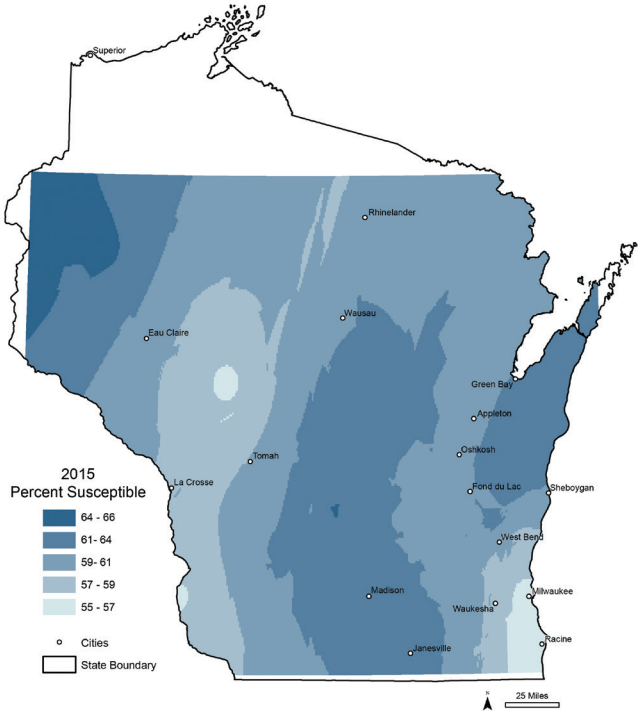
in each direction and is presented within state boundaries. Facility geocodes were masked from public display for confidentiality. City names were added for orientation. The mapping depicts regional differences, such as 2015 ampicillin susceptibilities ranging 55–64% (Figure 1). The maps provide a preliminary susceptibility prediction in areas where no AMR data were available. Average susceptibilities were compared across 2009, 2013, and 2015 to map areas with the highest rates of AMR change.

Conclusion. The described mapping provides a novel visualization of AMR across Wisconsin. The maps created will be utilized in continued efforts to improve the functionality of AMR data in clinical practice to optimize antimicrobial choice.

Figure 1: Interpolated Wisconsin *Escherichia coli* susceptibility to ampicillin



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

696. Mechanism of Cefiderocol high MIC mutants obtained in non-clinical FoR studies

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Background. Cefiderocol (S-649266, CFDC) is a novel siderophore cephalosporin with activity against a wide variety of Gram-negative bacteria including carbapenem-resistant strains. We previously reported that CFDC is efficiently transported into *Pseudomonas aeruginosa* via iron transporter PiuA. In this study, we examined frequency of resistance of *P. aeruginosa* to CFDC, and investigated the resistance mechanisms of appeared colonies.

Methods. Frequency of resistance (FoR) was determined by plating an overnight culture of *P. aeruginosa* PAO1 on Mueller–Hinton Agar containing 4× or 10×MIC of CFDC or ceftazidime (CAZ). Appeared colonies were analyzed by whole-genome sequencing (WGS) to identify genomic mutations. The mRNA expression was determined by real-time RT-PCR, and pyoverdine production was determined by MALDI-TOF/MS and expression of outer membrane protein was analyzed by SDS–PAGE and proteomic analysis.

Results. The FoR to CFDC was 2.9×10^{-8} and $<7.1 \times 10^{-8}$, which were lower than those to CAZ (3.1×10^{-7} and 3.4×10^{-8}) in the conditions of 4× and 10×MIC, respectively. MIC of CFDC against CFDC-derived mutant increased from 0.5 μg/mL (MIC against PAO1) to 2 μg/mL, and MICs of CAZ did not increase. In the case of CAZ-derived mutant, MICs of CAZ increased from 1 μg/mL (MIC against PAO1) to 16 μg/mL or higher, though MIC of CFDC did not increase, suggesting no cross-resistance between CFDC and CAZ. WGS identified mutations in upstream regions of *pvdS* (*pvdS* mutant), which regulates pyoverdine synthesis, or *fecI* (*fecI* mutant), which regulates the synthesis of iron transporter FecA contributing to the transport of iron citrate. The *pvdS* expression and pyoverdine production in the *pvdS* mutant were more than 4- and 6-fold higher than those in PAO1, respectively. The expression of *fecA* in the *fecI* mutant was more than ninefold higher than that in PAO1.

Conclusion. The MIC increase of CFDC against *P. aeruginosa* occurred due to the mutation of iron transporter-related genes. The resistance acquisition risks should be low as the frequency of resistance to CFDC was lower and the MIC increase of CFDC against the mutants was smaller than that of CAZ. In addition, no cross-resistance between CFDC and CAZ was observed.

Disclosures. **A. Ito**, Shionogi & Co., Ltd.: Employee, Salary. **T. Nishikawa**, Shionogi & Co., Ltd.: Employee, Salary. **R. Ishii**, Shionogi & Co., Ltd.: Employee, Salary. **M. Kuroiwa**, Shionogi & Co., Ltd.: Employee, Salary. **Y. Ishioka**, Shionogi & Co., Ltd.: Employee, Salary. **N. Kurihara**, Shionogi & Co., Ltd.: Employee, Salary. **I. Sakikawa**, Shionogi & Co., Ltd.: Employee, Salary. **T. Ota**, Shionogi & Co., Ltd.: Employee, Salary. **M. Rokushima**, Shionogi & Co., Ltd.: Employee, Salary. **M. Tsuji**, SHIONOGI & CO., LTD.: Employee, Salary. **T. Sato**, SHIONOGI & CO., LTD.: Employee, Salary. **Y. Yamano**, SHIONOGI & CO., LTD.: Employee, Salary.

697. *Pseudomonas aeruginosa* PcrV and Psl, the Molecular Targets of Bispecific Monoclonal Antibody MEDI3902, Are Conserved Among Diverse Hospital Isolates Collected From an International Surveillance Study

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Background. *Pseudomonas aeruginosa* is a frequent cause of life-threatening infections in mechanically ventilated patients and is associated with high mortality rates. Bispecific monoclonal antibody MEDI3902 targeting *Pa* type-3-secretion system (PcrV) and the Psl exopolysaccharide is currently under phase 2b development for the prevention of pneumonia in mechanically ventilated subjects with *Pa* colonization in the lower respiratory tract. In this study, we sought to survey a vast collection of global *Pa* clinical isolates for presence of *pcrV* and *psl* loci and MEDI3902 epitope conservation to evaluate the magnitude of *Pa* strain coverage by MEDI3902.

Methods. 913 *Pa* clinical isolates were collected from diverse patients and geographical locations in 2004–2014. Whole genome sequencing of the full collection was performed via MiSeq 2 × 250 runs (Illumina®). PcrV and Psl expression was detected by immunoblotting and ELISA, respectively. The crystal structure of anti-PcrV fab and PcrV fragment complex-crystals was solved at 2.8 Å resolution. MEDI3902 activity against representative isolates was tested in cytotoxicity and opsonophagocytosis assays and in a murine pneumonia model.

Results. Whole-genome sequencing revealed intact *pcrV* and *psl* genetic elements in 99% and 94% of isolates, respectively. We identified 46 variants of PcrV that were all bound by the anti-PcrV moiety of MEDI3902 and confirmed through crystal structure analysis that antibody-antigen contact residues were preserved in all variants. Similarly, anti-Psl binding was confirmed for selected isolates containing the complete Psl operon and strains lacking non-essential *psl* genes. Importantly, 99.9% of isolates contained the full complement of either genetic element. Consistent with these results, we observed potent MEDI3902 activity against diverse strain types, including strains that expressed only a single target.

Conclusion. Our results indicate PcrV and Psl are highly prevalent in recent clinical isolates from around the world, suggesting that MEDI3902 can mediate broad coverage against *Pa*.

Disclosures. **D. E. Tabor**, Astra Zeneca: employee, Salary.

698. Nacubactam Inhibits Class A β-lactamases

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Background. Nacubactam, formerly RG6080 and OP0595 (Figure 1A), is a bridged diazabicyclooctane (DBO) that inactivates class A and class C β-lactamases. Unlike avibactam, the DBO that is approved for use in combination with ceftazidime, nacubactam also inhibits penicillin binding proteins (i.e., PBP2) in Enterobacteriaceae. We set out to determine the effectiveness of meropenem-nacubactam against *Klebsiella pneumoniae* clinical strains and to elucidate the structure–function relationships.

Methods. Minimal inhibitory concentration (MIC) measurements using broth microdilution according to Clinical and Laboratory Standards Institute for meropenem (MERO) ± nacubactam (fixed concentration of 4 mg/L or fixed 1:1 ratio) was performed on 50 clinical *K. pneumoniae* strains (6 having OXA-48-like β-lactamases and 44 harboring KPC-2 or KPC-3) and 47 isogenic *Escherichia coli* strains harboring *bla* genes encoding *K. pneumoniae* carbapenemase (KPC) variants with single amino acid substitutions in residues that are involved in catalysis. IC_{50}s for selected KPC-2 variants were determined on periplasmic extracts with varying concentrations of nacubactam using nitrocefin as a reporter substrate.

Results. The MERO combinations with either 4 mg/L or a 1:1 ratio of nacubactam effectively lowered the MERO MICs of *K. pneumoniae* strains (Figure 1B). Similarly, all *E. coli* strains expressing bla_{KPC-2} variants were susceptible to the MERO-nacubactam