33ème Congrès de la STPI
09 - 11 mai 2024

PROFIL MOLECULAIRE DES BACTERIES HAUTEMENT RESISTANTES EN TUNISIE

RÉSULTATS D'UNE ÉTUDE MULTICENTRIQUE

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Introduction

Infection à *Enterobacterales, A. baumannii et P. aeruginosa* carbapénèmes R

- Taux élevé de mortalité
- Haut potentiel de transmission épidémique
- Résistance transférable entre différentes espèces du tube digestif (carbépénémases)
- Portage digestif prolongé
- Manque de molécules pour le traitement / décolonisation des patients
- Coût élevé

☛ OMS :

  - ☛ Agents pathogènes de 1ère priorité (CRITIQUE) pour la recherche-développement de nouveaux antibiotiques
  - ☛ Recommandations spécifiques pour le prévention et le contrôle de ces souches (**surveillance des infections,** ….)

(Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities. Geneva: World Health Organization; 2017)

Ambler molecular classification

Catalytic Center

- **Non-metal (Ser)**
  - Class A:
    - Classical narrow-spectrum (PSE, CARB)
    - ESBLs (Extended-spectrum β-lactamase)(TEM, SHV, CTX-M)
    - Class A carbapenemases (GES, KPC, SME, IMI/NMC-A, SHV-38, SFC-1) — GES-1, GES-2, GES-4, GES-5
  - Class C:
    - AmpC
    - ESAC (Extended-spectrum AmpC) — CMY-10, CMY-19, CMY-37
  - Class D:
    - ESBLs (Extended-spectrum β-lactamase,)(Oxacillinases, OXA)
    - CHDLs (carbapenem-hydolyzing class D β-lactamases) — OXA-23, OXA-48
- **Metal (Zinc)**
  - Class B: MBL (Metallo-β-lactamase)
    - Subclass B1: (IMP, VIM, SPM, IND, NDM, DIM, GIM, SIM)
    - Subclass B3: (AIM, CAU-1, GOB-1,FEZ-1)
    - Subclass B2: (CphA, Sfh-I, ImiS)

Carbapenemases

Bush-Jacoby-Medeiros functional classification

Group 1: cephalosporinases (Ambler Class C)

Group 2: serine- β -lactamase (Ambler Class A and D)

Group 3: metallo- β -lactamase (Ambler Class B)

Teiji Sawa et al. Molecular diversity of extended-spectrum β-lactamases and carbapenemases, and antimicrobial resistance Journal of Intensive Care (2020) 8:13

Caractéristiques

	Spectre						Inhibiteurs
	Pénicillines	C3G – C4G	Monobactame	carbapénèmes	Ceftolozane - tazobactam	Ceftazidime - avibactam	
A	+++	+++	+++	+++	++	-	**Acide clavulanique** **Acide boronique**
B	+++	+++	-	+++	+++	+++	**EDTA** **Acide dipicolinique**
D	+++	-/+	-/+	+	+	-	

Type de cabapénémase ☛ Détection / traitement

TABLE 1 | The advantages and limitations of common detection methods.

Detection methods	Advantages	Limitations
Phenotypic detection assays		
Modified Hodge test (MHT)	1. Detecting KPC 2. Simple and inexpensive	1. False-positive and false-negative 2. Insufficient for MBLs 3. Time consuming
Colorimetric assay	1. Detecting KPC and most MBLs 2. Type carbapenemases 3. Simple and inexpensive	1. Insufficient for OXA-48 2. Specific reagents 3. Various infecting factors
Modified carbapenem inactivation method (mCIM)	1. Detecting all carbapenemeses 2. Clear criteria of judgment 3. Simple and cost-effectiveness	1. Time consuming
Spectrophotometric method	1. High sensitivity and specificity 2. Time saving 3. Simple and inexpensive	1. Specific instrument (spectrophotometer) 2. Various influencing factors 3. No standard equation and cut-off value 4. Small sample size
MALDI-TOF-based methods	1. Detecting KPC and NDM 2. Time saving 3. Easy to perform 4. Low measurement cost	1. Insufficient for OXA-48 2. No clear protocol and standard analysis 3. Expensive equipment
Molecular-based detection methods	1. Gold standards 2. Detecting all carbapanemeses genes 3. Type carbapenemase genes 4. Time saving	1. High technical requirements 2. Insufficient for expression of genes 3. High measurement cost

TABLE 3 | The advantages and limitations of novel antimicrobial therapeutics.

Antimicrobial therapeutics	Advantages	Limitations	Mechanisms of resistance
Ceftazidime–avibactam	1. Inhibition of KPC, OXA-48, ESBLs 2. Effective for CR-hvKp 3. Effective for complicated urinary tract and intra-abdominal infections 4. Low mortality risk (Shields et al., 2016)	1. Poor inhibition of MBLs and the other OXA (Livermore et al., 2016) 2. Unclear efficacy on other infections	1. Mutation of Ompk35/Ompk36 and high expression of KPC and SHV (Nelson et al., 2017) 2. Point mutation (Shields et al., 2017)
Aztreonam–avibactam	1. Inhibition of KPC, MBLs, ESBLs, OXA	1. Insufficient phase III clinical trials data	
Imipenem–relebactam	1. Inhibition of KPC 2. Favorable *in vitro* activity (Lob et al., 2017) 3. Well tolerated (Sims et al., 2017) 4. Few adverse evens (Zhanel et al., 2018)	1. Poor inhibition of MBLs and OXA (Lapuebla et al., 2015a) 2. Insufficient phase III clinical trials data (Sims et al., 2017)	1. Low expression of OmpK36 (Hecker et al., 2015)
Meropenem–vaborbactam	1. Inhibition of KPC (Lapuebla et al., 2015b) 2. Well tolerated 3. Few adverse evens (Zhanel et al., 2018)	1. Poor inhibition of MBLs and OXA (Lapuebla et al., 2015b) 2. Insufficient clinical data support	1. Low expression of OmpK35 and OmpK36 (Ritchie and Garavaglia-Wilson, 2014)
Plazomicin	1. Inhibition of KPC and OXA (Castanheira et al., 2018) 2. More potent activity and lower side effects than other aminoglycosides	1. Poor inhibition of MBLs	1. Methylation of 16S rRNA (Livermore et al., 2011) 2. Aminoglycoside modifying enzyme (Castanheira et al., 2018)
Eravacycline	1. Well pharmacokinetics, pharmacodynamics, tolerability, and *in vitro* activity (Lan et al., 2019; McCarthy, 2019) 2. Performance in complicated intra-abdominal infections (Heaney et al., 2019) 3. Non-renal pathway clearance (Lee and Burton, 2019)	1. Suboptimal in complicated urinary tract infections (Lee and Burton, 2019)	1. Upregulation of efflux pumps (Livermore et al., 2011) 2. Mobile resistance genes, *tet*(X3) and *tet*(X4) (He et al., 2019)
Cefiderocol	1. Inhibition of kinds of carbapenemases 2. Well tolerability 3. High microbiological response rates and eradication rates (Zhanel et al., 2019)	1. Unclear optimal dose 2. Insufficient phase III clinical trials data	

(Cui X et al., Front. Microbiol. 2019;10:1823)

Type de cabapénémase ☛ Détection / traitement

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Meropenem–vaborbactam	1. Inhibition of KPC (Lapuebla et al., 2015b) 2. Well tolerated 3. Few adverse evens (Zhanel et al., 2018)	1. Poor inhibition of MBLs and OXA (Lapuebla et al., 2015b) 2. Insufficient clinical data support	1. Low expression of OmpK35 and OmpK36 (Ritchie and Garavaglia-Wilson, 2014)
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(Cui X et al., Front. Microbiol. 2019;10:1823)

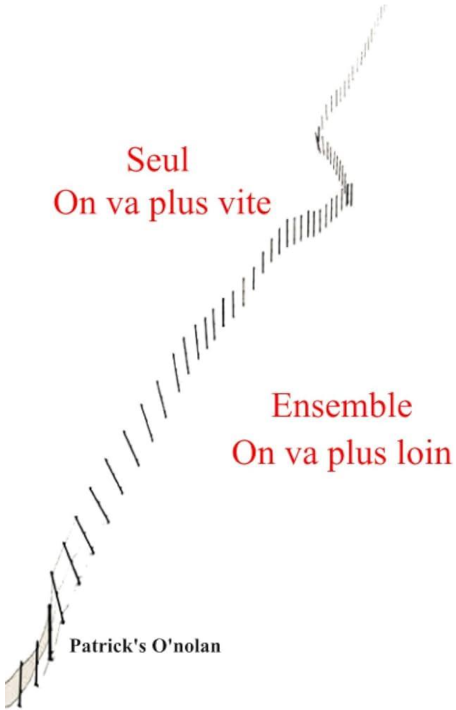
Objectifs

- Etudier le profil moléculaire des carbapénémases en Tunisie
- Etudier la clonalité des souches résistantes

Matériel et Méthodes (I)

- **Etude multicentrique prospective**

1. Grand Tunis	1. Tunis	**1. HCN** **2. Hôpital La Rabta** **3. HET** **4. HMPIT** **5. HAO** **6. CNGMO**
	2. Ariana	**7. H. Abderrahmen Mami**
	3. Ben Arous	**8. CTGB**
	4. Manouba	**9. IMKO**
2. Sousse / Monastir	5. Sousse	**10. H Farhat Hached Sousse**
	6. Monastir	**11. H. Fattouma Bourguiba Monastir**
3. Sfax	7. Sfax	**12. H. Habib Bourguiba Sfax**



Matériel et Méthodes (II)

- **Population bactérienne**

Souches incluses	Souches non incluses	Souches exclues
Souches non répétitives, *Enterobacterales, P. aeruginosa, A. baumannii*, Prélèvement réalisés du 05 février au 03 mars 2024, Responsables d'infections, R ou SFP (pour A. baumannii) aux carbapénèmes	Souches de *P. aeruginosa* ayant une résistance isolée à l'imipénème	Souches dont les subcultures étaient contaminées

Matériel et Méthodes (III)

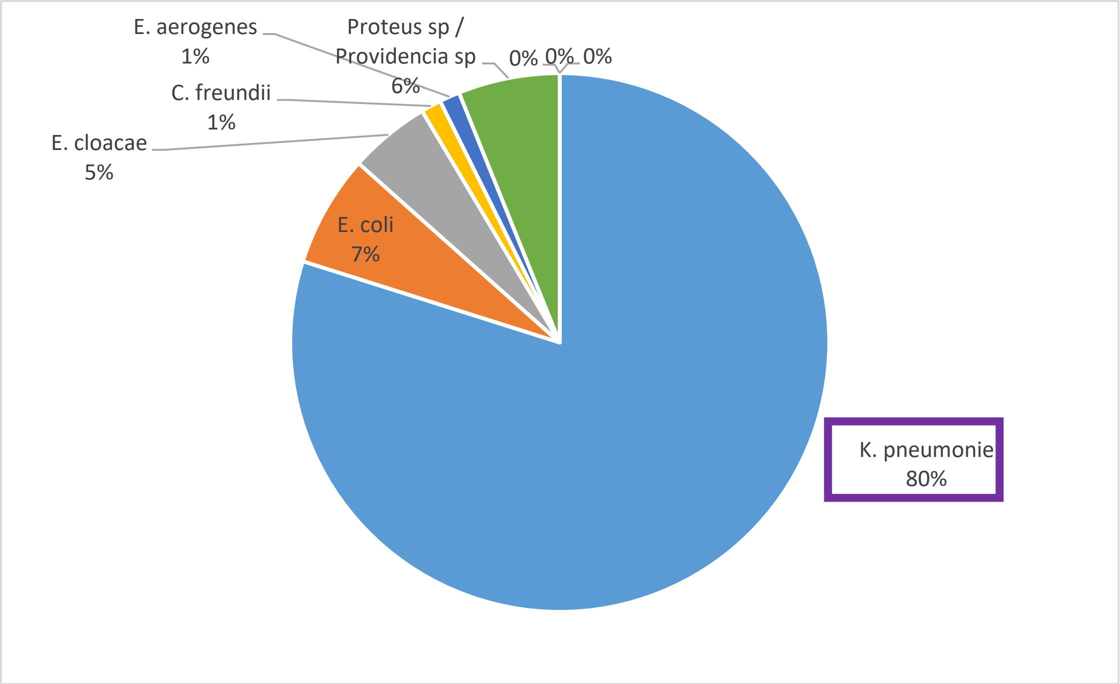
- **Collecte des souches / données épidémiologiques**
  - Service des Laboratoires du CNGMO
- **Etude phénotypique et génotypique**
  - **PhD A. Raddaoui**
- **Recherche des gènes de carbapénémases**
  - Extraction de l'ADN
    - Choc thermique
  - Amplification PCR simplex des gènes de carbapénémases
  - Révélation des produits d'amplification :
    - Electrophorèse horizontale sur gel d'agarose 1,5%
  - Visualisation
    - Transilluminateur UV (Gel Doc™ XR+) (BIORAD)

Amorces (Sequence 5′ to 3′)	Taille (pb)	Reference
KPC KPC- F : GTATCGCCGTCTAGTTCTGC KPC-R : GGTCGTGTTTCCCTTTAGCC	638	(Hong, et al., 2012)
IMI IMI-F : TGCGGTCGATTGGAGATAAA IMI-R : CGATTCTTGAAGCTTCTGCG	399	
GES GES-F : GCTTCATTCACGCACTATT GES-R : CGATGCTAGAAACCGCTC	323	
VIM VIM-F : GATGGTGTTTGGTCGCATA VIM-R : CGAATGCGCAGCACCAG	390	(Ellington, et al., 2007)
IMP IMP-F : GGAATAGAGTGGCTTAAYTCTC IMP-R : CCAAACYACTASGTTATCT [a]	188	
NDM NDM-F : GCTTTGGCGATCTGGTTTTC NDM-R : CGGAATGGCTCATCACGATC	620	(Poirel, et al., 2011)
OXA-48 OXA-48-F : TTGGTGGCATCGATTATCGG OXA48-R : GAGCACTTCTTTTGTGATGGC	743	(Poirel, et al., 2004)
OXA-23 ***OXA-23-F :*** GATCGGATTGGAGAACCAG ***OXA-23-R :*** ATTTCTGACCGCATTTCCAT	501	(Woodford, et al., 2019)

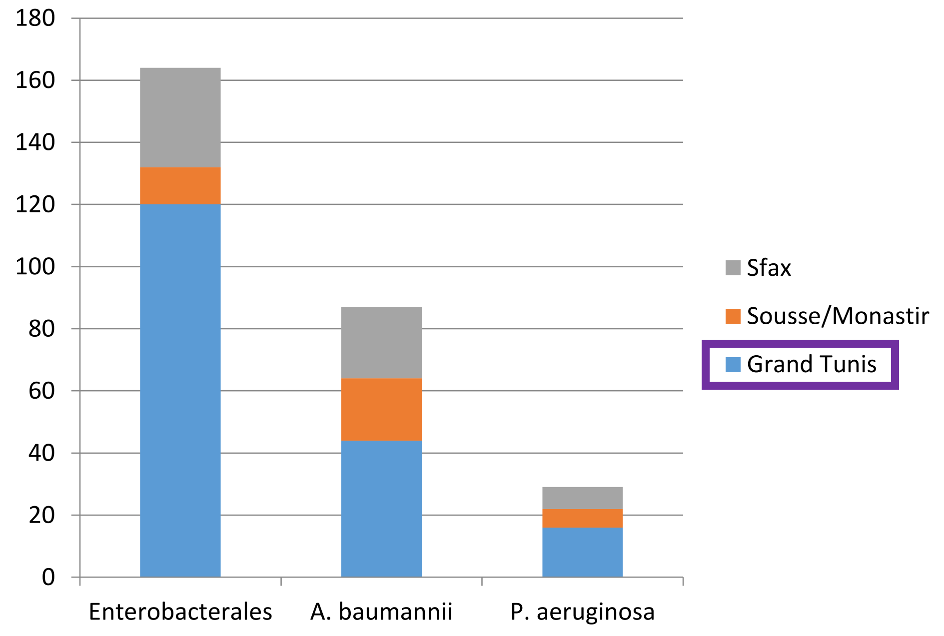
Résultats préliminaires et Discussion

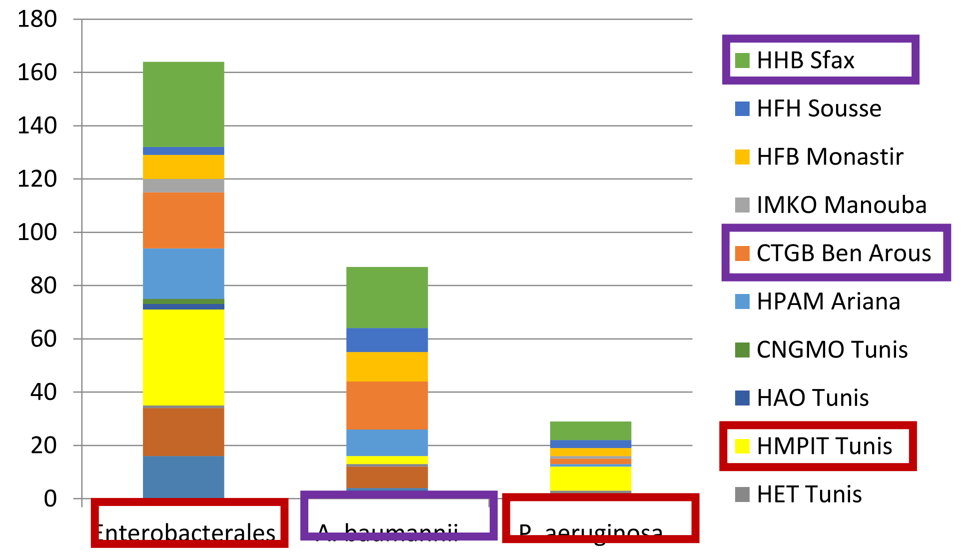
Répartition des souches par espèce

Enterobacterales	*A. baumannii*	*P. aeruginosa*
N=164	**N=87**	**N=29**

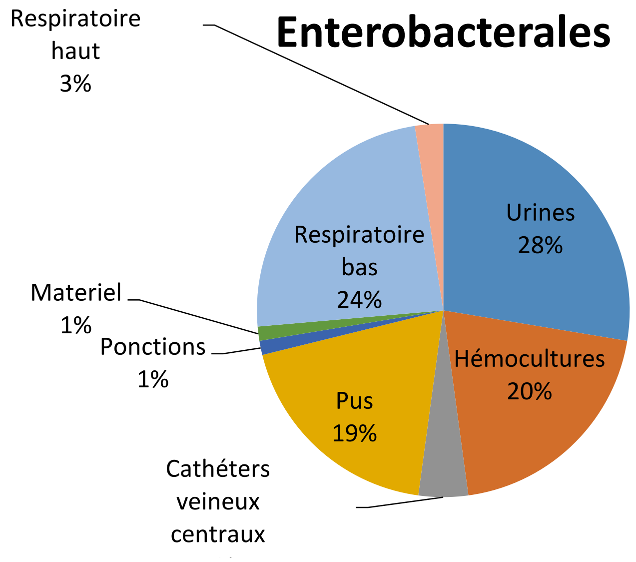


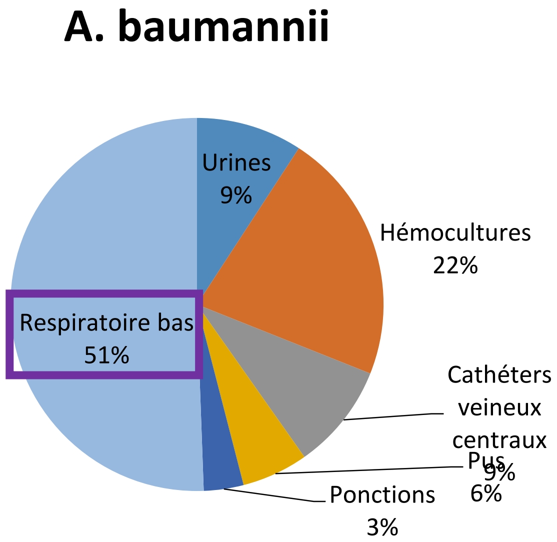
Répartition des souches par région et par hôpital

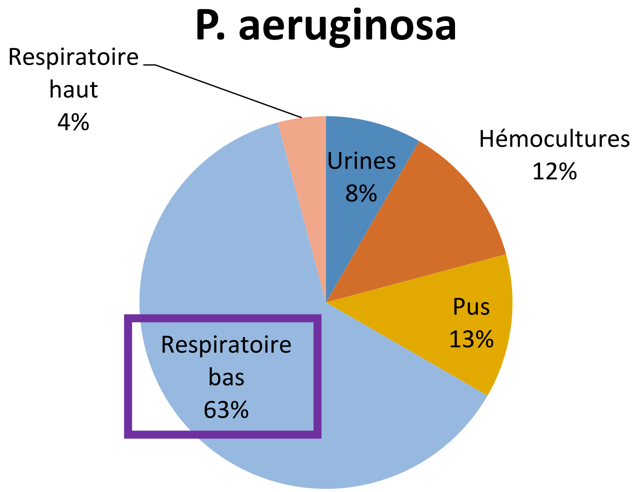




Répartition des souches par prélèvement et par service





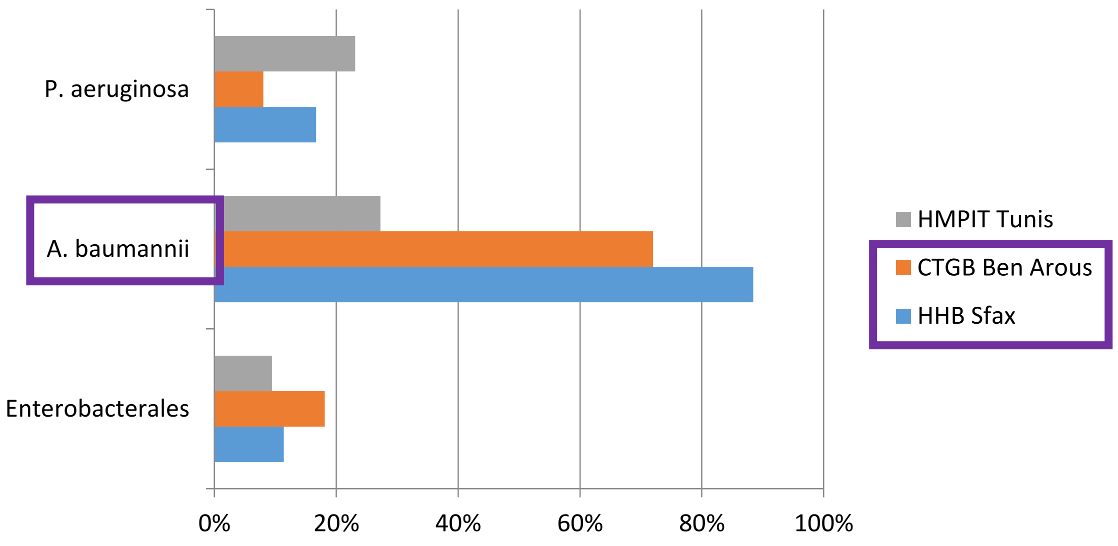


Prévalence de la résistance aux carbapénèmes

Enterobacterales
10,12%

A. baumannii
71,9%

P. aeruginosa
11,23%



Prévalence de la résistance aux carbapénèmes

	E. coli	*K. pneumoniae*	*A. baumannii*	*P. aeruginosa*
	Enterobacterales		***A. baumannii***	***P. aeruginosa***
Cette étude	**10,12%**		**71,9%**	**11,23%**
	Ertapénème R			
LART 2022	***E. coli***	***K. pneumoniae***		
	0,7% (sur 7780)	18,5% (sur 4023)	**79,5%** (sur 1033)	12,9% (sur 2448)
ECDC 2021	0.2%	11.7%	**39.9%**	8.1%

Fig. 13 *Escherichia coli*. Percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country, EU/EEA, 2021

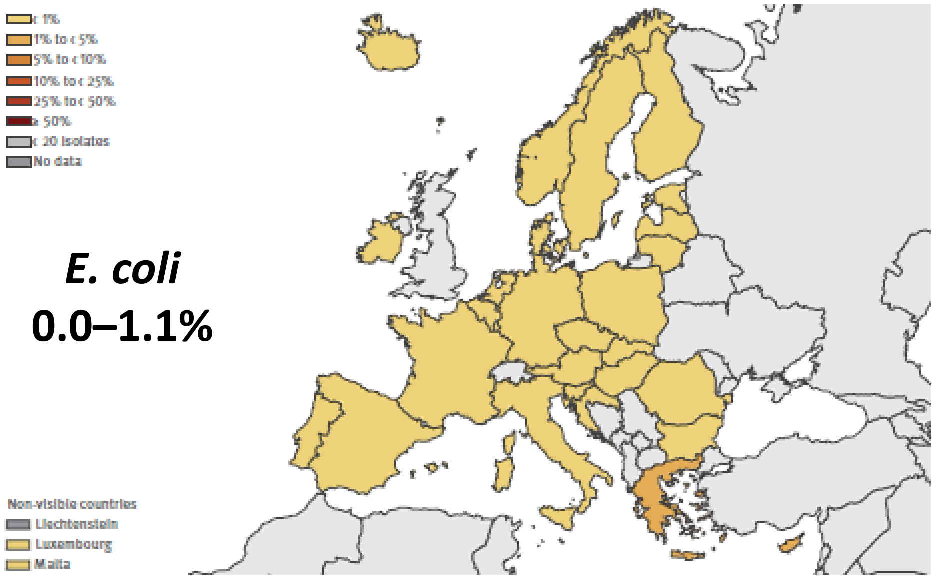


Fig. 17 *Acinetobacter* species. Percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country, EU/EEA, 2021

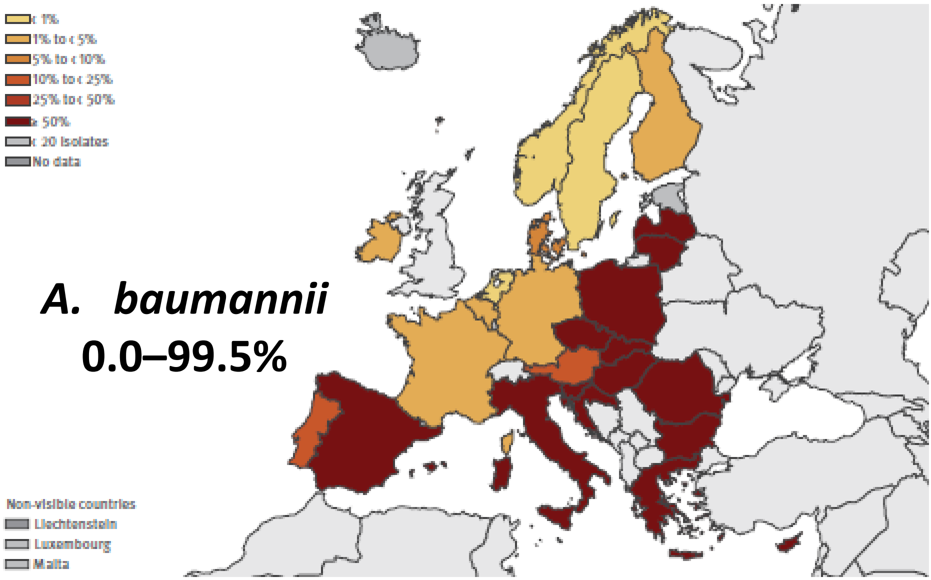


Fig. 15 *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country, EU/EEA, 2021

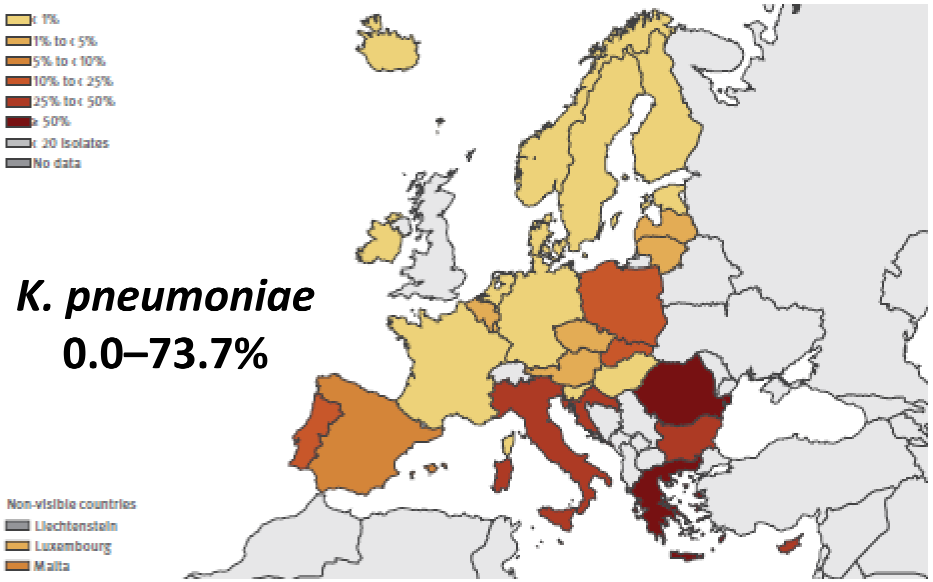
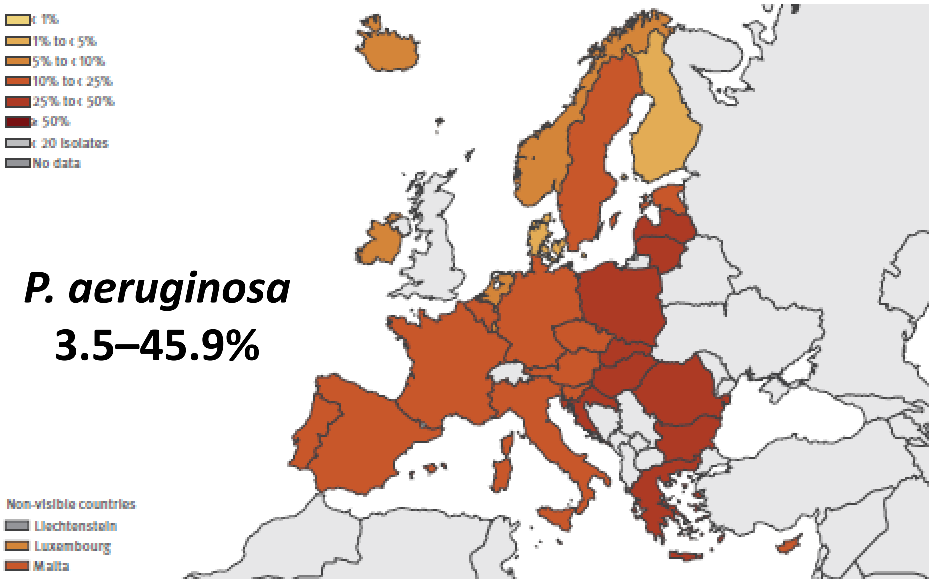


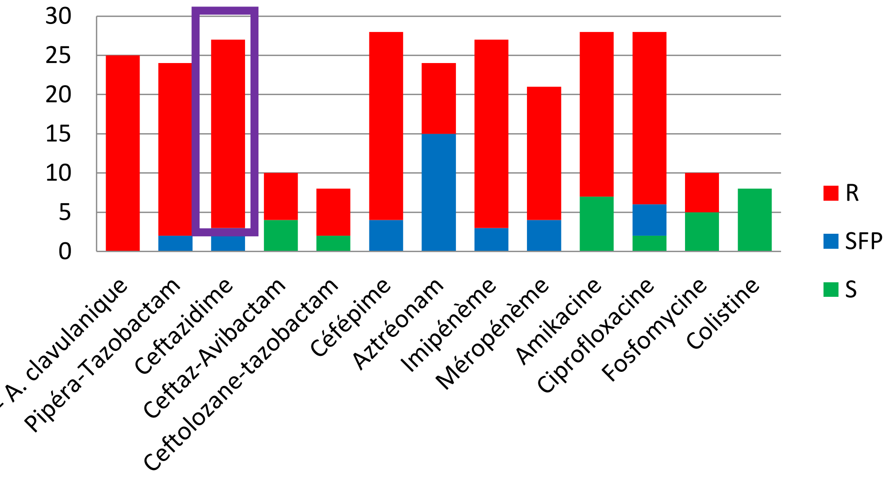
Fig. 16 *Pseudomonas aeruginosa*. Percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country, EU/EEA, 2021



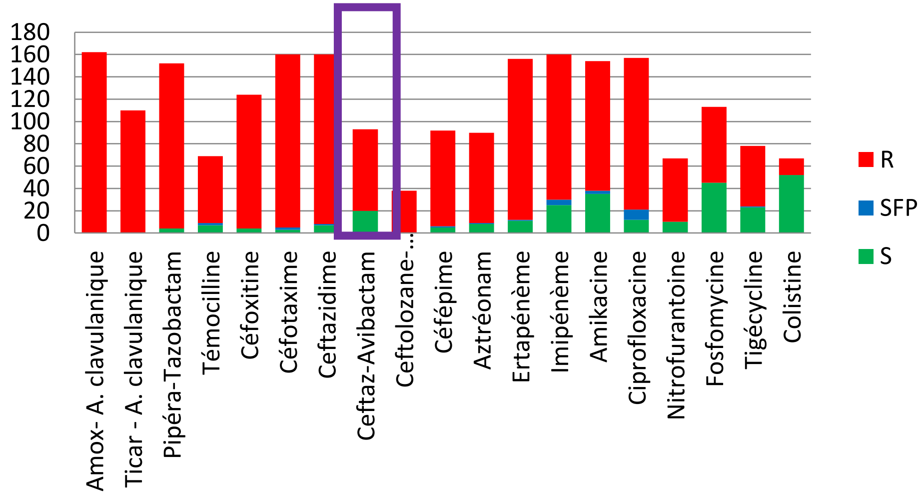
Antimicrobial resistance surveillance, in Europe 2023 - 2021 data. Stockholm: European Centre for Disease Prevention and Control and World Health Organization; 2023

Résistances associées aux antibiotiques

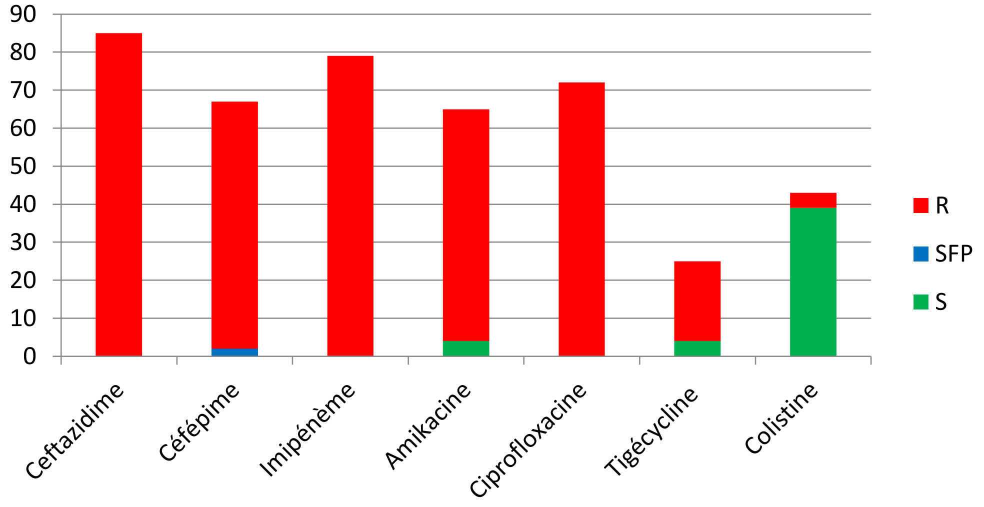
A. baumannii



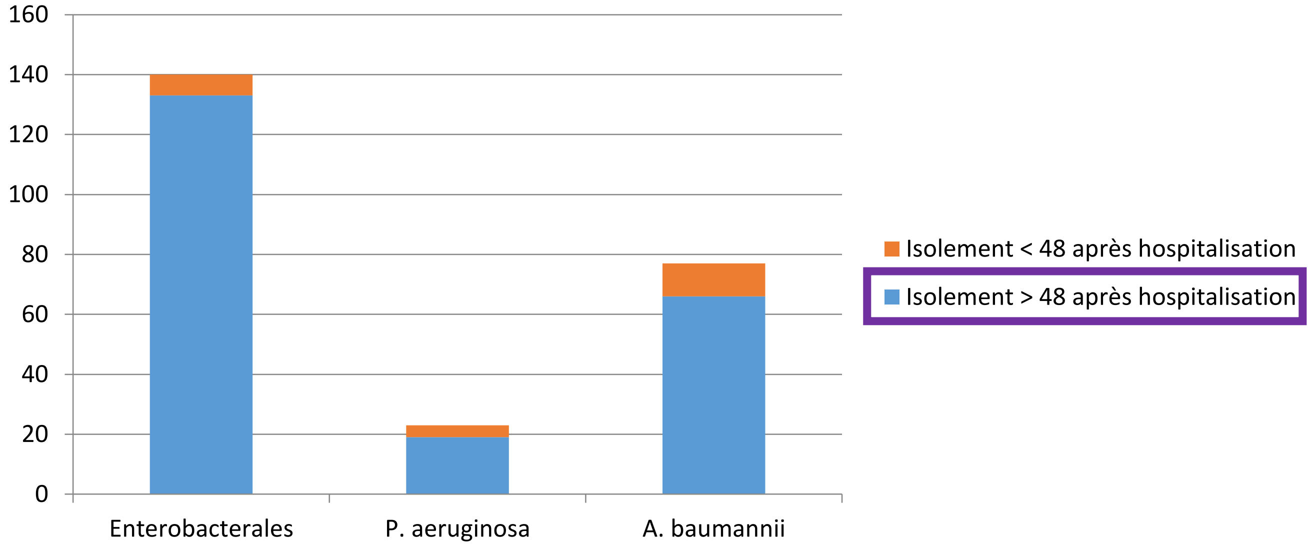
Enterobacterales



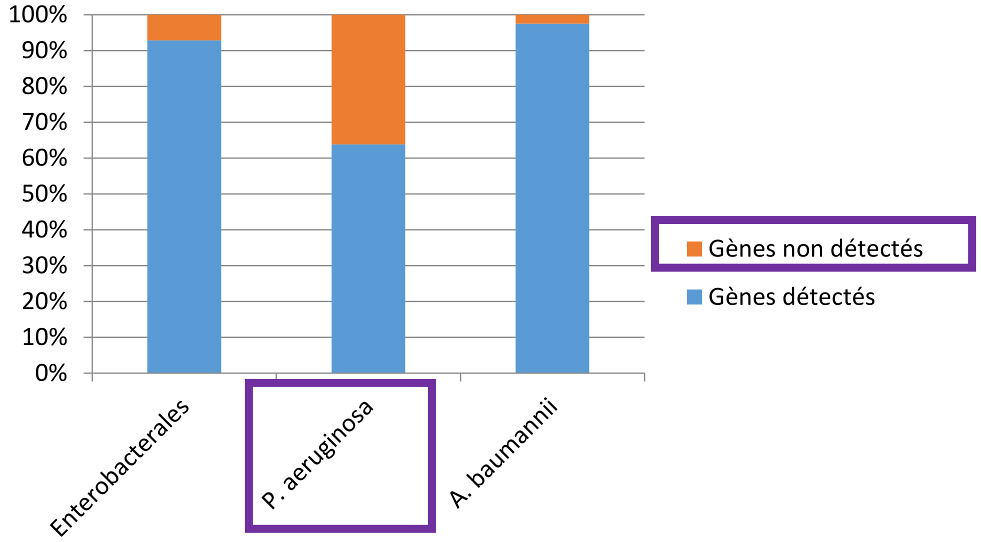
P. aeruginosa

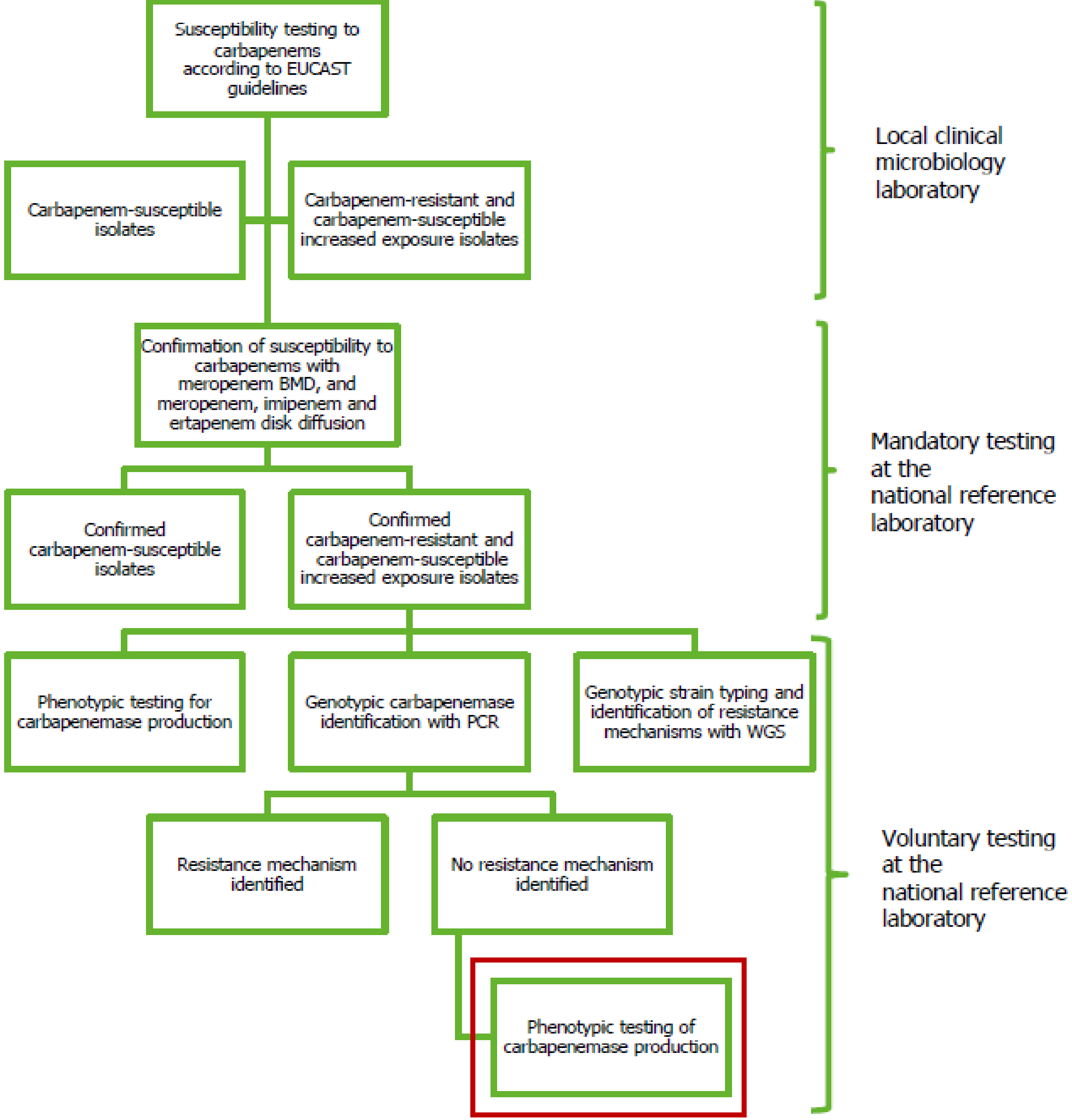


Délai d’isolement par rapport à l’hospitalisation



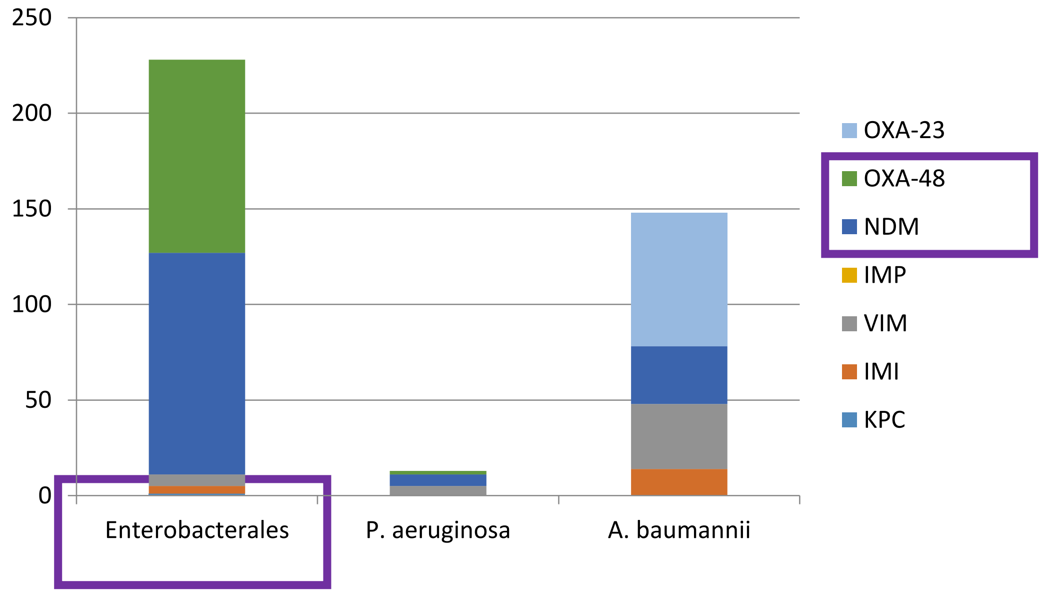
Gènes de carbapénémases





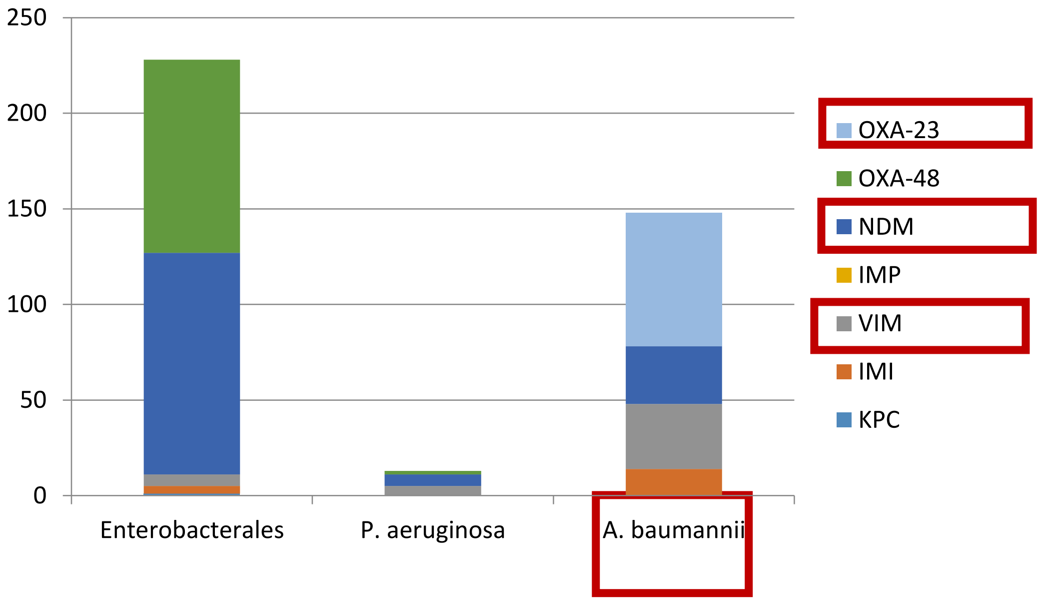
European Centre for Disease Prevention and Control. Expert consensus protocol on carbapenem resistance detection and characterisation for the survey of carbapenem- and/or colistin-resistant Enterobacteriaceae – Version 3.0. Stockholm: ECDC; 2019

Gènes de carbapénémases



OXA-48+NDM (n= 76)

Gènes de carbapénémases



OXA-23+VIM (n= 26)

Gènes de carbapénémases

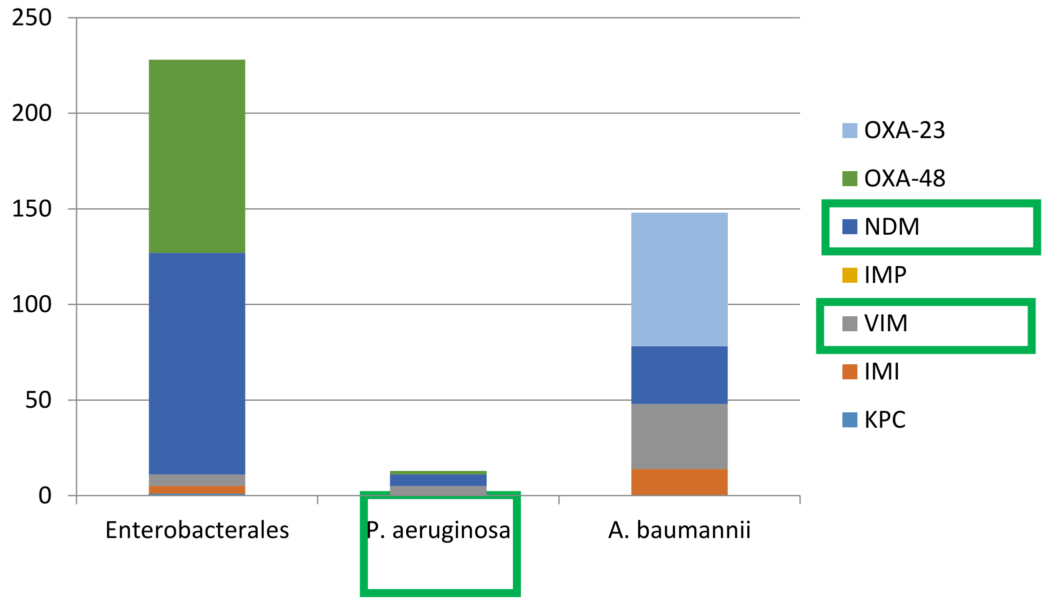


Table 2 The Frequencies of Carbapenemases Detected in Each Species in Tunisia from 2006 to 2019

	KPC		VIM		NDM-1		IMP		OXA-48		OXA-23		OXA-51		OXA-58		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
A. baumannii	–	–	–	–	14	12.28	–	–	–	–	424	100	230	100	20	100	688	55.62
P. aeruginosa	–	–	95	65.07	–	–	–	–	–	–	–	–	–	–	–	–	95	7.68
K. pneumoniae	20	90.91	39	26.71	99	86.84	25	100	222	86.72	–	–	–	–	–	–	405	32.74
E. coli	2	9.09	4	2.74	–	–	–	–	6	2.34	–	–	–	–	–	–	12	0.97
P. mirabilis	–	–	–	–	1	0.88	–	–	1	0.39	–	–	–	–	–	–	2	0.16
C. freundii	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
E. cloacae	–	–	1	0.69	–	–	–	–	11	4.30	–	–	–	–	–	–	12	0.97
*E. aerogenes**	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
P. stuartii	–	–	–	–	–	–	–	–	13	5.08	–	–	–	–	–	–	13	1.05
S. enterica	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
H. pylori	–	–	7	4.79	–	–	–	–	–	–	–	–	–	–	–	–	7	0.57
Total	22	1.78	146	11.80	114	9.22	25	2.02	256	20.69	424	34.28	230	18.59	20	1.62	1237	100

Note: **Enterobacter aerogenes* has been recently renamed *Klebsiella aerogenes*.[35]

(Olfa Dziri et al. Infect Drug Resistance : 13 4177–4191)

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P. aeruginosa	–	–	95	65.07	–	–	–	–	–	–	–	–	–	–	–	–	95	7.68
K. pneumoniae	20	90.91	39	26.71	99	86.84	25	100	222	86.72	–	–	–	–	–	–	405	32.74
E. coli	2	9.09	4	2.74	–	–	–	–	6	2.34	–	–	–	–	–	–	12	0.97
P. mirabilis	–	–	–	–	1	0.88	–	–	1	0.39	–	–	–	–	–	–	2	0.16
C. freundii	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
E. cloacae	–	–	1	0.69	–	–	–	–	11	4.30	–	–	–	–	–	–	12	0.97
*E. aerogenes**	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
P. stuartii	–	–	–	–	–	–	–	–	13	5.08	–	–	–	–	–	–	13	1.05
S. enterica	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
H. pylori	–	–	7	4.79	–	–	–	–	–	–	–	–	–	–	–	–	7	0.57
Total	22	1.78	146	11.80	114	9.22	25	2.02	256	20.69	424	34.28	230	18.59	20	1.62	1237	100

Note: **Enterobacter aerogenes* has been recently renamed *Klebsiella aerogenes*.[35]

(Olfa Dziri et al. Infect Drug Resistance : 13 4177–4191)

Table 2 The Frequencies of Carbapenemases Detected in Each Species in Tunisia from 2006 to 2019

	KPC		VIM		NDM-1		IMP		OXA-48		OXA-23		OXA-51		OXA-58		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
A. baumannii	–	–	–	–	14	12.28	–	–	–	–	424	100	230	100	20	100	688	55.62
P. aeruginosa	–	–	95	65.07	–	–	–	–	–	–	–	–	–	–	–	–	95	7.68
K. pneumoniae	20	90.91	39	26.71	99	86.84	25	100	222	86.72	–	–	–	–	–	–	405	32.74
E. coli	2	9.09	4	2.74	–	–	–	–	6	2.34	–	–	–	–	–	–	12	0.97
P. mirabilis	–	–	–	–	1	0.88	–	–	1	0.39	–	–	–	–	–	–	2	0.16
C. freundii	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
E. cloacae	–	–	1	0.69	–	–	–	–	11	4.30	–	–	–	–	–	–	12	0.97
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P. mirabilis	–	–	–	–	1	0.88	–	–	1	0.39	–	–	–	–	–	–	2	0.16
C. freundii	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
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S. enterica	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
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S. enterica	–	–	–	–	–	–	–	–	1	0.39	–	–	–	–	–	–	1	0.08
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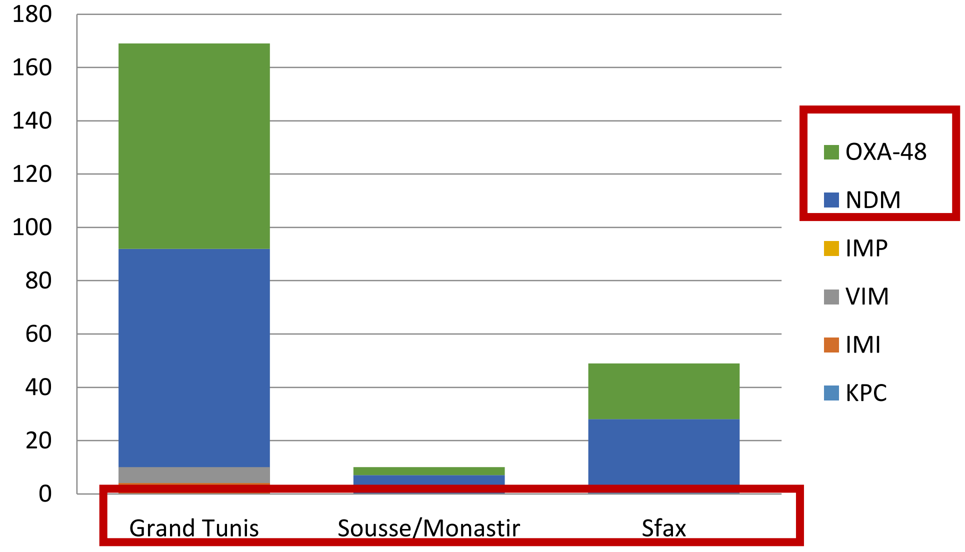
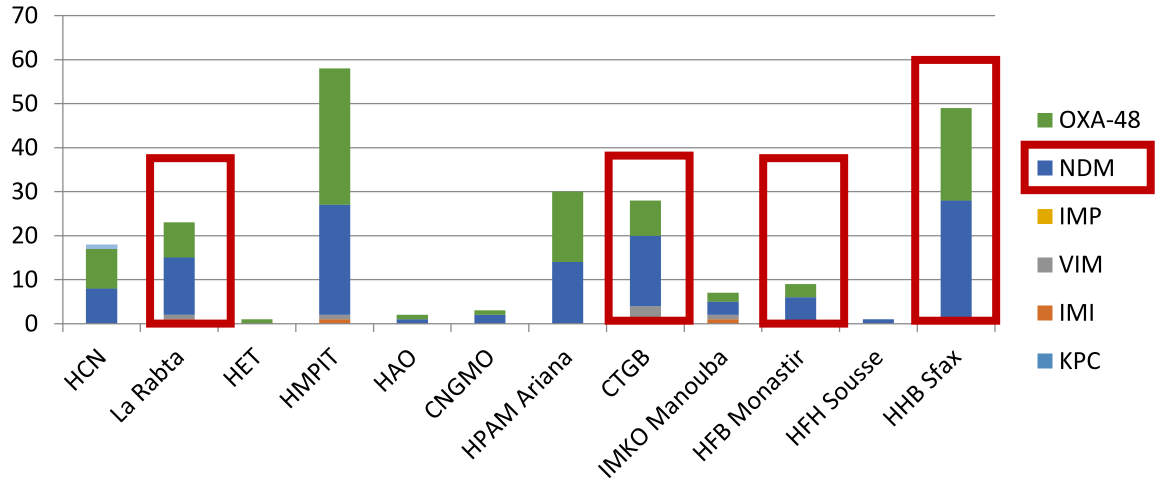
(Olfa Dziri et al. Infect Drug Resistance : 13 4177–4191)

Gènes de carbapénémases
Enterobacterales

Fonction de la région



Fonction du CHU



Gènes de carbapénémases
Enterobacterales

HHB	7 *Enterobacterales* (Portage digestif des restaurateurs : 0.33% sur 2135)	2012-17	**blaOXA-48-like (85%)** (N. Sallem, J Antimicrob Chemother 2022; 77: 2142–52)
H. Sahloul	240 K. Pneumoniae	2012-14	**$bla_{OXA\text{-}48\text{-}like}$ genes (81.7%)** (Messaoudi A et al., J Glob Antimicrob Resist 2020;20:87-93)
H. A. Mami	45 K. Pneumoniae	2015-16	**OXA-48 (87 %), NDM-1 (20 %),** association de ces deux gènes (11 %) (Bouattour H et al., Med Mal Infect. 2019;49(3):225-6)
HMPIT	102 *Enterobacterales* (85.2% K. pneumoniae)	2014-16	**$bla_{OXA\text{-}48}$ (n=84), $bla_{NDM\text{-}1}$ (n=8), $bla_{OXA\text{-}48}$ + bla_{VIM} (n=5),** $bla_{OXA\text{-}48}$ + $bla_{NDM\text{-}1}$ (n=5) (Ben Helal R et al., Microb Drug Resist. 2018 Nov;24(9):1361-7)
HMPIT	197 EB (170 K. pneumoniae)	2014-18	**$bla_{OXA\text{-}48}$ (n=153), bla_{NDM} (n=14), bla_{BIC} (n=5), and bla_{VIM}(n=3)** (Kollenda H, et al. Eur J Microbiol Immunol. 2019;9(1):9-13)
HMPIT	13 *K. pneumoniae* métallo-β-lactamases (+)	2017	***$bla_{NDM\text{-}1}$* (n=8)**, ***$bla_{VIM\text{-}1}$* (n=6)**, 1ère description, en Tunisie, de *$bla_{NDM\text{-}1}$*+*$bla_{VIM\text{-}1}$* (n=1) et, dans le monde, de nouveaux ST de *K. pneumoniae* métallo-β-lactamases (+) (Dziri R et al., Microb Drug Resist. 2019 Nov;25(9):1282-6)
IMKO	K. pneumoniae (n = 7) P. mirabilis (n = 1)	2017-18	**blaOXA-48 (n = 8), blaNDM-1 (n = 4)** (D. Miniaoui et al.,.J Infect Dev Ctries 2023; 17(11):1591-7)
MENA (HCN, HHB)	103 *Enterobacterales*	2019	***$bla_{OXA\text{-}48}$* et *$bla_{NDM\text{-}1}$* +++** (Dos Santos S et al., Front Microbiol. 2024;15:1370553)

Intégration du WGS dans la surveillance de la résistance aux antibiotiques en Tunisie

D. Itani (Travail en cours)

TARSS
I. Boutiba
M. Zribi
W. Achour
L. Thabet
H. Smaoui

Holt Lab Kat Holt
E. Foster-Ny

Quadram Institute
D. Bakerarko

Wellcome Sanger
N. Thomson

WHO CO Tunisia
R. Ouhichi

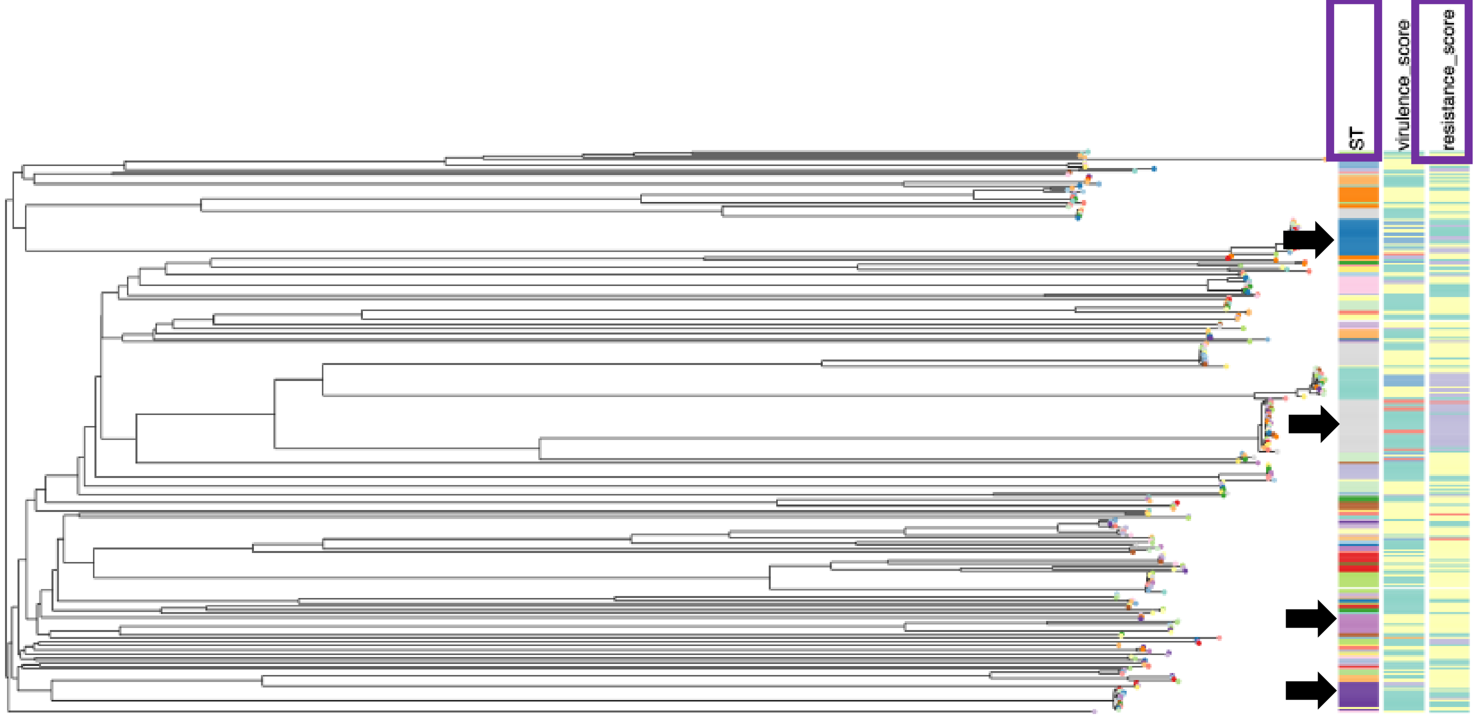
289 *K. pneumoniae*

CTGB, HCN, La Rabta, HET, CNGMO

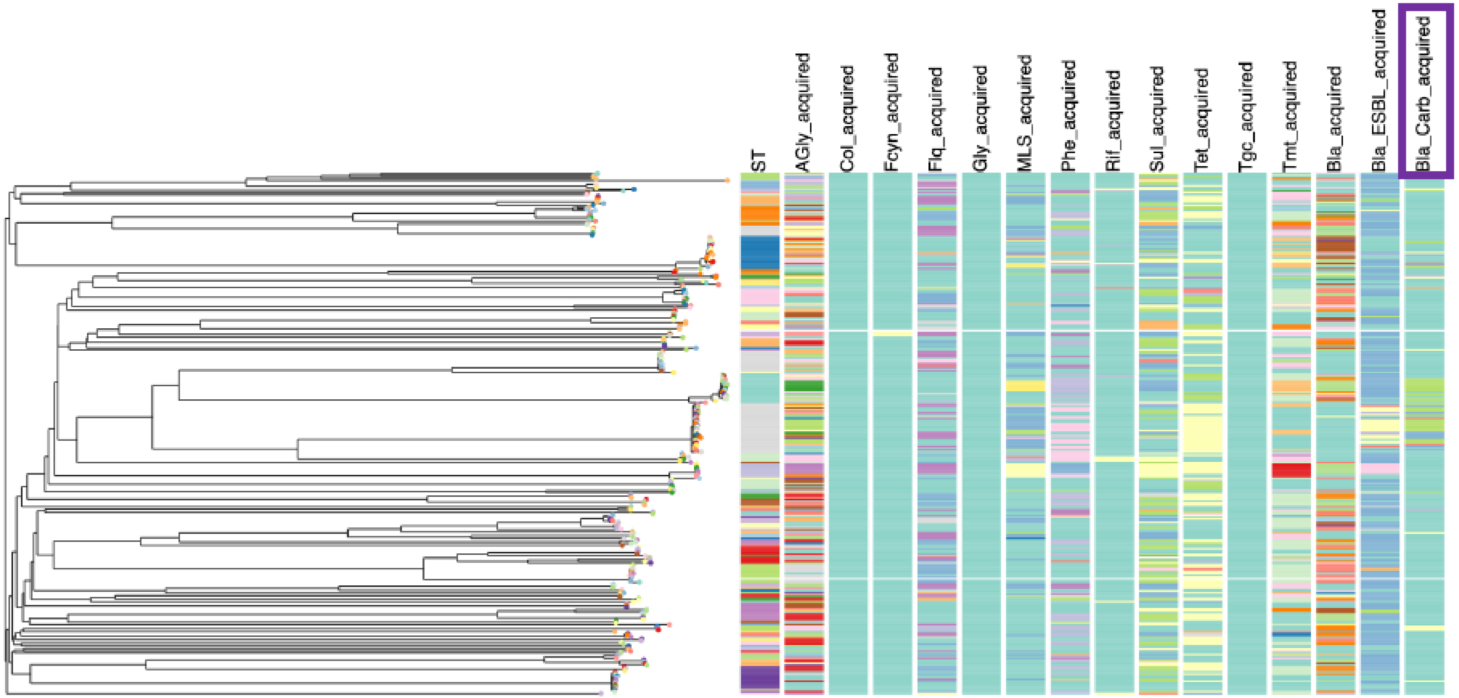
Illumina NextSeq 500 system, Quadram Institute, Royaume Uni

Intégration du WGS dans la surveillance de la résistance aux antibiotiques en Tunisie

D. Itani (Résultats préliminaires)



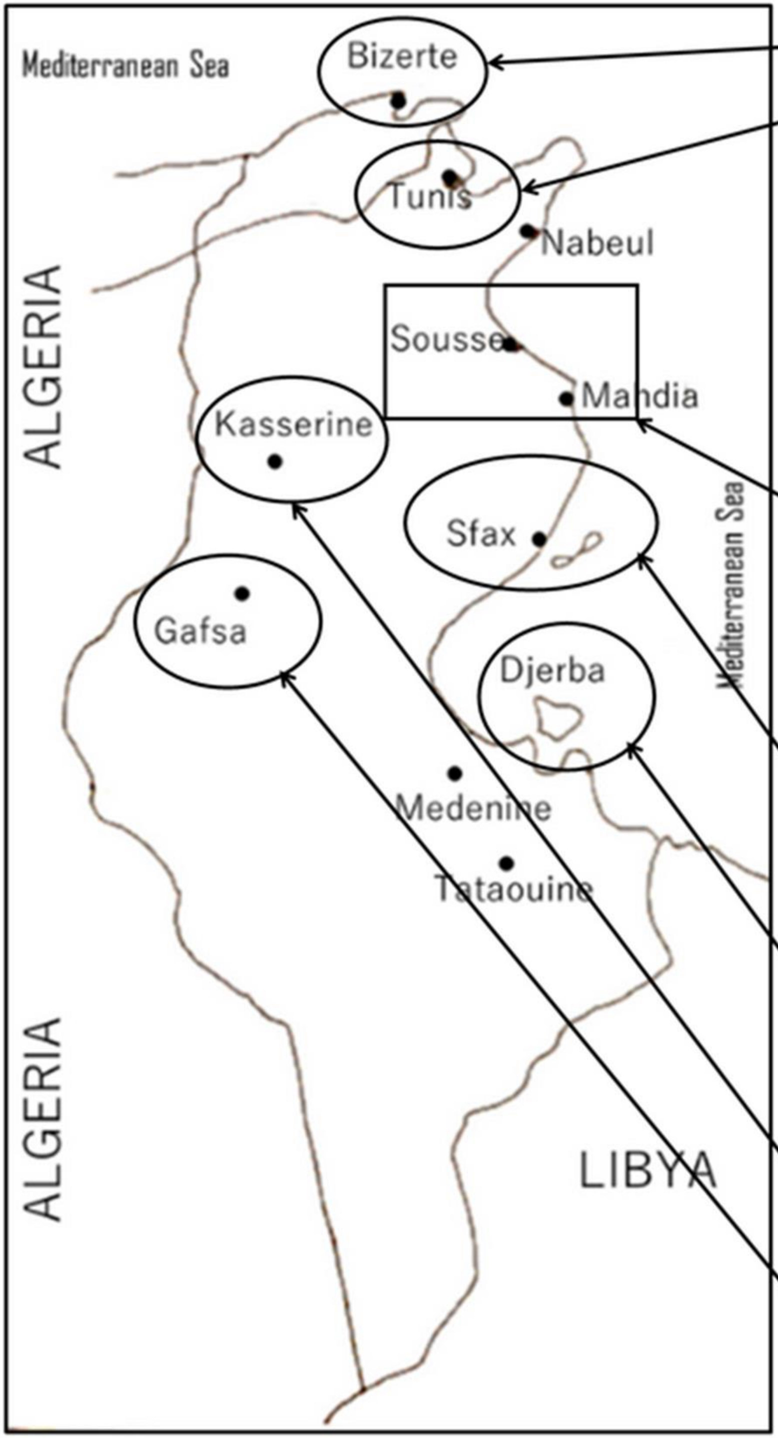
- Prédominance de quelques clones :
    - ST45 (haut risque épidémique)
    - ST307 (haut risque endémique aux USA)
    - ST383, ST147, ST101, ST39 (épidémiques)
    - ST13 (internationaux)
- 0 à 1 gènes de virulence (86,8%)
- gènes de carbapénémases (18.6%)
    - OXA-48 (14%) > NDM-1 (4%)



Gènes de carbapénémases
Enterobacterales

Fruits de mer	641 poissons d'élevage 1075 coquillages	**blaNDM-1** (1 souche) et **blaOXA-48** (1 souche) isolées de coquillages	(Sola, M. Microorganisms **2022, 10,** 1364)
Oiseaux sauvages	150oiseaux, 7 régions, Tunisie ➔ 2/99 souches imipénème R	1ère description de **KPC-2** (1 K. oxytoca) et **KPC-3** (1 E. fergusonii) chez les *Enterobacterales* isolées d'oiseaux sauvages en Afrique	(H. Ben Yahia. Africa. Microbial Ecology. 2020;79:30–37)
Vaux diaahéiques	100 Vaux diarrhéiques**,** Bizerte ➔ 2/77 E. coli imipénème R	1ère description de carbapénémases chez les vaux en Afrique du Nord : ***bla*** $_{\mathbf{OXA\text{-}48}}$**+*bla*** $_{\mathbf{IMP}}$ (1 souche) et ***bla*** $_{\mathbf{IMP}}$ (1 souche)	(A. Ben Haj Yahia et al., Microb Drug Resist. 2023;29(4):150-62)
Lapins sains	16 /39 carbapénèmes R	1ère description de **bla** $_{\mathbf{VIM}}$ (2 souches dont 1 en association) et **bla** $_{\mathbf{IMP}}$ (1 souche) chez le bétail en Tunisie	(S Lengliz LettApplMicrobiol. 2021;73(6):708-17)

Gènes de carbapénémases chez les BGN (2006 – 2019)



OXA-23 (*A. baumannii*)

VIM (*P. aeruginosa / K. pneumoniae / H. pylori*)
NDM-1 (*K. pneumoniae / A. baumannii / P. mirabilis /* Wastewater effluents)
IMP (*K. pneumoniae*)
KPC (*K. pneumoniae / E. coli /* Wastewater effluents)
OXA-48 (*K. pneumoniae / E. coli / C. freundii / E. cloacae / E. aerogenes /* Wastewater effluents)
OXA-23 (*A. baumannii*)
OXA-51 (*A. baumannii*)
OXA-58 (*A. baumannii*)

VIM-2 (*P. aeruginosa*)
NDM-1 (*K. pneumoniae / A. baumannii /* Wastewater effluents)
KPC (Wastewater effluents)
OXA-48 (*K. pneumoniae / E. coli /* Wastewater effluents)
OXA-23 (*A. baumannii*)
OXA-51 (*A. baumannii*)
OXA-58 (*A. baumannii*)

VIM (*K. pneumoniae / P. aeruginosa*)
NDM (Wastewater effluents)
OXA-48 (*K. pneumoniae / P. stuartii / S. enterica /* Wastewater effluents)

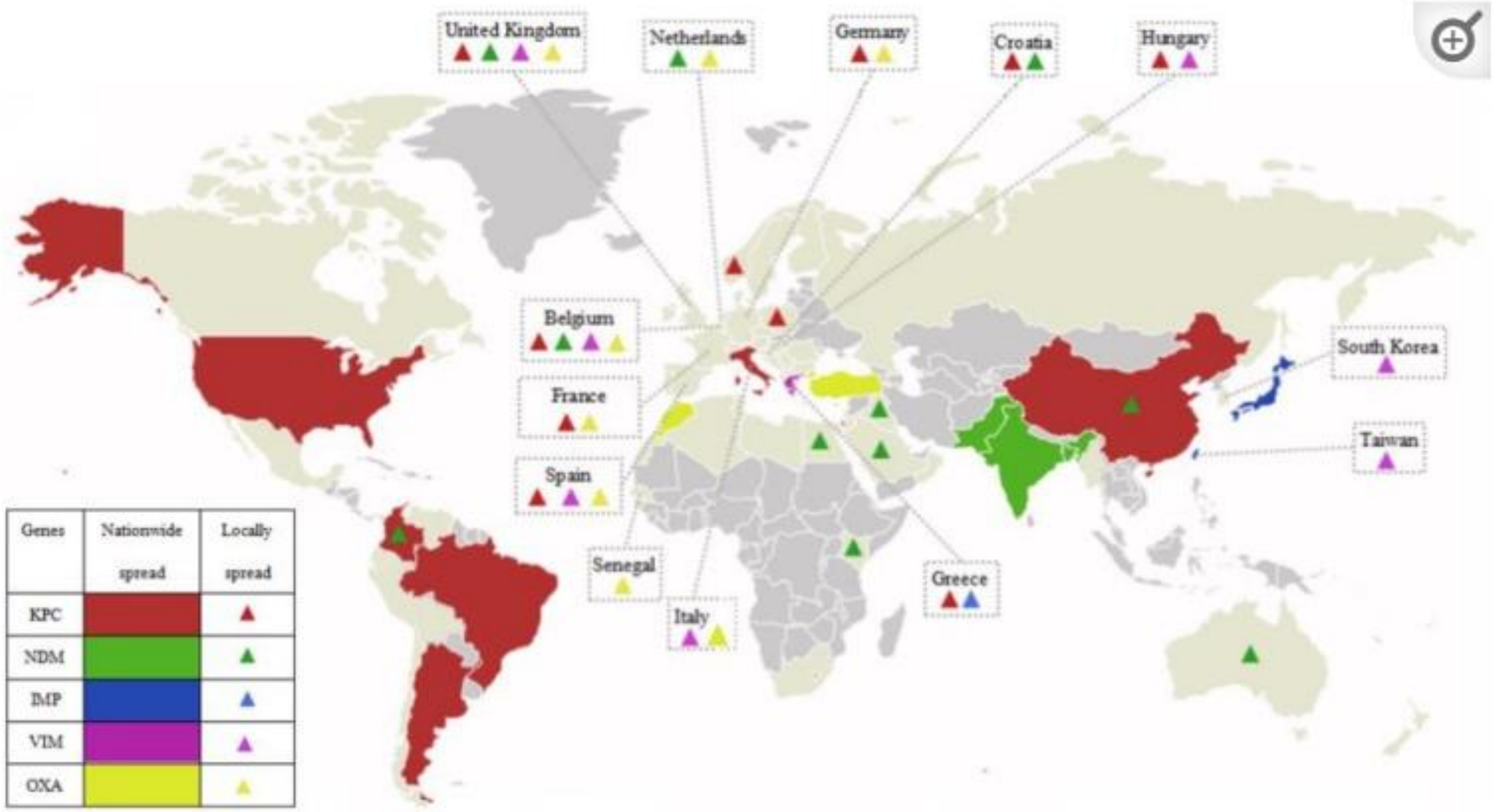
VIM-2 (*E. cloacae*)
NDM-1 (*K. pneumoniae*)
OXA-48 (*K. pneumoniae / P. mirabilis*)
OXA-23 (*A. baumannii*)

IMP-1 (*K. pneumoniae*)
VIM-2 (*E. coli*)

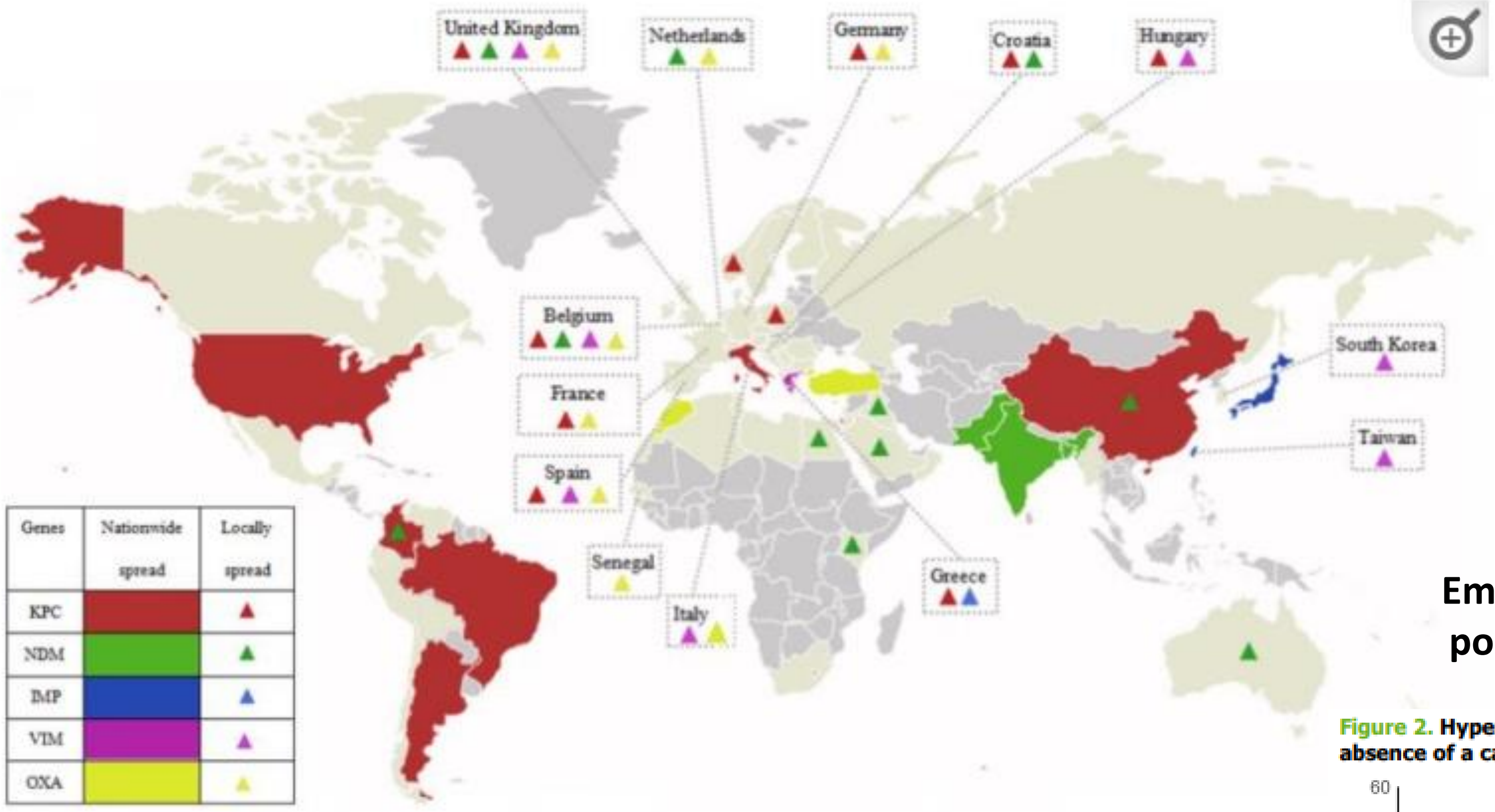
NDM (Wastewater effluents)
OXA-48 (Wastewater effluents)

☛ Présence de carbapénémases (OXA-48, NDM-1 et KPC) dans les effluents

(Olfa Dziri et al. Infect Drug Resistance : 13 4177–4191)



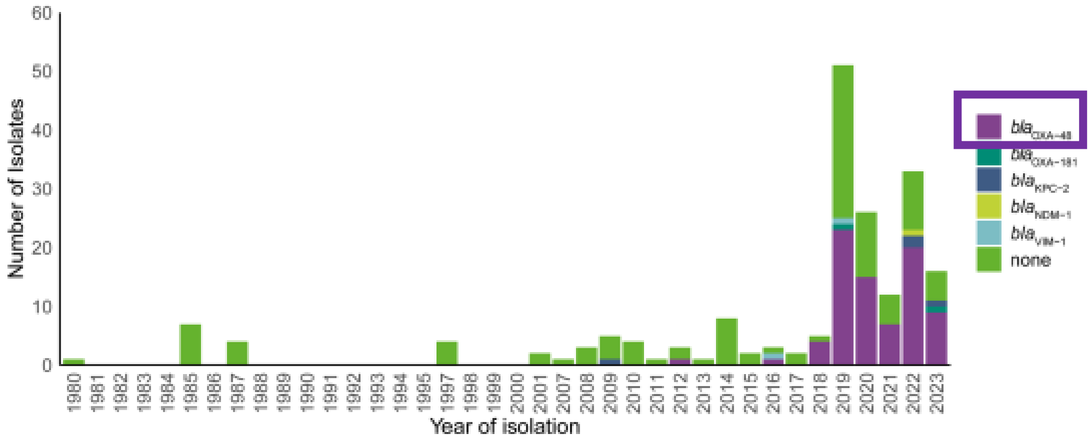
(Cui X et al., Front Microbiol. 2019;10:1823)



(Cui X et al., Front Microbiol. 2019;10:1823)

Emergence de *K. pneumoniae* ST23 hypervirulente porteuse de gènes de carbapénémases en Europe

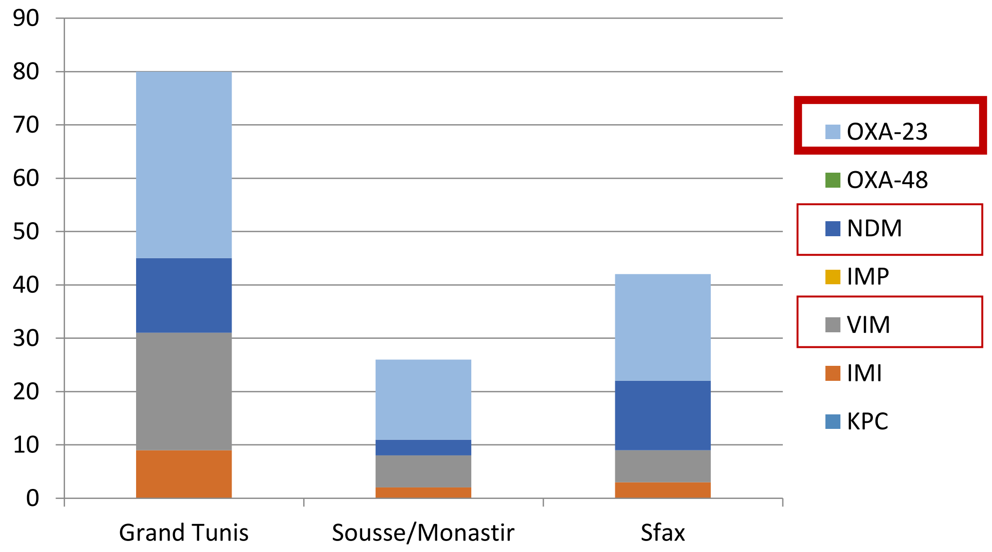
Figure 2. Hypervirulent *Klebsiella pneumoniae* (hvKp) ST23-K1 lineage isolates, by presence or absence of a carbapenemase gene and year of isolation, EU/EEA (n=194)*†



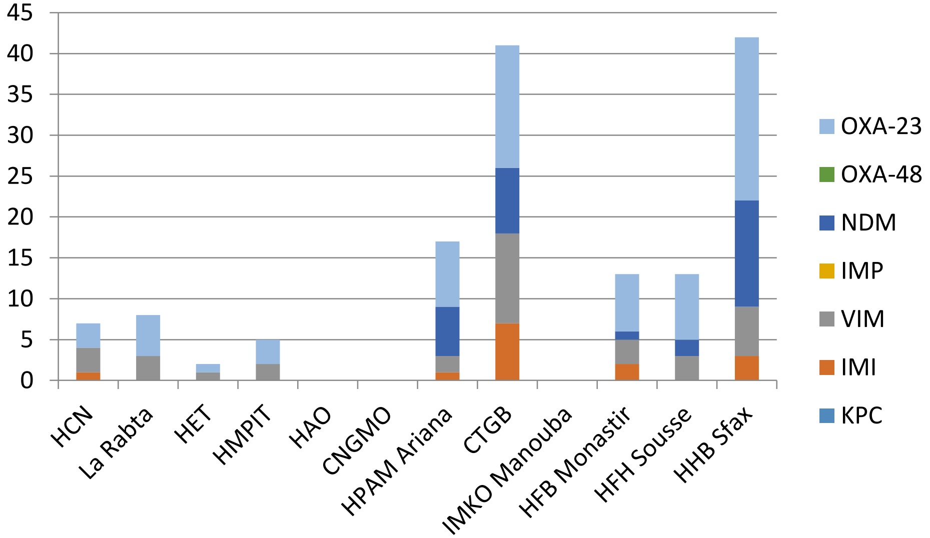
(ECDC, first update 14 February 2024)

Gènes de carbapénémases
A. baumannii

Fonction de la région

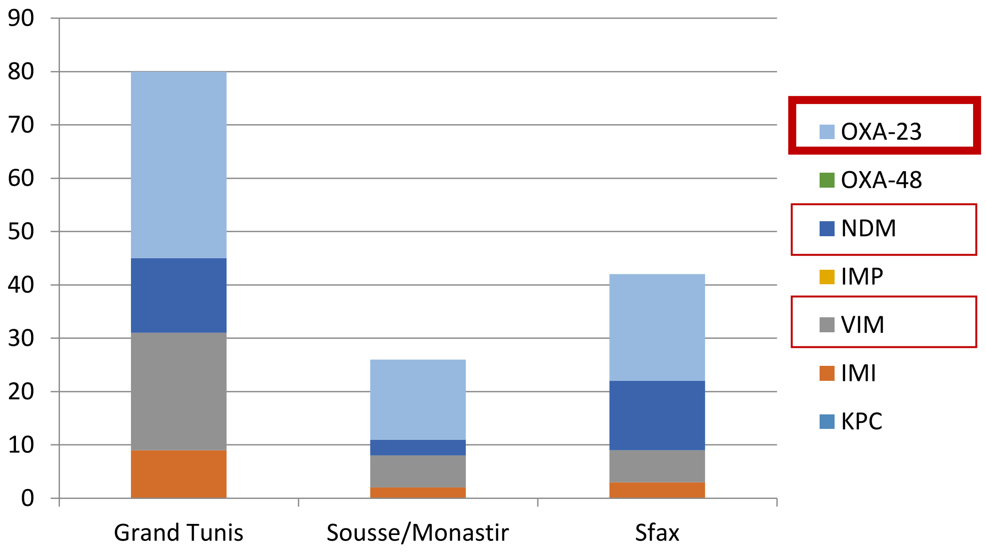


Fonction du CHU



Gènes de carbapénémases
A. baumannii

Fonction de la région

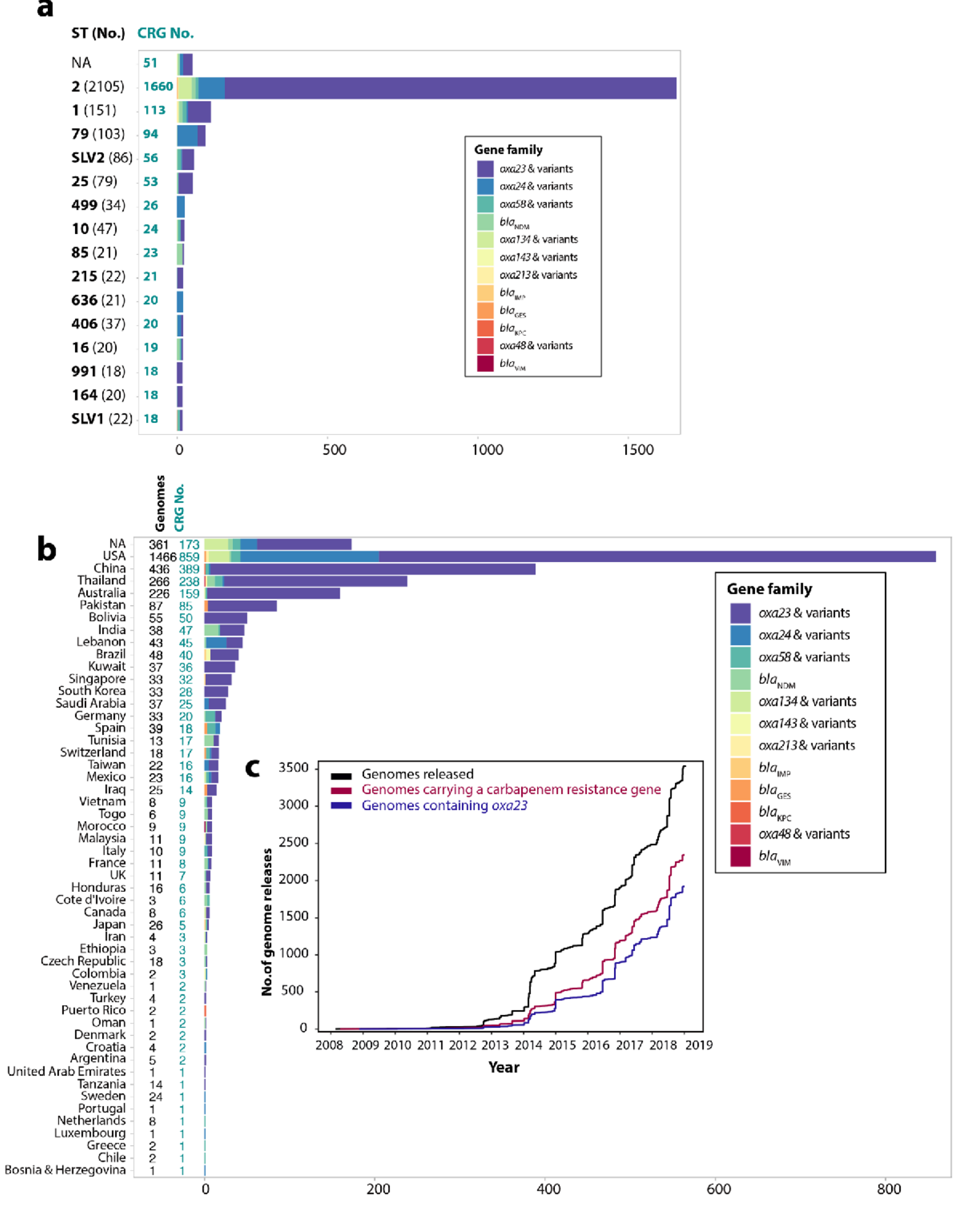


☛IMKO et HMPIT : 2 souches, **blaOXA-23** (Chihi H et al. J Glob Antimicrob Resist. 2016 Jun;5:47-50)

☛ CTGB : 1ère description en Tunisie de diffusion clonale d'*A. baumannii* blaPER-1 + **blaOXA23** + blaADC, origine environnementale probable (A. . MABROUK, Acta Microbiol Immun Hung 2020); 67 (4): 222–7)

☛ IMKO : 13 souches, **OXA-23**, en association avec KPC-2 chez une souche ➔ 1ère description de cette enzyme en Tunisia chez *A. baumannii* (D. Miniaoui et al.,.J Infect Dev Ctries 2023; 17(11):1591-7)

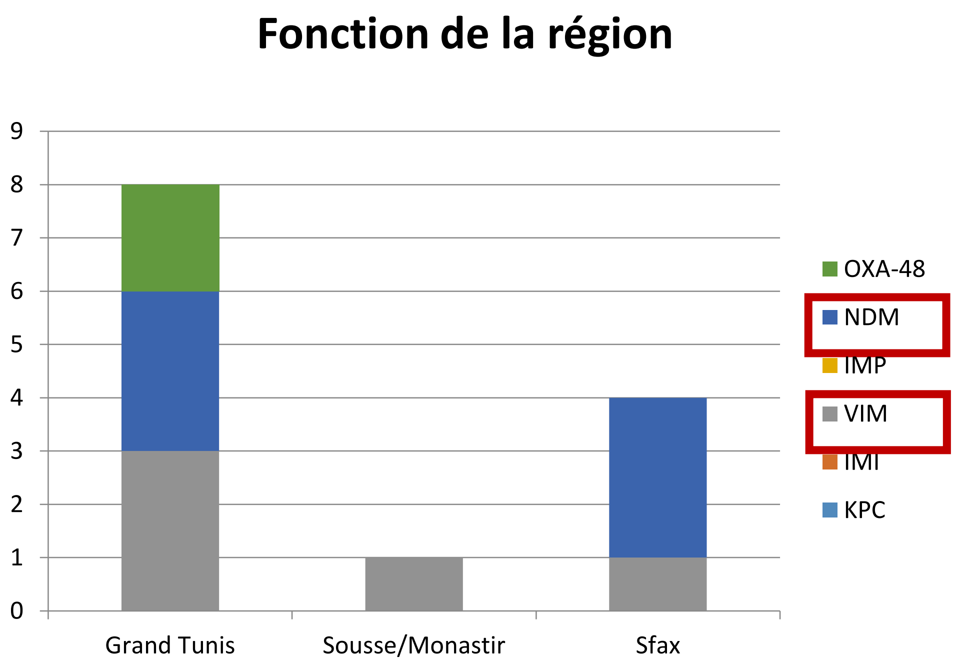
Génomes d'*A. baumannii* (2008- 2019)



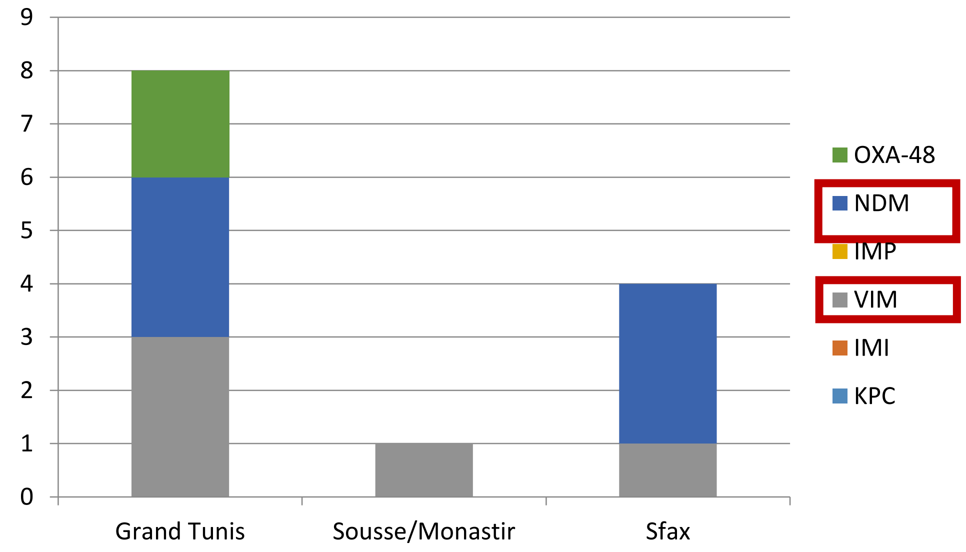
(Hamidian and Nigro, *Microbial Genomics 2019;5)*

Gènes de carbapénémases

P. aeruginosa



Gènes de carbapénémases
P. aeruginosa

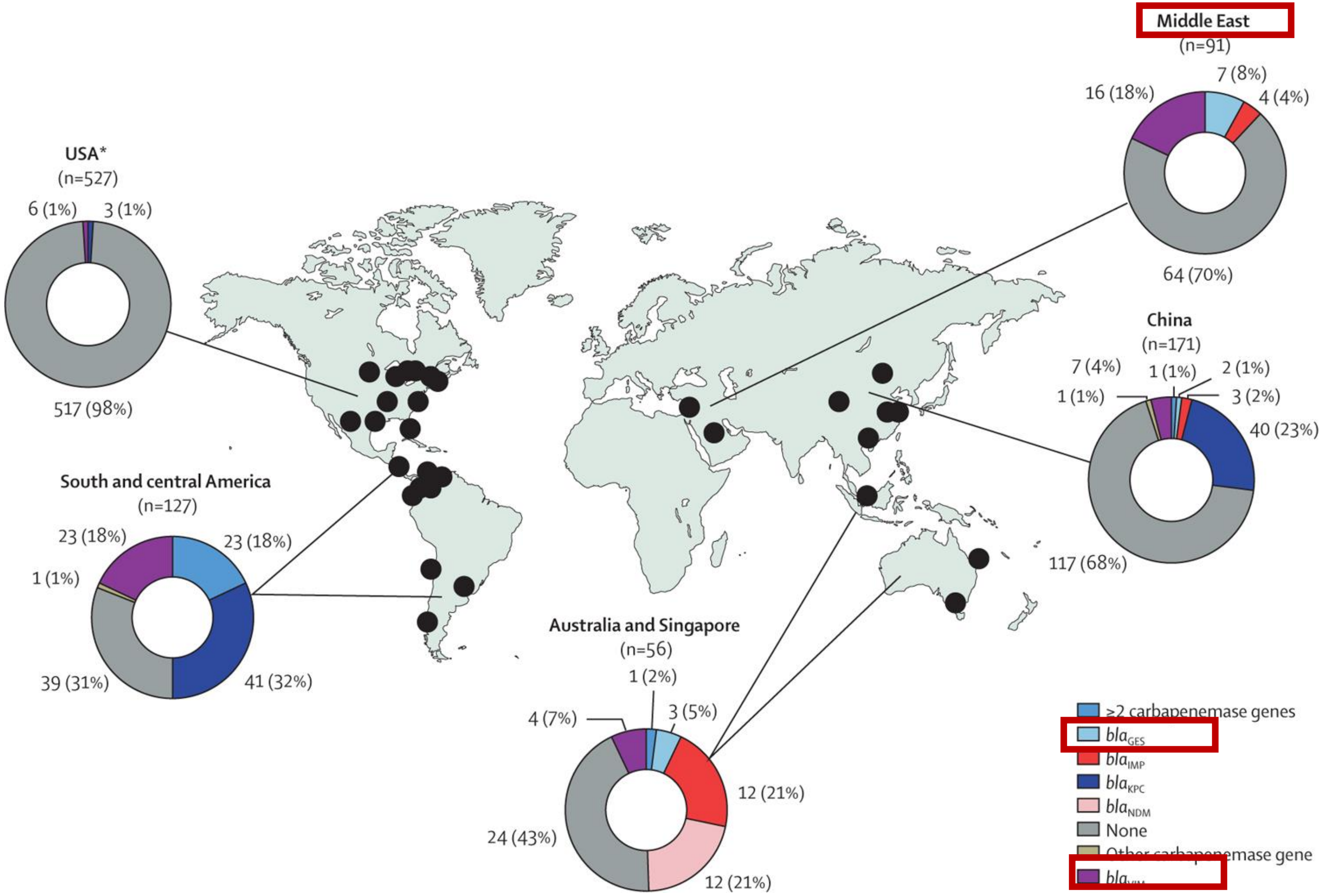


☛HCN : 35 souches, 2014-2017, **bla GES** (n=16, GES-5+++) et **bla VIM** (n=11, VIM-2+++) (S. Ferjani. et al, Antibiotics 2022, 11, 858)

☛ HMPIT : 57 souches, 2018 –2019, **bla GES** (n=36, GES-5+++) et **bla VIM-2** (n=4), altérations OprD (n=18), nouveaux intégrons portant bla_{GES-29}, bla_{GES-45} et bla_{VIM-2}, 24 pulsotype, 13 ST (3 nouveaux) (Fethi M et al., Antibiotics 2023;12(9):1394)

☛ CTGB : 67 souches, 2018, **blaVIM** (n=58) et **bla GES** (n=55), 1ère description de *P. aeruginosa* blaVIM-2+blaGES-5 (n=48) (S Hmissi et al., Acta Microbiol Immunol Hung. 2023;70(3):199-205)

☛ IMKO : 1 souche, **blaVIM-2** (D. Miniaoui et al.,.J Infect Dev Ctries 2023; 17(11):1591-7)



(J. Reyes, Lancet Microbe 2023; 4: e159–70)

En cours de réalisation

- Pour les souches ayant des PCR (-)
  - Vérification de la production de carbapénémase par les tests phénotypiques
  - Recherche des types rares (par PCR) ou de nouveaux types de carbapénémases (par séquençage du génome total

  ☛ Identification des mécanismes de résistance aux carbapénèmes

- Typage moléculaire des souches par RAPD / ERIC-PCR (screening) et MLST (souches clonales) ☛ Circulation des souches en Tunisie

Conclusion (I)

- *Enterobacterales* :
  - bla NDM et bla OxA-48, associations +++
- *A. baumannii* :
  - bla OXA-23, suivi de bla NDM et bla VIM, associations ++
- *P. aeruginosa* :
  - bla NDM et bla VIM

Conclusion (II)

Mesures de prévention et de contrôle des BGN carbapénèmes R
(*Enterobacterales, A. baumannii* et *P. aeruginosa*)

- Implementation of multimodal infection prevention and control strategies
- Importance of hand hygiene compliance for the control of CR bacteria
- Environmental cleaning
- Surveillance cultures of the environment for CR bacteria colonization/contamination
- Surveillance of CR bacteria infection and surveillance cultures for asymptomatic CR Enterobacterales colonization
- Contact precautions
- Patient isolation
- Antimicrobial stewardship
  Monitoring, auditing and feedback
- Monitoring, auditing and feedback

CRE: carbapenem-resistant

(Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities. Geneva: World Health Organization; 2017)

Conclusion (II)

Mesures de prévention et de contrôle des BGN carbapénèmes R (*Enterobacterales, A. baumannii* et *P. aeruginosa*)

Implementation of multimodal infection prevention and control strategies	Importance of hand hygiene compliance for the control of CR bacteria	Environmental cleaning
Surveillance cultures of the environment for CR bacteria colonization/contamination	Surveillance of CR bacteria infection and surveillance cultures for asymptomatic CR Enterobacterales colonization	Contact precautions
Patient isolation	Antimicrobial stewardship Monitoring, auditing and feedback	Monitoring, auditing and feedback

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Corrélation consommation / R aux carbapénèmes

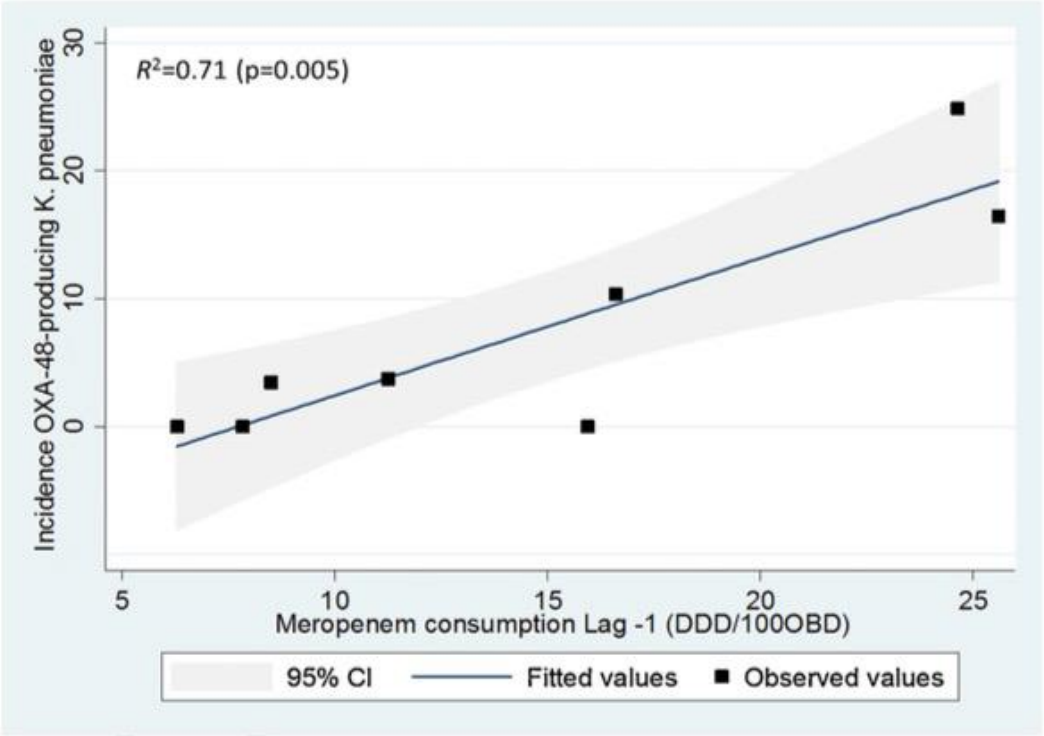

Fig. 1. Cross-correlation between meropenem consumption lag −1 (the preceding year) and the incidence rate of OXA-48-producing *Klebsiella pneumoniae* in a West London renal unit from 2008–2009 to 2013–2014.

(Gharbi M. Forecasting carbapenem resistance From antimicrobial consumption surveillance: Lessons learnt from an OXA-48-producing Klebsiella pneumoniae outbreak in a West London Renal unit. Int J Antimicrob Agents (2015)

Merci pour votre attention