

1 Supplementary Table 1: Genomic variants across all *E. hormaechei* isolates.

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Isolate	Gene_name	Gene_id	Var_type
E_1	ampD	CPT31_04100	IS110
E_43	wecA	CPT31_00845	NONSEN
E_43	ampD	CPT31_04100	NONSYN
E_43	mdoH	CPT31_08425	NONSYN
E_100	ampD	CPT31_04100	IS110
E_100	ampD	CPT31_04100	INTERGENIC
E_100	ampD	CPT31_04100	INTERGENIC
E_100	ampD	CPT31_04100	INTERGENIC
E_100	z14285/z14295	CPT31_14285/CPT31_14295	INDEL
E_100	igaA	CPT31_21550	NONSYN
E_100	pstC	CPT31_23350	NONSYN
E_134	ampD	CPT31_04100	IS110
E_134	ampD	CPT31_04100	INTERGENIC
E_134	ampD	CPT31_04100	INTERGENIC
E_134	ampD	CPT31_04100	INTERGENIC
E_134	z14285/z14295	CPT31_14285/CPT31_14295	INDEL
E_134	igaA	CPT31_21550	NONSYN
E_134	pstC	CPT31_23350	NONSYN
E_134	z00130	CPT31_00130	FRAMESHIFT
E_134	ramR	CPT31_05845	FRAMESHIFT
E_134	Plasmid1-z24450	CP023570-CPT31_24450	INTERGENIC
E_243	ampD	CPT31_04100	NONSYN
E_243	z08735	CPT31_08735	FRAMESHIFT
E_243	z14285	CPT31_14285	IS5
E_243	Plasmid2	CP023571	PLASMID_LOSS
E_243	Plasmid1	CP023570	INDEL
E_243	z05910	CPT31_05910	INTERGENIC
E_276	ampD	CPT31_04100	NONSYN
E_276	z08735	CPT31_08735	FRAMESHIFT
E_276	z14285	CPT31_14285	IS5
E_276	mdtK	CPT31_09220	IS5
E_276	mgrB	CPT31_12870	IS6
E_276	ompC	CPT31_15015	IS6
E_276	z15915	CPT31_15915	IS6
E_276	z16020	CPT31_16020	IS6
E_276	Plasmid1-z24230	CP023570-CPT31_24230	NONSEN
E_276	Plasmid1-z24095	CP023570-CPT31_24095	FRAMESHIFT

E_276	z00945	CPT31_00945	FRAMESHIFT
E_276	z00945	CPT31_00945	INTERGENIC
E_276	hflC	CPT31_02495	NONSEN
E_276	Plasmid1-z24975	CP023570-CPT31_24975	IS6
E_276B	ampD	CPT31_04100	NONSYN
E_276B	z08735	CPT31_08735	FRAMESHIFT
E_276B	z14285	CPT31_14285	IS5
E_276B	Plasmid2	CP023571	PLASMID_LOSS
E_276B	mdtK	CPT31_09220	IS5
E_276B	mgrB	CPT31_12870	IS6
E_276B	ompC	CPT31_15015	IS6
E_276B	z15915	CPT31_15915	IS6
E_276B	z16020	CPT31_16020	IS6
E_276B	Plasmid1-z24230	CP023570-CPT31_24230	NONSEN
E_276B	Plasmid1-z24095	CP023570-CPT31_24095	FRAMESHIFT
E_276B	treC	CPT31_02890	NONSYN
E_276B	phoE	CPT31_07945	IS6
E_276B	mdtH	CPT31_08495	IS6
E_276B	phoQ	CPT31_08825	NONSYN
E_276B	mdtK	CPT31_09620	NONSYN
E_276B	z10995	CPT31_10995	NONSYN
E_276B	z15040	CPT31_15040	NONSYN
E_276B	z15710	CPT31_15710	IS6
E_276B	hisD	CPT31_17420	FRAMESHIFT
E_277	ampD	CPT31_04100	NONSYN
E_277	z08735	CPT31_08735	FRAMESHIFT
E_277	z14285	CPT31_14285	IS5
E_277	mdtK	CPT31_09220	IS5
E_277	mgrB	CPT31_12870	IS6
E_277	ompC	CPT31_15015	IS6
E_277	z15915	CPT31_15915	IS6
E_277	z16020	CPT31_16020	IS6
E_277	Plasmid1-z24230	CP023570-CPT31_24230	NONSEN
E_277	z00945	CPT31_00945	FRAMESHIFT
E_277	z00085	CPT31_00085	SYN
E_277	deoR	CPT31_07370	INDEL
E_277	deoR	CPT31_07370	INTERGENIC
E_277	phoE	CPT31_07945	IS6
E_277	z15020/z15035	CPT31_15020/CPT31_15035	IS6-INDEL
E_277	z18300	CPT31_18300	FRAMESHIFT

E_277	z21555	CPT31_21555	NONSYN
E_277	Plasmid1	CP023570	INDEL
E_277	Plasmid2	CP023571	INDEL
E_277	z21410	CPT31_21410	NONSYN
E_277	rluC	CPT31_08610	NONSYN
E_279	ampD	CPT31_04100	NONSYN
E_279	z08735	CPT31_08735	FRAMESHIFT
E_279	z14285	CPT31_14285	IS5
E_279	mdtK	CPT31_09220	IS5
E_279	mgrB	CPT31_12870	IS6
E_279	ompC	CPT31_15015	IS6
E_279	z15915	CPT31_15915	IS6
E_279	z16020	CPT31_16020	IS6
E_279	Plasmid1-z24230	CP023570-CPT31_24230	NONSEN
E_279	Plasmid1-z24095	CP023570-CPT31_24095	FRAMESHIFT
E_279	z00945	CPT31_00945	FRAMESHIFT
E_279	Plasmid2	CP023571	PLASMID_INTEGRATION
E_279	ompD	CPT31_11335	IS5
E_279	z15560	CPT31_15560	IS6
E_279	mgrB/z13060	CPT31_12870/CPT31_13060	IS6-INDEL
E_279	z15515/z15560	CPT31_15515/CPT31_15560	IS6-INDEL
E_279	Plasmid1-z24760	CP023570-CPT31_24760	IS6
E_279	mgrB/z12915	CPT31_12870/CPT31_12915	IS6-INDEL
E_279	z15915/z15925	CPT31_15915/CPT31_15925	IS6-INDEL

4 **Supplementary Table 2. FICI scores for all isolates and four different combinations.**

Isolate	Combination	FICI
E_1	Meropenem (A) + Cefepime (B)	0.5
E_43		0.6
E_100		0.8
E_134		0.3
E_243		0.8
E_276		2.6
E_276B		2.5
E_277		5.1
E_279		2.5
E_1	Meropenem (A) + Gentamiicin (B)	0.3
E_43		0.9
E_100		0.6
E_134		0.5
E_243		0.6
E_276		0.7
E_276B		0.7
E_277		0.9
E_279		0.7
E_1	Meropenem (A) + Ciprofloxacin (B)	0.7
E_43		0.7
E_100		0.9
E_134		0.6
E_243		1
E_276		0.9
E_276B		1
E_277		1
E_279		0.7
E_1	Meropenem (A) + Sulfamethoxazole/trimethoprim (B)	0.5
E_43		0.7
E_100		2
E_134		2
E_243		0.4
E_276		1.4
E_276B		1
E_277		0.4
E_279		0.7

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6 **Synergistic interactions are shown in red, additive interactions in grey and antagonistic interactions in blue.**