ContraFect
MOLECULAR TREATMENTS
FOR INFECTIOUS DISEASE

ContraFect Corporation (CFRX)

Direct Lytic Agents: differentiated, first-in-class biologics for the treatment of life-threatening and drug-resistant infections

Therapeutics Pipeline Corner
ECCMID, Amsterdam 2019
Sunday, 14 April 2019 - 12:15 - 13:15

Raymond Schuch, Ph.D.

VP of Research
ContraFect Corporation
Yonkers, NY

https://www.contrafect.com/

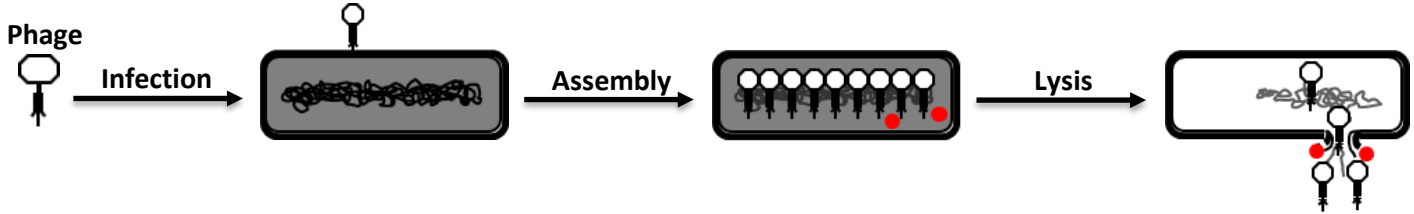
ContraFect Corporation Overview

- **Late clinical-stage biotech leading the development of direct lytic agents (DLA): first-in-class biologics for the treatment of life-threatening and drug-resistant infections**
- **Lysin platform technology**
  - Novel class of non-traditional, direct-acting anti-infectives derived from bacteriophage
  - Proprietary discovery program at ContraFect and in collaboration with Rockefeller University
- **Exebacase (CF-301) – first-in-class lysin for *S. aureus* bacteremia including endocarditis**
  - Demonstrated substantial added clinical benefit when used in addition to conventional antibiotic therapy vs antibiotics alone in Phase 2 superiority-design study, including 42.8% higher clinical responder rates in MRSA patients treated with exebacase in addition to antibiotics vs. antibiotics
- **Broad pipeline**
  - Novel lysins directed at drug-resistant Gram-negative (GN) pathogens
  - Novel phage derived peptides with broad spectrum activity against GN pathogens
  - CF-296 – engineered exebacase variant – potential line extension

Lysins Strategy: Based on a Novel MOA

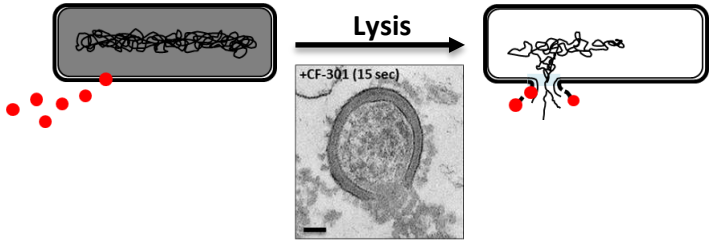
Lysins are enzymes (cell wall hydrolases) that cleave bacterial peptidoglycan, causing osmotic lysis

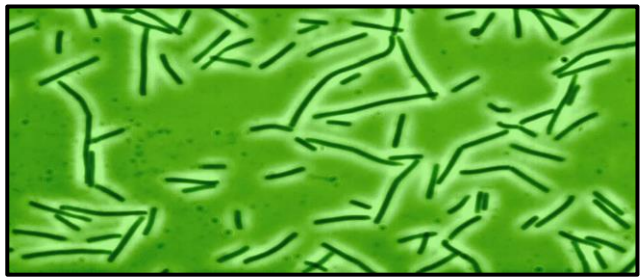
Bacteriophage infect bacteria, replicate and produce lysins to rupture the host cell:



We use lysins as purified therapeutic proteins, driving cell wall hydrolysis and rapid bacterial killing

Lysins are applied externally to a target pathogen to effect bacteriolysis:

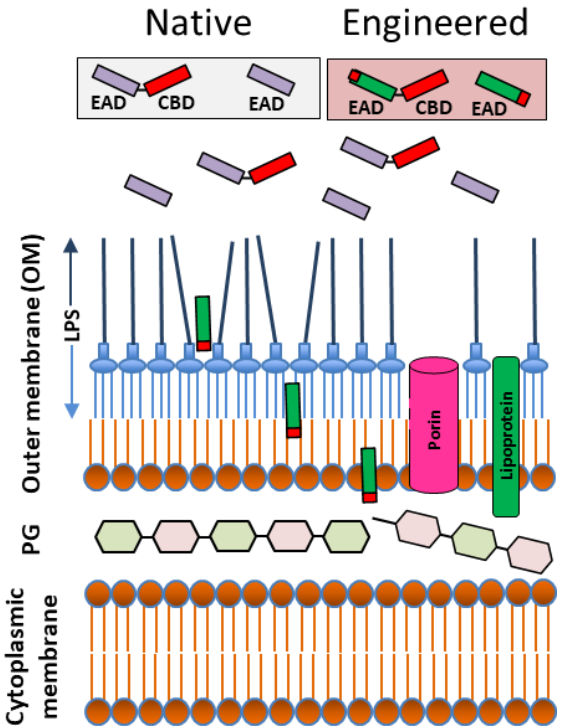




Lysis video (real time)

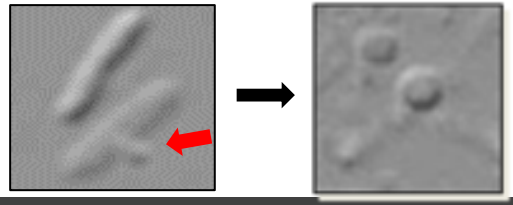
Targeting *P. aeruginosa* with Lysins

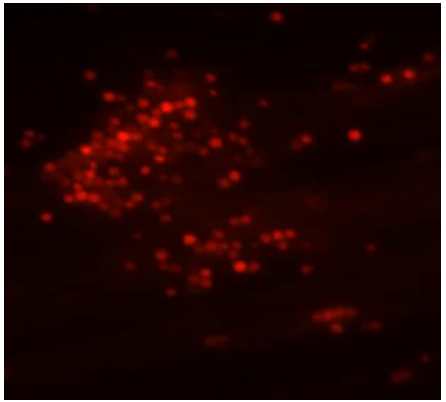
- **Engineered lysins can overcome the outer membrane (OM) barrier in the context of human blood matrices:**



- **Core activities:**
  - Rapid, potent and targeted bactericidal activity
  - Eradicates biofilms
  - Synergy with conventional antibiotics
  - Low propensity for resistance
  - Active against antibiotic-resistant strains
  - Resensitization of antibiotic-resistant strains

- **Rapid killing in human serum (rounding up, then lysis):**



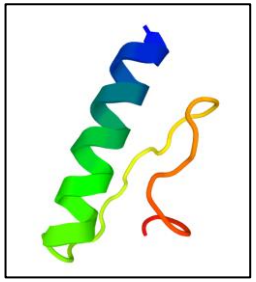


Targeting Gram-negatives with Amurin Peptides

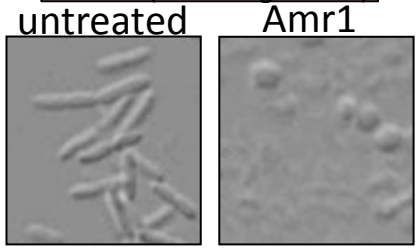
- Novel phage lytic agents with potent bactericidal activities vs GN ESKAPE pathogens
- CARBX-funded discovery program to identify lead candidate and conduct IND-enabling studies for the treatment of infections caused by MDR GN pathogens
- Features supporting development:

Broadly active

Organism	N	MIC_{100} (µg/mL)				
		Amr1	Amr2	Amr3	Amr4	Amr5
P. aeruginosa	14	2	2	1	2	0.5
E. coli	10	2	1	2	1	0.5
E. cloacae	10	4	2	2	2	1
K. pneumoniae	10	2	2	1	2	1
A. baumannii	10	1	4	2	2	0.5
S. typhimurium	2	2	2	2	4	n.d.
S. aureus	10	>64	>64	>64	>64	>64



5 min (*P. aeruginosa*)



- Rapid, potent and broad bactericidal activity
- Non-hemolytic
- Active in serum
- Eradicates biofilms
- Synergy with conventional antibiotics
- Active against antibiotic-resistant strains
- Resensitization of antibiotic-resistant strains

Therapeutic Potential of DLAs (Lysins and Amurins)

Attributes

- Rapid bacterial killing
- Biofilm eradication
- Synergy with SOC antibiotics
- Potential to re-sensitize antibiotic resistant strains

Unmet needs

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

Challenges

- Overcome the outer membrane (mitigation: engineer native lysins)
- Potential lack of activity in human blood matrices (mitigation: engineer native lysins)
- Scale up for in vivo studies eventual clinical trials (mitigation: partner with CMO)

Potential therapeutic uses

- In addition to conventional 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

ContraFect Corporation Pipeline

Program	Target Pathogen	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Exebacase (CF-301)	*Staphylococcus aureus*	**Bacteremia including endocarditis**				
CF-296	*Staphylococcus aureus*					
GN lysin	*Pseudomonas aeruginosa*	CARB-X Xccelerating global antibacterial innovation				
GN lysins	*Klebsiella pneumoniae* *Escherichia coli* *Enterobacter cloacae* *Acinetobacter baumannii*					
Amurin peptides	GN ESKAPE *pathogens* *E. coli*	CARB-X Xccelerating global antibacterial innovation				
GP lysins	*Streptococcus pneumoniae* *Enterococcus faecalis* Group B *streptococcus* *Bacillus anthracis*					

GN – Gram-negative
GP – Gram-positive

ContraFect Corporation

NASDAQ: CFRX

First in class anti-infectives for life-threatening, drug-resistant infections