2351 *Pa* isolates were collected. MICs were determined using CLSI broth microdilution and breakpoints.

Results. *Pa* isolates from BSI tended to show higher susceptibility than IAI, UTI, and especially LRTI isolates (Table). Susceptibility to the tested comparator β-lactams was 11-12 percentage points lower among LRTI than BSI isolates, while C/T and IMI/REL susceptibility was only 2-5% lower. Even among BSI isolates, the comparator β-lactams were active against only 75-88% of isolates, while C/T and IMI/REL were active against >95%. Only amikacin showed higher activity. Analyzing coverage by either C/T or IMI/REL, 98.7% of *Pa* isolates from BSI were susceptible to one or both agents. C/T and IMI/REL maintained activity against 89% and 69% of meropenem-nonsusceptible (MEM-NS) *Pa* isolates from BSI (n=36), respectively, and 87% and 76% of piperacillin/tazobactam (P/T)-NS *Pa* (n=38).

Results Table

	% Susceptible								
Organism/Source (n)	C/T	IMI/REL	MEM	IMI	P/T	FEP	CAZ	LVX	AMK
BSI (224)	97.8	95.1	83.9	75.0	83.0	88.4	87.1	74.1	98.7
IAI (261)	96.6	91.6	79.7	69.4	80.1	85.4	82.8	74.0	98.1
LRTI (1647)	95.6	90.5	72.3	63.2	71.8	76.8	75.8	60.5	94.3
UTI (219)	97.7	94.5	88.1	74.0	81.7	85.8	85.4	65.8	99.1

C/T, ceftolozane/tazobactam; IMI/REL, imipenem/relebactam; MEM, meropenem; IMI, imipenem; P/T, piperacillin/tazobactam; FEP, cefepime; CAZ, ceftazidime; LVX, levofloxacin; AMK, amikacin; BSI, bloodstream infections; IAI, intraabdominal infections; LRTI, lower respiratory tract infections; UTI, urinary tract infections.

Conclusion. Even among BSI isolates, which were generally more susceptible than those from other infection types, *Pa* susceptibility to commonly used β-lactams like MEM and P/T was < 90%, 7-23% lower than C/T and IMI/REL. Given the desirability of β-lactams among clinicians and the >98% coverage by either C/T or IMI/REL of *Pa* isolates from BSI, both agents represent important options in the treatment of patients with BSI.

Disclosures. **Sibylle Lob, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Meredith Hackel, PhD MPH**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **C. Andrew DeRyke, PharmD**, **Merck & Co., Inc.** (Employee, Shareholder) **Kelly Harris, PharmD, BCPS**, **Merck & Co. Inc** (Employee) **Katherine Young, MS**, **Merck** (Employee) **Mary Motyl, PhD**, **Merck & Co., Inc.** (Employee, Shareholder) **Daniel F. Sahm, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor)

1275. Dynamics of *Enterococcus faecalis* Cardiolipin Synthase Gene Expression Reveal Compensatory Roles in Daptomycin Resistance

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Session: P-72. Resistance Mechanisms

Background. Daptomycin (DAP) is a lipopeptide antibiotic targeting membrane anionic phospholipids (APLs) at the division septum, and resistance (DAP-R) has been associated with activation of the *E. faecalis (Efs)* LiaFSR response and redistribution of APL microdomains (predicted to contain cardiolipin) away from the septum. *Efs* encodes two putative cardiolipin synthase genes, *cls1* and *cls2*. While changes in Cls1 are associated with DAP-R, the exact roles of each enzyme in resistance are unknown. This work aims to establish the contributions for both enzymes in the development of DAP-R.

Methods. *cls1* and *cls2* were deleted individually and in tandem from *Efs* OG117Δ*liaX* (a DAP-R strain with an activated LiaFSR response). Mutants were characterized by DAP minimum inhibitory concentration (MIC) using E-test and localization of APL microdomains with 10-N-nonyl-acridine orange staining. Quantitative PCR (qRT-PCR) was used to study gene expression profiles of *cls1* and *cls2* in *Efs* OG117Δ*liaX* relative to *Efs* OG117. Membrane lipid content was analyzed using hydrophilic interaction chromatography-mass spectrometry (HILIC-MS).

Results. *cls1* was highly upregulated in stationary phase concurrent with a decrease in *cls2* expression. However, independent deletion of *cls1* or *cls2* in the DAP-R background resulted in no significant phenotypic changes from the parent strain. Interestingly, qRT-PCR showed that *cls2* expression was upregulated upon deletion of *cls1* (and vice-versa), suggesting a compensatory role for one enzyme upon deletion of the other (Fig 1). When comparing membrane lipid content between *Efs* OG117Δ*liaX*Δ*cls1* and *Efs* OG117Δ*liaX*Δ*cls2,* there were no significant differences in both the overall amount or species of cardiolipin generated, further supporting a potential redundancy between the cardiolipin synthases (Fig 2). Ultimately, double deletion of both *cls* genes lowered the DAP MIC relative to the parent strain and restored septal localization of APL microdomains.

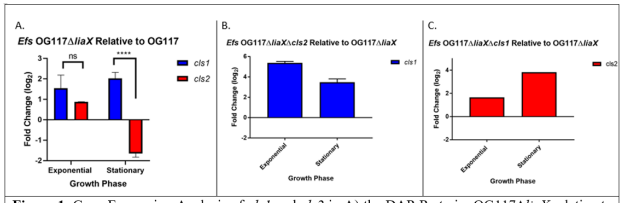

Figure 1. Gene Expression Analysis of *cls1* and *cls2* in A) the DAP-R strain, OG117Δ*liaX* relative to the DAP-S strain OG117, B) the *cls2* deletion strain relative to the parental strain, and C) the *cls1* deletion strain relative to the parental strain. ****p<0.001

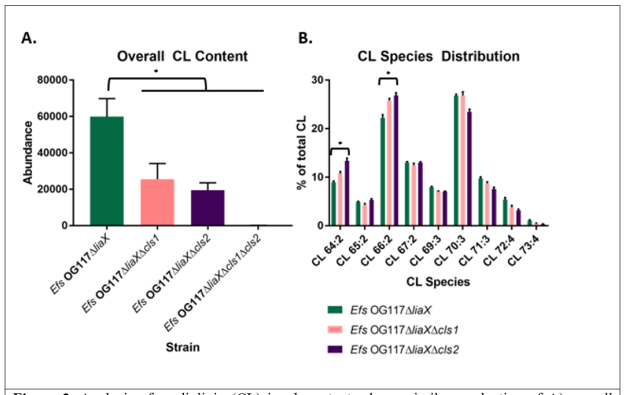

Figure 2. Analysis of cardiolipin (CL) in *cls* mutants shows similar production of A) overall cardiolipin content and B) cardiolipin content by species. *p<0.05

Conclusion. Overall, Cls1 has a predominant role in the development of DAP-R in *E. faecalis*. However, here, we describe a novel compensatory role for Cls2 under conditions in which there is no functional Cls1 to maintain the DAP-R phenotype.

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1276. Assessment of Anti-biofilm Activity of *Staphylococcus aureus* Bacteriophages Against Clinical Isolates from Patients with Left Ventricular Assist Device Infections

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Session: P-72. Resistance Mechanisms

Background. *Staphylococcus aureus* is a common cause of biofilm-mediated left ventricular device (LVAD) infections which are difficult to resolve with antibiotics alone and are associated with substantial morbidity and mortality. Recently, bacteriophages (phage) therapy has been used to resolve LVAD infections in a few cases. Our goal was to assess *in vitro* susceptibility and anti-biofilm activity of two *S. aureus* bacteriophages against clinical isolates from patients with *S. aureus* LVAD infections in order to develop a *S. aureus* phage cocktail for clinical use.

Methods. Two bacteriophages, OMS1 and OMS2, from the Israeli Phage Bank, were assessed for lytic activity against 15 *S.aureus* isolates (9 methicillin resistant, MRSA and 6 methicillin susceptible, MSSA) via agar overlay method and plaque forming units (PFU)/mL were enumerated. We then formed bacterial biofilms after overnight incubation at 120 rpm in a 96-well plates in duplicate; experiments were repeated thrice. Wells were then treated with tryptic soy broth (TSB, control) or TSB containing phage at 109 PFU/mL for 24 hours. After washing, biofilms were stained with crystal violet and biomass quantified via optical density at 570mm.

Results. All bacterial isolates were susceptible to both phages via agar overlay to varying degrees as determined by phage titers obtained via serial dilutions (Figure 1a, 1b). OMS1 led to significant reduction in biofilm of 7/9 MRSA and 3/6 MSSA isolates and OMS2 reduced biofilms in 9/9 MRSA and 4/6 MSSA isolates (Figure 1c).

Phage titers and Biofilm Biomass