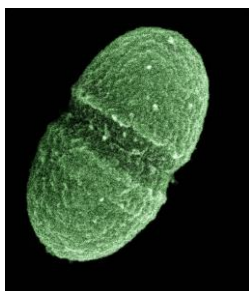




Journée Régionale de Formation CPias CVL - ETH-MS

Espace Malraux, Joué-lès-Tours - Mardi 23 juin 2026 9h30-10h30



Les ERV en France et dans le monde aujourd'hui

Pr. Vincent CATTOIR

Service de Bactériologie-Hygiène Hospitalière, CHU de Rennes

CNR de la Résistance aux Antibiotiques (laboratoire associé 'Entérocoques')

Unité Inserm U1230 BRM & Faculté de Médecine, Université de Rennes



**Université
de Rennes**

Plan



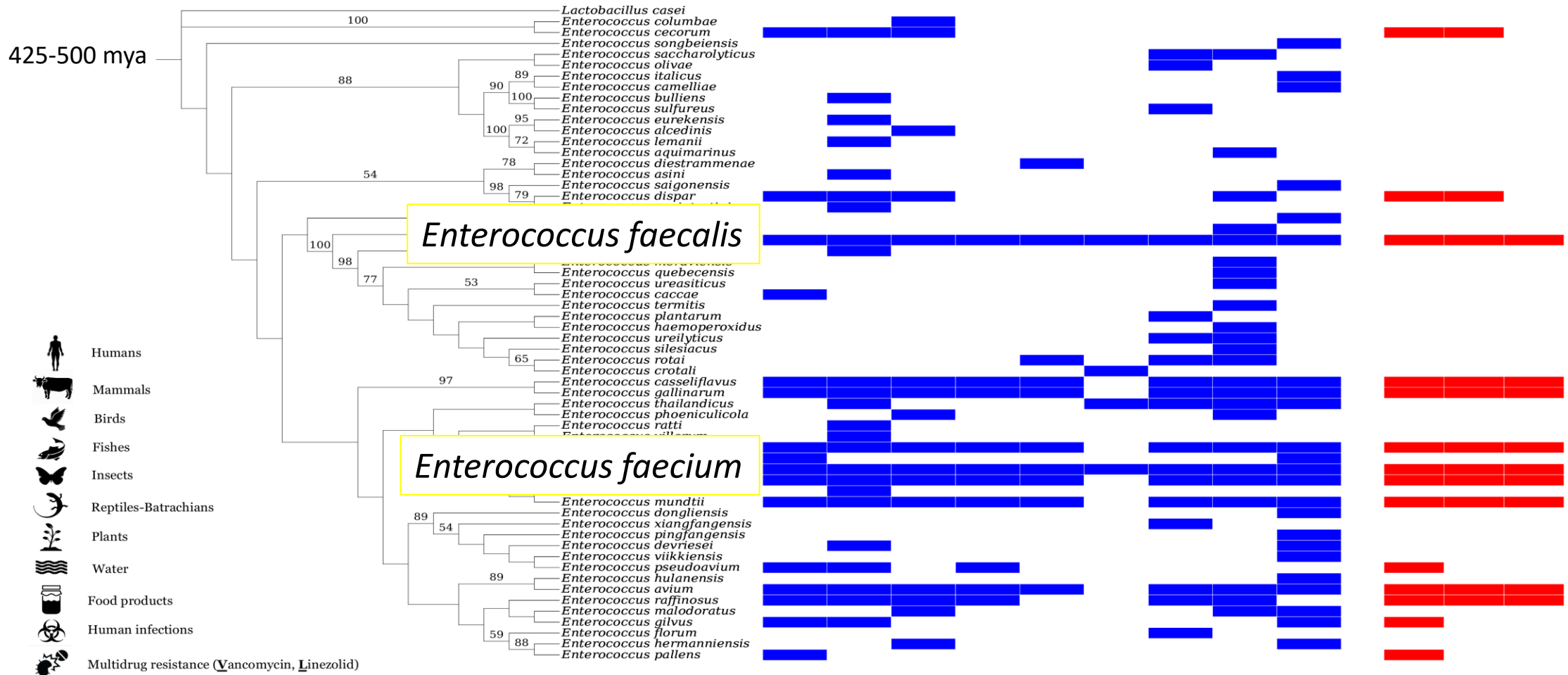
Généralités sur les entérocoques

Diversité, pathogénicité, résistance, phylogénétique

1

Enterococcus spp.

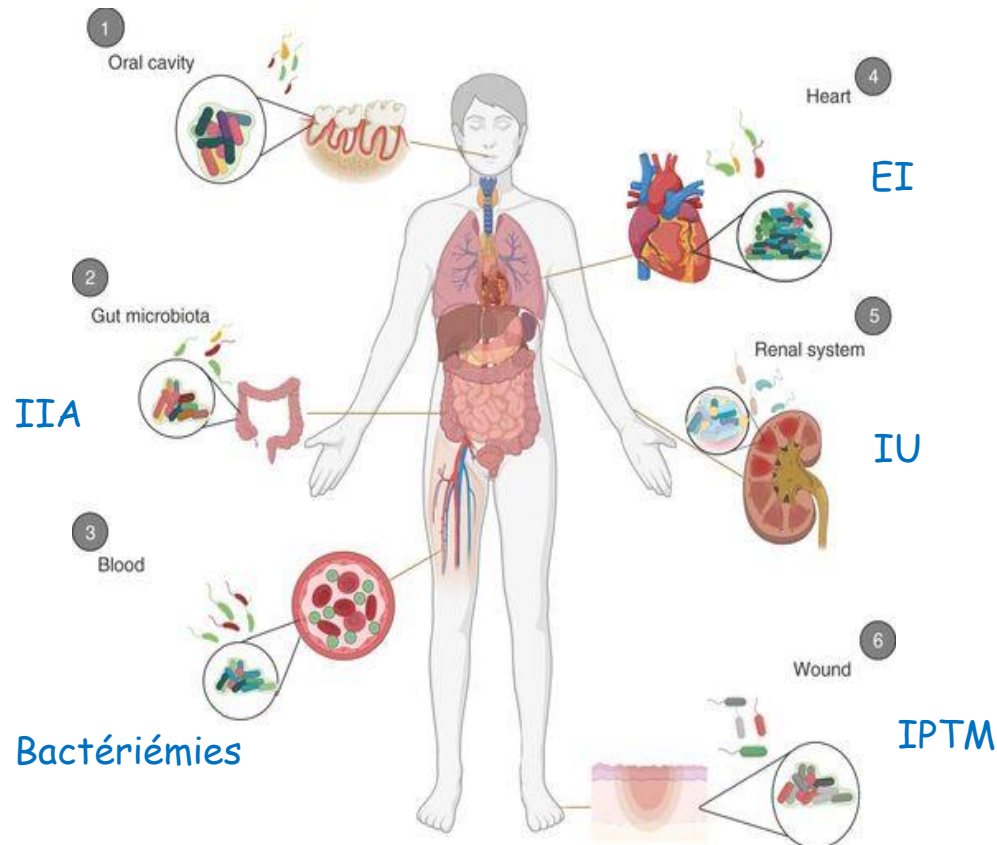
>60 espèces (<https://www.bacterio.net/>)



Infections à entérocoques

Bactéries commensales du microbiote intestinal

Pathogènes opportunistes majeurs :



3^{ème} cause d'infections nosocomiales (1059 ES) :

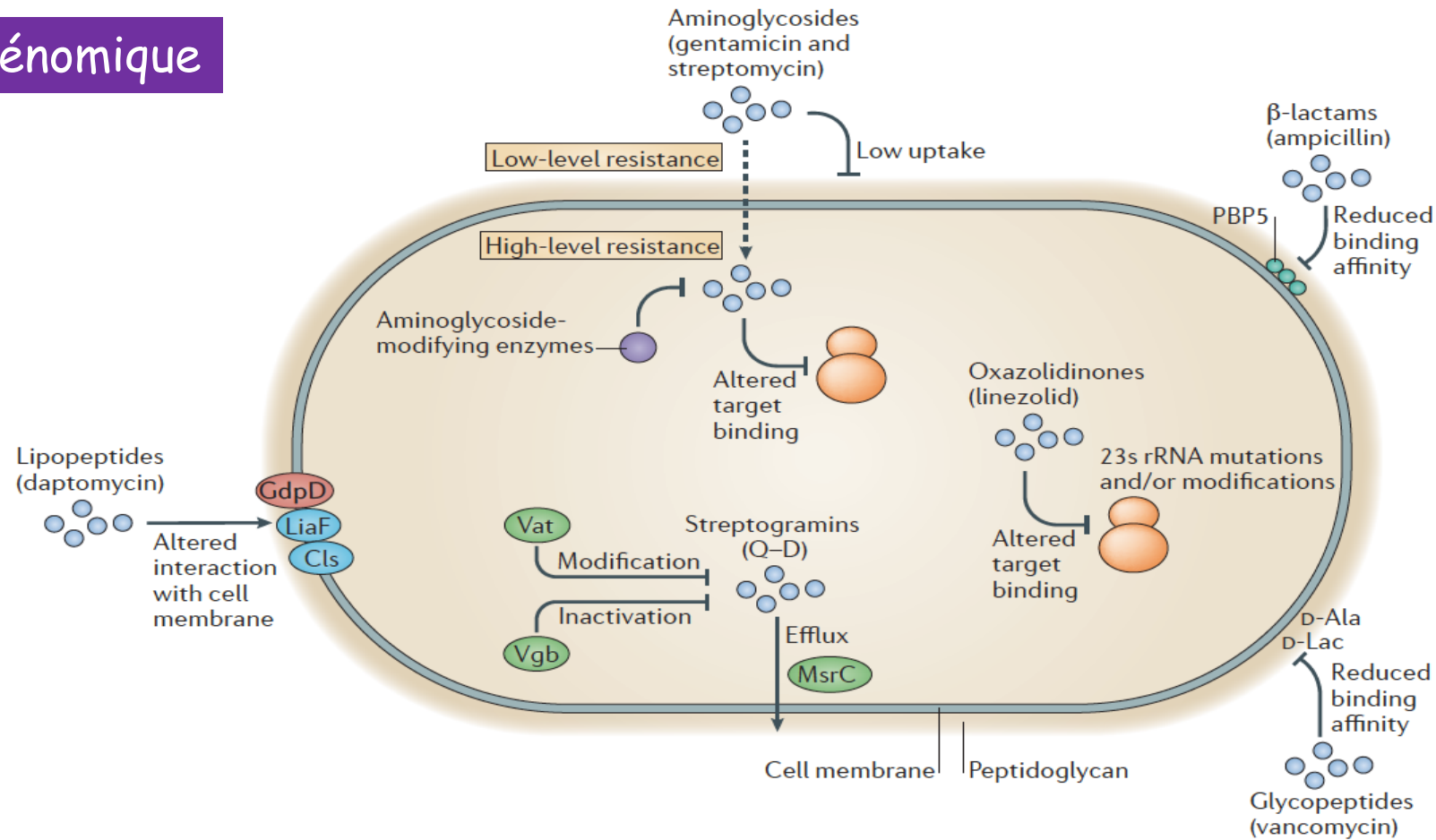
Espèce bactérienne	Nb souches	Répartition (%)
Total Enterobacterales	430 052	70,2%
<i>Escherichia coli</i>	237 052	38,7%
<i>Klebsiella pneumoniae</i>	54 451	8,9%
<i>Enterobacter cloacae</i> complex	29 700	4,8%
Autres Enterobacterales	108 849	17,8%
<i>Pseudomonas aeruginosa</i>	43 604	7,1%
<i>Acinetobacter baumannii</i>	1 797	0,3%
<i>Staphylococcus aureus</i>	68 134	11,1%
<i>Enterococcus faecalis</i>	53 177	8,7%
<i>Enterococcus faecium</i>	15 827	2,6%
Total	612 591	100,0%

11,3 %

E. faecalis / *E. faecium* : **77 / 23**

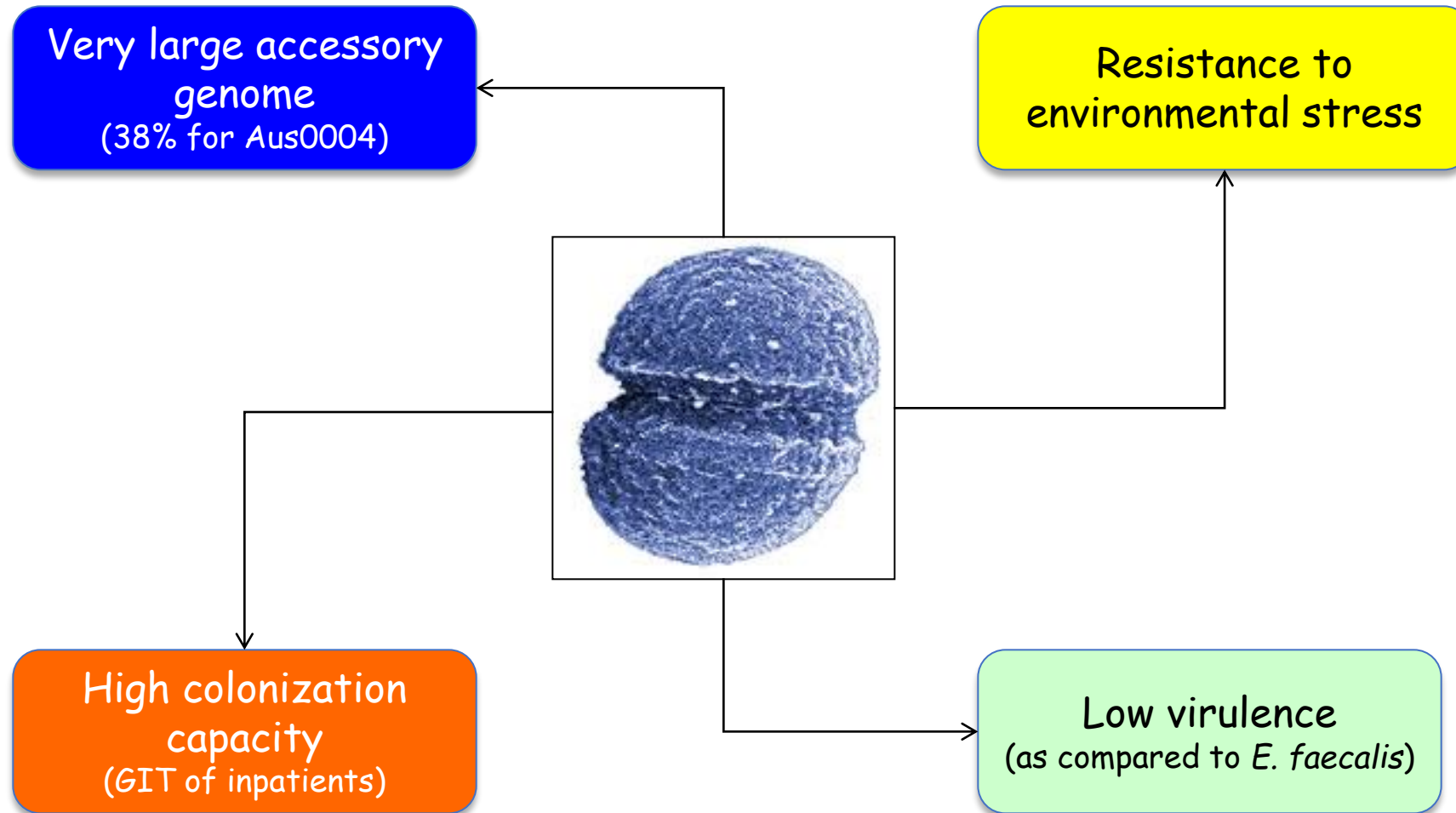
Multirésistance chez *E. faecium*

Plasticité génomique



→ Résistance possible à toutes les classes d'antibiotiques

Succès épidémiologique d'*E. faecium*

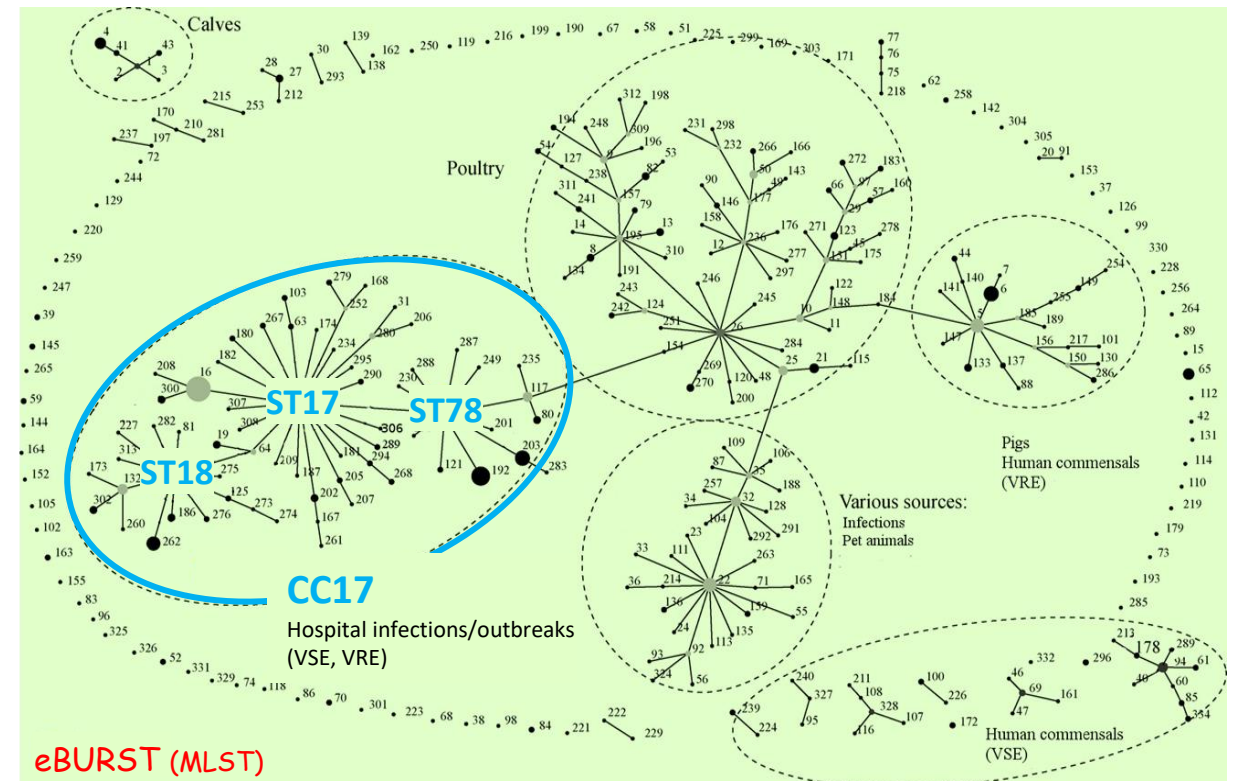


Complexe clonal 17 (CC17)

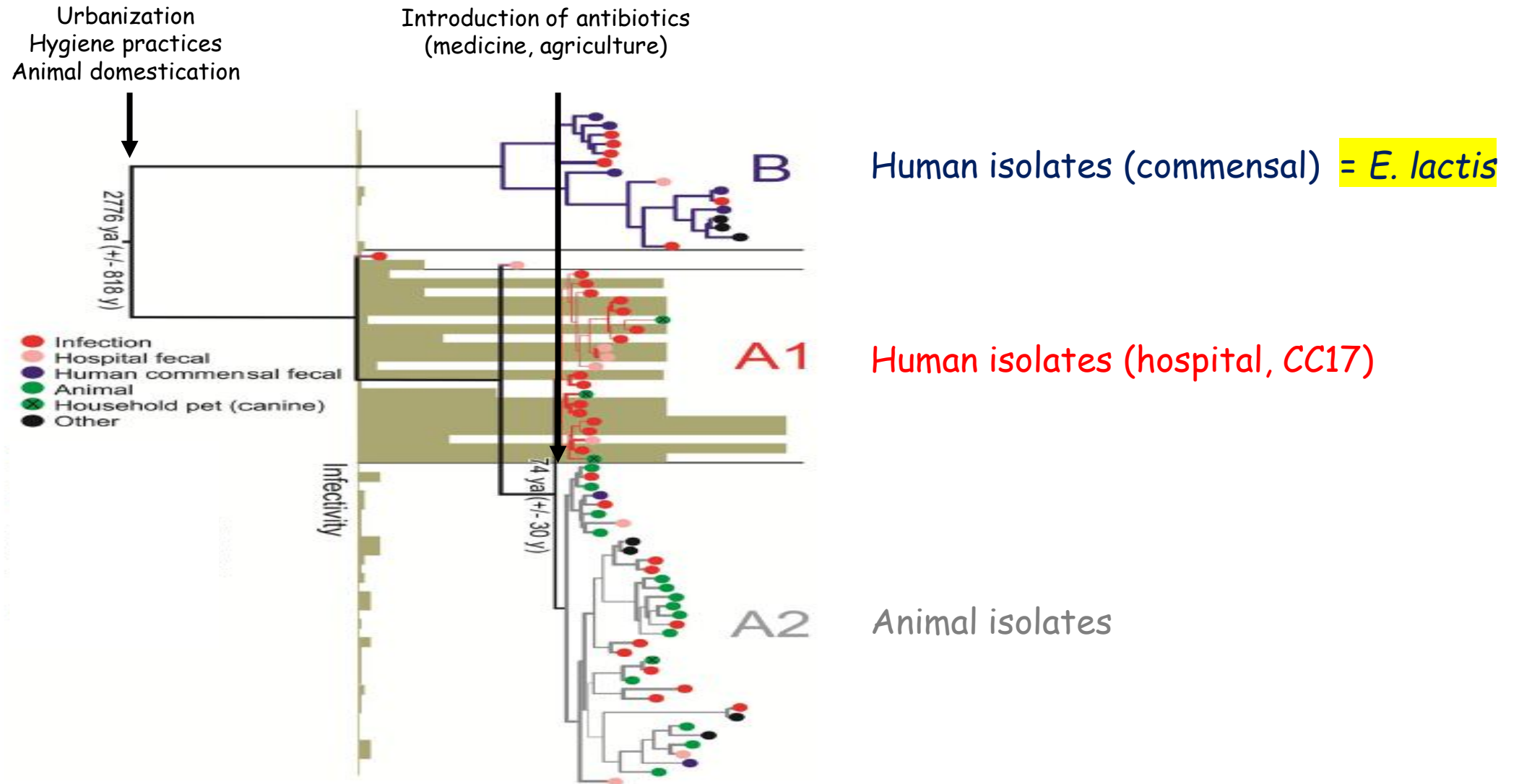
❖ Sous-population de clones d'*E. faecium* adaptés à l'environnement hospitalier ayant acquis par la suite la résistance à la vancomycine (VRE_fm)

❖ Plusieurs caractéristiques communes :

- Haut niveau de résistance aux aminopénicillines et aux FQ
- Présence d'un îlot de pathogénicité, portant des gènes de virulence (*esp* et *hyl*_{Efm})
- Présence d'IS16



Clades phylogénétiques



Alphabet Van

	Résistance acquise								Résistance intrinsèque
	Haut niveau		Variable	Modérée	Bas niveau				Bas niveau
	VanA	VanM	VanB	VanD	VanE	VanG	VanL	VanN	VanC1/C2/C3
Sensibilité									
Vancomycine	R	R	r-R	R	r	r	r	r	r
Téicoplanine	R	R	S	r-R	S	S	S	S	S
Transférabilité	+	+	+	-	-	+	-	+	-
Espèces principales	Efm/Efs	Efm	Efm/Efs	Efm/Efs	Efs	Efs	Efs	Efm	Ega/Eca
Expression	I	?	I	C	I/C	I	I	C	I/C
Localisation génétique	Plasmide	Plasmide (Chr)	Plasmide (Chr)	Chr (plasmide)	Chr	Chr	Chr	Plasmide	Chr
Précurseurs	D-Ala-D-Lac	D-Ala-D-Lac	D-Ala-D-Lac	D-Ala-D-Lac	D-Ala-D-Ser	D-Ala-D-Ser	D-Ala-D-Ser	D-Ala-D-Ser	D-Ala-D-Ser

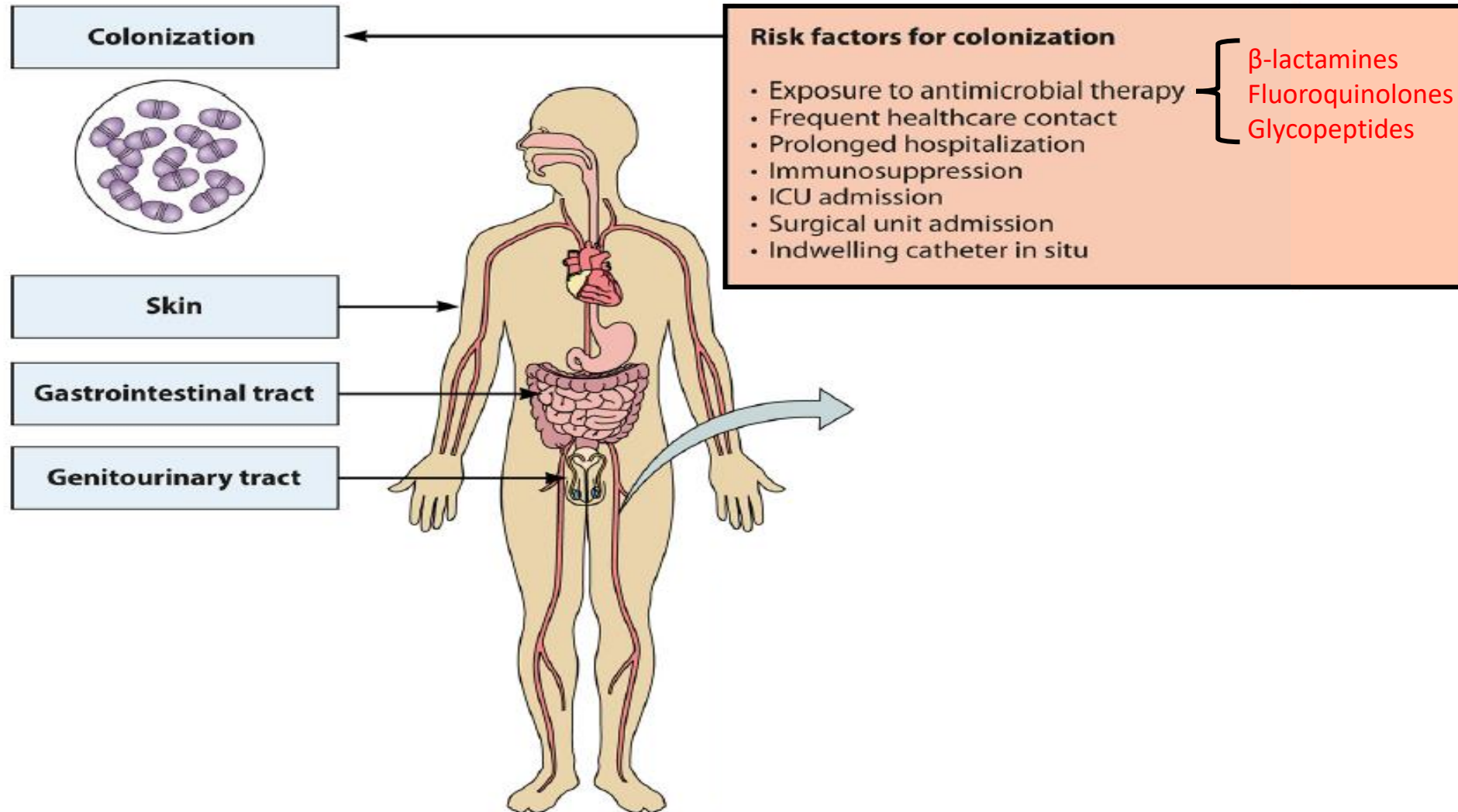
Impact clinique des ERV

Facteurs de risque, mortalité et statut de priorité

A blue circular graphic element is located in the bottom-left corner of the slide. It is a solid blue circle that is partially cut off by the left edge of the frame.

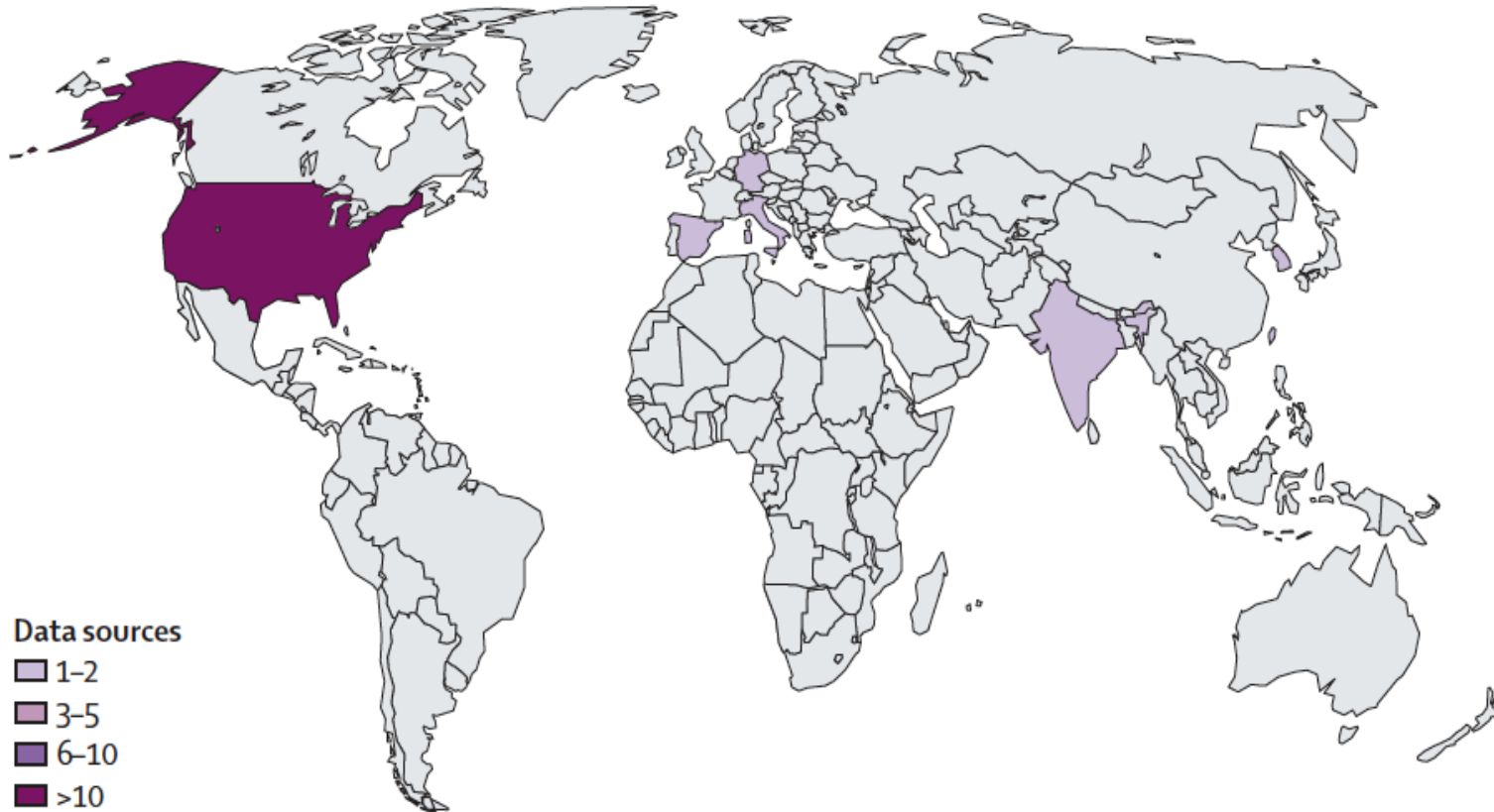
2

Colonisation à infection à ERV



Risque d'infection chez les porteurs

Systematic review & meta-regression analysis (14 études, 4 pays, 1995-2022)

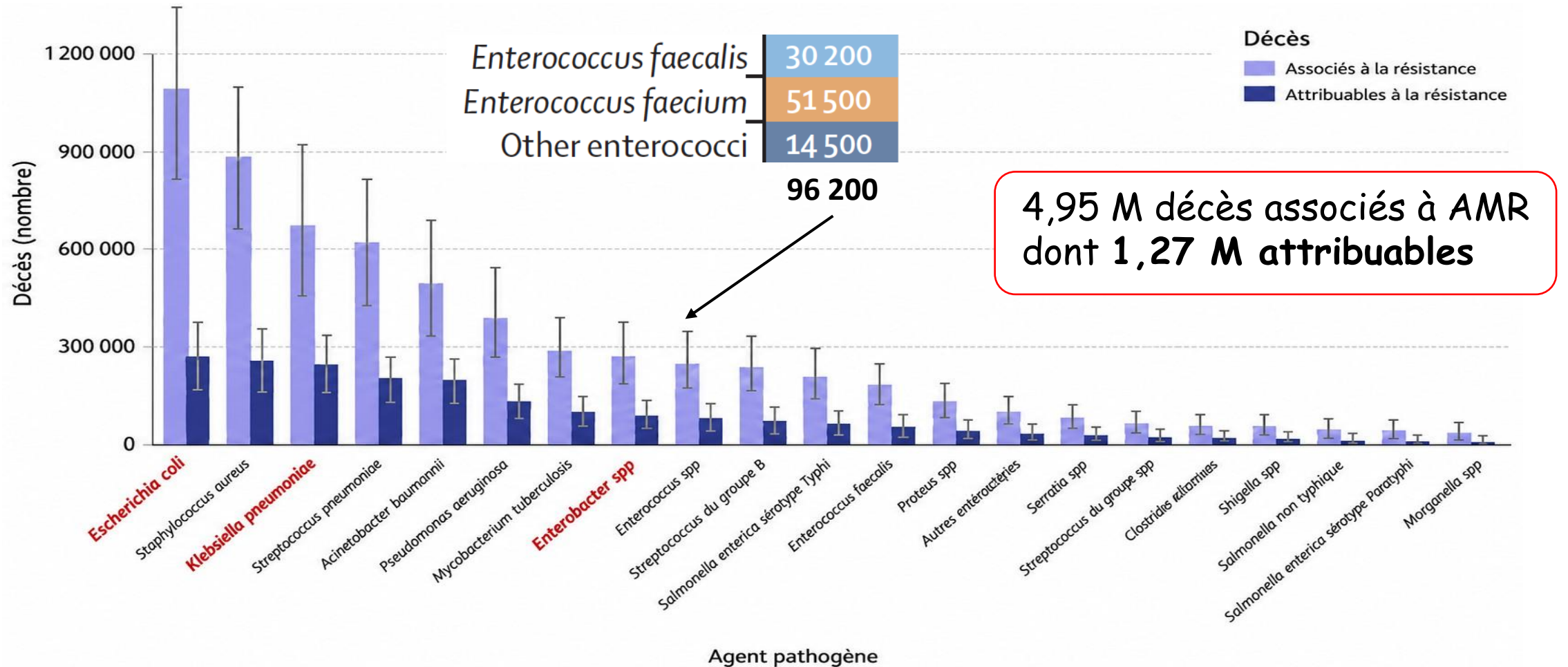


Incidence
cumulée
d'infection chez
porteurs d'ERV
= 8 % à 30 j
(229/4747)

vs 14 % pour BGN MDR

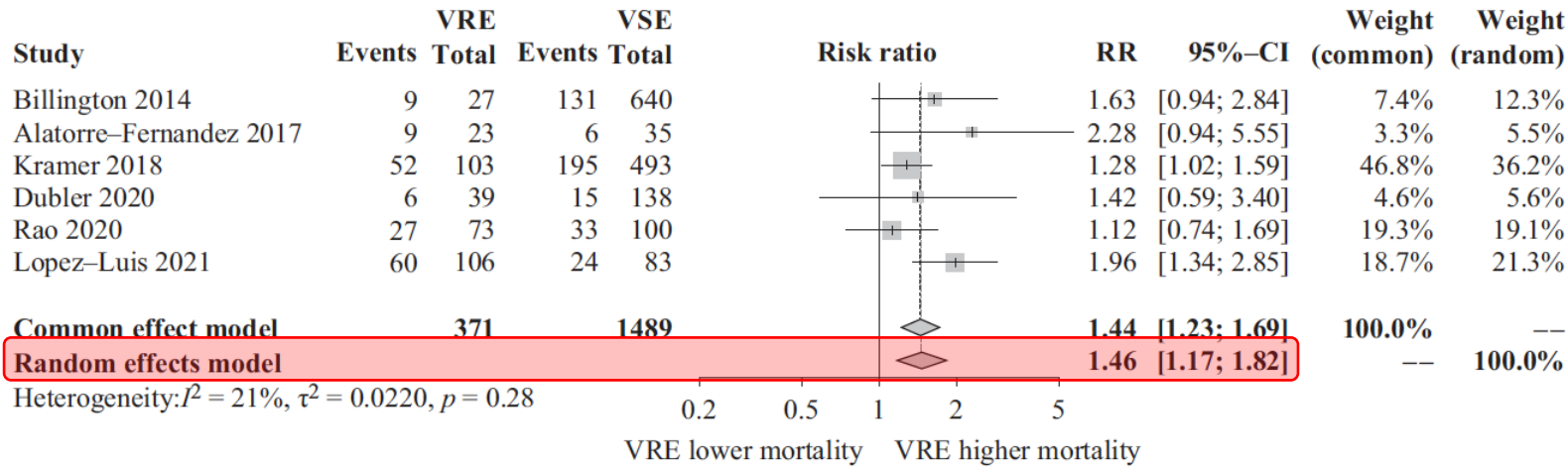
Mortalité attribuable des infections à entérocoques

23 pathogènes (204 pays, 2019)



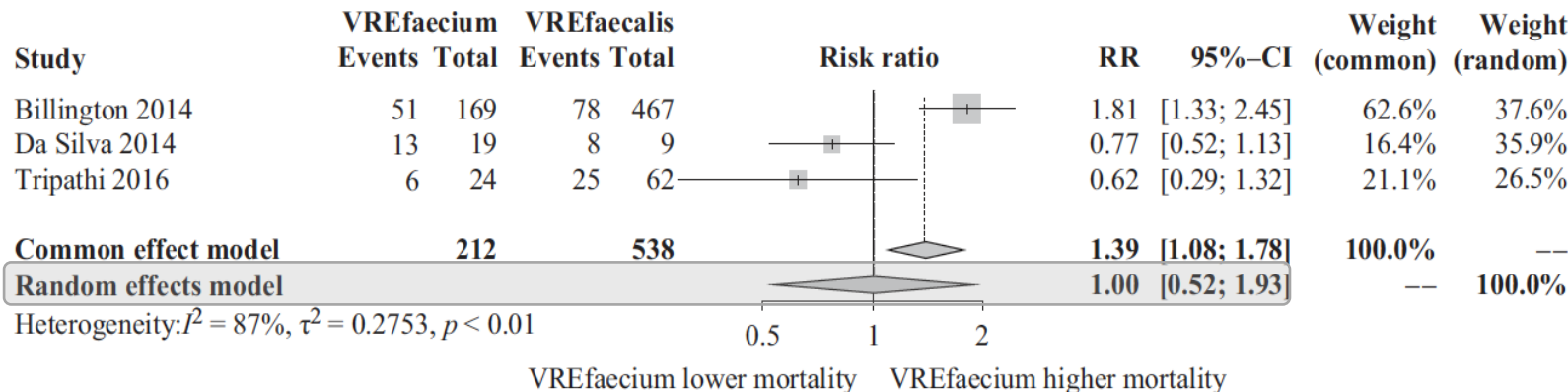
Surmortalité des bactériémies à ERV

Méta-analyse (57 études, 2014-2020)



RR 1,46

Surmortalité des bactériémies à *E. faecium*
VR vs sensible (IC95 % 1,17-1,82)



Pas de différence

Bactériémies à *E. faecium* VR vs *E. faecalis*
VR (RR 1,00 ; IC95 % 0,52-0,93)

Surmortalité des bactériémies à ERV

US (2016-2018)

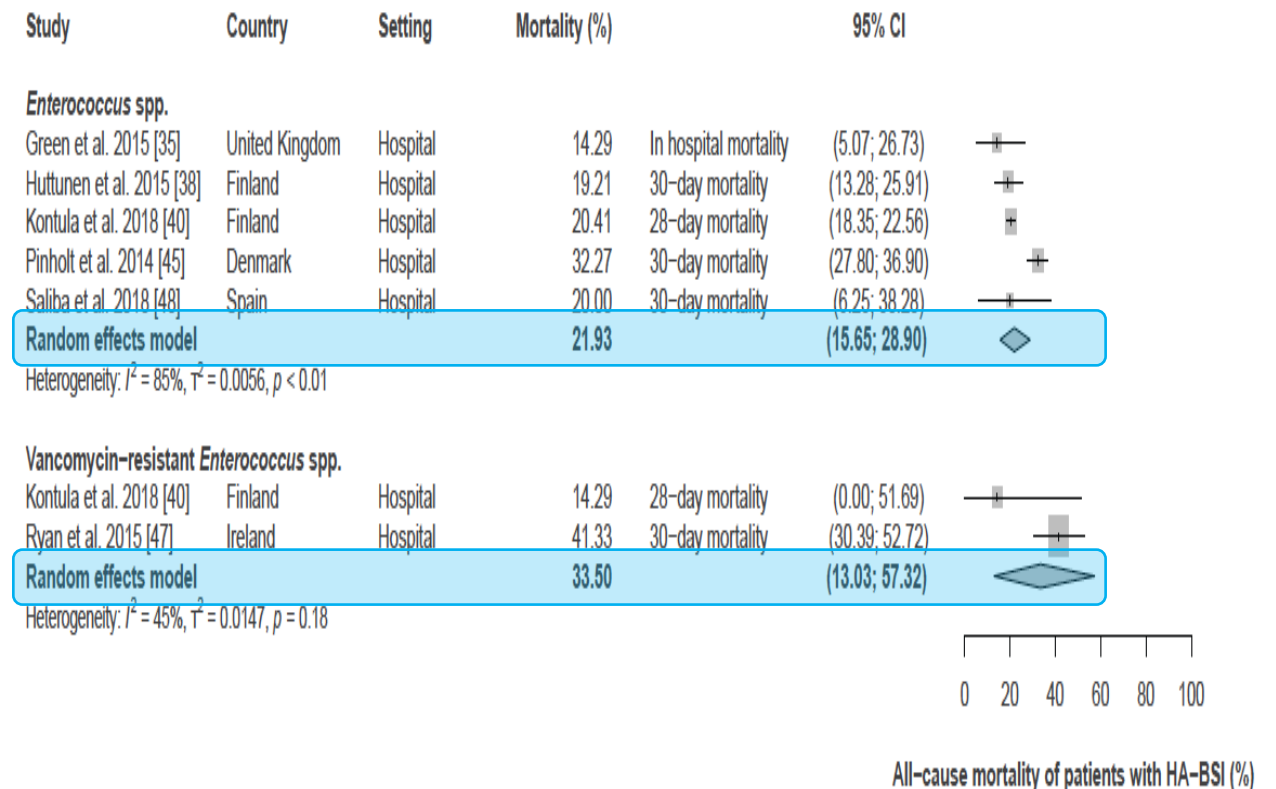
Prospective multicenter study (VENOUS I)

Variables	VSE (n = 176)	VRE (n = 56)	Total Population (N = 232)	PValue
Clinical outcomes				
In-hospital mortality	22 (12.50)	20 (35.71)	42 (18.10)	<.001

Variable	Adjusted Conventional ^{a,b}		PValue
	HR	(95% CI)	
Intensive care unit admission	
Pitt bacteremia score ≥2	1.83	(1.47–2.28)	<.001
Neutropenia, defined as <500 cells/μL	3.13	(2.89–3.39)	<.001
Central line placement	
Urinary catheter	1.85	(1.17–2.93)	.009
Mechanical ventilation	
VRE BSI	2.13	(1.54–2.93)	<.001
Microbiological failure	2.4	(1.34–4.31)	.003

Europe (2010-2020)

Systematic review & Meta-analysis

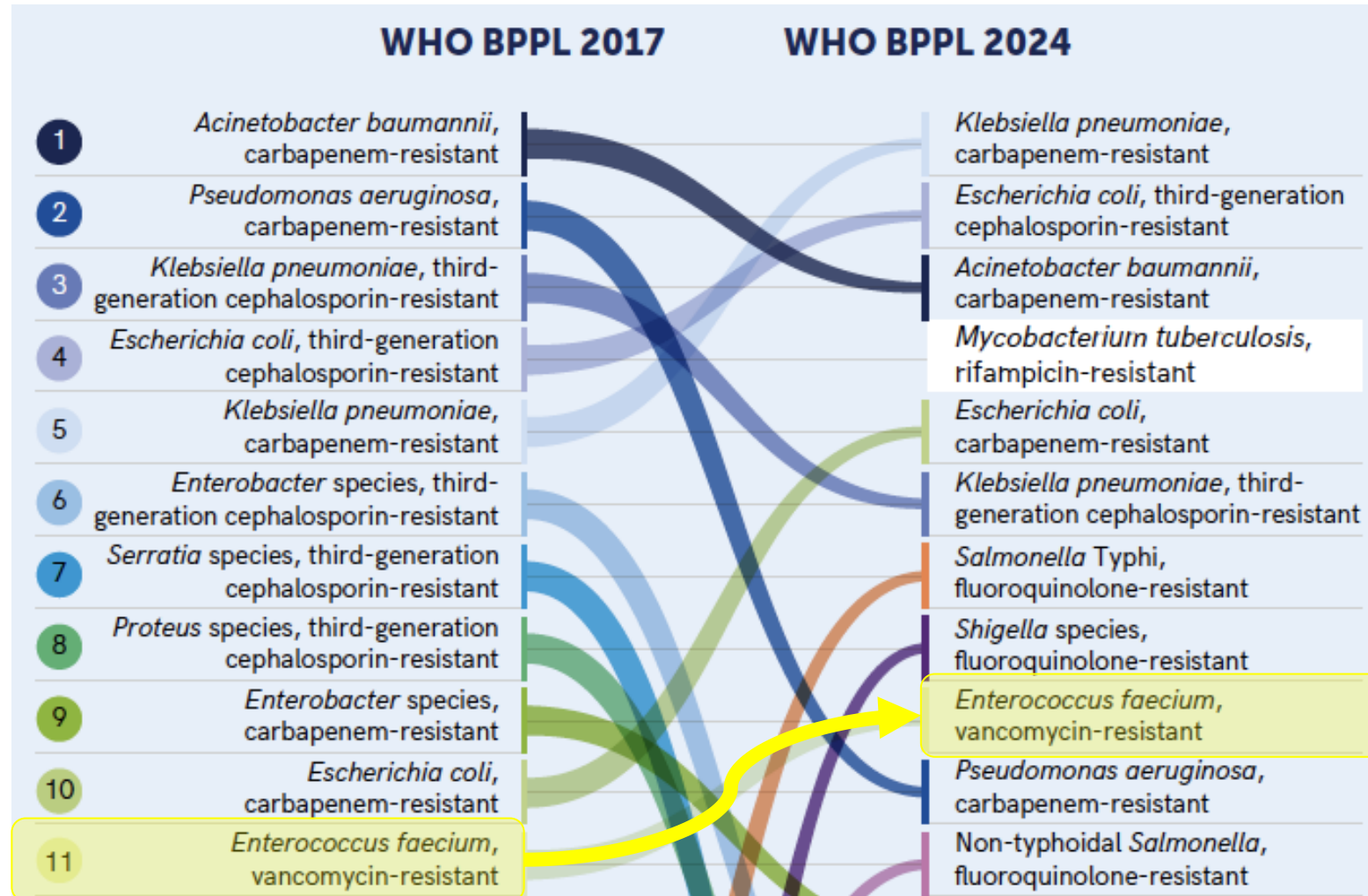


BMR & BHRe

Bacteria (WHO category)	WHO	CDC	ESKAPE
<i>Acinetobacter baumannii</i> , carbapenem-R	Critical	Serious (MDR)	Yes
<i>Pseudomonas aeruginosa</i> , carbapenem-R	Critical	Serious (MDR)	Yes
<i>Enterobacteriaceae</i> , carbapenem-R, 3 rd -gen cep-R (ESBL+)	Critical	Urgent (carbapenem-R) Serious (ESBL+)	Yes
<i>Enterococcus faecium</i> , vancomycin-R	High	Serious (VRE)	Yes
<i>Staphylococcus aureus</i> , methicillin-R, vancomycin-I/R	High	Serious (MRSA) Concerning (VRSA)	Yes
<i>Helicobacter pylori</i> , clarithromycin-R	High		
<i>Campylobacter</i> spp., fluoroquinolone-R	High	Serious (drug-R)	
<i>Salmonellae</i> spp., fluoroquinolone-R	High	Serious (drug-R)	
<i>Neisseria gonorrhoeae</i> , 3 rd -gen cep-R, fluoroquinolone-R	High	Urgent (drug-R)	
<i>Streptococcus pneumoniae</i> , penicillin-NS	Medium	Serious (drug-R)	
<i>Haemophilus influenzae</i> , ampicillin-R	Medium		
<i>Shigella</i> spp., fluoroquinolone-R	Medium	Serious	
<i>Clostridium difficile</i>		Urgent	
<i>Candida</i> spp. fluconazole-R		Serious (Flu-R)	
<i>M. tuberculosis</i>		Serious (drug-R)	
Group A <i>Streptococcus</i>		Concerning (erythro-R)	
Group B <i>Streptococcus</i>	WHO PPL, CDC, & ESKAPE	Concerning (clinda-R)	1

} BHRe

Classification OMS



Classification CDC (2019)



Serious threat



Classification CDC (2022)

	Threat	Change in Rates or Number of Infections***			
		2020 vs. 2019	2021 vs. 2020	2022 vs. 2021	2022 vs. 2019
URGENT*	Hospital-onset CRE	▲ Increase	▲ Increase	▬ Stable	▲ Increase
	Hospital-onset Carbapenem-resistant <i>Acinetobacter</i>	▬ Stable	▬ Stable	▬ Stable	▲ Increase**
	Clinical Cases of <i>C. auris</i>	▲ Increase	▲ Increase	▲ Increase	▲ Increase
SERIOUS*	Hospital-onset MRSA	▲ Increase	▬ Stable	▼ Decrease	▬ Stable
	Hospital-onset VRE	▲ Increase	▲ Increase	▬ Stable	▲ Increase
	Hospital-onset ESBL-producing Enterobacterales	▲ Increase	▬ Stable	▬ Stable	▲ Increase
	Hospital-onset MDR <i>Pseudomonas aeruginosa</i>	▲ Increase	▲ Increase	▬ Stable	▲ Increase

Epidémiologie des ERV en France, en Europe et dans le Monde

3

Découverte des ERV



PLASMID-MEDIATED RESISTANCE TO VANCOMYCIN AND TEICOPLANIN IN *ENTEROCOCCUS FAECIUM*

ROLAND LECLERCQ, M.D., ELIANE DERLOT,
JEAN DUVAL, M.D., AND PATRICE COURVALIN, M.D.

E. faecium strains BM4147 and BM4152 were isolated in 1986 from the feces of two patients with acute leukemia who had not been treated with vancomycin and who had undergone selective digestive tract decontamination with oral kanamycin, sisomicin, nitrofurans, and colistin five days before a bone marrow transplantation. The patients had been hospitalized in a hematology unit where vancomycin was included in a regimen of empirical antibiotic therapy of febrile patients with neutropenia. The strains were isolated as pure cultures from the stools of the patients with neutropenia but did not provoke infection.



VANCOMYCIN-RESISTANT ENTEROCOCCI

SIR,—Vancomycin resistance among gram-positive organisms is rare,^{1,2} except in some strains of *Leuconostoc* spp, lactobacilli, and pediococci.³ Since November 1986, 55 strains of vancomycin-resistant enterococci derived from twenty-two patients with end-stage renal failure or multiple organ failure, including acute renal failure, have been isolated at the Dulwich Public Health Laboratory. The sources of these enterococci included blood (8), intra-abdominal sepsis (8), urine (5), peritoneal fluid (2), pleural fluid (1), and bile (1). Colonisation of four central venous lines was detected at their exit sites. Faecal carriage of resistant organisms was present in some infected patients and in 1 without evidence of infection.

Two patients were infected with both species. All strains are resistant to vancomycin at a concentration in excess of 64 mg/L.

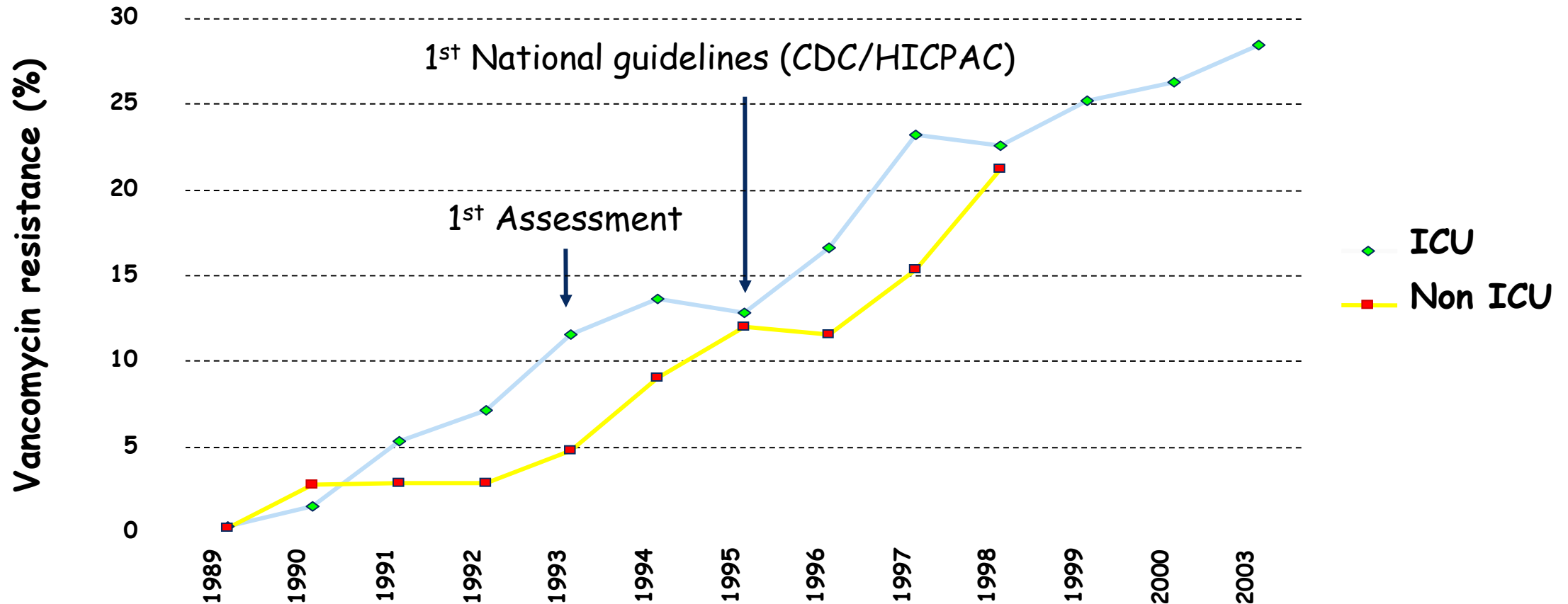
Public Health Laboratory,
Dulwich Hospital,
London SE22 8QF

ANNE H. C. UTTLEY
C. H. COLLINS

Antibiotics Reference Laboratory,
Division of Hospital Infection,
Central Public Health Laboratory,
London NW9

JAY NAIDOO
R. C. GEORGE

Diffusion rapide des ERV aux Etats-Unis



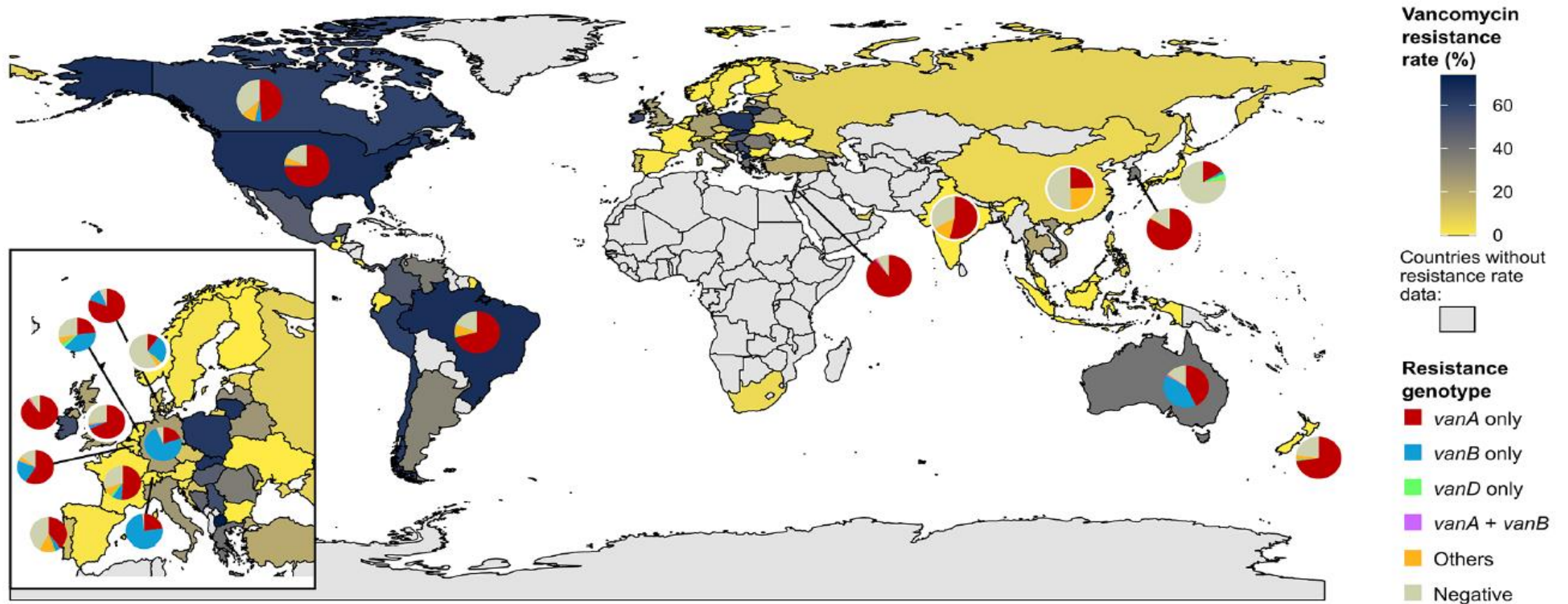
First cases of VRE = *E. faecalis* in 1987 (Saint Louis, MO)
First outbreaks = *E. faecium* in 1989 (New York City, NY)

Actuellement aux Etats-Unis

Pathogen, Antimicrobial Phenotype	Device-associated HAIs			Surgical Site Infections		
	# Reported	% Tested	%R	# Reported	% Tested	%R
<i>Enterococcus faecalis</i>	22,258			16,871		
Vancomycin-resistant (VRE)		89.1	5.5		89.0	2.4
<i>Enterococcus faecium</i>	10,754			6,150		
Vancomycin-resistant (VRE)		91.5	77.0		91.8	48.8

Actuellement dans le monde

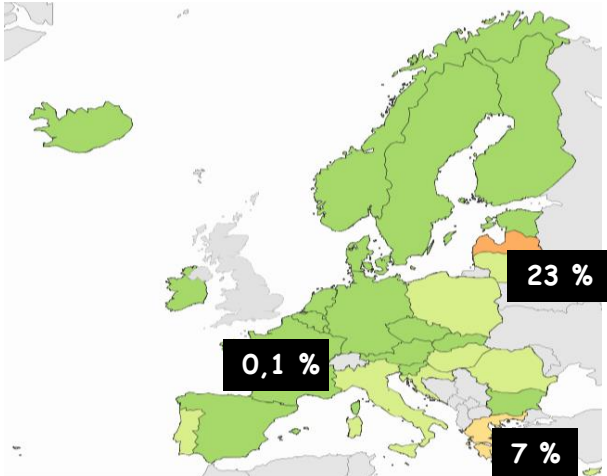
Prévalence des ERV (12 171 souches, 66 pays)



0 à 74 % (médiane = 21,8 %, IQR = 1,2-48,6 %)

Actuellement en Europe (2024)

E. faecalis



E. faecium

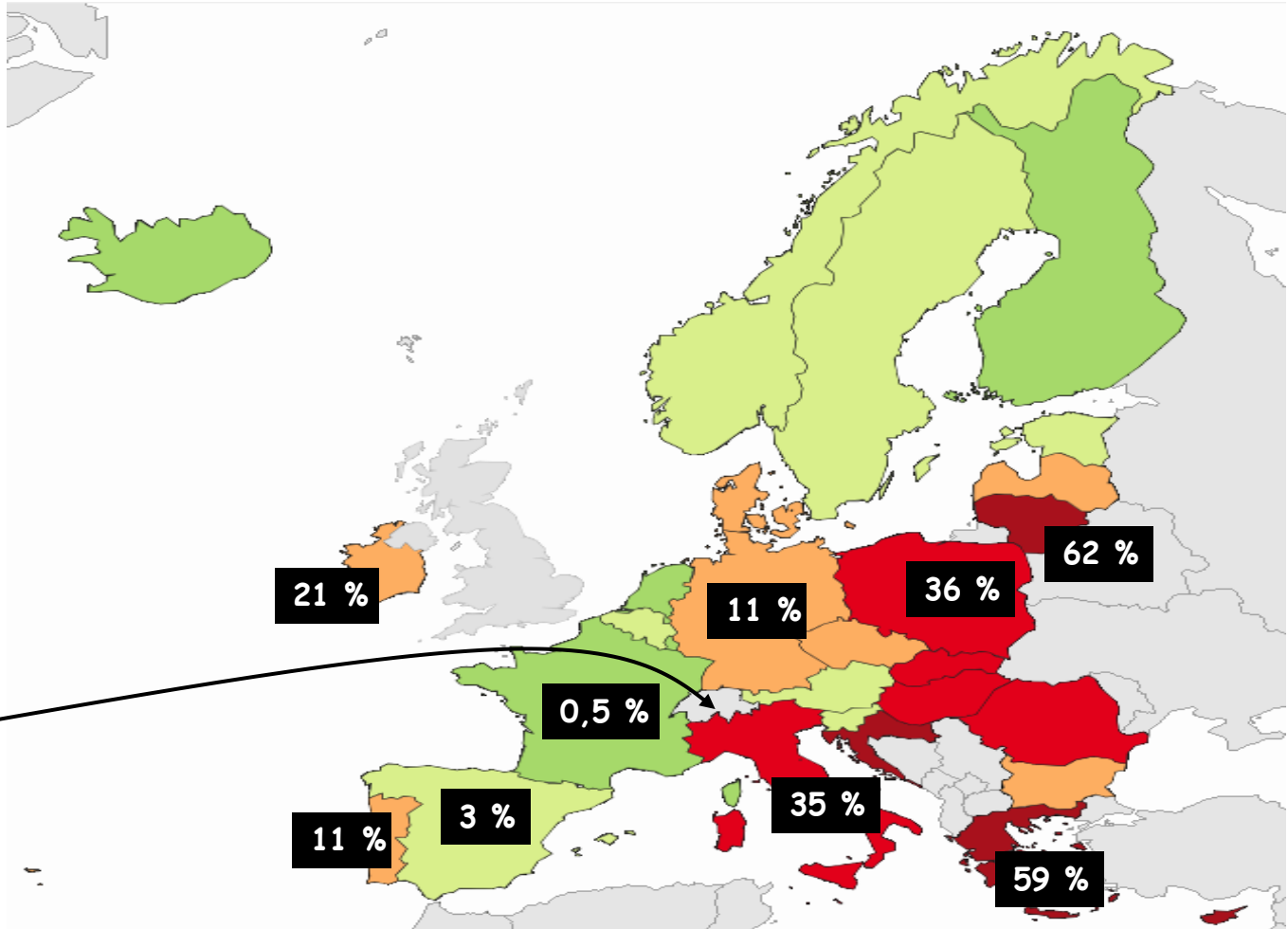
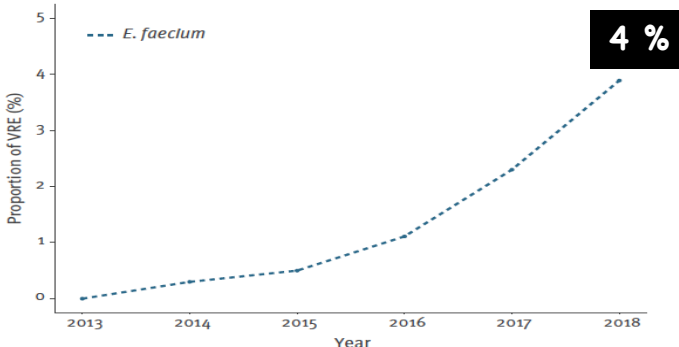
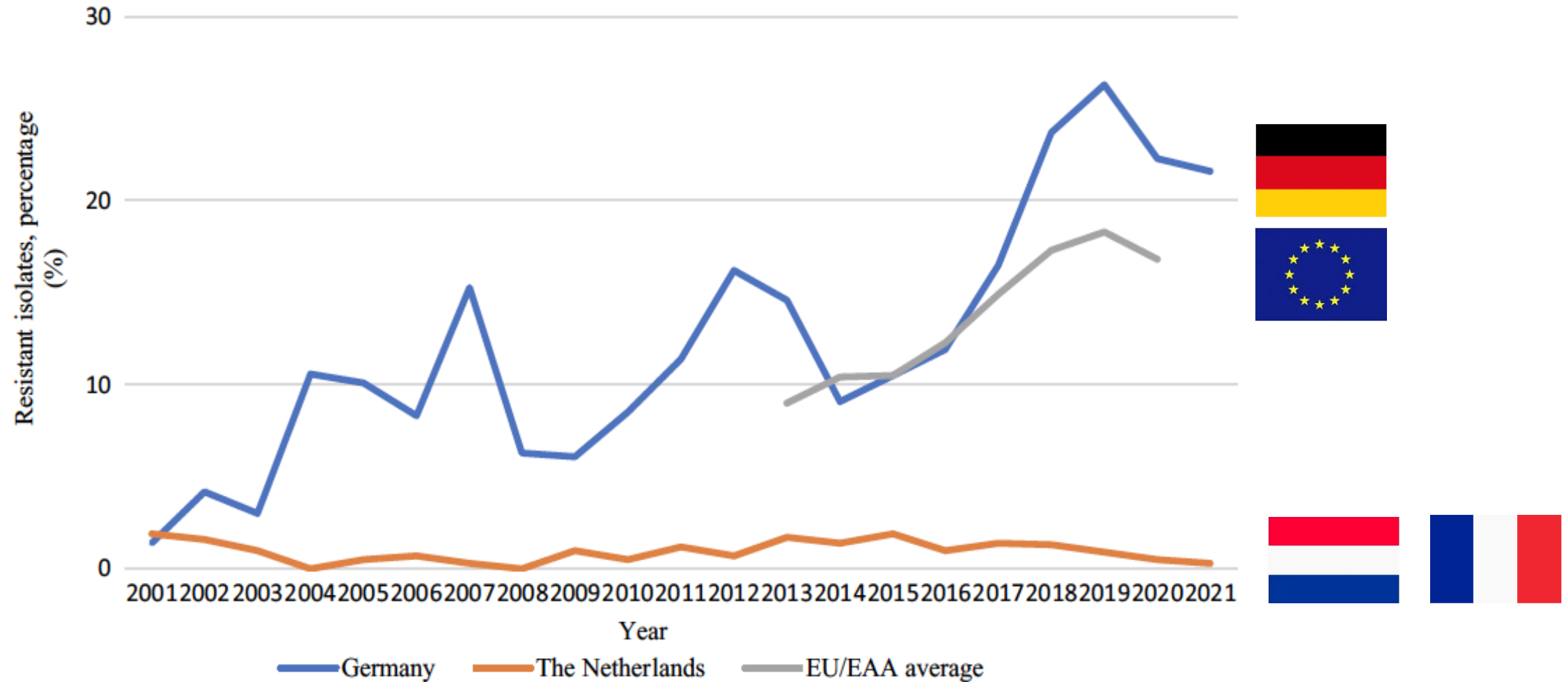


FIGURE 4
Time trend for the proportion of vancomycin resistance among *Enterococcus faecium* bacteraemias, Switzerland, 2013–2018 (n = 2,173 *E. faecium* bacteraemias)

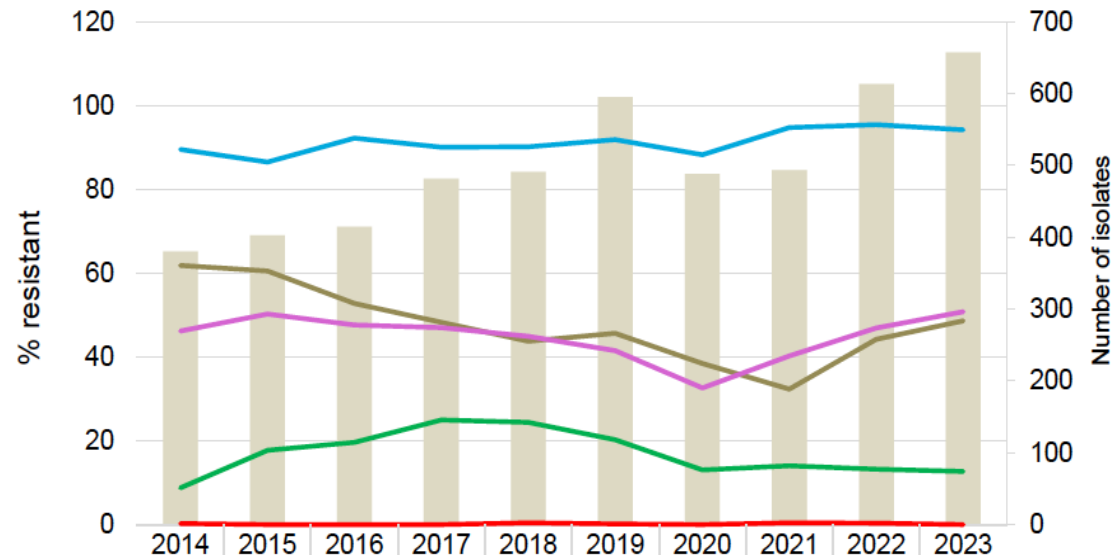


Hétérogénéité en Europe



Actuellement en Australie

Programme AGAR (2023) - 1599 épisodes de bactériémies
93 % dues à *E. faecalis* et *E. faecium*



	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Total, n	380	402	414	481	491	595	488	493	613	657
Ampicillin	89.4	86.5	92.2	90.0	90.1	91.9	88.2	94.7	95.4	94.2
Gentamicin (high-level)	61.8	60.5	52.7	48.2	43.7	45.6	38.4	32.3	44.2	48.6
Vancomycin	46.2	50.2	47.6	47.0	44.9	41.5	32.6	40.2	46.9	50.8
Teicoplanin	8.8	17.7	19.6	24.9	24.4	20.2	13.0	14.0	13.2	12.7
Linezolid	0.3	0.0	0.0	0.0	0.4	0.2	0.0	0.4	0.3	0.0

Organism	Total
<i>Enterococcus</i> species	1,599
<i>Enterococcus faecalis</i>	828
Vancomycin-resistant, percent*	0.0
Vancomycin-susceptible, percent*	100.0
<i>Enterococcus faecium</i>	657
Vancomycin-resistant, percent*	50.8
Vancomycin-susceptible, percent*	49.2
Other enterococcal species	114

Actuellement dans le Monde

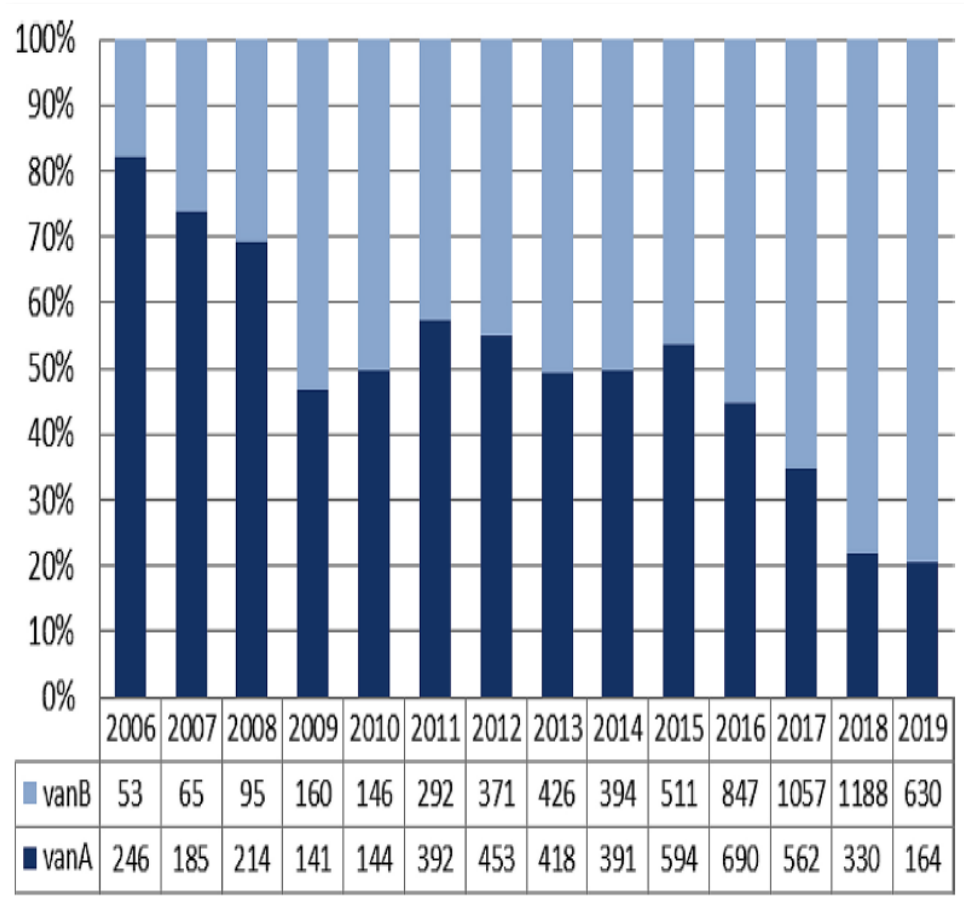
Programme SENTRY (1997-2016) - 49 491 souches testées (298 centres) dont **7 615 ERV**

Organism/Organism Group	Asia-Pacific	Europe	Latin America	North America	Total
<i>Enterococcus</i> spp., No. (%)	3476	16 054	4755	25 206	49 491
Vancomycin-susceptible (≤ 4 mg/L)	3135 (90.2)	14 626 (91.1)	4249 (89.4)	19 544 (77.5)	41 554 (84.0)
Vancomycin-resistant (VanA)	232 (6.7)	1095 (6.8)	426 (9.0)	5035 (20.0)	6788 (13.7)
Vancomycin-resistant (VanB)	89 (2.6)	279 (1.7)	44 (0.9)	415 (1.6)	827 (1.7)
<i>Enterococcus faecium</i> , No. (%)	1089	5229	876	7166	14 360
Vancomycin-susceptible (≤ 4 mg/L)	780 (71.6)	3990 (76.3)	517 (59.1)	2268 (31.6)	7555 (52.6)
Vancomycin-resistant (VanA)	227 (20.8)	992 (19.0)	323 (36.8)	4637 (64.7)	6179 (43.0)
Vancomycin-resistant (VanB)	82 (7.5)	246 (4.7)	36 (4.1)	259 (3.6)	623 (4.3)
<i>Enterococcus faecalis</i> , No. (%)	2225	10 078	3524	16 188	32 015
Vancomycin-susceptible (≤ 4 mg/L)	2213 (99.5)	9942 (98.6)	3413 (96.8)	15 631 (96.6)	31 199 (97.5)
Vancomycin-resistant (VanA)	5 (0.2)	103 (1.0)	103 (3.0)	398 (2.5)	609 (1.9)
Vancomycin-resistant (VanB)	7 (0.3)	33 (0.3)	8 (0.2)	156 (1.0)	204 (0.6)

Rapport VanA/VanB = 10

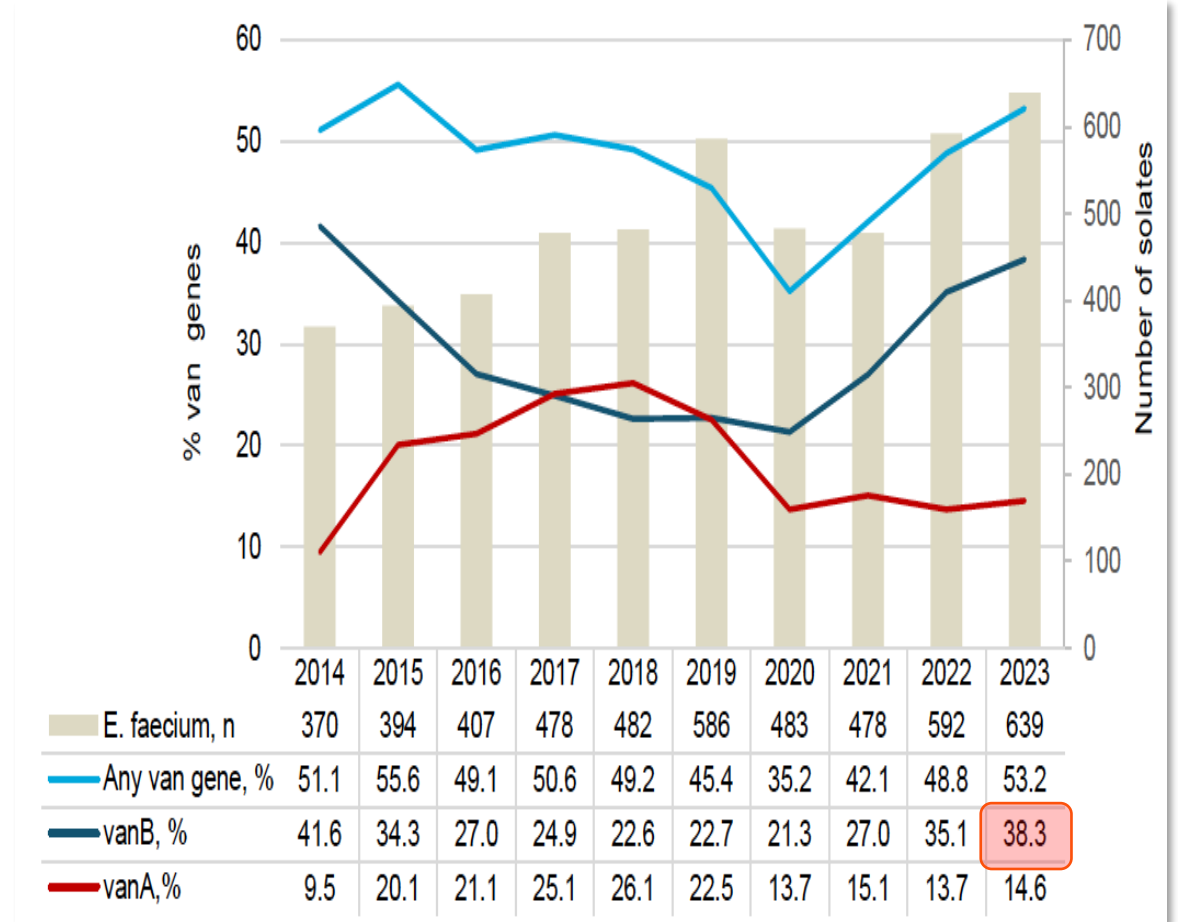
Pays à épidémiologie *E. faecium* VanB

Allemagne



79 %

Australie



Actuellement en France (2024)

Résistance chez *E. faecalis*

Antibiotique	Tous prélèvements confondus		Hémocultures	
	Nb total de souches	% (R)	Nb total de souches	% (R)
Ampicilline-amoxicilline	49 252	0,4	5 122	0,4
Nitrofurantoïne	37 199	0,5	3 241	0,6
Teicoplanine	45 194	0,1	4 674	0,1
Vancomycine	47 738	0,1	5 094	0,1

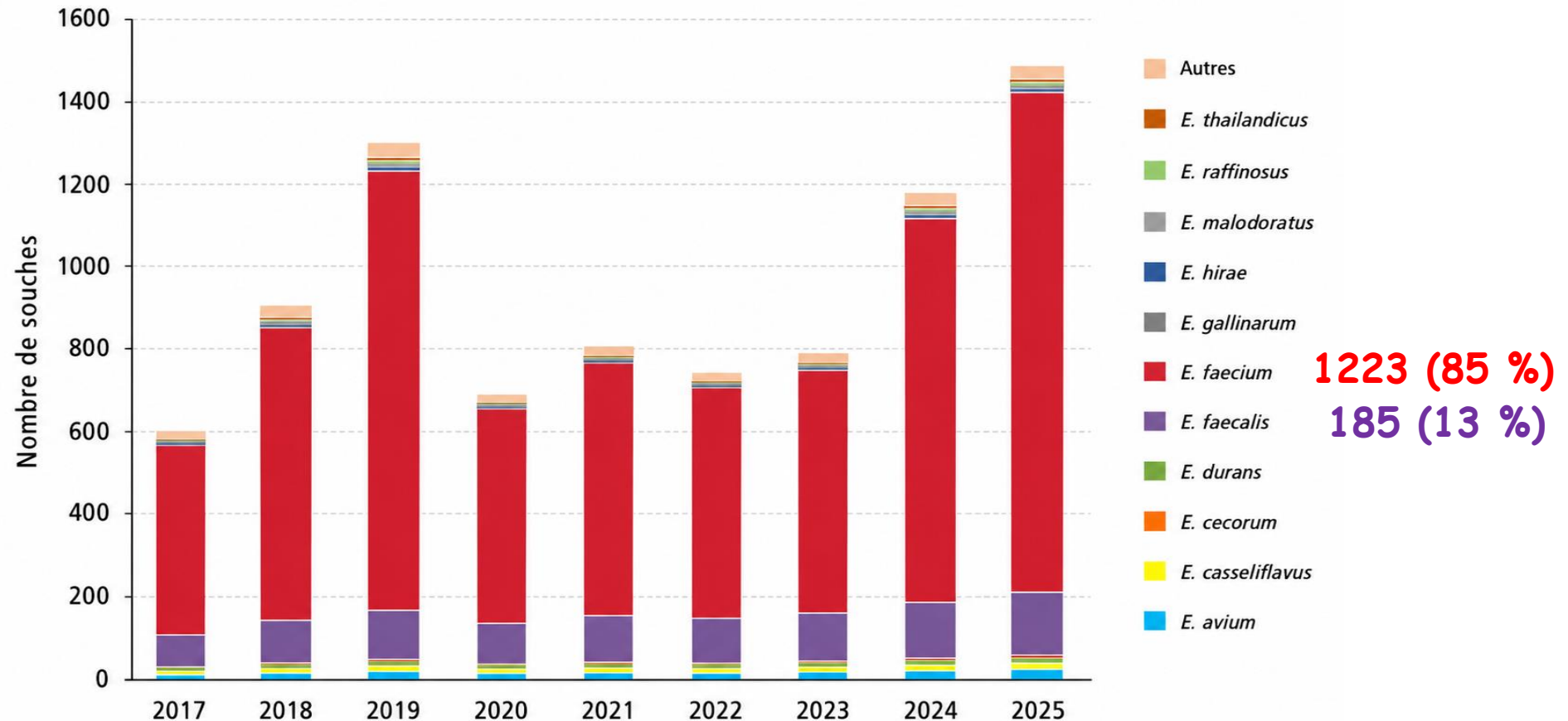
Résistance chez *E. faecium*

Antibiotique	Tous prélèvements confondus		Hémocultures	
	Nb total de souches	% (R)	Nb total de souches	% (R)
Ampicilline et/ou amoxicilline	14 649	78,5	2 144	81,3
Nitrofurantoïne	10 781	32,6	1 384	34,3
Teicoplanine	13 665	1,2	1 958	0,6
Vancomycine	14 658	1,2	2 149	0,6
Linézolide	12 801	0,8	1 844	1,1
Daptomycine	979	10,5	338	10,1

Activité du CNR en 2025

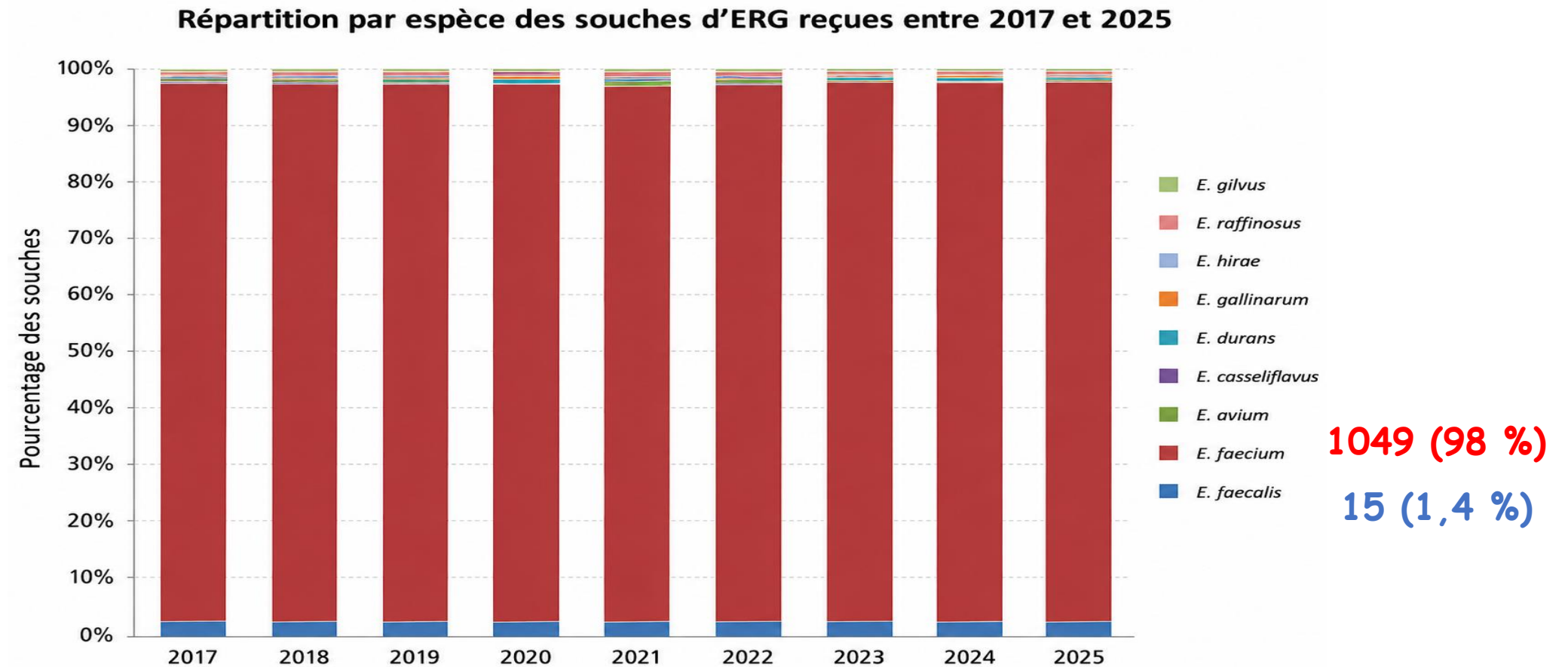
1434 souches reçues

Répartition par espèce des souches reçues entre 2017 et 2025



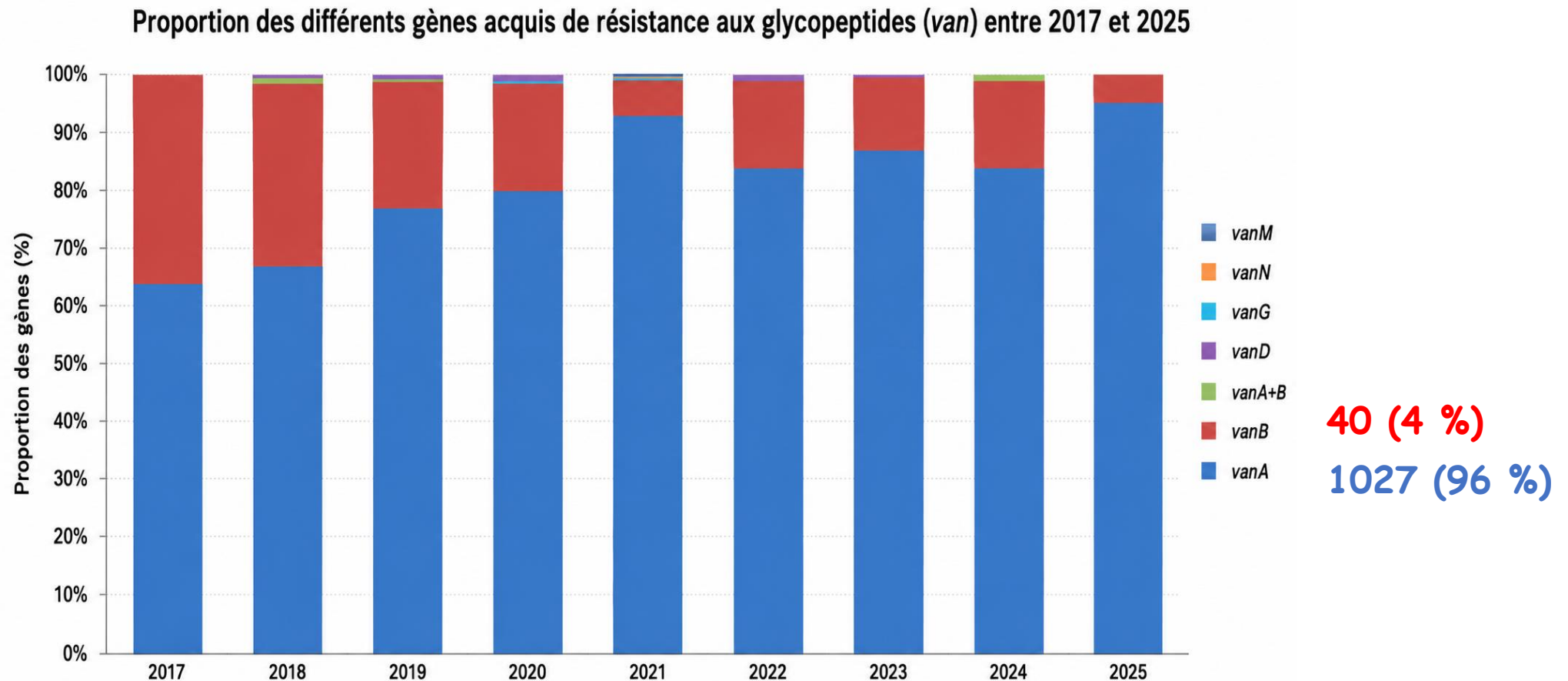
Souches d'ERV reçues au CNR en 2025

1068 souches (74 %) avec une résistance acquise



Souches d'ERV reçues au CNR en 2025

1068 souches (74 %) avec une résistance acquise



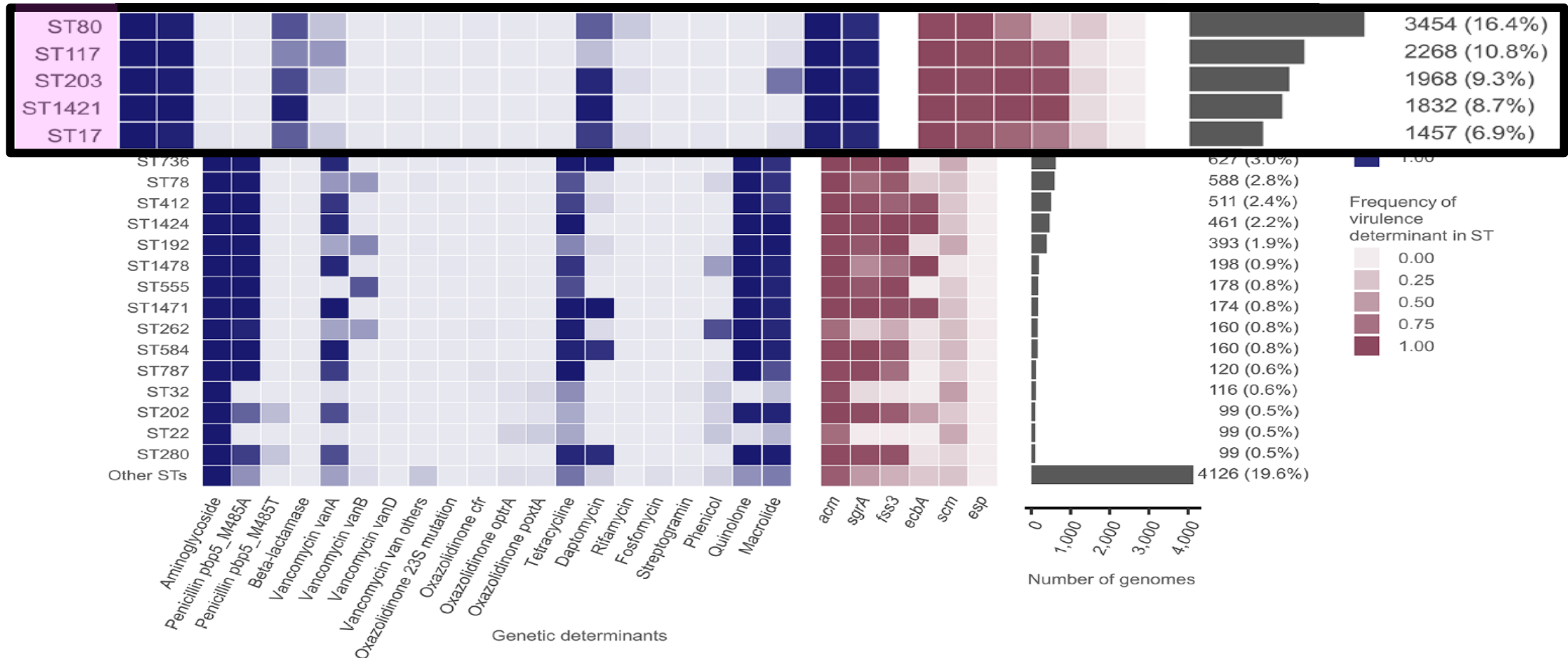
Dynamique clonale & génomique

Transition ST17 / ST18 → ST80 / ST117 et émergence de nouveaux ST

4

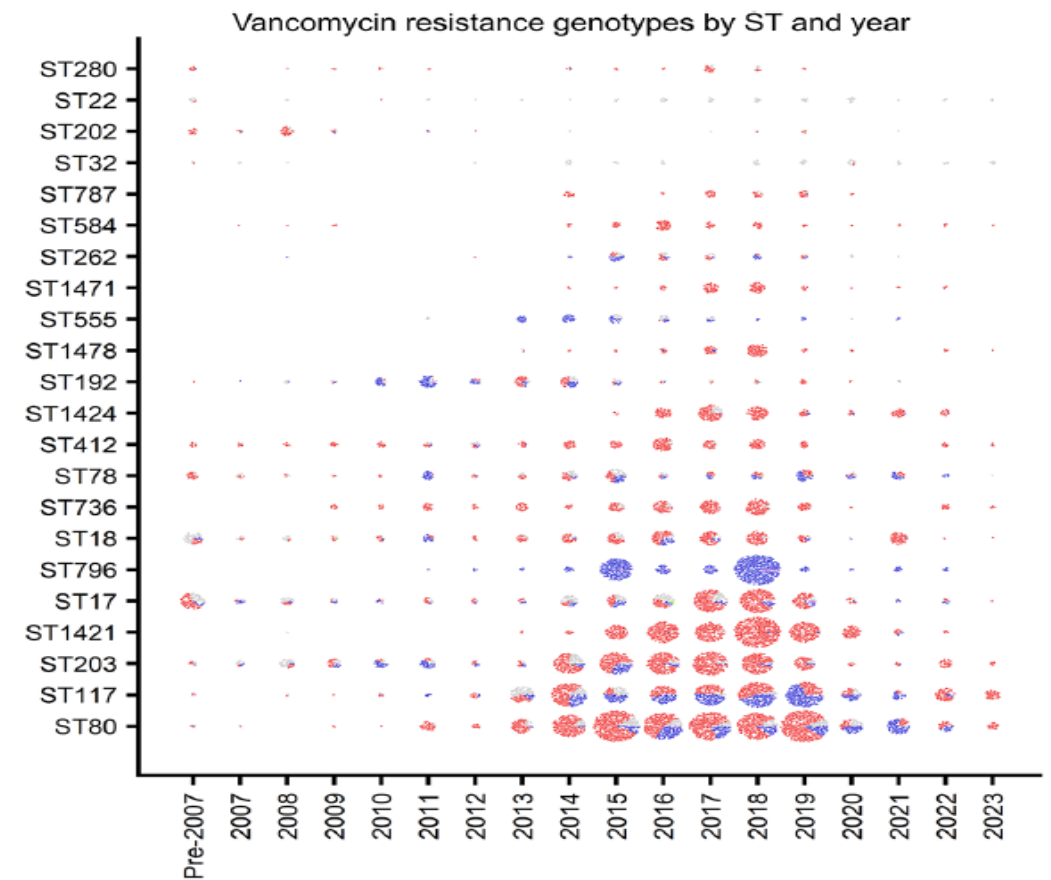
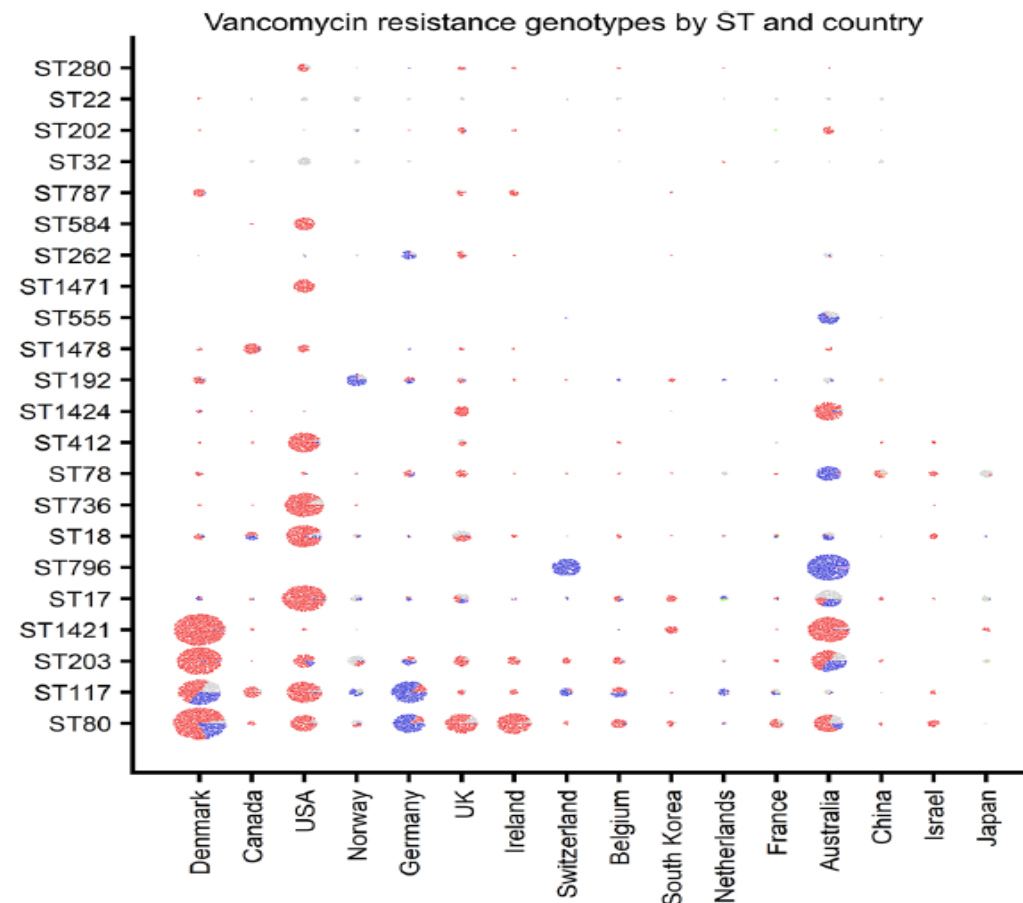
Principaux ST d'*E. faecium* dans le monde

Analyse génomique sur 21 058 génomes NCBI (80 pays, 1956-2024, 780 ST)



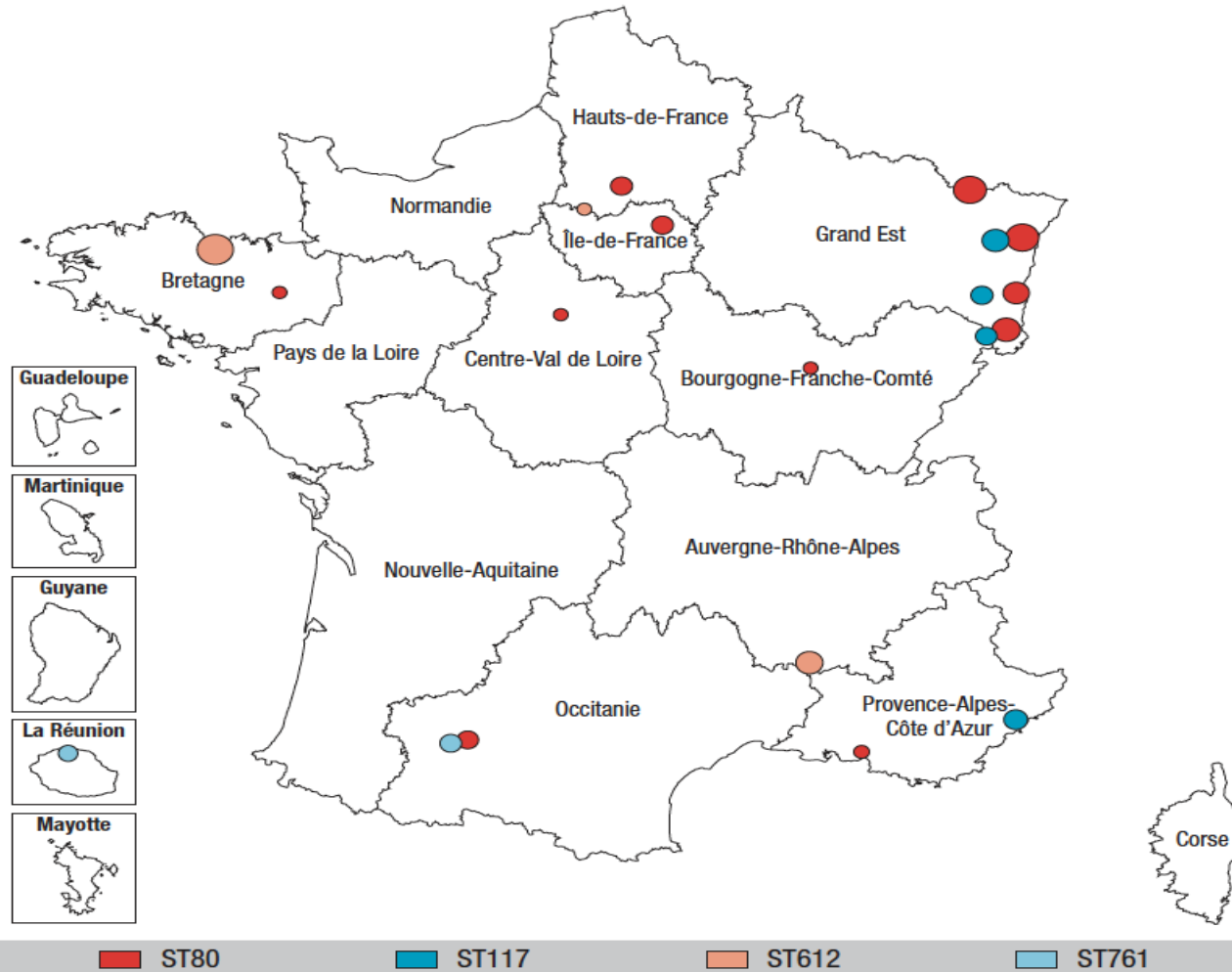
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Analyse génomique sur 21 058 génomes NCBI (80 pays, 1956-2024, 780 ST)

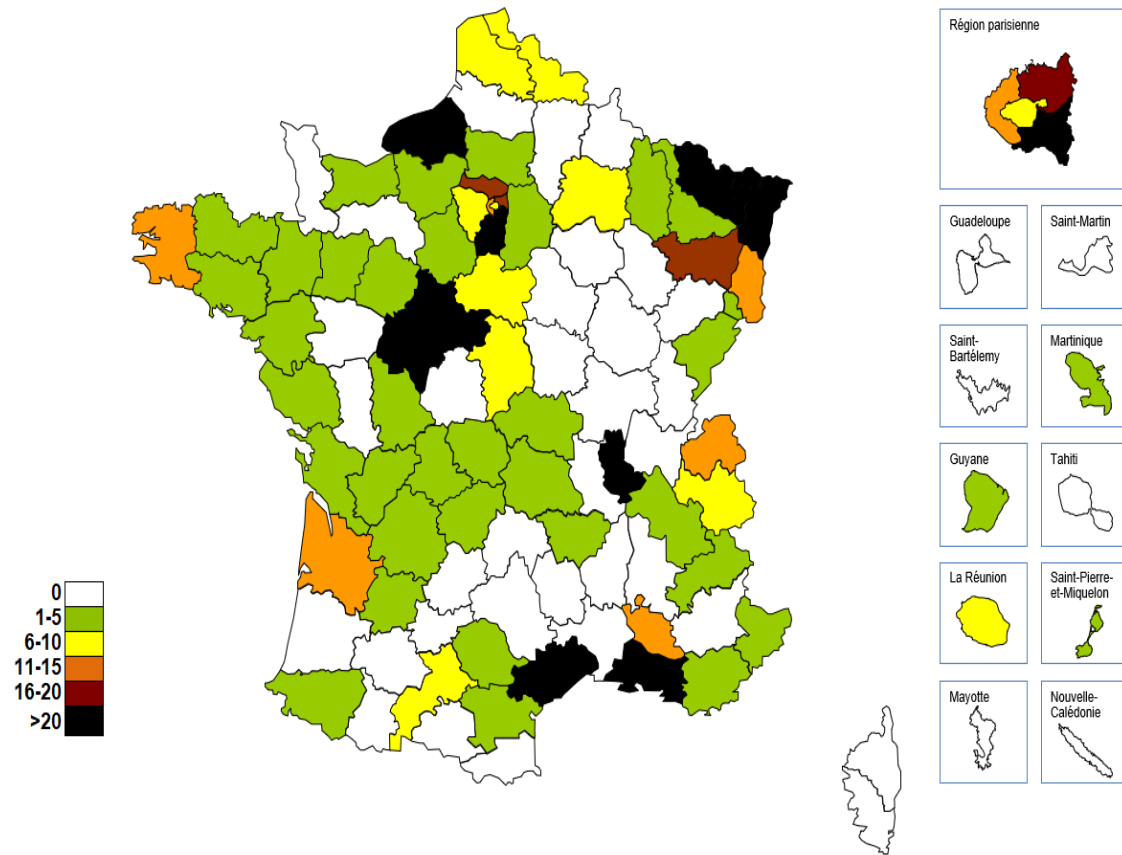


Principaux ST d'*E. faecium* en France

Localisation géographique des principaux ST (*Sequence Type*) identifiés dans les souches d'*E. faecium* par séquençage entier du génome (approche MLST *in silico*) entre 2019 et 2022



Souches d'*E. faecium* vanA en 2025



Principales épidémies 2025

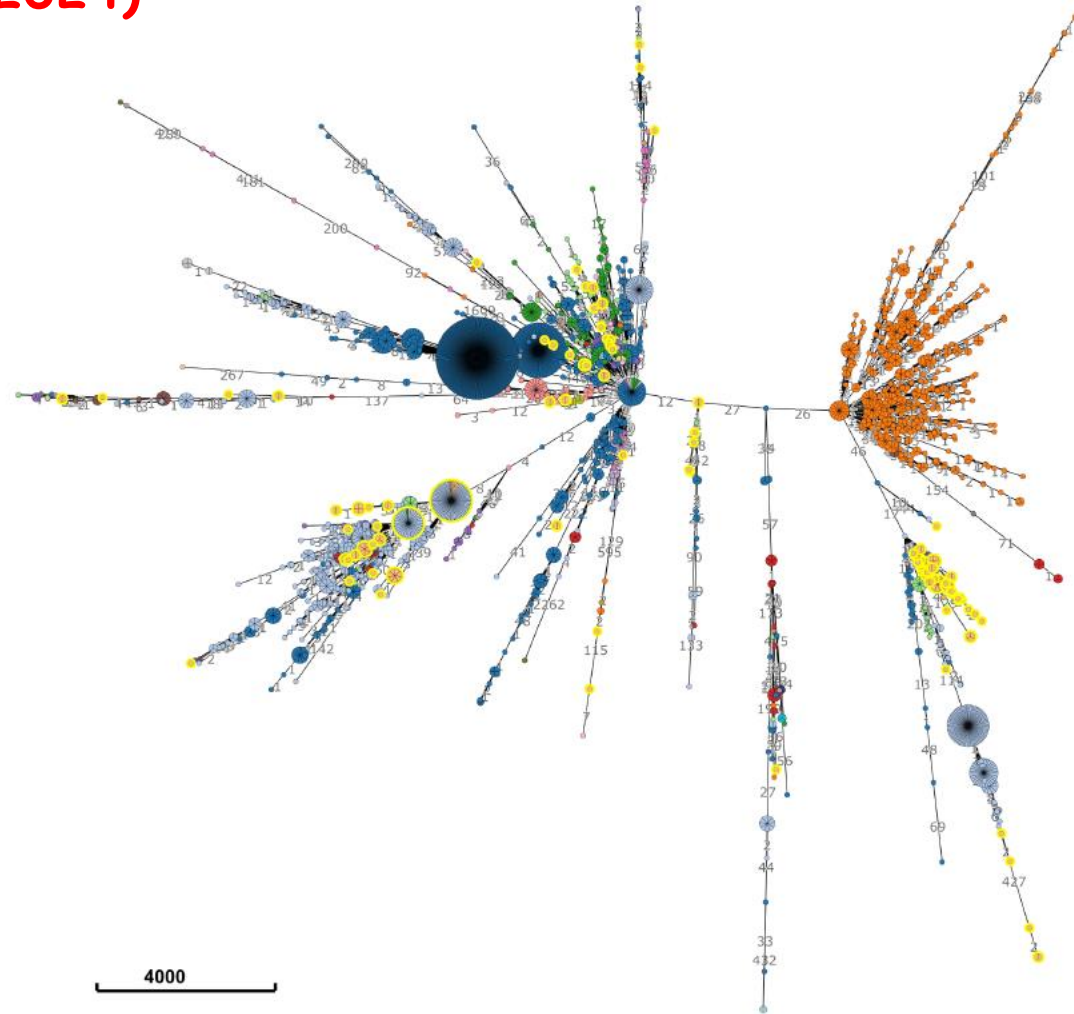
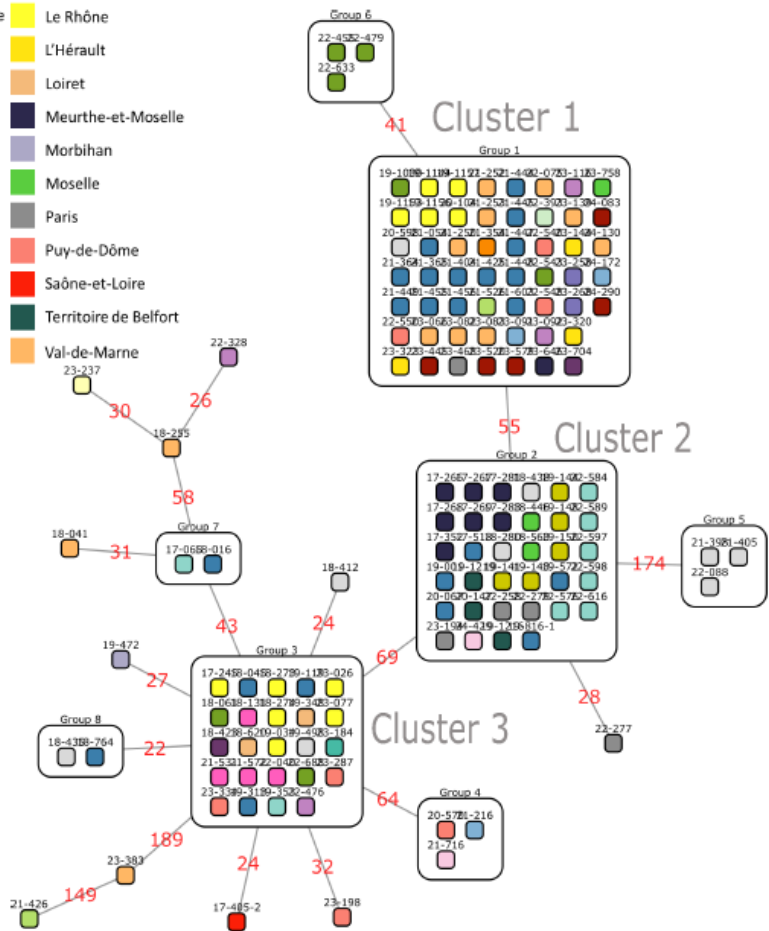
Ville	Souches	Clones	Sequence types (n souches)
Blois (41)	47	3	ST817 · 43 ST80 · 4
Metz (57)	37	2	ST80 · 36 ST1228 · 1
Béziers (34)	36	3	ST80 · 36
Muret (31)	24	1	ST117 · 24
Tours (37)	20	2	ST612 · 18 ST80 · 2
Total	164	11	5 ST distincts

 ST80 (lignée partagée)
 ST817
 ST1228
 ST117
 ST612

Diffusion du ST117 en France

136 souches (2017-2024)

French Administrative Departments



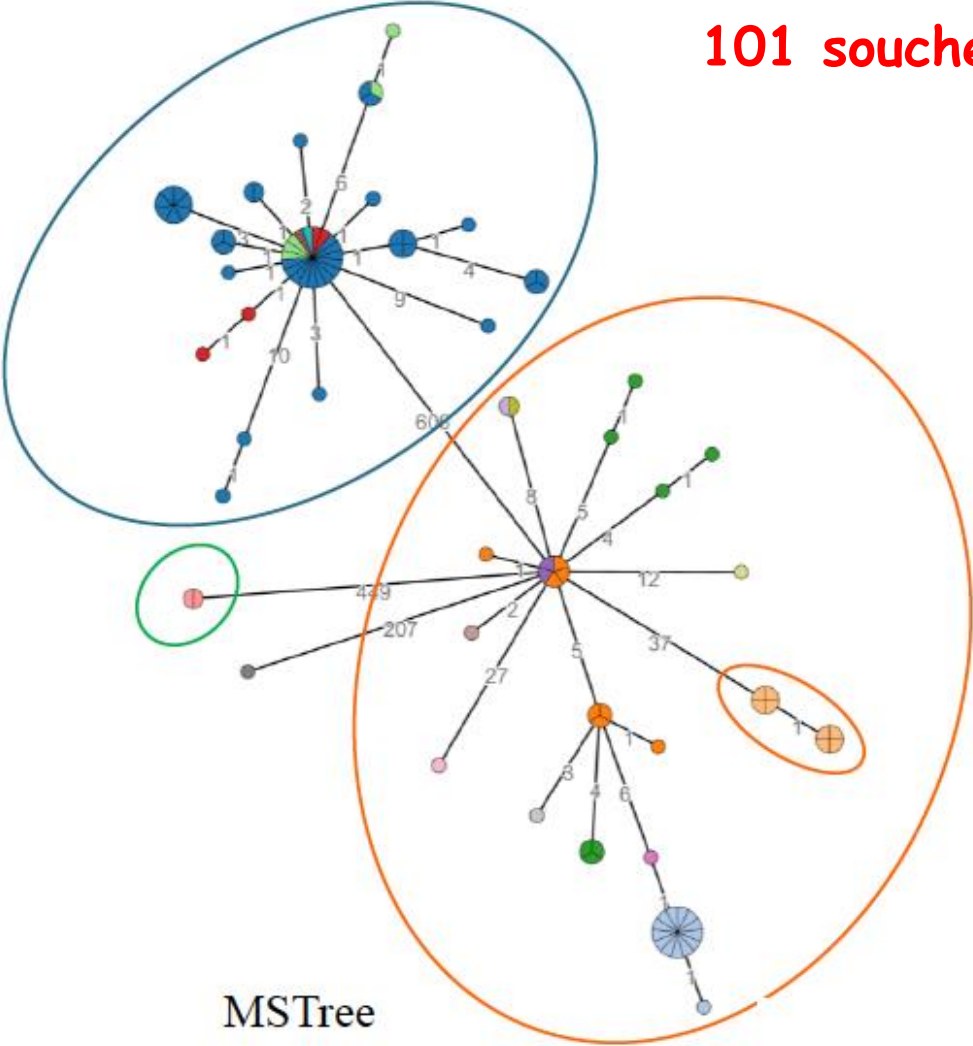
Country



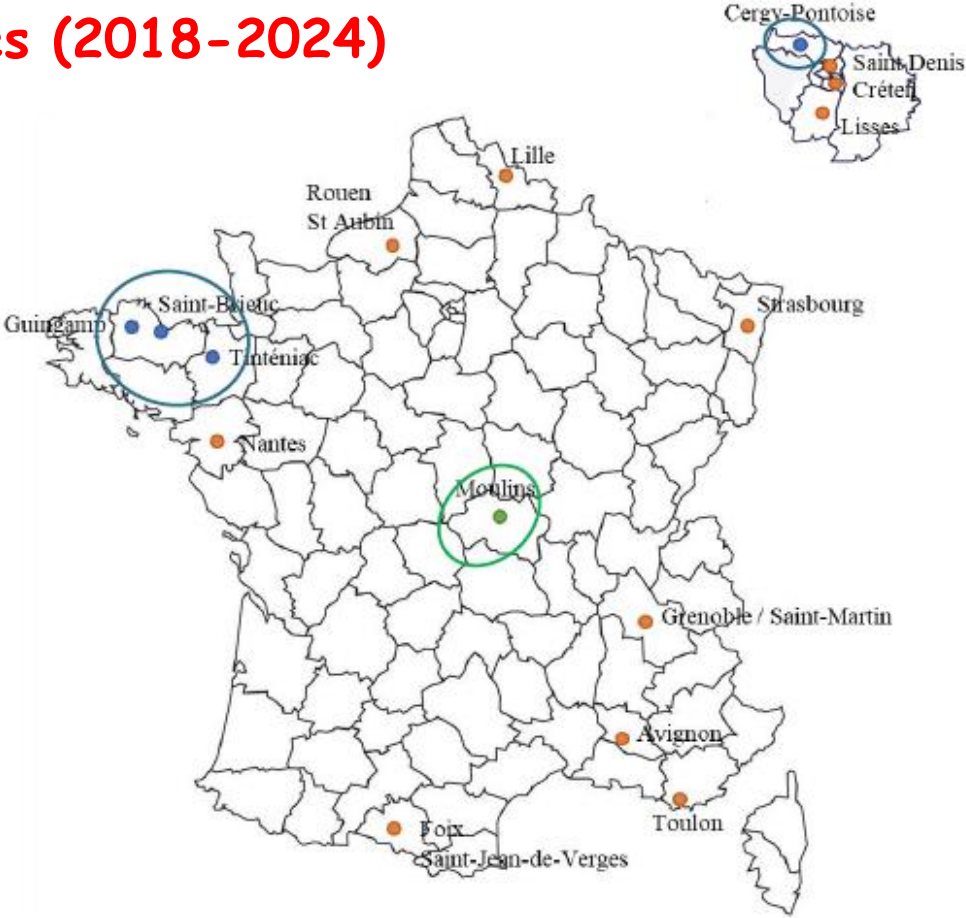
Diffusion du ST612 en France

101 souches (2018-2024)

- City
- Saint-Brieuc [41]
 - Avignon [14]
 - Grenoble [8]
 - Toulon [8]
 - Rouen [7]
 - Plerin [5]
 - Cergy-Pontoise [4]
 - Moulins [2]
 - Saint-Martin [2]
 - Foix [1]
 - Guingamp [1]
 - Lille [1]
 - Lisses [1]
 - Nantes [1]
 - Saint-Aubin-les-Elbeuf [1]
 - Saint-Denis [1]
 - Saint-Jean de Verges [1]
 - Strasbourg [1]
 - Tinténiac [1]

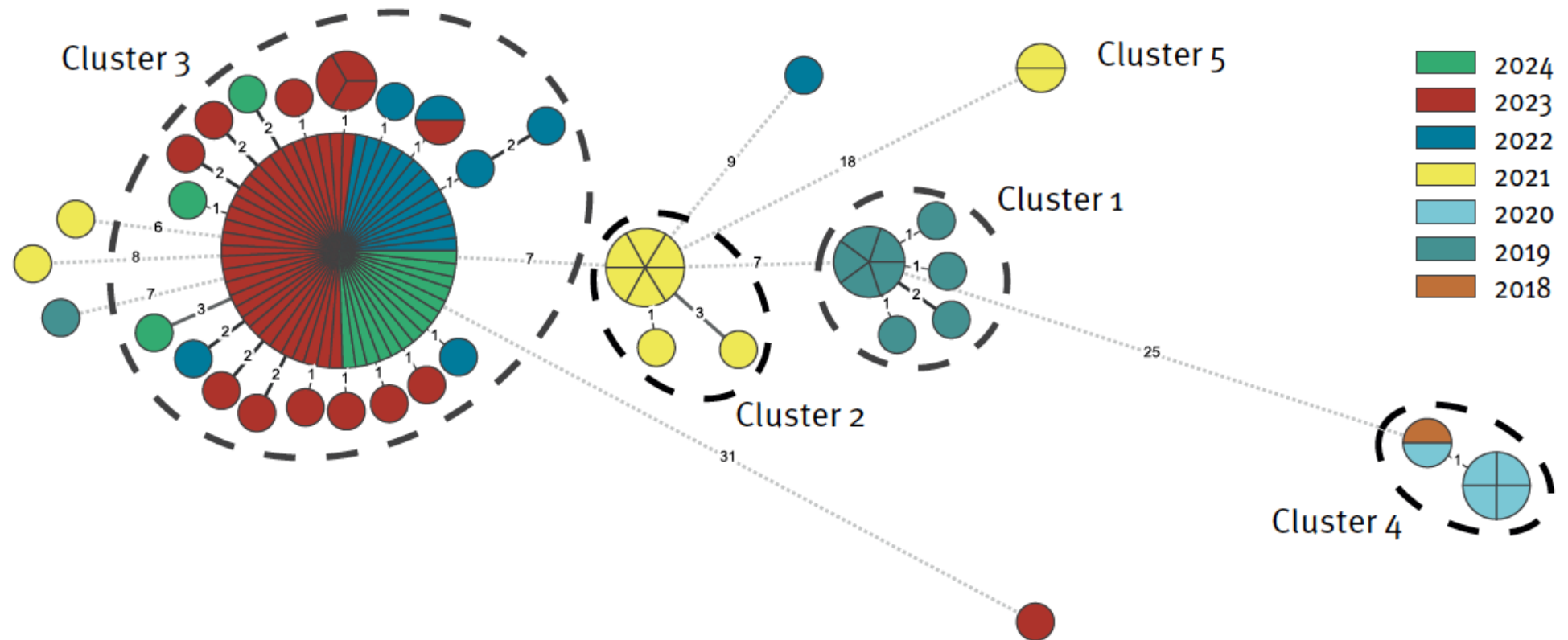


MSTree



Diffusion du ST612 en Suisse

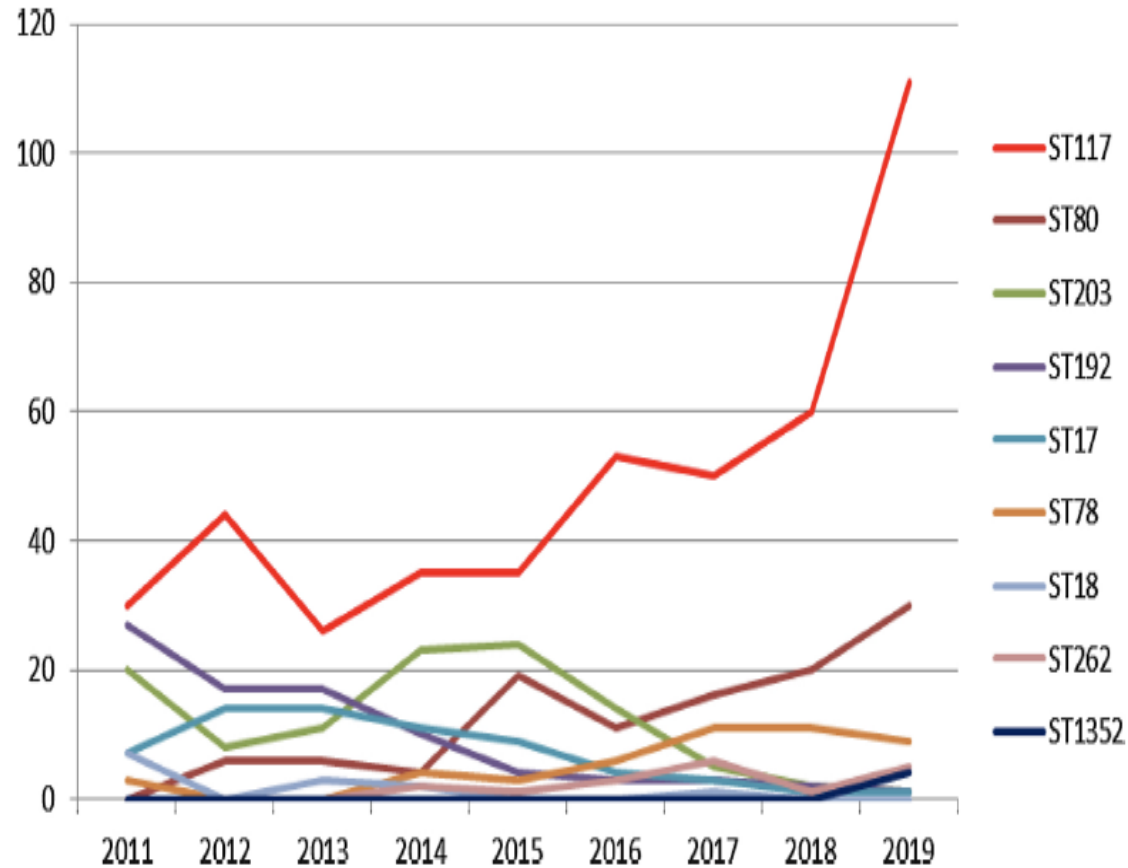
Diffusion en Suisse - 114 cas de VREfm *vanA* (2018-2024)



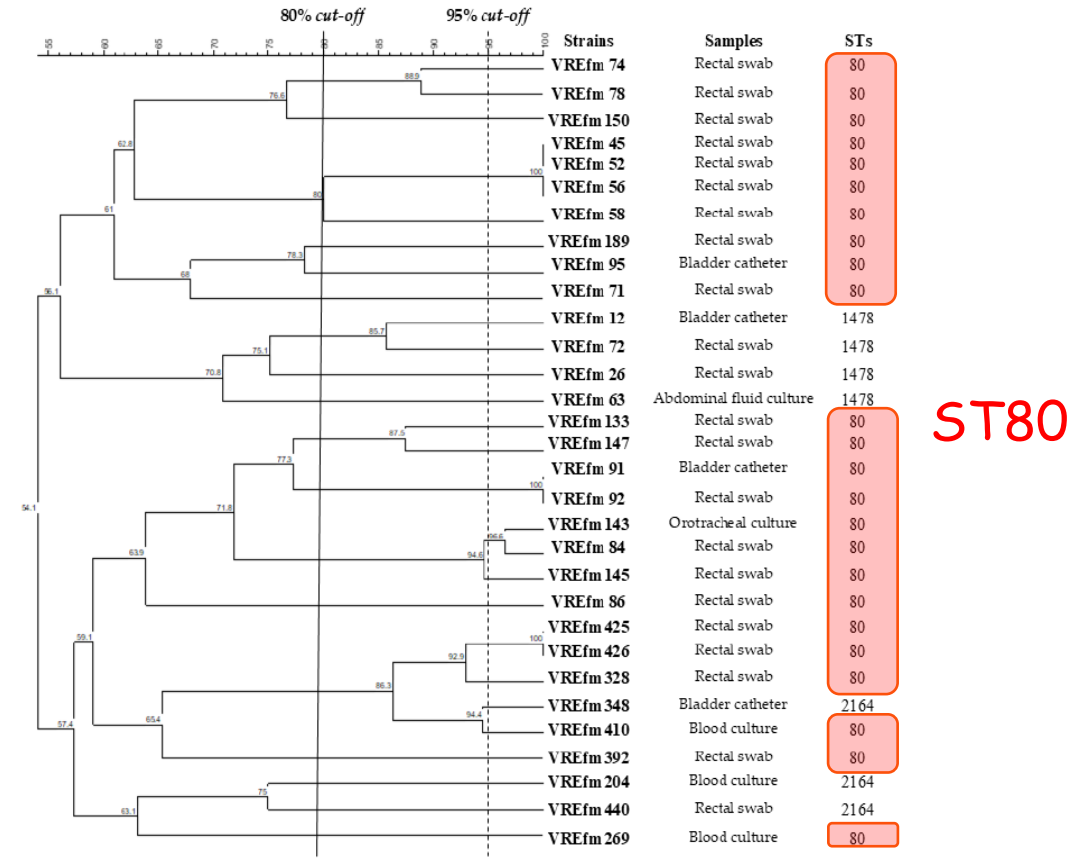
Sensibilité diminuée à la daptomycine

Principaux ST en Europe

Allemagne (2011-2019)

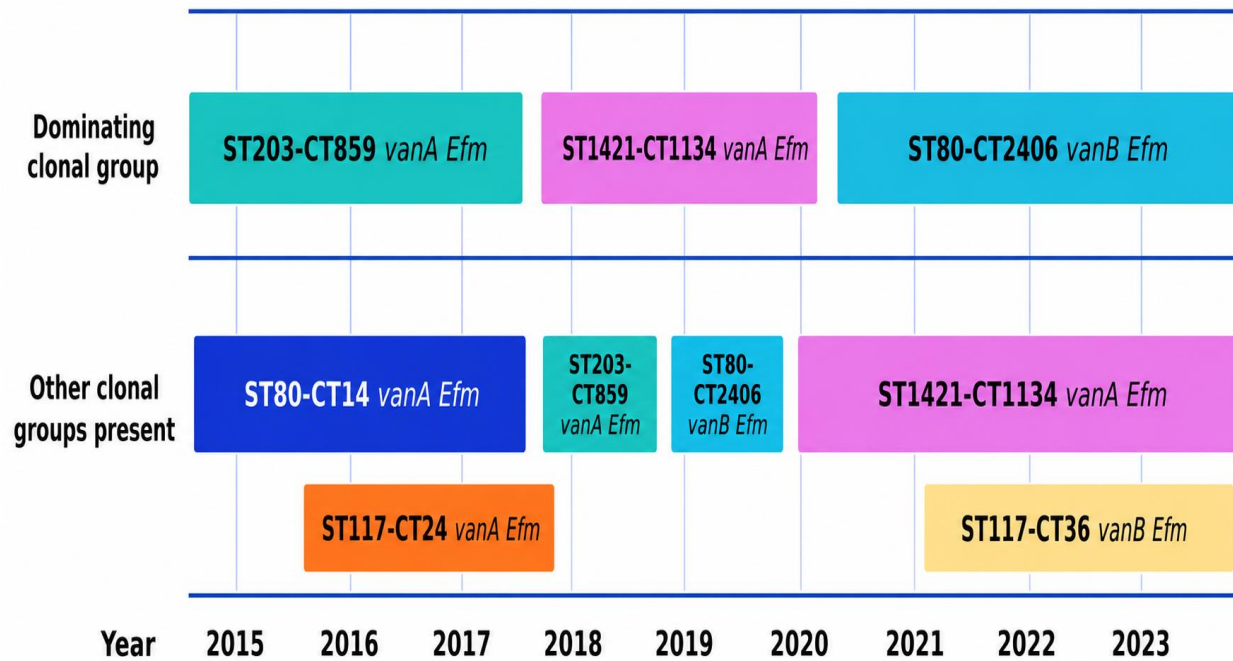


Italie (Molise) (2022-2024)



Principaux ST en Europe

Danemark
(2015-2023)
516 souches de bactériémies



Irlande
(2019-2022)
378 souches (330 de dépistage)

Tree scale: 0.1

(a) Ward location

- Ward A
- ★ Ward B

(b) Sequence type

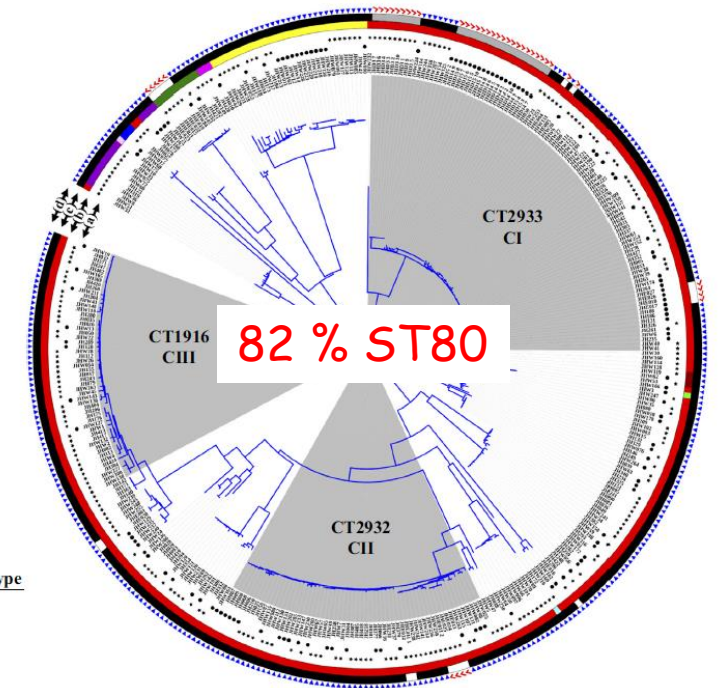
- ST17
- ST18
- ST80
- ST117
- ST203
- ST612
- ST787
- ST789
- ST1395
- Novel

(c) Isolate source

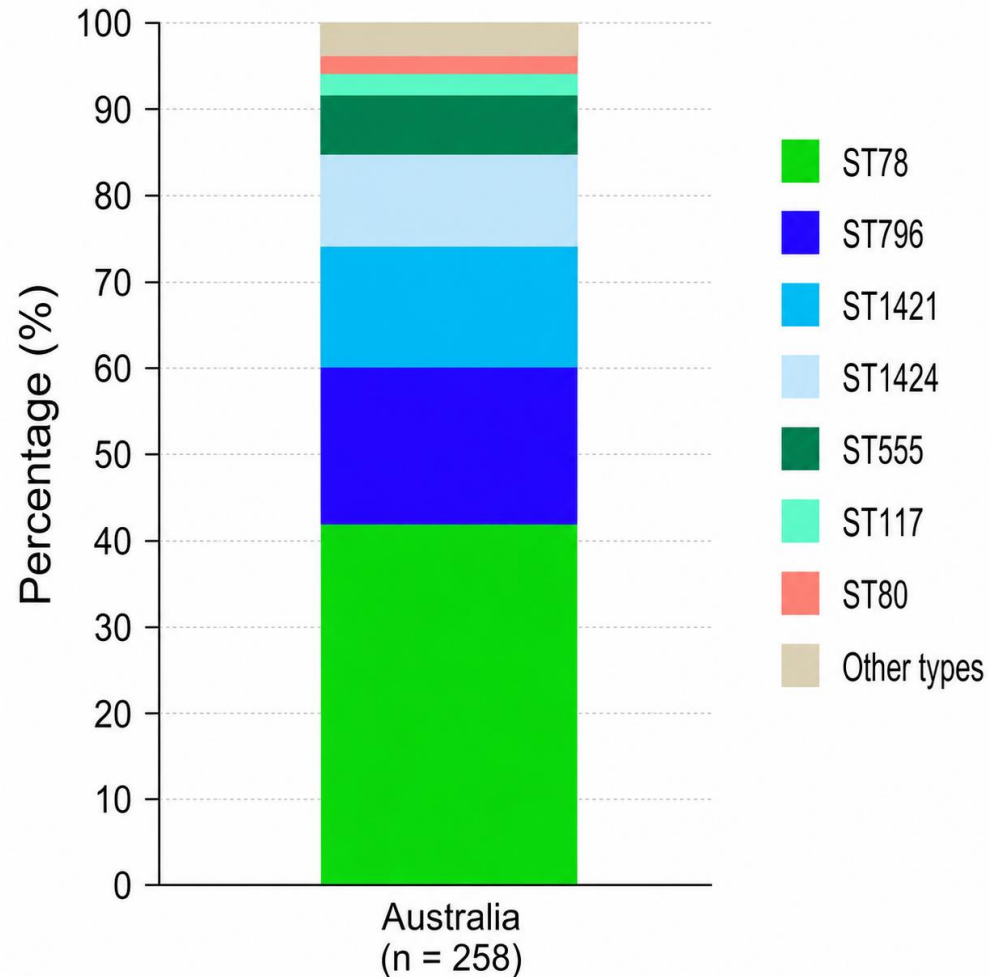
- Rectal screening
- Handwash basin drain outlet
- Environmental

(d) Vancomycin susceptibility phenotype

- ◀ Resistant
- ✓ Susceptible



Principaux ST en Australie (2023)

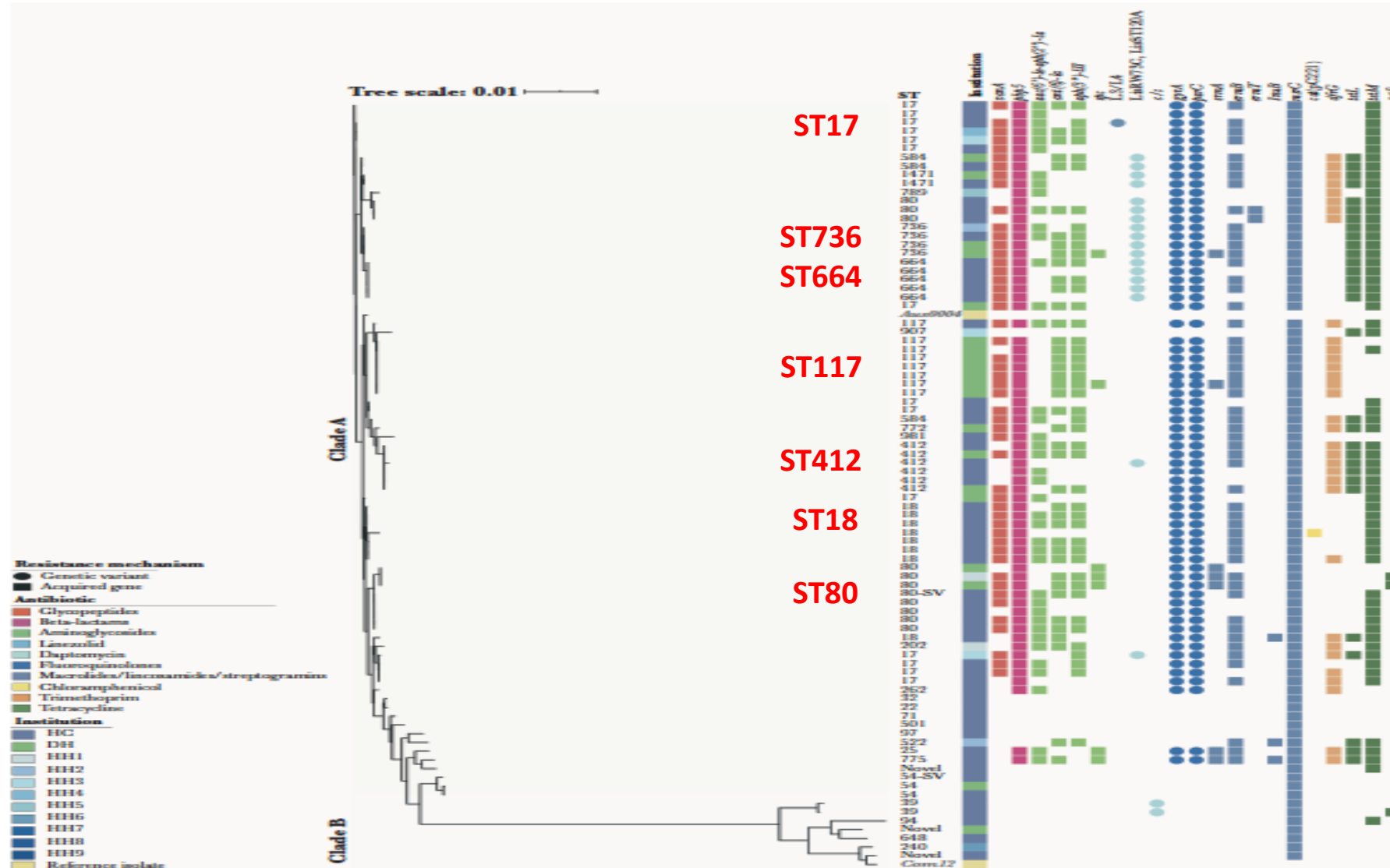


MLST	vanA	vanB	vanA + vanB	van non détecté	Total, n
ST78	0.0 (0)	100.0 (141)	0.0 (0)	0.0 (0)	141
ST1424	39.8 (45)	3.5 (4)	0.0 (0)	56.6 (64)	113
ST17	2.1 (2)	8.3 (8)	0.0 (0)	89.6 (86)	96
ST80	1.4 (1)	10.0 (7)	1.4 (1)	87.1 (61)	70
ST796	0.0 (0)	97.9 (46)	2.1 (1)	0.0 (0)	47
ST1421	83.8 (31)	2.7 (1)	0.0 (0)	13.5 (5)	37
ST555	0.0 (0)	89.5 (17)	0.0 (0)	10.5 (2)	19
Autres types (n=51)	6.9 (6)	10.3 (9)	0.0 (0)	82.8 (72)	87
Total	13.9 (85)	38.2 (233)	0.3 (2)	47.5 (290)	610

Valeurs : pourcentage (n). Intensité de couleur ∝ pourcentage.

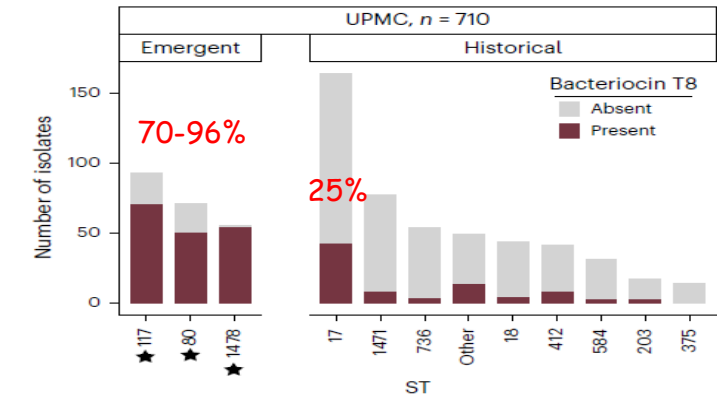
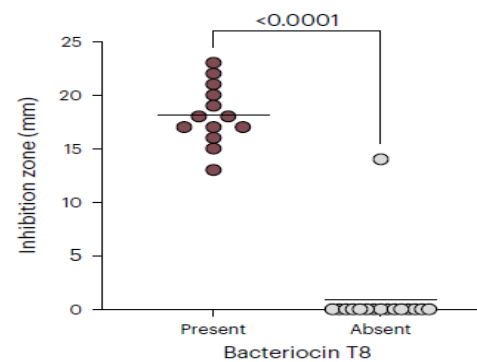
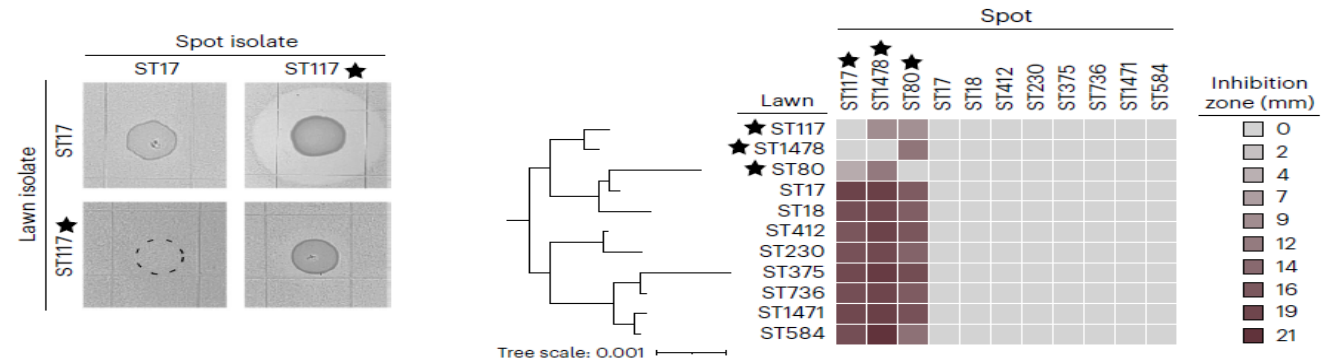
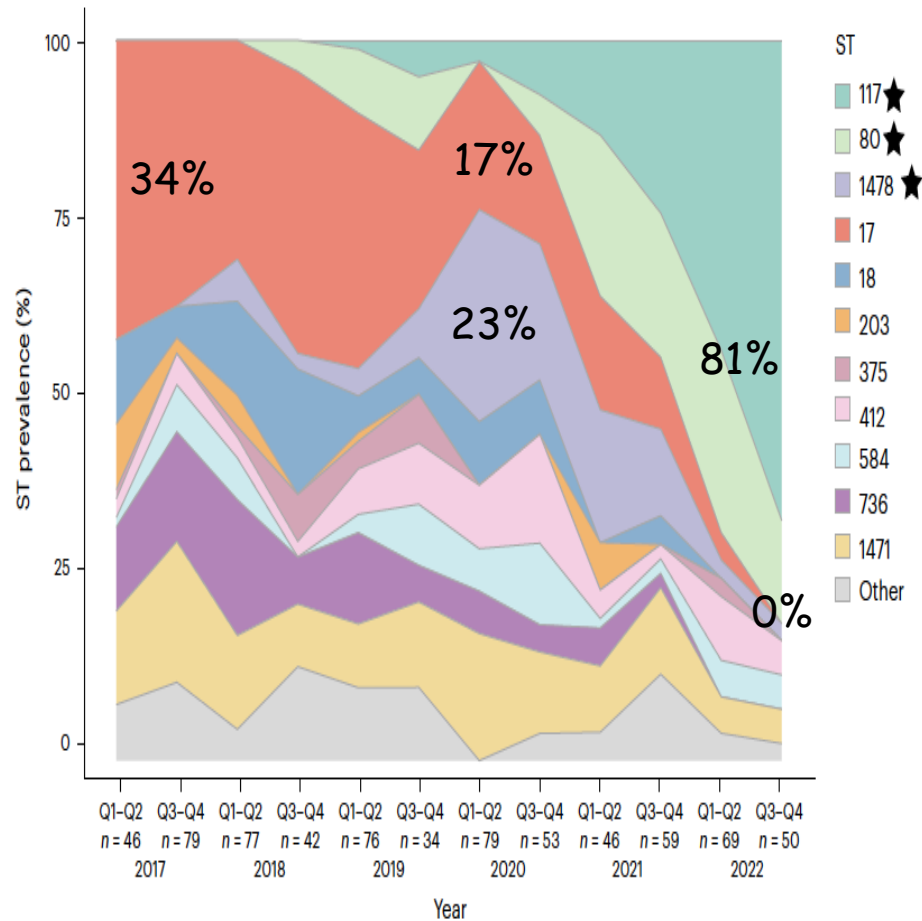
vanA vanB vanA+vanB non détecté

Principaux ST de *E. faecium* Aux Etats-Unis



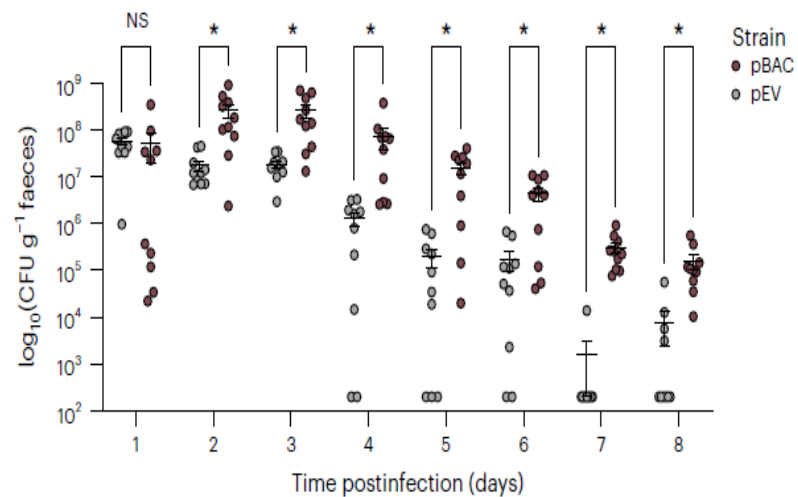
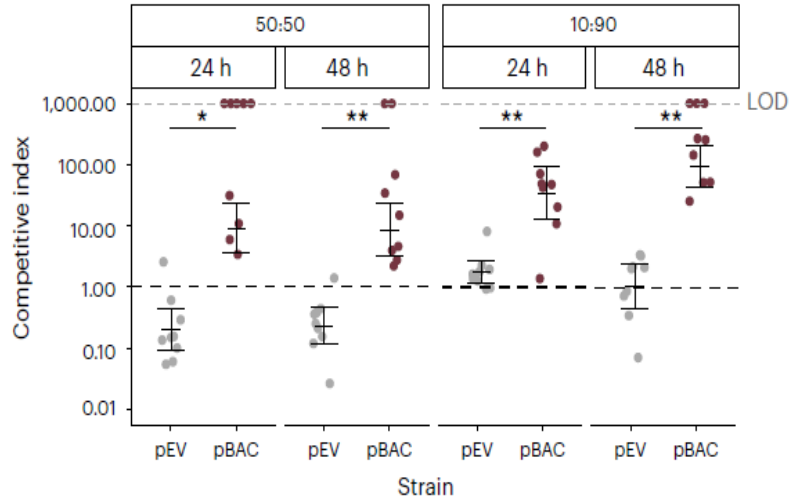
Transition des ST

710 VREfm isolates
(UPMC, 2017-2022)

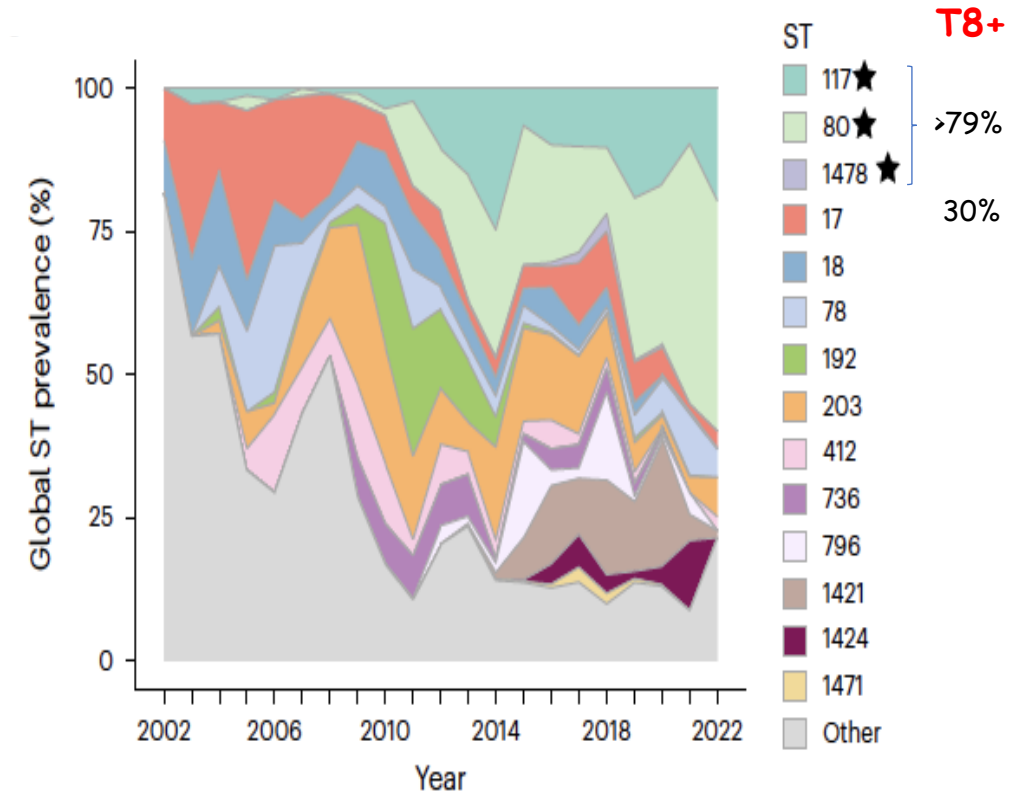


→ Bacteriocin T8 is associated with growth inhibition and more prevalent in emergent lineages (ST117-ST80-ST1478)

Transition des ST



15,631 VREfm genomes
(53 countries, 2002-2022)



Emergence des VVE

Diffusion nationale (Danemark, 2015-2019) d'un clone d'*E. faecium* VVE *vanA*

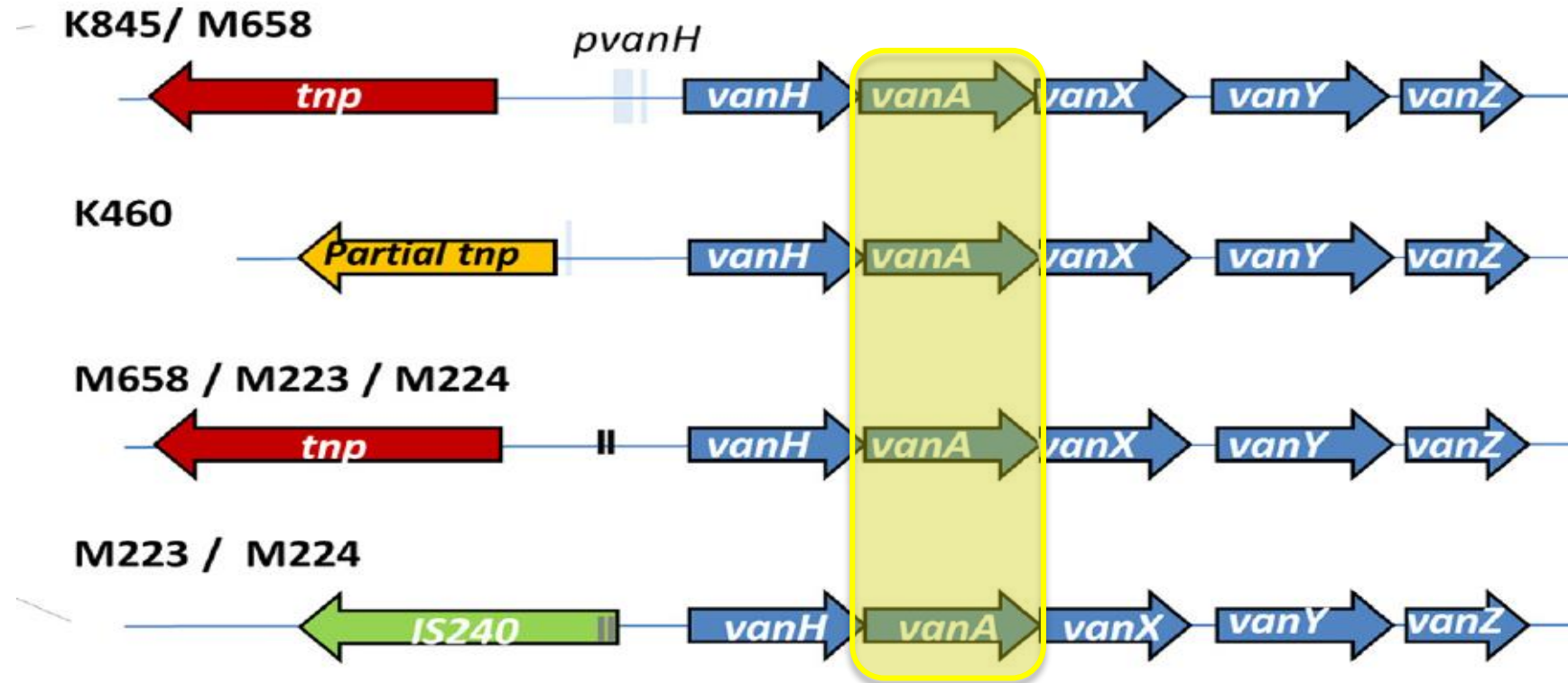
Types	2015 (n = 369)		2016 (n = 427)		2017 (n = 425)		2018 (n = 515)		Q1 2019 (n = 174)	
	n	%	n	%	n	%	n	%	n	%
■ ST80-CT14 <i>vanA</i>	81	22	38	9	15	4	1	<1	ND	
■ ST80-CT24 <i>vanA</i>	23	6	19	4	11	3	2	<1	4	2
■ ST80-CT860 <i>vanA</i>	7	2	11	3	ND		ND		ND	
■ ST80-CT866 <i>vanA</i>	14	4	10	2	7	2	ND		ND	
■ ST80-CT991 <i>vanA</i>	ND		11	3	9	2	6	1	ND	
■ ST80-CT1160 <i>vanA</i>	ND		ND		7	2	10	2	ND	
■ ST80-CT1064 <i>vanA/vanB</i>	ND		2	<1	8	2	23	5	4	2
■ ST80-CT1729 <i>vanA</i>	ND		ND		ND		22	4	2	1
■ ST117-CT873 <i>vanA</i>	5	1	12	3	ND		ND		ND	
■ ST117-CT1180 <i>vanA</i>	ND		ND		9	2	30	6	7	4
■ ST117-CT36 <i>vanB</i>	ND		ND		ND		2	<1	16	9
■ ST203-CT859 (sous-types CT1051 et CT1507) <i>vanA</i>	188	51	271	64	265	63	161	31	20	12
■ ST1421-CT1134 <i>vanA</i>	ND		2	<1	13	3	176	34	77	44
Autres types	51	14	51	12	81	19	82	16	44	25

ND : non détecté. Intensité de bleu ∝ pourcentage.

% 3 10 25 45 64 ■ *vanA* ■ *vanB* ■ *vanA/vanB*

Vancomycin-variable enterococci (VVE)

Souches *vanA*+ mais sensibles phénotypiquement (perte de *vanRS*)



Réversion vers un phénotype d'ERV (et risque d'échec de traitement)

Résistance aux alternatives thérapeutiques

Linézolide, daptomycine

5

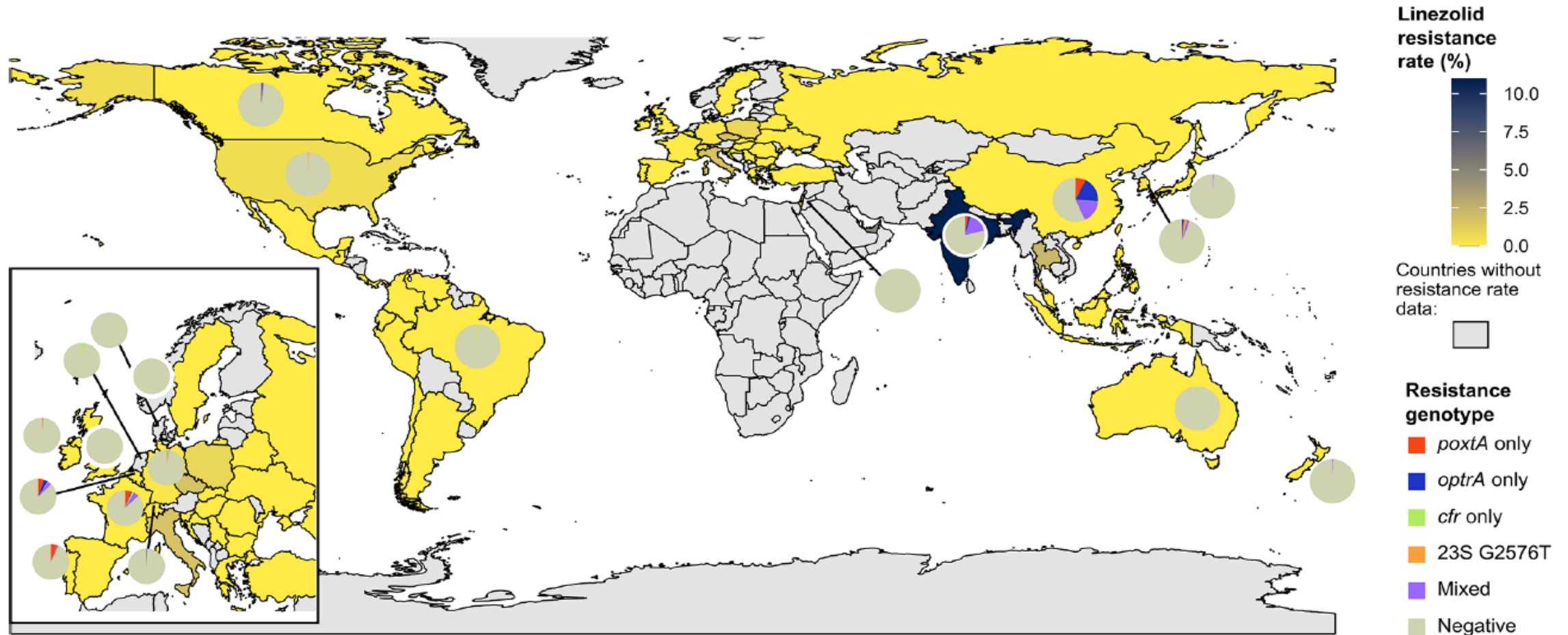
Résistance au linézolide

Systematic review & meta-analysis (114 studies, **2000-2020**): Asia (35%), Europe (25%), America (39%) and Africa (1%)

Isolate	Category	Subcategory	No. of studies	No. of strains	Prevalence (%) (95% CI)	I2
ARE	Overall	ARE/Enterococcus	161	2,600/362,604	0.7 (0.4-1.1)	0.0%
AREF	Overall	AREF/Enterococcus	72	1,593/180,917	0.9 (0.4-1.4)	0.0%
AREFA	Overall	AREFA/Enterococcus	89	1,007/181,687	0.6 (0.1-1.0)	0.0%
LREF	Overall	LREF/ <i>E. faecalis</i>	43	1,646/69,291	2.2 (1.5-2.8)	0.0%
TREF	Overall	TREF/ <i>E. faecalis</i>	9	25/10,449	0.3 (0.0-2.2)	0.0%
DREF	Overall	DREF/ <i>E. faecalis</i>	4	32/11,821	0.1 (0.0-0.3)	88.5%
<i>E. faecalis</i>	Overall	<i>E. faecalis</i> /Enterococcus	22	3,061/6,036	47.6 (43.8-51.3)	92.0%
<i>E. faecium</i>	Overall	<i>E. faecium</i> /Enterococcus	39	49,613/115,406	40.6 (38.3-42.8)	88.9%
DREFA	Overall	DREFA/ <i>E. faecium</i>	11	295/7,226	9.0 (3.8-14.2)	62.5%
TREFA	Overall	TREFA/ <i>E. faecium</i>	9	58/6,134	1.0 (0.0-3.5)	0.0%
LREFA	Overall	LREFA/ <i>E. faecium</i>	51	574/52,605	1.1 (0.3-1.9)	0.0%

ERL dans le monde

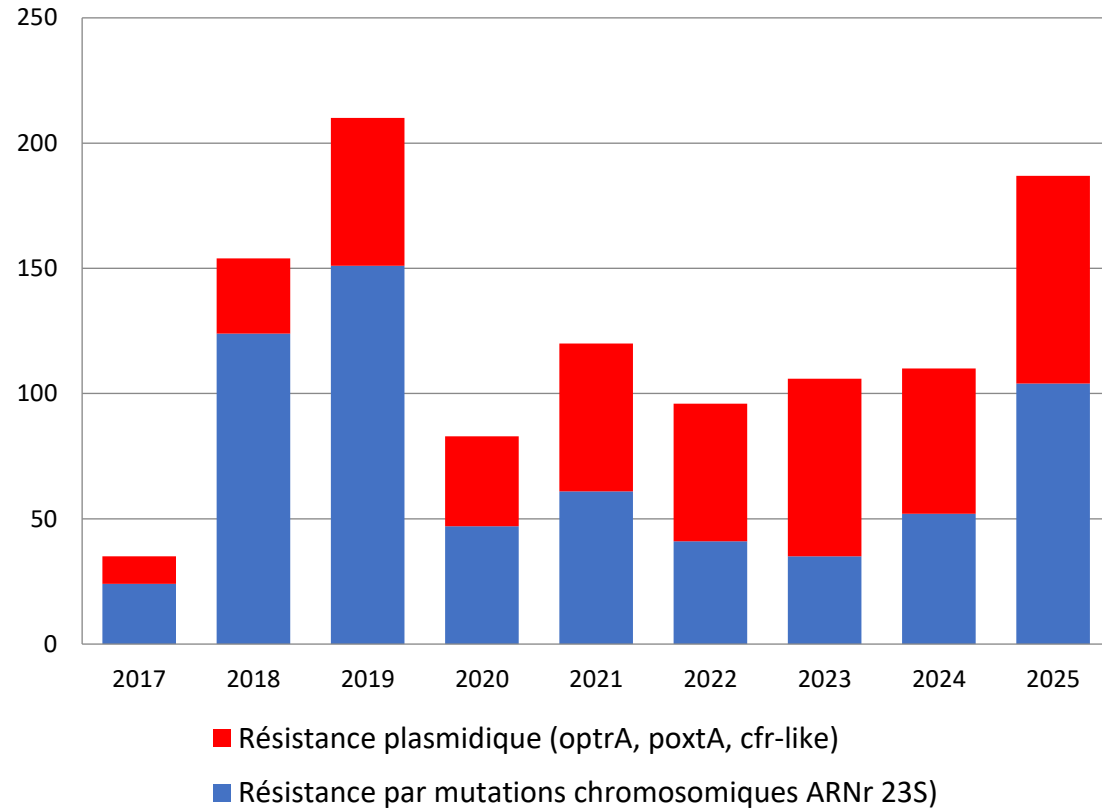
Prévalence des ERL (7 109 souches, 51 pays)



0 à 11 % (médiane = 0,0 %, IQR = 0,0-0,0 %)

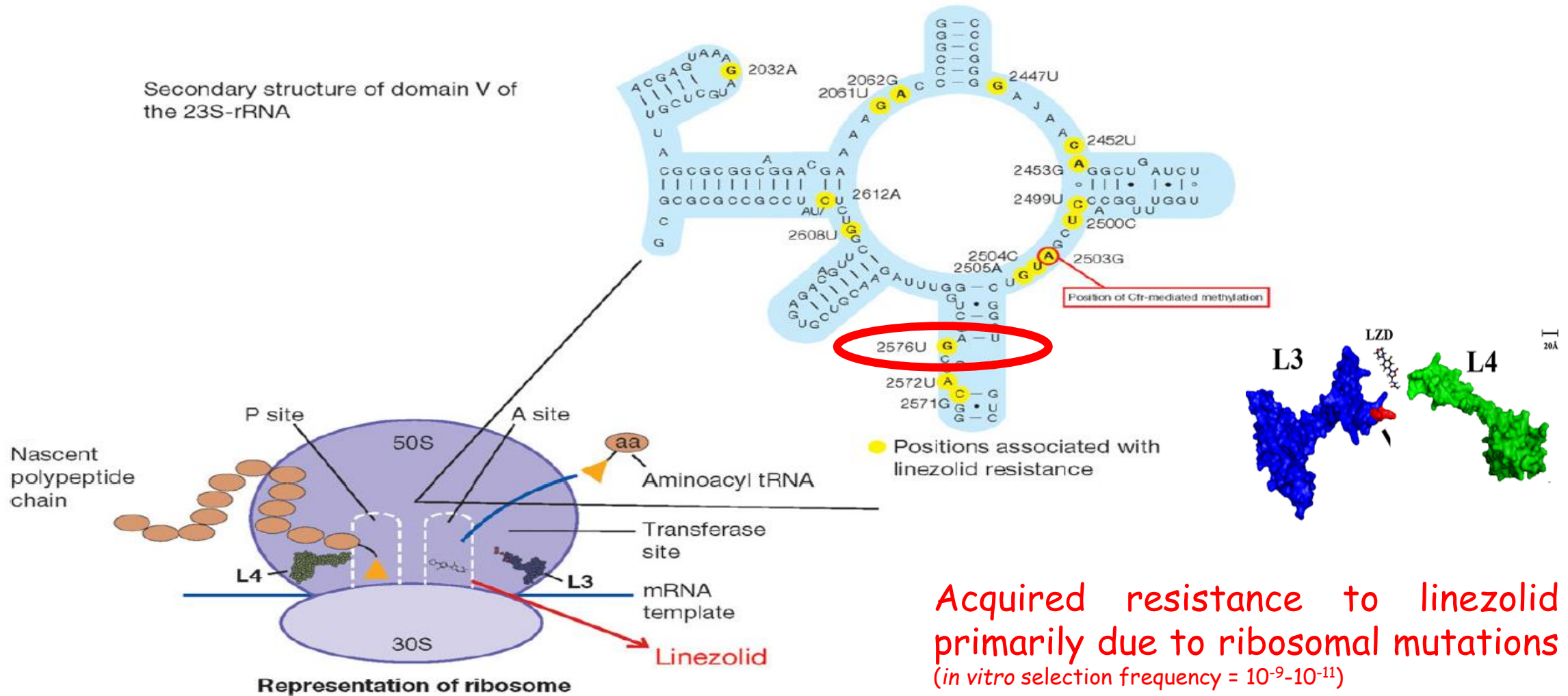
Souches d'ERL en France

Nombre de souches résistantes au linézolide reçues entre 2017 et 2025



Espèce	Génotype	Mécanismes de résistance au linézolide (nombre)				TOTAL
		optrA	optrA + poxtA	poxtA	Mutations ARNr 23S	
<i>E. faecalis</i>	van(-)	63	2	1	9	75
	vanA	3	-	1	59	63
<i>E. faecium</i>	van(-)	5	2	6	35	48
	vanA	-	-	-	1	1
TOTAL		71	4	8	104	187

Résistance chromosomique



Résistance plasmidique : Cfr

Oxazolidinones
(pas TZD)

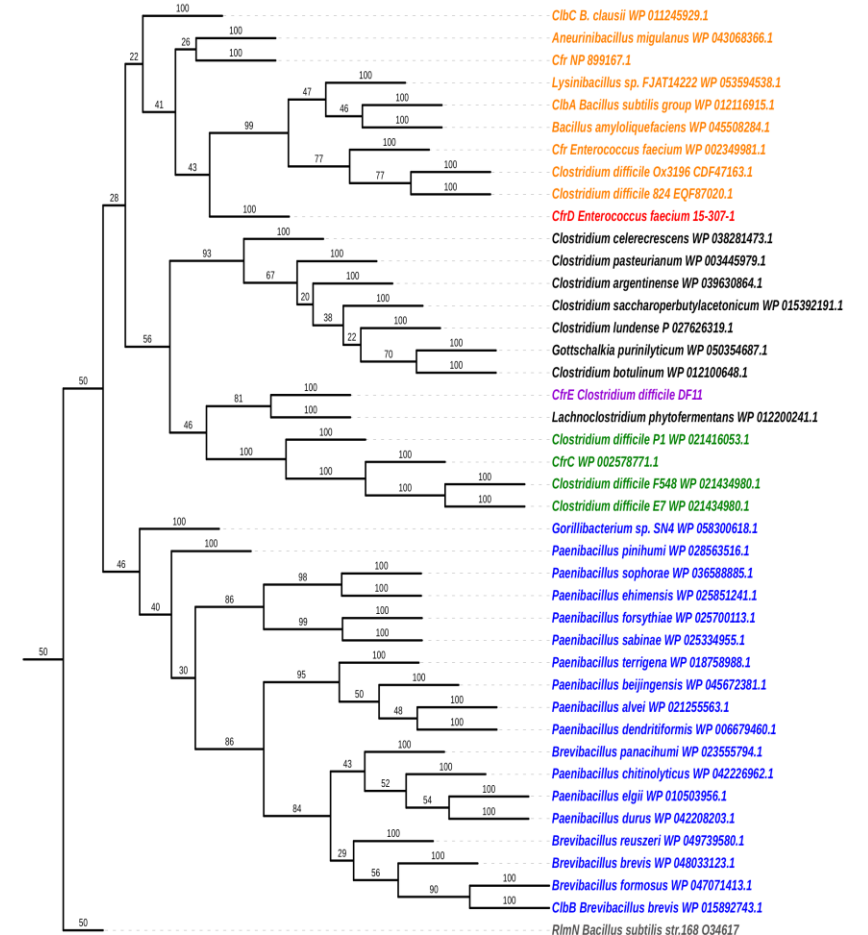
Antibiotic	MIC (µg/ml) ^a			
	<i>E. faecalis</i>			
	603-50427X	OG1RF	Tc6	Tc11
Linezolid	32	1	8	8
Linezolid ^b	24	2	8	6
Ampicillin	2	4	1	1
Vancomycin	1	2	2	2
Teicoplanin	≤1	≤1	≤1	≤1
Daptomycin	1	2	1	1
Ciprofloxacin	>4	2	1	1
Levofloxacin	>4	2	1	1
Chloramphenicol	64	4	64	64
Tigecycline	0.06	0.12	0.12	0.12
Quinupristin/dalfopristin	4	16	>16	>16
Tiamulin	64	>64	>64	>64
Clindamycin	>128	32	>128	>128
Fusidic acid	8	>128	>128	>128
Rifampin	0.25	>128	>128	>128

Phenolics

Streptogramins A
Pleuromutilins
Lincosamides

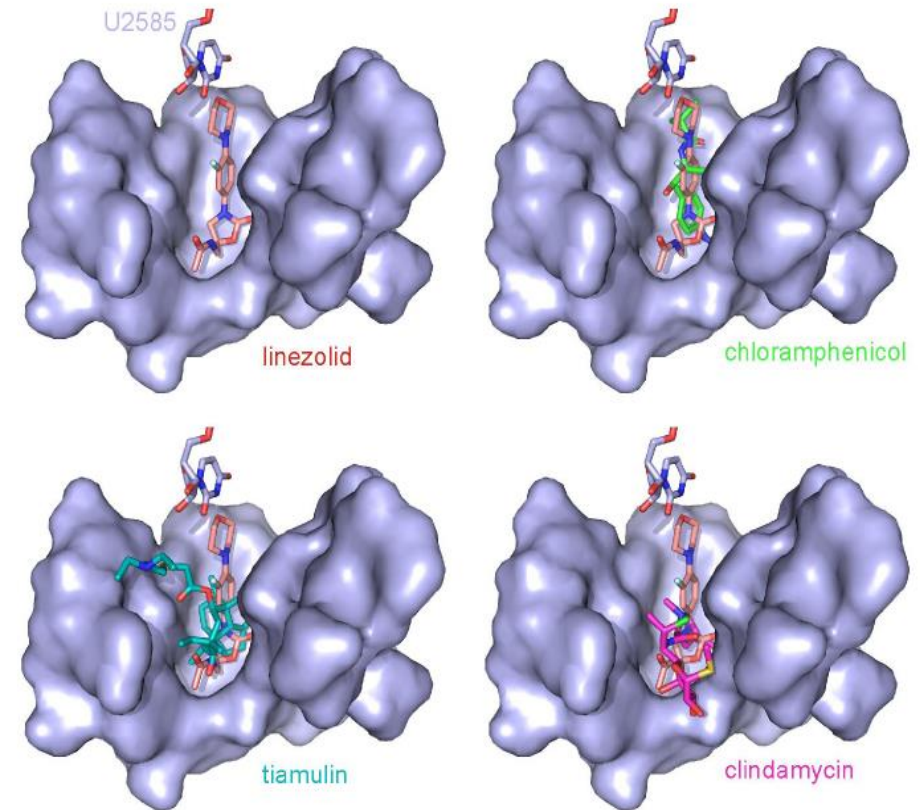
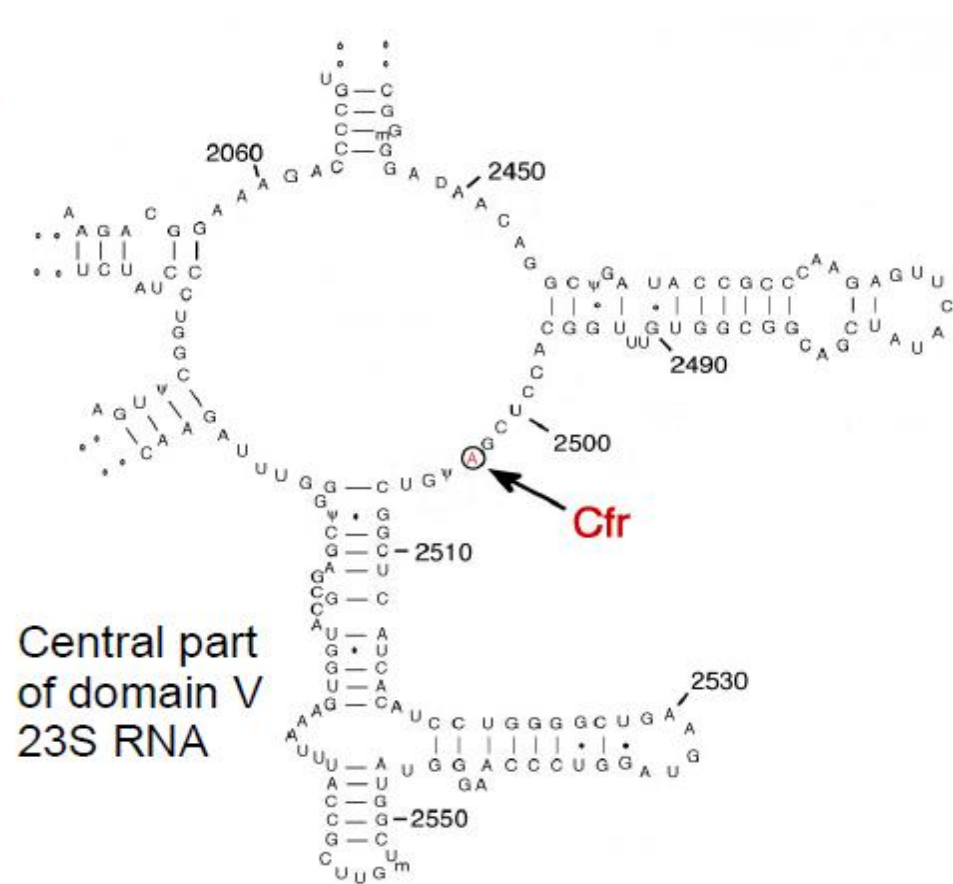
Phenotype PhLOPS_A

Tree scale: 100



Résistance plasmidique : Cfr

Gene coding for a 23S rRNA methyltransferase (A2503)



Résistance plasmidique : Optra & PoxTA

Optra

Bacterial isolate	MIC (mg/L)				
	CHL	FFC	LZD	TZD	VAN
Clinical <i>E. faecalis</i> E349 (with <i>optra</i> -carrying pE349)	64	64	8	2	1
<i>E. faecalis</i> FA2-2	4	2	2	0.5	1
	x8	x32	x4	x4	
Transconjugant <i>E. faecalis</i> FA2-2-E349	32	64	8	2	1

→ Phénotype PhO

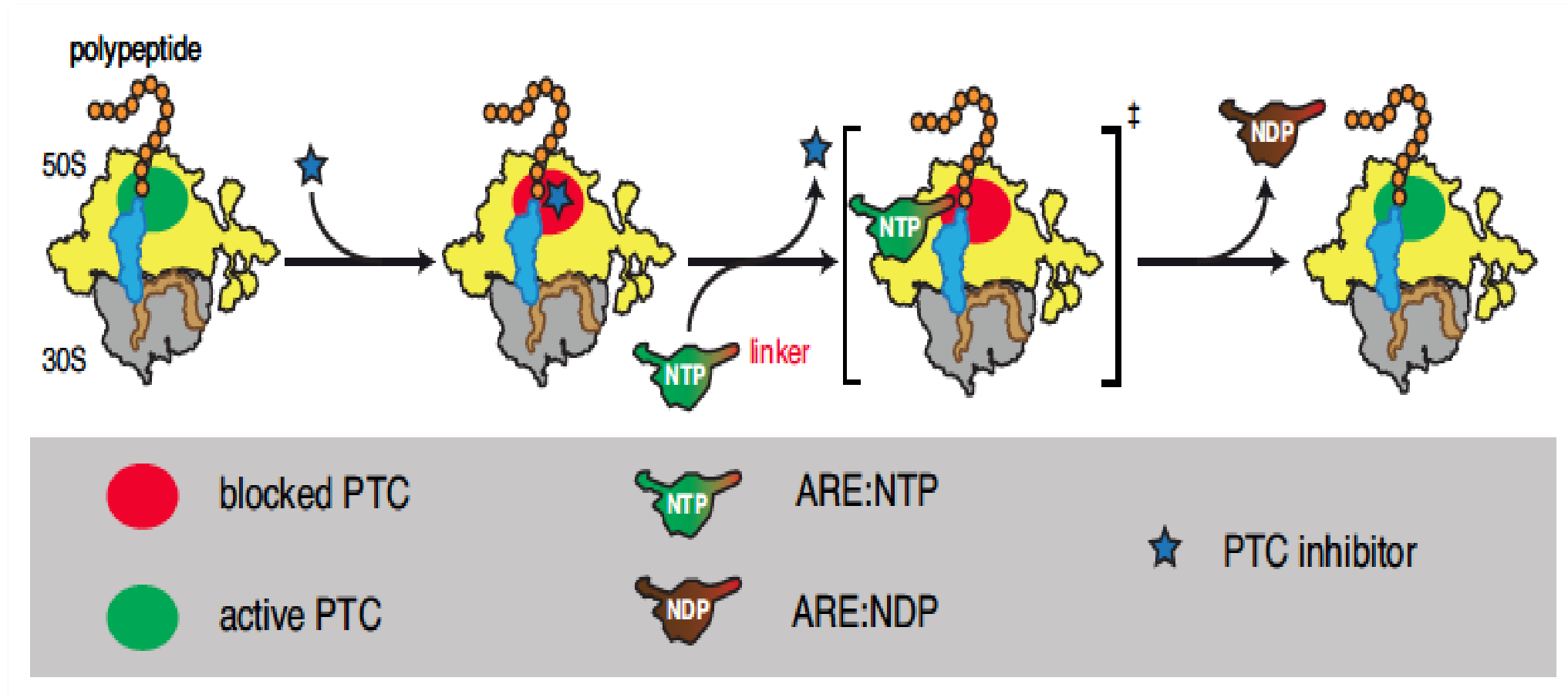
PoxTA

Antibiotic	MIC (mg/L)				
	<i>S. aureus</i> ^a		<i>E. faecalis</i> ^b		
	RN4220 (pMU- <i>poxTA</i>)	RN4220 (pMU-E)	JH2-2 (pMU- <i>poxTA</i>)	JH2-2 (pMU-E)	
Linezolid	2	1	4	1	x2-4
Tedizolid	0.5	0.25	0.5	0.25	x2
Chloramphenicol	8	4	8	4	x2
Florfenicol	16	2	16	2	x8
Tigecycline	0.25	0.25	0.25	0.25	
Tetracycline	0.25	0.125	0.25	0.125	x2
Doxycycline	0.25	0.125	0.125	≤0.06	

→ Phénotype PhOT

Protéines ABC-F

Mechanism : **Ribosomal protection**

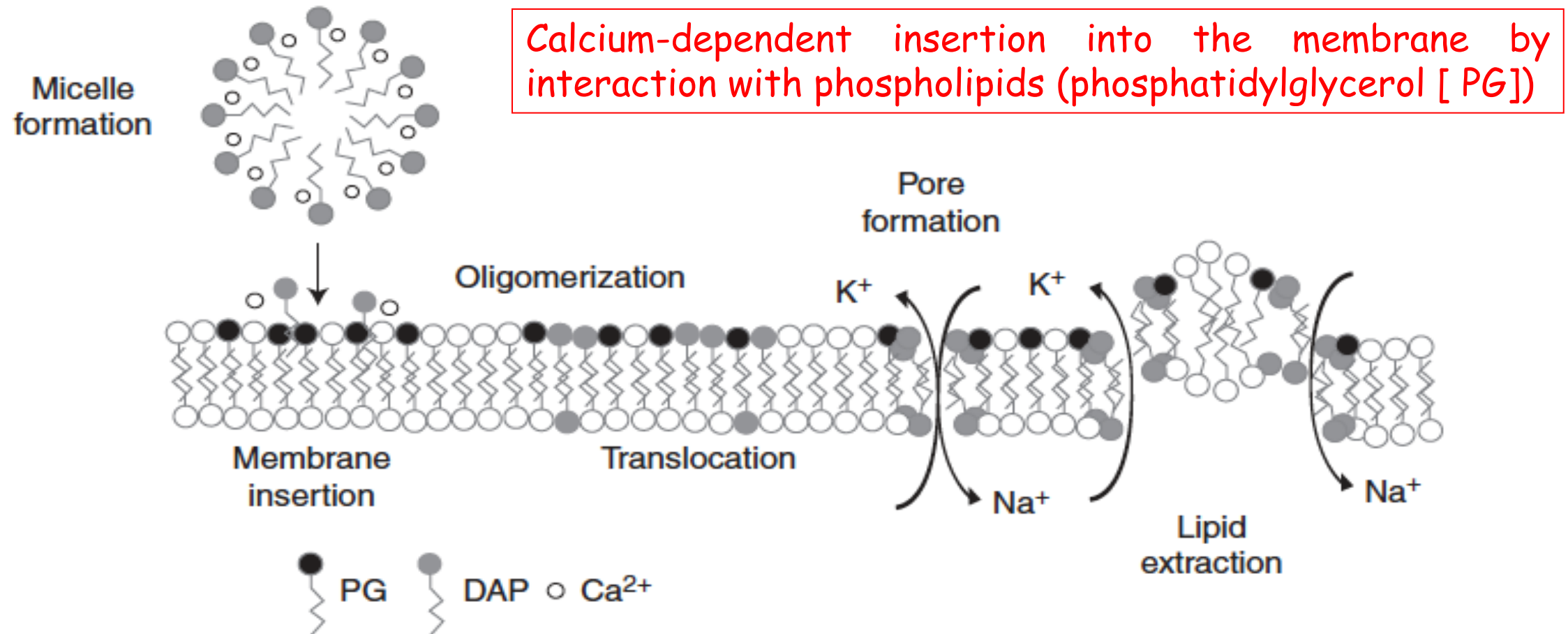


Résistance à la daptomycine

Systematic review & meta-analysis (114 studies, **2000-2020**): Asia (35%), Europe (25%), America (39%) and Africa (1%)

Isolate	Category	Subcategory	No. of studies	No. of strains	Prevalence (%) (95% CI)	I2
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LREFA	Overall	LREFA/ <i>E. faecium</i>	51	574/52,605	1.1 (0.3-1.9)	0.0%

Mode d'action

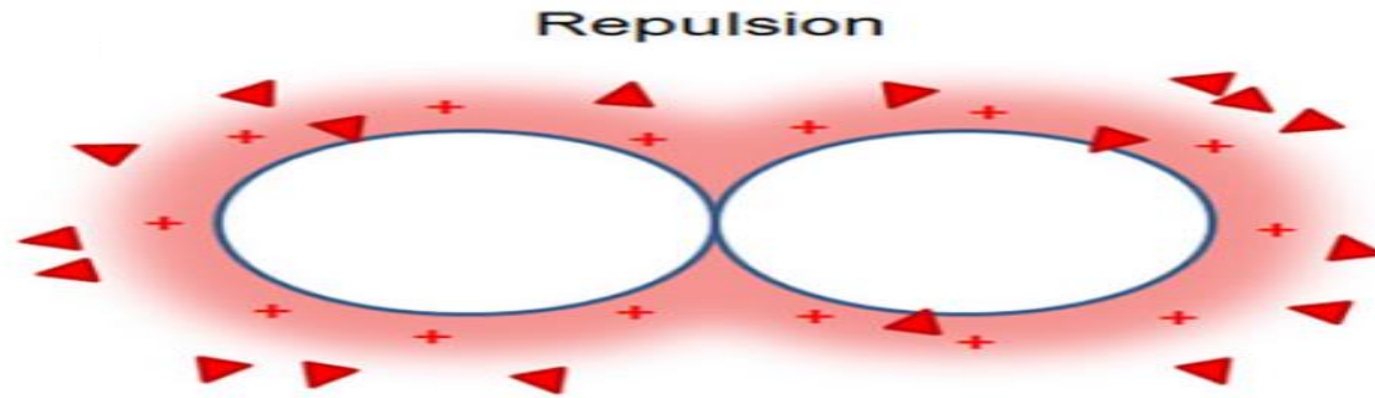


Résistance chromosomique classique

Due to multiple chromosomal mutations, especially in genes involved in cell-envelope homeostasis and stress response and phospholipid metabolism

Organism	Gene	Predicted function
<i>E. faecalis</i>	<i>liaFSR</i>	Three-component regulatory system as part of the cell envelope stress response
	<i>cls</i>	Cardiolipin synthase
	<i>gdpD</i>	Glycerophosphoryl diester phosphodiesterase
<i>E. faecium</i>	<i>liaSR</i>	Histidine kinase and response regulator of three-component regulatory system
	<i>cls</i>	Cardiolipin synthase
	<i>yycFG</i>	Two-component regulatory system of cell wall synthesis and homeostasis

Mécanisme de résistance chez *E. faecium*



Article

Rifaximin prophylaxis causes resistance to the last-resort antibiotic daptomycin

<https://doi.org/10.1038/s41586-024-08095-4>

Received: 25 July 2022

Accepted: 20 September 2024

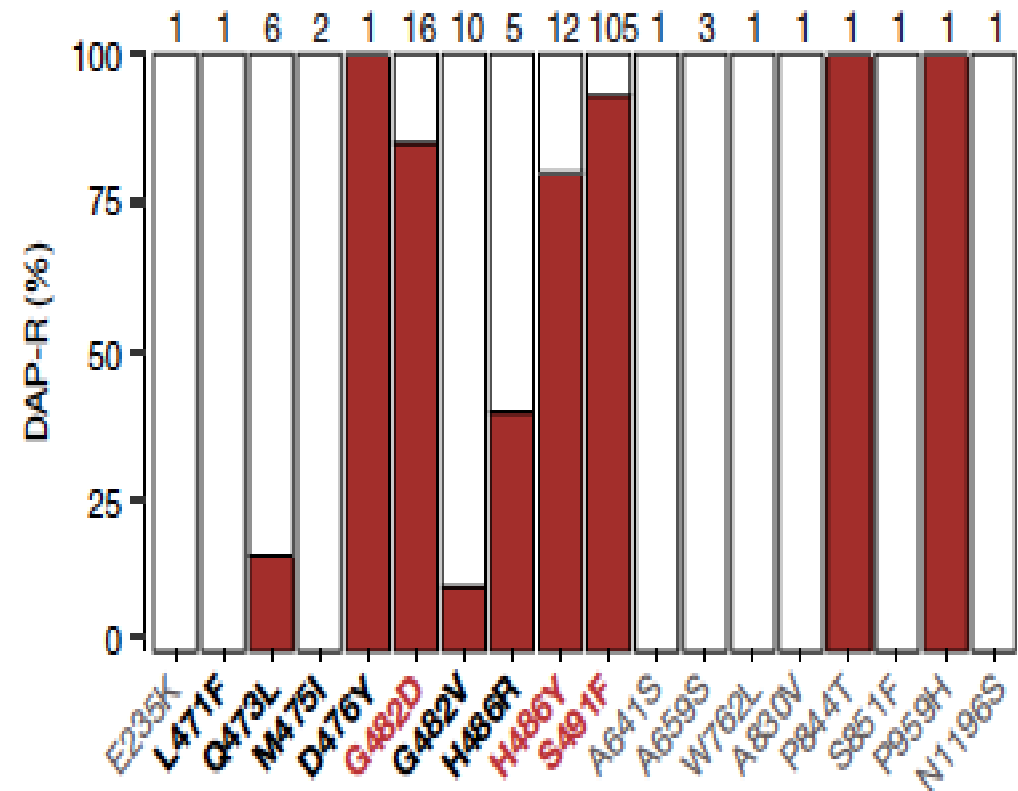
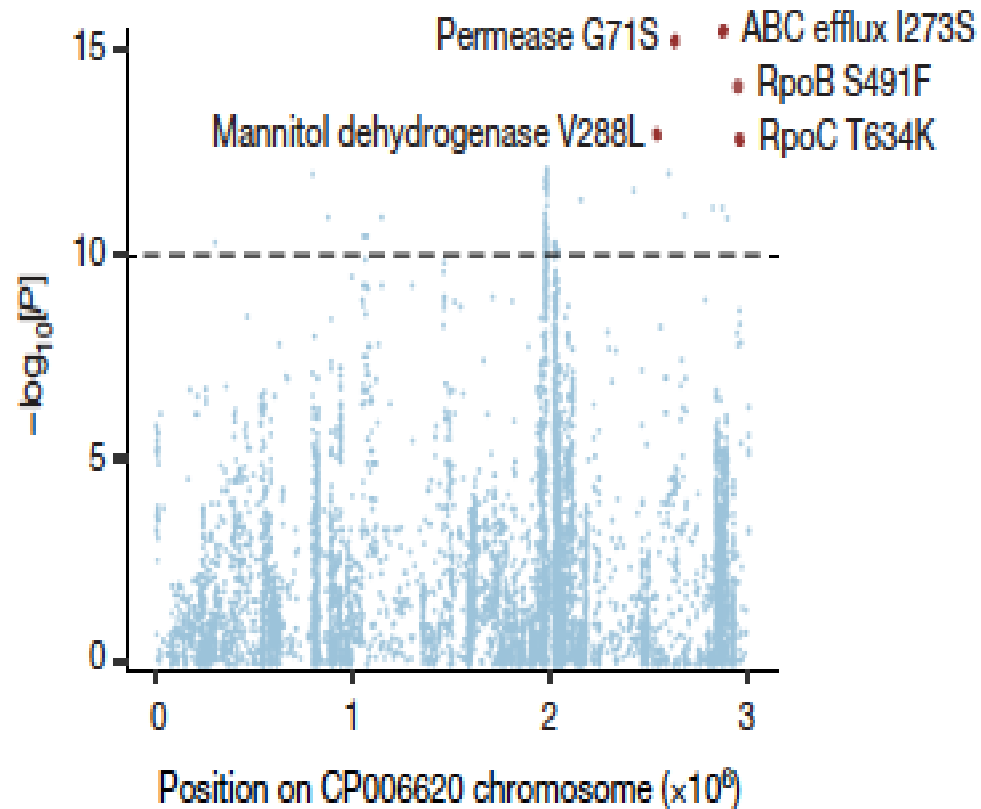
Published online: 23 October 2024

Open access

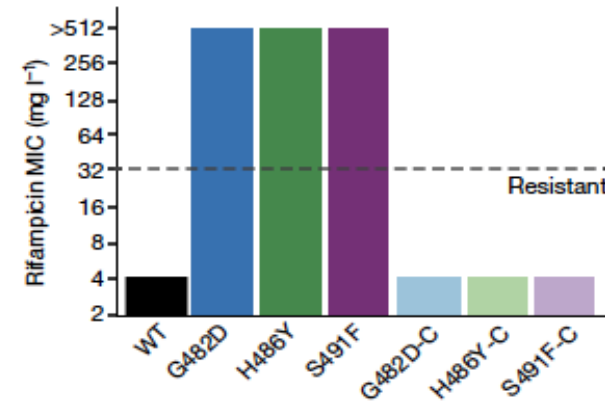
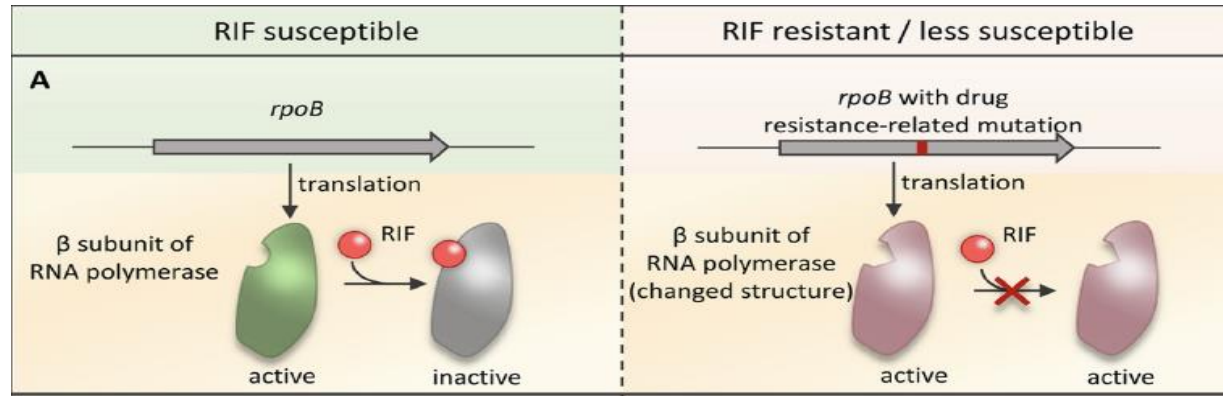
Adrianna M. Turner¹, Lucy Li¹, Ian R. Monk¹, Jean Y. H. Lee^{1,2}, Danielle J. Ingle¹, Stephanie Portelli^{3,4}, Norelle L. Sherry^{1,5,6}, Nicole Isles¹, Torsten Seemann^{1,5,7}, Liam K. Sharkey¹, Calum J. Walsh^{1,7}, Gavin E. Reid^{8,9,10}, Shuai Nie¹¹, Bart A. Eijkelkamp¹², Natasha E. Holmes^{6,13}, Brennan Collis⁶, Sara Vogrin^{6,14}, Andreas Hiergeist¹⁵, Daniela Weber¹⁶, Andre Gessner¹⁵, Ernst Holler¹⁶, David B. Ascher^{3,4}, Sebastian Duchene^{1,17}, Nichollas E. Scott¹, Timothy P. Stinear^{1,7}, Jason C. Kwong^{1,6}, Claire L. Gorrie^{1,5,7,18}, Benjamin P. Howden^{1,5,6,7,18} ✉ & Glen P. Carter^{1,7,18} ✉

Recent emergence of DAP resistance

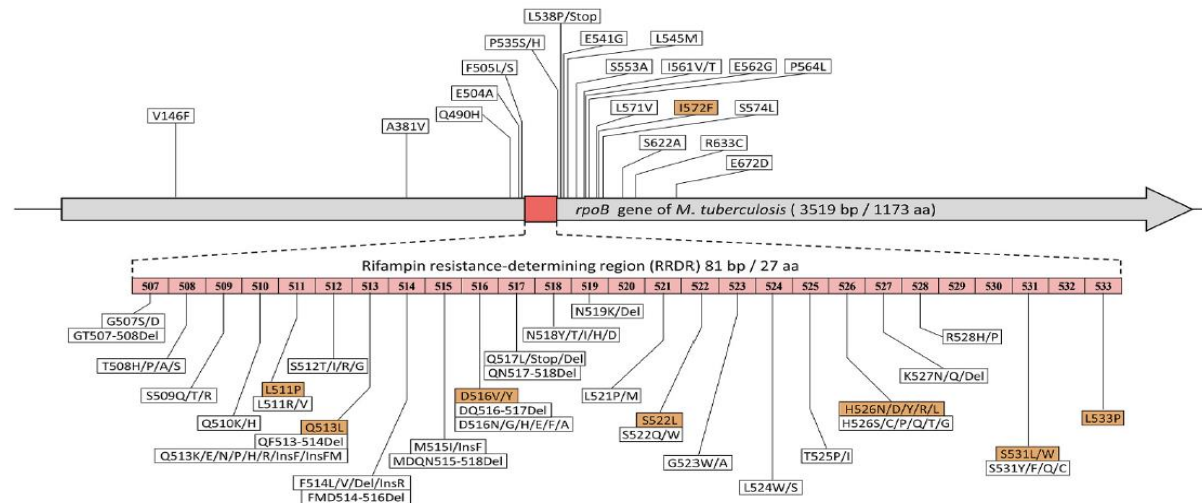
194/998 (19.4%) **VREfm isolates** resistant to DAP (Victoria, Australia, 2015-2018)



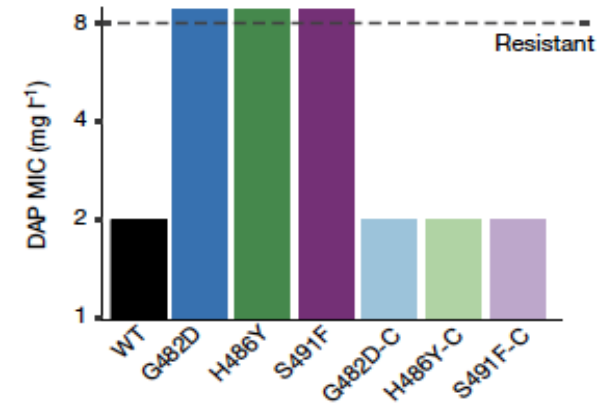
Résistance croisée rifampicine/daptomycine



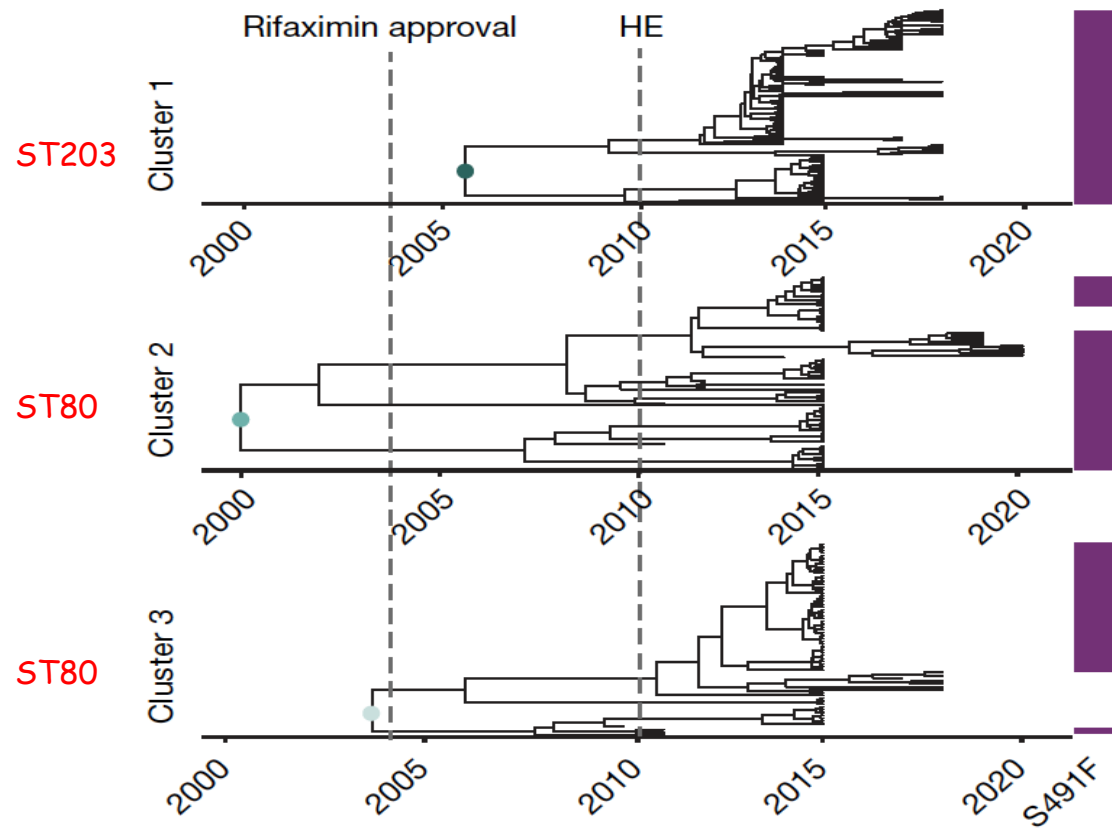
Cross-R to DAP and rifampicin



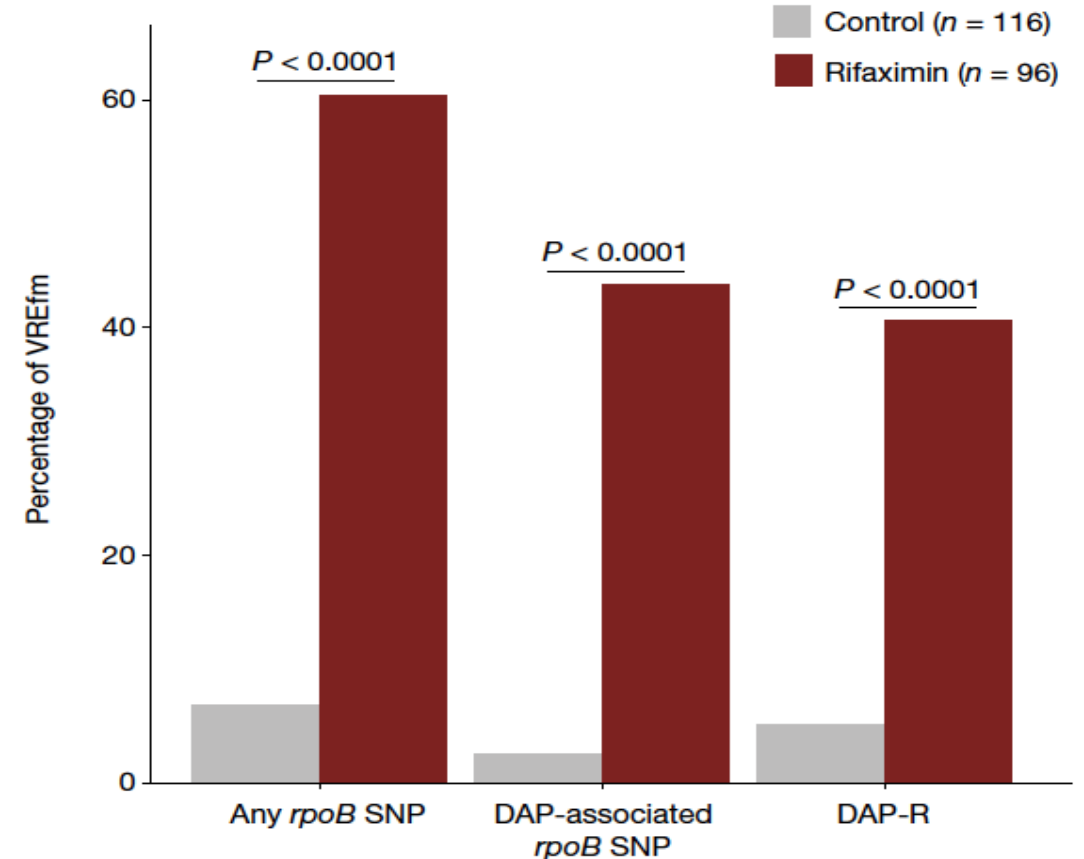
Rifampicin resistance-determining region (RRDR) - 81 bp



Rifaximine et émergence de résistance à la daptomycine



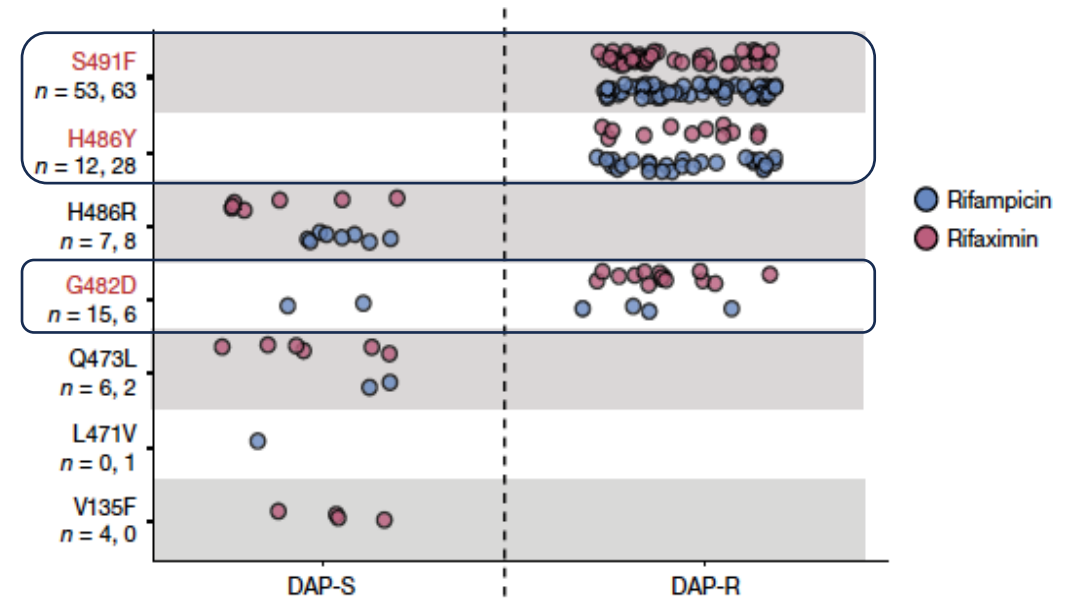
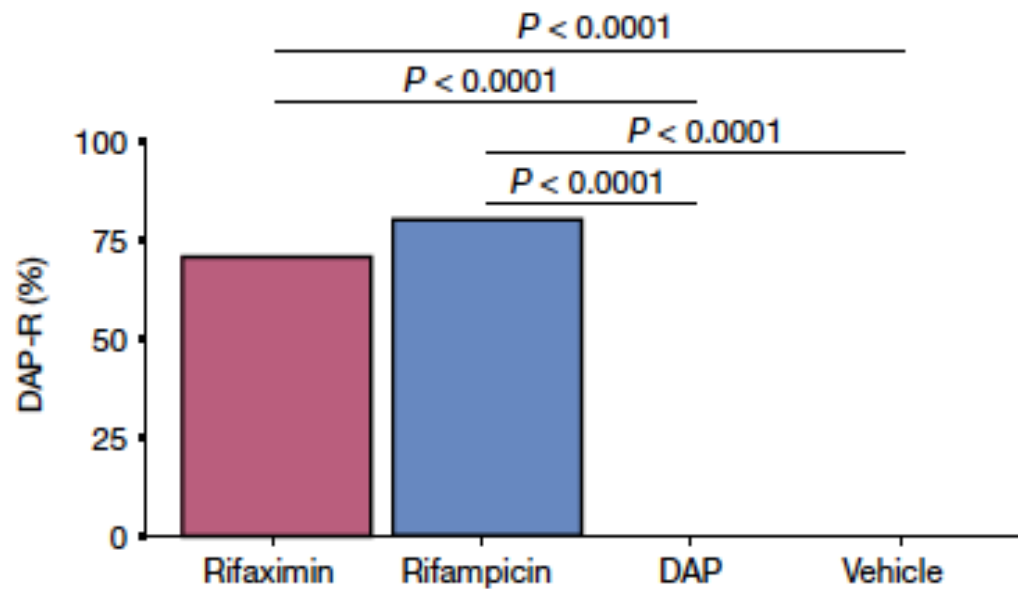
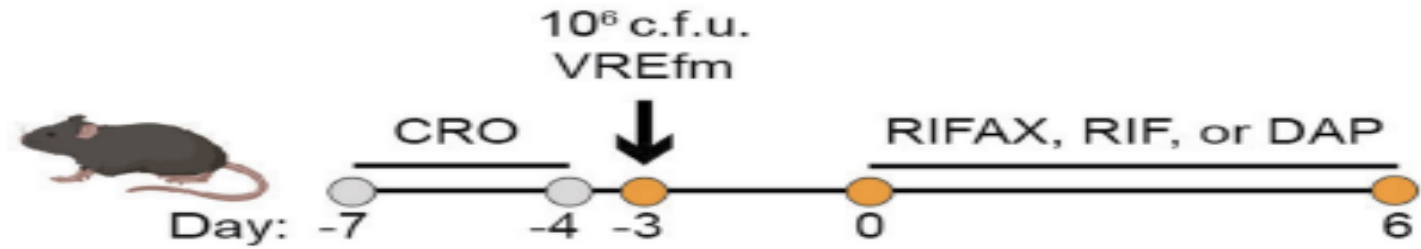
➔ Rifaximin exposure associated with DAP-R VREfm emergence in humans



➔ Recent rifaximin = independent predictor of DAP-R VREfm (OR = 4.37; 95% CI = 1.70-12.84; $P = 0.004$)

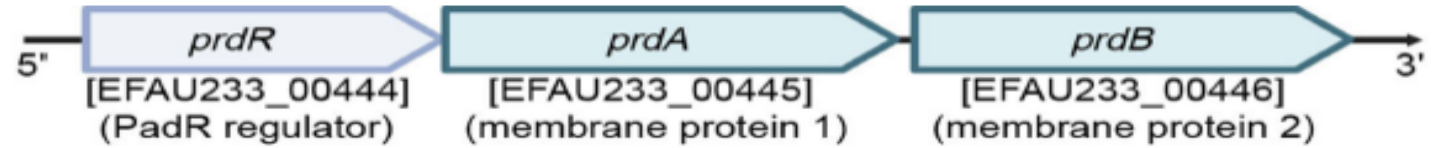
Sélection *in vivo* de la résistance par rifaximine

In vivo emergence of DAP resistance in mice

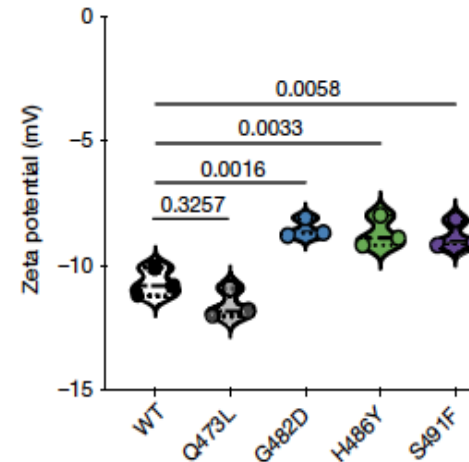
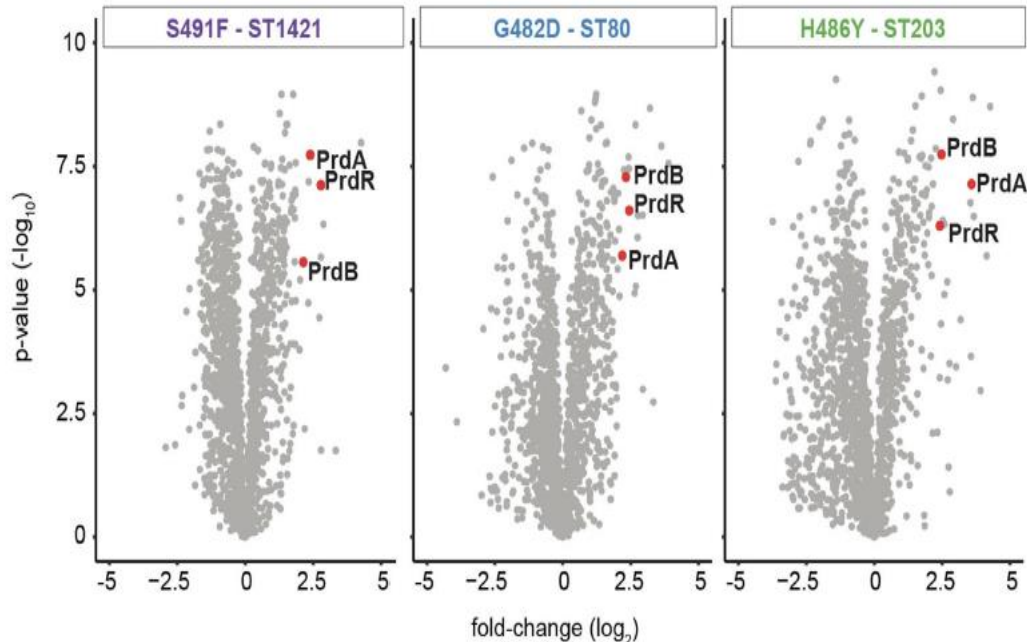


Nouveau mécanisme de résistance

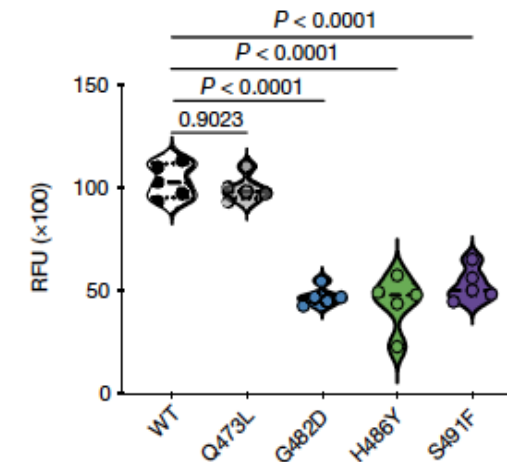
Overexpression of the *pdrR* locus



Changes in the abundance of charged phospholipids:



→ Reduced negative charge of cell membrane

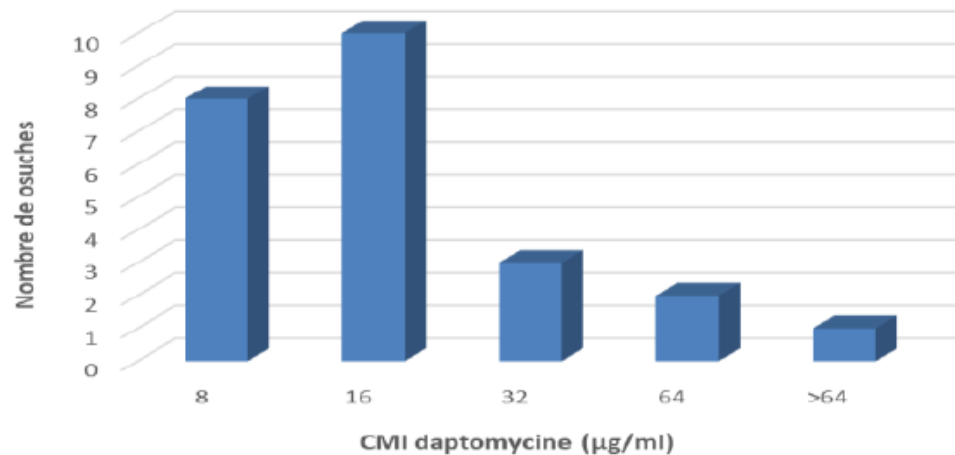


→ Decrease in BoDIPY-Dap binding

Résistance associée aux mutations *rpoB* en France

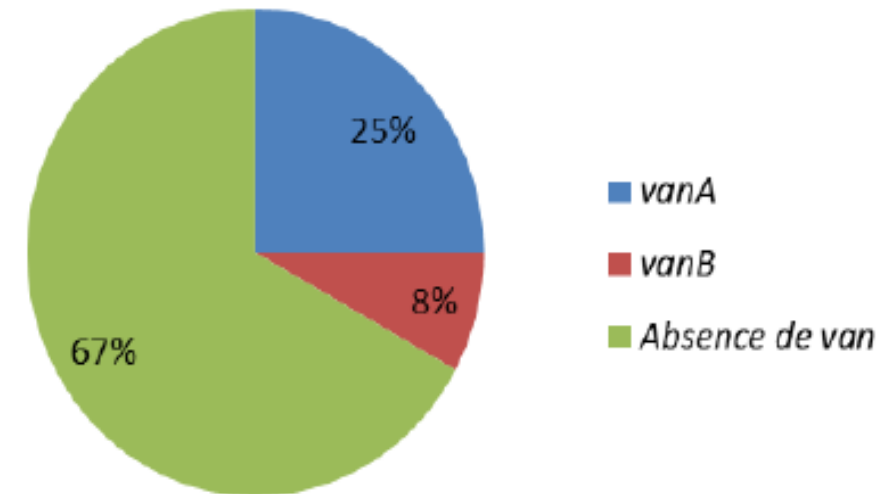
>9,200 clinical isolates received to the NRC (2006-2024)

24 DAP-R strains (0.3%):



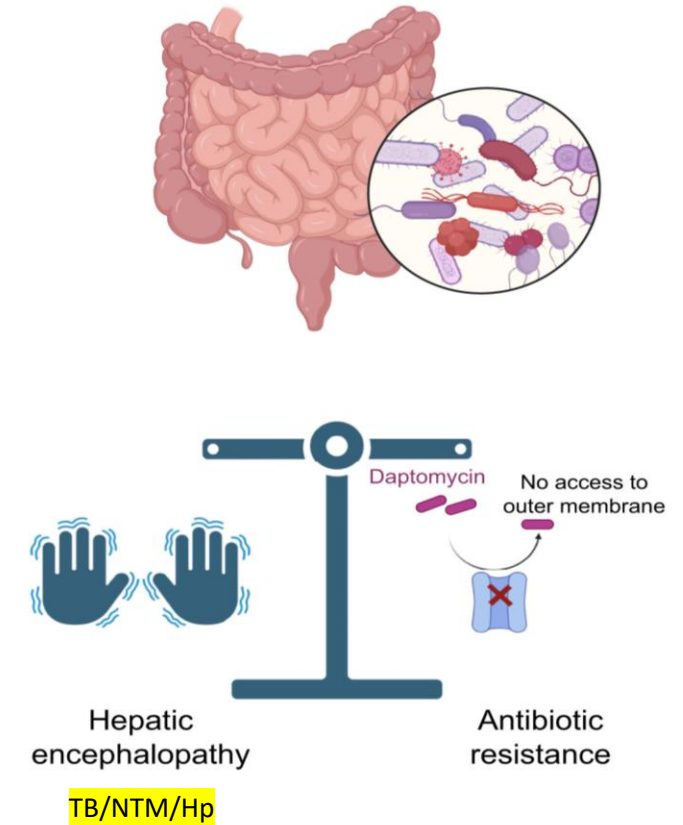
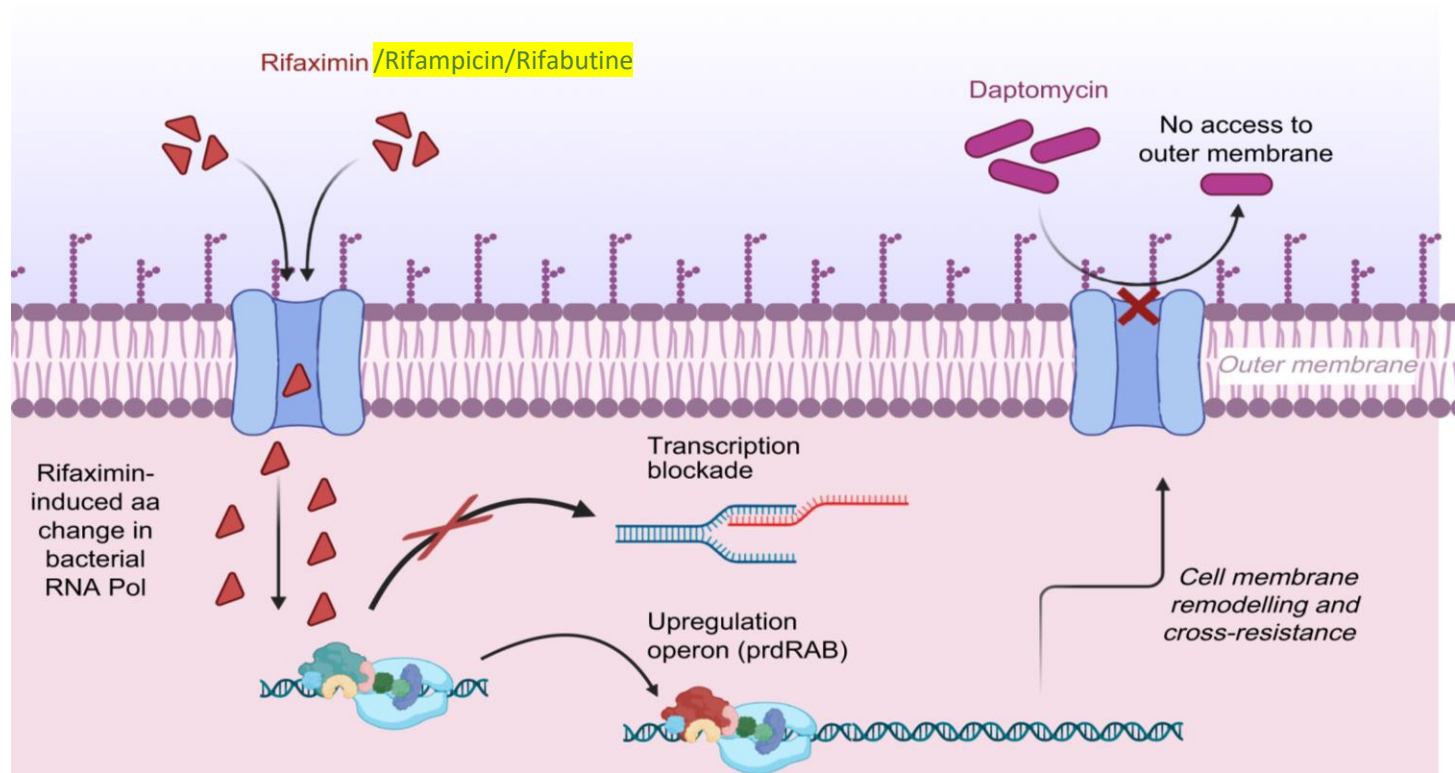
18/24 (75%) isolated after 2020

67% of VSE isolates:



13/24 (54%) of DAP-R strains with S491F RpoB mutation
38% ST80 and 29% ST117

Conclusion



→ Surveillance étroite de la résistance à la daptomycine chez *E. faecium*, notamment chez les patients recevant des rifamycines

Résistance transférable à la daptomycine

Identified in the chromosome of *Mammaliicoccus* (formerly *Staphylococcus*) *sciuri* TS92 (DAP MIC = 64 mg/L)

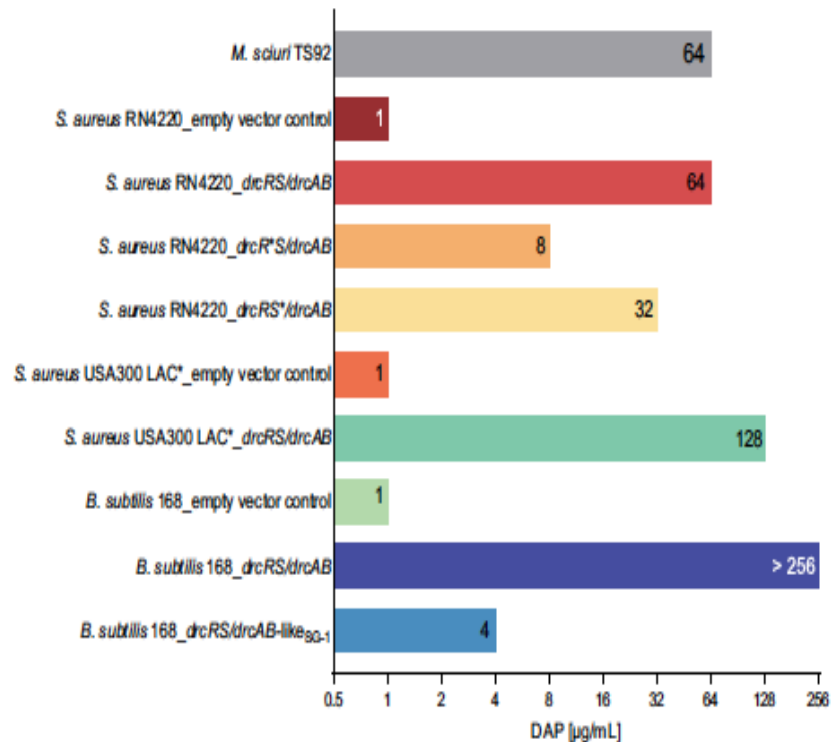
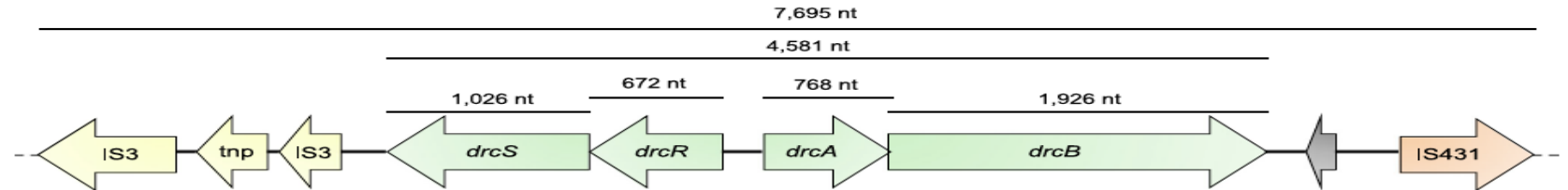
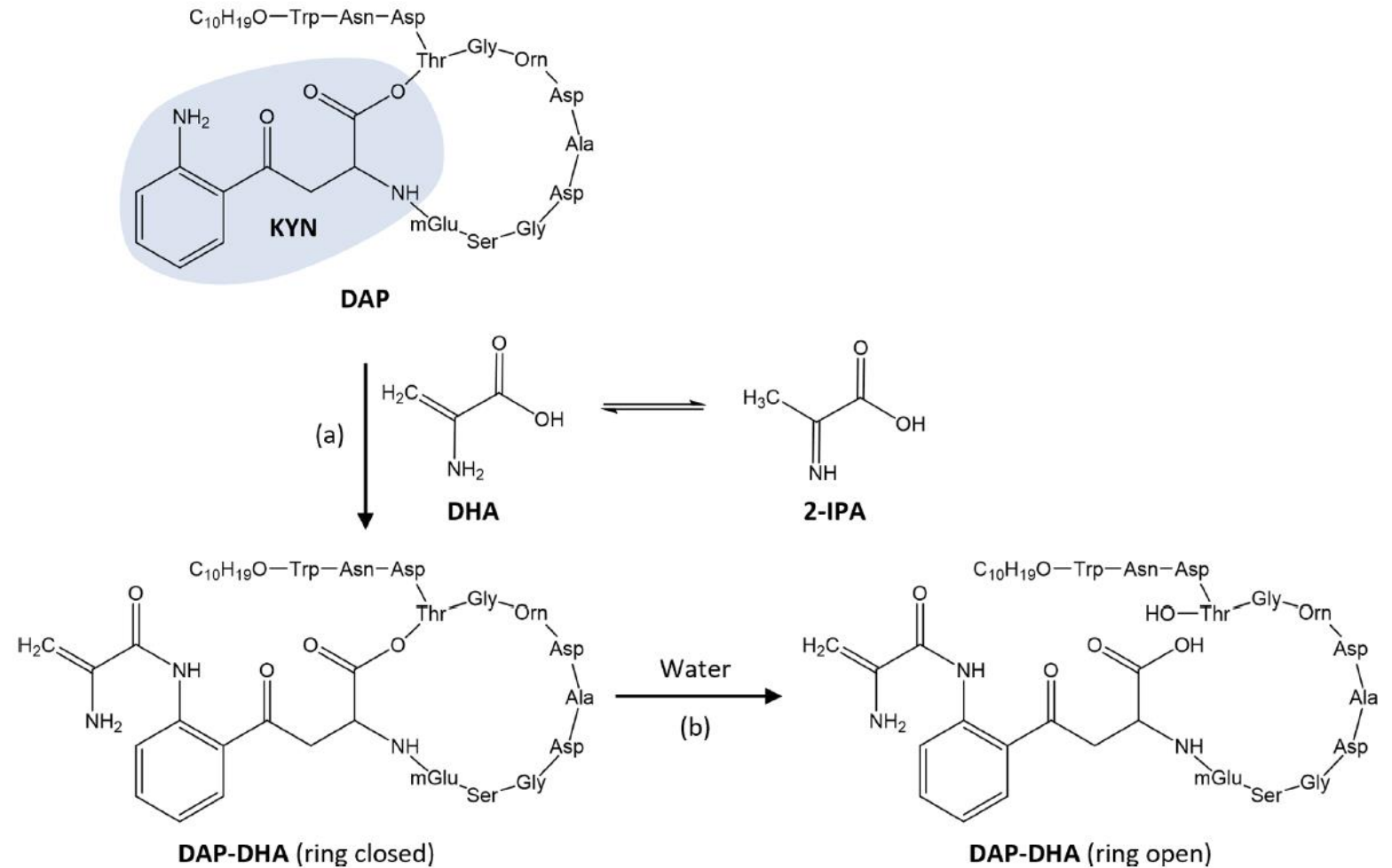


Table 1 | Detection of the *drc* locus (*drcRS/drcAB*) in staphylococci and enterococci

Species Strain	Isolate source; Geographic region; Collection date	Accession BioProject BioSample	DAP MIC (µg/mL)	References	Alignments with <i>drcRS/drcAB</i> _{TS92%} nucleotide identity (Gaps)	MGE association of <i>drc</i>
<i>Mammaliicoccus sciuri</i> TS92	Pig farm, surface dust; Germany; 2013	PP236779 PRJNA1074542 SAMN39864404	64	This study	-	IS3 - <i>drc</i> - IS431 <i>mec</i> (SCC element)
<i>Mammaliicoccus sciuri</i> SNUC 5594	Dairy cow, subclinical mastitis; Canada, Quebec; 2007	PZGV01000123.1 PRJNA342349 SAMN06173142	n.d.	63	99.98% (0)	IS3 - <i>drc</i> - IS431 <i>mec</i>
<i>Mammaliicoccus lentus</i> 7048	<i>Camelus dromedarius</i> , nose; Algeria, M'sila; 2021	NZ_CP118848.1 PRJNA937407 SAMN33407027	n.d.	64	99.64% (0)	n.d. - <i>drc</i> - ISL3 (family)
<i>Mammaliicoccus lentus</i> C9	Not specified; United Kingdom; 2016	NZ_JAAQRX010000032 PRJNA610046 SAMN14273045	n.d.	Direct submission	99.28% (0)	n.d. - <i>drc</i> - IS431 <i>mec</i>
<i>Enterococcus faecalis</i> CVM N59689F	Market swine; USA, Iowa; 2014	PTUJ01000031.1 PRJNA292669 SAMN07982045	>16	24	97.40% (0)	Tn3 family recombinase - <i>drc</i>
<i>Enterococcus faecalis</i> FSIS 12032216	Dairy cow; USA, Texas; 2020	AAXCZN01000013.1 PRJNA292669 SAMN15856852	n.d.	Direct submission	97.23% (0)	Tn3 family recombinase - <i>drc</i> (on plasmid?)
<i>Enterococcus faecalis</i> FSIS 11808951	Cattle (steer); USA, Pennsylvania; 2018	AAXEJZ010000069.1 PRJNA292669 SAMN10482714	n.d.	Direct submission	97.21% (0)	Tn3 family recombinase - <i>drc</i>

Inactivation de la daptomycine

Two-step DrcAB-mediated DAP inactivation



DHA: dehydroalanine; 2-IPA: 2-iminopropanoic acid; KYN: kynurenine

Messages-clés & perspectives

6

Messages-clés



Grande majorité des ERV = **VREfm Clade A1** (anc. CC17)



Surmortalité des infections invasives à ERV
VREfm = **Top 9 OMS** des priorités de l'AMR



Prévalence des ERV en France faible (<2 %) mais épidémies récurrentes
Prévalence très hétérogène (**élevée en Amérique**)



Bascule clonale **ST17 → ST80/ST117** (avantage de colonisation, T8)
+ clones émergents **ST612, ST1421** (VVE)



Emergence des ERL et de nouveaux mécanismes
de **résistance à la daptomycine**

Remerciements

Un grand merci aux membres du CNR

Ainsi qu'à tous les collègues qui nous envoient les souches



Merci pour votre attention !

Contact : vincent.cattoir@chu-rennes.fr