Lysin CF-370 Exhibits Broad Spectrum Antimicrobial Activity Against Gram-Negative (GN) ESKAPE Pathogens

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Yonkers, New York

New Agents Discovery Summary Session: Early New Antimicrobial Agents
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11:50-12:05

ContraFect
MOLECULAR TREATMENTS FOR INFECTIOUS DISEASE

CARB-X
Combating Antibiotic-Resistant Bacteria

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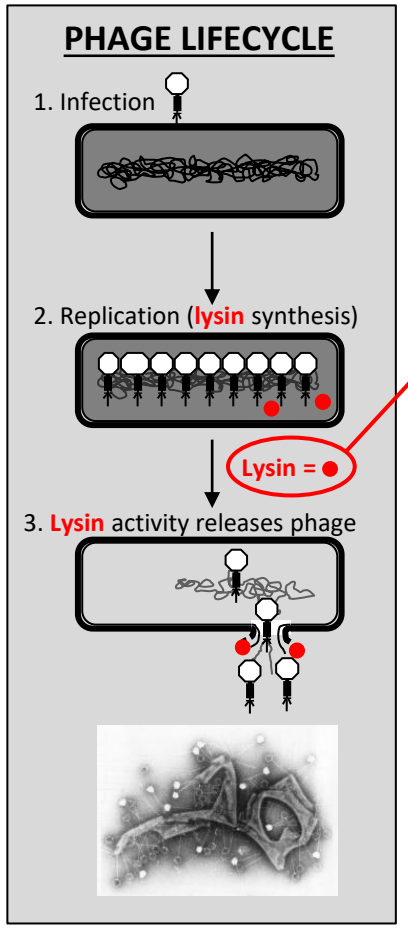
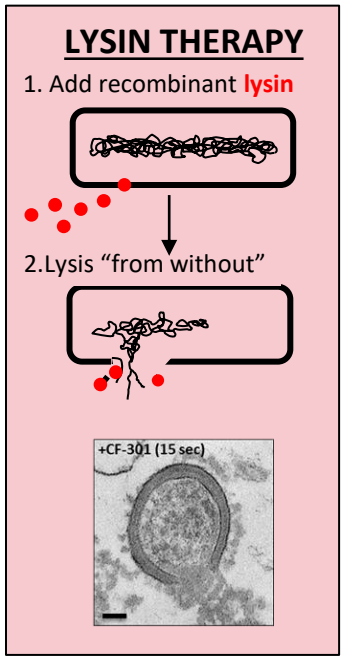
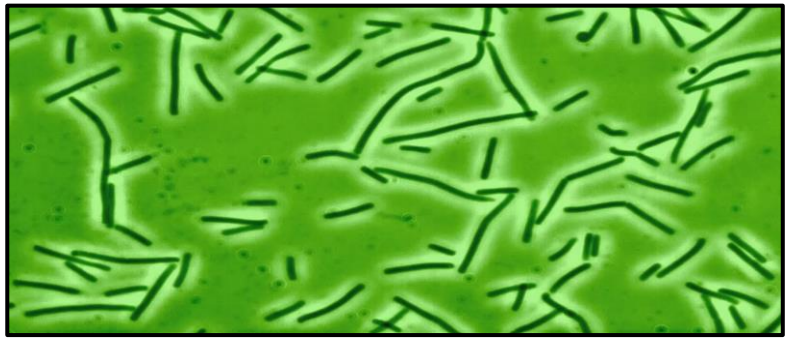
ContraFect is a late clinical-stage biotechnology company leading the development of direct lytic agents (DLAs), which include lysins and amurin peptides, as new medical modalities for the treatment of life-threatening and antibiotic-resistant infections

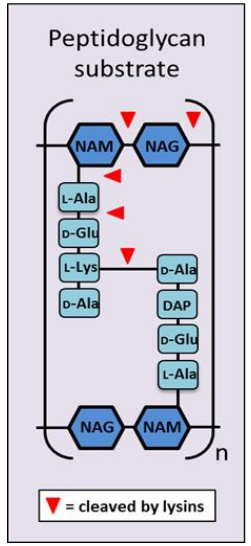
Lysins: Novel Antimicrobial Modalities

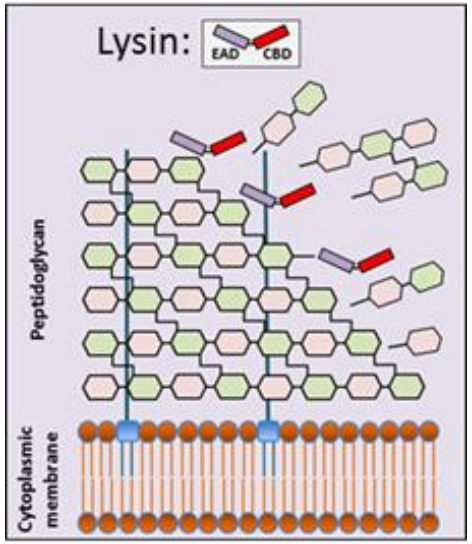






MOA: Peptidoglycan Hydrolysis





Core Microbiologic Features*

- Rapid, potent bactericidal activity
- Eradicates biofilm
- Synergy with standard of care antibiotics
- Low propensity of resistance
- Antibiotic rensensitization
- Extended postantibiotic/sub-MIC effects

*PMID: 24286983, 30670427, 28461319, 31712212

ContraFect Direct Lytic Agent Platform

Exebacase: First-in-Class Lysin Candidate

- 26 kDa modular bacterial cell wall hydrolase enzyme
- Highly potent against *Staphylococcus aureus* and unique lysis and eradication of biofilms
- Potent synergy with broad range of anti-staphylococcal antibiotics

Exebacase clinical-stage program

- Advancing with FDA Breakthrough Therapy designation
- Ongoing Phase 3 DISRUPT superiority trial
- Completed Phase 2 superiority study with positive results
  - Significant improvement in MRSA patient responder rates with over 40% increase over standard-of-care antibiotics alone
  - Demonstrated favorable safety and tolerability data in patients

Broad pipeline of new agents

- Second generation antistaphylococcal lysin
- **Novel phage-derived lytic agents targeting a broad range of GN pathogens (ESKAPE)**

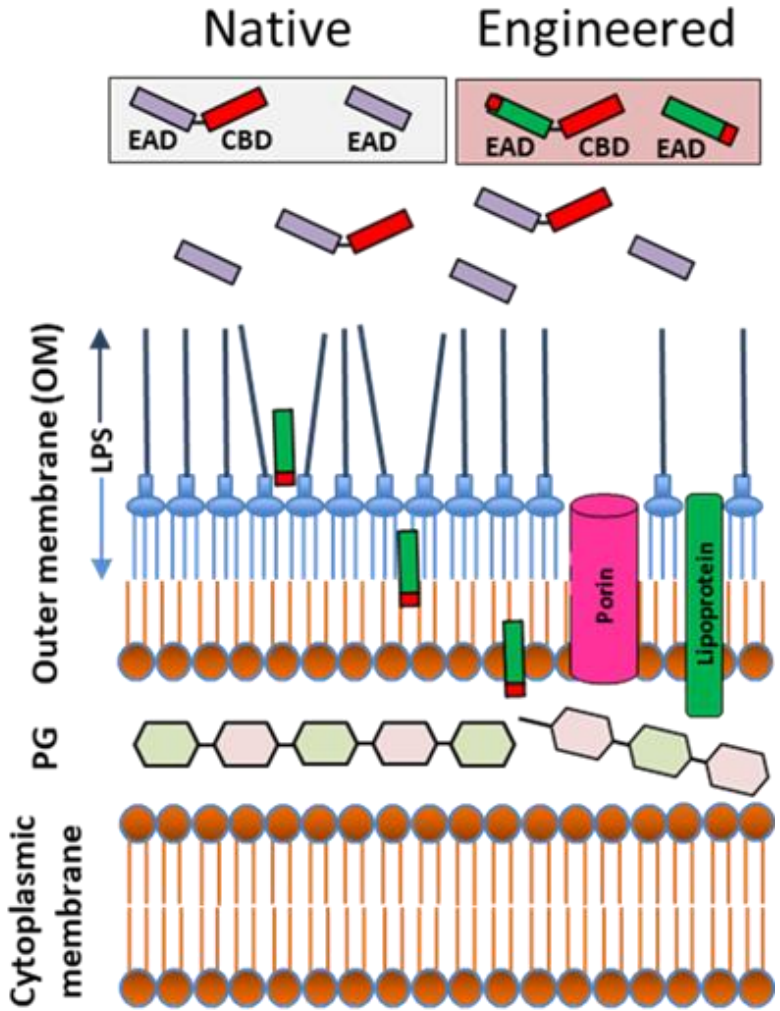
CF-370 Targeting GN Bacteria Advancing as Next IND Candidate

Based on novel lysin platform

- Engineered to cross the outer membrane of GN bacteria and for potent activity in human blood
- Potential to improve clinical response and cure rates for resistant GN infections

IND-enabling activities are in progress

- Results from in vitro studies are presented here:
  - ✓Define activity range
  - ✓Demonstrate rapid, potent bactericidal activity
  - ✓Synergy with SOC antibiotics
  - ✓Eradication of biofilms
- In vivo efficacy studies are ongoing in multiple animal models (Poster 6871, Lehoux et al.)



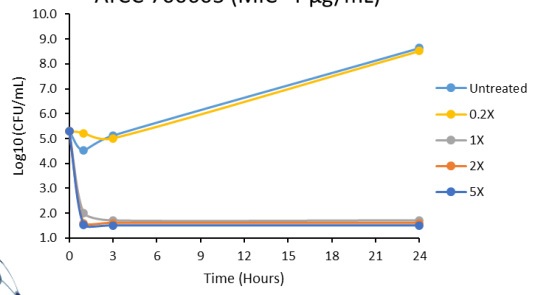
CF-370: Broad Spectrum Activity vs Gram-negatives

MICs were determined by broth microdilution for CF-370 vs range of organisms including MDR and XDR isolates from the CDC Antibiotic Resistance (AR) Bank, which includes carbapenem resistant *Acinetobacter* (CRA), *Enterobactericae* (CRE), and *Pseudomonas* (CRP) in addition to colistin-resistant isolates:

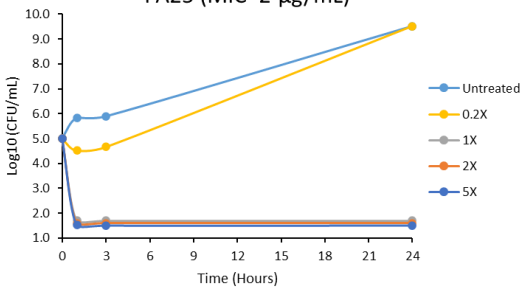
		MIC (µg/mL)												
Organism	**n**	**0.016**	**0.032**	**0.064**	**0.125**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**MIC_{50}**	**MIC_{90}**	**Range**
P. aeruginosa	124					3	20	67	34			1	2	0.25 - 2
A. baumannii	80					6	27	44	3			1	1	0.25 - 2
E. coli	44		1	2	4	16	16	5				0.25	1	0.032 - 1
K. pneumoniae	73				3	7	10	16	27	10		2	4	0.125 - 4
E. cloacae	37	1				4	7	8	12	4	1	1	4	0.016 - 8

Broad spectrum bactericidal activity vs ESKAPE pathogens observed in the time-kill assay format:

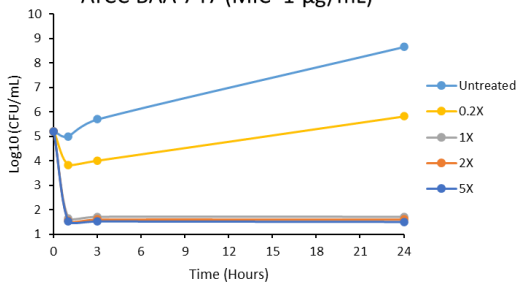
K. pneumoniae
ATCC 700603 (MIC=4 µg/mL)



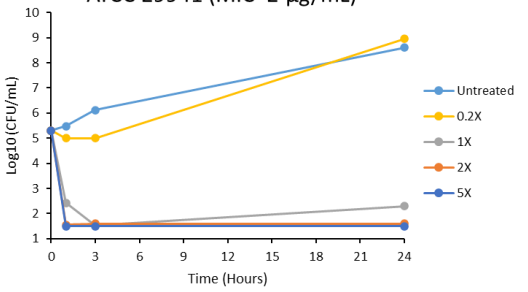
P. aeruginosa
PA25 (MIC=2 µg/mL)



A. baumannii
ATCC BAA 747 (MIC=1 µg/mL)

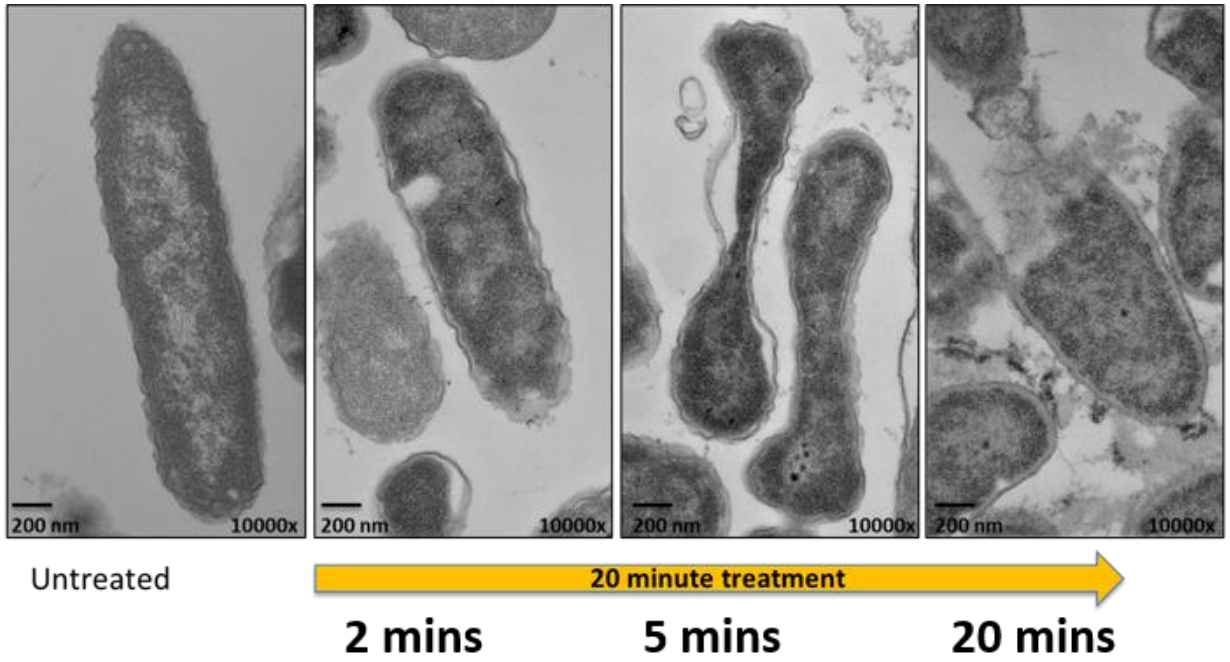


E. cloacae
ATCC 29941 (MIC=2 µg/mL)

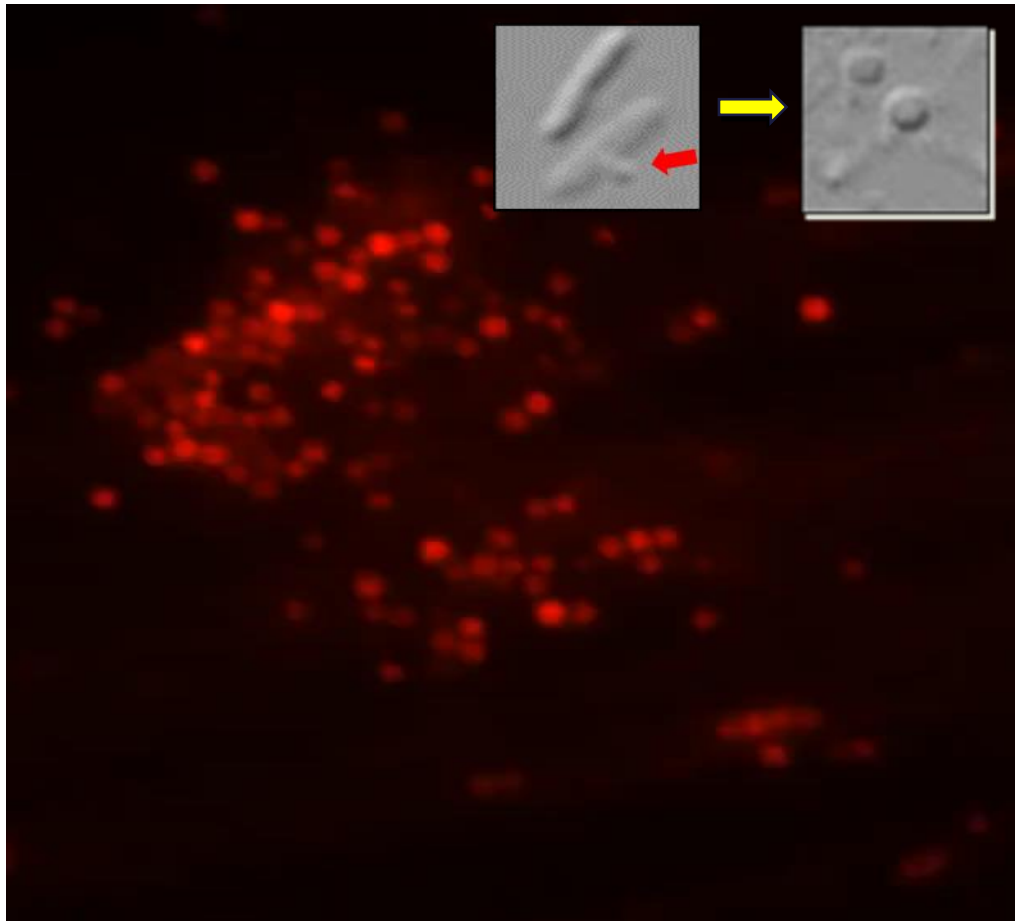


CF-370: Visualize Rapid Killing

Rapid killing in saline:



Rapid killing in 100% serum:



CF-370: Synergy and Antibiofilm Activity

Synergy with antibiotics in the checkerboard assay:

Fractional inhibitory concentration index (FICI) values are indicated; FICI values ≤0.5 (in green) are consistent with synergy:

Antibiotic	*P. aeruginosa* ATCC 27853 (MIC = 1 µg/mL)	*A. baumannii* ATCC BAA-747 (MIC = 1 µg/mL)	*E. coli* ATCC 25922 (MIC = 0.5 µg/mL)	*E. cloacae* ATCC 13047 MIC = 2 µg/mL)	*K. pneumoniae* HM-44 (MIC = 4 µg/mL)
Amikacin	0.375	0.625	0.25	0.75	0.375
Aztreonam	0.375	0.313	0.375	0.25	0.375
Cefazolin	n.d.	0.5	n.d.	n.d.	0.375
Ciprofloxacin	n.d.	n.d.	0.156	0.25	0.156
Colistin	0.499	0.375	0.375	0.25	0.187
Gentamicin	0.531	0.563	0.312	0.25	0.375
Meropenem	0.375	0.5	0.5	0.531	0.5
Tobramycin	0.5	0.5	0.25	0.5	0.375

- CF-370 synergized with a broad range of antibiotics, with multiple different MOAs

Potent antibiofilm activity:

Antibiofilm activity was determined in the minimal biofilm eliminating concentration (MBEC) assay format using a range of MDR and XDR isolates:

		MBEC (µg/mL)							
Organism	n	0.25	0.5	1	2	4	$MBEC_{50}$	$MBEC_{90}$	Range
P. aeruginosa	9			4	4	1	2	4	1 - 4
A. baumannii	22		2	12	8		1	2	0.5 - 2
E. coli	11	2	5	2	2		0.5	2	0.25 - 2
K. pneumoniae	11		3	3	4	1	1	2	0.5 - 4
E. cloacae	14		1	9	4		1	2	0.5 - 2

- MBEC values of ≤4 µg/mL were observed, and were similar to MIC values for each strain

Therapeutic Potential of CF-370

Exhibits favorable microbiologic profile including key core features of the DLA class of protein therapeutics

- Broad spectrum activity vs GN ESKAPE pathogens with no cross resistance
- Rapid bacterial killing
- Synergy with SOC antibiotics
- Biofilm eradication
- Low propensity for resistance

Unmet needs

- HAP/VAP
- Cystic fibrosis pulmonary exacerbations
- Intra abdominal infections
- Bacteremia
- Burns

Potential therapeutic uses

- Alone or in addition to standard of care antibiotics to improve clinical cure rates compared to antibiotics alone
- To treat infections caused by XDR (extreme drug-resistant) and PDR (pan drug resistant) GN pathogens, including ESKAPE organisms

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