

Supplemental Material

Imipenem heteroresistance but not tolerance in *Haemophilus influenzae* during chronic lung infection associated with chronic obstructive pulmonary disease

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Table S1. AcrB truncated variants identified in the *H. influenzae* strain collection under study.

Table S2. AcrR truncated variants identified in the *H. influenzae* strain collection under study.

Table S3. Summary of FtsI, ArcA, ArcB and ArcR variant distribution across *H. influenzae* strain collection.

21 **Table S1.** AcrB truncated variants identified in the *H. influenzae* strain collection under study. “.” indicates no amino acid substitution; * indicates
 22 early stop codon.

Strain Amino acid substitution for:

Rd	M	K	F	T	D	I	F	I	R	R	P	V	L	A	V	S	I	S	L	L	M	I	I	L	G	L	Q	A	I	S	K	L	A	V	R	E	Y	P	K	M	T	T	T	v	I	T	V	S	T					
KW20	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49					
P615	
P616	
P600	
P601	
P602

Rd	Y	P	G	A	D	A	N	L	I	Q	A	F	V	T	S	K	L	E	E	S	I	A	Q	A	D	N	I	D	Y	M	S	S	T	S	A	P																							
KW20	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86																							
P615			
P616			
P600		
P601		
P602

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Table S2 (continued).

Strain	Amino acid substitution for:							
	Rd	T	I	L	S	N	L	K
KW20	100	101	102	103	104	105	106	
P612	P	L	F	Y	P	I	*	
P615	P	L	F	Y	P	I	*	
P616	P	L	F	Y	P	I	*	
P620	P	L	F	Y	P	I	*	
P621	P	L	F	Y	P	I	*	
P623	P	L	F	Y	P	I	*	
P624	P	L	F	Y	P	I	*	
P629	P	L	F	Y	P	I	*	
P600	P	L	F	Y	P	I	*	
P601	P	L	F	Y	P	I	*	
P602	P	L	F	Y	P	I	*	
P613	P	L	F	Y	P	I	*	
P614	P	L	F	Y	P	I	*	
P618	P	L	F	Y	P	I	*	
P622	P	L	F	Y	P	I	*	
P632	P	L	F	Y	P	I	*	
P633	P	L	F	Y	P	I	*	

37 **Table S3.** Summary of FtsI, ArcA, ArcB and ArcR variant distribution across *H. influenzae*
 38 strain collection. Information summarized in four groups: (i) four-gene variant combinations
 39 present in susceptible, heteroresistant and resistant strains; (ii) four-gene variant combinations
 40 present in susceptible strains; (iii) four-gene variant combinations present in heteroresistant
 41 strains; (iv) four-gene variant combinations present in resistant strains.

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Clonal Type (CT)	Patient	Phenotype	Allelic variant FtsI	Allelic variant AcrA	Allelic variant AcrB	Allelic variant AcrR
14	2, 10	S, H1	12	10	11	8
17, 47	8, 12	S, H1	13	11	12	4
48	4, 6	S, H1, H2	8	6	Truncated	Truncated
48	6, 7, 8	S, H2	8	6	8	Truncated
27, 72	1, 5	S, H1	14	4	6	4
95	7, 13	R, H2	5	3	5	3
3, 28, 106	12, 13	S	19	4	12	4
6	7	S	20	14	16	3
7	13	S	1	6	17	11
16	3	S	19	4	18	4
35	6	S	19	4	19	4
38	10	S	21	15	20	Truncated
45	3	S	22	16	21	12
52	5	S	15	17	22	6
54	10	S	17	13	23	10
59	2	S	23	18	24	13
76	12	S	23	18	25	14
100	11	S	23	19	13	Truncated
107	1	S	24	7	26	Truncated
119	5	S	25	20	27	15
137	4, 8	S	17	4	28	4
138	6	S	14	4	25	4
140	3	S	26	21	29	Truncated
145	5	S	21	11	12	4
146	1	S	27	21	30	Truncated
8, 87	6, 10	H1, H2	10	8	9	3
9	1	H1	11	9	10	7
18	10	H2	6	4	6	4
40	5	H1, H2	7	5	7	5
73	4, 10	H1, H2	9	7	5	6
83	10	H1	15	7	5	6
91	10	H1	16	12	13	8
105	11	H1	17	13	14	9
124	8	H1	18	4	12	4
135	2	H1	17	13	15	10
44	6, 9	R	2	2	2	2
44	6, 9	R	3	2	3	2
44	6, 9	R	4	2	4	2

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