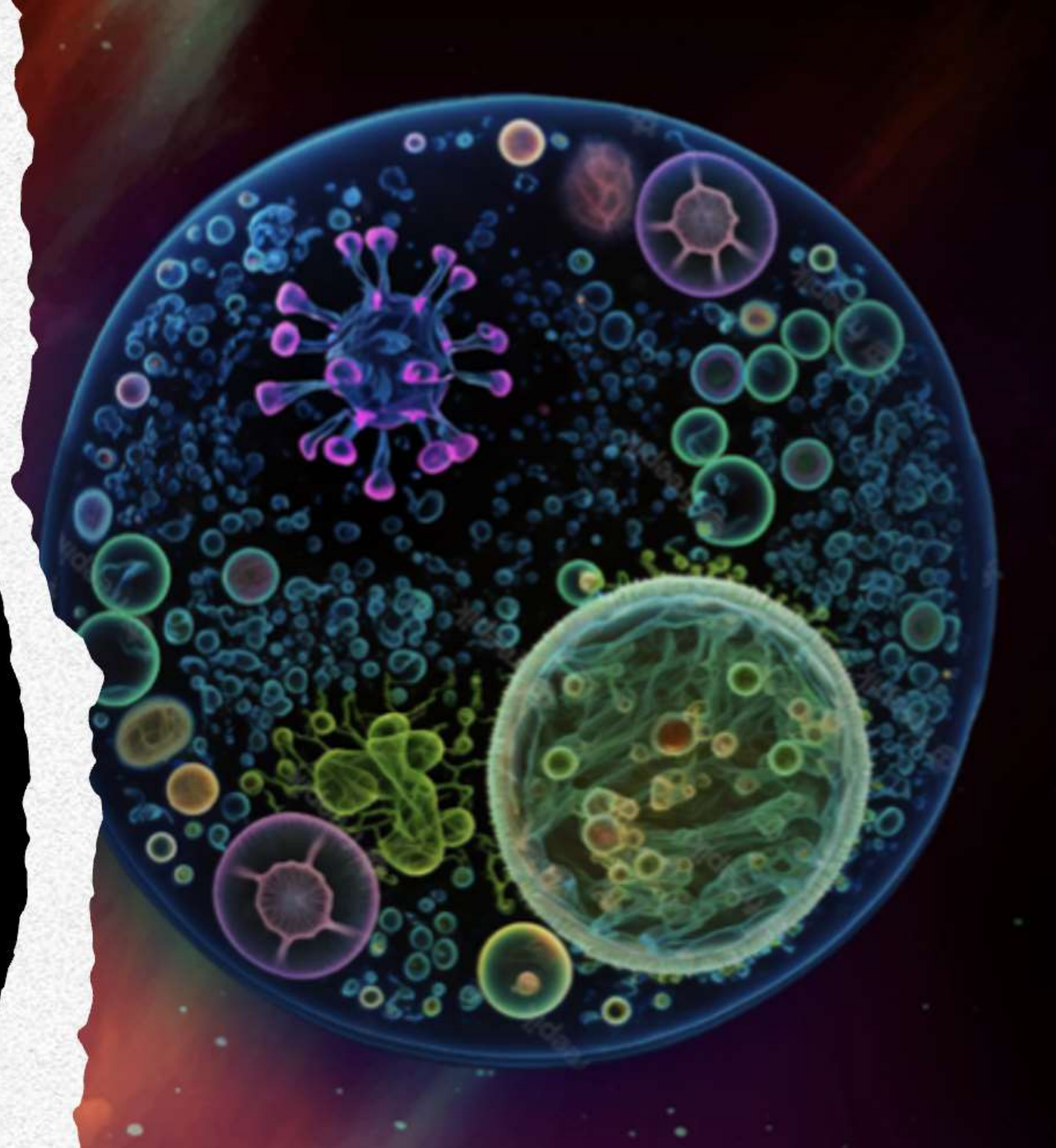
I. VİRAL İNFEKSİYONLAR VE BAĞIŞIKLAMA SİMPOZYUMU

19-21 EYLÜL 2024

ALİ EMİRİ EFENDİ KÜLTÜR MERKEZİ / İSTANBUL



Virusların Evrimi

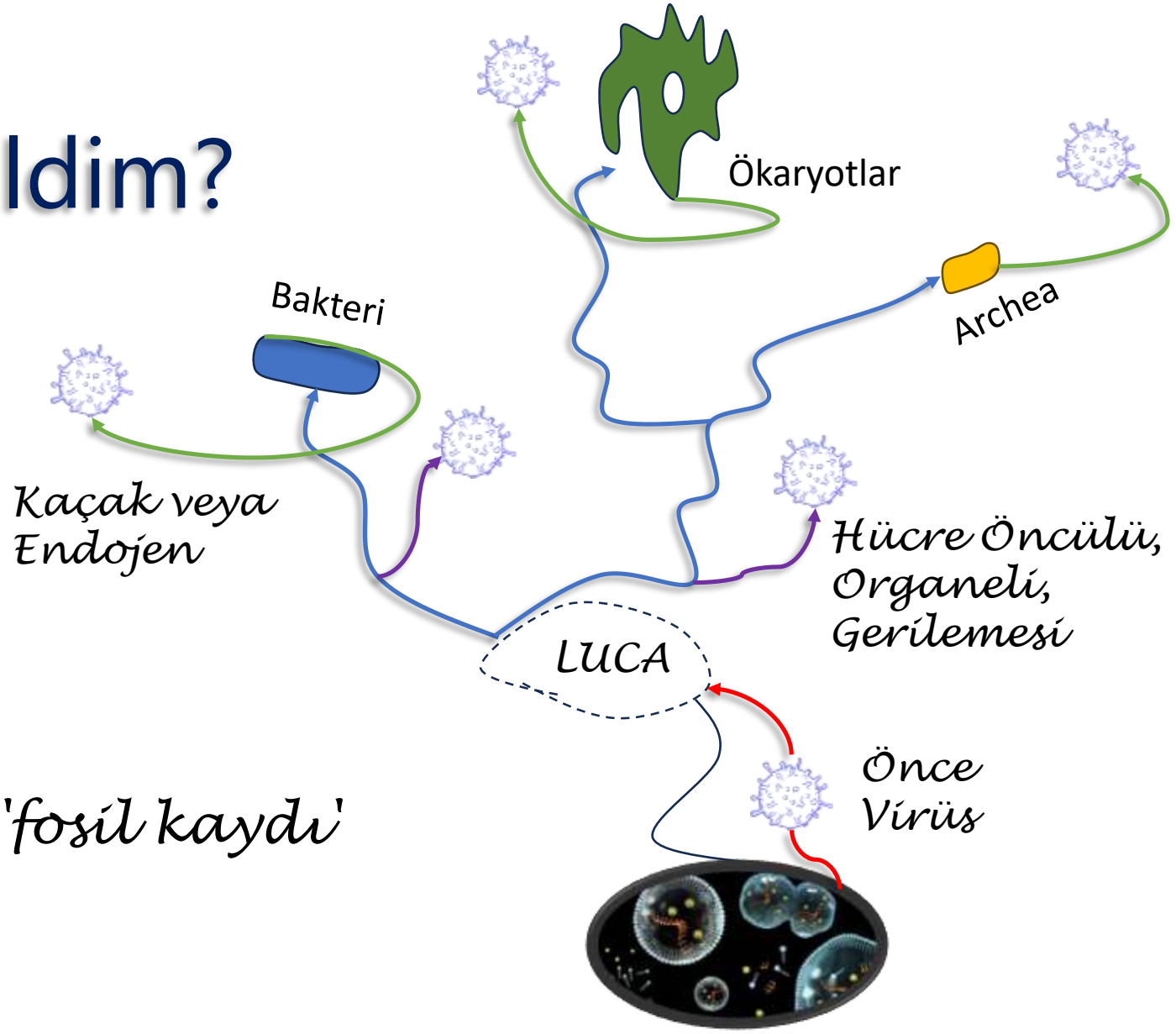
Viral Evrimin Lokomotifleri

Dr. Mert A. KUŞKUCU

Koç Üniversitesi, Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı

Koç Üniversitesi – İş Bankası Bulaşıcı Hastalıklar Merkezi

Ben Nereden Geldim?



Virüslerin fiziksel bir 'fosil kaydı' yoktur !!!

LUCA: Last Universal Cellular Ancestor

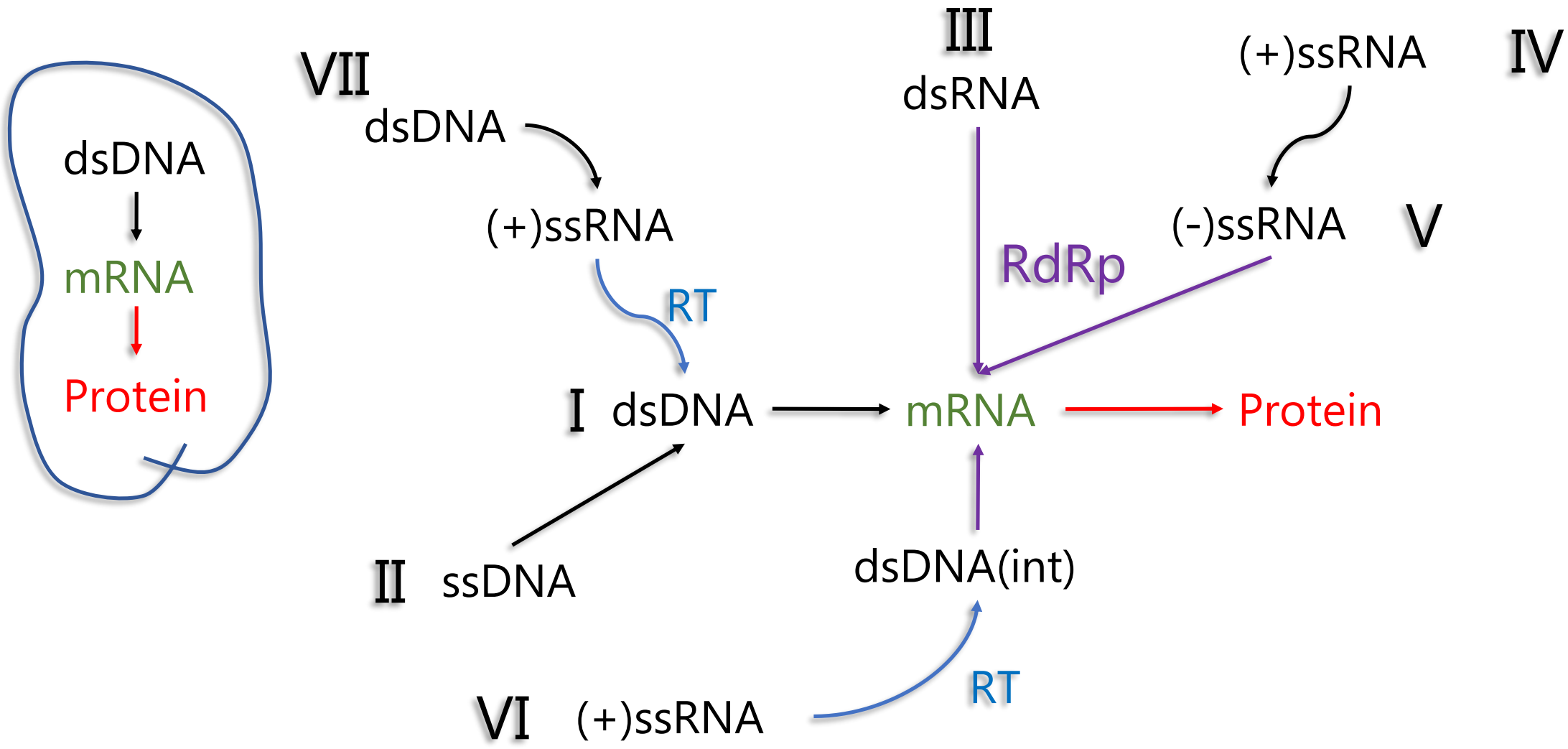
Paleoviroloji

Paleovirology: inferring viral evolution from host genome sequence data

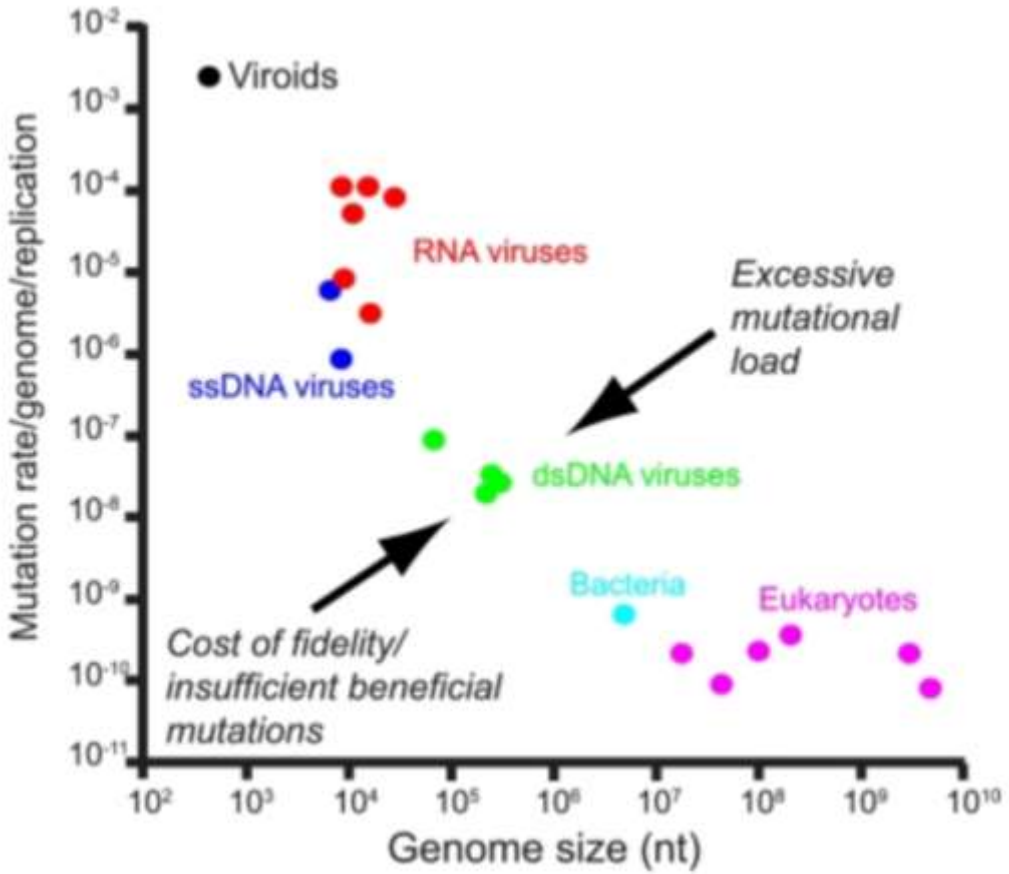
Aris Katzourakis

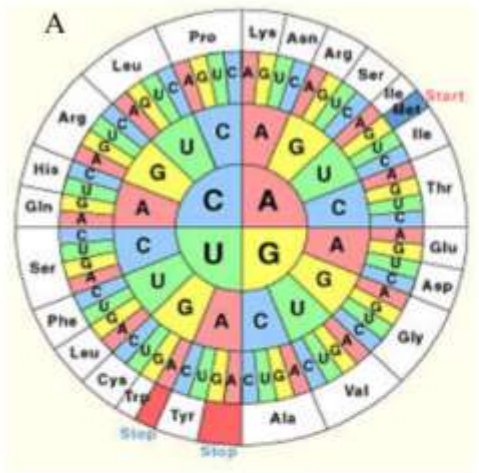
Department of Zoology, University of Oxford, Oxford OX1 3PS, UK

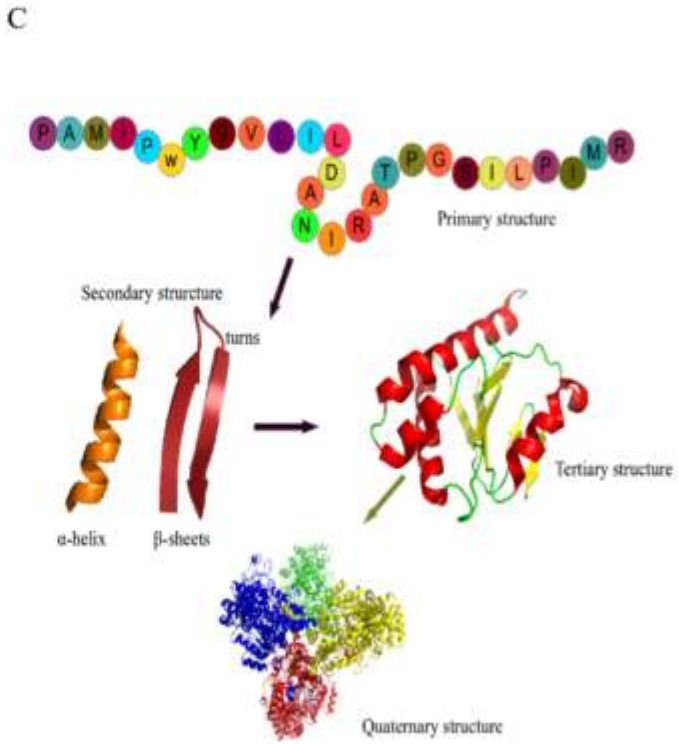
Ezber Bozan Bir Yaşam Formu !!!



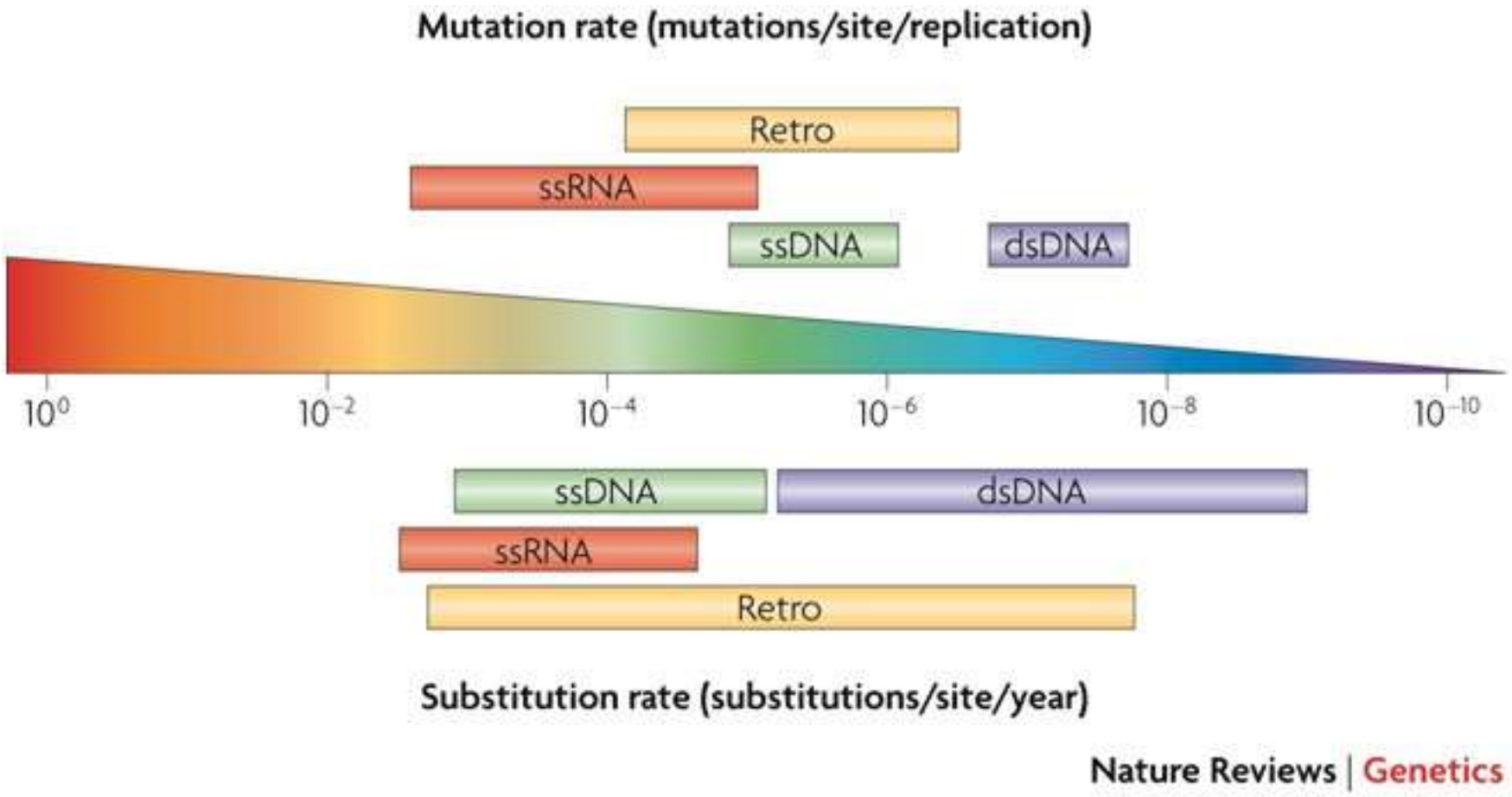
Genomun Kaderindir



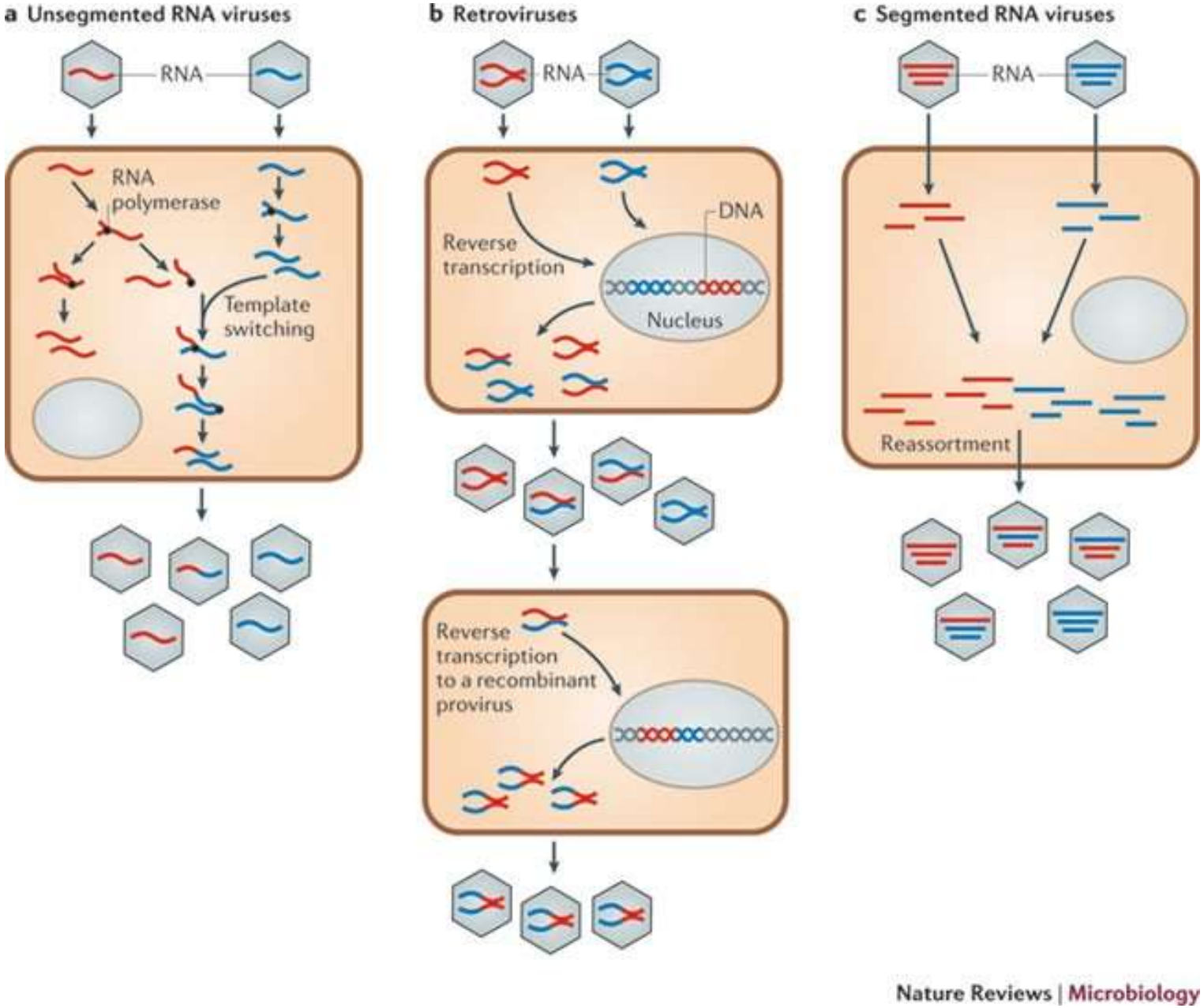




Genomun Kaderindir



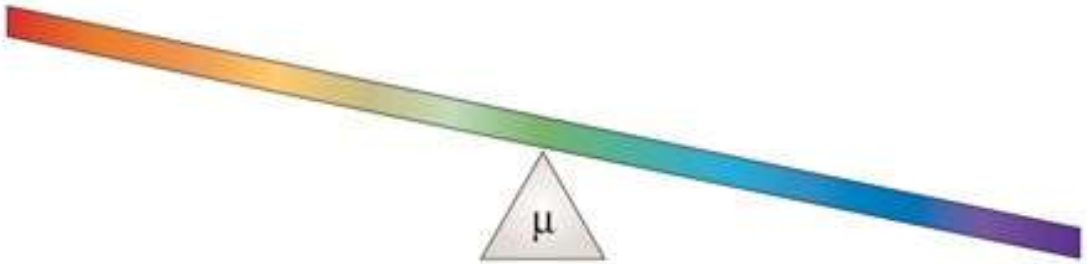
Rekombinasyon



Temel Belirleyiciler;

Effects on substitution rate

Generation time	Shorter		Longer
Transmission	Direct		Vector borne
	Horizontal		Vertical
Selection	Positive		Purifying

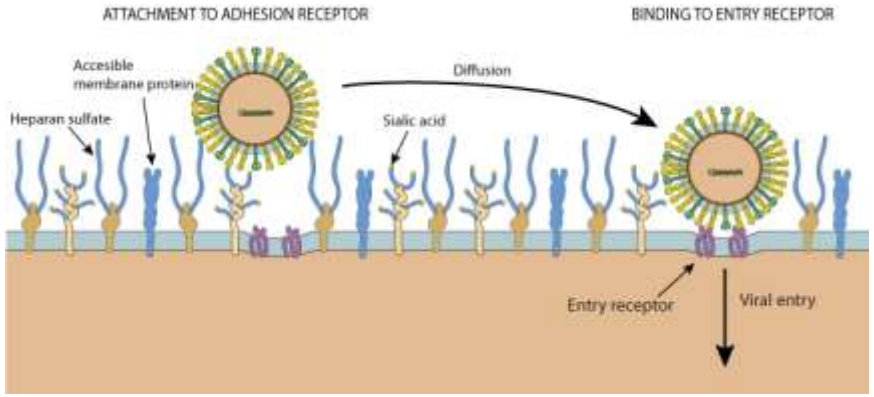


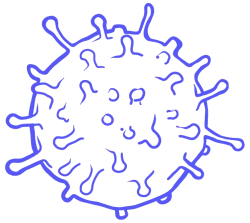
Effects on mutation rate

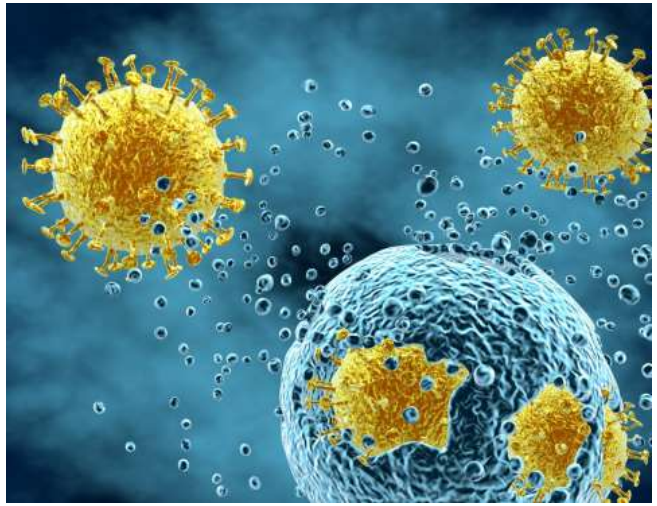
Genomic architecture	Single stranded		Double stranded
	RNA		DNA
	Smaller		Larger
Replication speed	Faster		Slower
Viral enzymes	–		DNA repair
Host enzymes	Deamination, oxidation		–
Environmental effects	Deamination, oxidation, UV		–

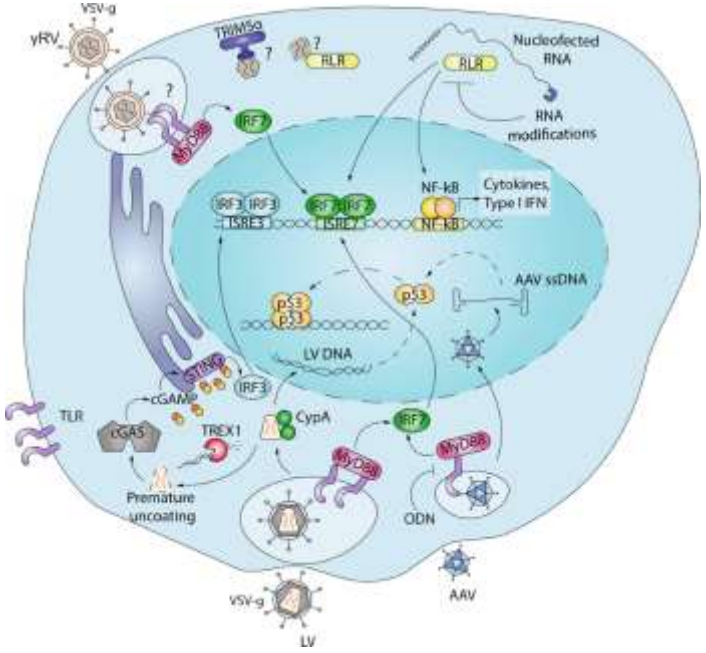
Nature Reviews | Genetics

Virüs Olmanın Zorluğu









Paleovirology: inferring viral evolution from host genome sequence data

Aris Katzourakis

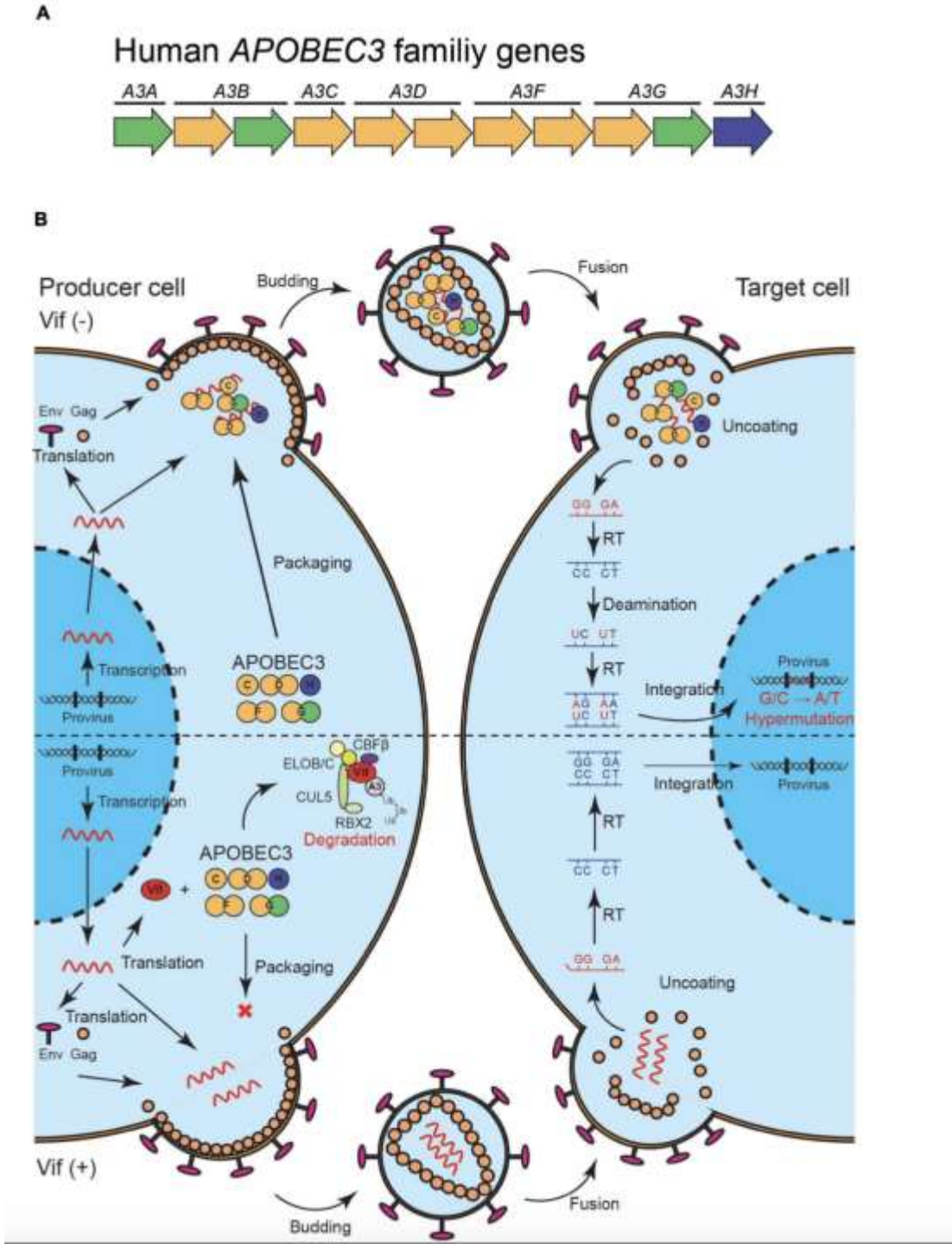
Department of Zoology, University of Oxford, Oxford OX1 3PS, UK

APOBEC giller

TRIM5a

TRIMCyp

SAMHD1



Potential Utilization of APOBEC3-Mediated Mutagenesis for an HIV-1 Functional Cure

Terumasa Ikeda[1], Yuan Yue[1,2], Ryo Shimizu[1,2] and Hesham Nasser[1]*

[1] Division of Molecular Virology and Genetics, Joint Research Center for Human Retrovirus Infection, Kumamoto University, Kumamoto, Japan, [2] Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

Suppression of HIV-1 Infection by APOBEC3 Proteins in Primary Human CD4$^+$ T Cells Is Associated with Inhibition of Processive Reverse Transcription as Well as Excessive Cytidine Deamination

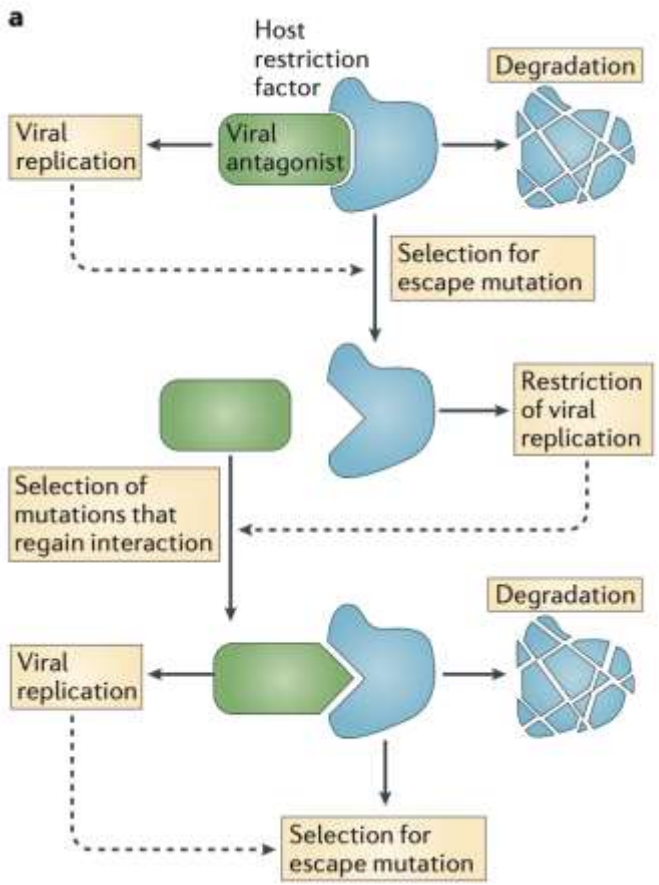
Kieran Gillick,[a] Darja Pollpeter,[a] Prabhjeet Phalora,[a] Eun-Young Kim,[b] Steven M. Wolinsky,[b] Michael H. Malim[a]

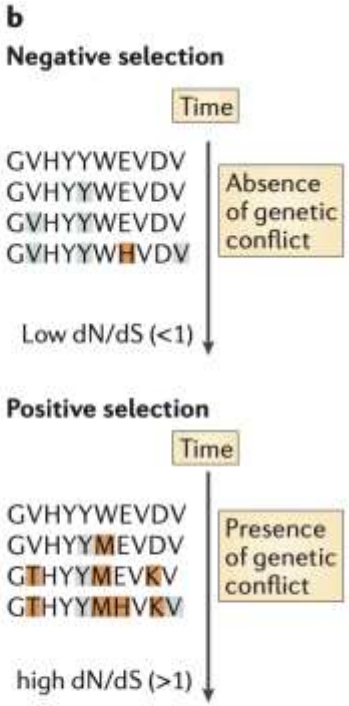
Department of Infectious Diseases, King's College London, London, United Kingdom[a]; Division of Infectious Diseases, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA[b]

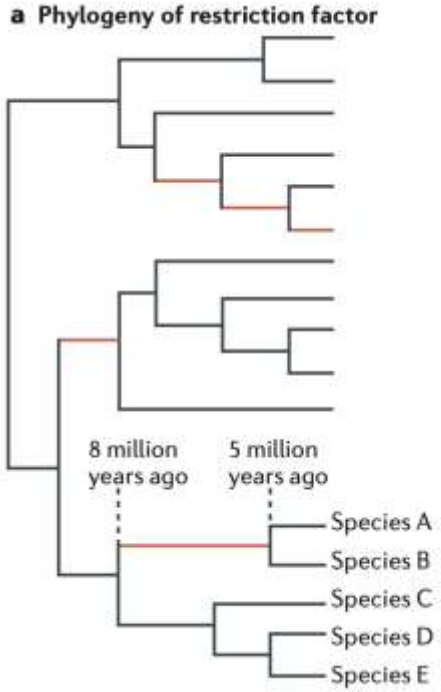
Table 1 | **Characteristics of some well-studied examples of restriction factors**

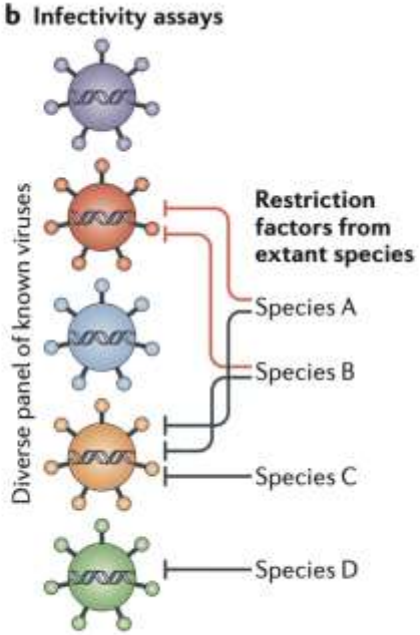
Restriction factor	IFN induced?	Viral targets*	Viral lifecycle stage inhibited	Viral antagonists	Under positive selection?
Fv1	No	Retroviruses	Capsid uncoating[93]	None known	Yes[94]
TRIM5α and TRIM–CYP	Yes	Retroviruses	Capsid uncoating[9,93]	None known (escape through capsid mutations)	Yes[53,95]
APOBEC3 family	APOBEC3A	Retroviruses, retrotransposons, hepadnaviruses	Reverse transcription[80,93]	Vif (lentiviruses), Bet (spumaviruses), Gag (gammaretroviruses)	APOBEC3DE, APOBEC3G, APOBEC3H[45,49,50]
SAMHD1	Yes	Retroviruses	Reverse transcription[88]	Vpx (some SIVs), Vpr (some SIVs)	Yes[81,82]
ZAP	Yes	Retroviruses, filoviruses, alphaviruses	Viral protein translation[93]	None known	Yes[96]
Tetherin	Yes	Retroviruses, flaviviruses, herpesviruses, rhabdoviruses, paramyxoviruses, arenaviruses	Budding[93]	Nef (some SIVs), Vpu (HIV-1), Env (HIV-2), glycoprotein (Ebola virus), K5 (KSHV)	Yes[97,98]
Viperin	Yes	Orthomyxoviruses, flaviriruses, herpesviruses, alphaviruses, paramyxoviruses	Budding[99]	None known	Yes[100]
MxA and Mx1	Yes	Orthomyxoviruses, paramyxoviruses, hepadnaviruses, rhabdoviruses, alphaviruses, bunyaviruses, togaviruses, picornaviruses	Nucleocapsid transport or another early lifecycle step[101]	None known	ND
IFITM1, IFITM2 and IFITM3	Yes	Orthomyxoviruses, flaviviruses, coronaviruses	Endosomal fusion or uncoating[99]	None known	ND
PKR	Yes	Poxviruses	Viral protein translation[101]	K3L and E3L (vaccinia virus), TRS1 and IRS1 (HCMV)[102], and many others[103]	Yes[104]

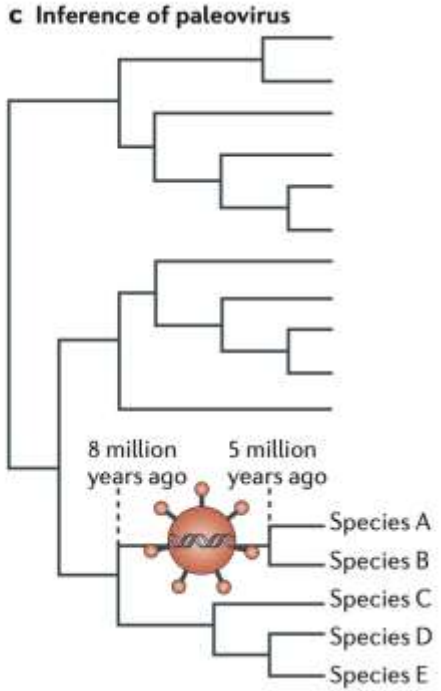
Genomlarımızda Derin İzler;



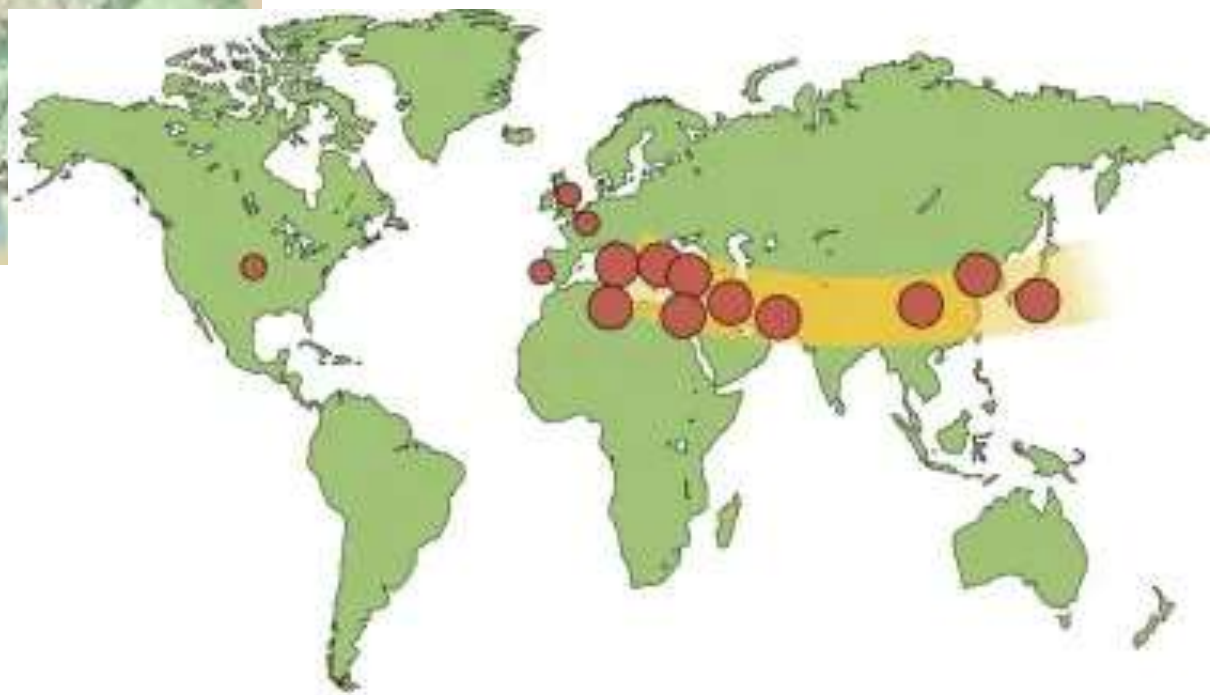


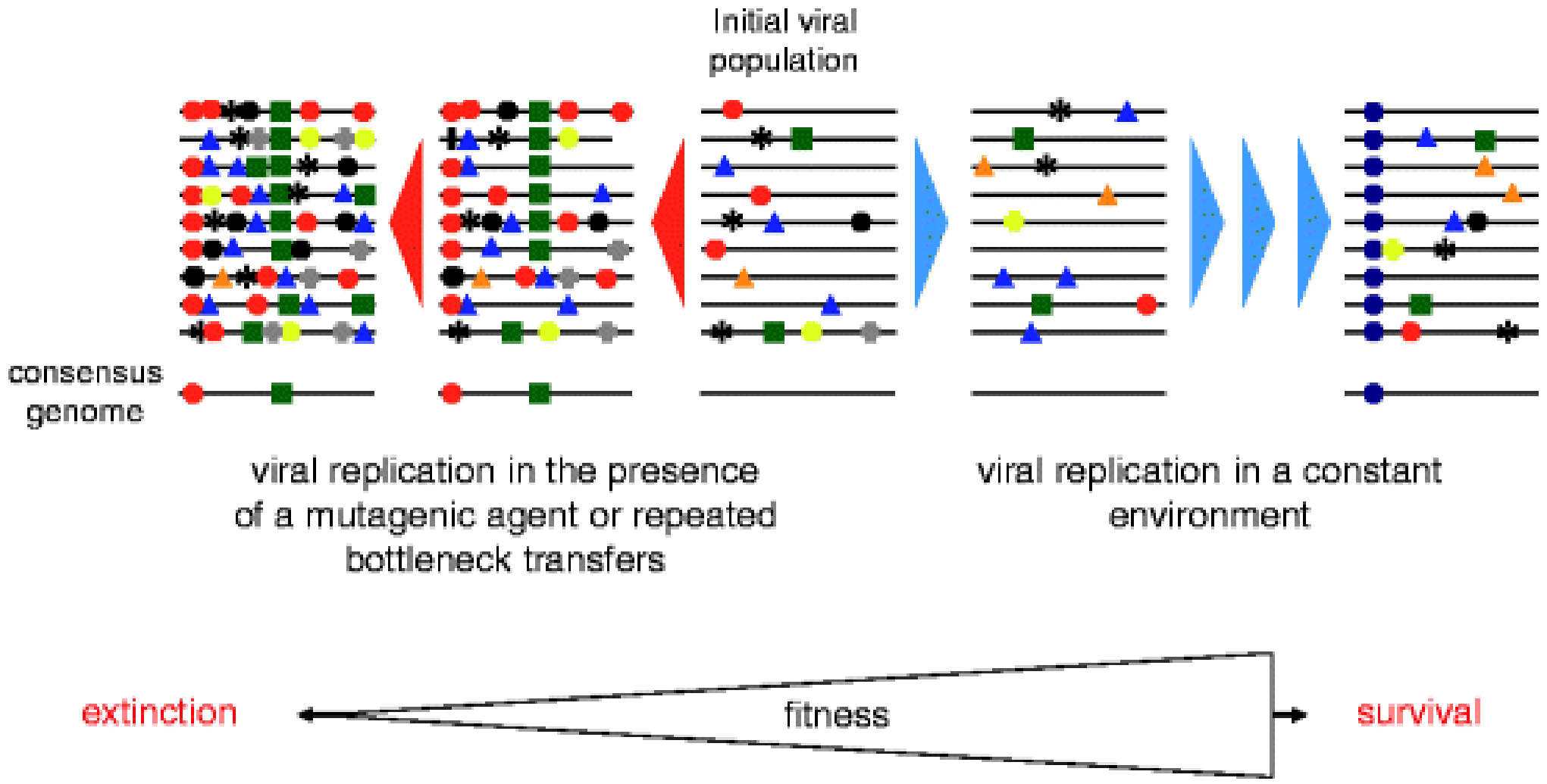


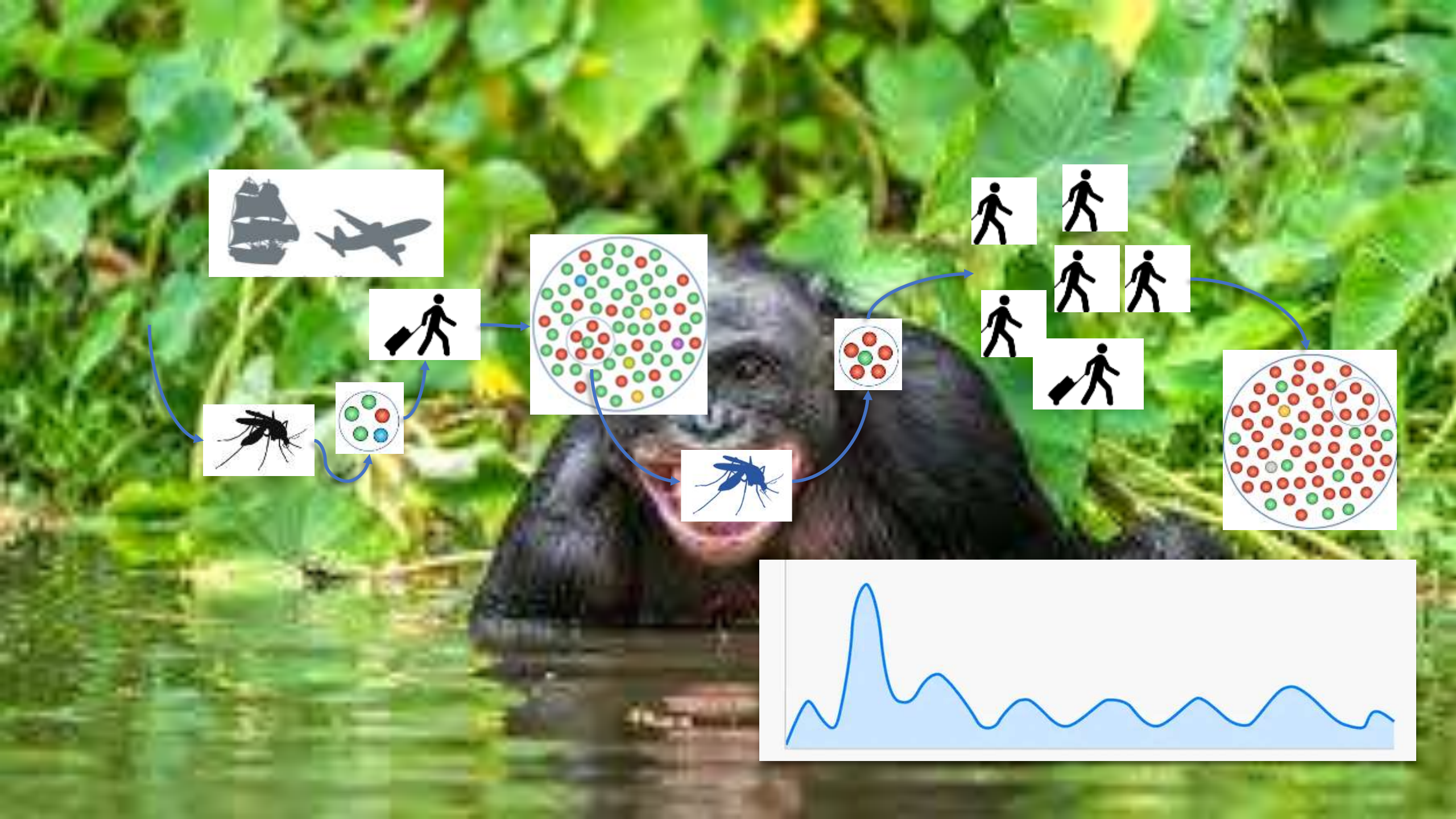





Ancient Silk Road
CHINA
INDIA

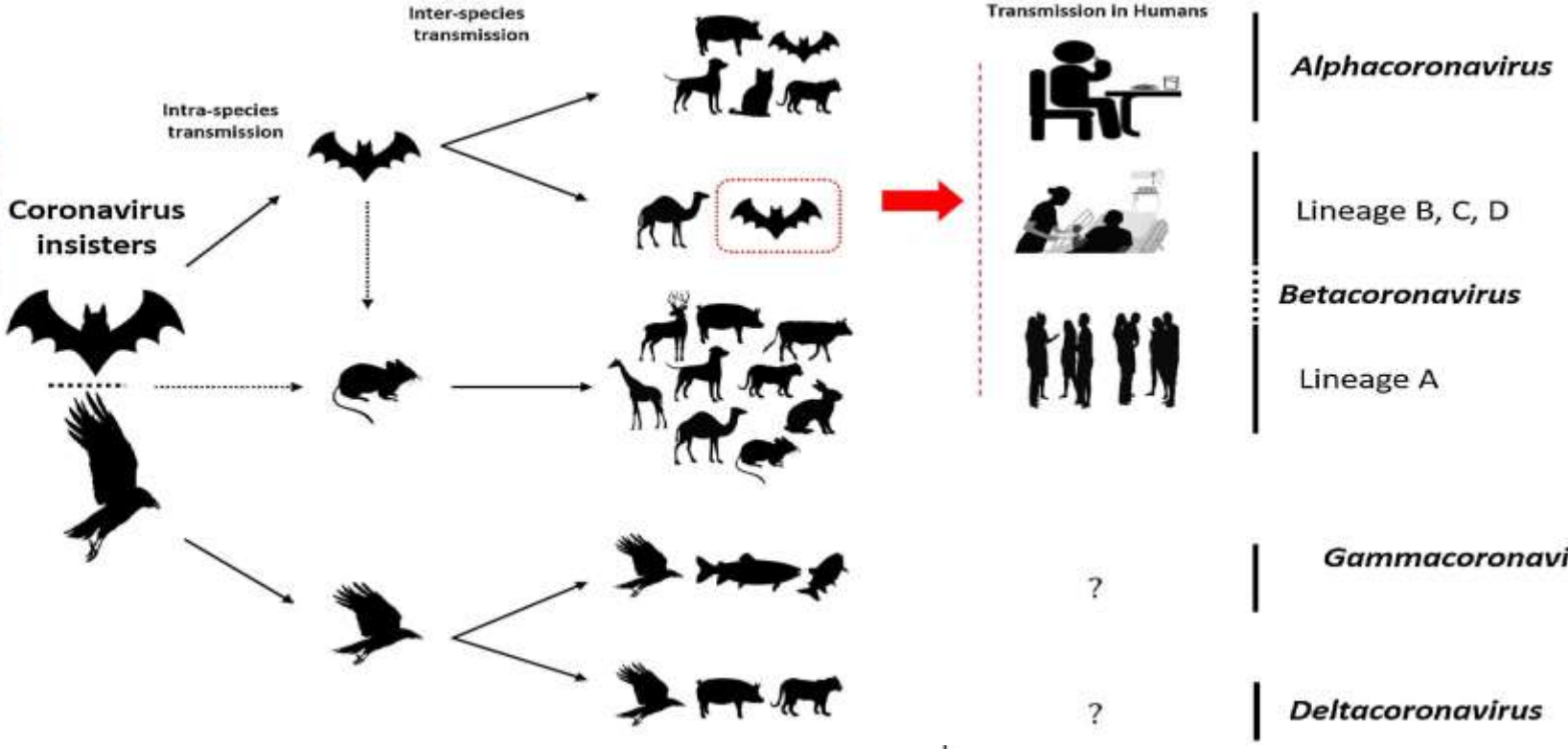

Country with high incidence of Behçet's disease

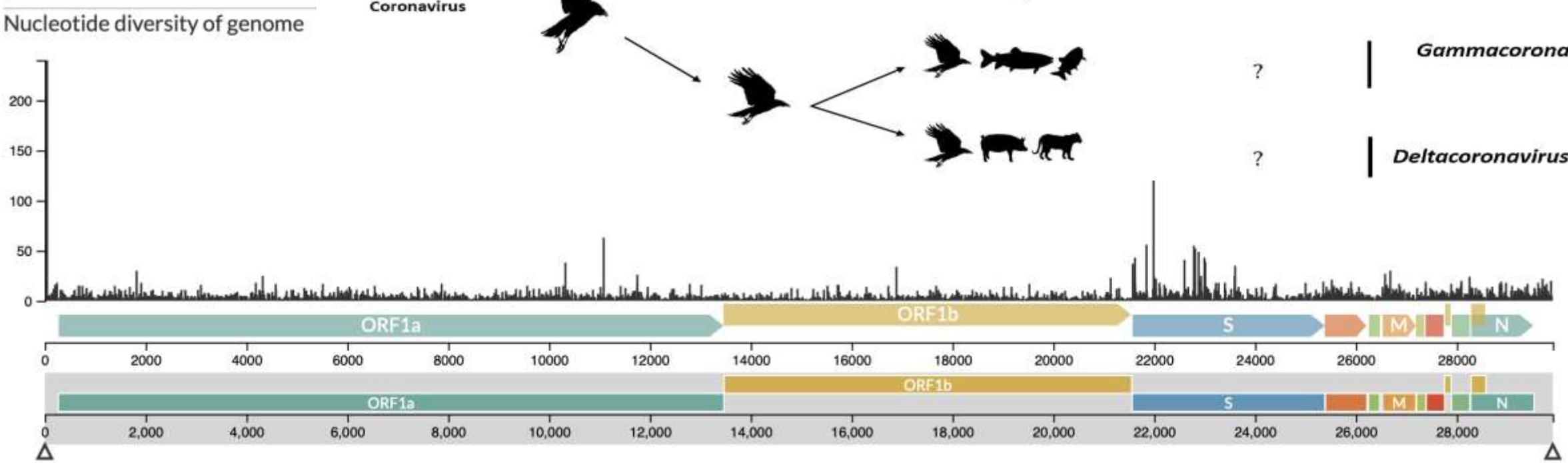

Initial viral population
consensus genome
viral replication in the presence of a mutagenic agent or repeated bottleneck transfers
viral replication in a constant environment
extinction
fitness
survival
horizontal lines represent single viral genomes
symbols on lines represent mutations



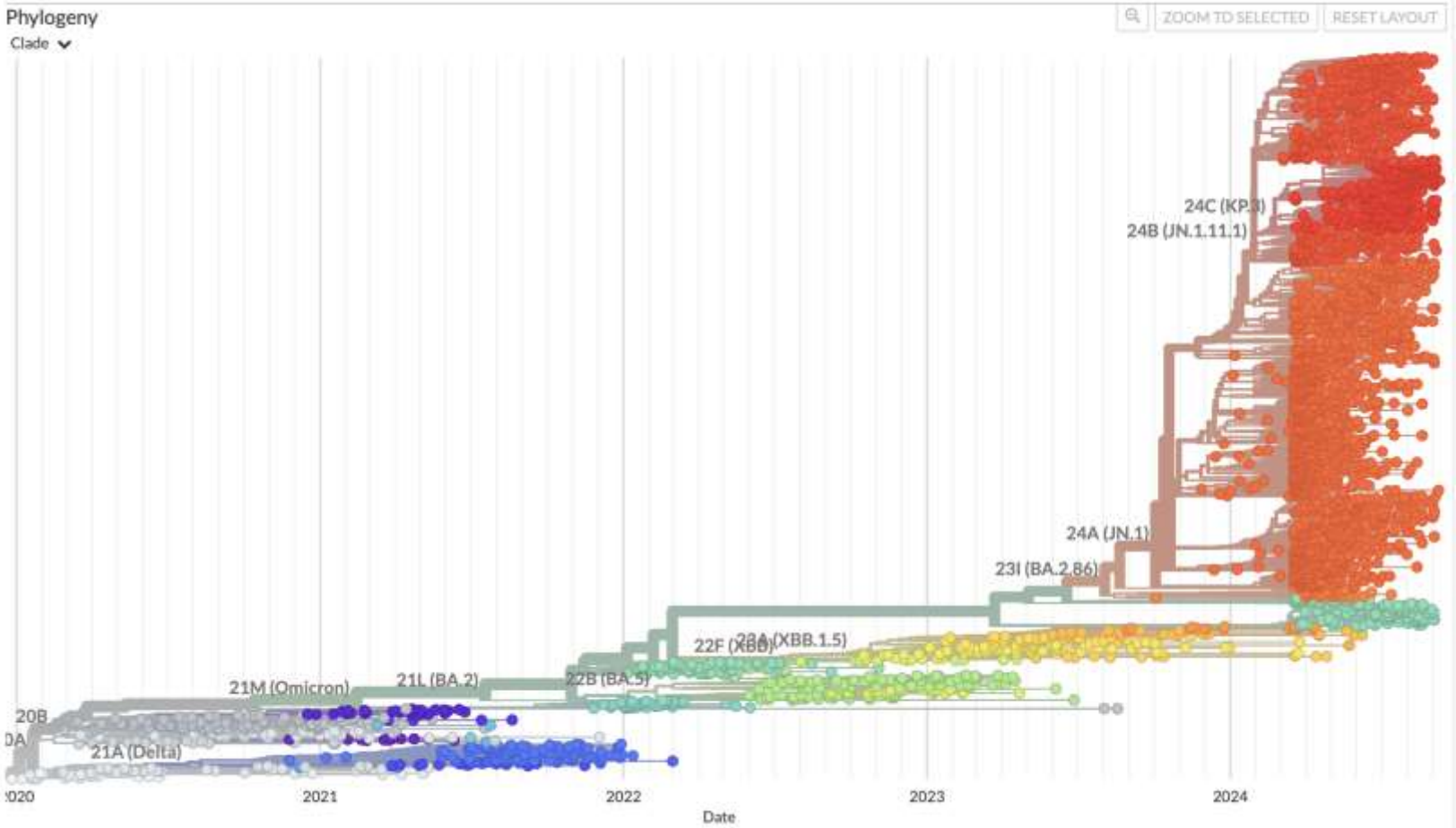
Koronaviruslar

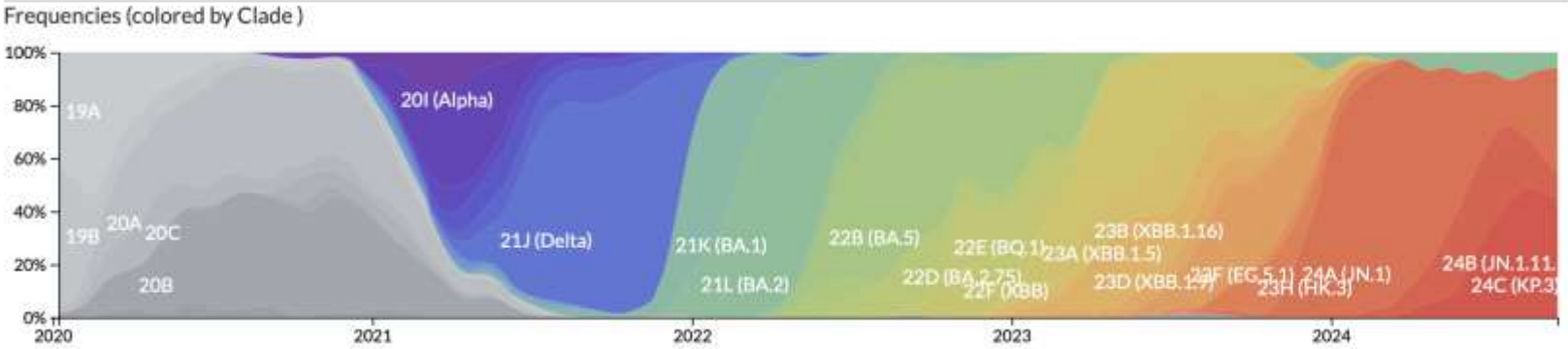
Coronavirus

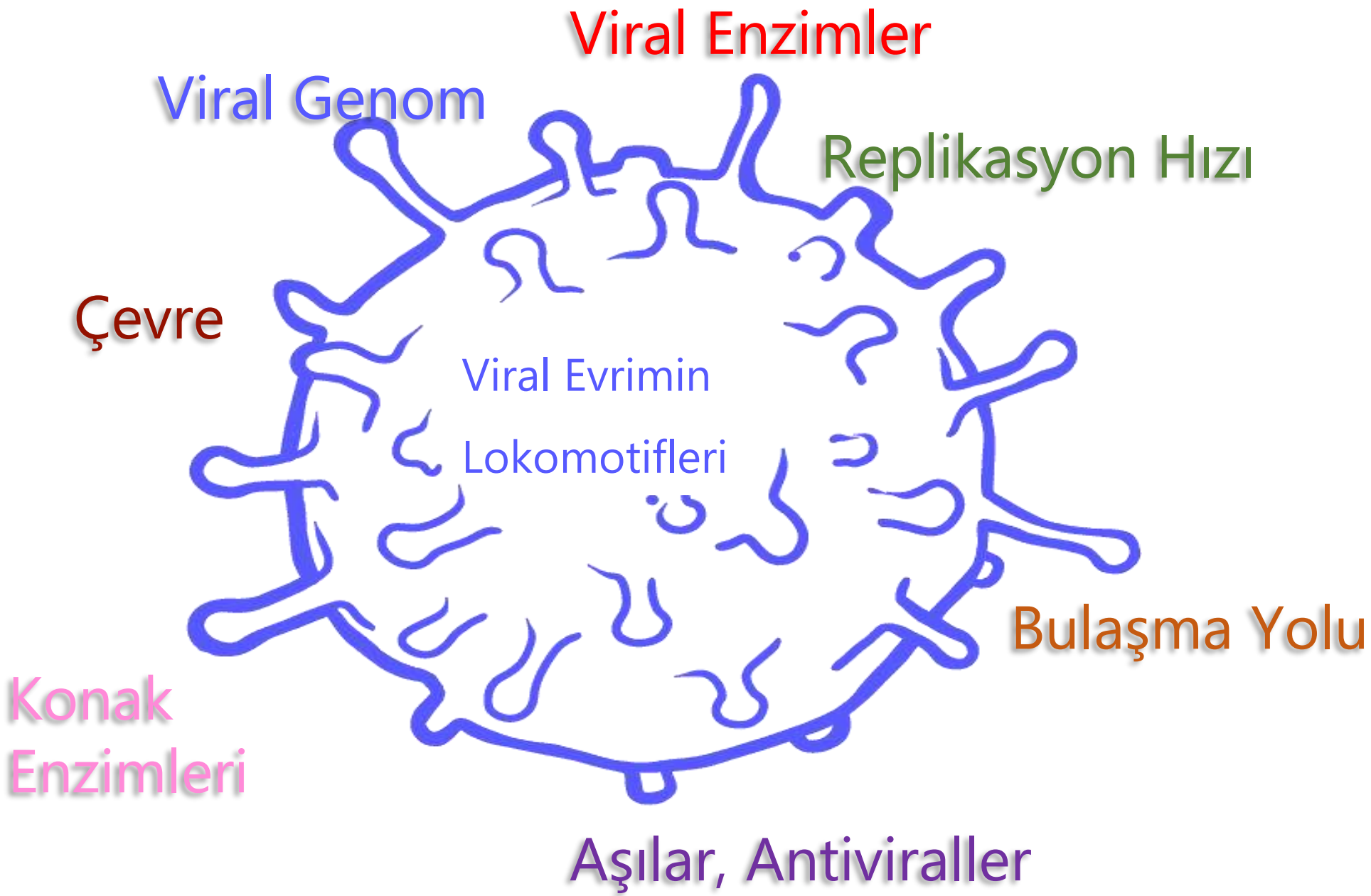




Sars Cov-2


Phylogeny
Clade
ZOOM TO SELECTED
RESET LAYOUT
24C (KP.3)
24B (JN.1.11.1)
24A (JN.1)
23I (BA.2.86)
22F (XBB)
23A (XBB.1.5)
22B (BA.5)
21L (BA.2)
21M (Omicron)
20B
21A (Delta)
2020
2021
2022
2023
2024
Date


Frequencies (colored by Clade)
100%
80%
60%
40%
20%
0%
19A
19B
20A
20C
20B
20I (Alpha)
21J (Delta)
21K (BA.1)
21L (BA.2)
22B (BA.5)
22E (BQ.1)
22D (BA.2.75)
22F (XBB)
23A (XBB.1.5)
23B (XBB.1.16)
23D (XBB.1.9)
23F (EG.5.1)
23H (FLK.3)
24A (JN.1)
24B (JN.1.11.
24C (KP.3)
2020
2021
2022
2023
2024


Viral Enzimler
Viral Genom
Replikasyon Hızı
Çevre
Viral Evrimin
Lokomotifleri
Bulaşma Yolu
Konak
Enzimleri
Aşılar, Antiviraller