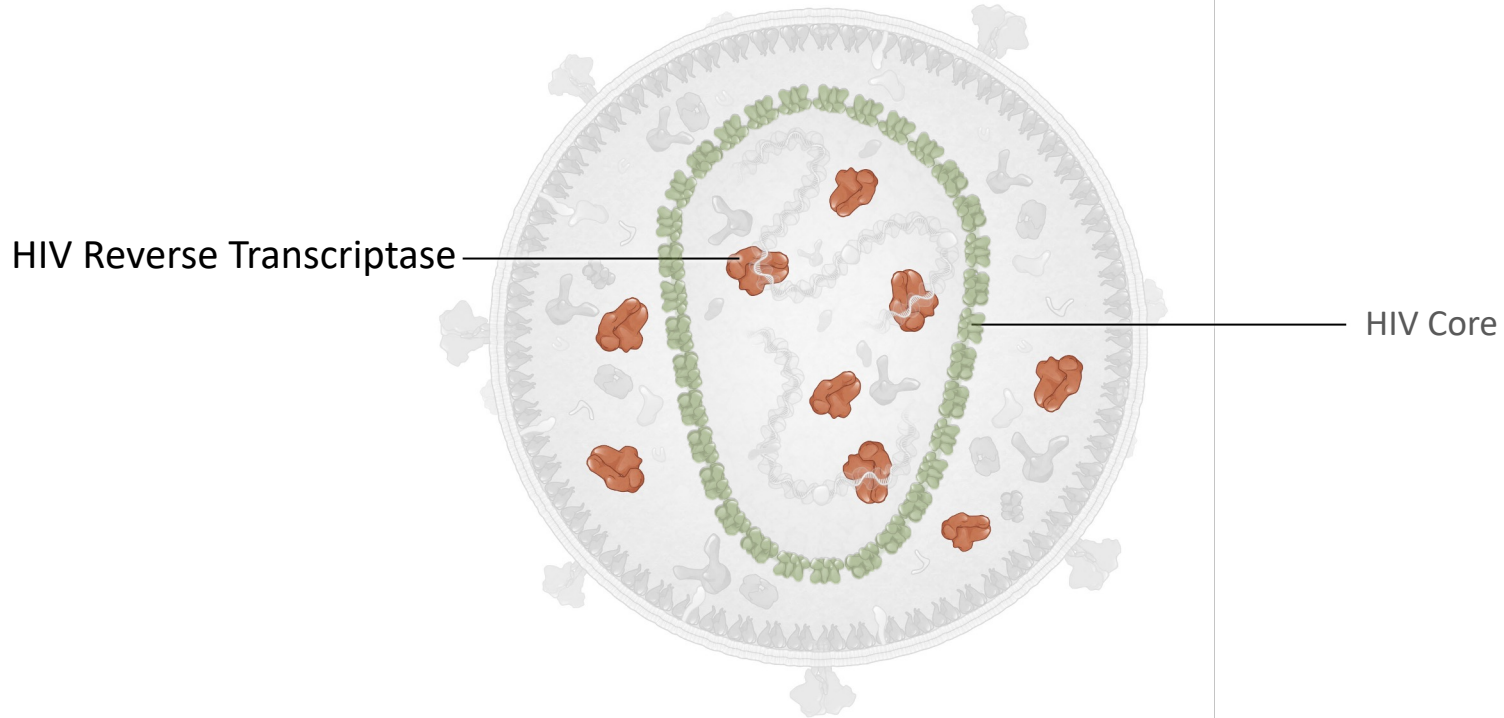


HIV Reverse Transcriptase

HIV Reverse Transcriptase



HIV Reverse Transcriptase



Enzyme

HIV Reverse Transcriptase: Subunits



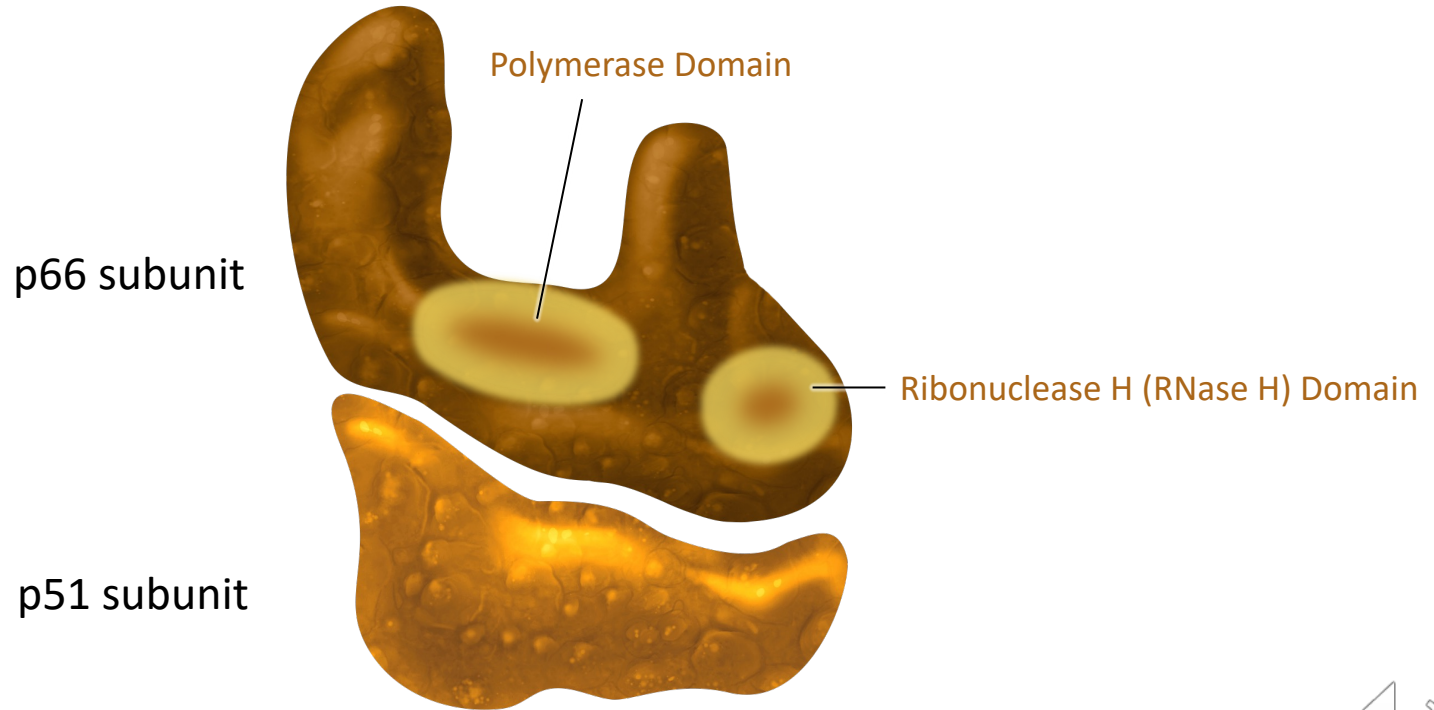
HIV Reverse Transcriptase: Subunits

p66 subunit

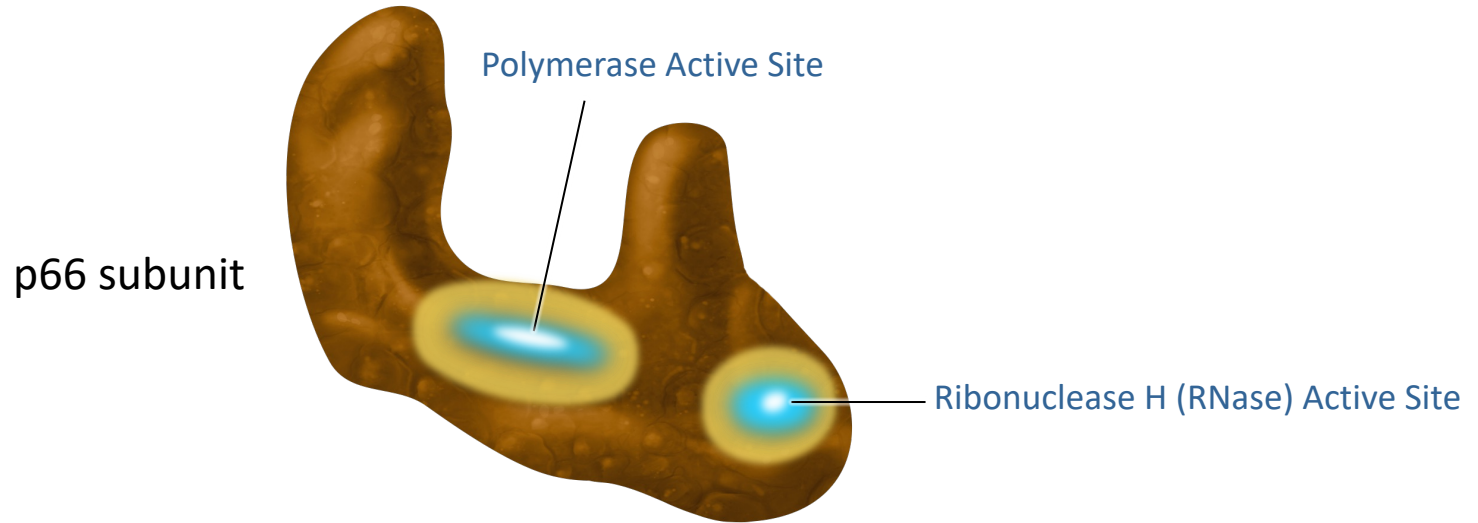
p51 subunit



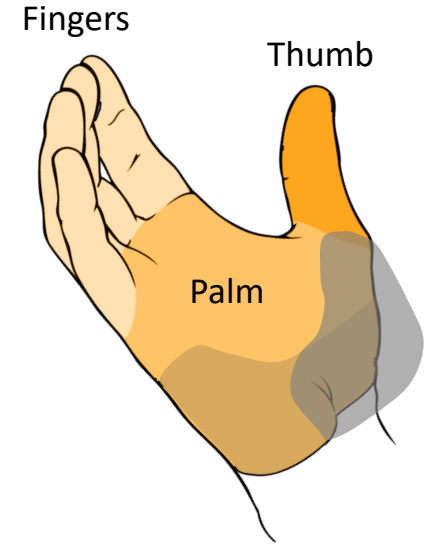
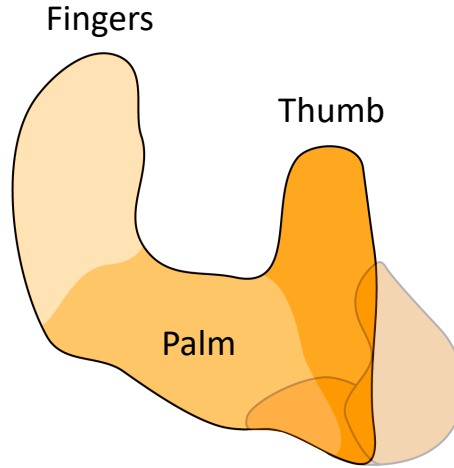
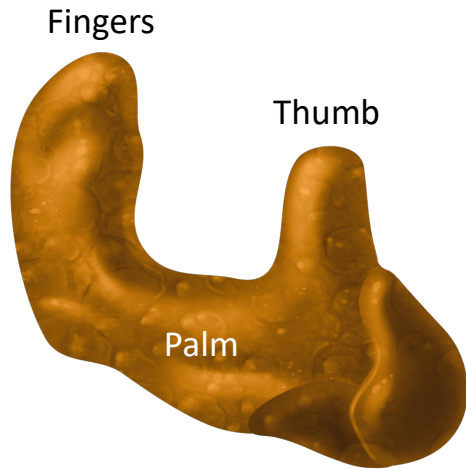
HIV Reverse Transcriptase: Enzymatic Domains



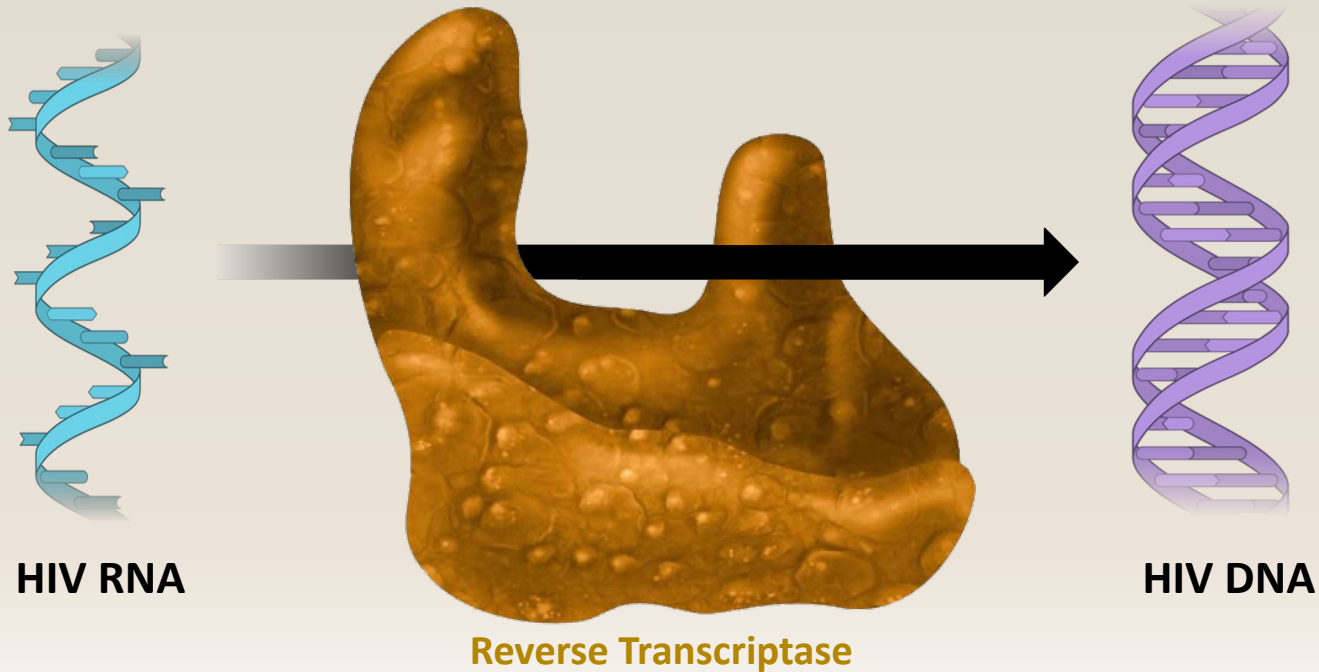
HIV Reverse Transcriptase: Enzyme Active Sites



HIV Reverse Transcriptase: p66 Subunit Right Hand Structure

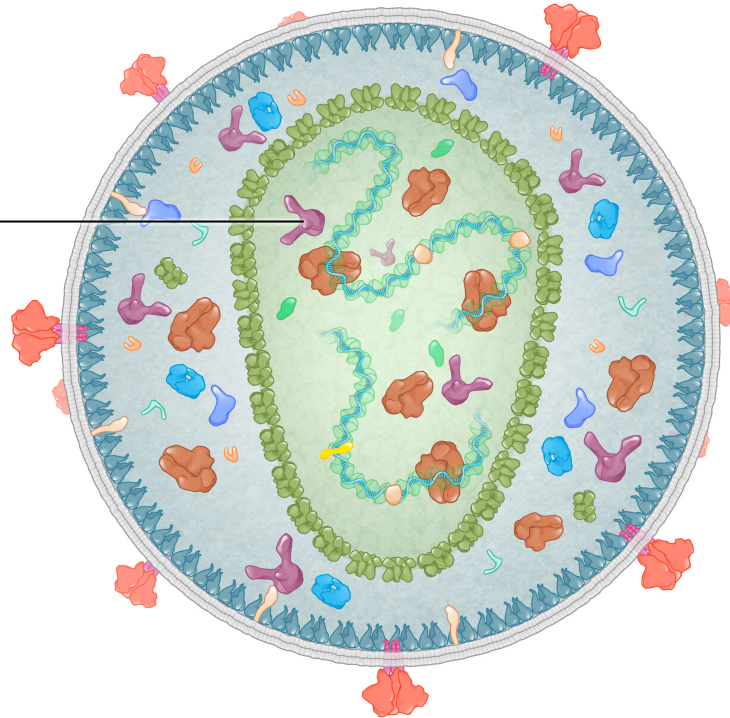


HIV Reverse Transcriptase: Reverse Transcription



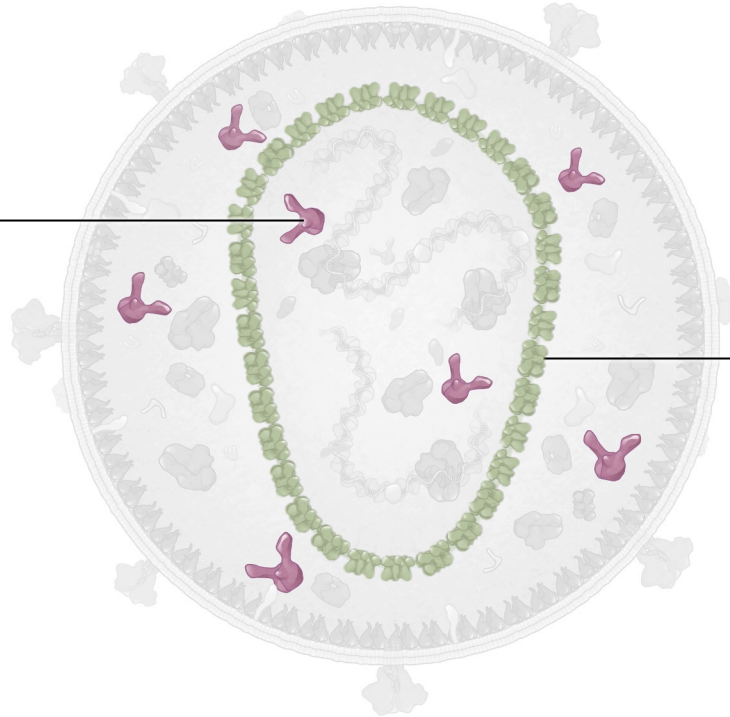
HIV Integrase

HIV Integrase



HIV Integrase

HIV Integrase

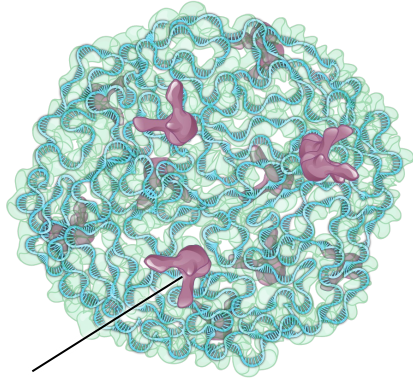


HIV Core

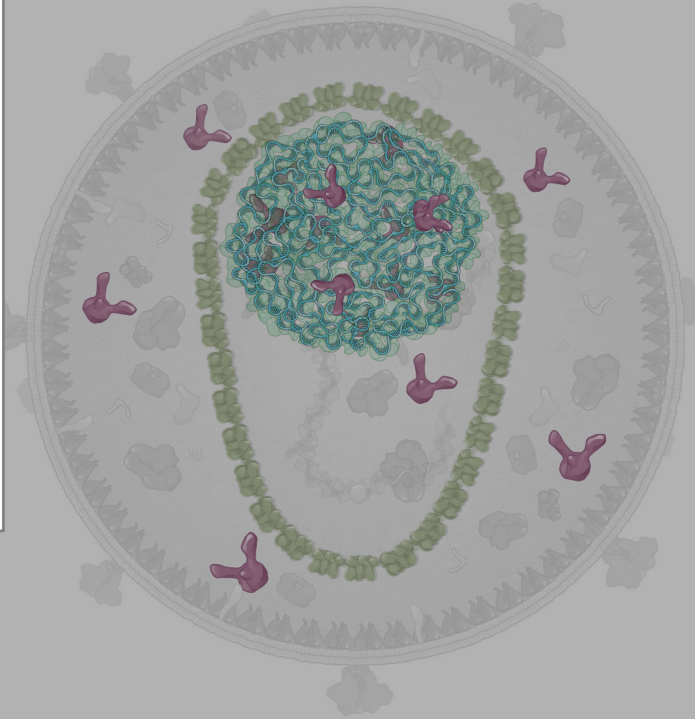
Enzyme

HIV Integrase: Component of Ribonucleoprotein Complex

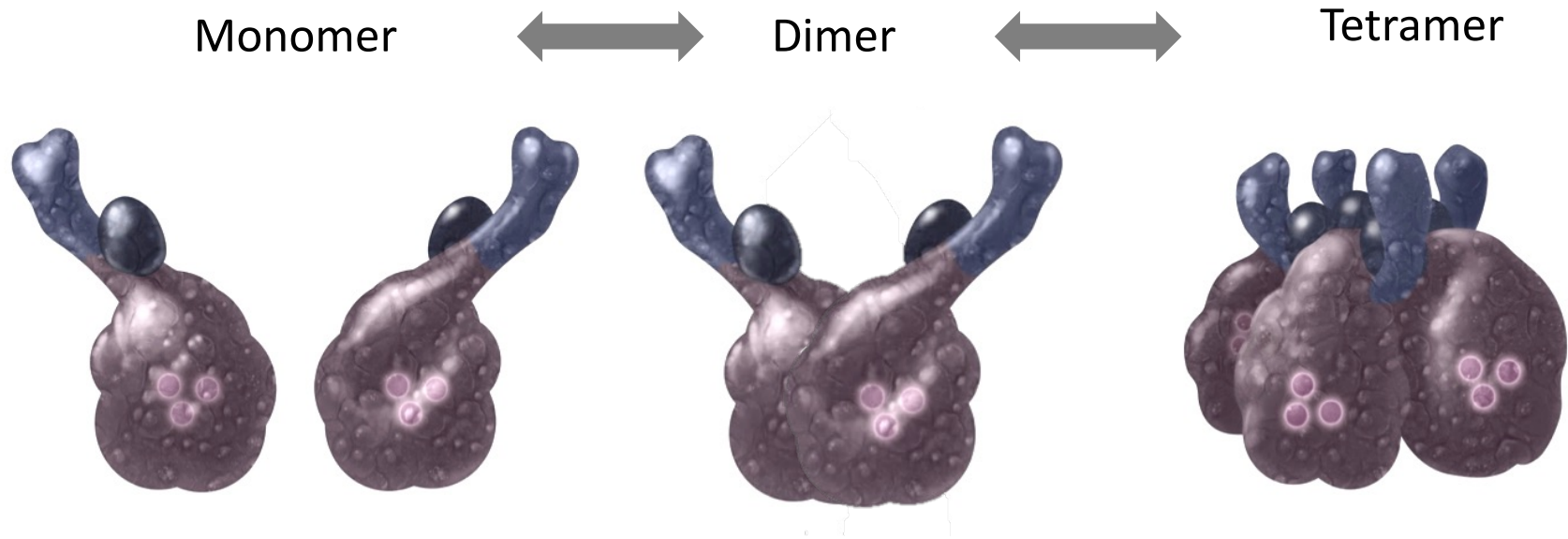
HIV Ribonucleoprotein Complex



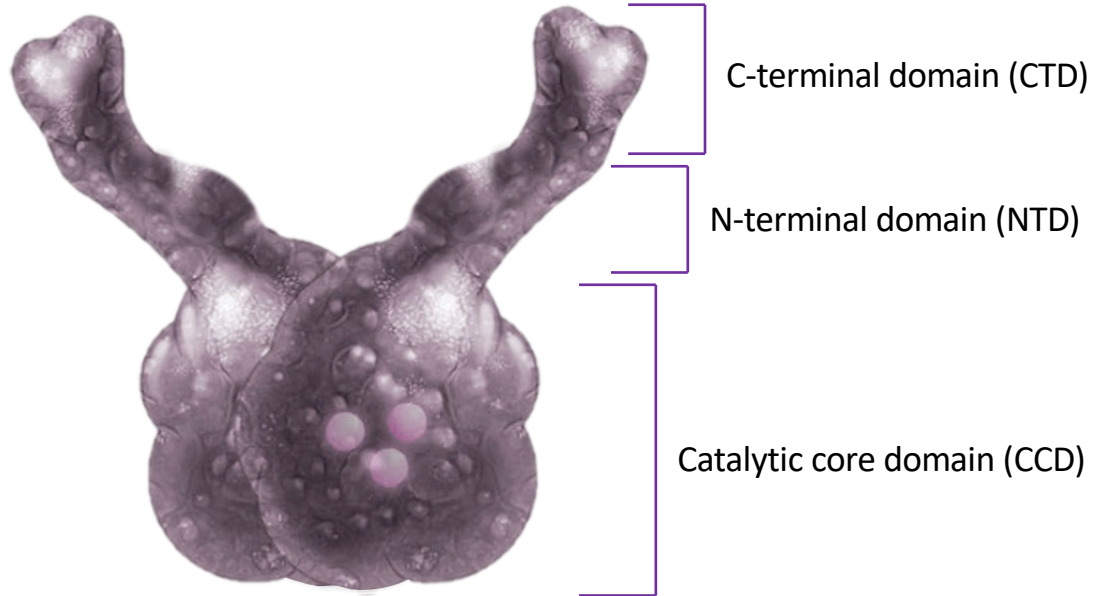
Integrase



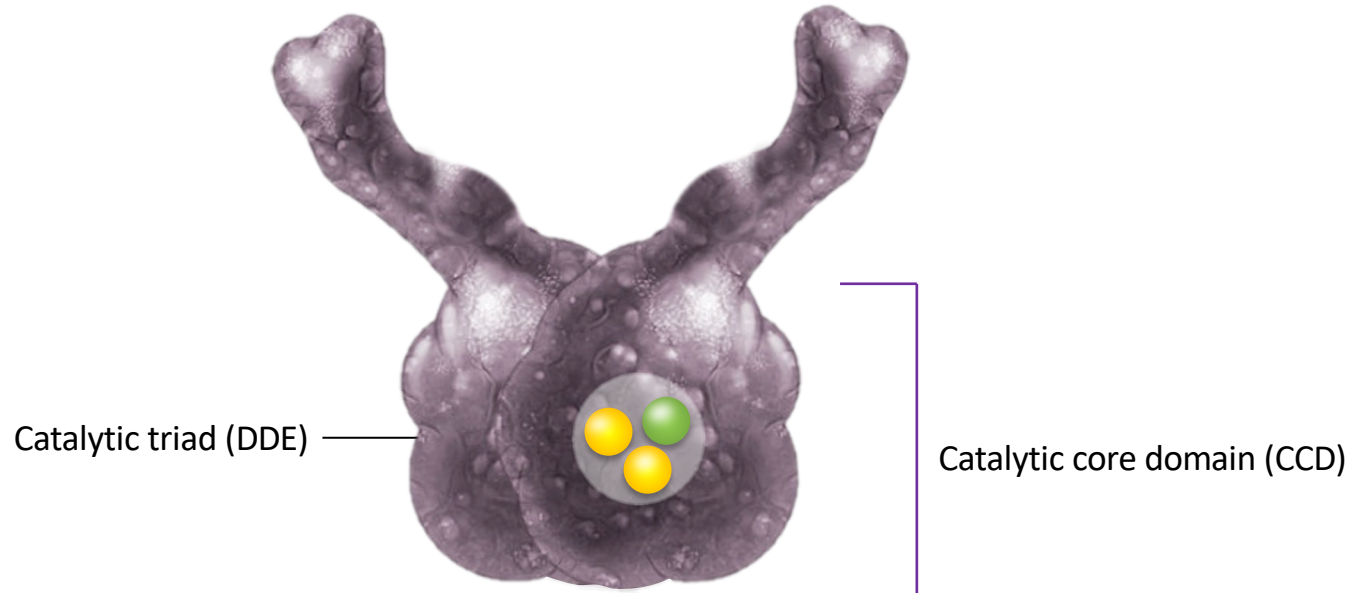
HIV Integrase: Complexes



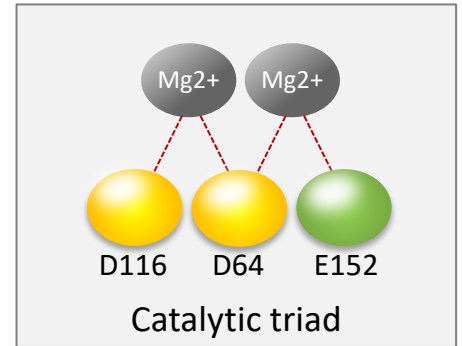
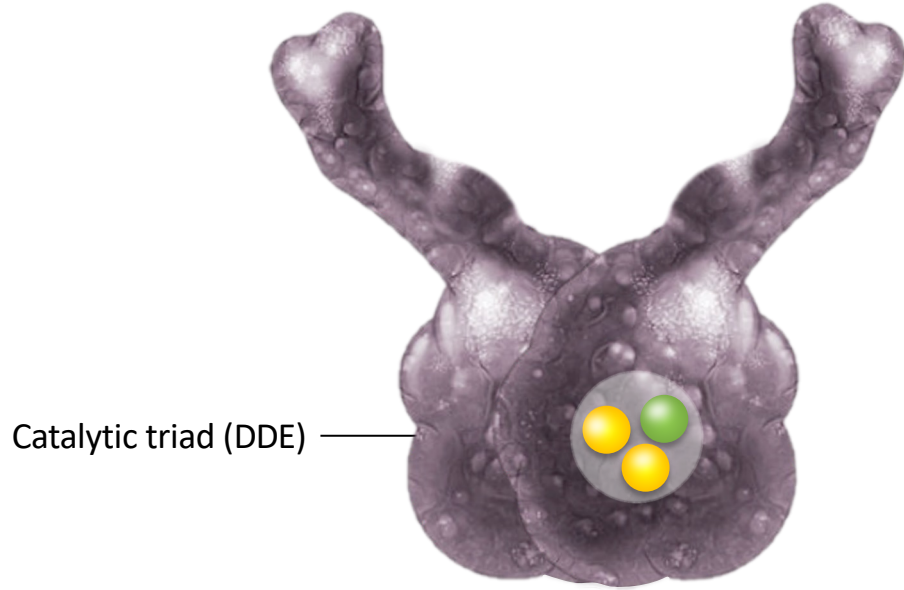
HIV Integrase: Dimer Structure



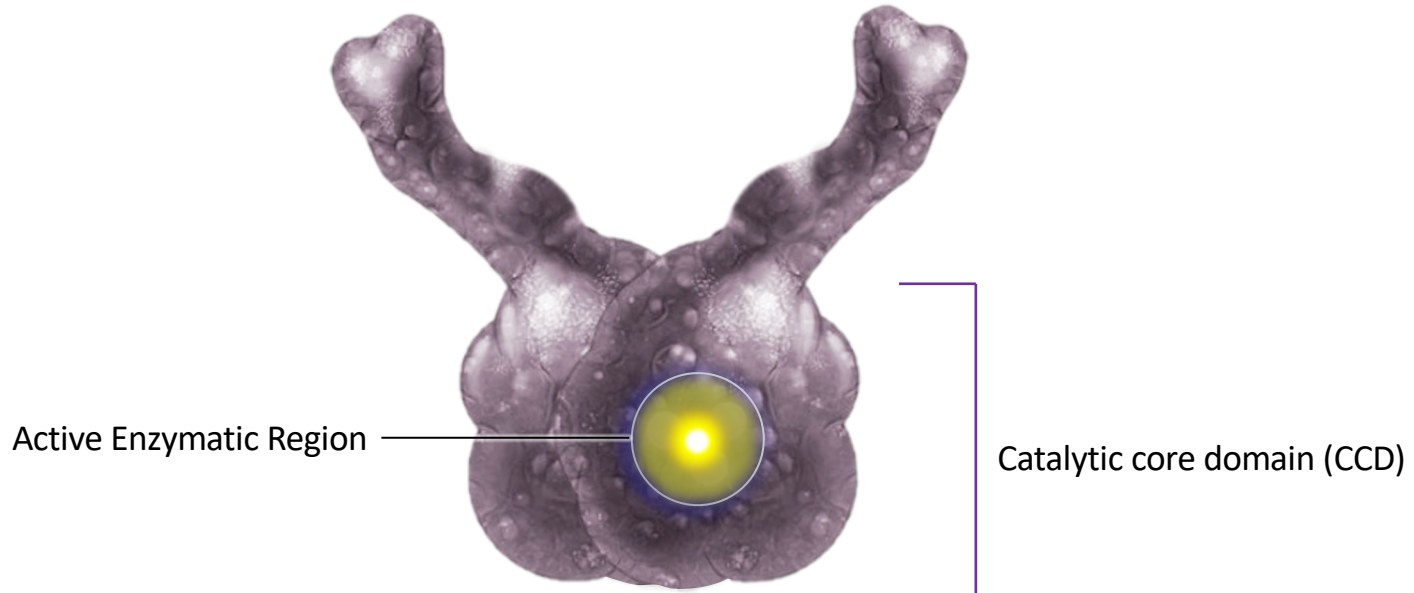
HIV Integrase: Catalytic Core Domain



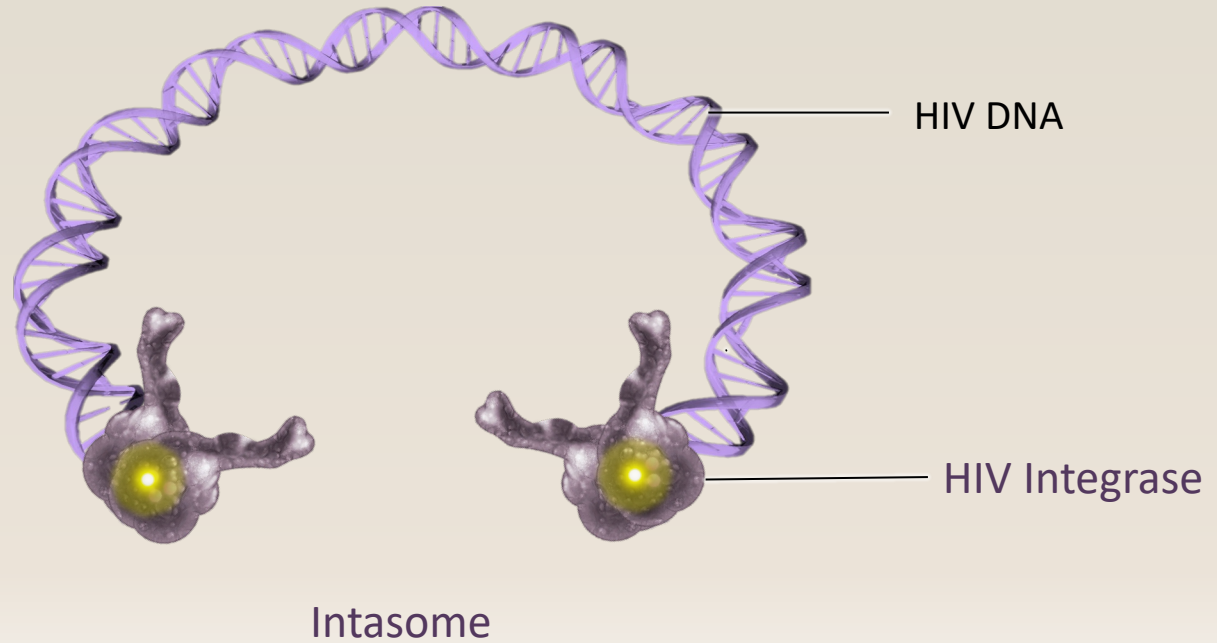
HIV Integrase: Catalytic Core Domain



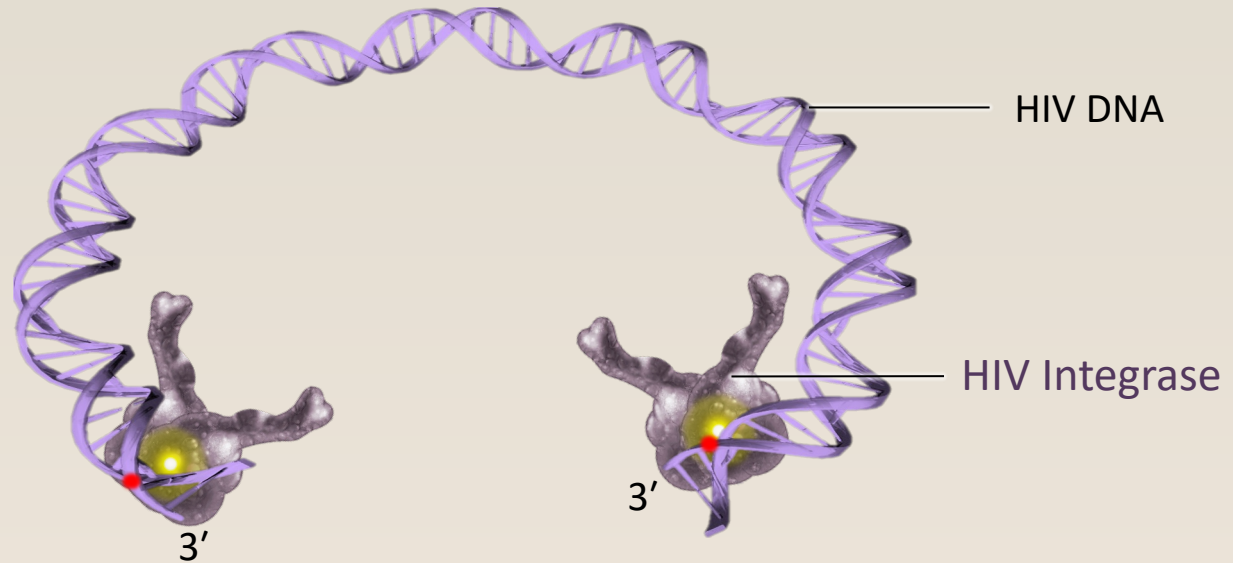
HIV Integrase: Active Enzymatic Region



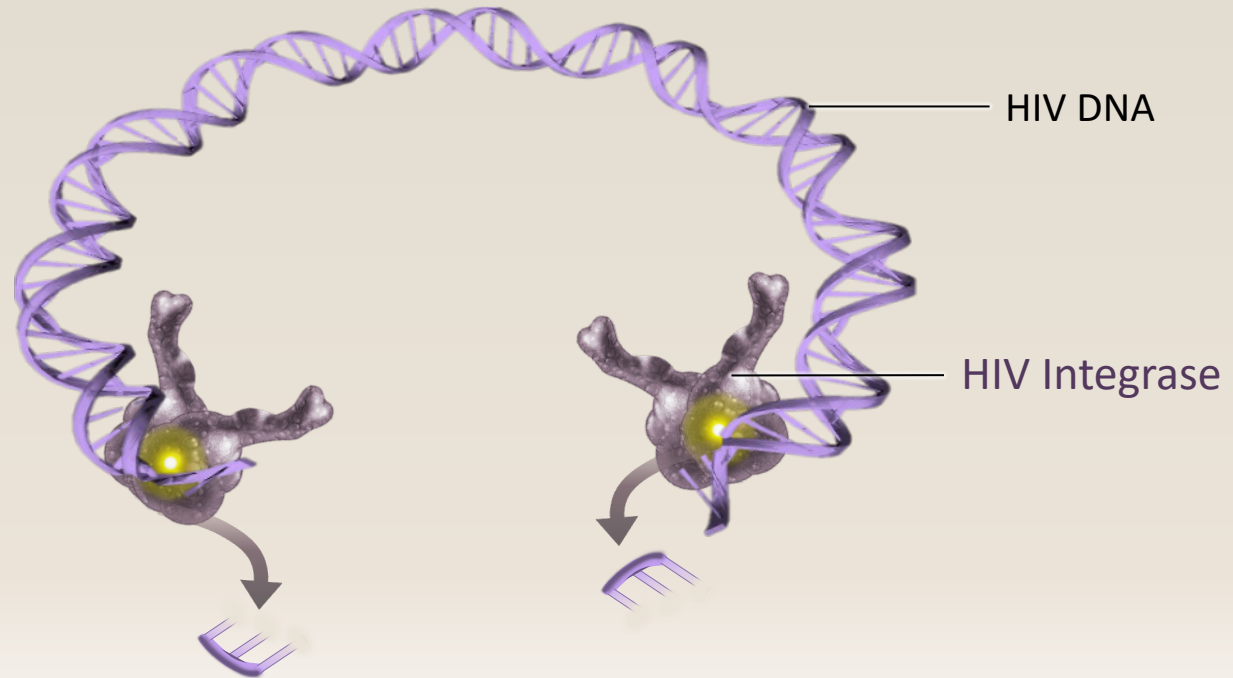
HIV Integrase: Intasome Formation



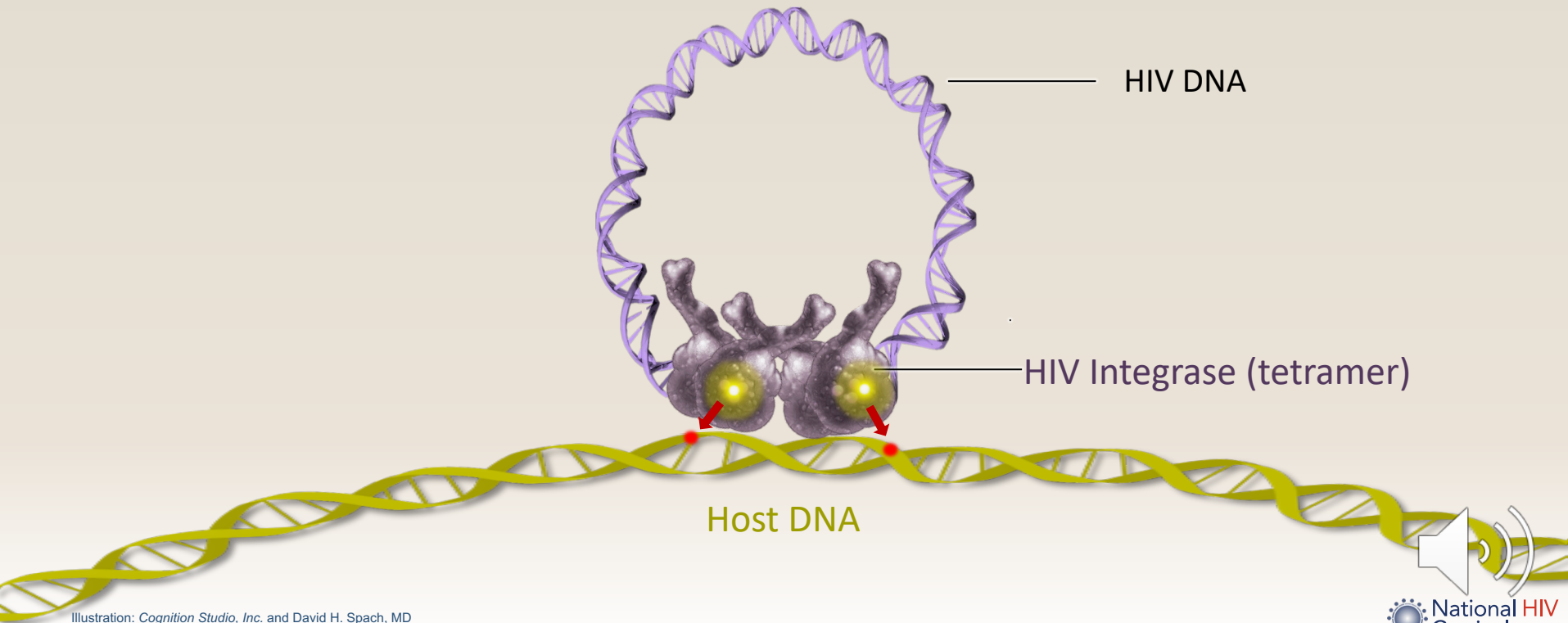
HIV Integrase: 3' Processing of HIV DNA



HIV Integrase: 3' Processing of HIV DNA



HIV Integrase: Strand Transfer

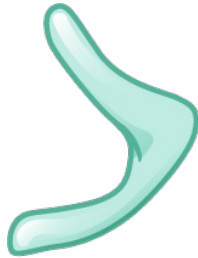


HIV Accessory and Regulatory Proteins

HIV Accessory Proteins



Vif



Vpr



Vpu



Nef

Viral Infectivity Factor (Vif)

Accessory Protein



Vif

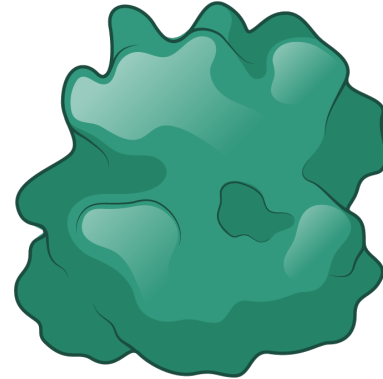
Vif and Host Restriction Factor APOBEC3G

Accessory Protein



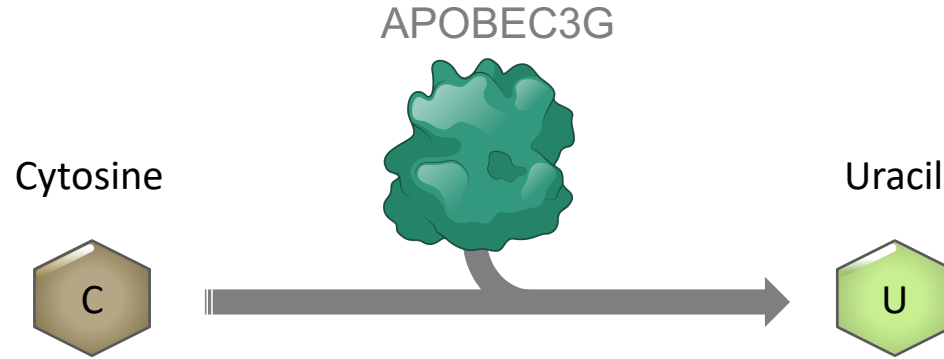
Vif

Host Restriction Factor

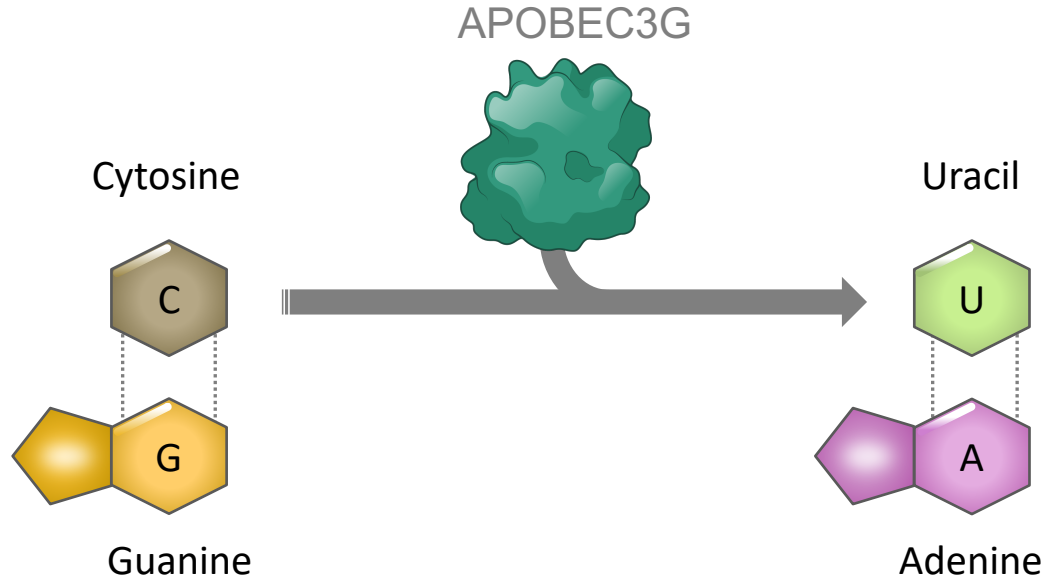


APOBEC3G

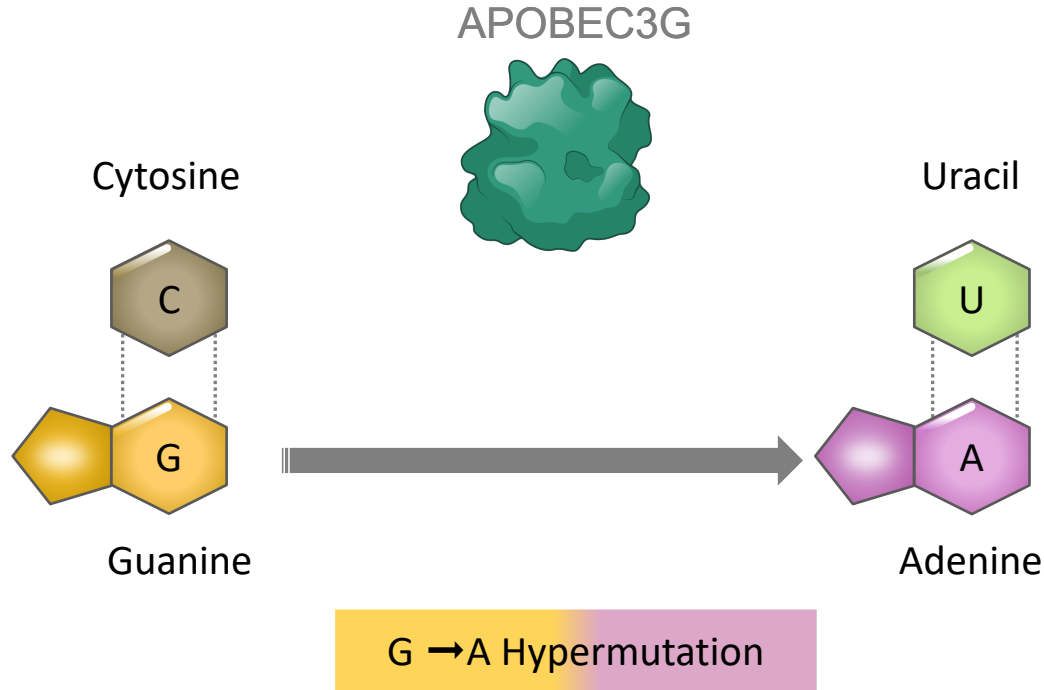
APBOPEC3G Conversion of Cytosine to Uracil



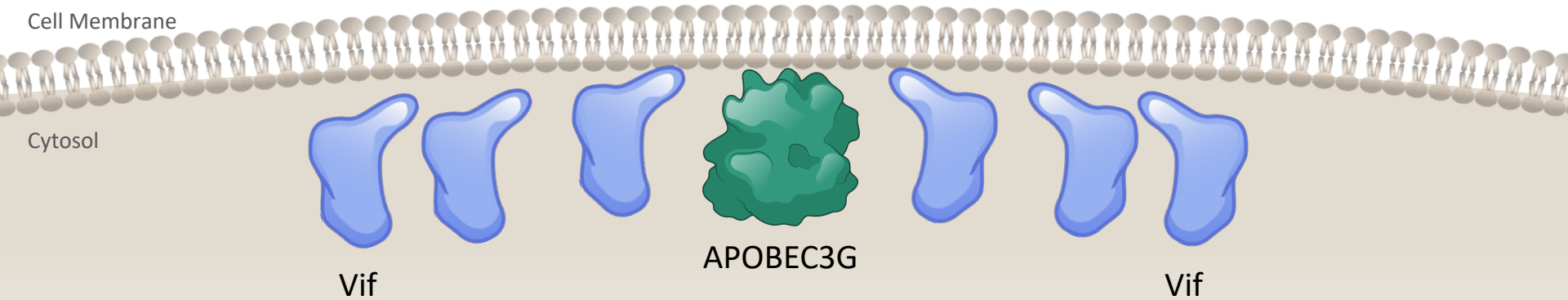
APOBEC3G-Induced Altered Base Pairing



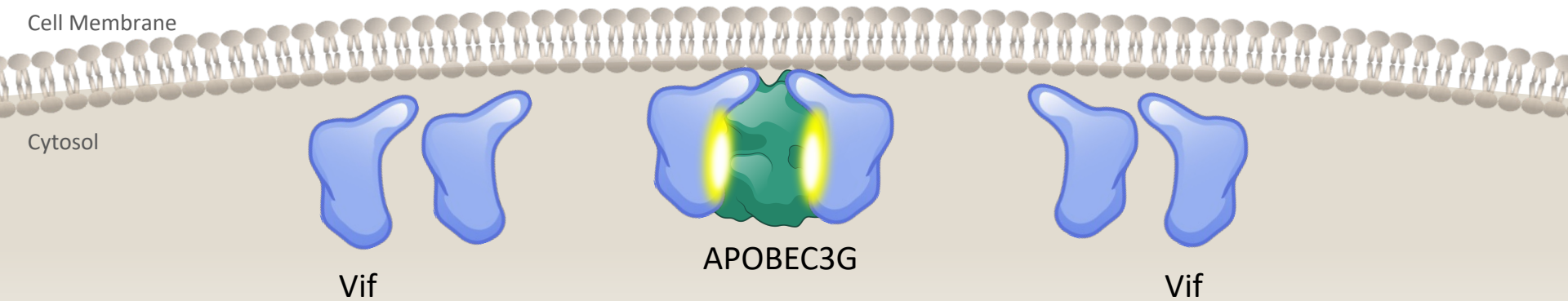
APBOPEC3G-Induced “G to A” Hypermuration



Vif: Clustering at Host Cell Membrane



Vif: Binding to APOBEC3G at Host Cell Membrane

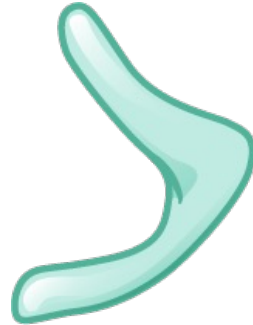


Vif: Neutralizing Action of APOBEC3G



Viral Protein R (Vpr)

Accessory Protein



Vpr

Vpr: Component of HIV Core

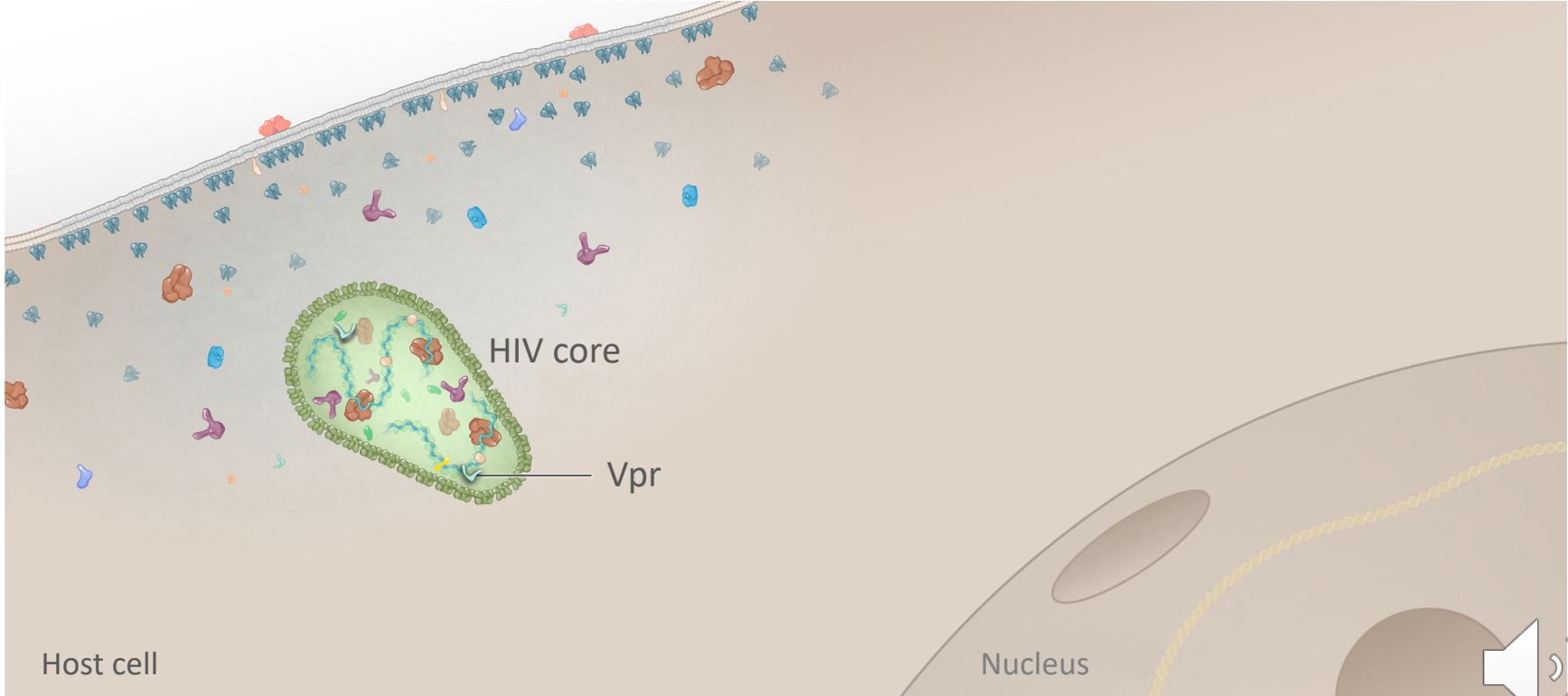
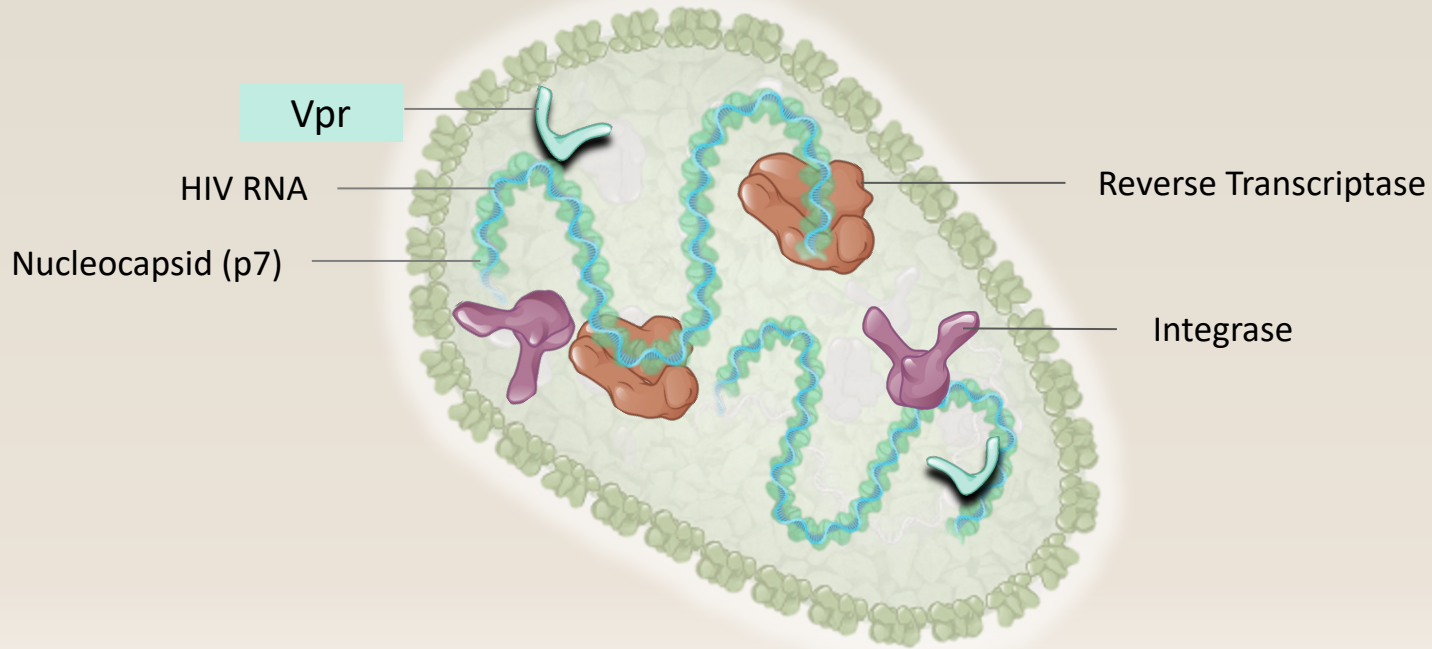
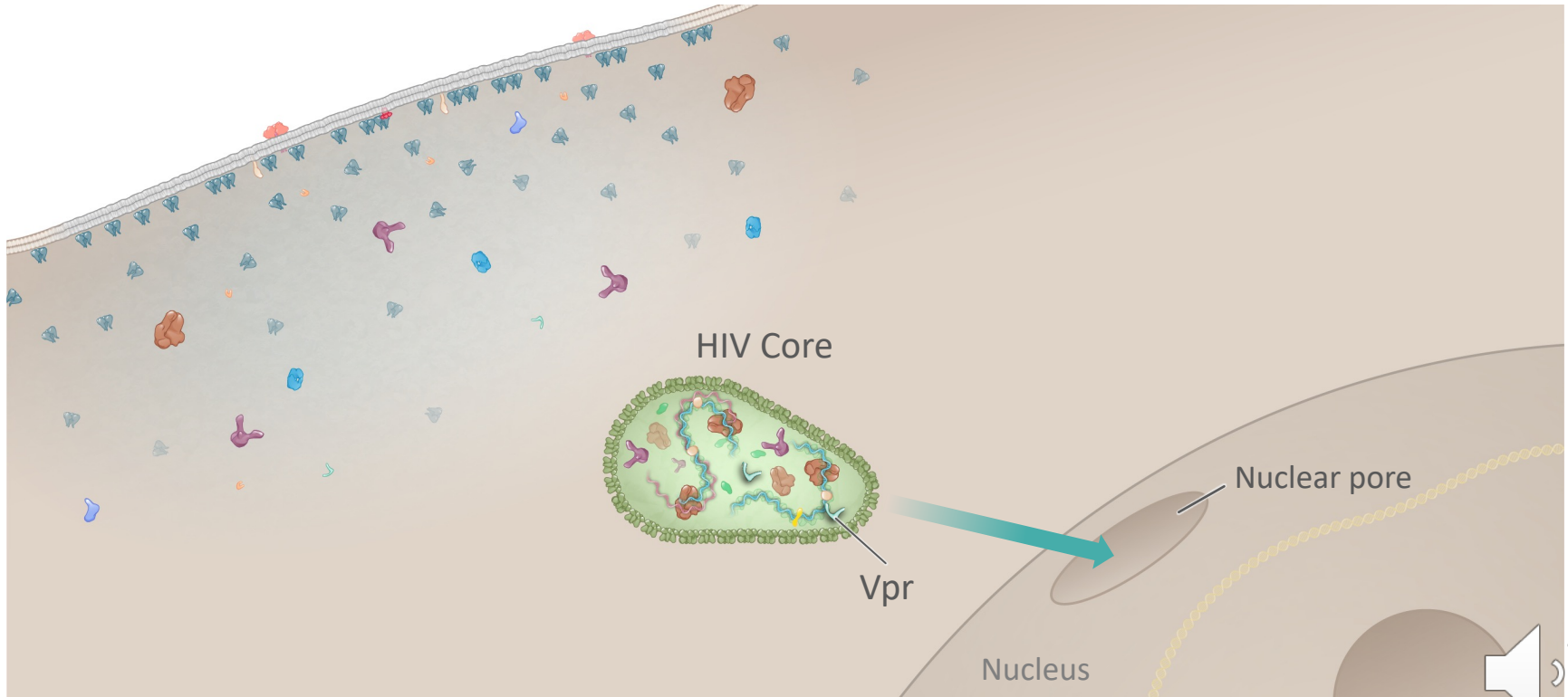


Illustration: Cognition Studio, Inc. and David H. Spach, MD

Vpr: Role in HIV Reverse Transcription



Vpr: Role in Nuclear Import



Viral Protein U (Vpu)

Accessory Protein



Vpu and Host Restriction Factor Tetherin

Accessory Protein



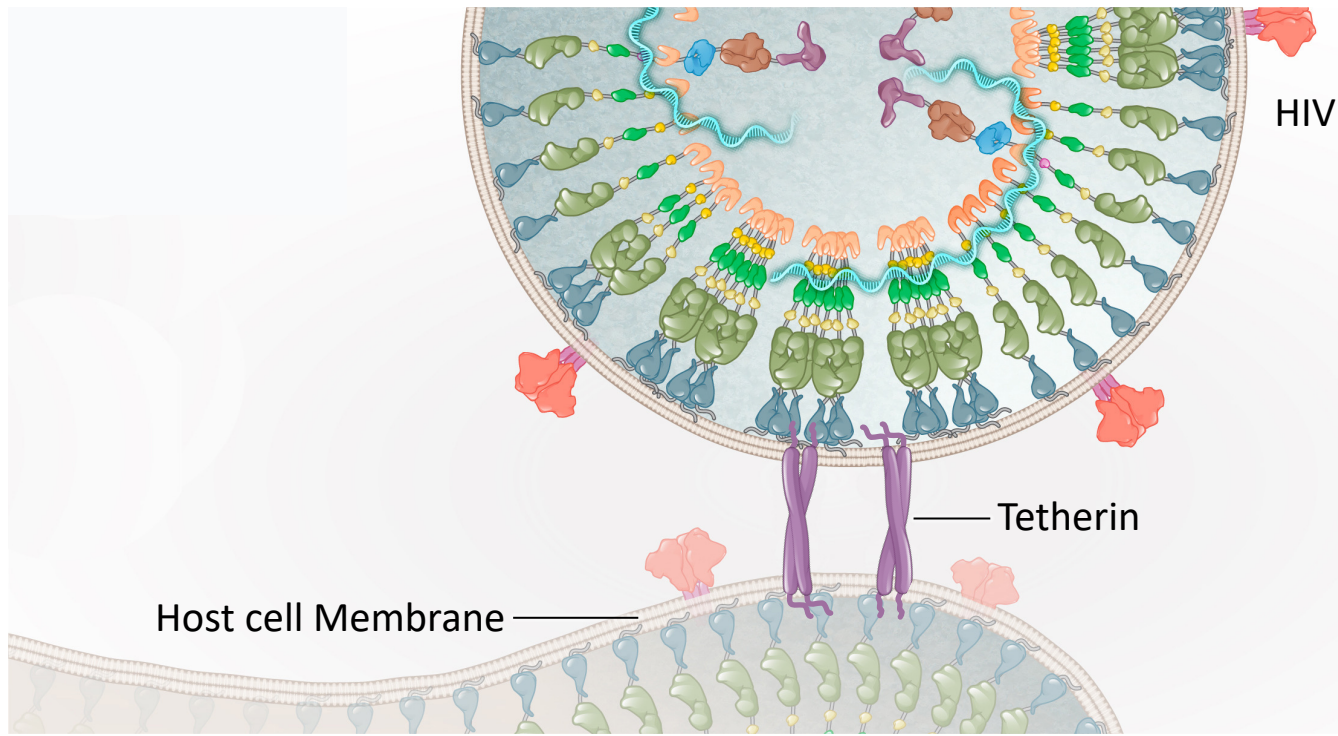
Vpu

Host Restriction Factor

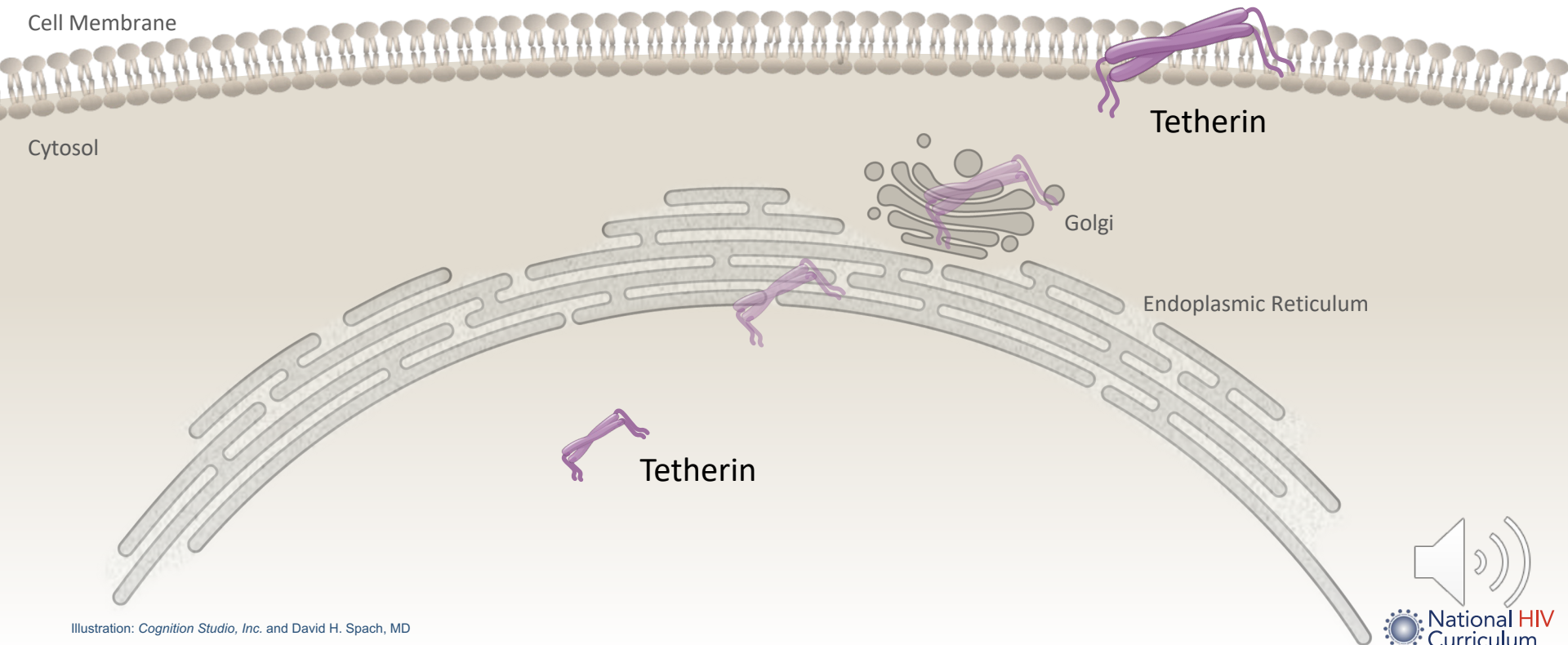


Tetherin (BST-2)

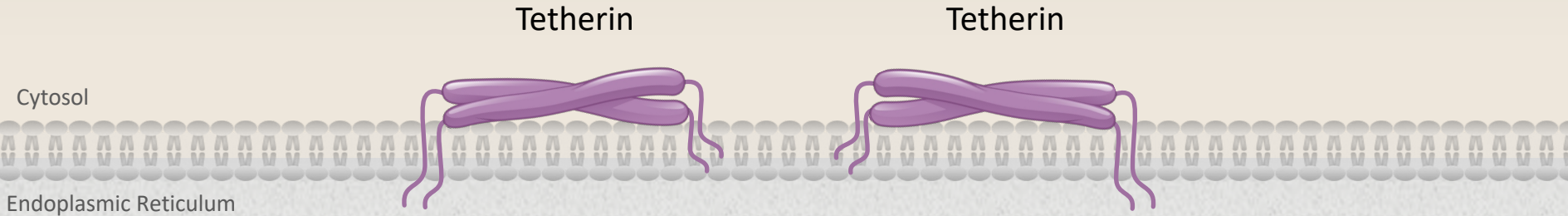
Tetherin: Prevention of Budding



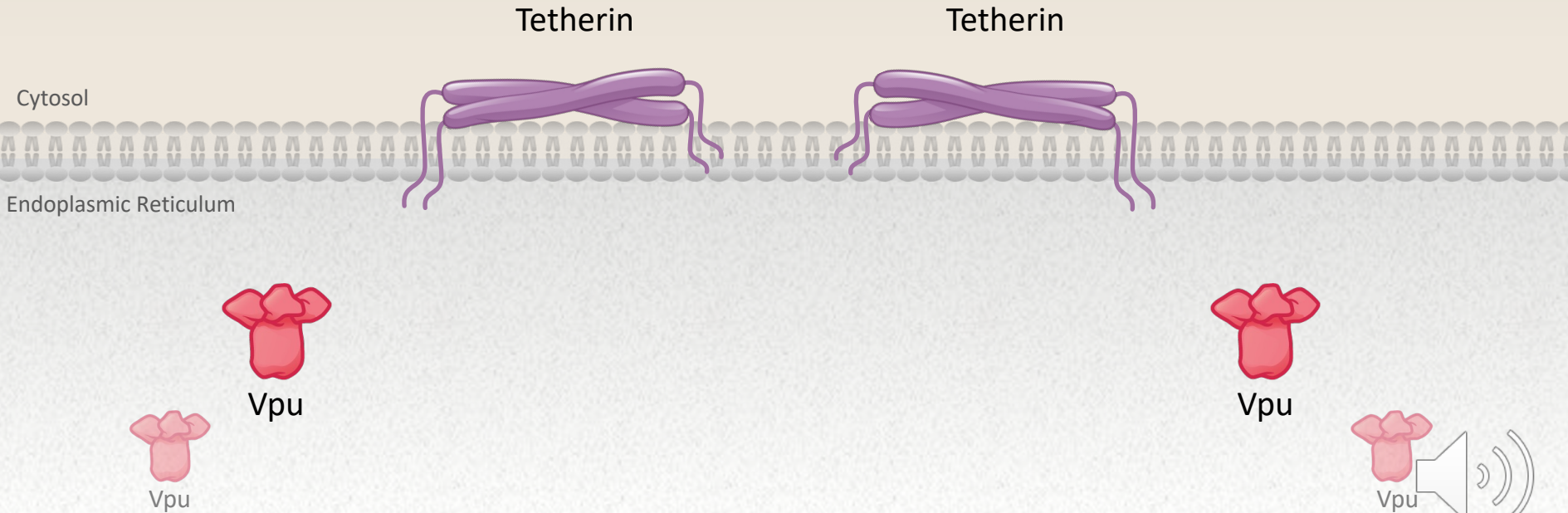
Tetherin: Synthesis in Endoplasmic Reticulum and Golgi



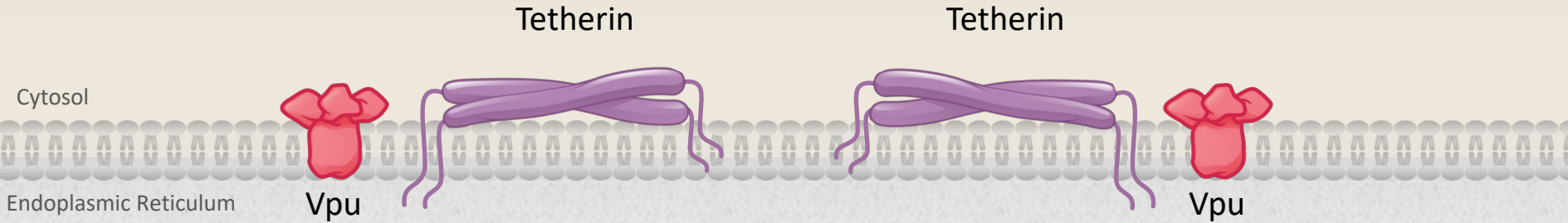
Tetherin: Bound to Endoplasmic Reticulum Membrane



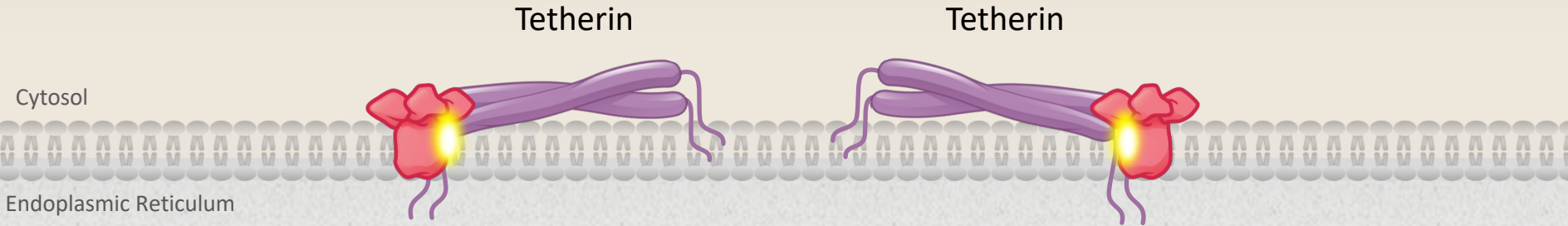
Vpu: Synthesis



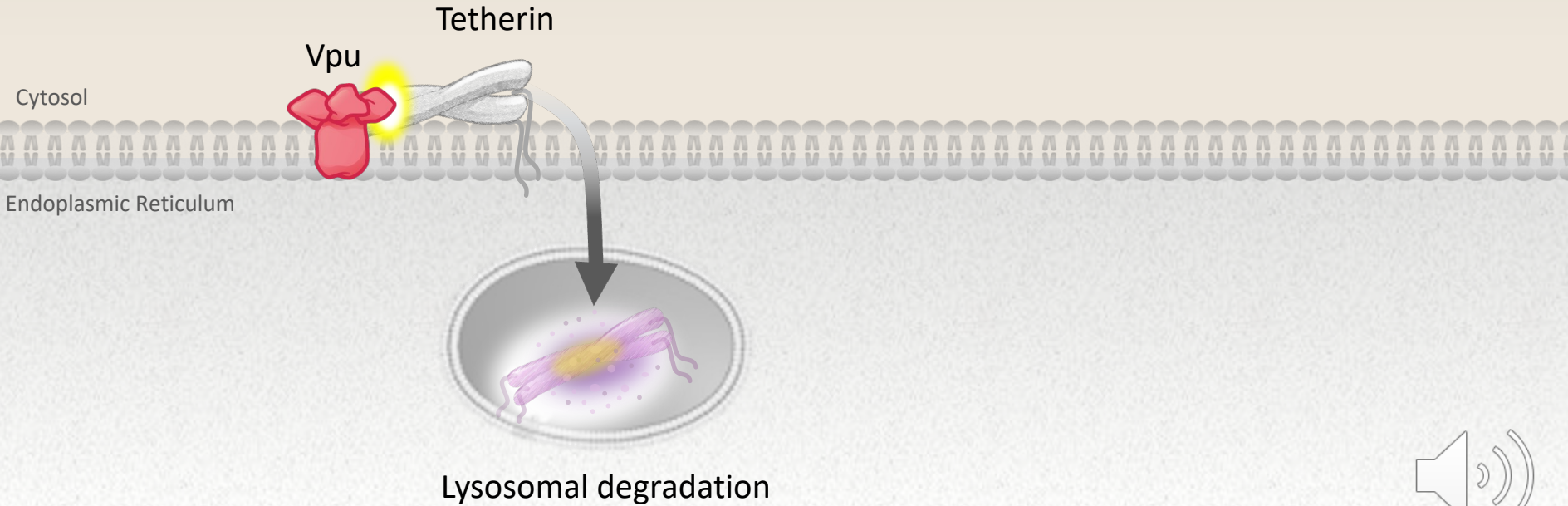
Vpu: Accumulation at Endoplasmic Reticulum Membrane



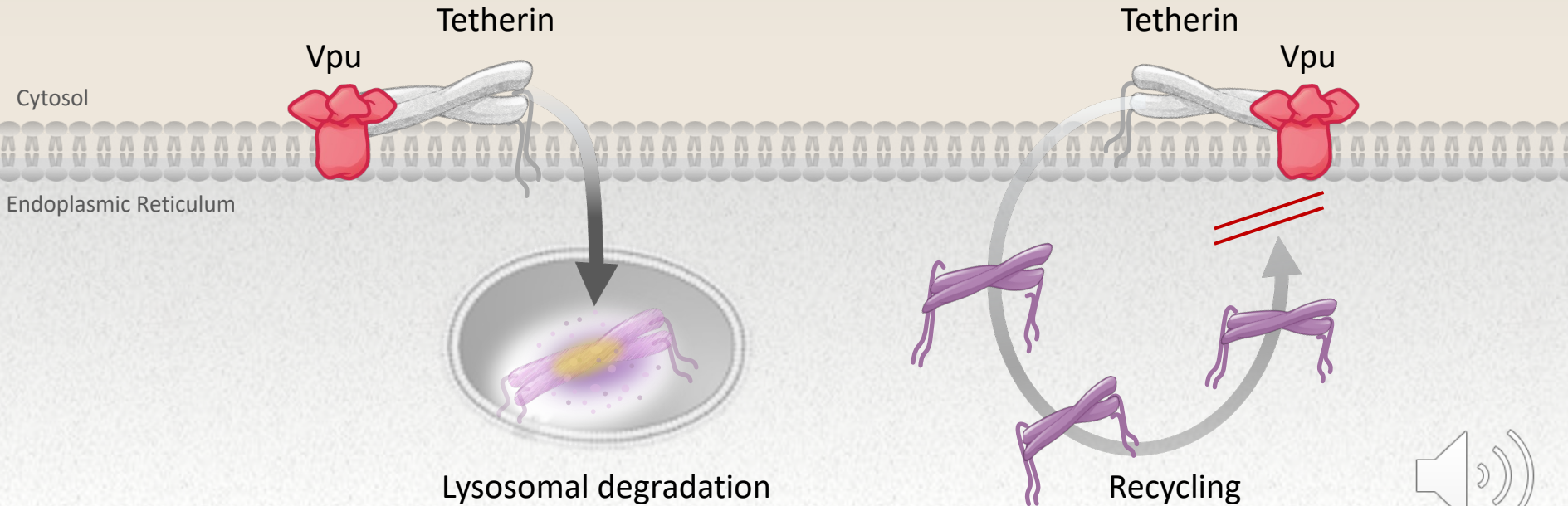
Vpu: Binding to Tetherin



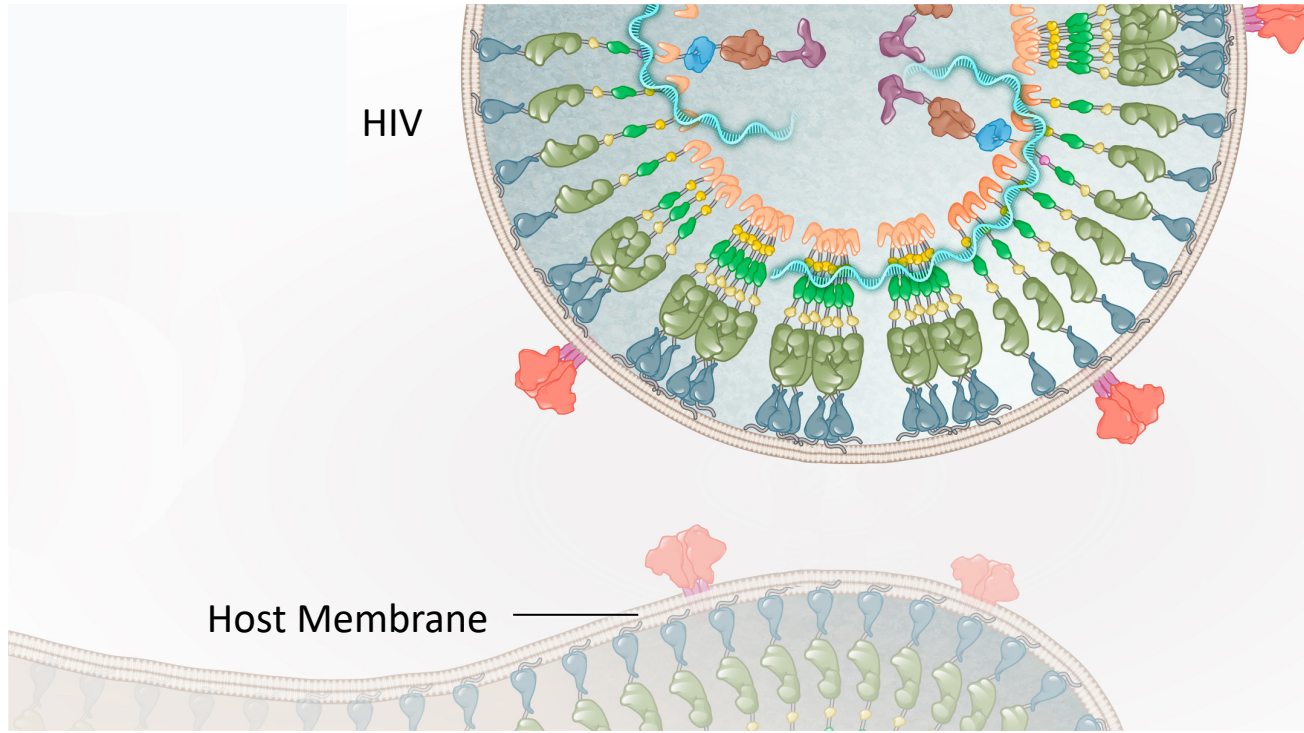
Vpu: Destruction of Tetherin



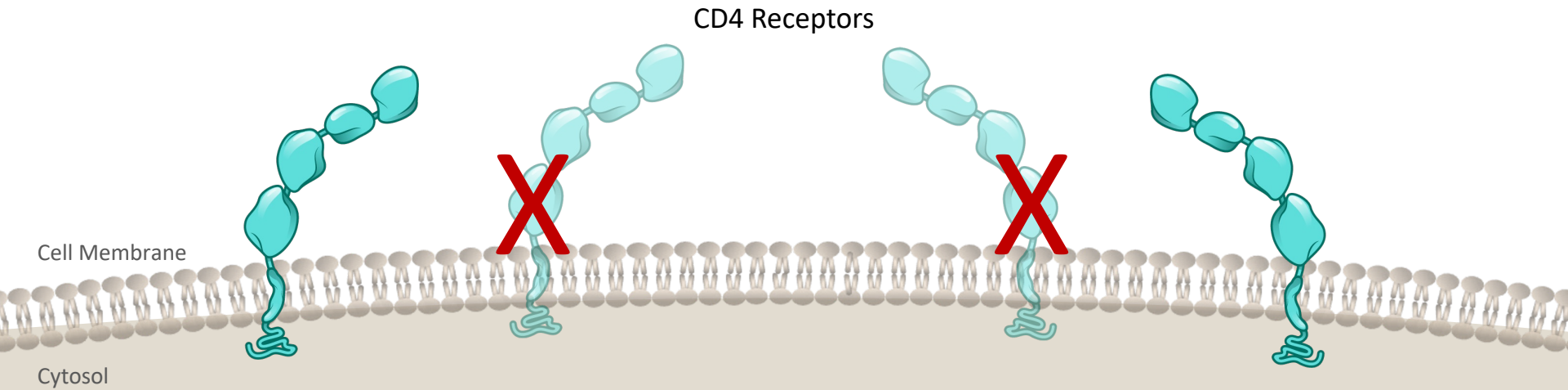
Vpu: Blocked Recycling of Tetherin



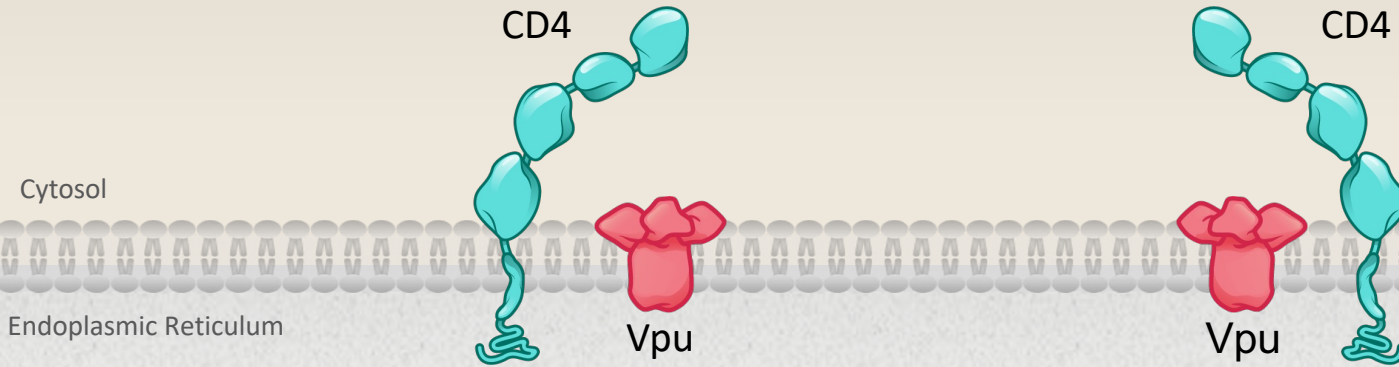
Vpu: Neutralizing Action of Tetherin



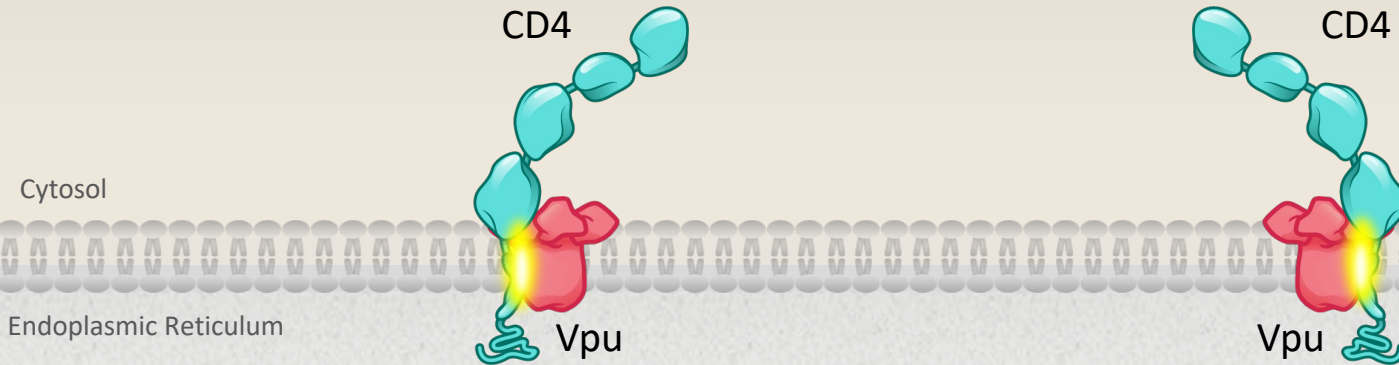
Vpu: Downregulation of Host Cell CD4 Receptor



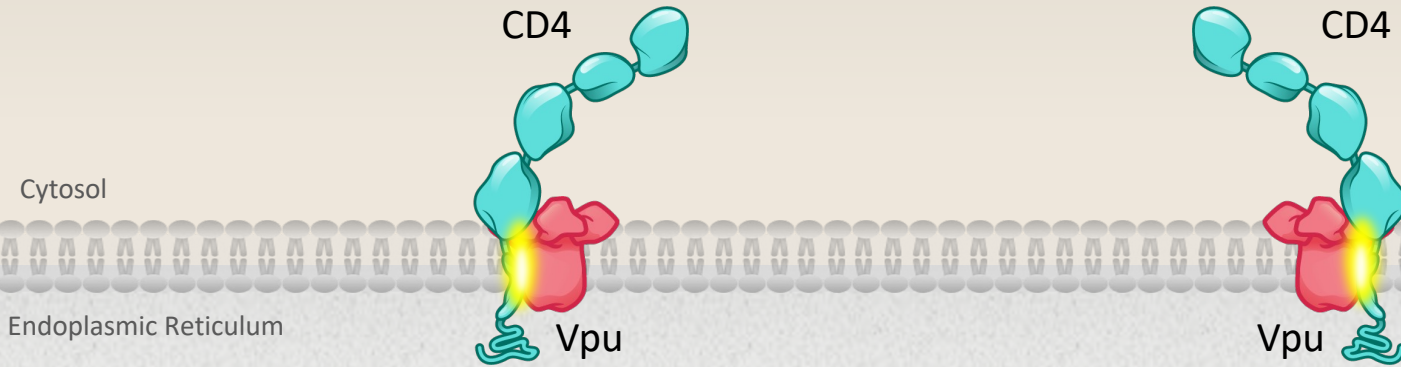
Vpu and CD4 Interaction



Vpu: Interaction with Host CD4 Receptor



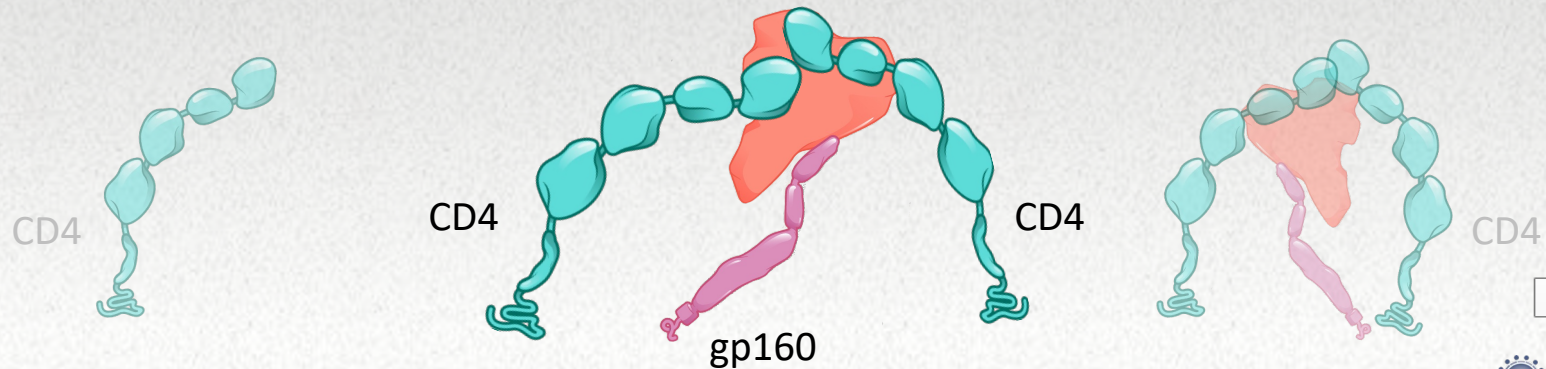
Vpu: Destruction of CD4 Molecule



CD4 Trapping of HIV Envelope in Endoplasmic Reticulum

Cytosol

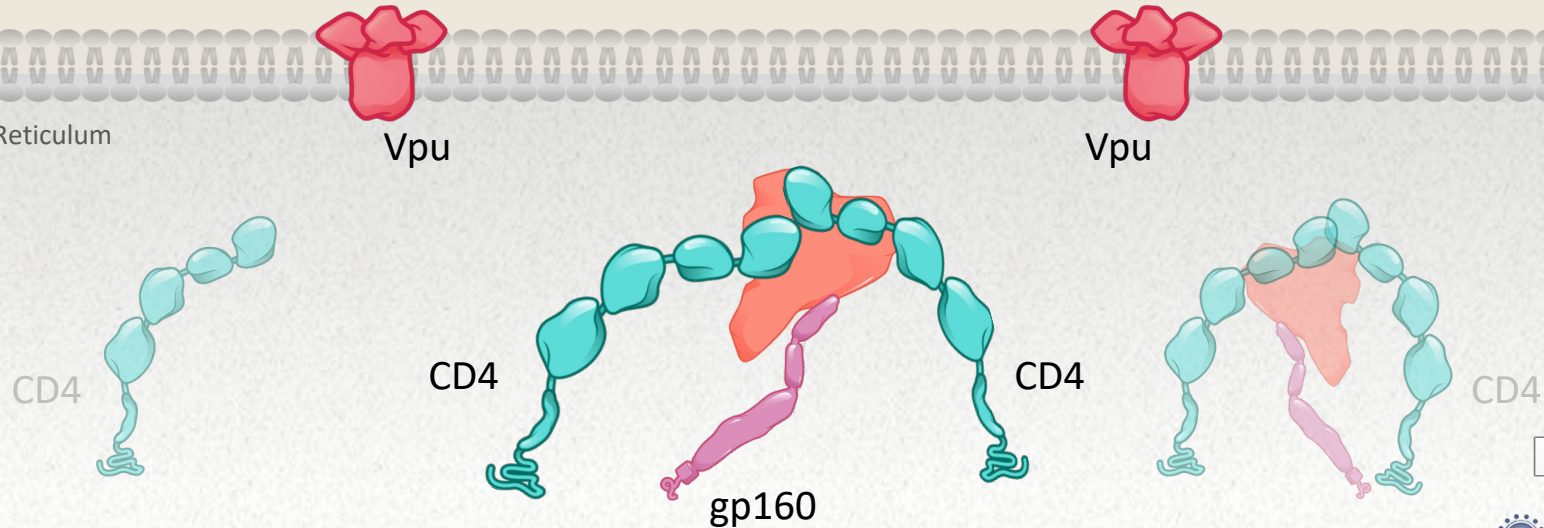
Endoplasmic Reticulum



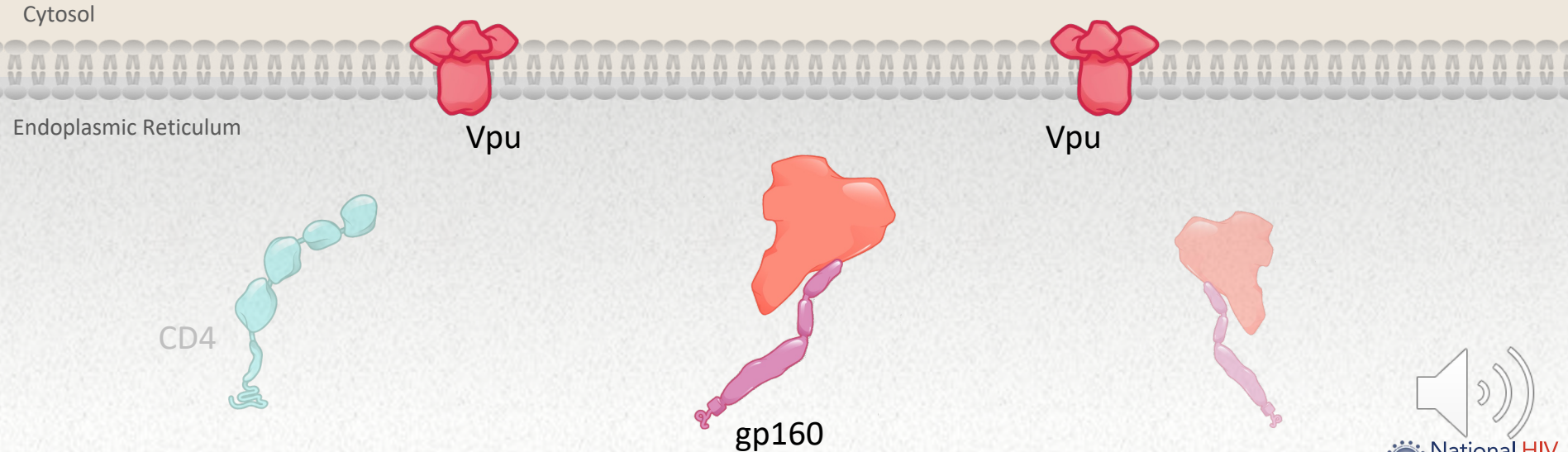
Vpu: Production Correlates with Amount of CD4

Cytosol

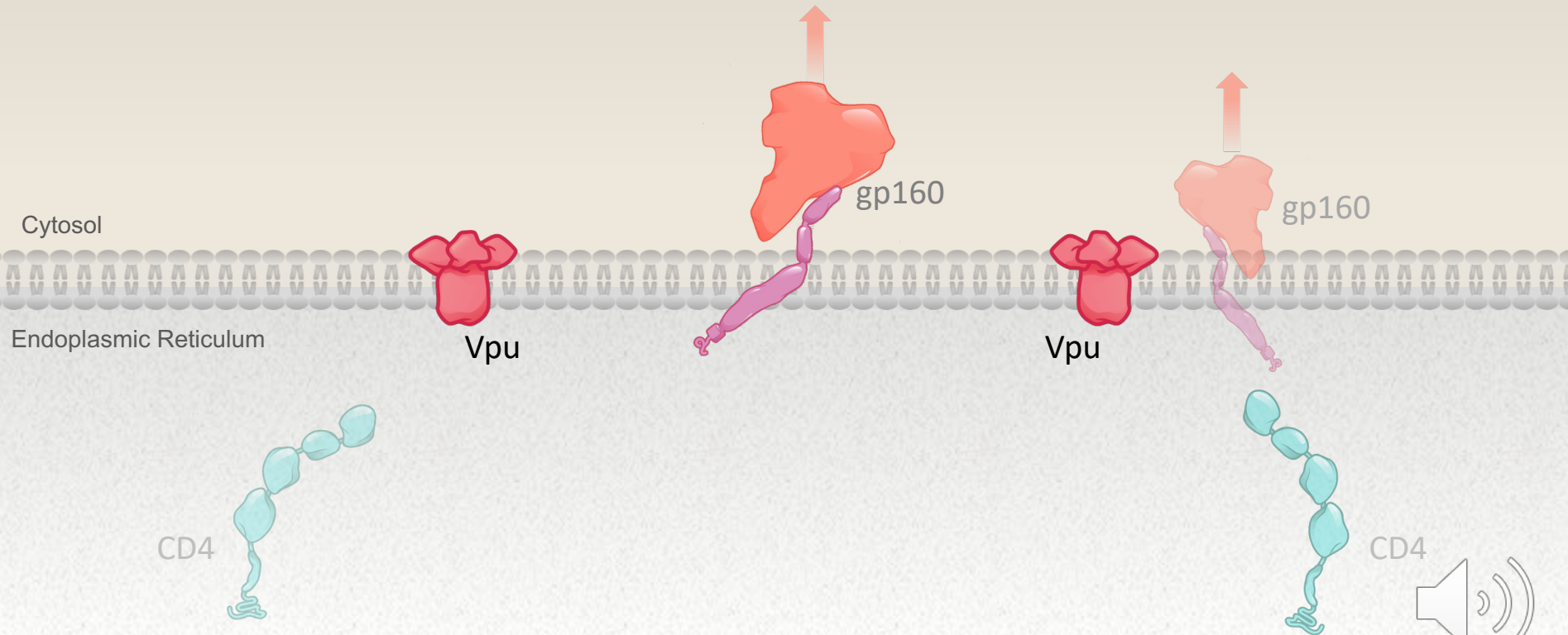
Endoplasmic Reticulum



Vpu Production: Reduces Amount of CD4



Vpu: Augments HIV Envelope Migration to Cell Surface

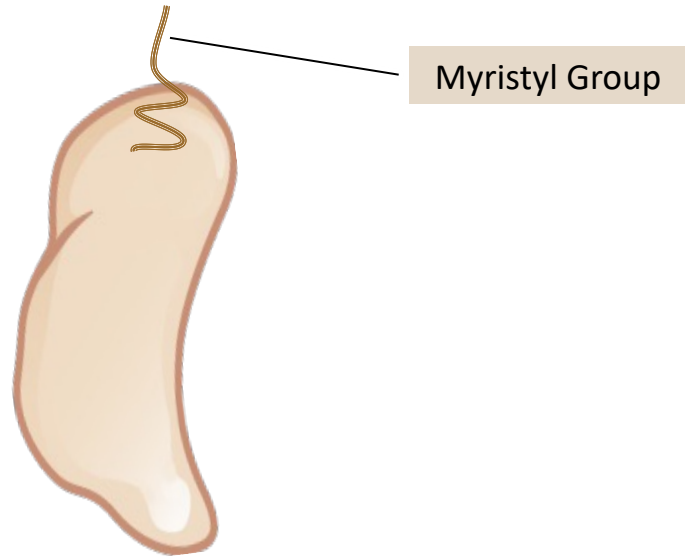


Negative Regulatory Factor (Nef)

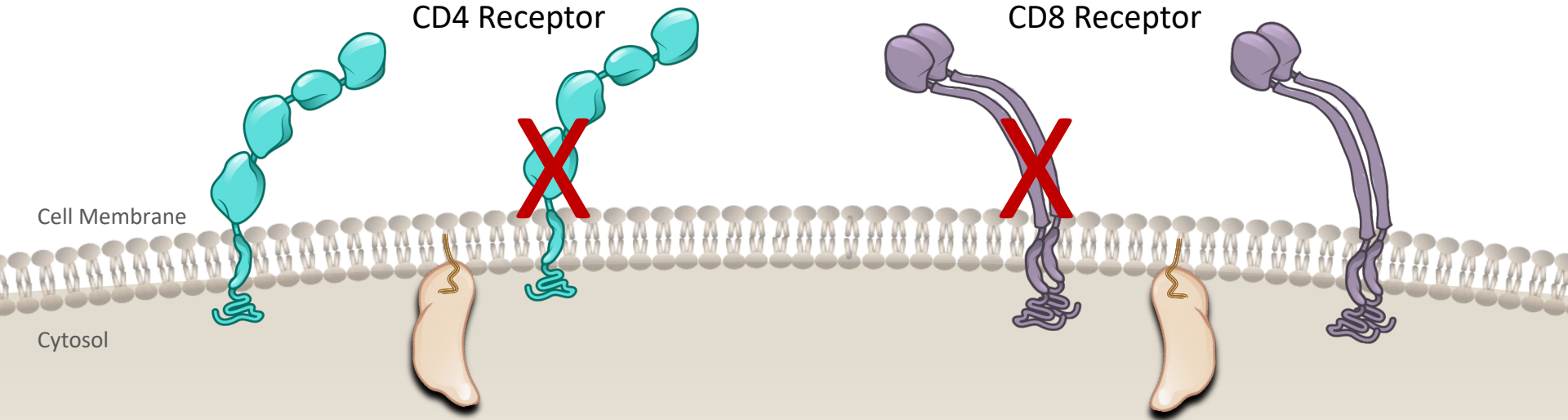
Accessory Protein



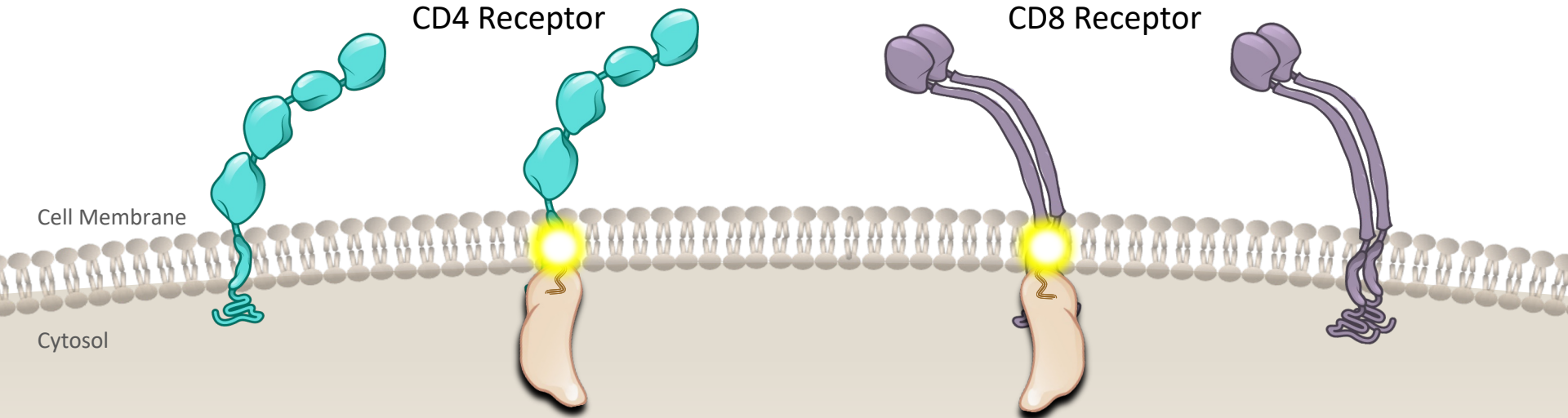
Nef: Myristyl Group



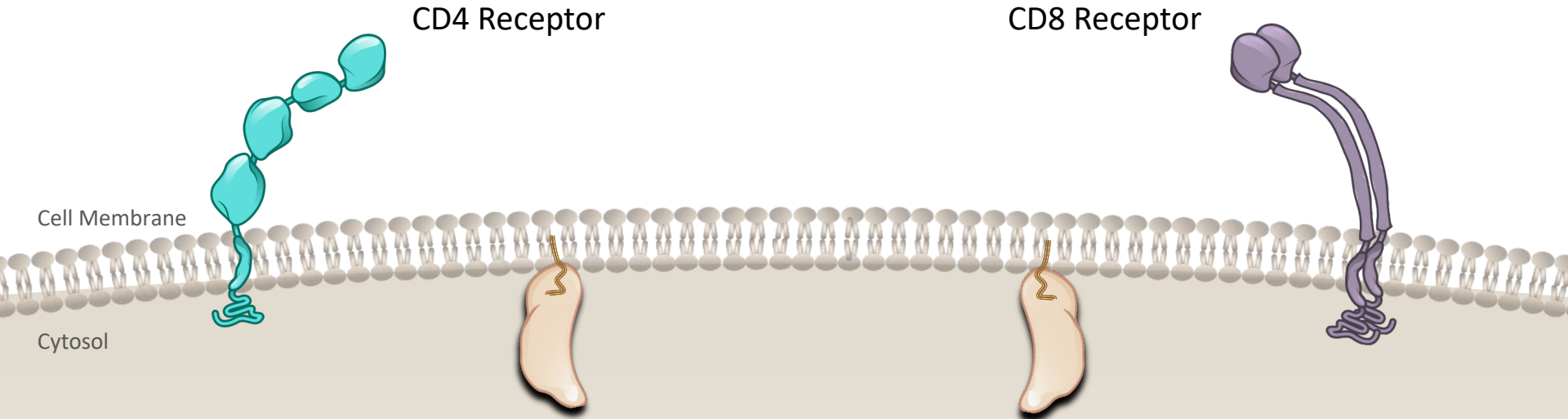
Nef: Downregulation of Cellular Receptors



Nef: Binding to Host Cell Receptors



Nef: Destruction of Host Cell Receptors



HIV Regulatory Proteins

HIV Transcription



Tat

HIV Translation



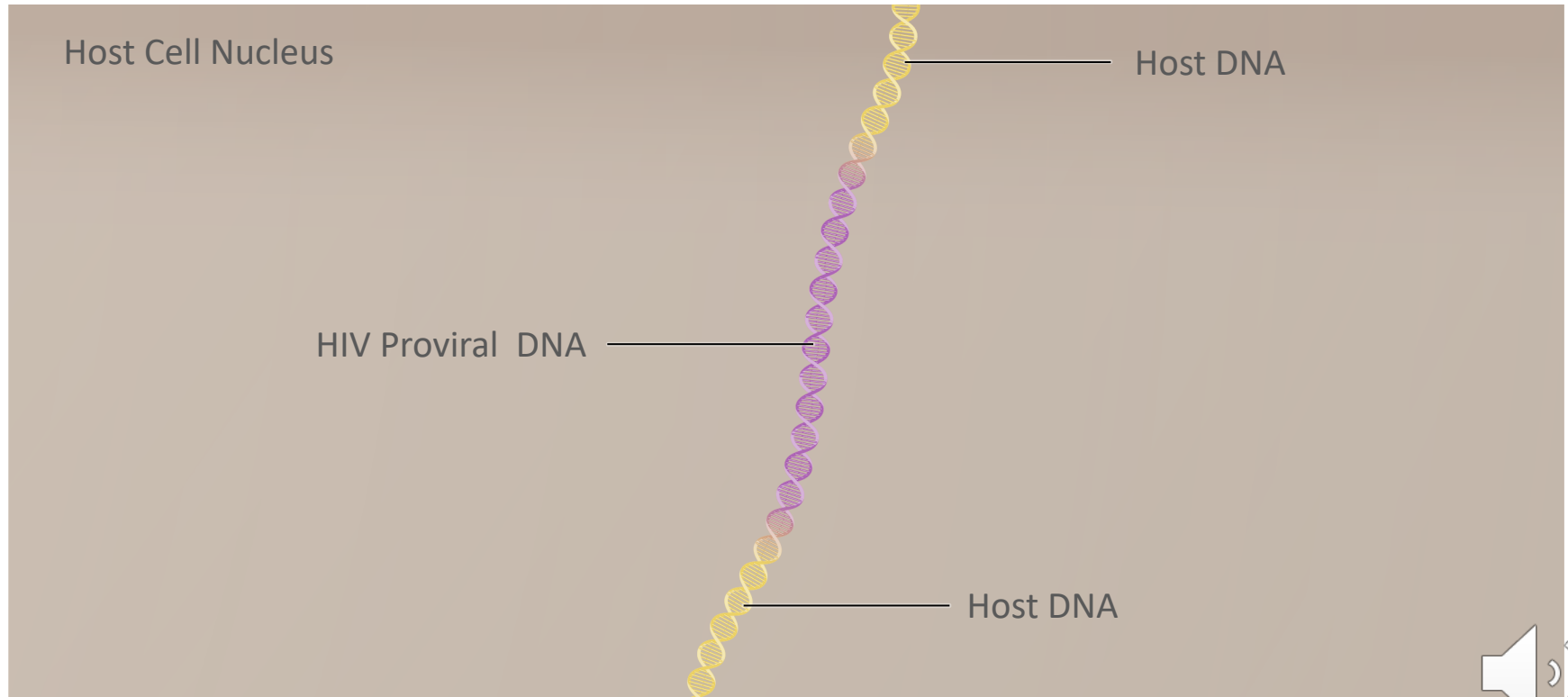
Rev

Transactivator of Transcription (Tat)

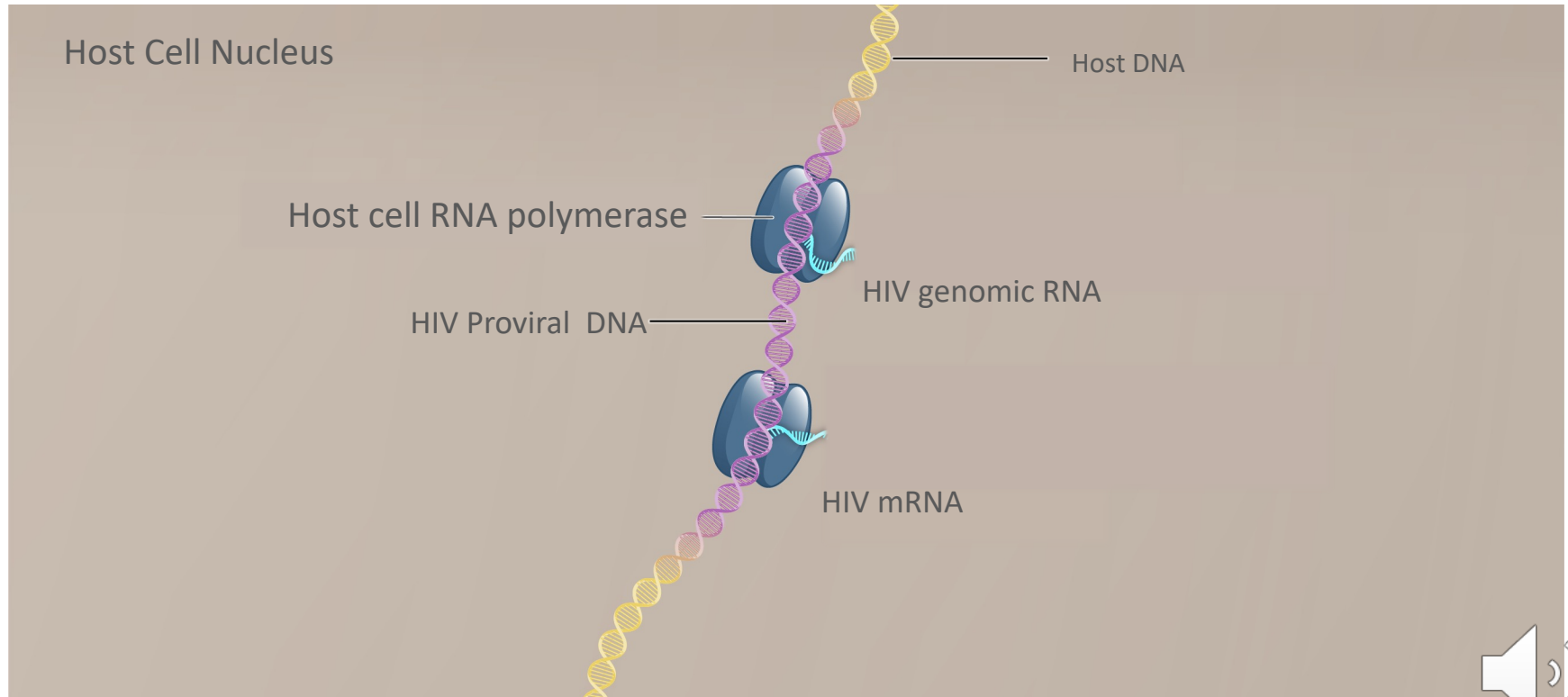
Regulatory Protein



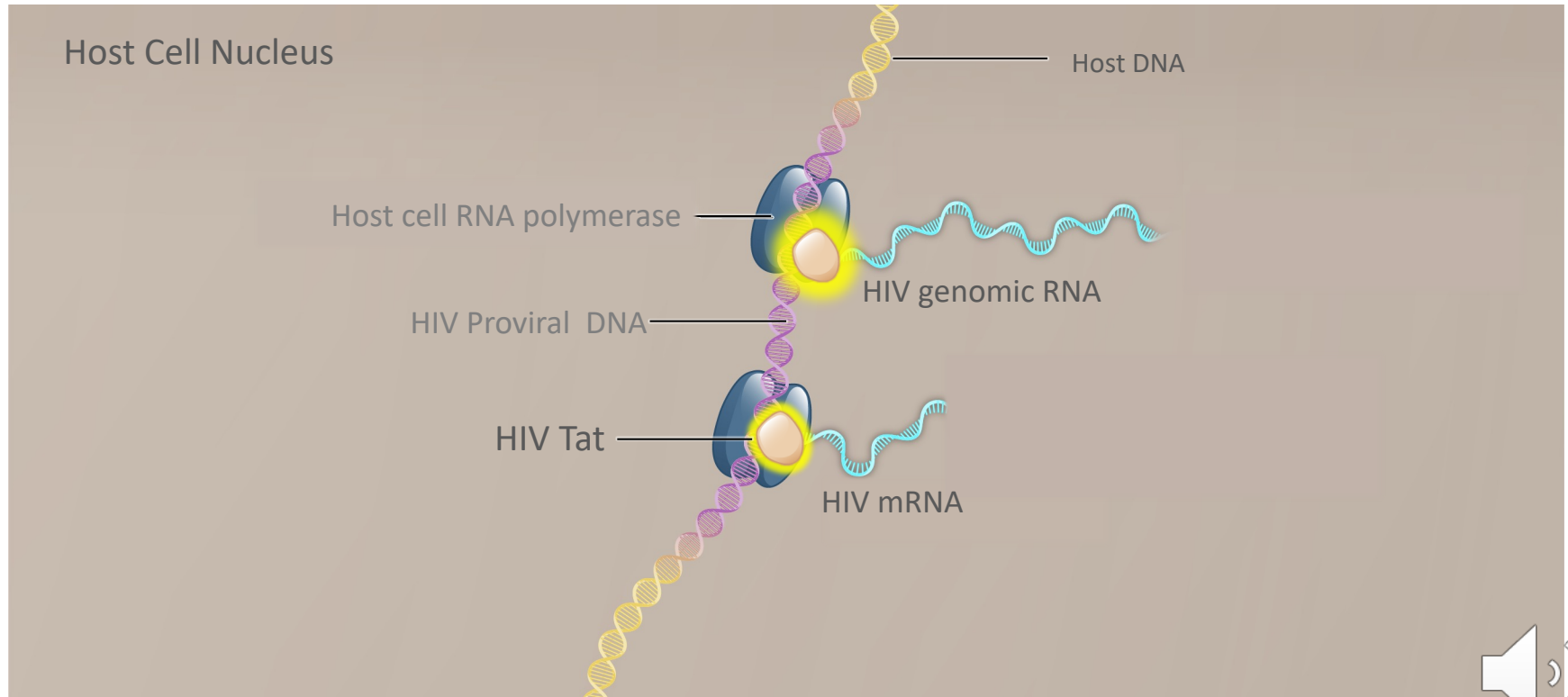
Latent Proviral HIV DNA



Activation of Transcription



Tat: Activation of Transcription

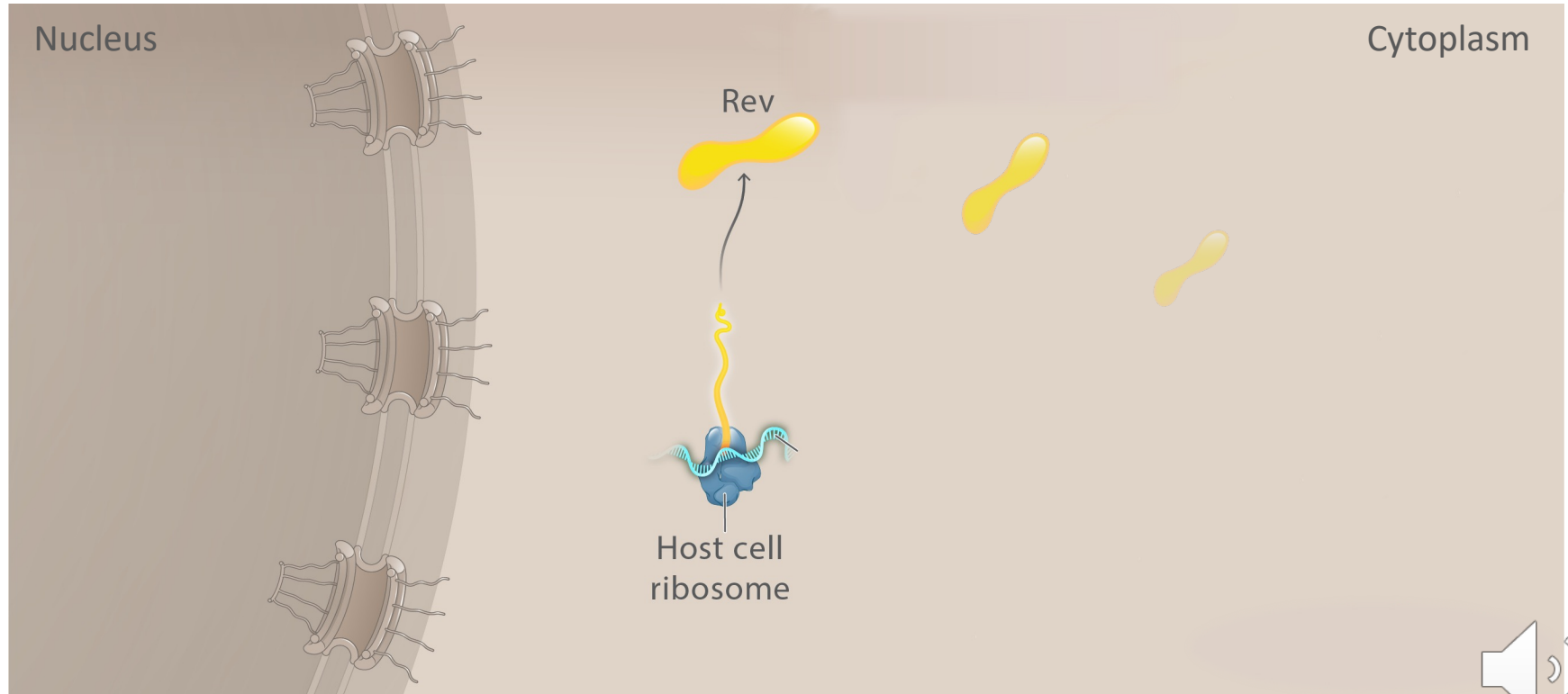


Regulator of Expression of Virion Proteins (Rev)

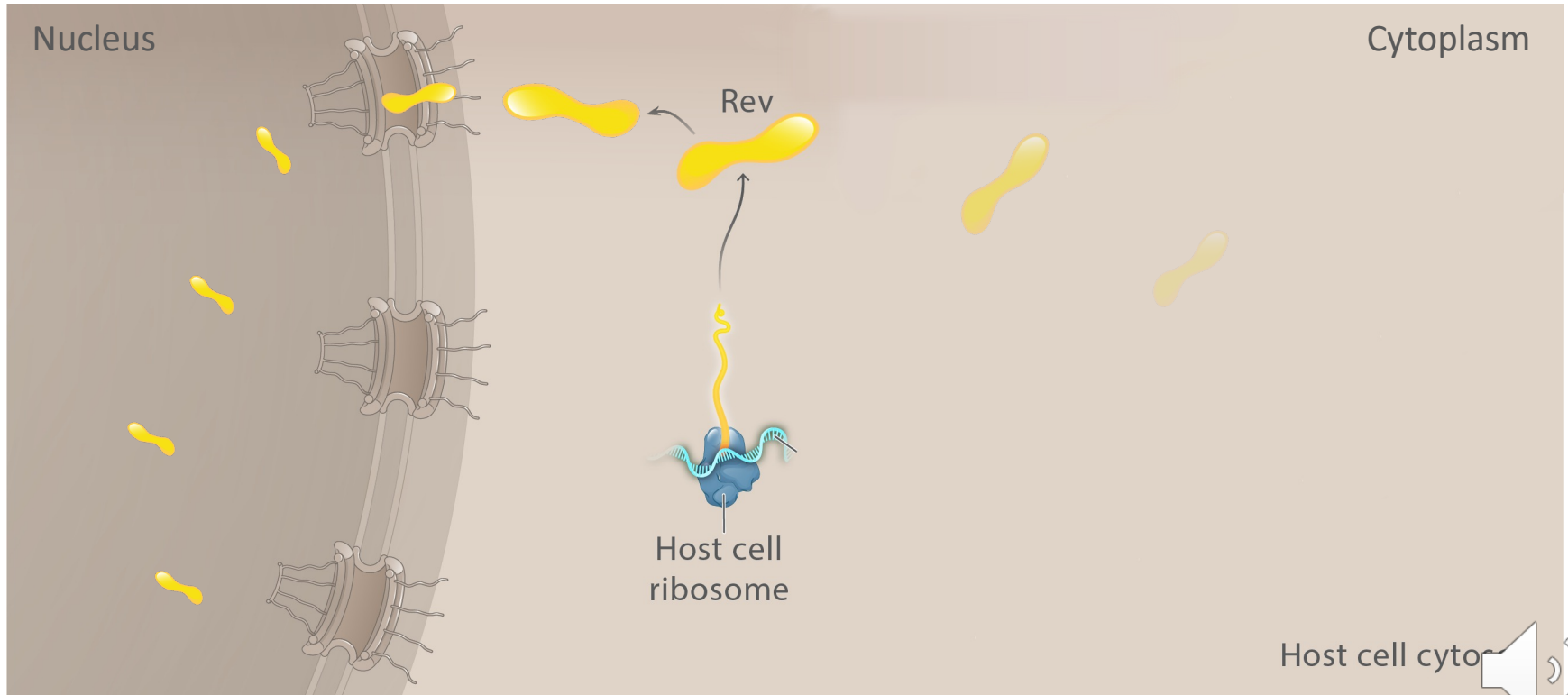
Regulatory Protein



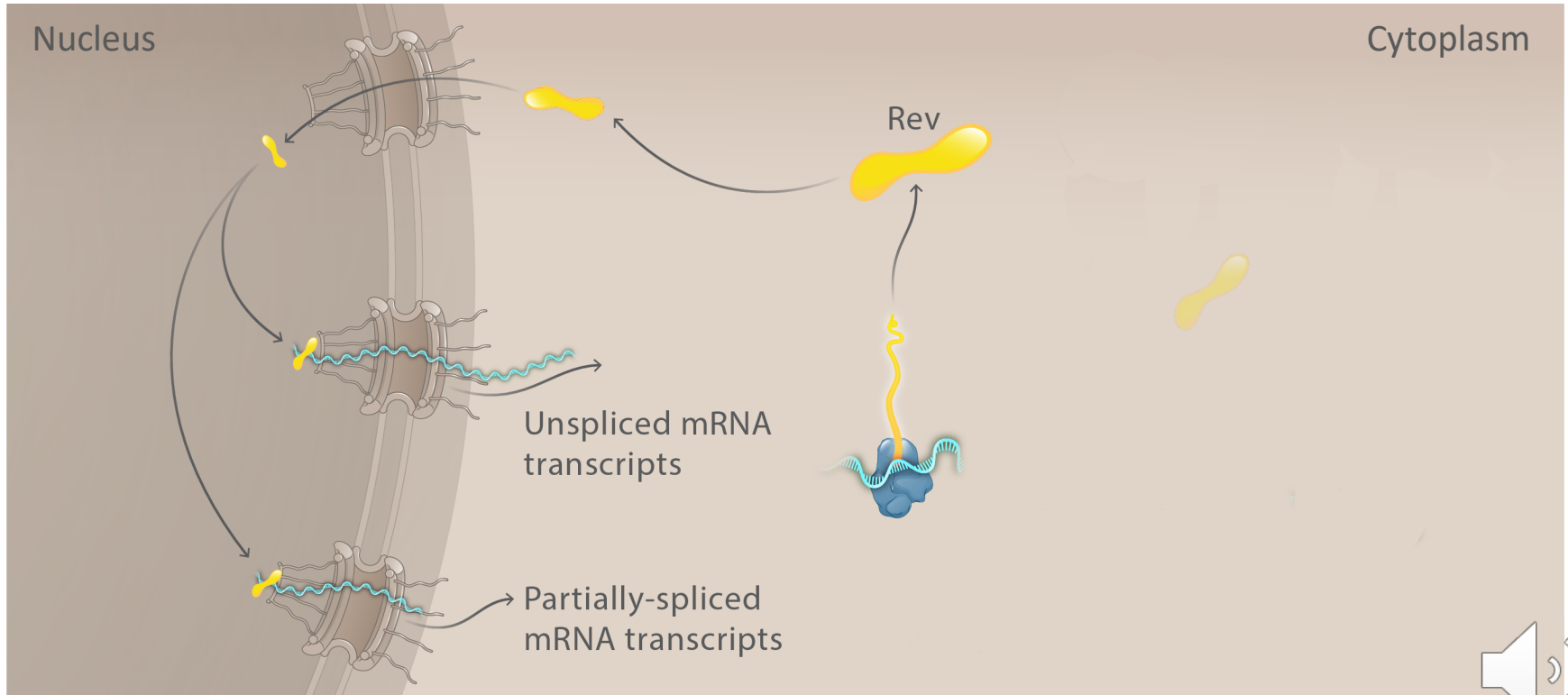
Rev: Early Synthesis



Rev: Migration into Nucleus



Rev: Enhanced Shuttling of mRNA to Cytoplasm



Summary

Introduction to the Biology of HIV-1: Summary

Structure

Genome

Structural Proteins

Enzymes

Accessory and Regulatory Proteins

Acknowledgment

The production of this **National HIV Curriculum** Mini-Lecture was supported by Grant U10HA32104 from the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS). Its contents are solely the responsibility of University of Washington IDEA Program and do not necessarily represent the official views of HRSA or HHS.

