

Evolution génétique virale

causes et conséquences

UE M1 Microbiologie
06 février 2026 Dr C.Bressollette-Bodin

-
- Evolution génétique virale = changements dans la structure génétique d'une population virale
 - Facteurs d'évolution multiples
 - Hôte infecté
 - Vecteur
 - Environnement
 - Virus
 - Conséquences
 - Nouveaux variants > souches > espèces
 - Nouvelles propriétés biologiques > nouvel hôte

Taxonomie - classification

- ICTV = International Committee on Taxonomy of Virus

<https://ictv.global/news/search-visual-browser>

Release: 2023 (MSL 39) Font size: Zoom: Screenshot: PNG Search: pandemicum Include all ICTV releases: ☐

Show 10 entries

Release	Rank	Name
2023	Species	Riboviria › Orthornavirae › Pisuviricota › Pisoniviricetes › Nidovirales › Cornidovirineae › Coronaviridae › Orthocoronavirinae › Betacoronavirus › Sarbecovirus › Betacoronavirus pandemicum

Showing 1 to 1 of 1 entries

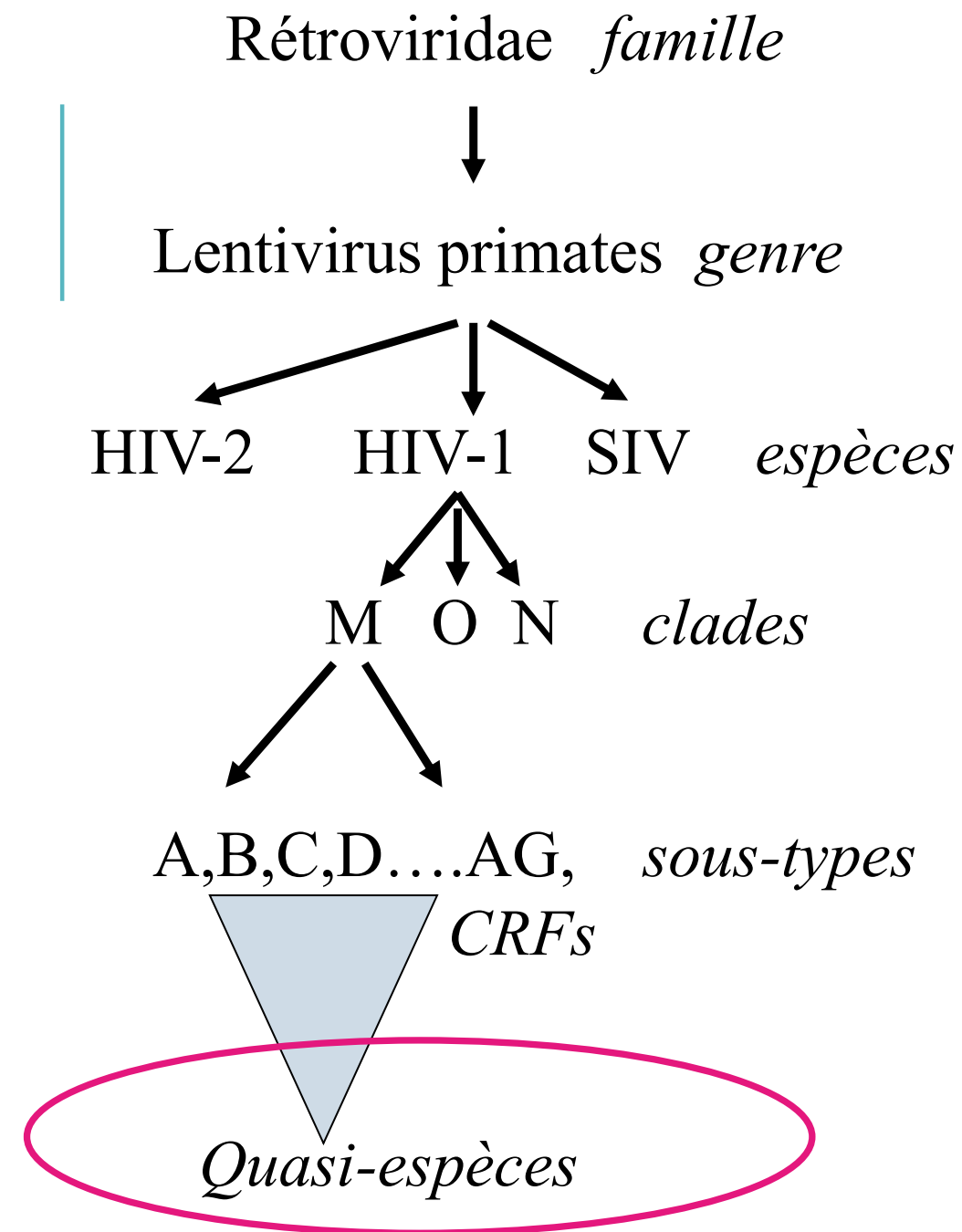
Previous 1 Next

Species of Subgenus **Sarbecovirus**

Betacoronavirus pandemicum

Diversité virale

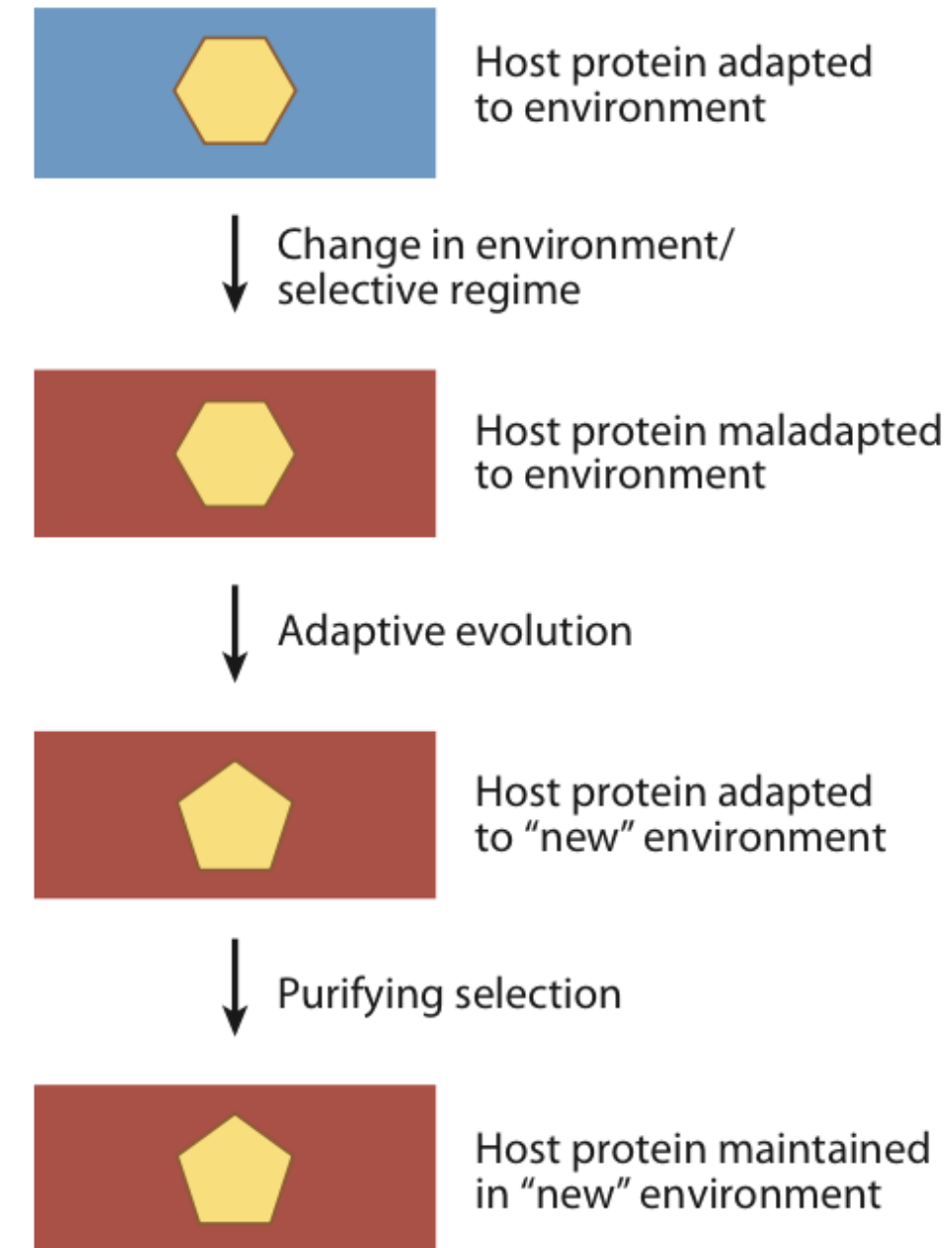
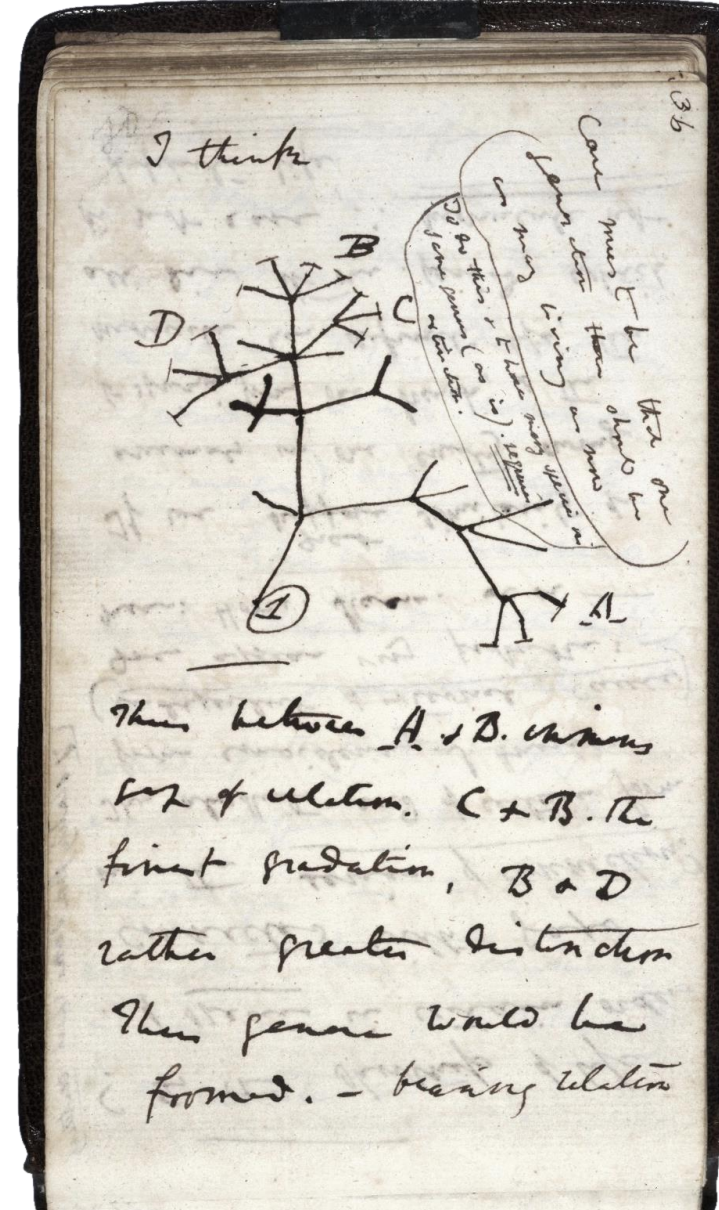
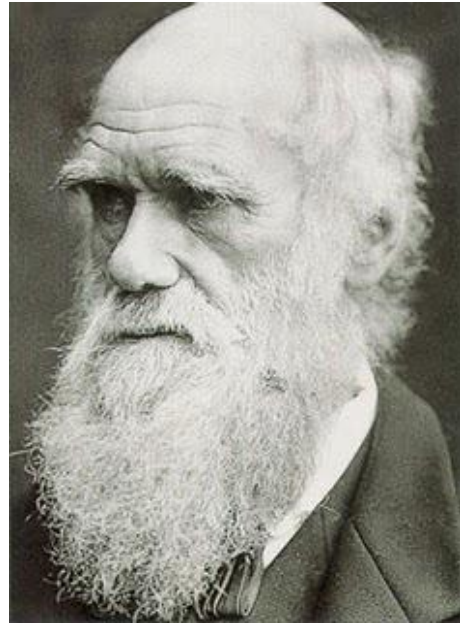
- Diversité génétique au sein d'une espèce de virus > notion de génotypes, clades, variants



Au sein d'une espèce :

- Différences antigéniques sérotypes
- Différences de séquences génétiques : génotypes

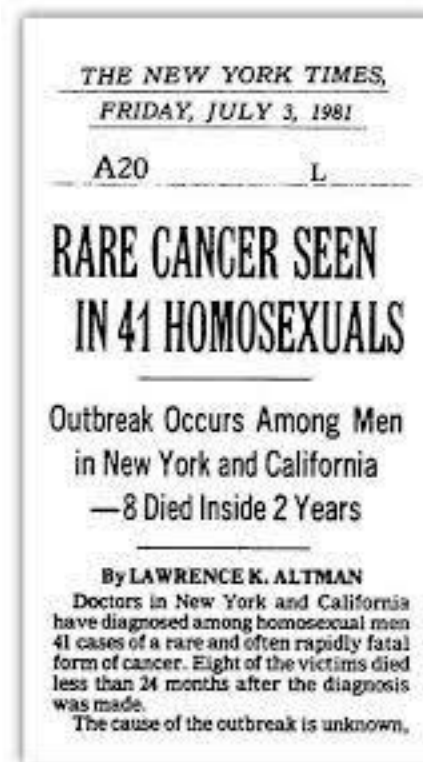
Evolution



- Evolution > succession de hasards /sélection

Evolution virale

- Nous sommes régulièrement confrontés aux conséquences de l'évolution virale
 - Nouveaux virus



HIV/AIDS



EBOLA



COVID-19

- Épidémies annuelles (grippe...)
- Résistance aux antiviraux (HIV)

Evolution virale

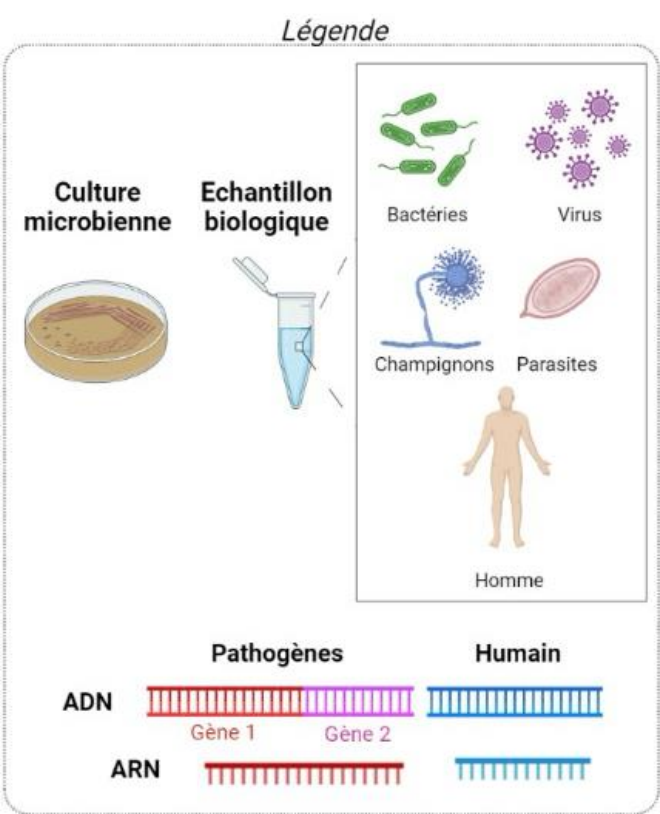
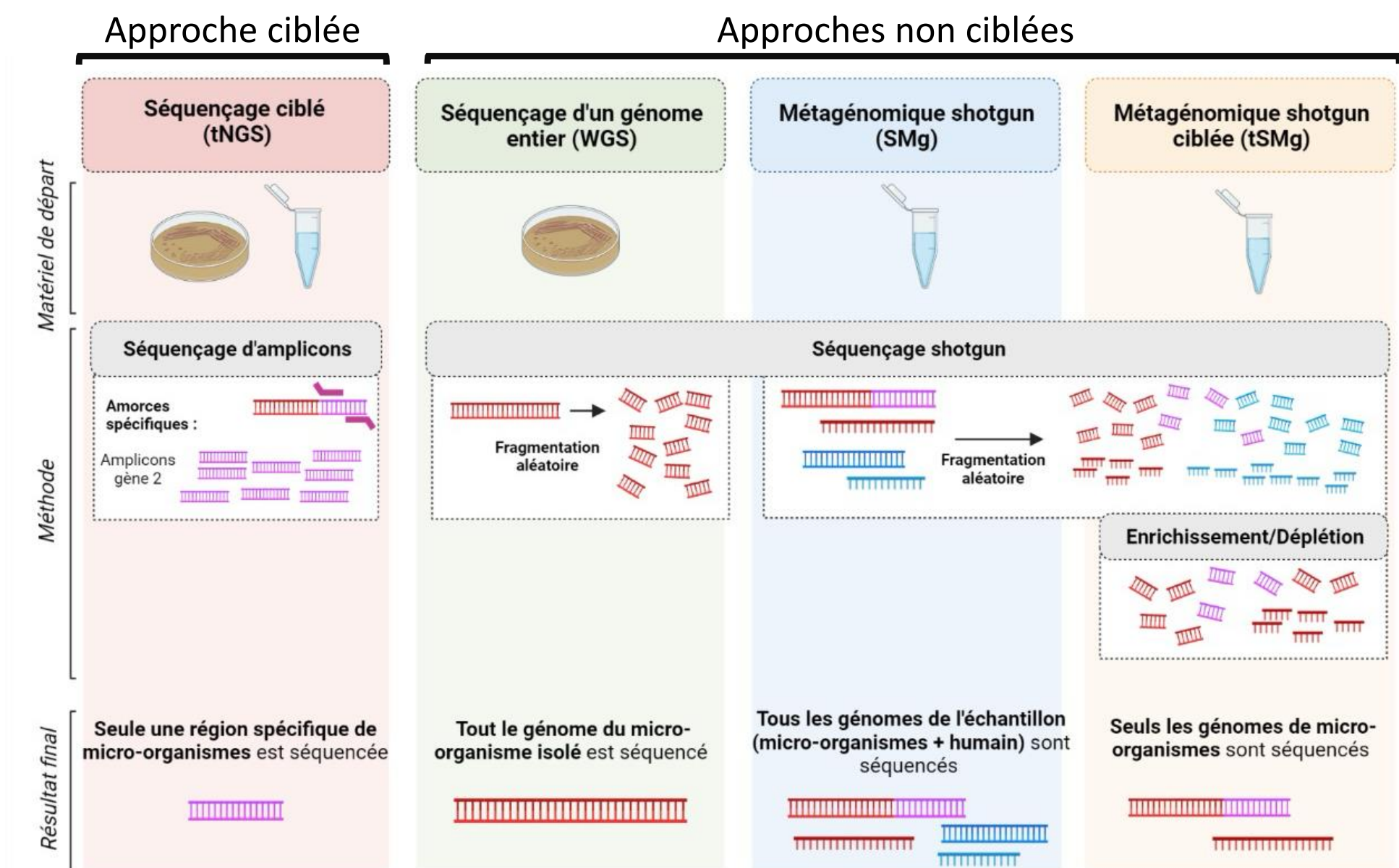
- Une population virale de grande taille
 - HIV: $\frac{1}{2}$ vie d'une particule virale = 6h, turnover quotidien = 90%, nb total de particules virales $> 10^9$ dans plasma
- Des mutations fréquentes
 - Mutations ponctuelles
 - Recombinaisons et réassortiments
- Qui génèrent de la diversité > notion de quasi-espèce
- Un processus de sélection
 - Notion de goulot d'étranglement
 - Sélection / immunité, environnement

Comment étudier la diversité et l'évolution génétique

- Evolution ++ des techniques de séquençage



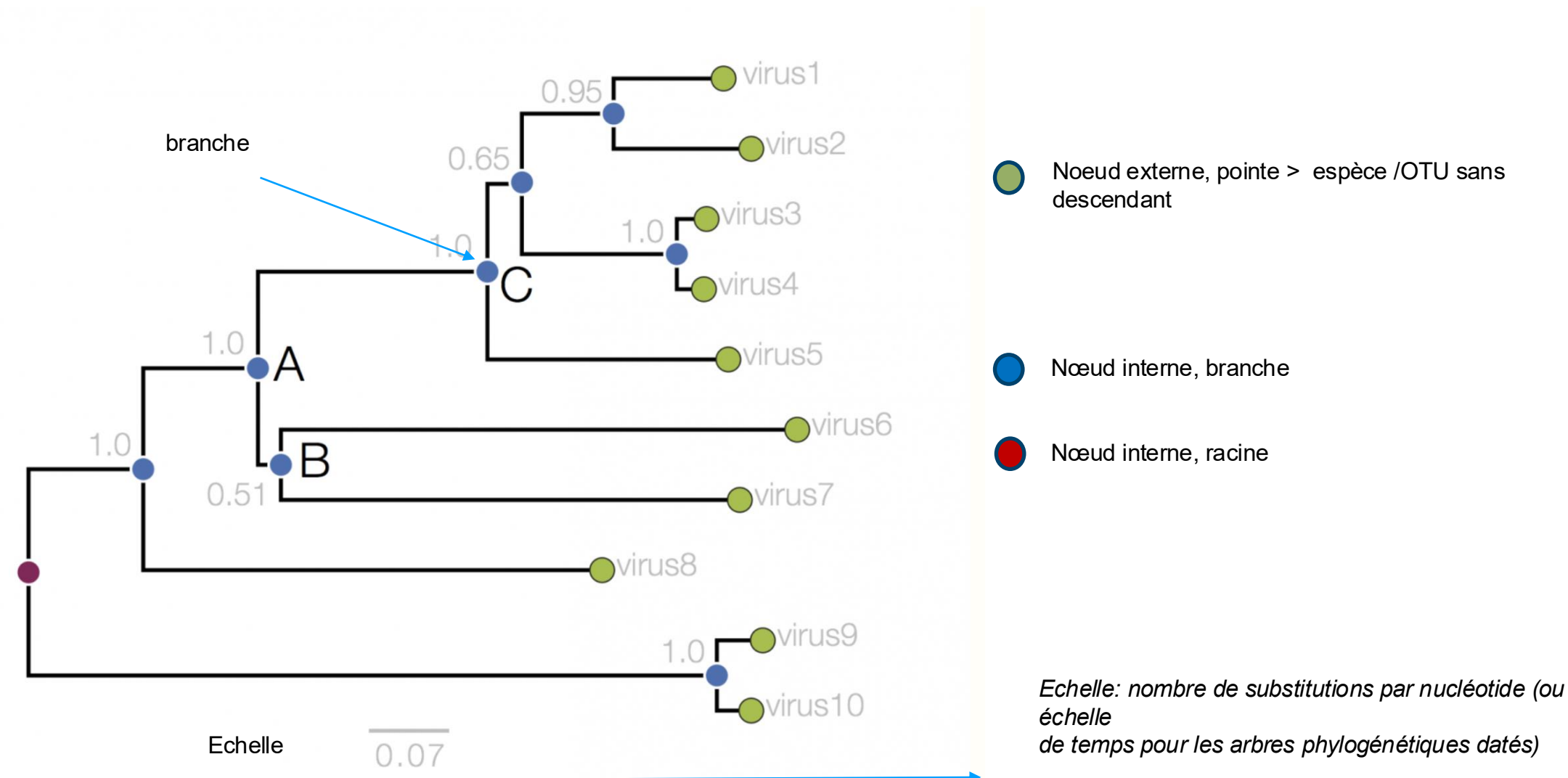
Les stratégies de séquençage à haut débit en microbiologie clinique :



Comment étudier la diversité et l'évolution génétique

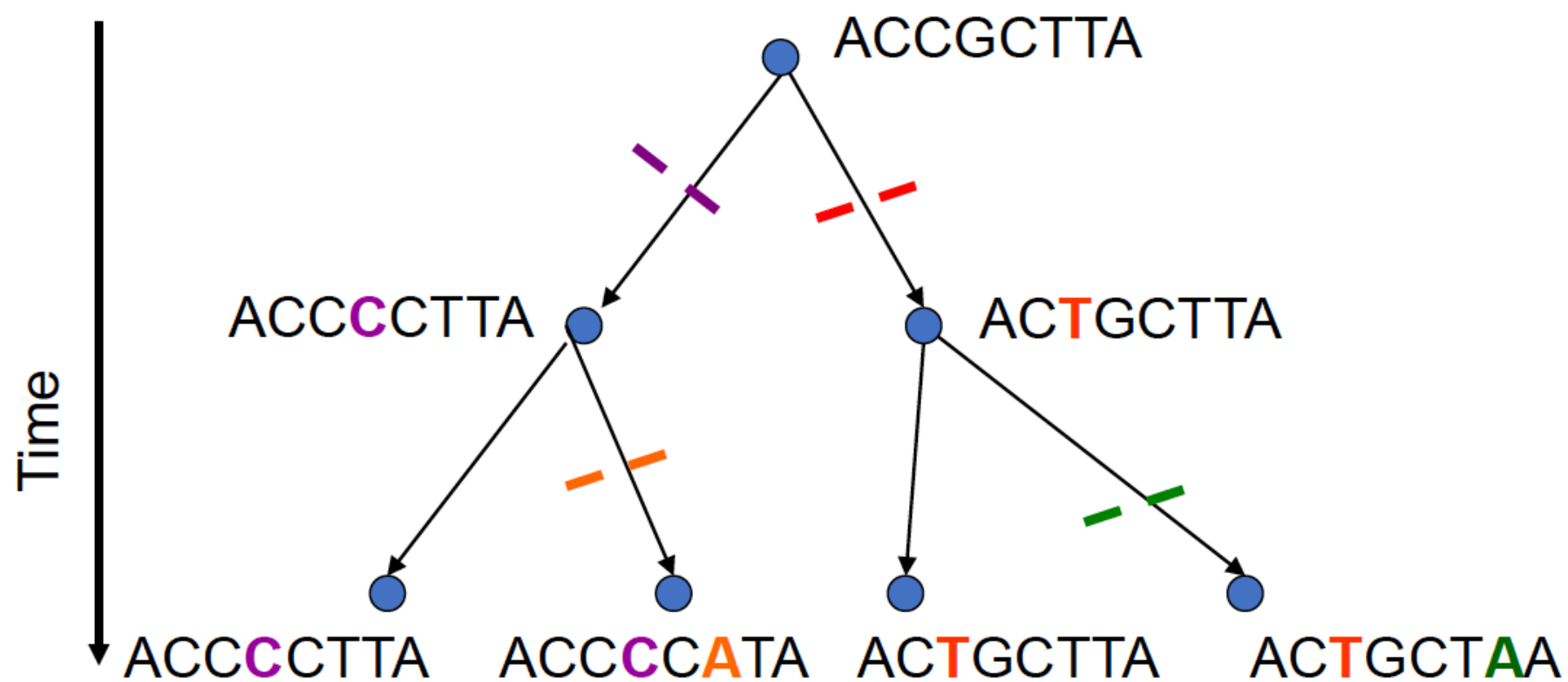
- La phylogénie ou arbre phylogénétique

= structure de classification hiérarchique qui représente des relations de parenté entre « objets » > en l'occurrence génomes viraux, sous la forme d'un arbre



Sequence-based phylogenetics

ACCCCTTA
ACCCATA
ACTGCTTA
ACTGCTAA

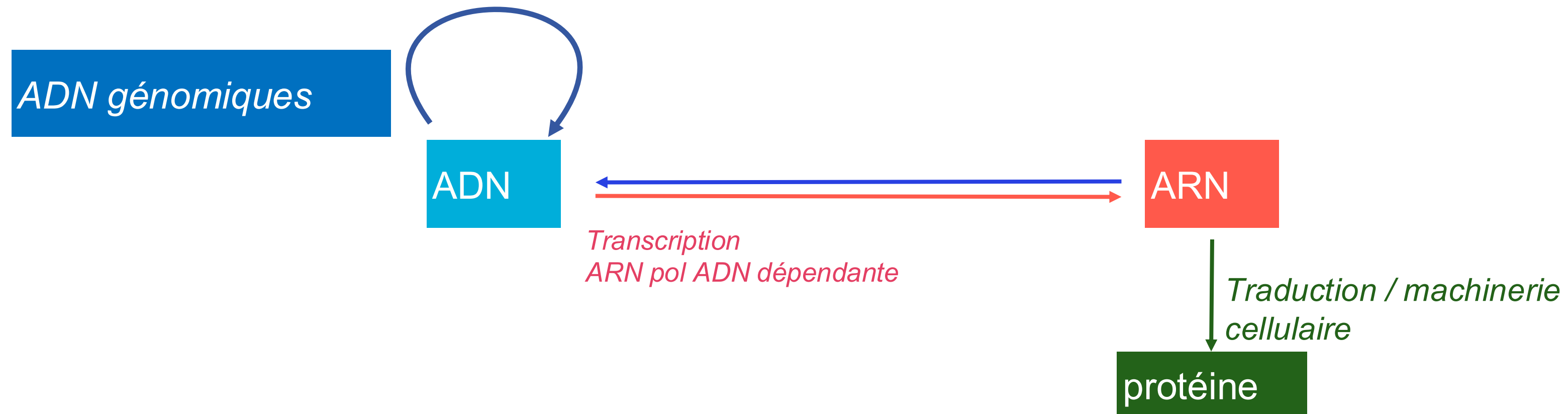


1. Sequence alignment
2. Evolutionary model

- Parsimony
 - Distance
 - Maximum likelihood
 - Bayesian
-
- Groups interpreted as common ancestry (acquired changes)
 - Branch lengths reflect number of changes

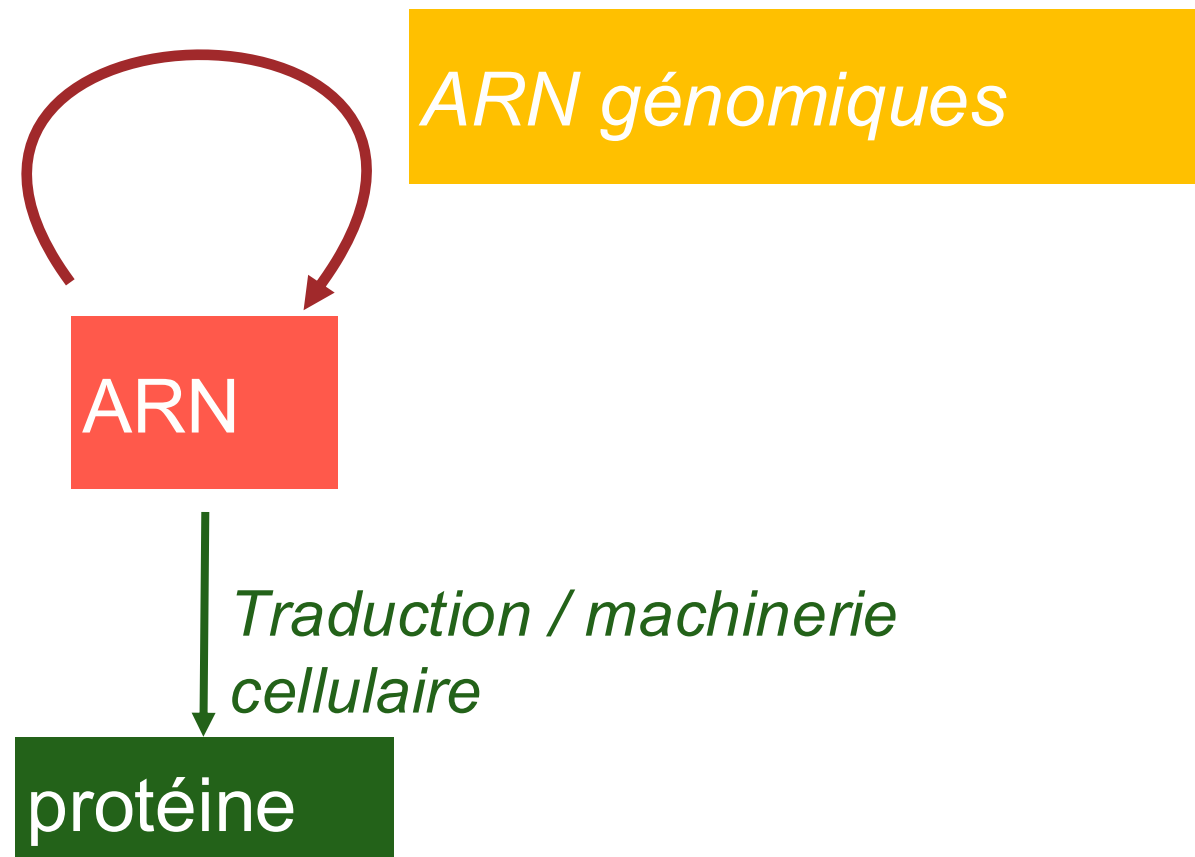
L'information génétique virale : virus ADN

*réplication (virus ADN)
> ADN polymérase ADN dépendante
(virale ou cellulaire)*

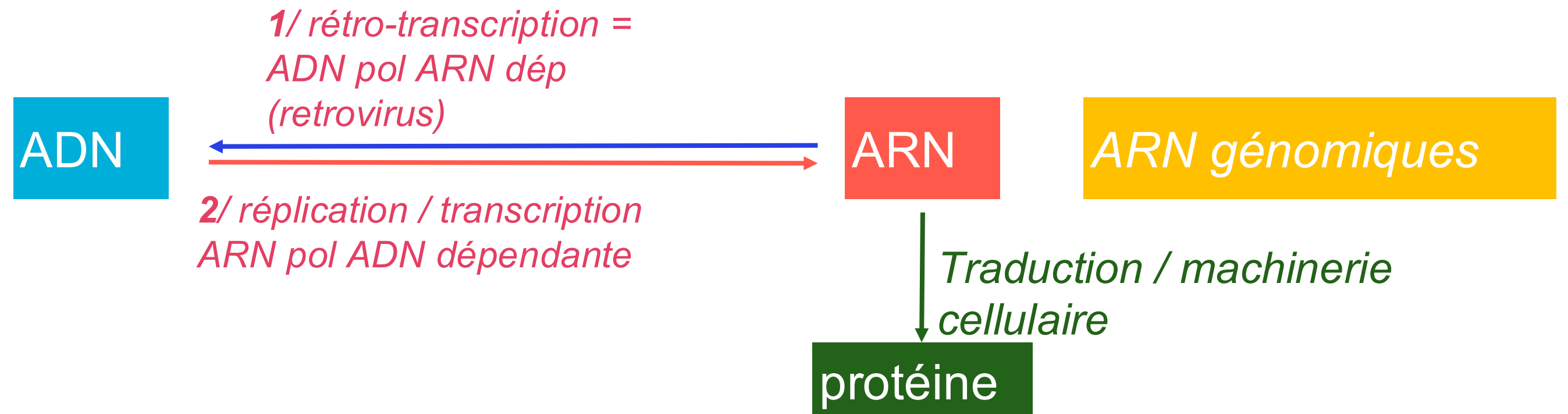


L'information génétique virale : virus ARN

Réplication / transcription (virus ARN)
> ARN polymérase ARN dépendante
(virale)



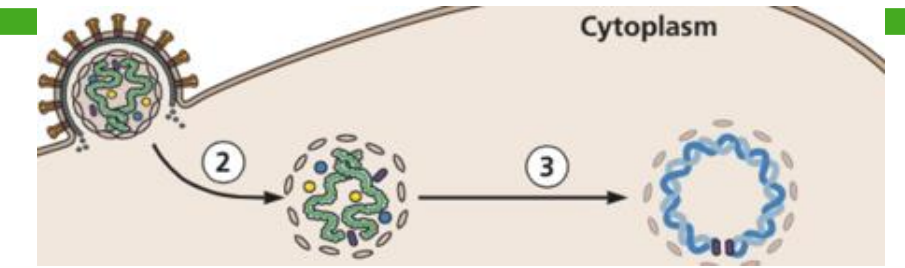
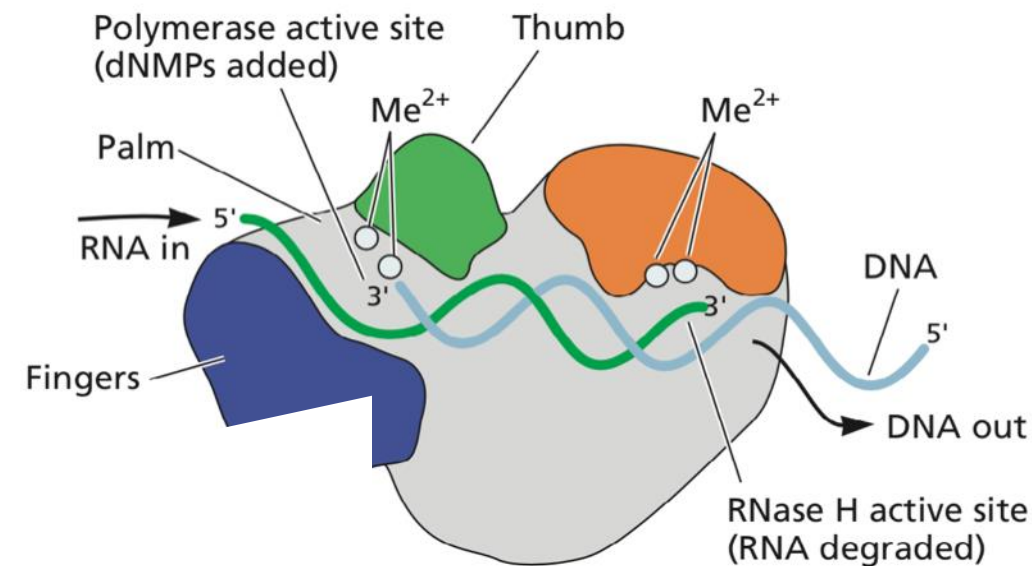
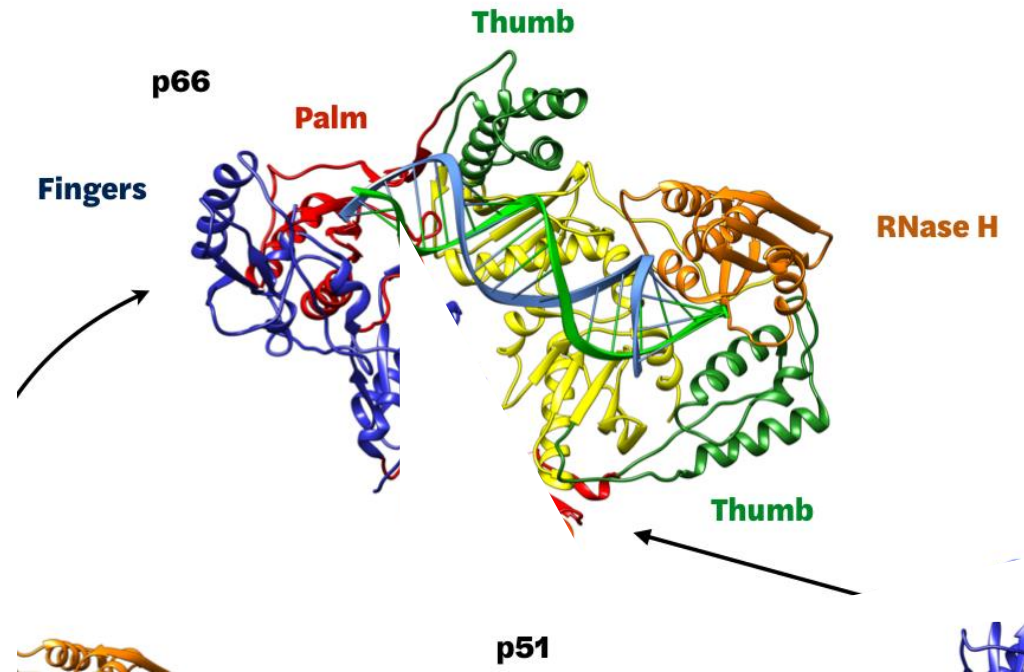
L'information génétique virale: rétrovirus



VIH

Transcriptase inverse virale

transcription inverse

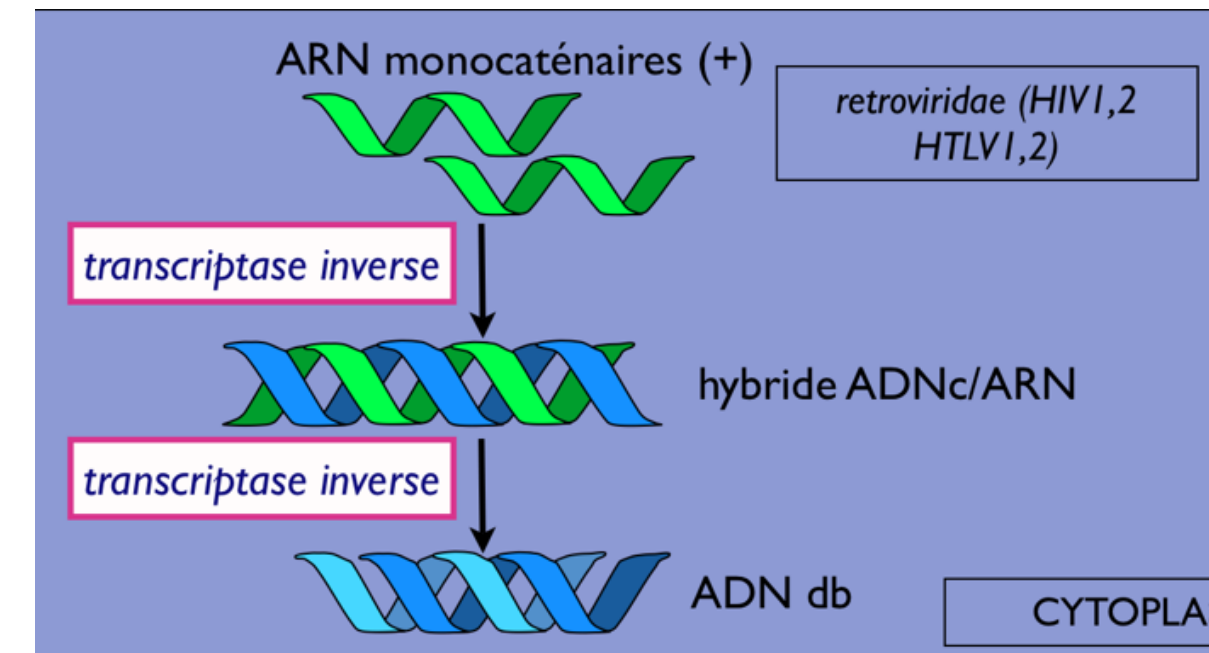


Virology Lectures 2021 • Prof. Vincent Racaniello • Columbia University

- synthèse d'une molécule d'ADN complémentaire de l'ARN: fonction **ADN polymérase ARN dépendante**
- dégradation de la molécule d'ARN: fonction **RNase H**
- synthèse d'un 2e brin d'ADN complémentaire du 1er = ADN db: **fonction ADN polymérase ADN dépendante**

Mais > absence d'activité correctrice d'erreurs à l'incorporation des nucléotides (activité proofreading) > mutations ponctuelles, 1-3 mutations / génome

> **Modifications conformations protéines cibles des traitements (cf cours HIV)**



Le concept de quasi-espèce

A Q β phage population is in a dynamic equilibrium with viral mutants arising at a high rate on the one hand, and being strongly selected against on the other. The genome of Q β cannot be described as a defined unique structure, but rather as a weighted average of a large number of different individual sequences.”

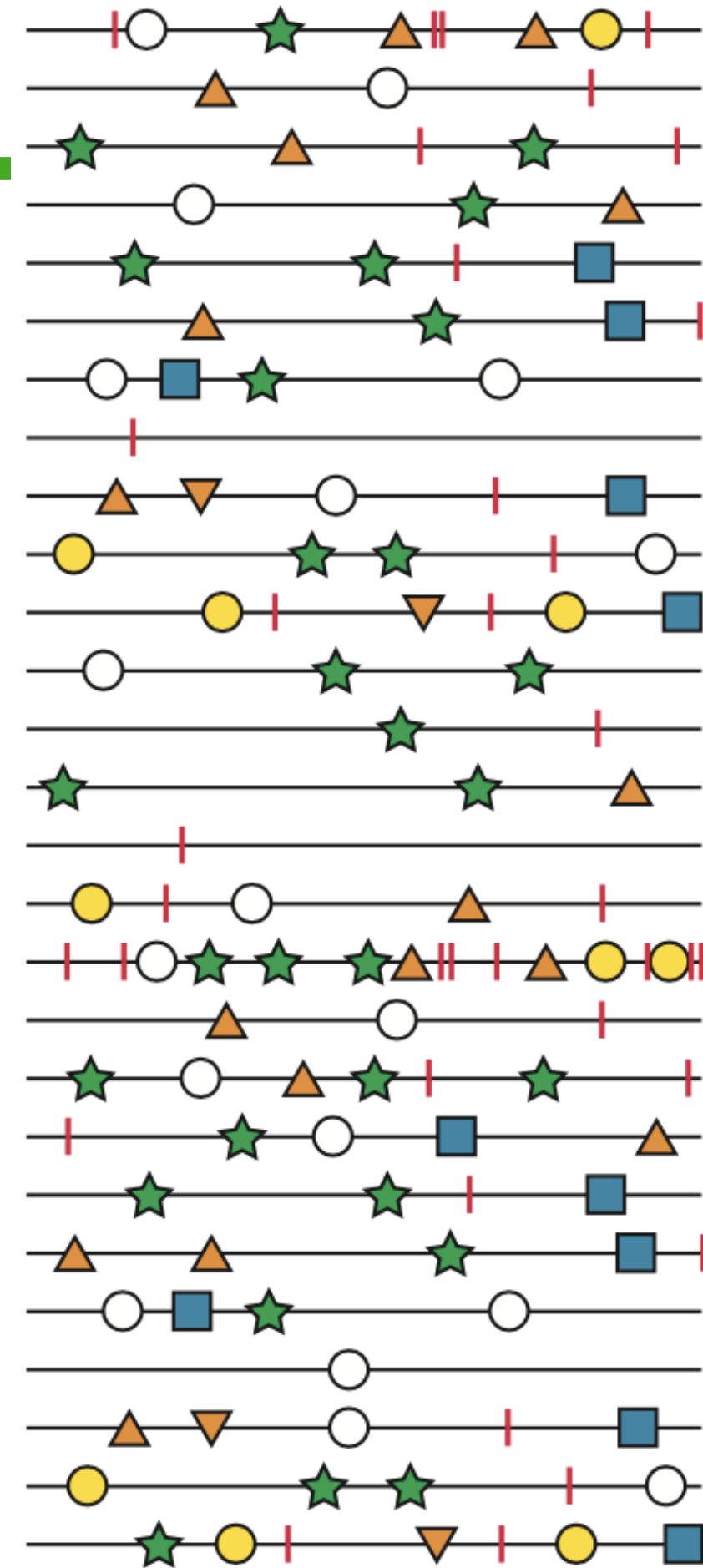
E. Domingo, D. Sabo, T. Taniguchi, C. Weissmann. 1978. Nucleotide sequence heterogeneity of an RNA phage population. Cell 13:735-744.

- Chez un individu infecté par une espèce virale, la population de virus n'est pas homogène, elle est constituée d'un ensemble de « réplicons », dont la distribution est dynamique dans le temps

Quasi-espèce = nuage de mutants

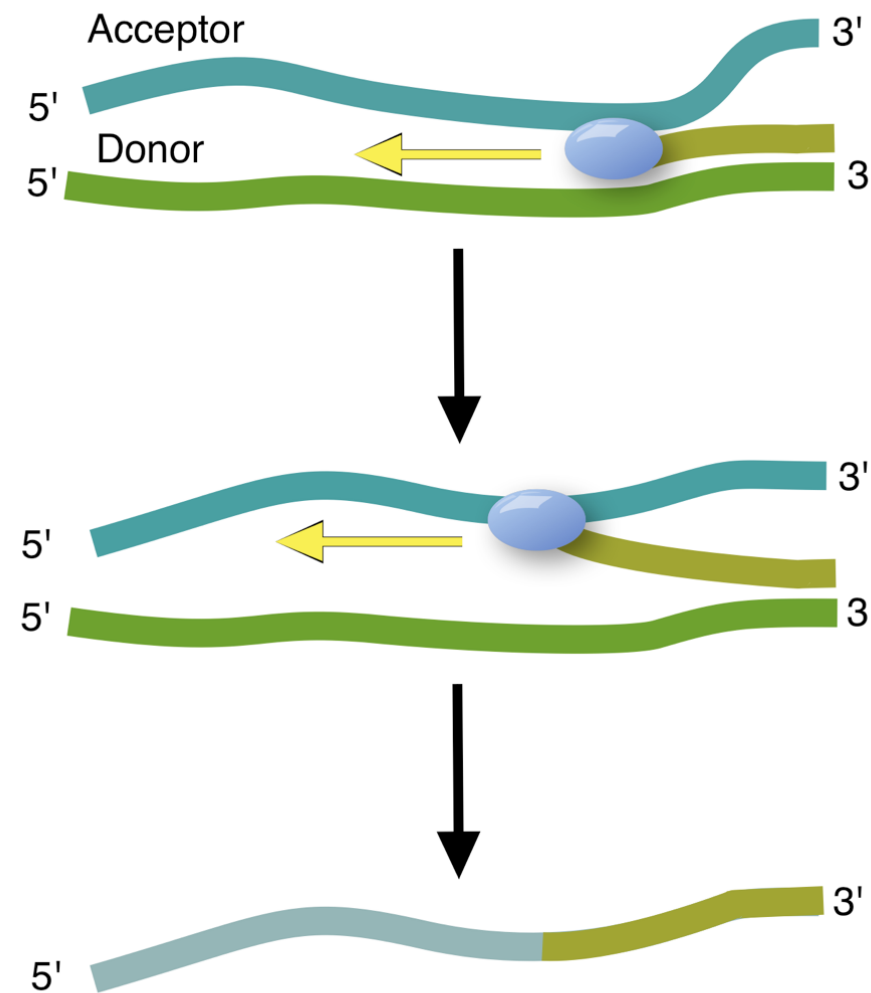
L'ensemble des mutants évoluent comme s'ils formaient « quasiment une seule et même espèce » (au sens chimique ou moléculaire et non biologique)

≠ séquence consensus obtenue par séquençage

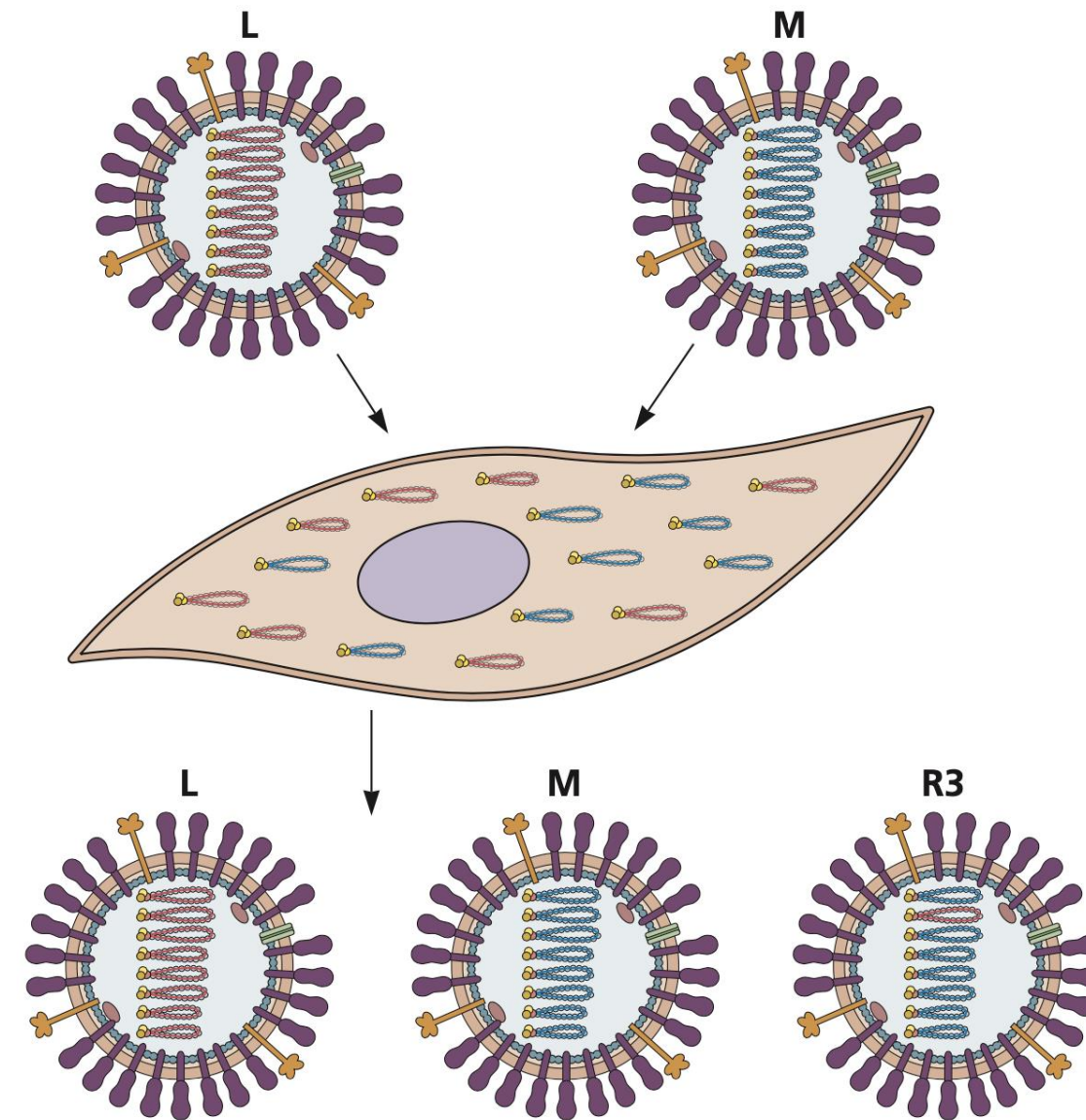


Autres mécanismes d'évolution génétique

Recombinaison



Réassortiment

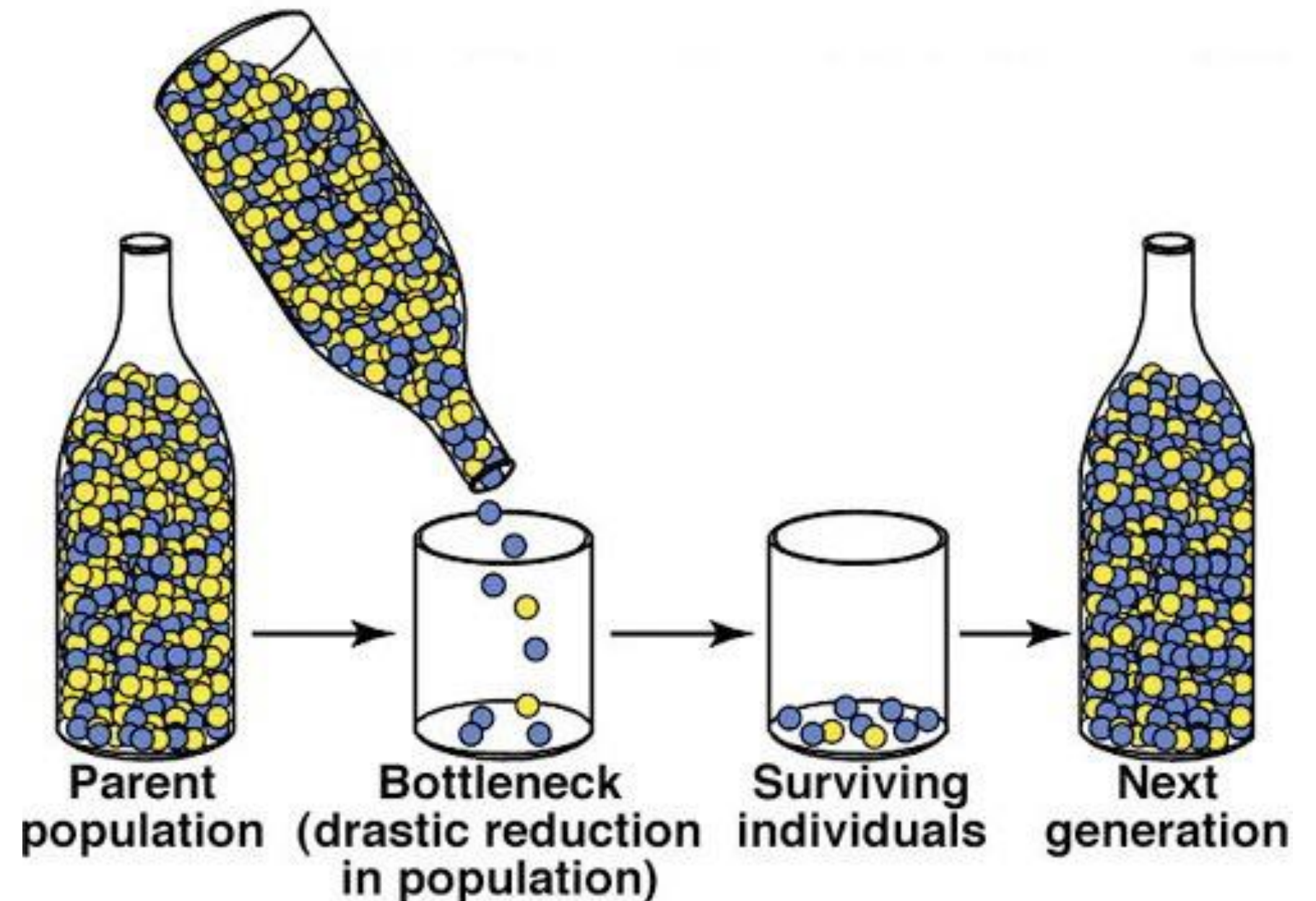


Sélection

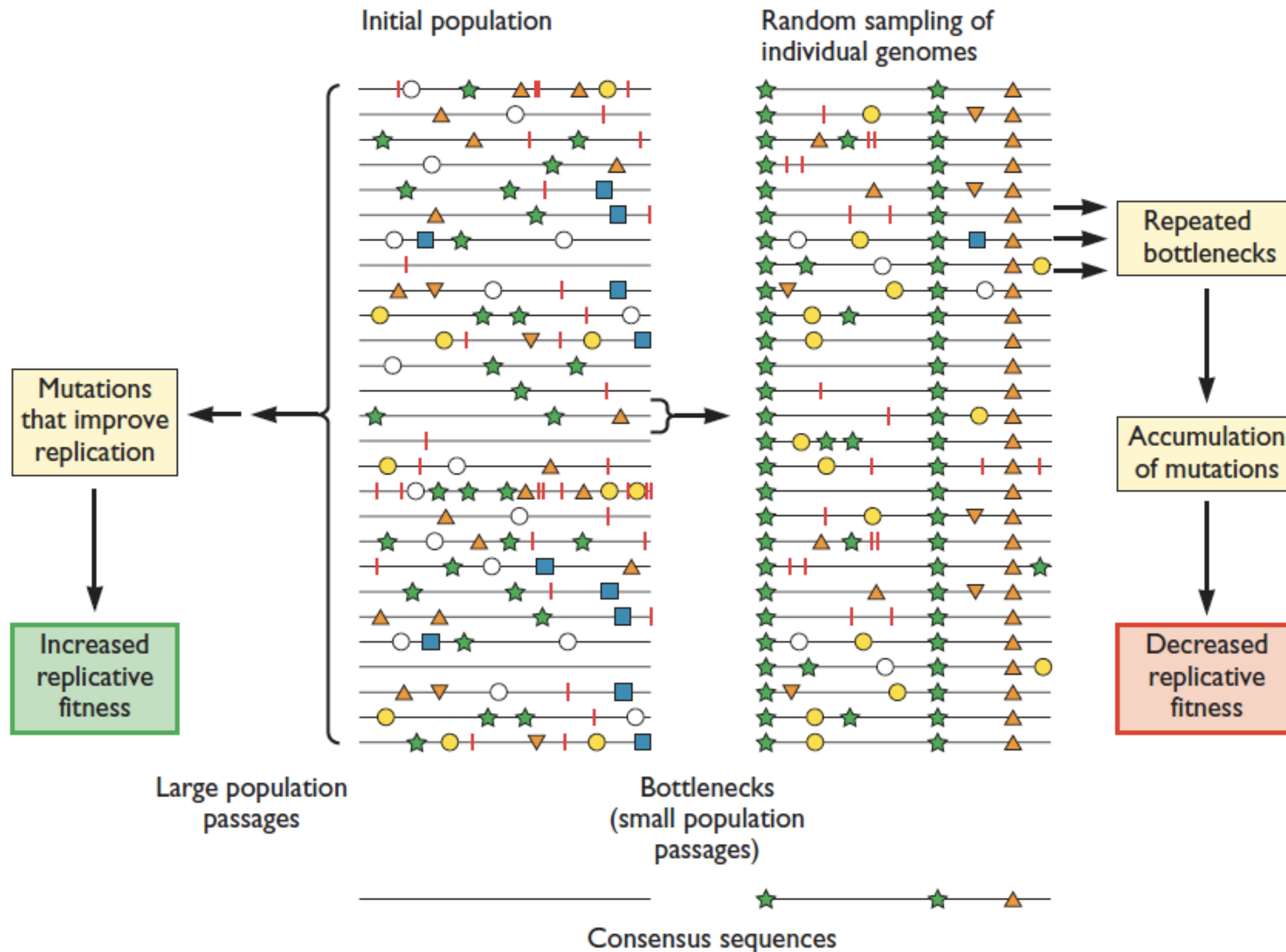
- Au sein d'une quasi-espèce, une/plusieurs mutation(s) peuvent être sélectionnées et persister dans le temps pour donner naissance à des quasi-espèces qui partagent cette/ces mutations leur ayant conféré un avantage
- Sélection ne signifie pas forcément plus de pathogénicité ou plus de transmissibilité, mais cela **favorise la survie du virus**
- **Seuil d'erreur : équilibre entre sélection/survie et taux de mutation**
 - Si taux de mutation dépasse le seuil d'erreur > perte d'infectivité
 - Si taux de mutation très inférieur > pas assez de mutation pour survivre à la sélection

Notion de goulot d'étranglement (« genetic bottlenecks »)

- Si un seul replicon survit au goulot d'étranglement > moins de diversité, fitness et survie diminués

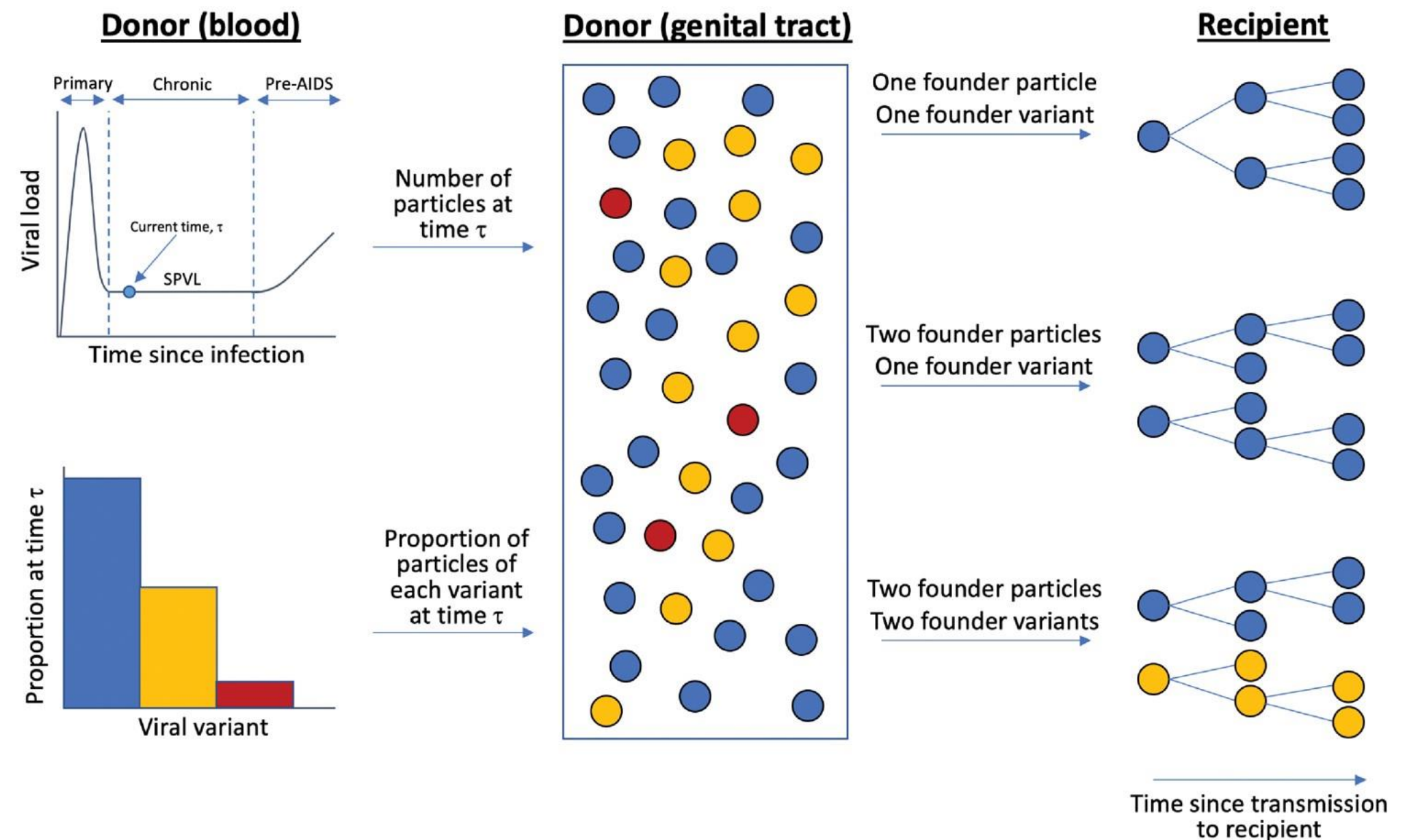


Notion de goulot d'étranglement (« genetic bottlenecks »)



Transmission du HIV et goulot d'étranglement

- Transmission HIV > évènement rare, contraint, faible diversité de la population virale initiale
- Notion de virus « founders »



Sélection

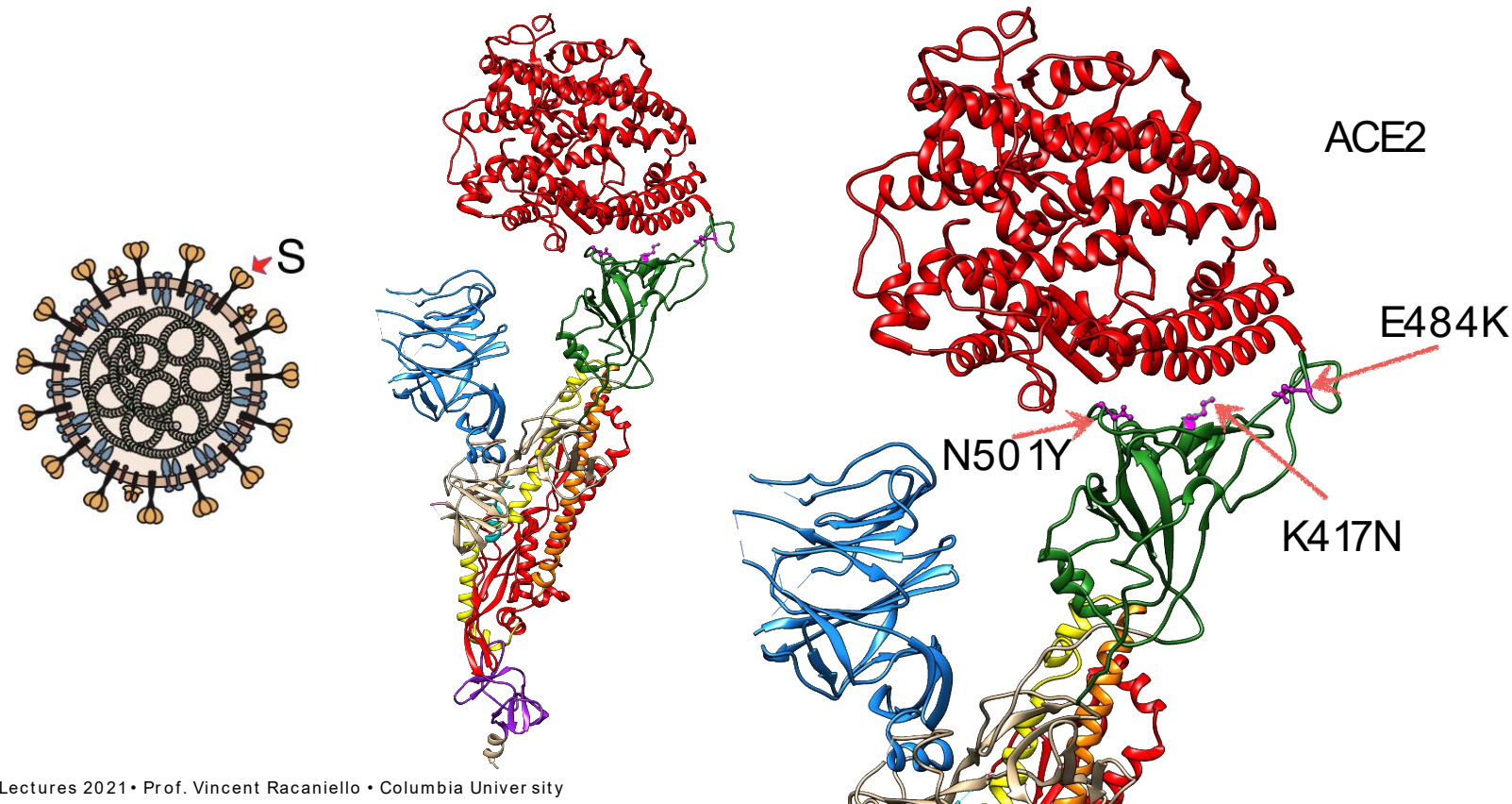
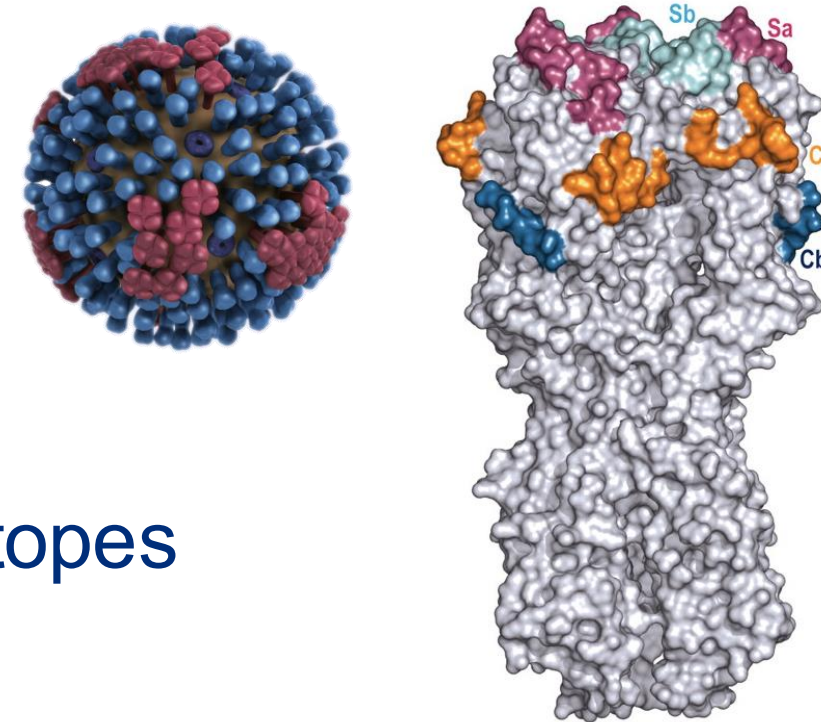
- La sélection favorise le variant adapté à un environnement donné
- Facteurs de sélection
 - Contraintes structurales de survie : sites actifs des enzymes
 - Facteurs liés à l'hôte :
 - Le système immunitaire
 - L'entrée dans la cellule cible
 - Adaptation sur protéines de surface
 - Sites antigéniques
 - Sites de reconnaissance des récepteurs cellulaires

Sélection

- Sélection de mutants résistants à l'élimination par les Ac ou les cellules T cytotoxiques > processus naturel au cours de la réplication virale chez un individu
 - **Drift = dérive** > diversité issue des erreurs de réplication, sélectionnées par la pression immunitaire
 - **Shift = cassure** > diversité issue des mécanismes de recombinaison ou réassortiment

Dérive antigénique

- Virus Influenza > sites de mutations ++ sur épitopes immunogènes de l'HA
- SARS CoV-2 > sites de mutations ++ sur épitopes immunogènes de la protéine Spike



Exemple du SARS CoV-2

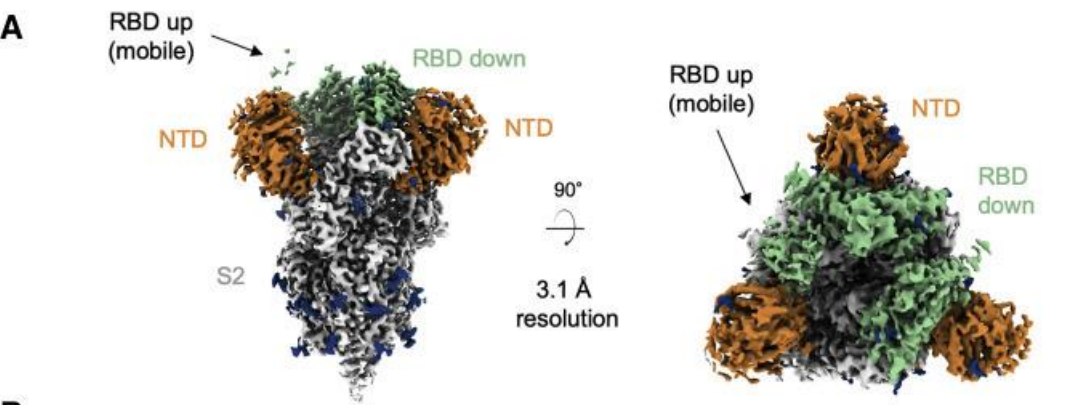
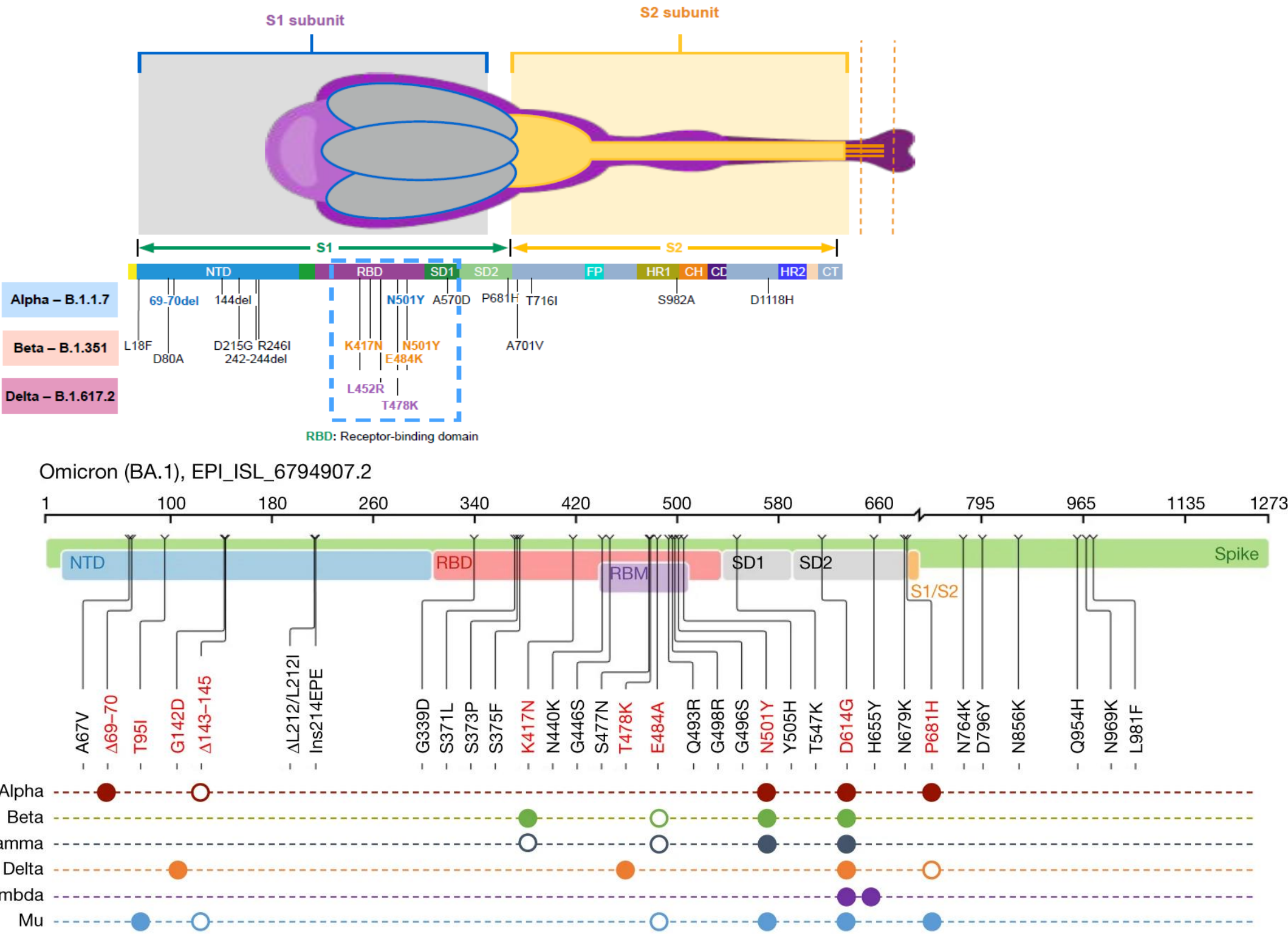
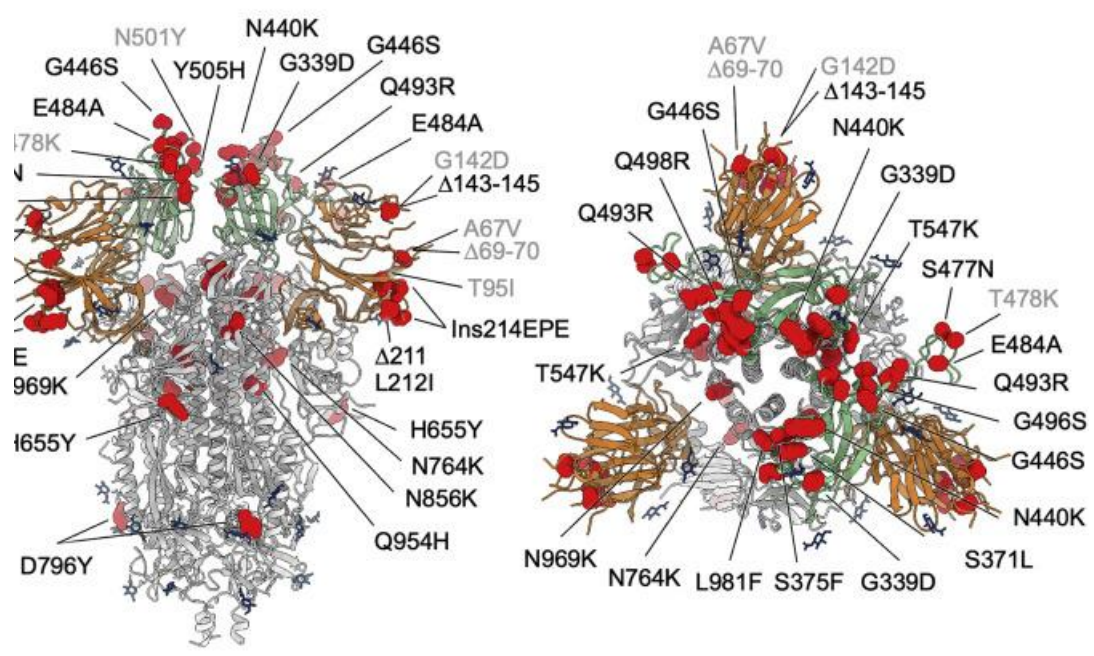


Figure B shows a table of RBD positioning data for various SARS-CoV-2 variants.

RBD positioning	WA1	D614G	Alpha	Beta	Gamma	Delta	Kappa	Omicron
3 down	0.45	0.05	0.25	0.2	-	0.3	0.55	-
1 up	0.55	0.36	0.75	0.7	1	0.7	0.45	1
2 up	-	0.29	-	0.1	-	-	-	-
3 up	-	0.20	-	-	-	-	-	-

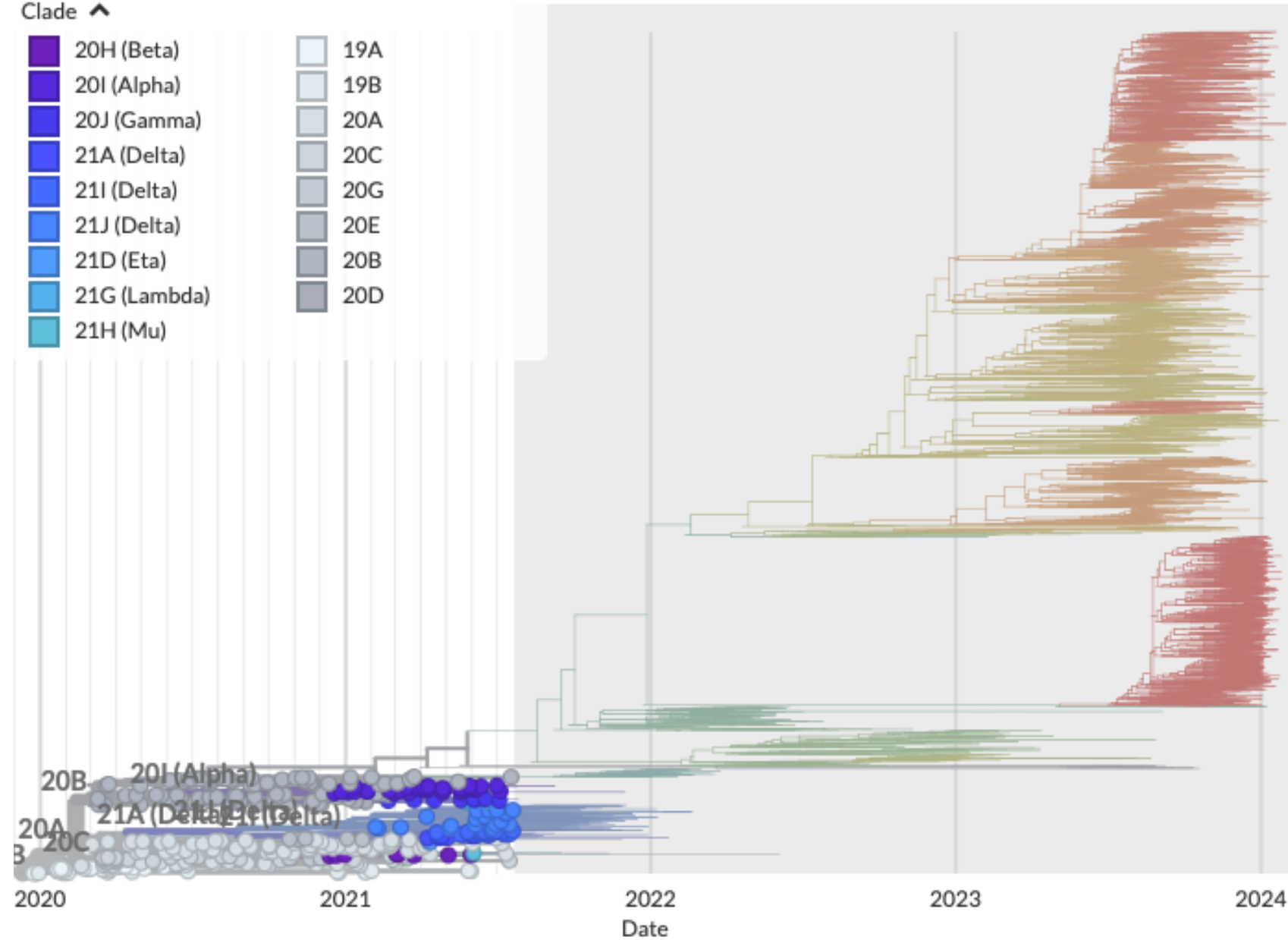
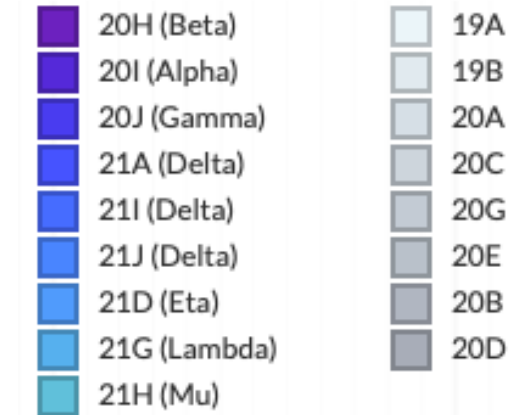


Diversité du SARS CoV-2

Showing 334 of 3915 genomes sampled between Dec 2019 and Jul 2021. Filtered to [Dec 2019 to Jul 2021](#) .

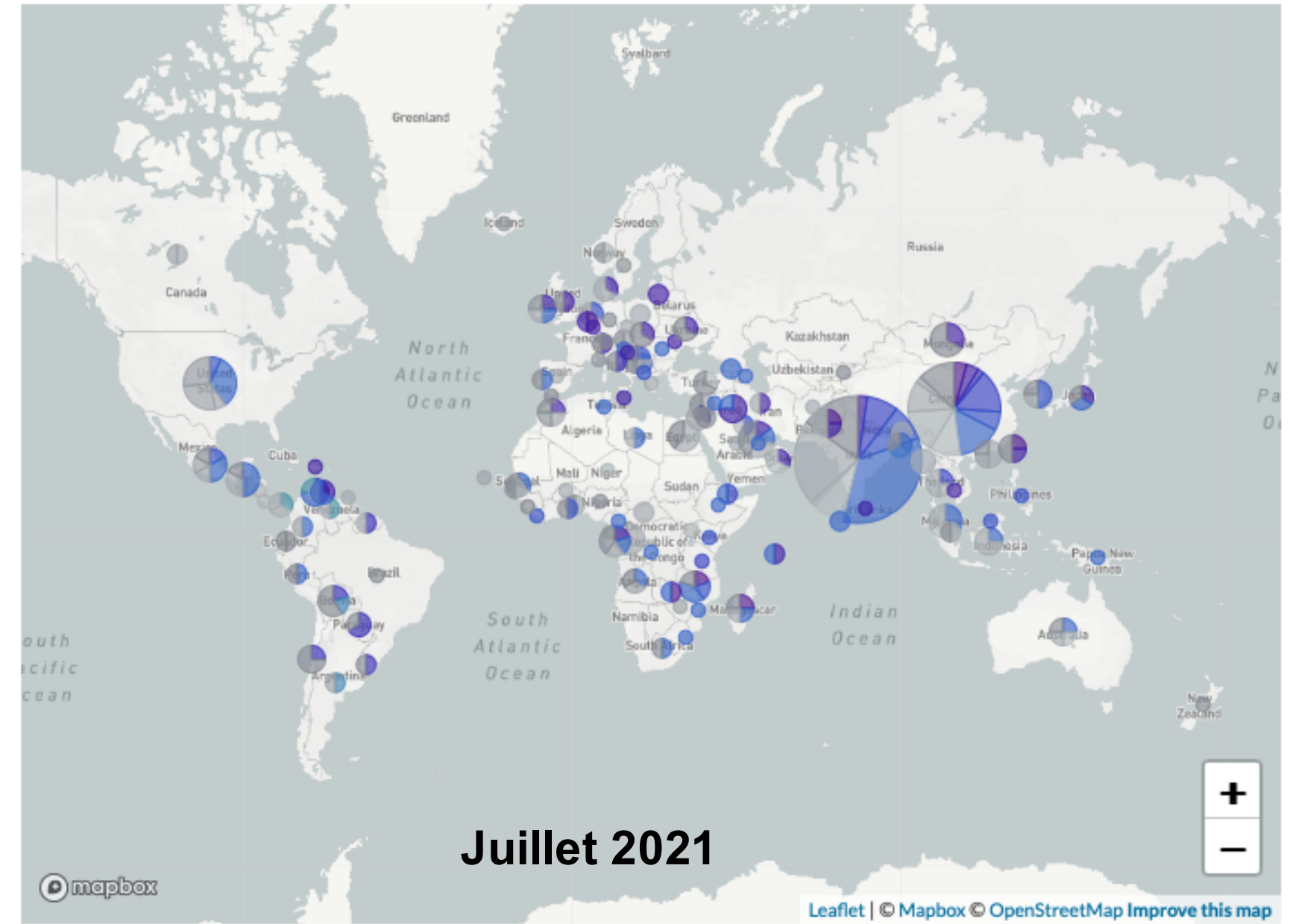
Phylogeny

Clade 



Geography

[RESET ZOOM](#)



Diversité du SARS CoV-2

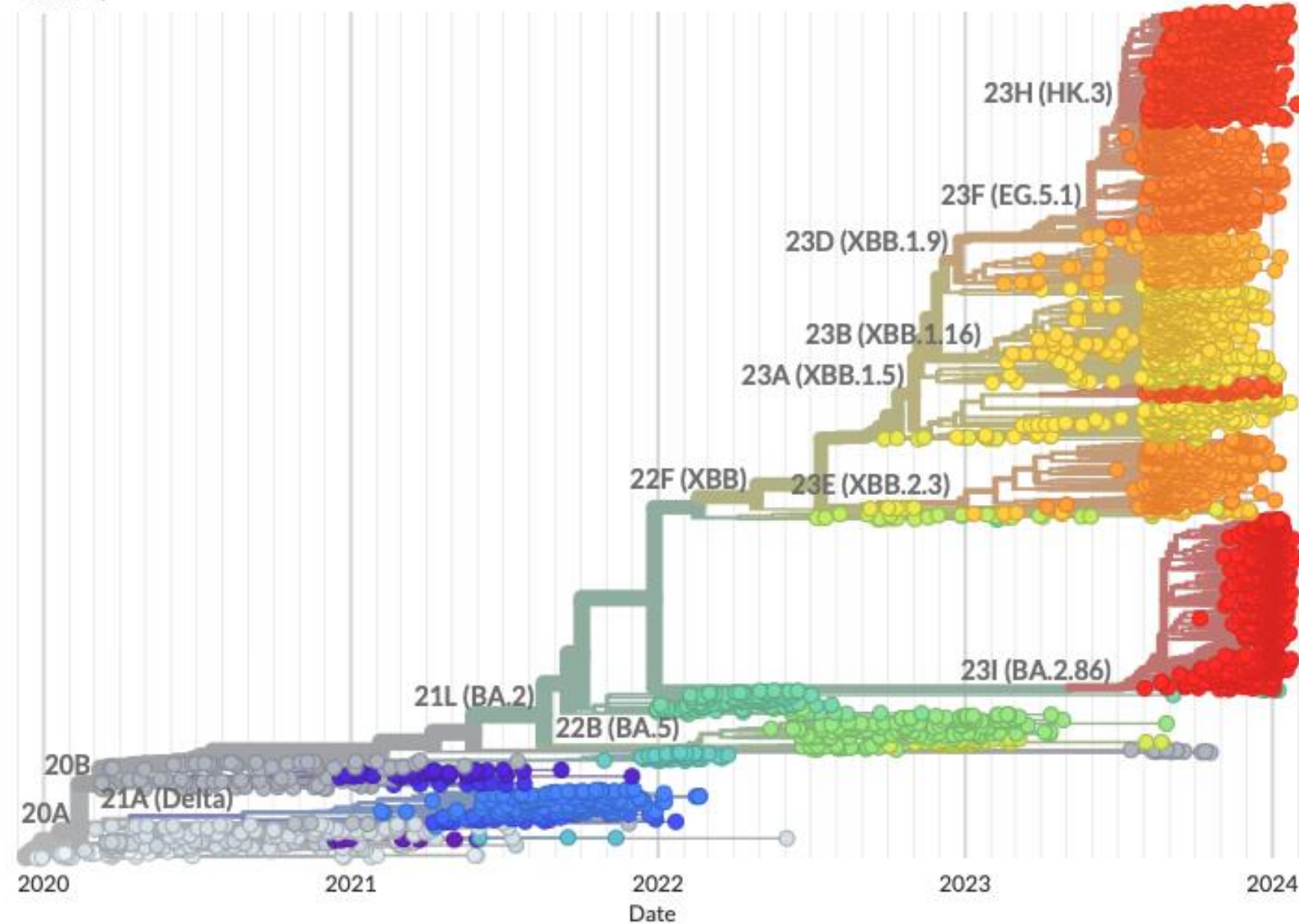
Genomic epidemiology of SARS-CoV-2 with subsampling focused globally over the past 6 months

Built with [nextstrain/ncov](#). Maintained by the [Nextstrain team](#). Data updated 2024-02-06. Enabled by data from [GISAID](#).

Showing 3915 of 3915 genomes sampled between Dec 2019 and Jan 2024.

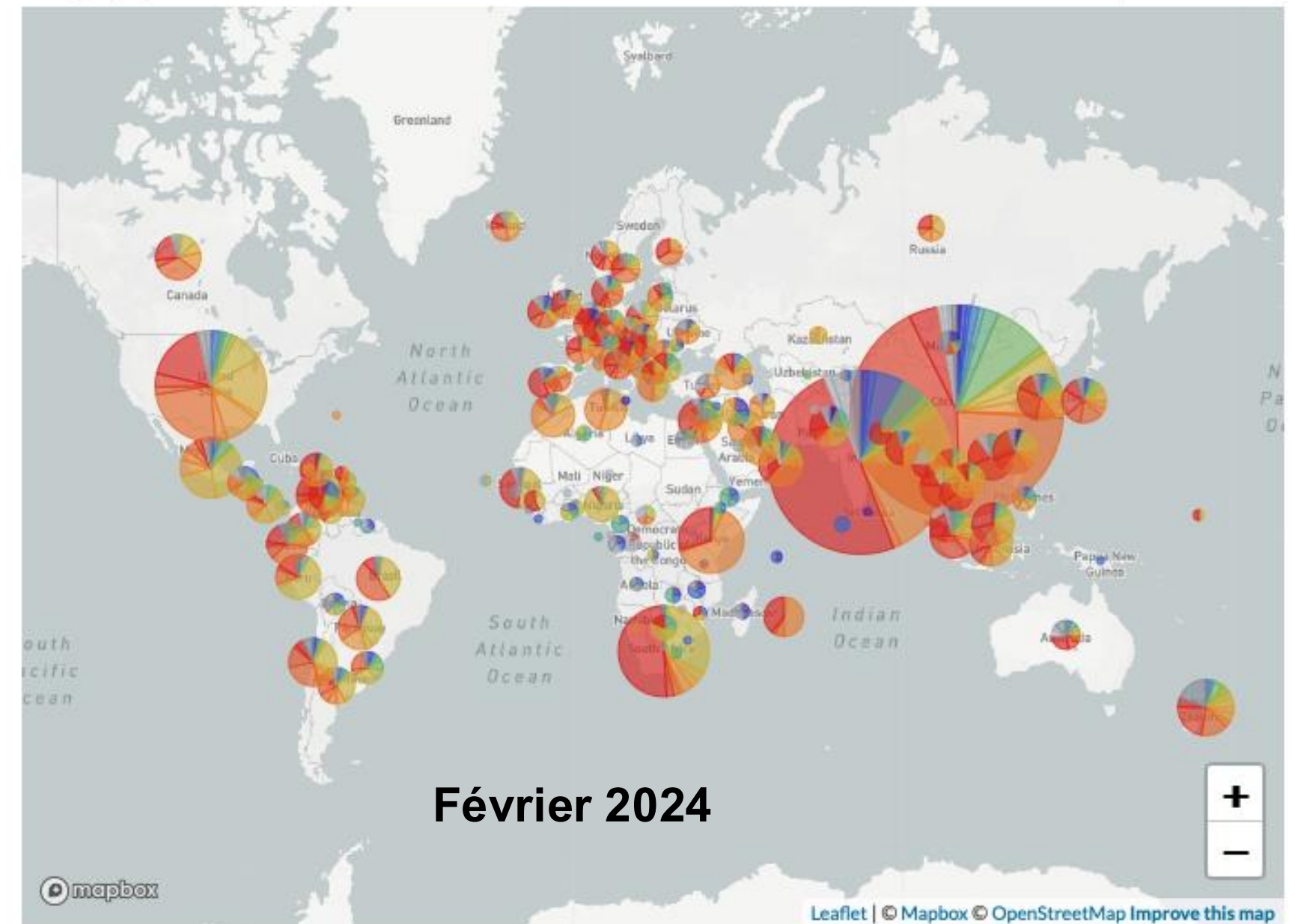
Phylogeny

Clade ▼



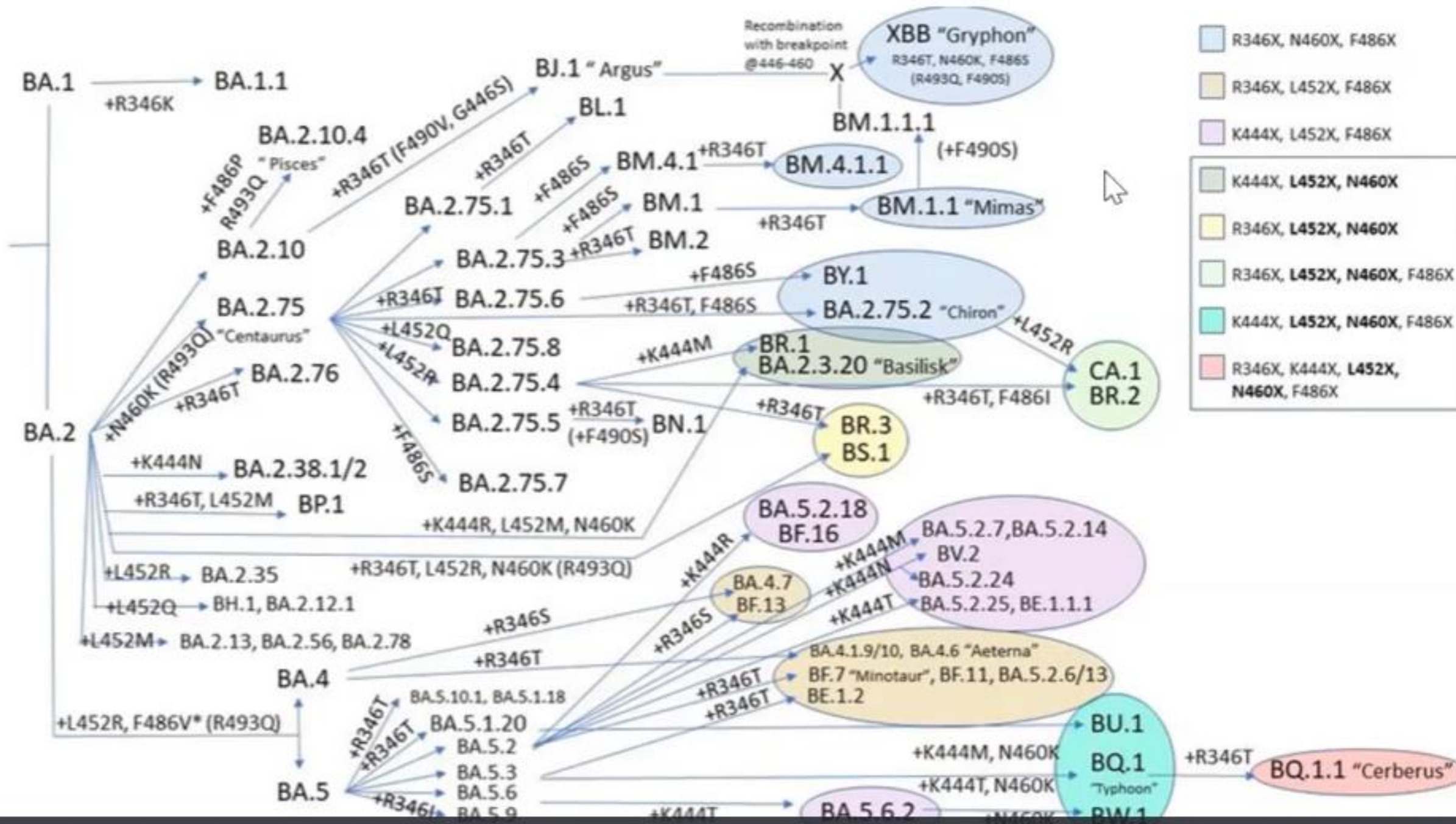
Geography

RESET ZOOM



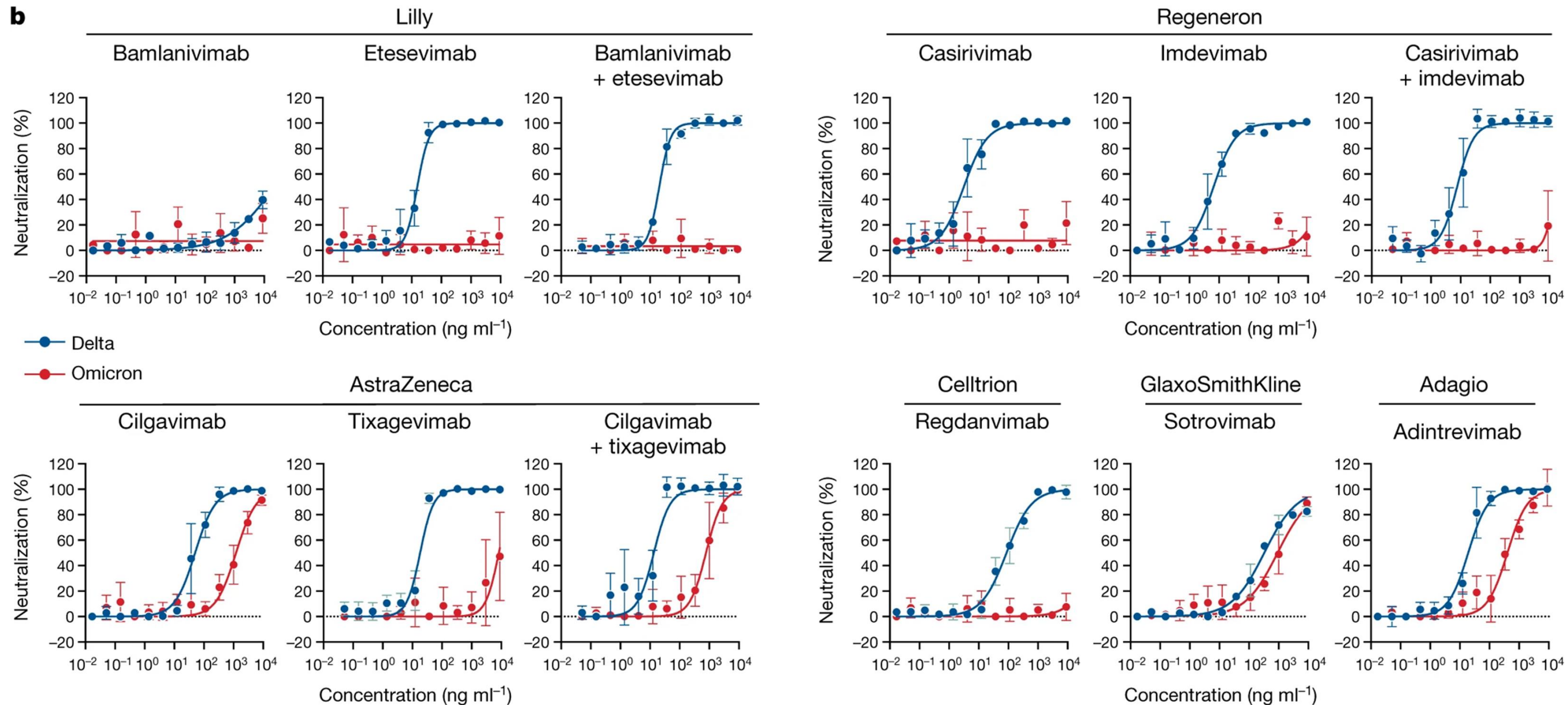
Diversité du SARS coV-2

- Mutations ponctuelles et mécanismes de recombinaison



Diversité du SARS CoV-2: conséquences

- Echappement à l'action neutralisante des AC



Article

Resurgence of Ebola virus in 2021 in Guinea suggests a new paradigm for outbreaks

<https://doi.org/10.1038/s41586-021-03901-9>

Received: 6 April 2021

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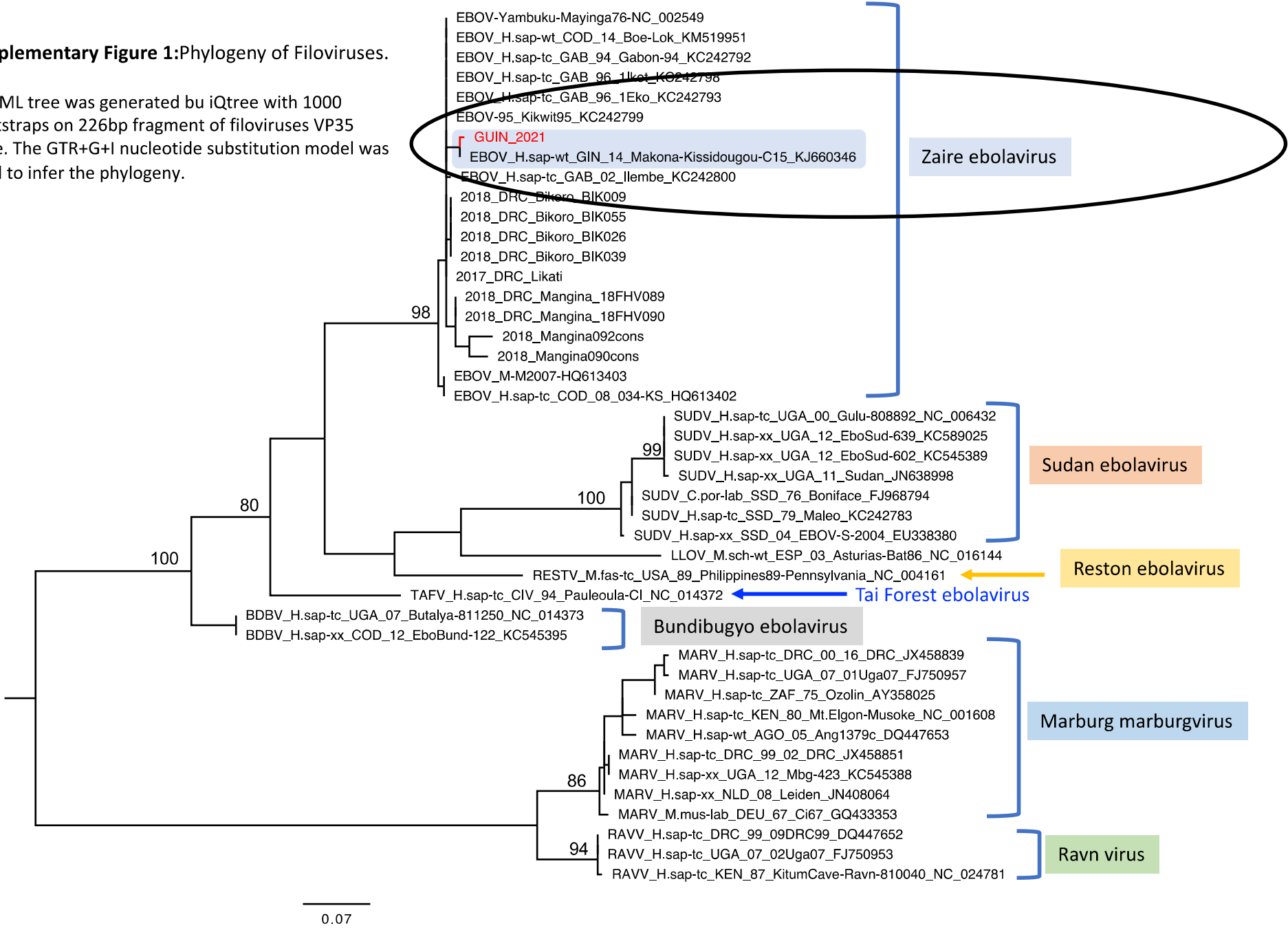
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Alpha Kabinet Keita^{1,2,26}✉, Fara R. Koundouno^{3,4,26}, Martin Faye^{5,26}, Ariane Dux^{6,26}, Julia Hinzmann^{4,7,8,26}, Haby Diallo¹, Ahidjo Ayoub², Frederic Le Marcis^{1,2,9}, Barré Soropogui³, Kékoura Ifono^{3,4}, Moussa M. Diagne⁵, Mamadou S. Sow^{1,10}, Joseph A. Bore^{3,11}, Sebastien Calvignac-Spencer⁶, Nicole Vidal², Jacob Camara³, Mamadou B. Keita¹², Annick Renevey^{4,7}, Amadou Diallo⁵, Abdoul K. Soumah¹, Saa L. Millimono^{3,4}, Almudena Mari-Saez⁶, Mamadou Diop⁵, Ahmadou Doré³, Fodé Y. Soumah¹⁰, Kaka Kourouma¹², Nathalie J. Vielle^{4,13}, Cheikh Loucoubar⁵, Ibrahima Camara¹, Karifa Kourouma^{3,4}, Giuditta Annibaldis^{4,13}, Assaïtou Bah³, Anke Thielebein^{4,7}, Meike Pahlmann^{4,7}, Steven T. Pullan^{8,11}, Miles W. Carroll^{8,11}, Joshua Quick¹⁴, Pierre Formenty¹⁵, Anais Legand¹⁵, Karla Pietro¹⁶, Michael R. Wiley^{16,17}, Noel Tordo¹⁸, Christophe Peyrefitte⁵, John T. McCrone¹⁹, Andrew Rambaut¹⁹, Youssouf Sidibé²⁰, Mamadou D. Barry²⁰, Madeleine Kourouma²⁰, Cé D. Saouromou²⁰, Mamadou Condé²⁰, Moussa Baldé¹⁰, Moriba Povogui¹, Sakoba Keita²¹, Mandiou Diakite^{22,23}, Mamadou S. Bah²², Amadou Sidibe⁹, Dembo Diakite¹⁰, Fodé B. Sako¹⁰, Fodé A. Traore¹⁰, Georges A. Ki-Zerbo¹³, Philippe Lemey²⁴, Stephan Günther^{4,7,13}, Liana E. Kafetzopoulou^{4,7,24}, Amadou A. Sall⁵, Eric Delaporte^{2,25}, Sophie Duraffour^{4,7,13,27}, Ousmane Faye^{5,27}, Fabian H. Leendertz^{6,27}, Martine Peeters^{2,27}, Abdoulaye Toure^{1,12,27} & N'. Faly Magassouba^{3,27}

Confirmation virologique du diagnostic

Supplementary Figure 1: Phylogeny of Filoviruses.

The ML tree was generated bu iQtree with 1000 bootstraps on 226bp fragment of filoviruses VP35 gene. The GTR+G+I nucleotide substitution model was used to infer the phylogeny.



Diagnostic d'espèce: séquençage
226 pb dans VP35
> **Ebola Zaire**

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Resurgence of Ebola virus in 2021 in Guinea suggests a new paradigm for outbreaks

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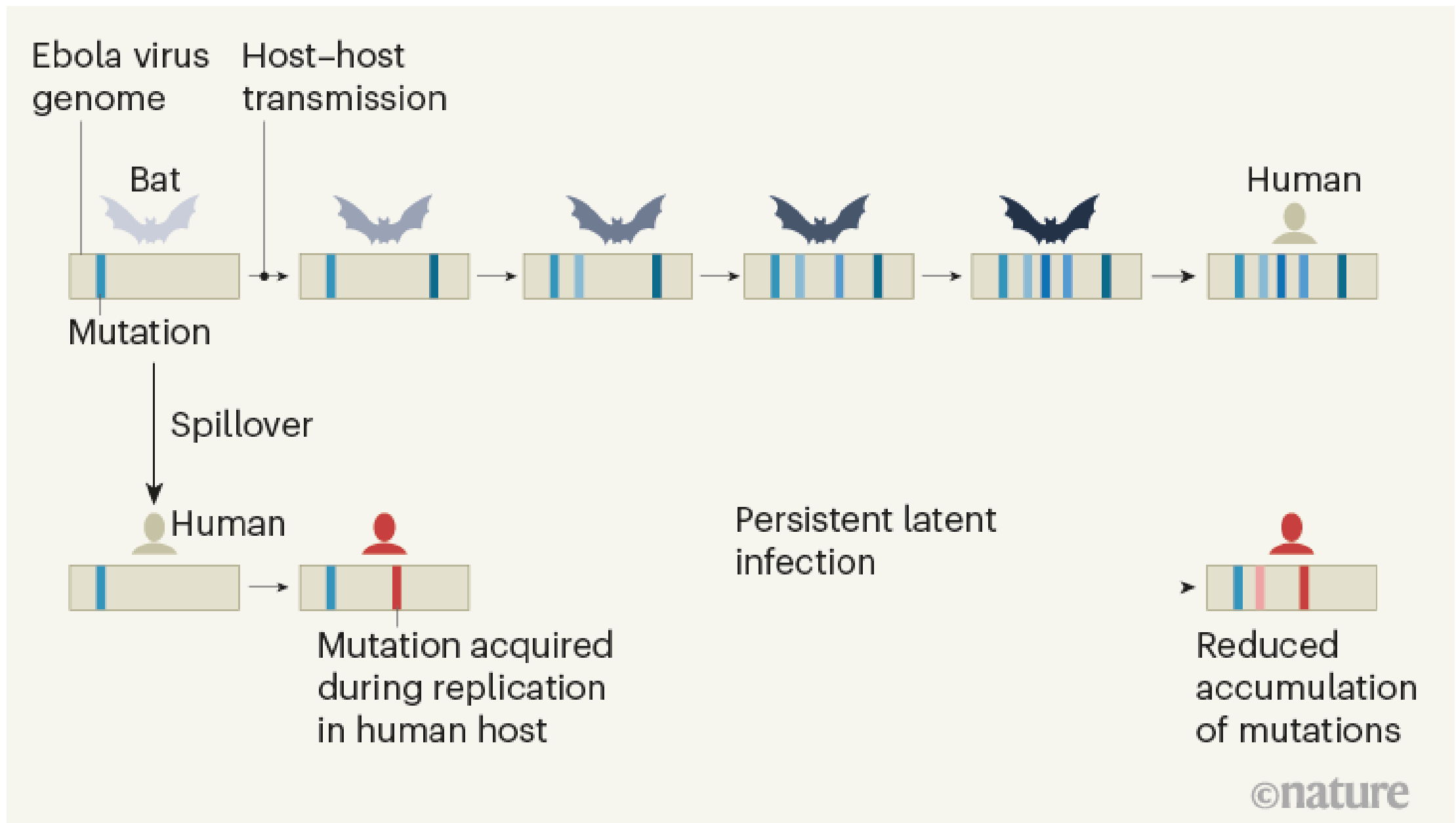
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2221,2222,2223,2224,2225,2226,2227,2228,2229,2230,2231,2232,2233,2234,2235,2236,2237,2238,2239,2240,2241,2242,2243,2244,2245,2246,2247,2248,2249,2250,2251,2252,2253,2254,2255,2256,2257,2258,2259,2260,2261,2262,2263,2264,2265,2266,2267,2268,2269,2270,2271,2272,2273,2274,2275,2276,2277,2278,2279,2280,2281,2282,2283,2284,2285,2286,2287,2288,2289,2290,2291,2292,2293,2294,2295,2296,2297,2298,2299,2300,2301,2302,2303,2304,2305,2306,2307,2308,2309,2310,2311,2312,2313,2314,2315,2316,2317,2318,2319,2320,2321,2322,2323,2324,2325,2326,2327,2328,2329,2330,2331,2332,2333,2334,2335,2336,2337,2338,2339,2340,2341,2342,2343,2344,2345,2346,2347,2348,2349,2350,2351,2352,2353,2354,2355,2356,2357,2358,2359,2360,2361,2362,2363,2364,2365,2366,2367,2368,2369,2370,2371,2372,2373,2374,2375,2376,2377,2378,2379,2380,2381,2382,2383,2384,2385,2386,2387,2388,2389,2390,2391,2392,2393,2394,2395,2396,2397,2398,2399,2400,2401,2402,2403,2404,2405,2406,2407,2408,2409,2410,2411,2412,2413,2414,2415,2416,2417,2418,2419,2420,2421,2422,2423,2424,2425,2426,2427,2428,2429,2430,2431,2432,2433,2434,2435,2436,2437,2438,2439,2440,2441,2442,2443,2444,2445,2446,2447,2448,2449,2450,2451,2452,2453,2454,2455,2456,2457,2458,2459,2460,2461,2462,2463,2464,2465,2466,2467,2468,2469,2470,2471,2472,2473,2474,2475,2476,2477,2478,2479,2480,2481,2482,2483,2484,2485,2486,2487,2488,2489,2490,2491,2492,2493,2494,2495,2496,2497,2498,2499,2500,2501,2502,2503,2504,2505,2506,2507,2508,2509,2510,2511,2512,2513,2514,2515,2516,2517,2518,2519,2520,2521,2522,2523,2524,2525,2526,2527,2528,2529,2530,2531,2532,2533,2534,2535,2536,2537,2538,2539,2540,2541,2542,2543,2544,2545,2546,2547,2548,2549,2550,2551,2552,2553,2554,2555,2556,2557,2558,2559,2560,2561,2562,2563,2564,2565,2566,2567,2568,2569,2570,2571,2572,2573,2574,2575,2576,2577,2578,2579,2580,2581,2582,2583,2584,2585,2586,2587,2588,2589,2590,2591,2592,2}

Pourquoi faire de l'épidémiologie moléculaire ?

