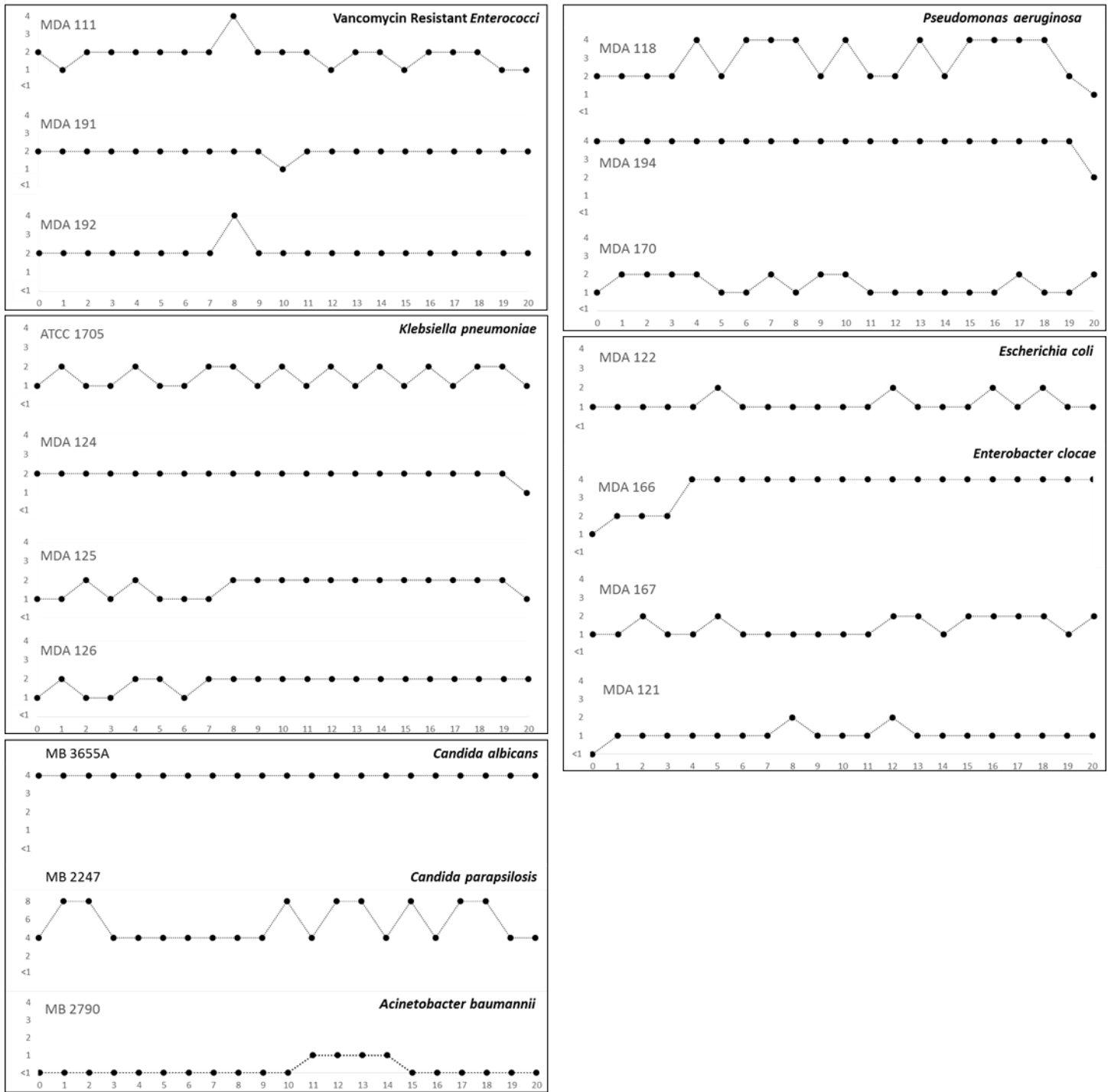


1 SUPPLEMENTAL MATERIAL -



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3 **Supplemental Material Figure S1 – Median MIC for MIN, RIF, and CHX in each sub-inhibitory passage for low**

4 **susceptibility organisms** - The median measured MIC values for MIN, RIF, and CHX in each passage are the circles in
 5 each plot. Dotted lines have been added to assist in visualizing the trend in MIC values. A vertical MIC trend (continually
 6 increasing MIC trending toward antimicrobial agent ineffectiveness) would be indicative of induced resistance for a
 7 particular organism. Conversely, a horizontal MIC trend would be indicative of the absence of induced resistance for a

8 particular organism. Low susceptibility organisms tested included the following susceptibility patterns: vancomycin
9 resistant *enterococci* (VRE MDA 111, 191, 192); carbapenem resistant *enterobacteriaceae* including *Klebsiella pneumoniae*
10 (ATCC 1705, MDA 124, 125, 126), *Escherichia coli* (MDA 122), *Enterobacter cloacae* (MDA 166, 167, 121); Multi-drug
11 resistant *Pseudomonas aeruginosa* (MDA 118, 194, 170); Other organisms *Acinetobacter baumannii* (MB2790), *Candida*
12 *albicans* (MB3655A), and *Candida parapsilosis* (MB 2247). The x-axis for each plot is the passage number and y-axis is
13 measured median MIC ($\mu\text{g/mL}$).

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30 **Table S1 - Susceptibility of Test Organisms**

31 Organisms were tested for susceptibilities of commonly used antibiotics as reported by University of Texas MD Anderson Clinical Microbiological Laboratory. All
32 definitions are per CLSI guidelines for susceptibility testing (1, 2). All testing is conducted by the CLIA certified UT MDACC Clinical Microbiology Laboratory using
33 a Biomerieux Vitek II system or using E-test strips for determining antibiotic profiles for each organism. Determination of which antibiotics were tested for which
34 organism was determined by standard operating procedures in the clinical microbiology laboratory, some antibiotics are not available or appropriate to be
35 tested for specific organisms.

36 Abbreviations and definitions are as follows: R – Resistant to antimicrobial based on interpretation of MIC/Etest; I – Intermediate to antimicrobial based on
37 interpretation of MIC/Etest; S – Sensitive to antimicrobial based on interpretation of MIC/Etest; MRSA – methicillin resistant Staphylococcus aureus; VRE –
38 vancomycin resistant enterococci; ECS – Extended Spectrum cephalosporin, resistant to at least one of the extended spectrum cephalosporin (cefepime,
39 cefotazime, ceftazidime, ceftriaxone); CRE – carbapenem resistant enterobacteriaceae, resistant to at least one carbapenem (ertapenem, imipenem,
40 meropenem, doripenem); MDR – multidrug resistant, must be intermediate or resistant to at least 1 drug in 3 of the 6 classes (extended spectrum
41 cephalosporin, fluoroquinolones, aminoglycosides, CRE, piperacillin/tazobactam, ampicillin/sulbactam).

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Enterococcus				Klebsiella pneumoniae			
ID	MDA 111	MDA 191	MDA 192	ID	MDA 124	MDA 125	MDA 126
Species	E. faecium	E. faecium	E. faecium	Species	K. pneumoniae	K. pneumoniae	K. pneumoniae
Year	2015	2017	2017	Year	2014	2014	2013
Source	Blood	Blood	Blood	Source	Blood	Blood	Blood
Category	VRE	VRE	VRE	Category	ESC, CRE, MDR	ESC, CRE, MDR	ESC, CRE, MDR
Beta lactamase	negative	n/a	n/a	Amikacin	R	I	S
Ampicillin	R	S	R	Amoxicillin/Clavulanate			
Daptomycin	S	S	S	Ampicillin	R	R	R
Gentamicin 500	R	n/a	n/a	Amp/Sulbactam	R	R	R
Levofloxacin	R	n/a	n/a	Aztreonam	R	R	R
Linezolid	S	I	S	Cefepime	I	R	R
Nitrofurantoin	I	n/a	n/a	Cefotaxime	R	R	R
Streptomycin	R	n/a	n/a	Cefpodoxime	R	R	R
Tetracycline	R	R	R	Ceftazidime	n/a	n/a	n/a
Vancomycin	R	R	R	Ceftazidime/Avibactam	n/a	n/a	n/a
Quinupristin/Dalfopristin	n/a	R	I	Ceftriaxone	R	R	R
				Cephalothin	R	R	R
				Ciprofloxacin	R	R	R
				Colistin-E	NO INTERP	NO INTERP	NO INTERP
				Ertapenem	n/a	R	R
				Gentamicin	S	R	R
				Imipenem	R	R	R
				Levofloxacin	R	R	R
				Meropenem	R	R	R
				Moxifloxacin	R	R	R
				Nitrofurantoin	R	R	R
				Pip/Tazo	R	R	R
				Tigecycline	S	I	I
				Tobramycin	R	R	S
				Sulfa/Trimeth	R	R	R
				Carbapenamase	POSITIVE	POSITIVE	POSITIVE

Escherichia coli				Enterobacter spp.			
ID	MDA 122	MDA 164	MDA 165	ID	MDA 121	MDA 166	MDA 167
Species	E. coli	E. coli	E. coli	Species	Eb. Clocae	Eb. Clocae	Eb. Clocae
Year	2015	2011	2011	Year	2015	2009	2011
Source	Blood	Blood	Blood	Source	Blood	Blood	Blood
Category	ESC, CRE, MDR	ESC, CRE, MDR	ESC, CRE, MDR	Category	ESC	ESC, MDR	ESC
Amikacin	R	S	I	Amikacin	S	S	n/a
Ampicillin	R	R	R	Ampicillin	n/a	R	n/a
Amp/Sulbactam	R	R	R	Amp/Sulbactam	n/a	R	n/a
Aztreonam	R	R	S	Aztreonam	R	I	R
Cefepime	I	R	R	Cefepime	S	S	S
Cefotaxime	R	R	S	Cefotaxime	R	R	R
Cefpodoxime	R	n/a	n/a	Cefpodoxime	R	n/a	n/a
Ceftazidime	R	R	I	Ceftazidime	R	R	R
Ceftriaxone	R	R	R	Ceftriaxone	R	R	R
Cephalothin	R	n/a	n/a	Cephalothin	R	n/a	n/a
Ciprofloxacin	R	R	n/a	Ciprofloxacin	S	S	S
Ertapenem	R	n/a	R	Ertapenem	I	n/a	NO INTERP
Gentamicin	R	S	S	Gentamicin	S	S	S
Imipenem	R	R	NO INTERP	Imipenem	S	No INTERP	NO INTERP
Levofloxacin	R	R	R	Levofloxacin	S	S	S
Meropenem	R	R	NO INTERP	Meropenem	S	No INTERP	NO INTERP
Moxifloxacin	R	R	n/a	Moxifloxacin	S	n/a	S
Nitrofurantoin	n/a	S	S	Nitrofurantoin	I	S	S
Pip/Tazo	R	R	R	Pip/Tazo	n/a	R	R
Tigecycline	I	S	S	Tigecycline	S	S	n/a
Tobramycin	R	S	R	Tobramycin	S	S	S
Sulfa/Trimeth	R	R	R	Sulfa/Trimeth	S	S	S
Carbapenamase	POSITIVE	POSITIVE	n/a	Carbapenamase	POSITIVE	n/a	POSITIVE

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Pseudomonas aeruginosa				Acinetobacter spp			
ID	MDA 118	MDA 170	MDA 194	ID	MB2875	MB2790	MB2761
Species	Ps. aeruginosa	Ps. aeruginosa	Ps. aeruginosa	Species	An. Ursingii	An. Baumannii	An baumannii
Year	2003	2016	2017	Year	2016	2016	2016
Source	Catheter site	Blood	Blood	Source	Blood	Blood	Blood
Category	MDR	MDR	MDR	Category	Suseptible	Suseptible	Suseptible
Amikacin	S	I	I	Amikacin	S	S	S
Aztreonam	R	R	R	Cefepime	S	S	S
Cefepime	I	R	I	Ciprofloxacin	S	S	S
Ceftazidime	I	R	S	Colistin	n/a	n/a	S
Ceftizoxime	R	n/a	n/a	Imipenem	S	S	S
Ceftriaxone	R	n/a	n/a	Meropenem	n/a	n/a	S
Ciprofloxacin	R	R	R	Minocycline	n/a	n/a	S
Gentamicin	S	n/a	n/a	Pip/Tazo	S	S	n/a
Imipenem	R	R	R	Tobramycin	S	S	S
Levofloxacin	R	n/a	n/a	Trimethoprim/Sulfa	S	S	S
Meropenem	R	R	R				
Norfloxacin	R	n/a	n/a				
Piperacillin	S	n/a	n/a				
Pip/Tazo	S	n/a	R				
Ticar/Clav	R	n/a	n/a				
Tobramycin	S	S	R				
Ceftazidime/Avibactam	n/a	S	n/a				
Ceftolozane/Tazobactam	n/a	R	S				

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