Prospective ex vivo activity of an engineered antimicrobial peptide, PLG0206, on chronic periprosthetic joint infection total knee arthroplasty components: the Knee Explant Analysis (KnEA) Study

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Disclosures/Disclaimer

“I and/or my co-authors have something to disclose.”

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Disclaimer: This research was sponsored by Peptilogics Inc. *Research reported in this presentation is supported by CARB-X. CARB-X’s funding for this project is sponsored by the Cooperative Agreement Number IDSEP160030 from ASPR/BARDA and by an award from Wellcome Trust. The content is solely the responsibility of the authors and does not necessarily represent the official views of CARB-X or any of its funders.*

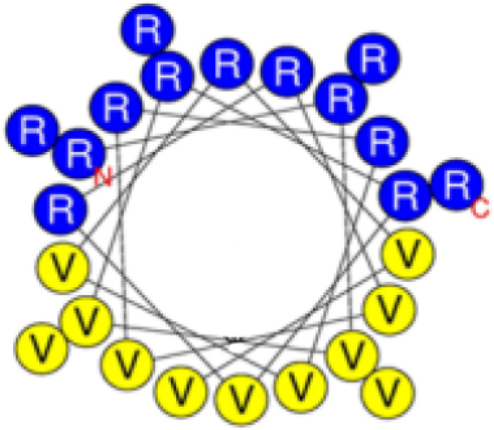
Background

- Total knee arthroplasty (TKA) is the most common surgery in US
- Most common reason for failure is periprosthetic joint infection (PJI)
- DAIR is an ideal treatment for PJI, but failure rates are 60%
- Failure is a result of biofilm antibiotic tolerance & low antibiotic penetration

Shah, CID, 2019

Background: PLG0206: A New Class of Antimicrobials

1	Biofilm Activity	Mandell 2017 Nature Sci Reports
2	Rapid Acting	Mandell 2017 Nature Sci Reports & AAOS 2022
3	Mechanism: Metabolic Independent Membrane Destabilization	Mandell 2017 Nature Sci Reports Kumagai 2019 Soft Matter
4	Broad Spectrum (ESKAPE)	AAOS 2022
5	Efficacy in Large Animal PJI	AAOS 2022



R Arginine

V Valine

W Tryptophan

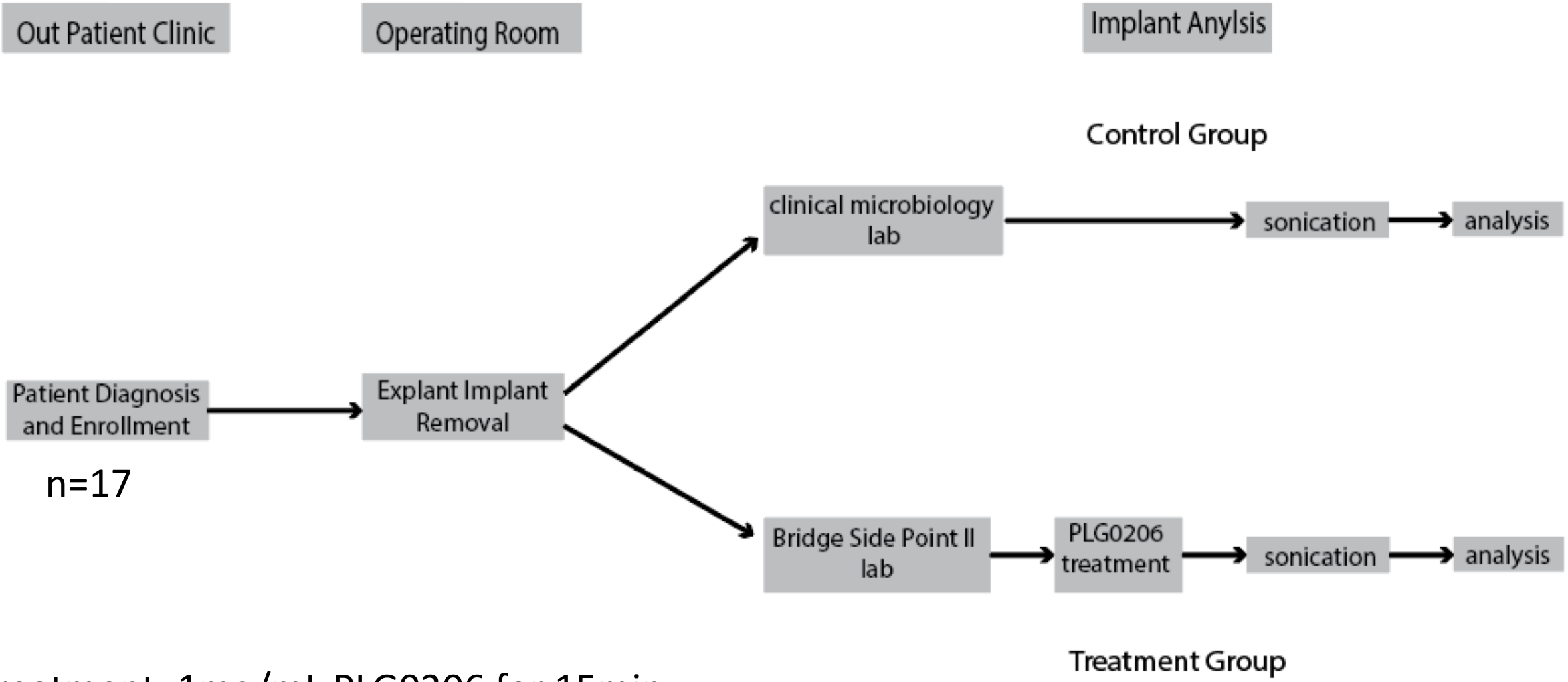
Purpose

Objective: To evaluate the efficacy of PLG0206 in decreasing bacterial burden on infected arthroplasty explants in the setting of chronic PJI

Hypothesis: PLG0206 will decrease implant associated biofilm CFU

Logic: Incremental study between large animal to FDA phase 1B

Methods



Treatment: 1mg/mL PLG0206 for 15min

Primary Endpoint: Treated Implants below $1x10^3$ CFU

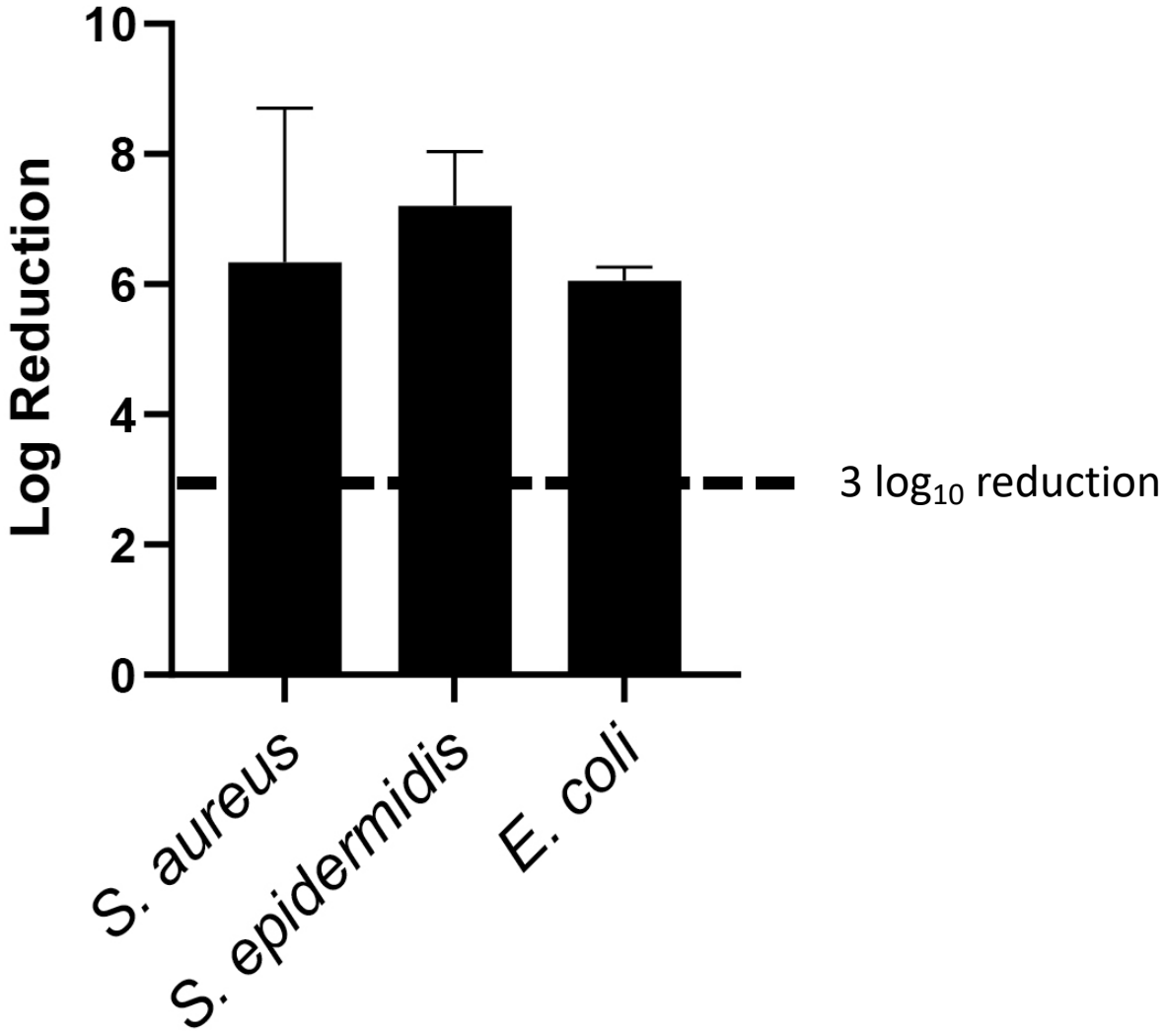
Secondary Endpoint: CFU on Implant; Treatment vs Untreated

Results: Log Reduction by Case

#	Culture	MDR	CFU/mL untreated	CFU/mL treated	Log reduction
1	*S. epidermidis*	Clindamycin, Erythromycin, Gentamicin, Oxacillin	$5.0x10^7$	0	7.7
2	*S. epidermidis*	Clindamycin, Erythromycin, Gentamicin, Oxacillin	$5.0x10^7$	0	7.7
3	*S. aureus* (MRSA)	Oxacillin, Erythromycin	$5.0x10^7$	0	7.7
4	*S. hemolyticus*	Clindamycin, Gentamicin, Oxacillin, Rifampin, Sulfa/Trimethoprim	$7.3x10^2$	0	2.9
5	*S. aureus* (MSSA)	None	$5.0x10^7$	$1.3x10^2$	3.6
6	*S. caprae*	None	$5.0x10^7$	0	7.7
7	*E. coli*	Ampicillin, Ampicillin/Sulbactam	$5.0x10^7$	30	6.2
8	*E. coli*	Ampicillin, Ampicillin/Sulbactam	$5.0x10^7$	60	5.9
9	*S. epidermidis*	None	$5.0x10^7$	90	5.7
10	*Haemophilus parainfluenzae*	None	$5.0x10^7$	0	7.7
11	*Haemophilus parainfluenzae*	None	$5.0x10^7$	0	7.7
12	*E. faecalis*	None	$5.0x10^7$	10	6.7
13	*S. aureus* (MRSA)	Oxacillin	$5.0x10^7$	0	7.7
14	*S. dysgalactiae*	None	$4.7x10^3$	60	4.0
15	*S. epidermidis*	Penicillin	$5.0x10^7$	0	7.7
16	*S. epidermidis*	Oxacillin, Tetracycline, Bactrim (sulfa/trimethoprim)	$5.0x10^7$	0	7.7
17	*S. epidermidis*	Oxacillin, Tetracycline, Bactrim (sulfa/trimethoprim)	$5.0x10^7$	10	6.7

- Range of Gram-(+) and gram-(-) bacteria; many were MDR.
- Primary Endpoint: All treated implants were below $1x10^3$ CFU/mL
- Secondary Endpoint: Treatment resulted in mean $\log_{10}$ reduction of 6 (range 2.9-7.70)
- 10 of the 17 (58%) infected implants were culture negative after treatment

Results: Log Reduction by Organism



Organisms in multiple cases had > $3\log_{10}$ reduction

Discussion

- 1 mg/mL PLG0206 successfully reduced explant biofilm CFU after 15 minutes of treatment when compared to the control.
- The average $\log_{10}$ reduction was 6.
- These findings support the development of PLG0206 as a local irrigation solution for patients undergoing PJI treatment.

Limitations:

- Most treated explants below the limit of detection on assay
- Difficult to compare treated and untreated

PLG0206: A New Class of Antimicrobials

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4	Broad Spectrum (ESKAPE)	AAOS 2022
5	Efficacy in Large Animal PJI	AAOS 2022
6	Activity on TKA Explants	AAOS 2022; Huang Microbiology Spectrum 2021
	Safety	
7	Systemic Safety & Pharmacokinetics	Phase I Clinical Study: ACTRN12618001920280 Huang AAC 2022
8	Acute Postop TKA PJI (Ongoing)	Phase 1b FDA: NCT05137314

Thank You

- **Ken Urish MD PhD**
- **Kimberly Brothers PhD**
- **Masashi Taguchi MD**
- **Jon Mandell MS**
- **Dana M Parker**
- Beth Knapick
- Nadine Sadaka
- Charles Gish
- Bill Li MD
- **John Koch**
- Sanathan Iyer

Peptilogics

- **David Huang**
- **Nicholas Pachuda**
- **Despina Dobbins**
- **Jonathan Steckbeck**

ClinicalTrials.gov NCT05137314

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Trial Questions - David Huang MD PhD: david.huang@peptilogics.com

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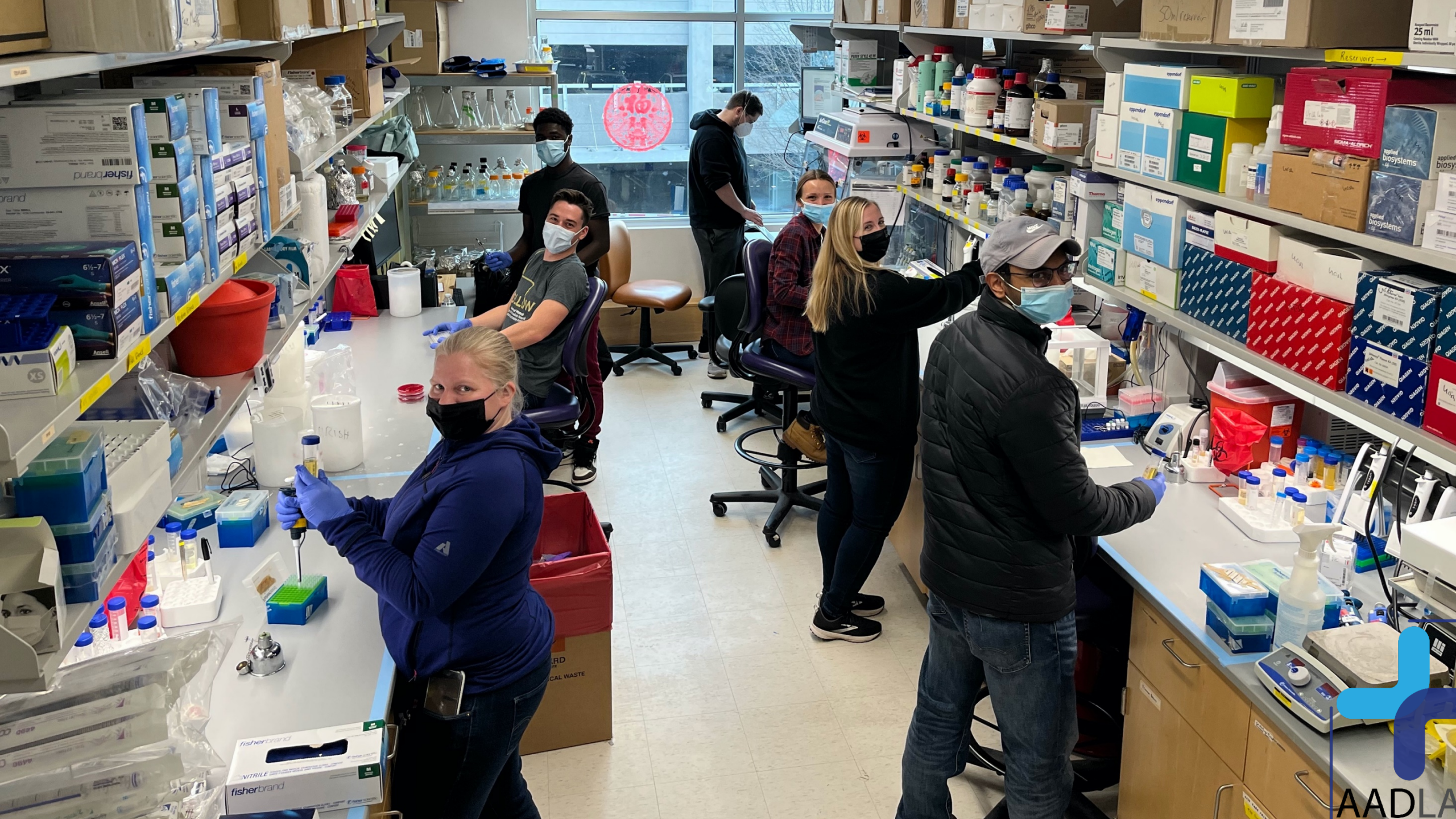
Combating Antibiotic-Resistant Bacteria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