TABLE S1 Susceptibility of the selected *P. aeruginosa* strains to therapeutic antipseudomonal ß-lactams.

Strains	Origin	Sample	*ampC* expression [a]	PDC	MIC (µg/mL) [b]							
					TIC	TZP	ATM	CAZ	FEP	CZ/T	IMP	MER
Strains producing wild-type AmpC												
PAO1	Reference		1	PDC-1	32	4	4	2 (1) [c]	2	0.5 (0.5)	1	≤0.25
4098	Reference		ND	PDC-1	16	4	4	1 (1)	1	0.5 (≤0.25)	≤0.5	≤0.25
PAO1Δ*dacB*	Reference		290	PDC-1	64	32	8	16 (2)	8	1 (0.5)	1	0.5
14.2028	Bourg S^{t} M^{ce}	Urine	239	PDC-3	128	16	16	4 (4)	16	2 (1)	16	8
13.1642	Nancy	Rectal swab	3,329	PDC-8	256	256	128	64 (4)	32	4 (1)	4	2
13.1781	Montpellier	CF sputum [d]	26.0	PDC-24	512	256	64	128 (8)	64	4 (2)	32	16
PA14	Reference		ND	PDC-34	16	≤2	2	1 (≤0.5)	1	≤0.25 (≤0.25)	≤0.5	≤0.25
11.773	Bellegarde	Urine	511	PDC-35	256	64	16	8 (8)	8	1 (1)	8	8
Strains producing ESAC												
12.1227	Besançon	Stool	737	PDC-44	64	16	16	32 (16)	>64	4 (1)	4	8
12.1255	Besançon	Catheter	2,895	PDC-44	128	128	64	512 (64)	>64	32 (4)	16	16
10.257	Besançon	COPD [e]	2,120	PDC-50	256	128	64	256 (64)*	32	8 (4)*	8	2
12.1285	S^{t} Denis R^{n}	Rectal swab	188	PDC-73	32	≤2	8	16 (1)*	16	0.5 (≤0.25)*	≤0.5	≤0.25
12.1111	Brest	CF sputum	1,233	PDC-74	128	4	16	16 (8)	8	1 (1)	16	8

13.1716	Pessac	CF sputum	12	PDC-74	>512	64	128	>512 (64)	>64	32 (32)	4	4
12.1129	Toulouse	CF sputum	267	PDC-75	256	≤2	64	64 (32)	8	4 (2)	16	8
13.1727	Toulouse	CF sputum	46.6	PDC-75	128	≤2	16	16 (4)	16	1 (0.5)	16	4
13.1415	Nantes	CF sputum	4.4	PDC-76	≤4	≤2	≤1	64 (32)*	8	16 (8)*	32	16
13.1404	Martigues	Wound	73.2	PDC-77	512	8	64	64 (32)	16	8 (4)	16	8
13.1696	Marseille	Tr. aspirate[f]	173	PDC-77	512	16	64	128 (64)	16	8 (4)	16	8
13.1760	Tours	CF sputum	112	PDC-77	256	16	64	64 (32)	16	8 (4)	16	8
11.571	Gap	COPD	688	PDC-78	256	16	64	64 (32)	16	8 (2)	8	4
11.516	Besançon	Tr. aspirate	202	PDC-79	256	16	32	256 (128)	16	64 (64)	2	4
13.1737	Amiens	Tr aspirate	114	PDC-80	512	128	64	256 (128)	16	64 (64)	1	4
13.1514	Besançon	CF sputum	31.4	PDC-81	>512	128	64	>512 (32)	>64	16 (8)	32	16
13.1770	Besançon	COPD	1,147	PDC-82	512	64	128	256 (128)	32	64 (64)	1	0.5
4836	Besançon	CF sputum	8.5	PDC-83	256	8	16	256 (32)*	64	4 (4)*	8	4
13.1482	Nancy	CF sputum	35.4	PDC-84	256	64	128	>512 (64)	>64	>64 (16)	2	2
12.961	Amiens	CF sputum	37.9	PDC-85	128	≤2	8	16 (8)	8	32 (16)	1	0.5
13.1755	Wissous	COPD	192	PDC-86	>512	32	64	>512 (512)	32	>64 (>64)	8	8
14.1999	Besançon	Tr. aspirate	2,351	PDC-86	>512	64	128	>512 (512)	32	>64 (>64)	≤0.5	≤0.25
11.698	Montpellier	Urine	1,439	PDC-87	>512	64	32	>512 (512)	32	8 (2)	16	8
13.1775	Montpellier	Urine	2,322	PDC-87	>512	32	32	512 (64)	32	8 (4)	16	4

13.1601	Grenoble	Blood	345	PDC-88	128	256	32	512 (32)	>64	16 (4)	16	16
09.236	Besançon	Stool	1,502	PDC-89	128	64	64	256 (64)	>64	16 (8)	8	8
13.1562	Besançon	Stool	1,238	PDC-90	16	16	8	64 (32)	>64	4 (2)	8	4
11.813	Paris	Rectal swab	289	PDC-91	32	16	8	64 (16)	>64	4 (2)	4	4
12.1121	Bordeaux	COPD	1,009	PDC-92	128	64	32	128 (64)	>64	8 (4)	8	16
13.1389	Bordeaux	Blood	449	PDC-92	128	32	32	128 (64)	>64	4 (4)	8	16
14.2036	Pau	Sputum	184	PDC-93	128	32	32	128 (32)	>64	4 (2)	8	8

[a] values from two independent cultures with duplicate determinations

[b] values from at least two independent experiments

[c] values in brackets represent the MIC for bacteria grown in the presence of 1,000 µg/mL of cloxacillin (* 250 µg/mL when inhibited by 1,000 µg/mL)

[d] cystic fibrosis sputum

[e] chronic obstructive pulmonary disease sputum

[f] tracheal aspirate

Abbreviations: TIC (ticarcillin), TZP (piperacillin plus tazobactam at a fixed concentration of 4 µg/mL), ATM (aztreonam), CAZ (ceftazidime), FEP (cefepime), CZ/T (ceftolozane plus tazobactam at a fixed concentration of 4 µg/mL), IMP (imipenem), MER (meropenem).

TABLE S2 ESAC-associated mutations in various class C ß-lactamases

Enzyme name	ESAC-associated mutations	Domain	Position in *P. aeruginosa* AmpC	Reference
E. coli AmpC	S duplication at position 282	H-9 helix	R283	(1)
	I duplication at position 283	H-9 helix	L284	(2)
	Δ(G286-D288)	H-9 helix near R2 loop	G287-S289	(3)
	S287C	H-9 helix near R2 loop	N288	(4)
	S287N	H-9 helix near R2 loop	N288	(5)
	A292V	R2 loop	**A293**	(6)
	L293S	R2 loop	**L294**	(7)
	AA insertion between L293-A294	R2 loop	**L294-Q295**	(8)
	LAA insertion at position 295	R2 loop	P296	(6)
	H/R/L/296P	R2 loop	H297	(4)
	V298L	R2 loop	I299	(4)
	V350F	H-11 helix	V351	(4)
Enterobacter AmpC	Δ(K193-G206)	omega loop	E194-D208	(9)
	tandem repeat A211 to R213	omega loop	P210-L211-**R212**	(10)
	Δ(S289-A294)	R2 loop	**T290-Q295**	(11)
	V291G	R2 loop	**M292**	(12)
	L293P	R2 loop	**L294**	(13)
	N346H/I	H-11 helix	**N347**	(9)
S. marcescens AmpC	T58I	H-2 helix	T70	(14)
	E219K	omega loop	**E221**	(15)
	S220Y	omega loop	G222	(16)
	Δ(M287-T290)	R2 loop	**L294-Q295**	(17)
C. freundii AmpC	R148H	near Y-X-N loop	R149	(18)

CMY	V211G (CMY-30) [a]	omega loop	**V213**	(19)
	V211S (CMY-42)	omega loop	**V213**	(20)
	V211A (CMY-95)	omega loop	**V213**	(7)
	G214E (CMY-32)	omega loop	**G216**	(21)
	I292S (CMY-19)	R2 loop	**A293**	(22)
	L316I (CMY-37)	R2 loop	H297	(23)
	N346I (CMY-10)	H-11 helix	**N347**	(24, 25)
ACC-1	V211G (ACC-4)	omega loop	**V213**	(26)
A. baumannii ADC	P210R and AA215 (ADC-33)	omega loop	**P215, A220**	(27)
	V208A (ADC-53)	omega loop	**V213**	(28)
	N283S (ADC-51)	H10 near R2 loop	N288	(28)
	R148Q (ADC-56)	not specified	R149	(29)
	P194A, G220D, R320G (ADC-68)	omega loop and C-loop	P193, **D219**, G322	(30)
P. aeruginosa AmpC	F121L	alpha3-alpha4 loop		This study and (31)
	P154L	H-5 helix		This study
	G157D	H-5 helix		(32)
	M175L	H-6 helix		This study
	Δ(R212-L218)	omega loop		(32)
	V213A	omega loop		This study
	G216R	omega loop		This study
	Δ(D219-Y223)	omega loop		(32)
	E221K	omega loop		This study and (31)
	E221G	omega loop		This study
	Y223H	omega loop		This study
	Δ(T290-P291)	R2 loop		This study
	Δ(T290-M292)	R2 loop		This study
	Δ(T290-A293)	R2 loop		This study

Δ(L294-Q295)	R2 loop	This study
L294P	R2 loop	This study
N347I	C3/C4-carboxylate binding	This study

[a] Name of ESAC

Amino acid positions indicated in bold have been found to be mutated both in *P. aeruginosa* AmpC and other class C ß-lactamases considered as ESAC.

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