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Resistance and persistence in *Staphylococcus aureus* clinical isolates from Vietnam

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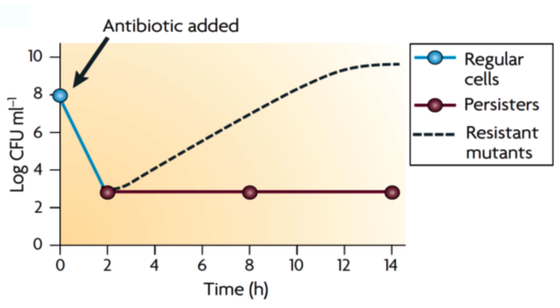
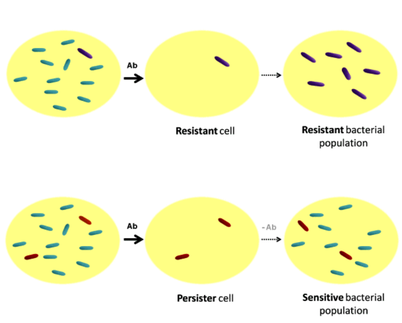
Background

Therapeutic failures may result from the development of resistant as well as persister phenotypes. Resistance is reaching alarming levels worldwide, especially in Asian countries like Vietnam. Persisters are defined as the fraction of antibiotic-treated bacteria that are refractory to antibiotic killing. This phenotype is not genetically-inherited, reversible upon antibiotic removal and associated to transient dormant lifestyles (1).





https://www.biw.kuleuven.be/dtp/cmpg/spi/research.aspx

Using *S. aureus* collected from persistent/recurrent infections in Vietnam, this work aims at studying their resistance to antibiotics as well as their persistent character after exposure to a selected antibiotic (moxifloxacin [MXF]) in broth.

Methods

➢ **Isolates:**
Clinical *S. aureus* isolates collected at the Bach Mai Hospital (Hanoi, Vietnam) from patients
- still infected after 5 days treatment with an active antibiotic
- or presenting a recurrence from a previous infection,
- and for whom data on antibiotic treatment were available.

Reference strain: ATCC 25923.

➢ **Typing:** *spa* typing (*Staphylococcus* protein A gene typing); PCR detection of *mecA* and *mecC* for MRSA.

➢ **MIC determinations:** microdilution (CLSI recommend-dations) with susceptibility assessed according to EUCAST criteria. MDR was defined strains presenting one or more of the following criteria (2):
- MRSA
- non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial categories

➢ **Persistence test in broth:** exposure of bacteria to antibiotics at 100 x MIC for 5 h; CFU counting; number of persisters and persister fraction calculated as follows:

$$\%\ \text{of persisters} = \frac{\text{CFU/mL for antibiotic-exposed cultures}}{\text{CFU/mL for controls (no antibiotic)}}$$

$$\text{Persister fraction} = \frac{\%\ \text{of persisters for clinical isolate}}{\%\ \text{of persisters for ATCC 25923}}$$

References

1. Cohen *et al, Cell Host Microbe* (2013) **13**: 632-642.
2. Magiorakos *et al*, *Clin Microbiol Infect* (2011) **18**: 268–281

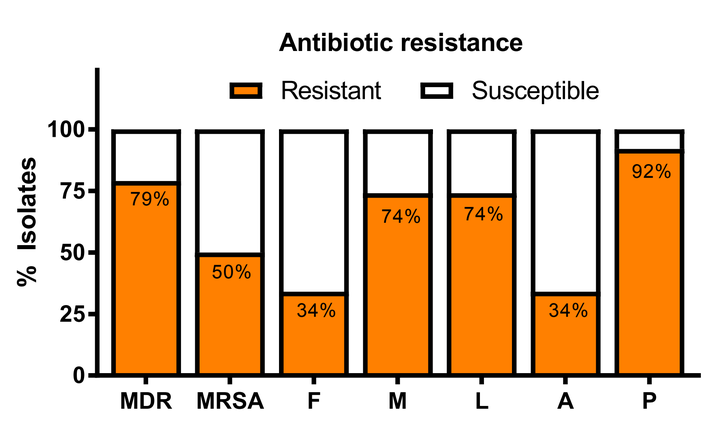
This poster will be made available for download after the meeting at http://www.facm.ucl.ac.be/posters.htm

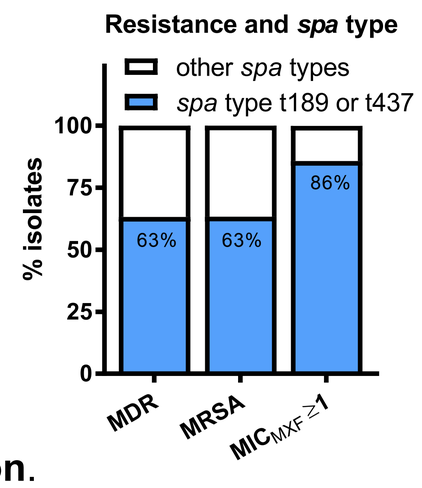
Results

The Table shows the *spa* type, phenotype of resistance as well as the moxifloxacin MIC and persister fraction after exposure to moxifloxacin for 38 clinical isolates from persistent infections

	Ref	*spa* type	Resistance[a]	MIC_{MXF}	P_{MXF}[b]		Ref	*spa* type	Resistance[a]	MIC_{MXF}	P_{MXF}[b]
MSSA, *mecA*, *mecC* negative	7	t056	A, K, L, M, P	0.06	1.4	MRSA, *mecA* positive	1	t008	K, L, M	0.06	1.2
	10	t189	K, L, M, P	0.06	2.4		3	t021	K, L, M	0.06	0.2
	11	t437	K, L, M, P	0.06	2.5		4	t1451	K, L, M	0.06	1.2
	12	t437	A, F, K, L, M, P	2	176.7		5	t008	P	0.06	1.8
	13	t437	P, F	2	29.0		6	t002	K, L, M	0.03	7.8
	14	t437	P, F	2	9.0		8	t657	K, L, M	0.25	1.0
	15	t034	A, C, F, K, L, M, P	2	138.3		9	t437	K, L, M	0.06	3.9
	18	t437	P, T	0.03	1.0		16	t437	A, M, L, T	0.06	4.9
	19	t437	P, T	0.03	0.8		17	t437	A, L, M	0.03	1.3
	20	t2883	A, C, F, K, L, M, P	2	60.7		22	t189	A, C, F, K, L, M, T	2	111.3
	21	t189		0.03	2.2		23	t189	A, C, F, K, L, M, T	2	100.7
	24	t437	A, F, K, L, M, P	2	403.3		28	t437	K, L, M	0.03	45.7
	25	t034	L, M, P	0.06	0.8		29	t437	K, L, M	0.03	6.2
	26	t189	F, L, M	1	289.3		30	t437	K, L, M	0.06	8.7
	27	t159	P	0.03	1.5		31	t189	A, C, F, K, L, M	1	91.7
	33	t304	P	0.03	6.7		36	t437	K, L, M	0.03	9.0
	34	t189	A,C, F, K, L, M, P	2	83.3		37	t1250	L, M, T	0.06	24.7
	35	t189	A,C, F, K, L, M, P	2	227.7		38	t189	A, C, F, K, L, M	2	175.7
	39	t159	P	0.03	79.2		40	t189	A, C, F, K, L, M	1	273.0

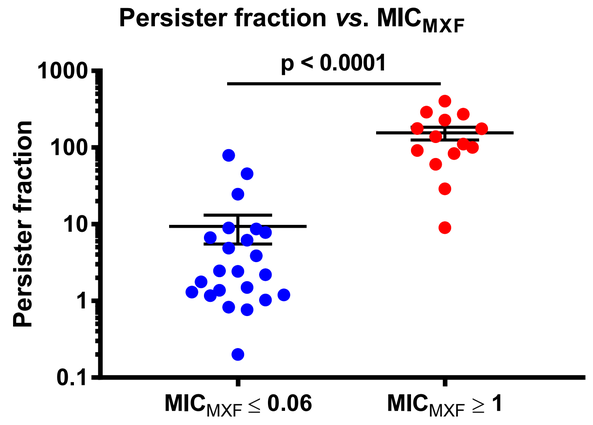
[a]A: Aminoglycoside; C: Co-trimoxazole; F: Fluoroquinolone; K: Ketolide; L: Lincosamide; M: Macrolide, P: Penicillin; T: Tetracycline. [b]Persister fraction.

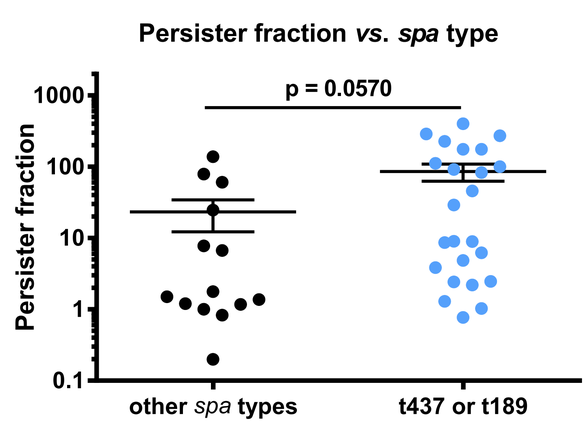




➢ **Resistance rates were high in this collection.**

➢ **12/14 isolates with elevated MIC to MXF belonged to *spa* types t189 or t437.** These *spa* types were also more frequent in MRSA and MDR isolates.





➢ **Persister fraction was higher in isolates with $MIC_{MXF} \geq 1$ mg/L**

➢ **There was only a trend to higher persister fraction in *spa* types t189 or t437**

Conclusion

Clinical isolates of *S. aureus* from Vietnam have high rate of resistance in specific *spa* types. Low susceptibility to MXF is associated with a higher propensity to form persisters after exposure to the drug, which may further contribute to therapeutic failures.

Acknowledgments

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