Table 2. Characteristics of clinical heteroresistant mother E. faecalis strains and heteroresistance-derived E. faecalis clones

Table 2. Characteristics of clinical heteroresistant mother *E. faecalis* strains and heteroresistance-derived *E. faecalis* clones.

NO.	TGC MIC (mg/L)	NO.	TGC MIC (mg/L)	TGC+CCCP	TGC+PABN
EF16C186	0.0625	Tig0.5-EF16C186-1	2	<=0.06	2
		Tig0.5-EF16C186-2	2	<=0.06	2
NEFA53	0.125	Tig0.5-NEFA53-1	1	<=0.06	2
		Tig0.5-NEFA53-2	1	<=0.06	2
NEFA5	0.25	Tig0.5-NEFA5-1	2	<=0.06	2
		Tig0.5-NEFA5-2	2	<=0.06	2
NEFA37	0.25	Tig0.5-NEFA37-1	2	<=0.06	2
		Tig0.5-NEFA37-2	2	<=0.06	2
NEFA26	0.5	Tig0.5-NEFA26-1	2	<=0.06	2
		Tig0.5-NEFA26-2	2	<=0.06	2
NEFA27	0.5	Tig0.5-NEFA27-1	2	<=0.06	1
		Tig0.5-NEFA27-2	2	<=0.06	1
NEFA32	0.5	Tig0.5-NEFA32-1	2	<=0.06	2
		Tig0.5-NEFA32-2	2	<=0.06	2

Table 3. List of mutation-related genes, amino acids and proteins by comparison of whole genome between the parental isolate and the TGC-induced resistant strains

Table 3. List of mutation-related genes, amino acids and proteins by comparison of whole genome between the parental isolate and the TGC-induced resistant strains

Name of gene	Locus name Deng	Gene	Mutation in the genome of *E. fecalis* strains		
			Deng-T10-3	Deng-T60-1	KOG
Membrane protein	DENG_ 00157		Ala54Glu His56Asn	Ala54Glu His56Asn	None
Recombinase/integrase	DENG_00476		Leu921Leu Pro925Pro Leu937Leu Glu926Asp Asp929Glu Met942Lys	Leu921Leu Pro925Pro Glu926Asp Asp929Glu Leu937Leu	None
Iron compound ABC transporter, substrate-binding protein	DENG_00164		Arg155Ser	Arg155Ser	K02016
Hypothetical protein	DENG_00426		Gly32Gly	Gly32Gly	None
PTS system, IIB component	DENG_00444	manX		Glu113Gly	K02794
Lipoprotein, YaeC family	DENG_02183	metQ		Ser355Asn	K02073
No	DENG_00473		Asp166Asp	Asp166Asp	None
Aspartyl/glutamyl-tRNA amidotransferase subunit B	DENG_00775	gatB	Gly210Gly	Gly210Gly	K02434
Hypothetical protein	DENG_01621		Gly32Gly	Gly32Gly	None
Hypothetical protein	DENG_01950		A446A T438T L437L P428P Y422Y E421E G419G A400A N399N	A446A T438T L437L P428P Y422Y E421E G419G A400A N399N	None
N0	DENG_00799		Gly261Gly	Gly261Gly	None
2-C-methyl-D-erythritol 2,4-cyclodiphosphate synthase	DENG_00043	ispF	267_268del	267_268del	K01770
Uncharacterized HTH-type transcriptional regulator in lacX 3'region	DENG_00489		L336fs	L336fs	None

Conclusion: Our data indicated that the main mechanism of TGC heteroresistance in *E. faecalis* might be associated with the efflux pumps. TGC resistance in *E. faecalis* was associated with mutations in the 16SrRNA site or 30S ribosome protein S10. The genetic mutations in several enzymes and transfer systems might also participate in the resistance development to TGC in *E. faecalis*.

Disclosures. **All Authors**: No reported disclosures

1457. Serial Passage of Enterobacteriaceae to Explore Development of Carbapenem Resistance

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Session: P-66. Resistance Mechanisms

Background. Carbapenems are broad-spectrum antibacterials that have seen increased usage for the Enterobacteriales family in recent years. While carbapenem usage has been associated with increased antibacterial resistance, there is currently a lack of data comparing the risk of reduced susceptibility selection by the two most commonly used carbapenems in the US, ertapenem (ERT) and meropenem (MER). We conducted a novel serial passage experiment with clinical isolates of Enterobacteriales to assess the impact of repeated exposure to ERT or MER on phenotypic susceptibility patterns.

Methods. Non-duplicate clinical Enterobacteriales isolates were selected randomly for inclusion. Antimicrobial susceptibility testing was performed by CLSI disc diffusion methods. Standardized suspensions of isolates were plated on Mueller-Hinton agar, and ERT (10mcg) and MER (10mcg) discs applied. Zones of inhibition were measured and recorded after 16-18 hours incubation. Growth from the innermost zone of inhibition around each disc was used to prepare subsequent suspensions for serial susceptibility testing. This process would be repeated daily for 10 days. Each subsequent serially-passaged isolated was tested against both ERT and MER. Daily zones of inhibition were measured and interpreted. Baseline & final susceptibilities were determined by automated methods (Vitek 2).

Results. Seventeen Enterobacteriaceae isolates were selected, including*: Klebsiella pneumoniae* (n=11), *Klebsiella oxytoca* (n=2), *Escherichia coli* (n=1), *Morganella morganii* (n=1), and *Enterobacter cloacae* (n=2). Despite a greater degree of reductions in zones of inhibition with repeated ERT exposure (vs MER), the overall 10 day trends were not found to be significant different (P=0.529). Resistance developed to ERT in six isolates compared to one MER-resistant isolate (P = 0.053). *E. cloacae* was the only species to show a significant change between drugs (P=0.010). Two of three isolates that developed reduced zone changes > 10mm to MER were initially exposed to ERT on an earlier plate.

Conclusion. This novel experiment identified the development of some nonsignificant reductions in susceptibility with ERT after serial exposure. Results from this pilot study should encourage larger well-designed studies in this area.

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1458. Uncharted territories: applying "precision medicine" to understand the treacherous landscape of extensively and multidrug resistant (XDR and MDR) Pseudomonas aeruginosa in a patient with cystic fibrosis and lung transplantation

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Session: P-66. Resistance Mechanisms

Background. *Pseudomonas aeruginosa* is a persistent and difficult-to-treat pathogen in many patients, especially those with cystic fibrosis (CF). Herein, we describe our experience managing a young woman suffering from CF with XDR *P. aeruginosa* who underwent lung transplantation. We highlight the contemporary difficulties reconciling the clinical, microbiological, and genetic information.

Methods. Mechanism-based-susceptibility disk diffusion synergy testing with double and triple antibiotic combinations aided in choosing tailored antimicrobial combinations to control the infection in the pre-transplant period, create an effective perioperative prophylaxis regimen, and manage recurrent infections in the post-transplant period. Thirty-six sequential XDR and PDR *P. aeruginosa* isolates obtained from the patient within a 17-month period, before and after a double-lung transplant were analyzed by whole genome sequencing (WGS) and RNAseq in order to understand the genetic basis of the observed resistance phenotypes, establish the genomic population diversity, and define the nature of sequence changes over time

Results. Our phylogenetic reconstruction demonstrates that these isolates represent a genotypically and phenotypically heterogeneous population. The pattern of mutation accumulation and variation of gene expression suggests that a group of closely related strains was present in the patient prior to transplantation and continued to evolve throughout the course of treatment regardless of antibiotic usage.Our findings challenge antimicrobial stewardship programs that assist with the selection and duration of antibiotic regimens in critically ill and immunocompromised patients based on single-isolate laboratory-derived resistant profiles. We propose that an approach sampling the population of pathogens present in a clinical sample instead of single colonies be applied instead when dealing with XDR *P. aeruginosa*, especially in patients with CF.

Conclusion. In complex cases such as this, real-time combination testing and genomic/transcriptomic data could lead to the application of true "precision medicine" by helping clinicians choose the combination antimicrobial therapy most likely to be successful against a population of MDR pathogens present.

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1459. Whole Genome Sequencing Analysis of Enterococcus faecium Clinical Isolates Reveals High Strain Diversity and High Accuracy Prediction of Antimicrobial Resistance

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