

~8% of the human genome has a viral origin representing molecular fossils of past infections

LTR retrotransposons = Endogenous retroviruses (ERV)

Category	Percentage
Intons	25.0%
Protein-coding genes	1.5%
LINEs	26.4%
SNEs	13.1%
DNA transposons	2.2%
Simple sequence repeats	4.2%
Segmental duplications	5.0%
Miscellaneous heterochromatin	6.0%
Miscellaneous unique sequences	11.0%
LTR retrotransposons (ERV)	8.3%

Venter et al. *Science* 291(5607):1304-1351 (2001)

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Retroviruses stably integrate their genetic material in the genome of the host cell

Overtime the genome of ERV accumulated mutations hampering the formation of infectious progeny viruses

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...overtime they are subjected to sequence divergence

Ancestral provirus with intact & functional ORFs

Modern provirus that underwent divergence (non-functional ORFs)

~700 000 known HERV loci in the human genome Not infectious (no production of viral particles) Expression of some transcripts Link with diseases (cancers, ALS)

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ERV are genetically & structurally related to infectious retroviruses

Who came first?

Monde K. *Retrovirology* 2017 Virology-Outbreaks 2025 10

ERV are present in virtually all eukaryotes

The presence of a provirus at a given locus in two different species indicates that infection of germ line occurred before separation.

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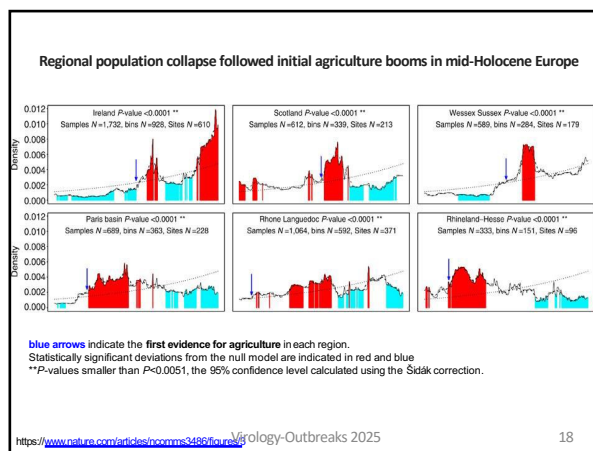
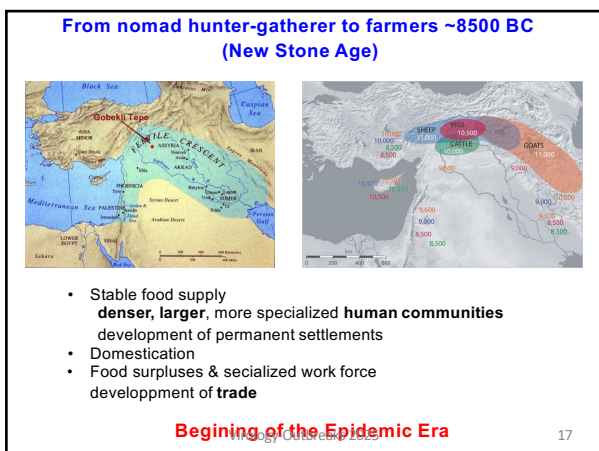
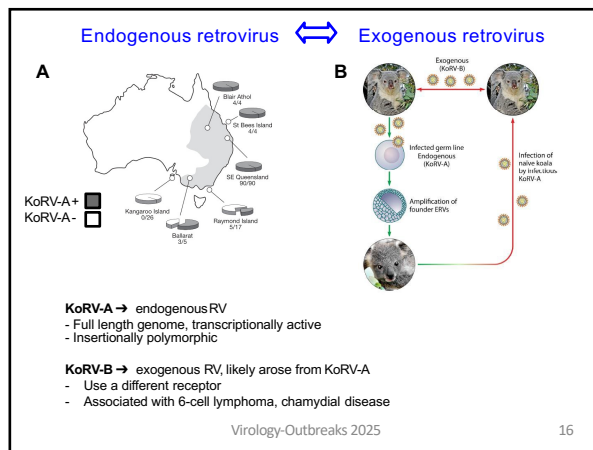
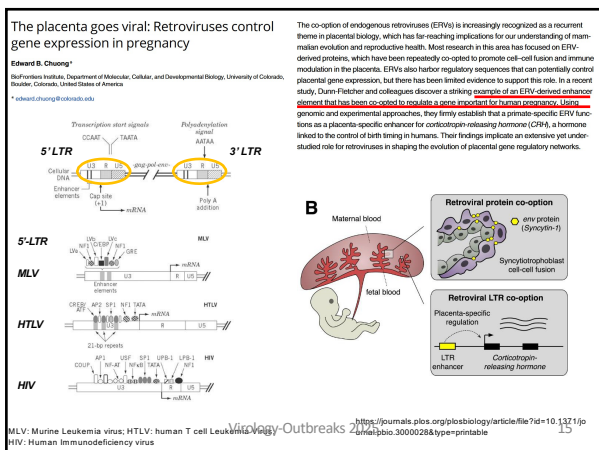
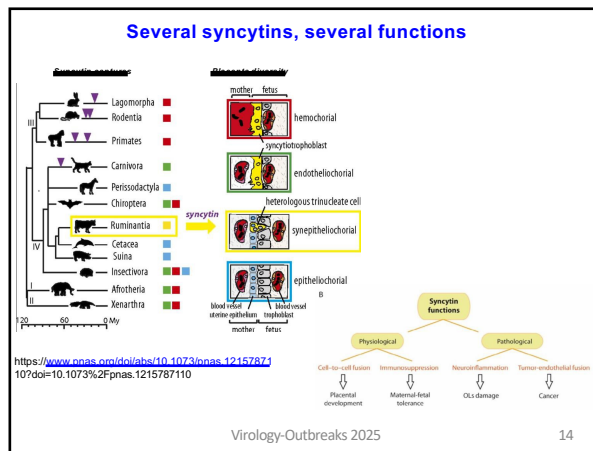
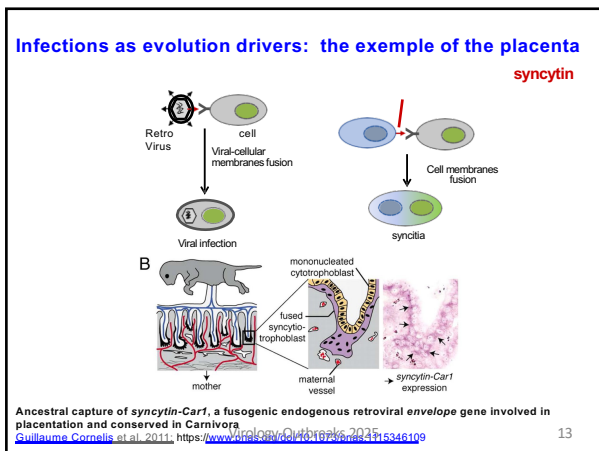
Infections as evolution drivers: the example of the placenta

Syncytin is a captive retroviral envelope protein involved in human placental morphogenesis

Sha M, Yin X, Li X, Zhang J, Li C, Guo Y, et al. *Development* 2005;132:111-119.

Many mammalian viruses have acquired genes from their hosts during their evolution. The rationale for these acquisitions is usually quite clear: the captured genes are subjected to provide a selective advantage to the virus. Here we describe the opposite situation, where a viral gene has been co-opted to serve an important function in the physiology of a mammalian host. This gene, encoding a protein that we here called syncytin, is the envelope gene of a recently identified human endogenous defective retrovirus, HERV-W. We find that the major sites of syncytin expression are placental syncytiotrophoblasts, multinucleated cells that originate from fetal trophoblasts. We show that expression of recombinant syncytin in a wide variety of cell types induces the formation of giant syncytia, and that fusion of a human trophoblastic cell line expressing endogenous syncytin can be inhibited by an anti-syncytin antibody. Our data indicate that syncytin may mediate placental cytotrophoblast fusion *in vivo* and thus may be important in human placental morphogenesis.

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Exploration, conquest, trade contributed to the spread of deadly infectious diseases, file: Enseignement 2021-2022, Outbreaks_History_Record_Arte.mp4

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Yersinia Pestis - Black Death. (bacteria !)

Origins of Black Death (disputed): near Lake Issyk-Kul of modern-day Kyrgyzstan, 2500 years ago

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4870133/>

Kaffa (now Feodosiya): the Black death port of entry in Europe

« The dying Tatars (Mongols), stunned and stupefied by the immensity of the disaster brought about by the disease, and realizing that they had no hope of escape, lost interest in the siege. BUT they ordered corpses to be placed in catapults and lobbed into the city in the hope that the intolerable stench would kill everyone inside. »
Gabriele De Mussi from Plorenza

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Yersinia Pestis - Black Death

- Both the vector (*Oriental rat flea*) and the vector host (*Rattus rattus*) migrated/were carried along the trade routes from East to West.
- Between 1347 and 1351 → 35 millions people died (30 to 60 % the European population)
- The bacteria *Yersinia pestis* was discovered by Alexandre Yersin in 1894 during the Hong Kong epidemics. Paul-Louis Simond (1898) discovered the vector.
- Today: about 2,000 cases/year mostly in Low-income countries; 5-15% case fatality rate

Disease outbreak news - Madagascar

1 octobre 2021

Le 29 août 2021, la Direction de la veille sanitaire, de la surveillance épidémiologique et riposte du Ministère de la santé publique de Madagascar a reçu une alerte du district sanitaire d'Anoronamano (région d'Itohy) concernant un décès dans la communauté et 15 cas suspects de peste pulmonaire, survenus dans la municipalité de Manonirina. Tous les cas présentaient les symptômes suivants: fièvre, maux de tête, faiblesse, essoufflement, douleurs thoraciques et toux. La peste est endémique à Madagascar et des foyers épidémiques sont souvent régulièrement, bien que chaque foyère épidémique soit préoccupante. En outre, la peste pulmonaire est une maladie à déclaration obligatoire en vertu du Règlement sanitaire international de 2005.

[https://www.who.int/emergencies/diseases/outbreak-news/item/20211001-madagascar/](https://www.who.int/emergencies/diseases/outbreak-news/item/20211001-madagascar)

How the Bubonic Plague Was Transmitted

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Variola Virus and Smallpox

- Phylogenetic studies indicate that Variola Virus infecting humans, and those infecting camels (CMLV) and gerbils (TATV) emerged almost simultaneously from a common ancestor
- Very contagious and deadly (mortality rate 15-30%)
- Earlier description in the 4th century CE in China
- Very narrow host specificity (tropism)

Ramses V (1157 BC)

humans
gerbils
camels
horses
monkeys
cows

<https://www.cdc.gov/sms/history/history.html>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC373269/>

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“Wherever the European had trod, death seemed to pursue the aboriginal.”
C. Darwin, The Voyage of the Beagle, Chapter XIX

Europe

←

→

Americas
Africa
Oceania

Smallpox
Measles
Diphtheria
Malaria
Whooping cough
Tuberculosis
Scarlet fever

Typhus
Mumps
Pneumonia
pertussis
Anthrax
Rubella
Influenza

15th – 19th century : 50 to 90% decrease of the indigenous population (Americas, Australia)

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Modeling of EID spreading dynamics depending on the preexisting immunity in the population

Day 1

Day N

Concept of Herd Immunity

<https://imgur.com/gallery/8M7c8#J7LANG4>

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Variolization was practiced in China & India since ~1000 aC




Reduced mortality from 30% to 2-3% upon infection

By 1700, variolation had spread to Africa, India and the Ottoman Empire.

https://fr.wikipedia.org/wiki/Mary_Wortley_Montagu
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Smallpox, Jenner, Blossom & James Philips

It was a common belief that dairymaids were in some way protected from smallpox: "I shall never have smallpox for I have had cowpox. I shall never have an ugly pockmarked face."



Gaston Mélingue, Lithography 1894

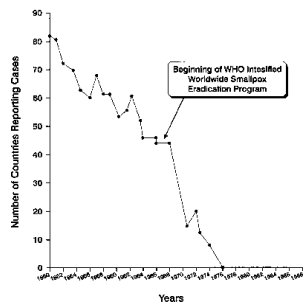
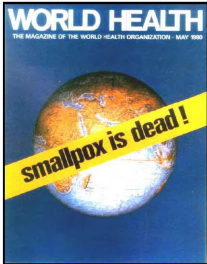
Edward Jenner performing the first smallpox vaccine in 1796. On the right, we observe a young woman who puts a bandage on her hand where the bubo taken for this "vaccine" is.

A month later, Jenner inoculated J. Philips with smallpox, who remained unscathed.

<https://www.nlm.nih.gov/bsd/Articles/PMC1200588>
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Number of Countries Reporting Smallpox Cases 1950-1976

I am among the last to be vaccinated (-:

1980

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The Cow Pock, James Gillray, 1802, Wellcome Library, London

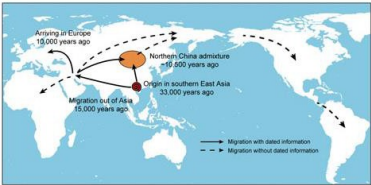

This 1802 cartoon by English caricaturist James Gillray (1756–1815) is a striking reminder that the controversy surrounding vaccination is as old as the earliest days of the procedure itself

cowpox, smallpox, vaccine et variole : orthopoxvirus

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Rabie

Dog domestication 33kya in N China; in Middle East by origin of farming. Rabies still in Europe but in decline

« Génétique moléculaire du virus de la rage, un siècle après pasteur », thèse 1988

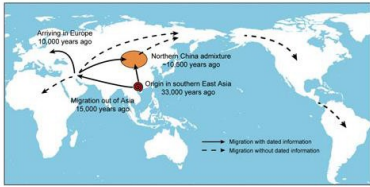
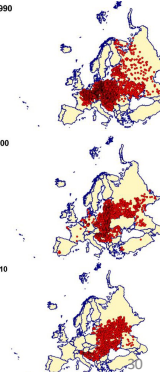
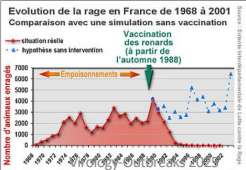
par Noël Tordo (Directeur Institut Pasteur de la Guinée)

<https://www.youtube.com/watch?v=s3CohwXZESc>

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Rabie

Dog domestication 33kya in N China; in Middle East by origin of farming. Rabies still in Europe but in decline

Evolution de la rage en France de 1968 à 2001
Comparaison avec une simulation sans vaccination

— situation réelle
— hypothèse sans intervention
— Vaccination des renards (à partir de l'automne 1988)

— Emploisements

Louis Pasteur
Vaccine against Rabie 1885

Modern epidemics and the discovery of the causative agents

Cholera epidemics
Starts in Asia (1817), reaches Europe (1832) and France (1832)
Vibio cholerae

Peste in China
1894 and 1910 (Hong Kong)
Yersinia pestis

Year	Disease or Organism	Scientist
1874	Leprosy	Hansen
1880	Malaria typhoid (organism seen in tissues)	Laveran and Eberth
1882	Tuberculosis glanders	Koch, Loeffler, and Schütz
1883	<u>Cholera streptococcus (ersipelae)</u>	<u>Koch and Fehleisen</u>
1884	Diphtheria	Klebs and Loettler
	Typhoid (bacilla isolate)	Gaffky
	Staphylococcus	Rosenbach
	Streptococcus	Nicolaier
	Tetanus	Fraenkel
1885	<i>Escherichia coli</i>	Escherich
1886	Pneumococcus	Yersin and Kitasato
1887	Malta fever, Soft chancre	Ducrey
1887	Gas gangrene	Welch and Nuttall
1892	<u>Plague</u>	<u>Yersin and Kitasato</u>
1894	Botulism	Van Ermengen
1898	Dysentery bacillus	Shiga
1896	<i>Hemophilus influenzae</i>	Pfeiffer

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The epidemics of the 20th century The Spanish flu 1917-18

1918 Influenza: the Mother of All Pandemics
Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 12, No. 1, January 2006
Jeffery K. Taubenberger* and David M. Morens†

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The epidemics of the 20th century The polio epidemic in the USA

History of Poliomyelitis (1971), John R. Pauly

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Global Polio Eradication Initiative (GPEI) was launched in 1988

WPV1 persists in Afghanistan and Pakistan in 2022

Figure 1. World map showing polio-endemic countries; outbreak of wild poliovirus in polio-free regions and countries at higher propensity of wild poliovirus outbreak in the year 2013.

Poliomyelitis: Historical Facts, Epidemiology, and Current Challenges in Eradication Man Mohan Mehndiratta et al. The Neurohospitalist 2014, Vol. 4(4) 223-229

The Fight against Poliovirus Is Not Over, Mbari et al. Microorganisms 2023

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FIGURE 1. Crude death rate* for infectious diseases — United States, 1900–1996†

*Per 100,000 population per year.
†Adapted from Armstrong GL, Conn LA, Pinner RW. Trends in infectious disease mortality in the United States during the 20th century. JAMA 1999;281:61-6.
‡American Water Works Association. Water chlorination principles and practices: AWWA manual M20. Denver, Colorado: American Water Works Association, 1973.

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The age of optimism

In 1967 the US Surgeon-General William Stewart famously declared "The time has come to close the book on infectious diseases"

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Impact of infectious diseases on human health today

Infectious diseases are responsible of
 ~26% deaths worldwide (~14 millions)
 ~16% of cancers - bacteria (*Helicobacter pylori*...) or viruses (hepatitis virus, Epstein Barr virus, papillomavirus...)

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<https://ourworldindata.org/causes-of-death>

Predicted hotspots for zoonotic infectious diseases

Primary drivers of past disease emergence

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What is the source of the EID?

- ~1400 known human pathogens
- 60% of known human pathogens are of zoonotic origin, and depend on an animal reservoir to survive
- 25-30% human-to-human transmitted
- 10-15% food-borne
- 75% of emerging pathogens originate in the wild → human-animal interface present a risk of emergence.

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Transfer of infectious diseases from wild to domestic animals

Anke K. Wiethoelter et al. PNAS 2015;112:9662-9667

Virology-Outbreaks 2025 PNAS 41

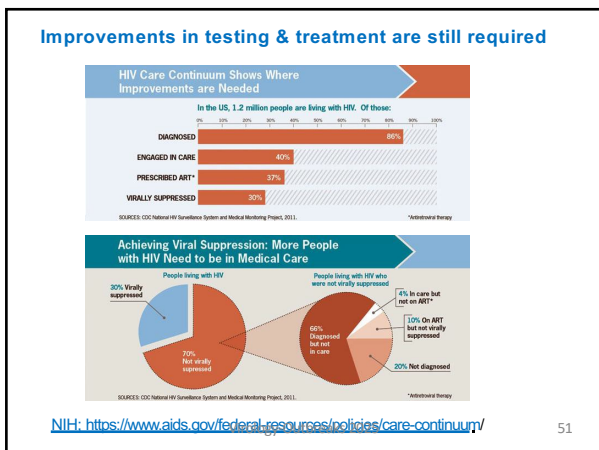
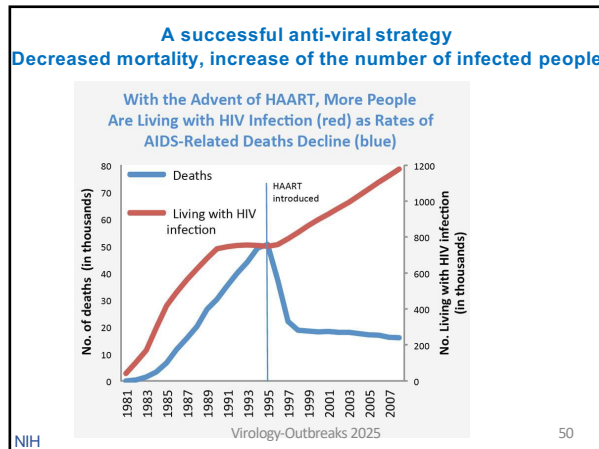
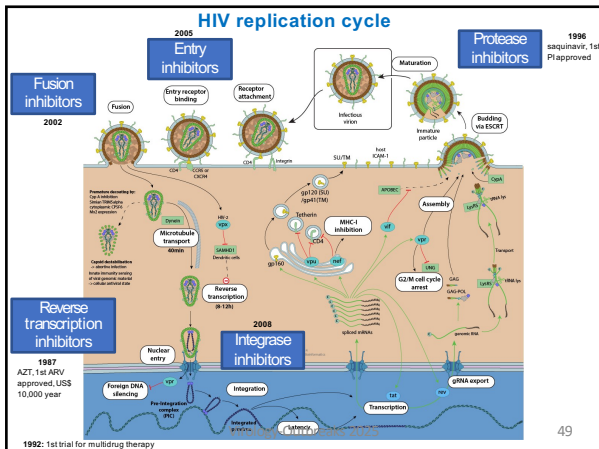
The HIV History by Mirko D. Grmek

Chapitre I: une maladie étrange est dénoncée: Los Angeles 1980
This is a very, very dramatic illness. I think, we can say quite assuredly that it is new (James Curran, Epidemiologist)
 CMV: cytomegalovirus, EBV: Epstein-Barr virus
 MMWR : morbidity and Mortality weekly report 1981
 Pneumocystis carinii (protozoaire), candidose
 Sarcome de Kaposi (dermatologie) New York et Los Angeles (20 et 6)

Chapitre II: l'enquête épidémiologique auprès des homosexuels américains
 hypothèse plurifactorielle (poppers); recherche biologique et biochimique, interrogatoires par le CDC, lymphadénopathie persistante
A la recherche du patient « 0 » commissaire de bord Air Canada, se déplaçait gratuitement en avion, 250 partenaires/0

Chapitre III: les premiers émois des européens (Danemark, Londres, Genève, Paris, Barcelone)

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Sociological and Geopolitical consequences of HIV

- Change of perception of the relationship between Doctor and Patient
- Change of intellectual property rights in Pharmaceutical Industry (Brazil played a Key role to declare they would not pay for IP since it was too much to pay for them)
- Strong success of individualization of treatment (the HAART allowed patient to survive in good conditions when they would have died)
- Failure of vaccine development
- Link of research between Virology and Bacteriology and Immunology (translational research and multi-disciplinary research)

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