

Antibactériens non conventionnels

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Centre de Référence des IOA complexes de Lyon (CRIOAc Lyon)

Président du Comité Scientifique des CRIOAc 2017-2022



Two major problems

Implantable
medical device
(connected)



Implant-associated
infections



Antimicrobial
resistance

Severe bacterial infections
(bone and joint, pneumonia, endocarditis, sepsis)

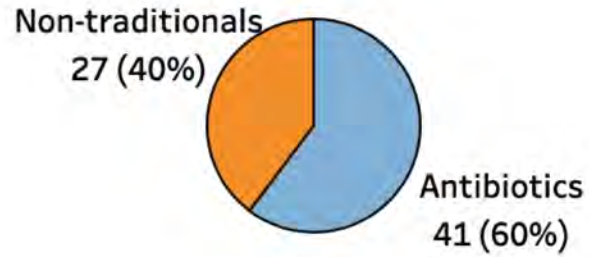
2020 ANTIBACTERIAL AGENTS IN CLINICAL AND PRECLINICAL DEVELOPMENT

an overview and analysis

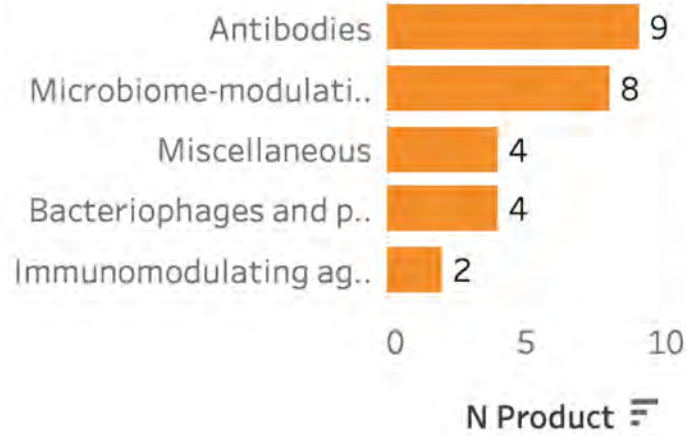


World Health
Organization

A.1. Products by type



A.2. No. of non traditional products by category



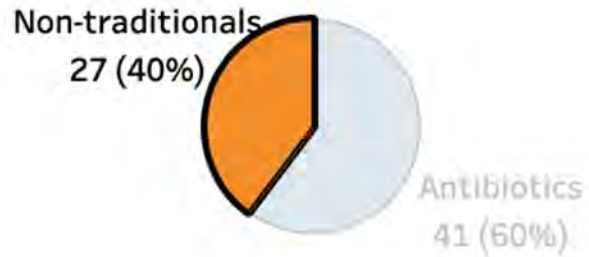
A.3. Products by pathogen category and phase

Pathogen category	Phase I	Phase II	Phase	Unkno..	Total
Priority pathogens	18	15	9	1	43
Mycobacterium tuberculosis	3	9			12
Clostridium difficile	3	8	2		13
Total	24	32	11	1	68

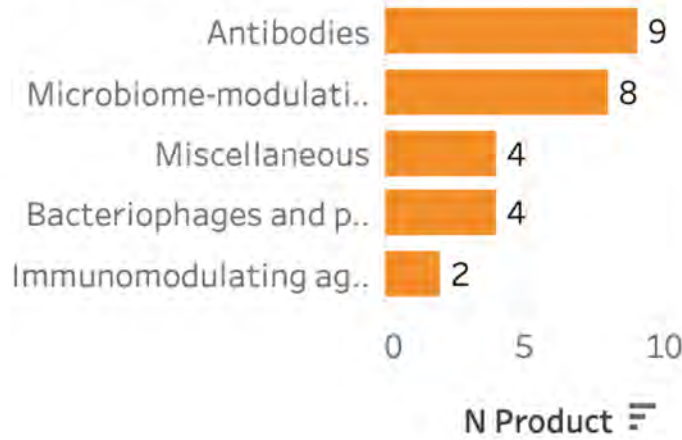
B. Expected activity against priority pathogens

Active?	Critical priority pathogens					Other priority pathogens							Subtotal	Total
	Acinetobac baumannii	Pseudomor aeruginosa	Enteroba..	All critical priority pathogens	Subtotal	Gram-positive priority p..	Neisseria gonnorrhoe:	Helicobact: pylori	Staphyloco aureus	Enterococc faecium	Streptococ pneumonia	Campyloba spp.		
Yes	7	7	14	3	21	17	3	2	17	3	2	2	21	38
Possibly	3	3	3	2	6	1	1	1	1	1			2	8
No	12	17	10	17	18	3	7	8	3	7	7	8	10	20

A.1. Products by type



A.2. No. of non traditional products by category



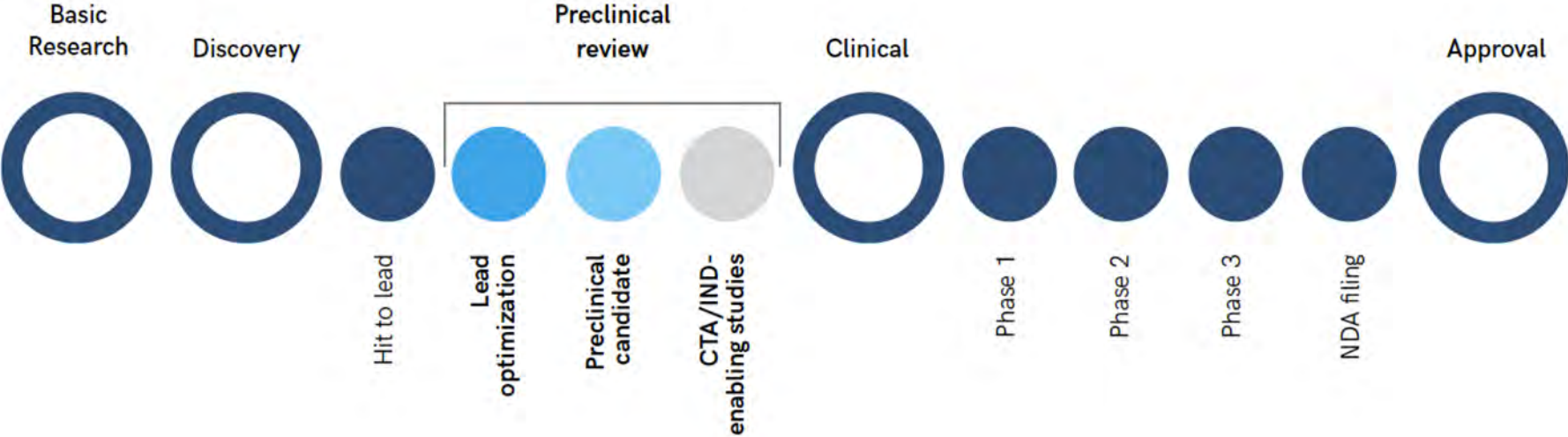
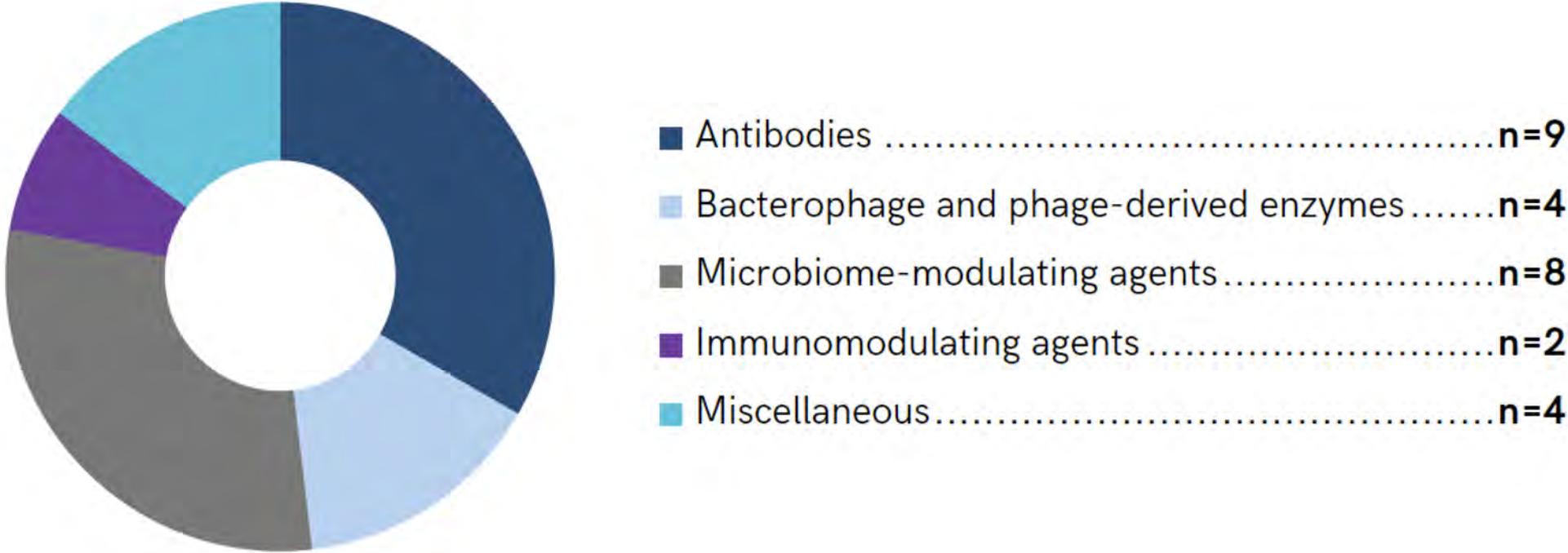
A.3. Products by pathogen category and phase

Pathogen category	Phase I	Phase II	Phase	Unkno..	Total
Priority pathogens	4	11	3	1	19
Clostridium difficile	2	5	1		8
Total	6	16	4	1	27

B. Expected activity against priority pathogens

Active?	Critical priority pathogens					Other priority pathogens							Subtotal	Total
	Acinetobac baumannii	Pseudomor aeruginosa	Enteroba..	All critical priority pathogens	Subtotal	Gram-positive priority p..	Neisseria gonnorrhoe;	Helicobact pylori	Staphyloco aureus	Enterococc faecium	Streptococ pneumonia	Campyloba spp.		
Yes	1	5	6	1	10	10	1	1	10	2	1	2	12	19

Fig. 7. Number of non-traditional antibacterials in the clinical pipeline.



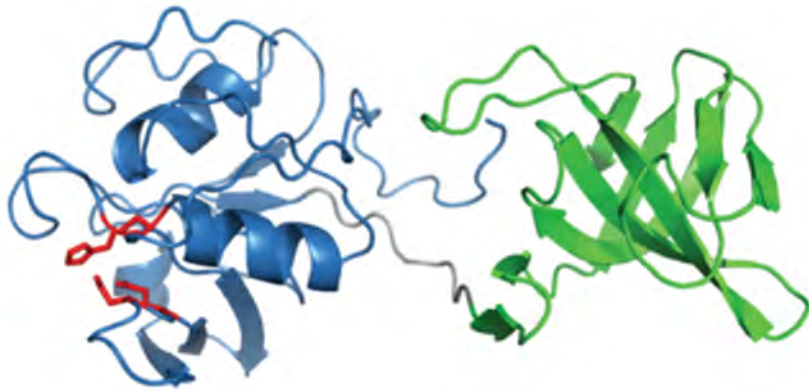
Non traditional anti-bacterial therapy



World Health
Organization

Lysins

Biological “natural”
enzymes



Bacteriophages
Natural viruses

Clinical officer



ESGNTA

European Society of Clinical Microbiology and Infectious Diseases

ESCMID STUDY GROUP
FOR NON-TRADITIONAL
ANTIBACTERIAL THERAPY


Bacteriophage Distributions and Temporal Variability in the Ocean's Interior



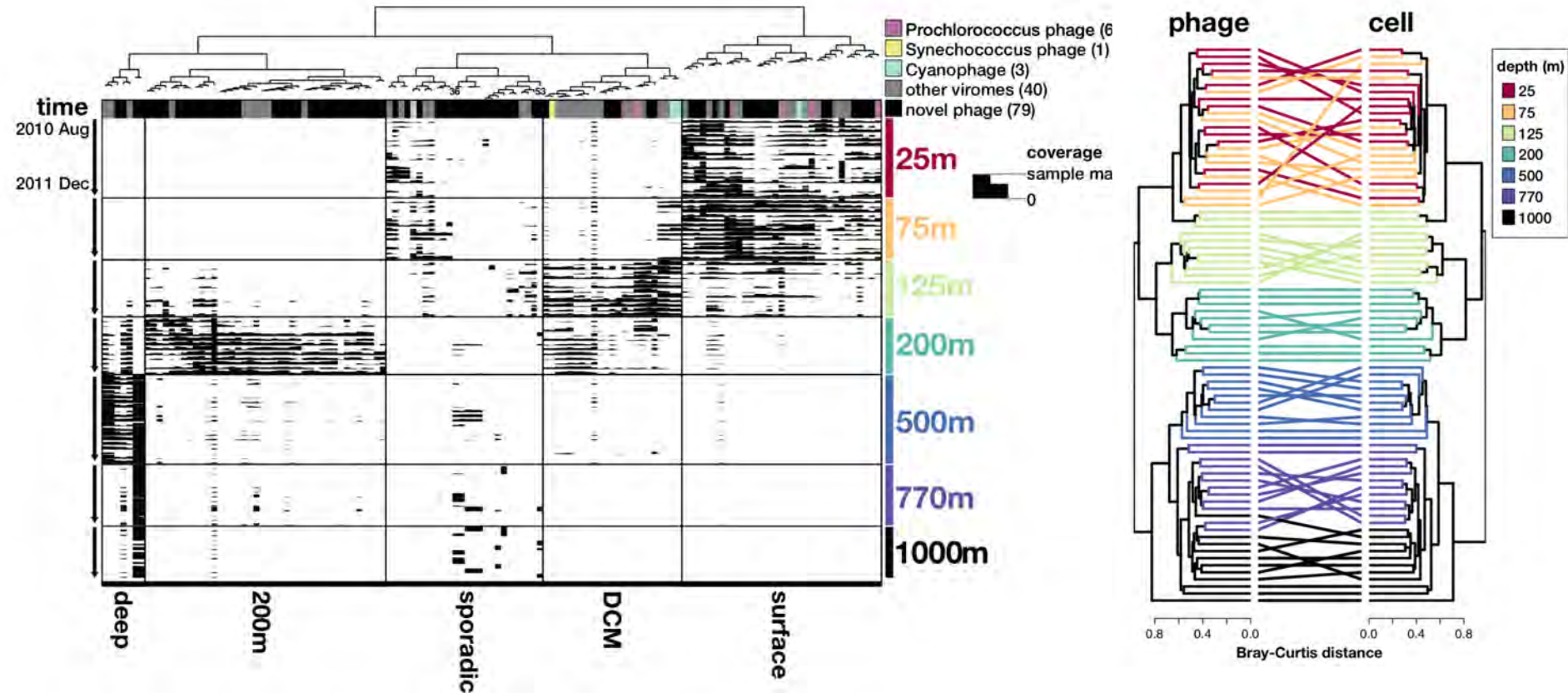
AMERICAN
SOCIETY FOR
MICROBIOLOGY



2017

Elaine Luo, Frank O. Aylward,* Daniel R. Mende,  Edward F. DeLong

Daniel K. Inouye Center for Microbial Oceanography: Research and Education, University of Hawaii, Honolulu, Hawaii, USA

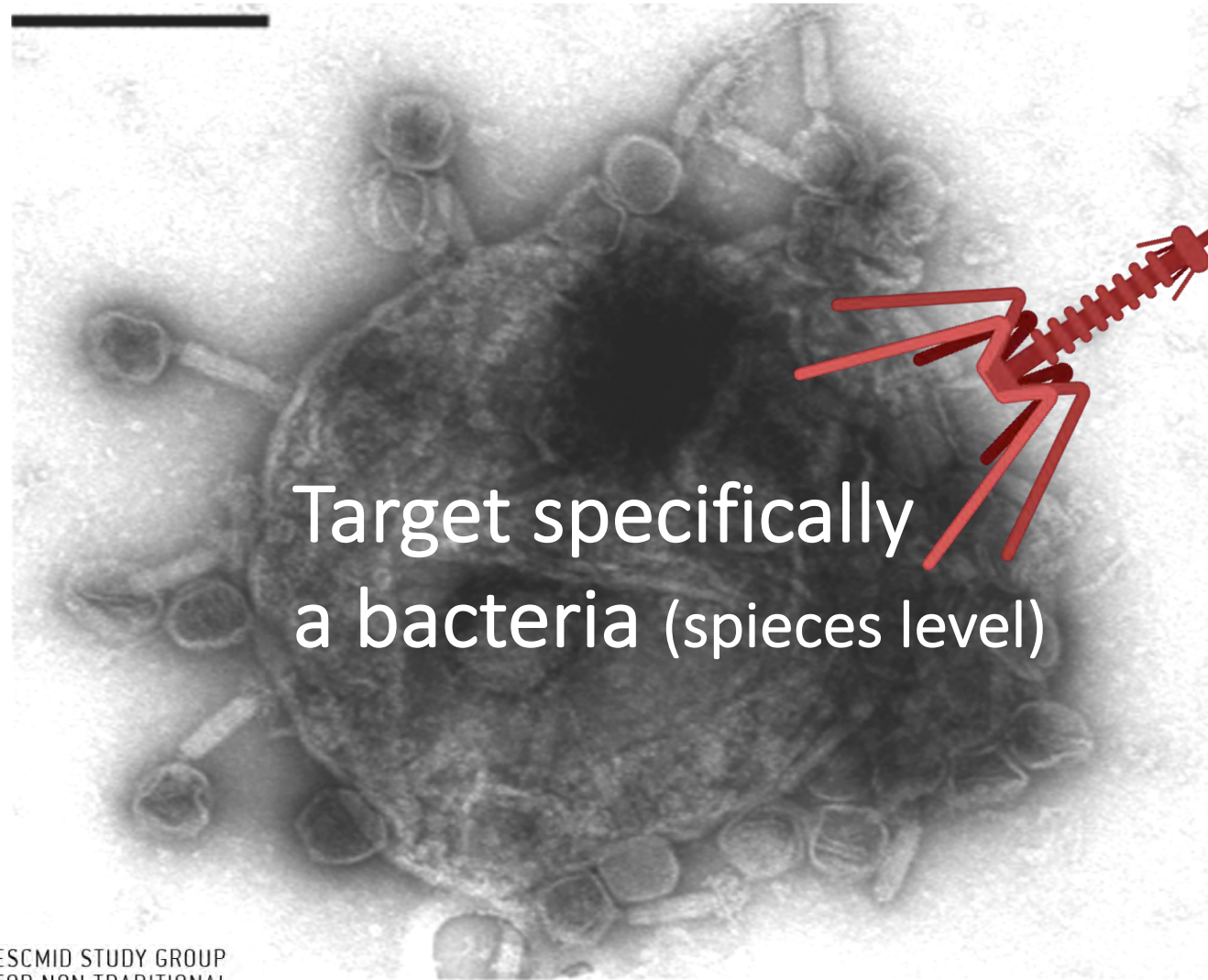


Bacteria have also their pandemics!



World Health
Organization

Non-**T**raditional
Antibacterial
therapy



Target specifically
a bacteria (species level)

Each virus



PHAGEⁱⁿLYON
Clinic

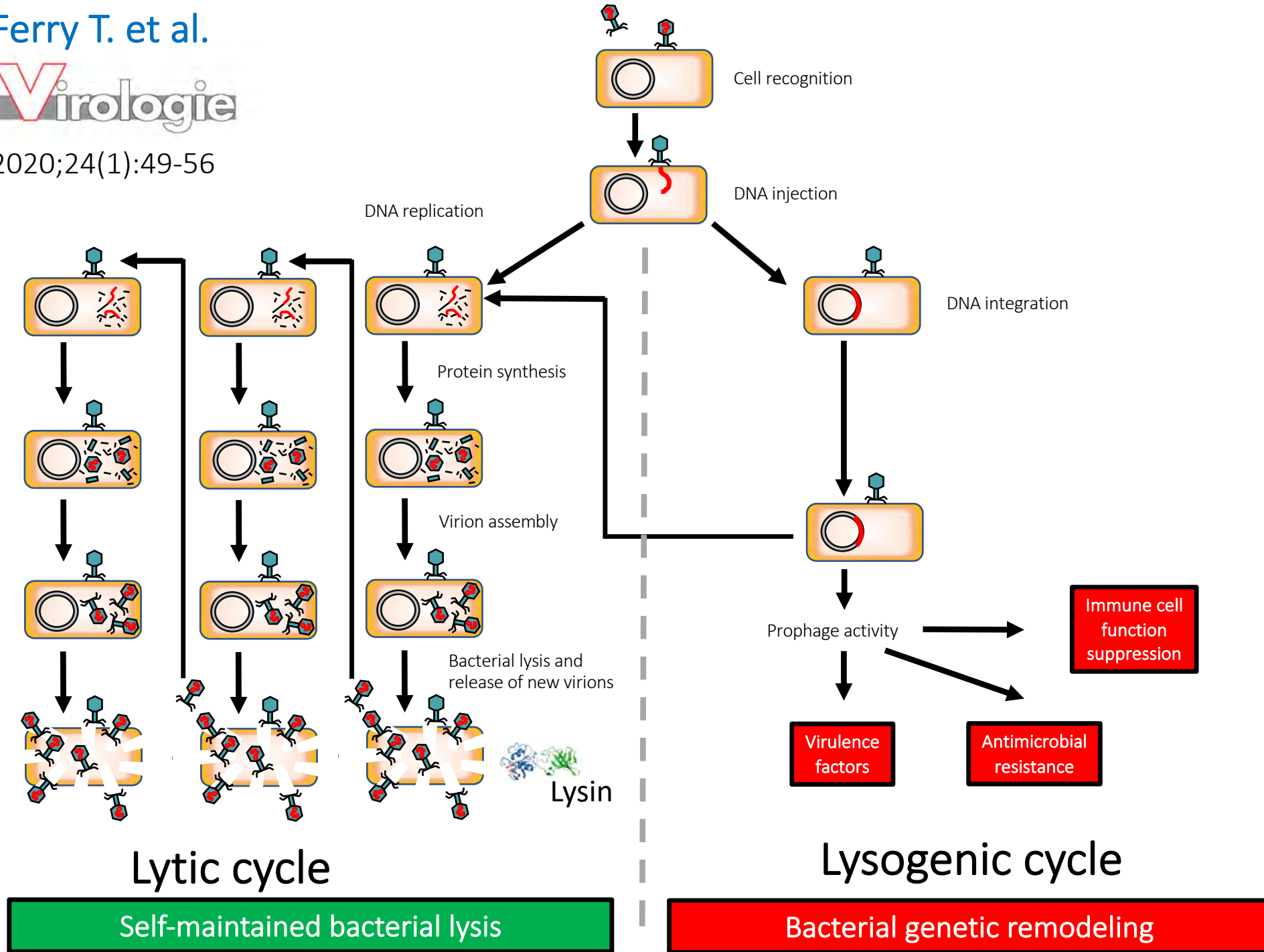


ESGNTA

European Society of Clinical Microbiology and Infectious Diseases

ESCMID STUDY GROUP
FOR NON-TRADITIONAL
ANTIBACTERIAL THERAPY

Merabishvili et al. *PloS ONE* 2009

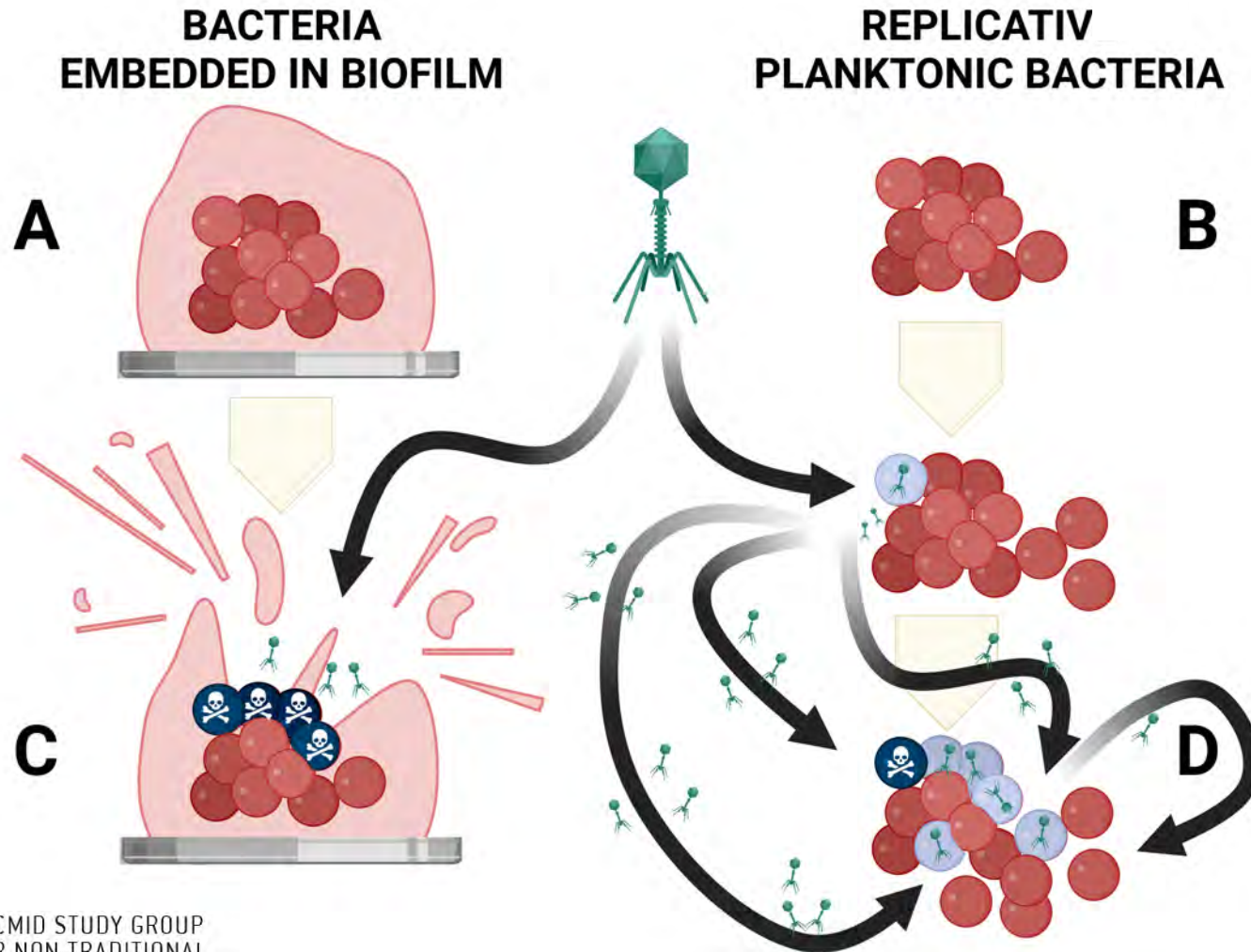


Bacteria have also their pandemics!



World Health Organization

Non-**T**raditional
Antibacterial
therapy



PHAGE_{in}LYON
Clinic



ESGNTA

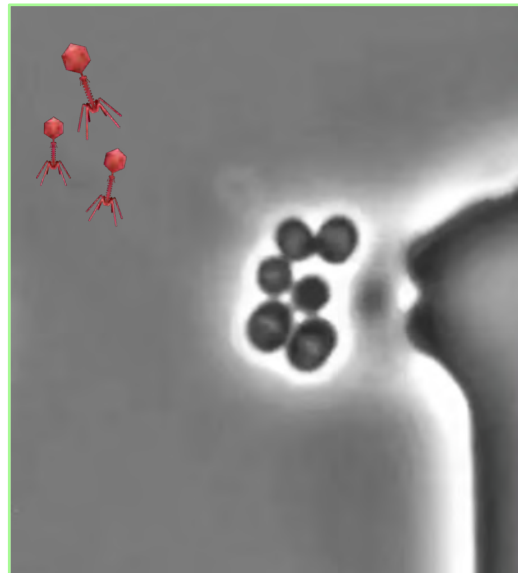
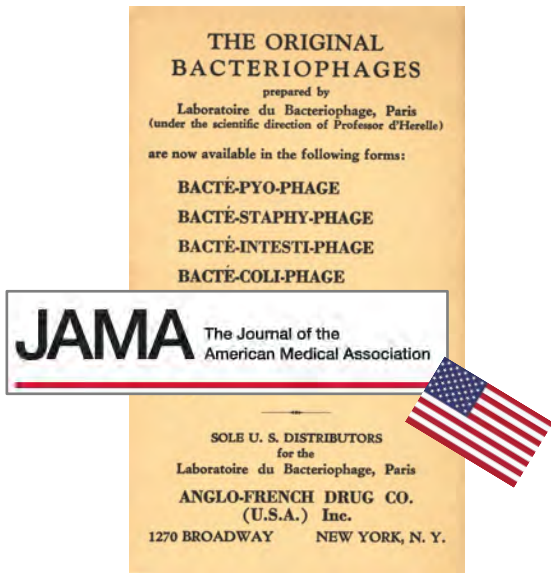
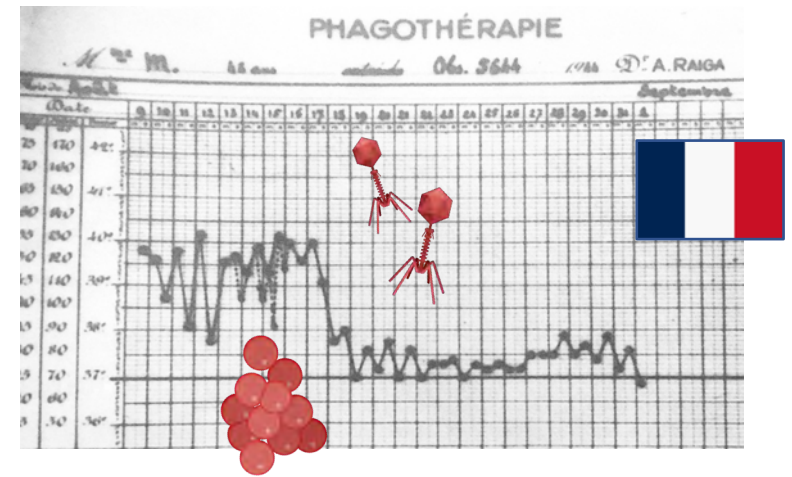
ESCMID STUDY GROUP
FOR NON-TRADITIONAL
ANTIBACTERIAL THERAPY

European Society of Clinical Microbiology and Infectious Diseases

T. Ferry. Springer 2023 In press

Phage therapy is fascinating

- Viral therapy for bacterial infections
- Story of phage therapy is connected to worldwide geopolitical events
- Potential incredible preclinical efficacy
- Failure to implement phage therapy in the west



S. aureus being lysed by the Sa2 phage

Bacterial DNA appeared in green

Courtesy Pascal Maguin
Luciano Marraffini Lab

THE ROCKEFELLER UNIVERSITY





Story of phage Therapy



Creation from F. d'Herelle (dismissed from Pasteur Institute):

- Laboratoire du bactériophage (Paris)
- Eliava Center (Georgia)
 - Fixed cocktails to treat digestive-tract infections
 - Fixed cocktails to treat skin and soft tissue infections



LE LABORATOIRE DU BACTÉRIOPHAGE
 Laboratoire de recherches dont les bénéfices sont destinés à des fins scientifiques
 sous le contrôle du
PROF. d'HERELLE

Bacté-coli-phage Colibacilluries . Pyelonephrites . Cystites	Bacté-rhino-phage Grippe . Coryza . Rhino-pharyngites
Bacté-intesti-phage Entérites . Colites . Diarrhées infantiles	
Bacté-pyo-phage Panaris . Phlegmons . Plaies Infectées	Bacté-staphy-phage Furonculose . Anthrax

AGENTS GÉNÉRAUX
LABORATOIRES ROBERT & CARRIÈRE - 37, rue de Bourgogne - Paris

BACTÉ-STAPHY-PHAGE

BACTÉ-PYO-PHAGE

T. Ferry

LE LABORATOIRE DU BACTÉRIOPHAGE
 FONDE PAR LE PROFESSEUR D'HERELLE
 75, RUE OLIVIER DE SERRES - PARIS (XV)
 Téléph. VAUgrad 55-62



Eliava Institute (Georgia)



100th anniversary



HELPING YOU LIVE LIFE

We offer highly specialized treatments

Therapy Services





Eliava Institute (Georgia)



Story of phage Therapy in Lyon



Dr. Emile PESCE

- Medical thesis "Contribution to the study of the treatment of furuncles and anthrax by bacteriophage", 1931



“Need for a microbiological analysis to select the phage, based on its activity on the patient’s strain”

“If microbiological analysis could not be done, use fixed cocktail”

Archives from Ferry T.

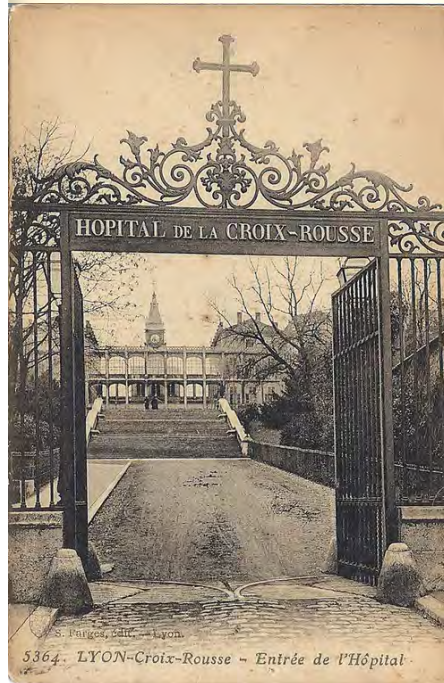


Le Journal de Médecine de Lyon

After d'Herelle, The story continued in Lyon

Traitement des infections à bacilles pyocyaniques par des bactériophages adaptés par sélection.

Par MM. André BERTOYE et A.-L. COURTIEU.



Les bacilles pyocyaniques sont fréquemment résistants aux antibiotiques usuels. Cette résistance, qui a été attribuée semble être en augmentation. Leur caractère rebelle est une de leurs caractéristiques. Cette résistance est différente de celle observée dans l'existence de bactéries de stock-bactériophages. L'adaptation par sélection a une variété de bactériophage à la souche isolée du malade permet de sélectionner un phage nutritif et indispensable pour le pouvoir intraveineux. Un tel phage est utilisé dans cette publication.

Antimicrobial resistance

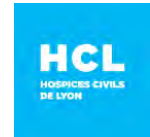
**Phage banking
Phage training**

**Meningitis
Skin and soft tissue
Bone and joint infection**



**Clinique des Maladies Infectieuses, Hôpital de la Croix-Rousse
Hospices Civils de Lyon**

1958-1960





Méningite purulente à colibacilles traitee par un bactériophage adapté intrarachidien

Par MM. P. SEDALLIAN, A. BERTOYE, J. GAUTHIER,
J.-M. MULLER et A.-L. COURTIEU.

Clinique des Maladies Infectieuses et Institut Pasteur de Lyon

Une injection intrarachidienne d'1/10 de centimètre cube n'ayant été suivie d'aucun accident, on commence, dès le lendemain 30 septembre, le traitement aux doses thérapeutiques : 1 centimètre cube de bactériophage intraventriculaire et 1 centimètre cube intrarachidien par vingt-quatre heures. Rapidement, le nombre des éléments du liquide céphalo-rachidien s'effondre à 356 contre 1.800 deux jours auparavant. Dès lors, la situation va s'améliorer très vite et on peut espérer la partie gagnée, malgré la persistance dans le liquide céphalo-rachidien d'un taux d'albumine aux alentours d'un gramme et de 50 à 200 éléments.

A une demande de **M. Roche**, **M. Bertoye** précise que nombre de germes peuvent être dotés d'un bactériophage. Il faut quatre à cinq jours pour l'adaptation du bactériophage : ce ne peut donc pas être une médication d'urgence.

Lyon Med. 1958 Mar 30;90(13):509-12

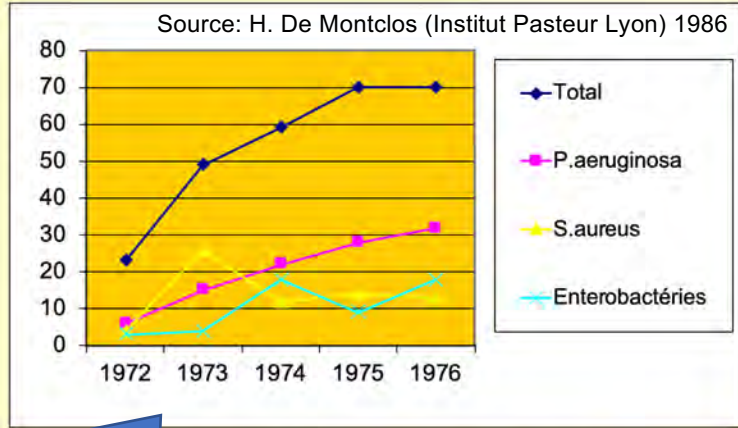


L'INSTITUT BACTÉRIOLOGIQUE



DE LYON

Lyon
Pasteur
Institute



Active and trained
bacteriophages

Technical development
Customisation of treatment
Academic multidisciplinary approach
70 patients/year!

Isolation of the isolates
responsible for the infection



1978

Pr. Bertoye

**Infectious
diseases
clinic**

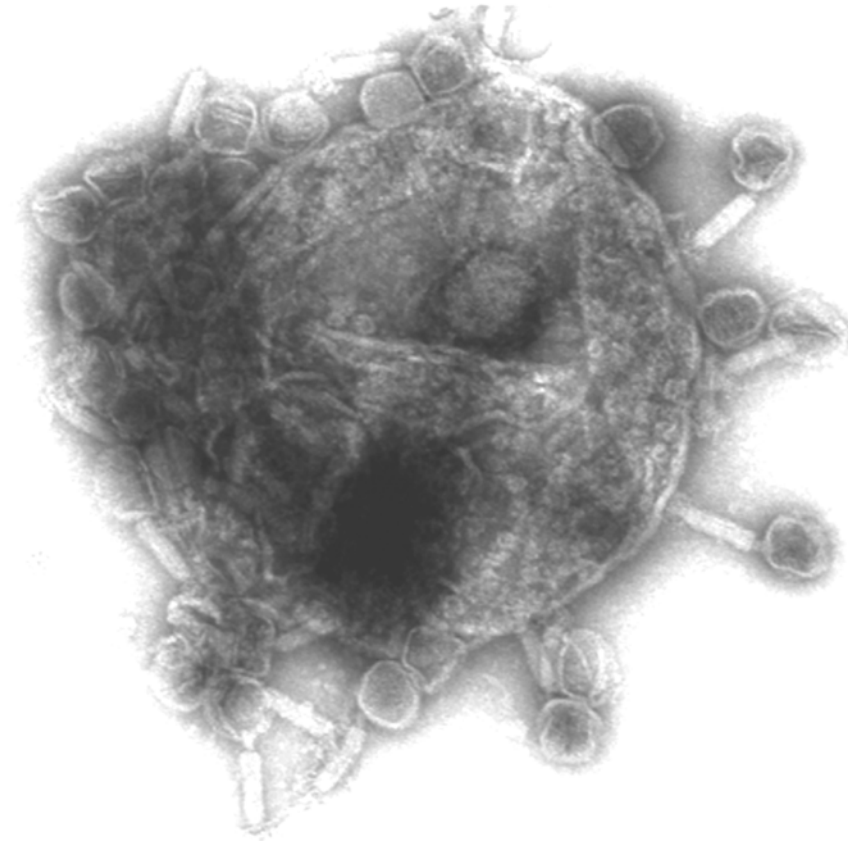


Eliava Institute (Georgia)



- PYO Bacteriophage
- FERSIS Bacteriophage
- STAPHYLOCOCCAL Bacteriophage
- SES Bacteriophage
- INTESTI Bacteriophage
- ENKO Bacteriophage

Bacteriophage (*Myoviridae*) targeting *S. aureus*



Merabishvili et al. PloS ONE 2009



Ferry T.



Professor Andrzej Górski



Doctor Ryszard Medyński with Anna Kubalska, one of the Medical Unit's patients.
Kalbar/TFN



The Institute of Immunology and Experimental Therapy's Medical Centre has been looking for a cure for patients who have lost all hope that their ailments could disappear.
Kalbar/TFN



"Our centre treats antibiotic-resistant infections. The great problem in medicine today is that we are becoming defenceless against the bacteria that cause them," says Professor Andrzej Górski.
Kalbar/TFN



The Institute is supported by the Bacteriophage Laboratory, which stores over 600 different phages.
Kalbar/TFN



We carry phages in our bodies says Doctor Beata Weber-Dąbrowska.
Kalbar/TFN

THEfirstNEWS

Wrocław clinic uses 'super viruses' to battle rebellious bacteria

JOANNA JASIŃSKA MARCH 22, 2020

Russian Phages



МИКРО  **ГЕН**

пиобактериофаг поливал.очищ.жидк.(
секста) 20мл фла г4

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ДП 01.08.2017
СГ 01.03.2019 РОССИЯ

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местного и наружного применения

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Способ применения – см. Инструкцию

1 000 000 000 boxes produced each year





Development and Use of Personalized Bacteriophage-Based Therapeutic Cocktails To Treat a Patient with a Disseminated Resistant *Acinetobacter baumannii* Infection

2017



Open Forum Infectious Diseases

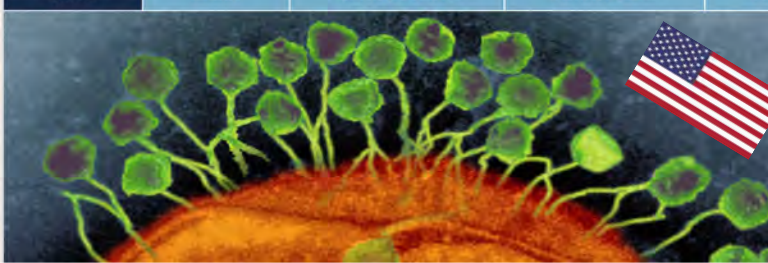
MAJOR ARTICLE



UC San Diego School of Medicine

Center for Innovative Phage Applications and Therapeutics
In the Division of Infectious Diseases & Global Public Health

HOME ABOUT NEWS & EVENTS PATIENT CARE



Lessons Learned From the First 10 Consecutive Cases of Intravenous Bacteriophage Therapy to Treat Multidrug-Resistant Bacterial Infections at a Single Center in the United States

Saima Aslam,^{1,2} Elizabeth Lampley,² Darcy Wooten,¹ Maile Karris,¹ Constance Benson,^{1,2} Steffanie Strathdee,^{1,2} and Robert T. Schooley^{1,2}

¹Division of Infectious Diseases and Global Public Health, University of California, San Diego, La Jolla, California, USA, and ²Center for Innovative Phage Applications and Therapeutics, University of California, San Diego, La Jolla, California, USA



Contemporary

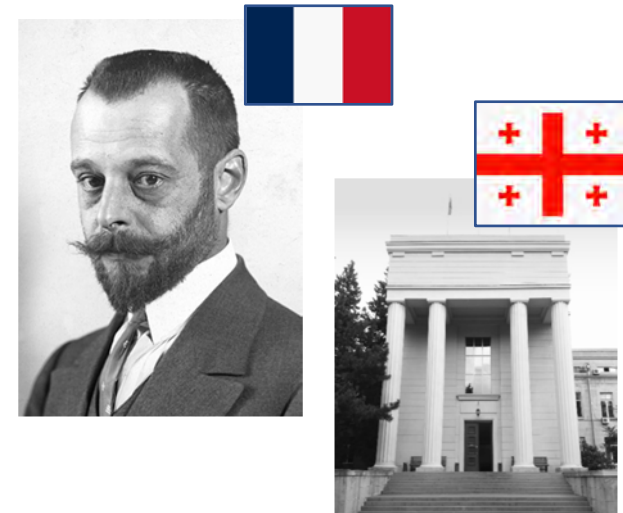
Previous clinical trials have not « failed »

- Most of them were phase I/IIa/IIb and **not phase III**
- Phages are **particular anti-infective agents** (≠ antibiotics)
- Need a **specific** purification process
- Purified phages or phage cocktails are potentially **not stable during time**
- **High specificity** of phages
- Potential need for a **phagogram** (like antibiogram) before treatment



Don't forget the lessons of the past

Respect the experience of the East



T. FERRY



KEEP CALM AND USE

PHARMACEUTICAL GRADE PHAGES

PHAGE 2.0 THERAPY

ESCMID MANAGING INFECTIONS PROMOTING SCIENCE

ESGNTA ESCMID STUDY GROUP FOR NON-TRADITIONAL ANTIBACTERIAL THERAPY European Society of Clinical Microbiology and Infectious Diseases

Elected Executive Committee:

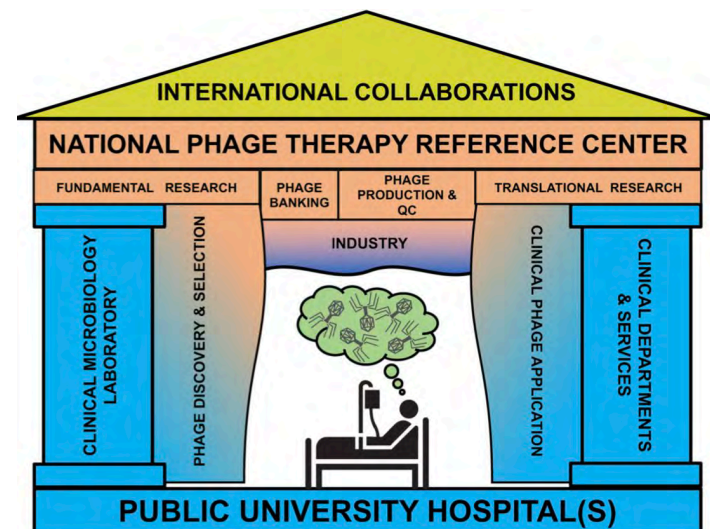
Ran Nir-Paz, Israël

Jean-Paul Pirnay, Belgium

Clinical officer: Tristan Ferry, France

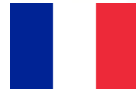
Shawna Mc Callin, Switzerland

Zuzanna Drulis-kawa, Poland

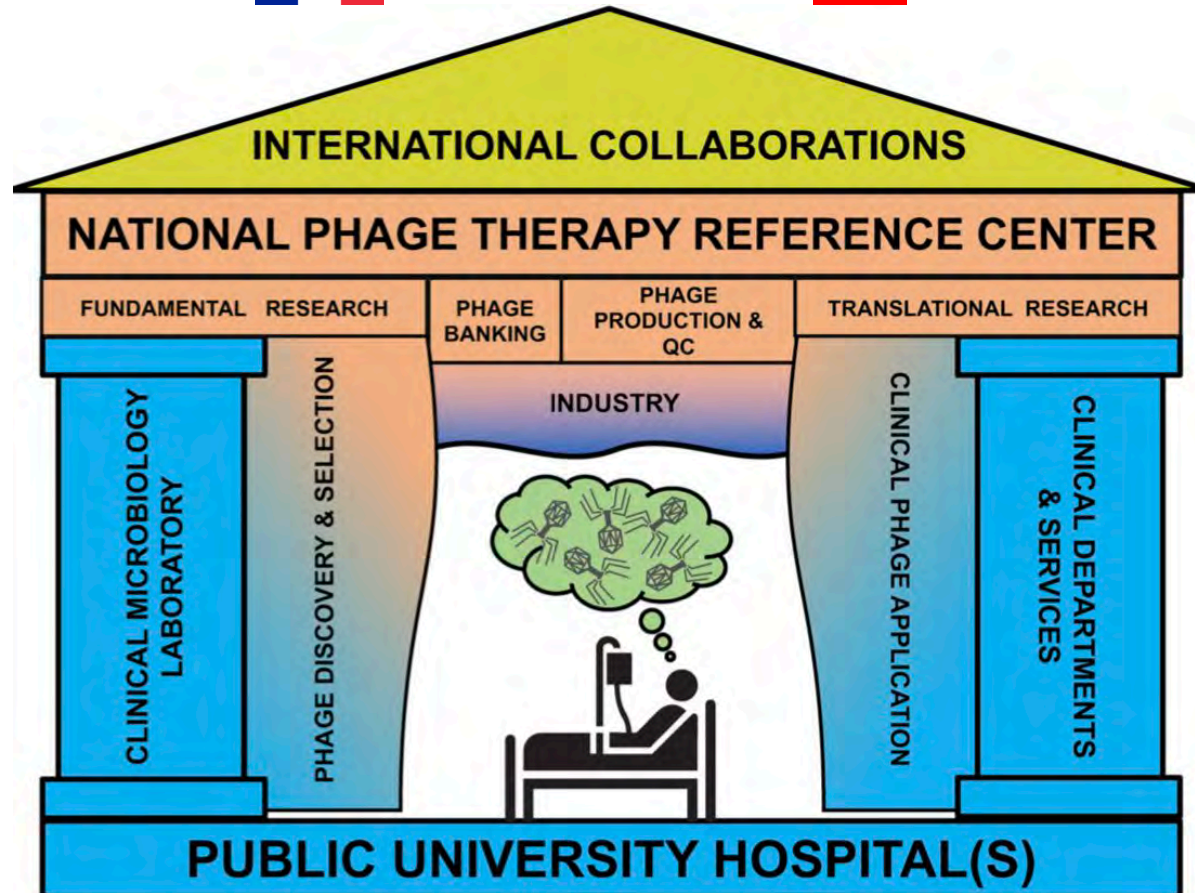
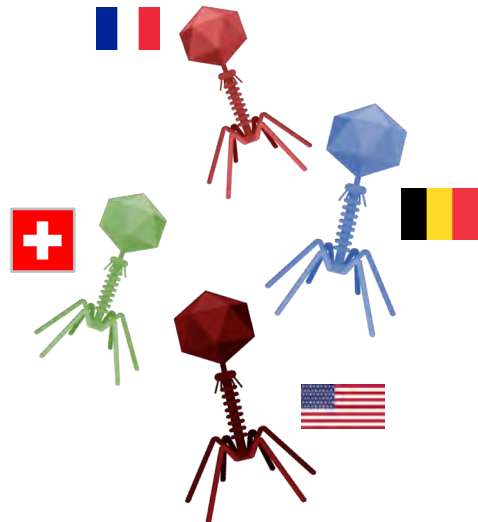


Recent progress toward the implementation of phage therapy in Western medicine

Jean-Paul Pirnay^{1,†}, Tristan Ferry^{2,3,†} and Grégory Resch^{4,*,†}



Phages



Lysins



**THE MYTHOLOGY
OF PHAGE THERAPY**



T. FERRY

vs.

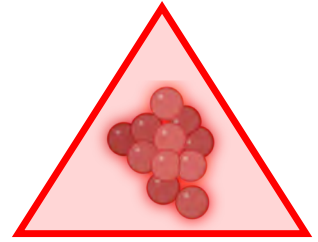


EBM

Clinical
Trials

T. FERRY

A large panel of severe bacterial infections



Central nervous system infections

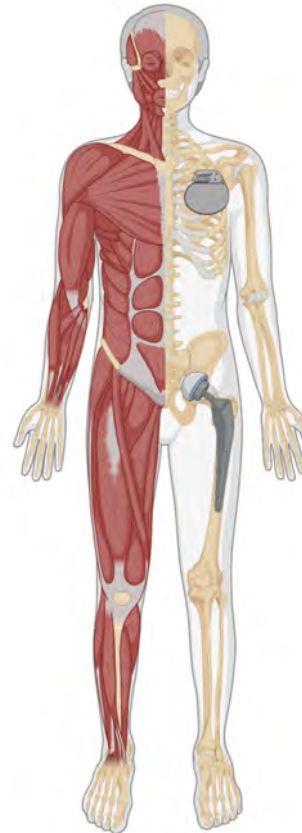
Implant-associated meningitis

Lung infections

Ventilator-associated pneumonia
Exacerbation in cystic fibrosis
Exacerbations in bronchiectasis

Urinary tract infections

Pyelonephritis
Ureteral stent-associated infection



Cardiovascular infections

Endocarditis
Cardiac electronic device infection
Prosthetic-valve endocarditis
Vascular graft infection

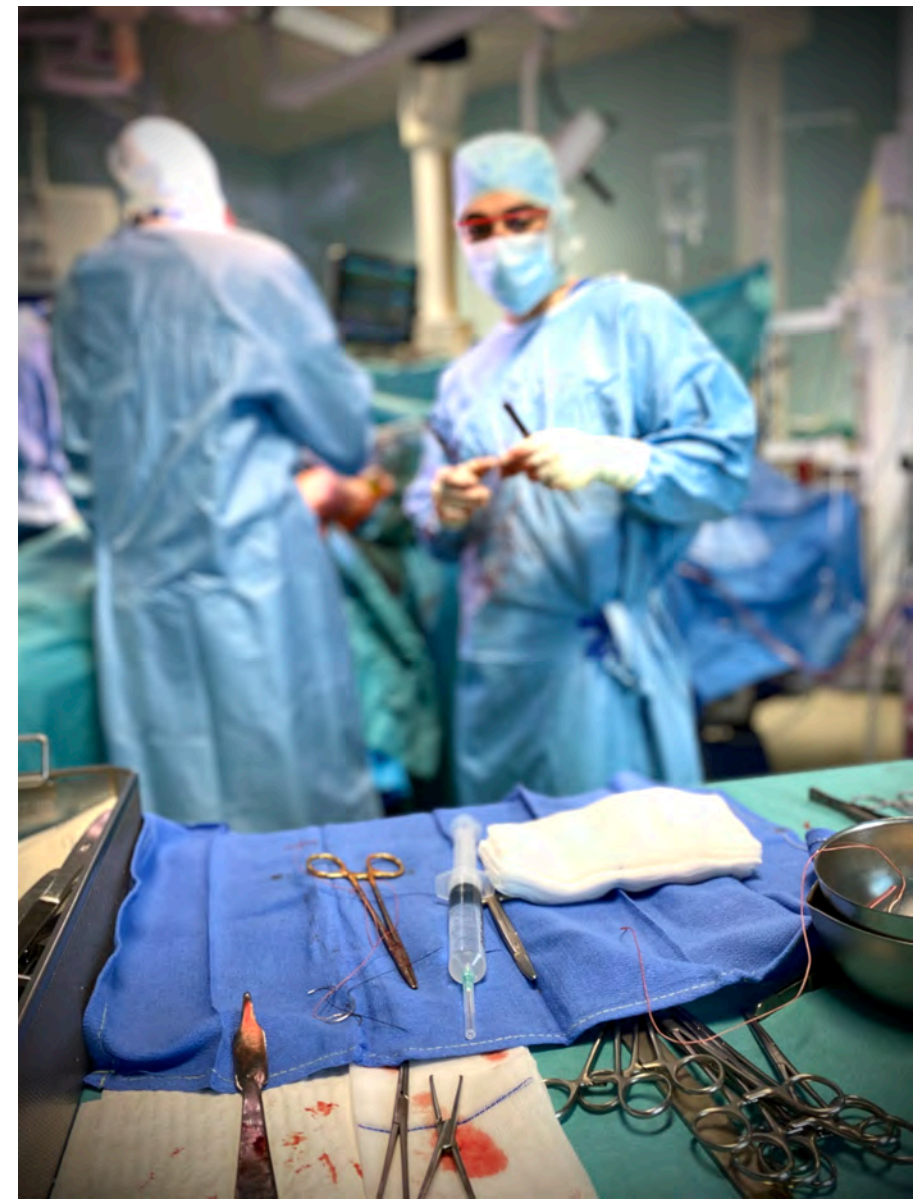
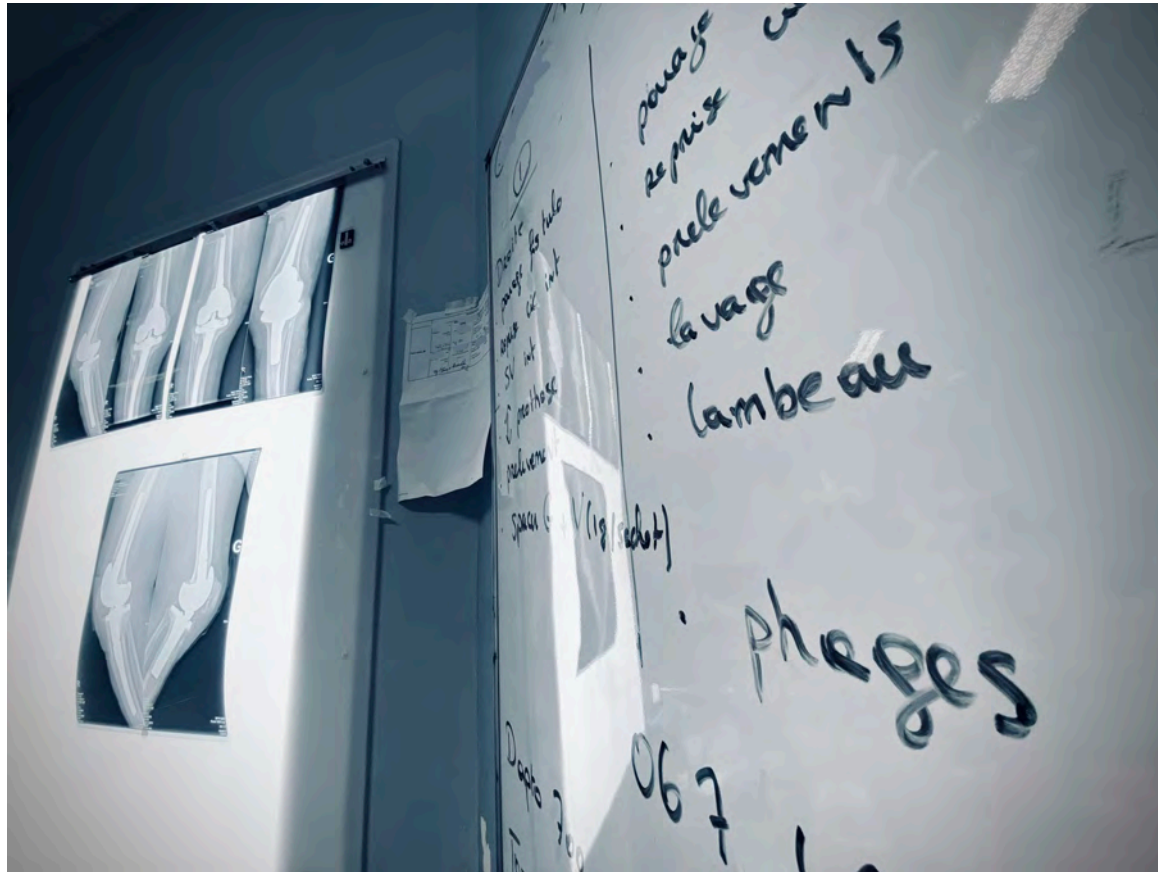
Muskuloskeletal infections

Wound infection
Osteomyelitis, fracture-related infection
Implant-associated bone and joint infection
Prosthetic joint infection

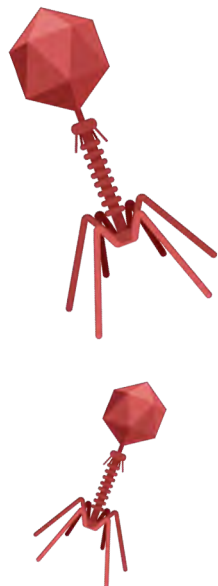
Digestive-tract infections

Typhoid fever, shigellosis
Cholera

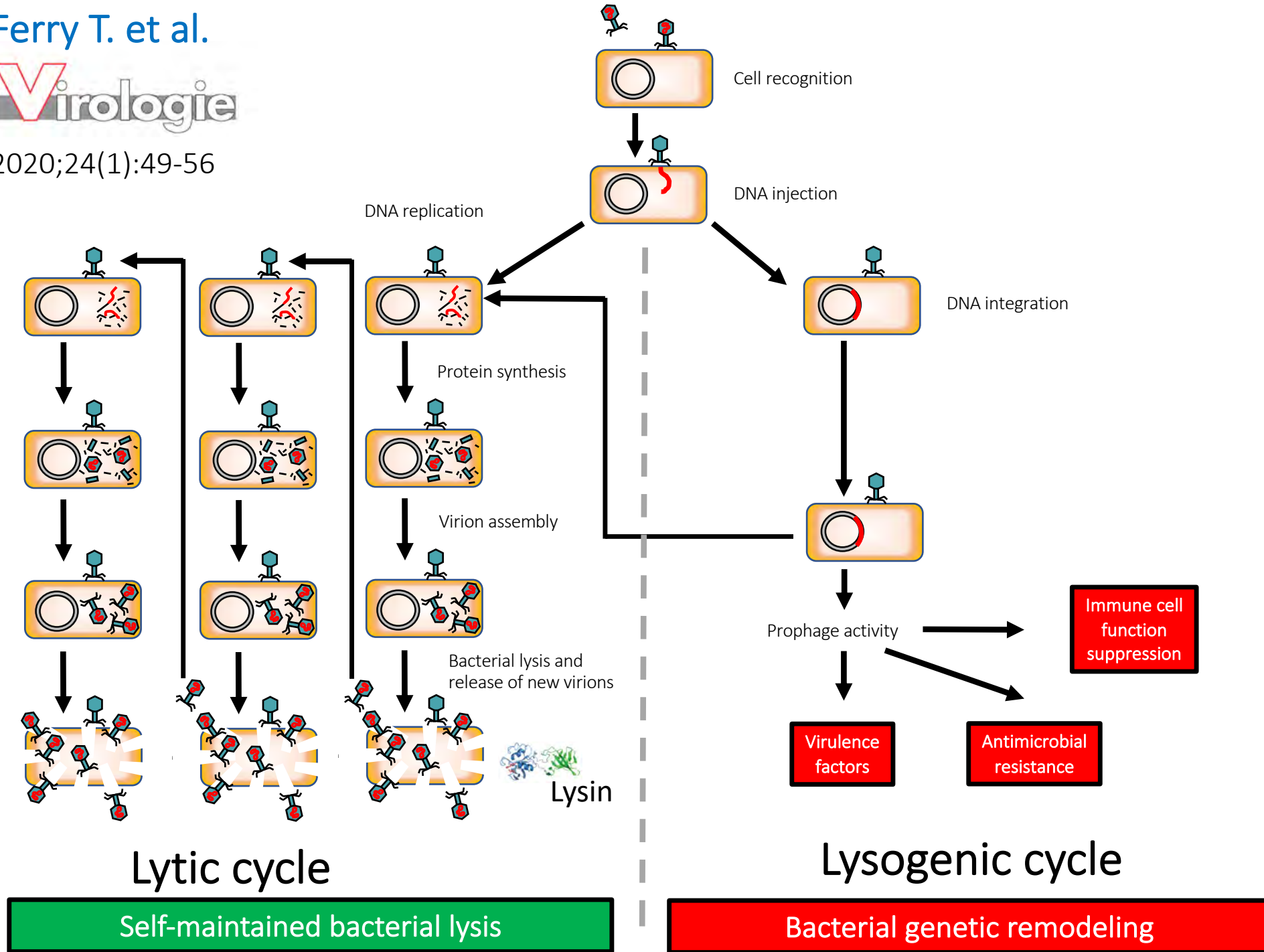
#PhagoDAIR procedure



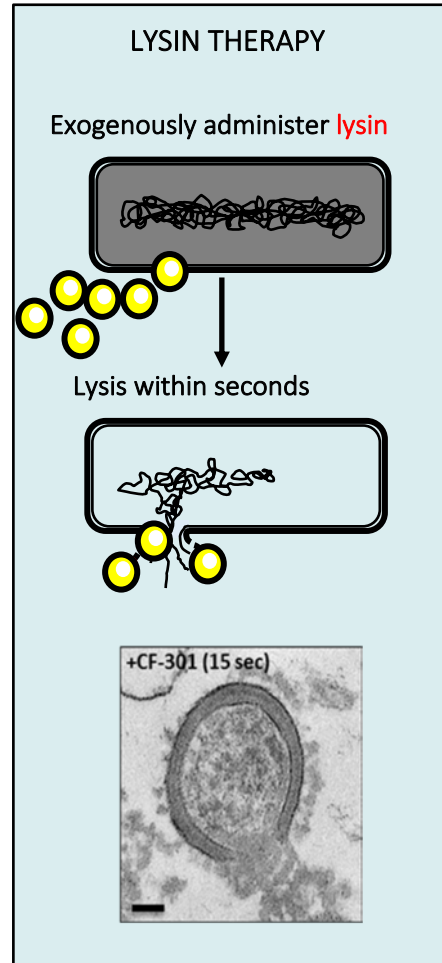
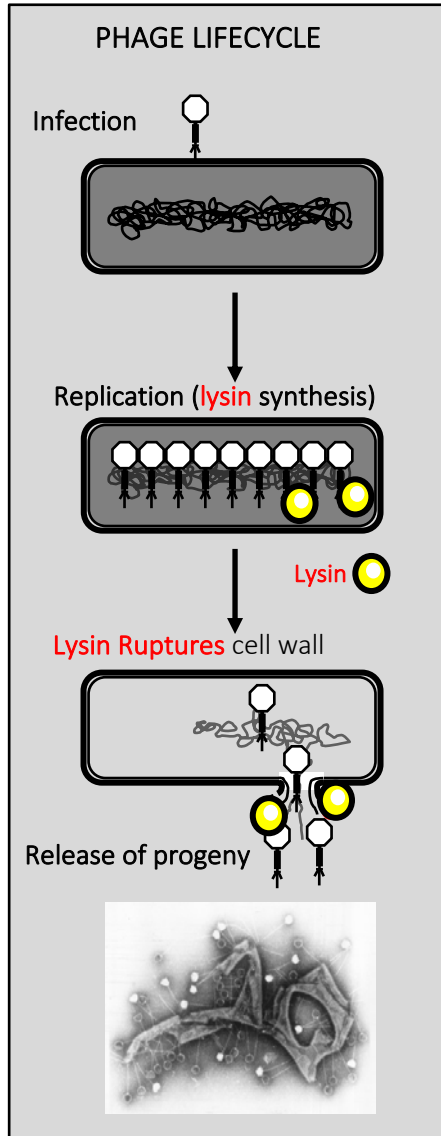
#PhagoDAIR procedure



>1 billion of **active viruses** infecting *S. aureus* in a syringe



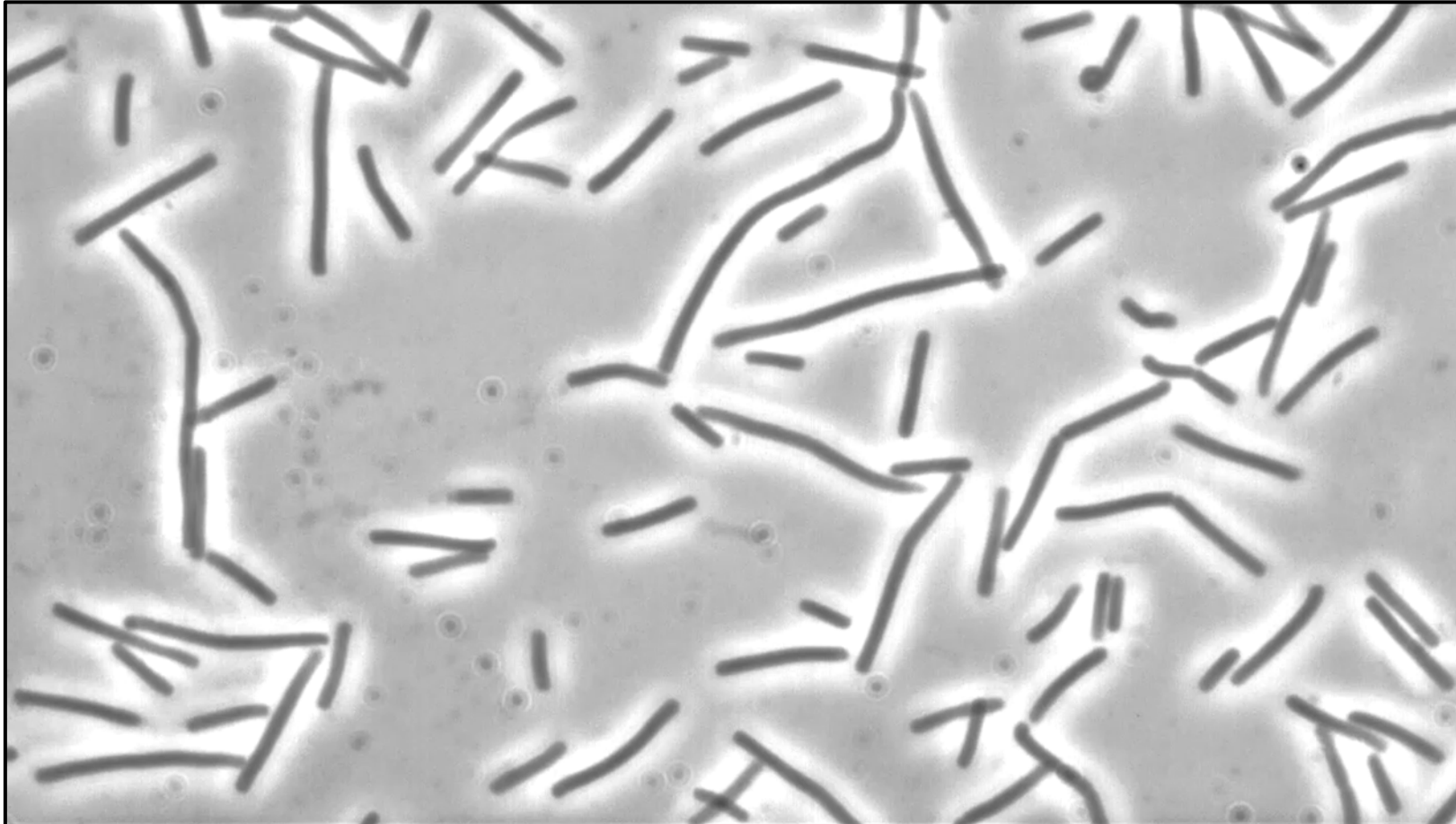
Lysins: A New Class of Antibacterial Biologics



- **Lysins are direct lytic agents** cloned/engineered leveraging genetic sequences found in bacteriophage
- **Novel mode of action:** peptidoglycan hydrolysis leading to osmotic lysis
- **Microbiological attributes:**
 - Rapid, potent and targeted activity
 - Eradication of biofilms
 - Synergy with conventional antibiotics
 - Low propensity for resistance development and no antibiotic cross-resistance

A Lysin in Action Real Time:

Peptidoglycan Hydrolysis and Osmotic Lysis



● Concentration = 1 $\mu\text{g}/\text{mL}$

Source: Ray Schuch

Exebacase (CF-301): A Novel Anti-staphylococcal Agent

A first-in-class anti-staphylococcal lysin (cell wall hydrolase)

- Key Microbiological Attributes

- Rapid, potent activity against *S. aureus* and coagulase-negative staphylococci (CNS) including multidrug resistant (MDR) phenotypes and beta-haemolytic streptococci
- Eradicates staphylococcal biofilms
- Synergy with conventional antibiotics
- Low propensity for resistance development and no antibiotic cross-resistance
- Suppression of antibiotic resistance

- Clinical Development

- Completed Phase 1: Safe and well tolerated with linear pharmacokinetics
- Completed Phase 2: Superiority design study compared exebacase + standard-of-care antibiotics (SoCA) vs SoCA alone in patients with *S. aureus* bacteremia including endocarditis
- Phase 3: Superiority design study comparing exebacase + SoCA vs SoCA alone in patients with *S. aureus* bacteremia including right-sided endocarditis



Bacteriophage Lysin CF-301, a Potent Antistaphylococcal Biofilm Agent

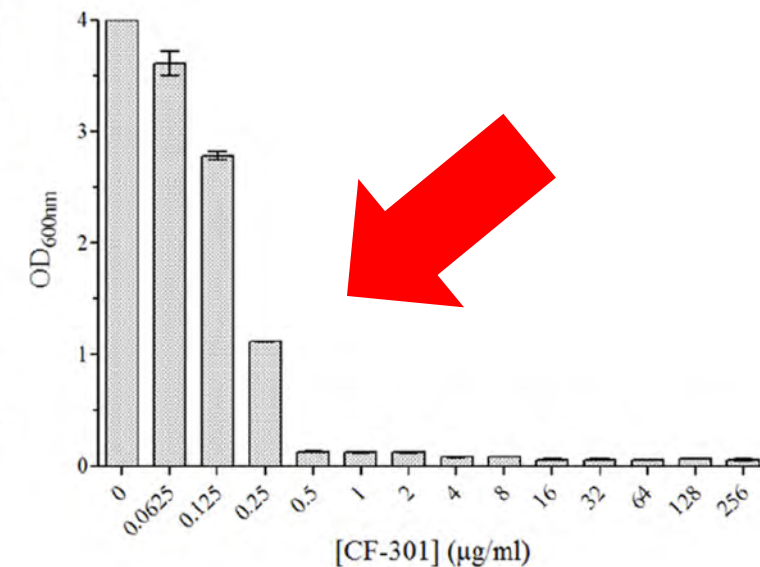
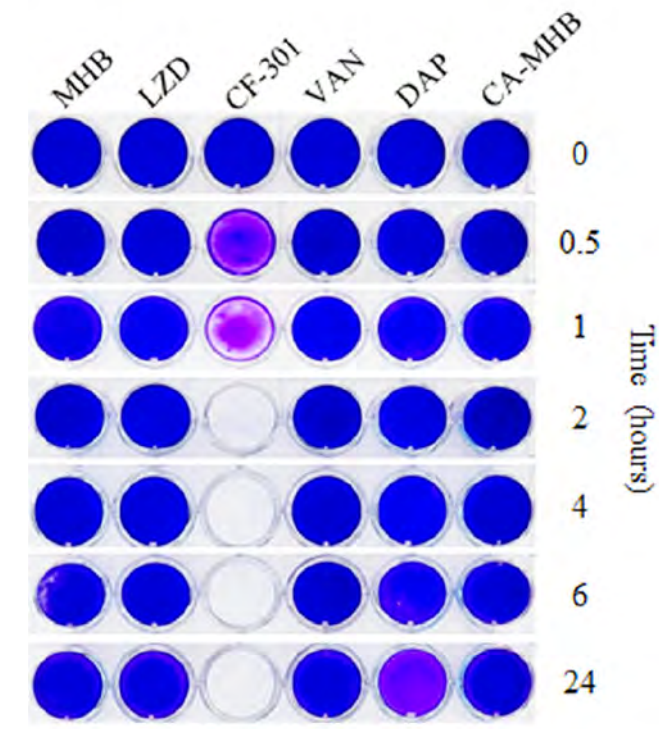
Raymond Schuch,^a Babar K. Khan,^{a*} Assaf Raz,^b Jimmy A. Rotolo,^a Michael Wittekind^a

ContraFect Corporation, Yonkers, New York, USA^a; Laboratory of Bacterial Pathogenesis and Immunology, The Rockefeller University, New York, New York, USA^b

TABLE 1 Activity of CF-301 and DAP against mature biofilms

Organism	n	Concn ($\mu\text{g/ml}$) of:			
		CF-301		DAP	
		MBEC ₉₀	Range	MBEC ₉₀	Range
MSSA	40	0.125	0.125 to 1	>1,024	512 to >1,024
MRSA	55	0.25	0.125 to 0.5	>1,024	>1,024
CoNS ^a	46	8	0.125 to 32	>1,024	256 to >1,024
<i>S. pyogenes</i> (group A)	27	0.25	0.03 to 1	>1,024	256 to >1,024
<i>S. agalactiae</i> (group B)	20	0.5	0.03 to 1	>1,024	512 to >1,024

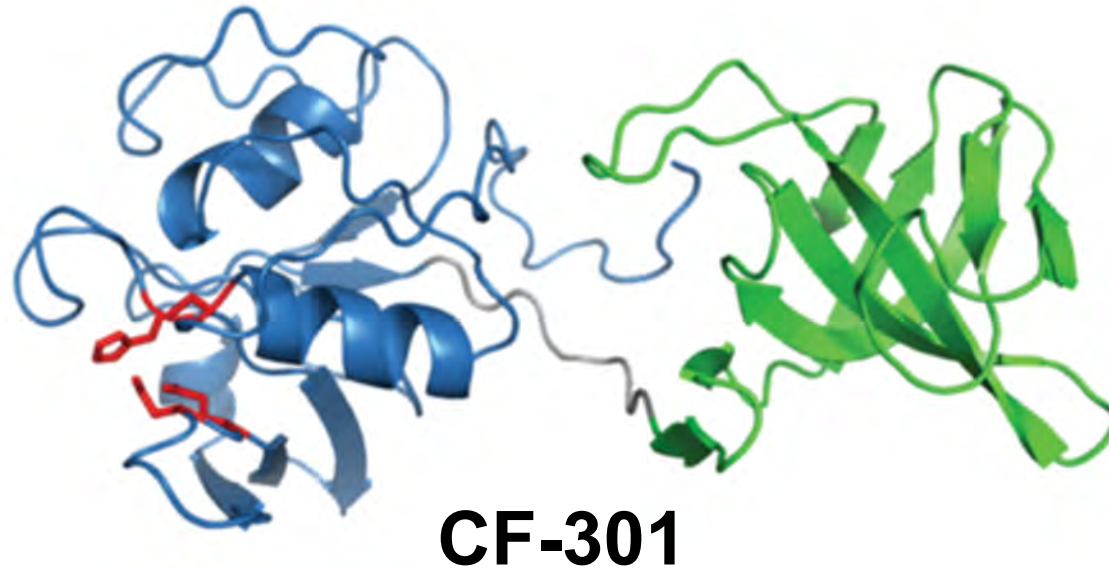
^aCoagulase-negative staphylococci examined in this study include the following (number of isolates in parentheses): *S. epidermidis* (21), *S. warneri* (9), *S. hominis* (5), *S. capitis* (2), *S. saprophyticus* (2), *S. cohnii* (1), *S. hyicus* (1), *S. lugdunensis* (2), *S. sciuri* (2) and *S. simulans* (1).



Combination Therapy With Lysin CF-301 and Antibiotic Is Superior to Antibiotic Alone for Treating Methicillin-Resistant *Staphylococcus aureus*-Induced Murine Bacteremia

Raymond Schuch,¹ Han M. Lee,¹ Brent C. Schneider,¹ Karen L. Sauve,¹ Christina Law,¹ Babar K. Khan,¹ Jimmy A. Rotolo,¹ Yuki Horiuchi,¹ Daniel E. Couto,¹ Assaf Raz,² Vincent A. Fischetti,² David B. Huang,¹ Robert C. Nowinski,¹ and Michael Wittekind¹

¹ContraFect Corporation, Yonkers, NY, and ²Department of Bacterial Pathogenesis and Immunology, The Rockefeller University, New York, New York



CF-301 is a lysin from a *Streptococcus suis* phage

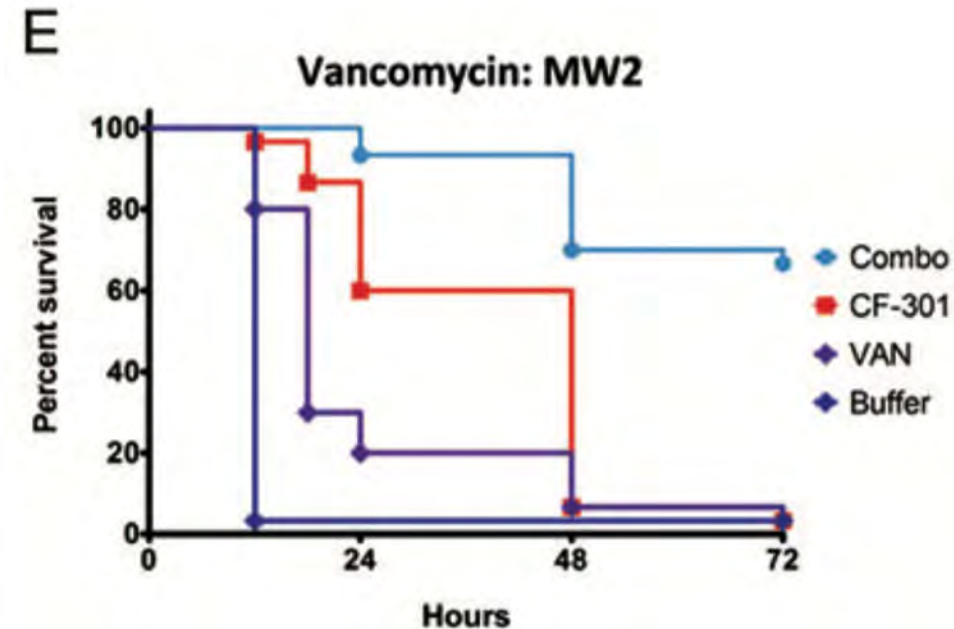
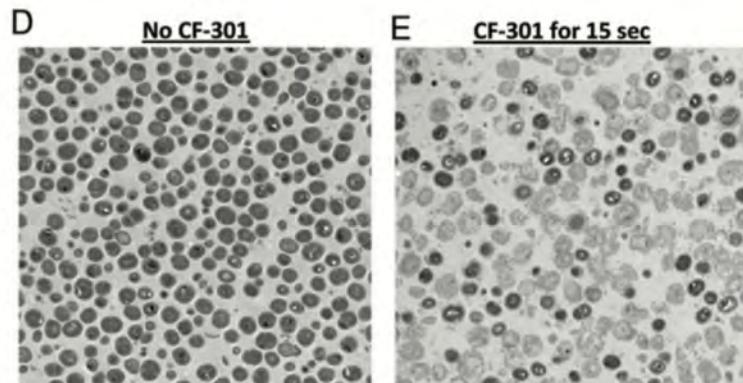
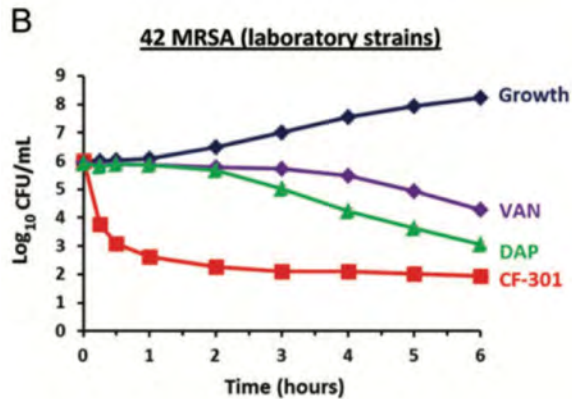
Broader spectrum of activity: against *S. aureus*, but also against coagulase-negative staphylococci

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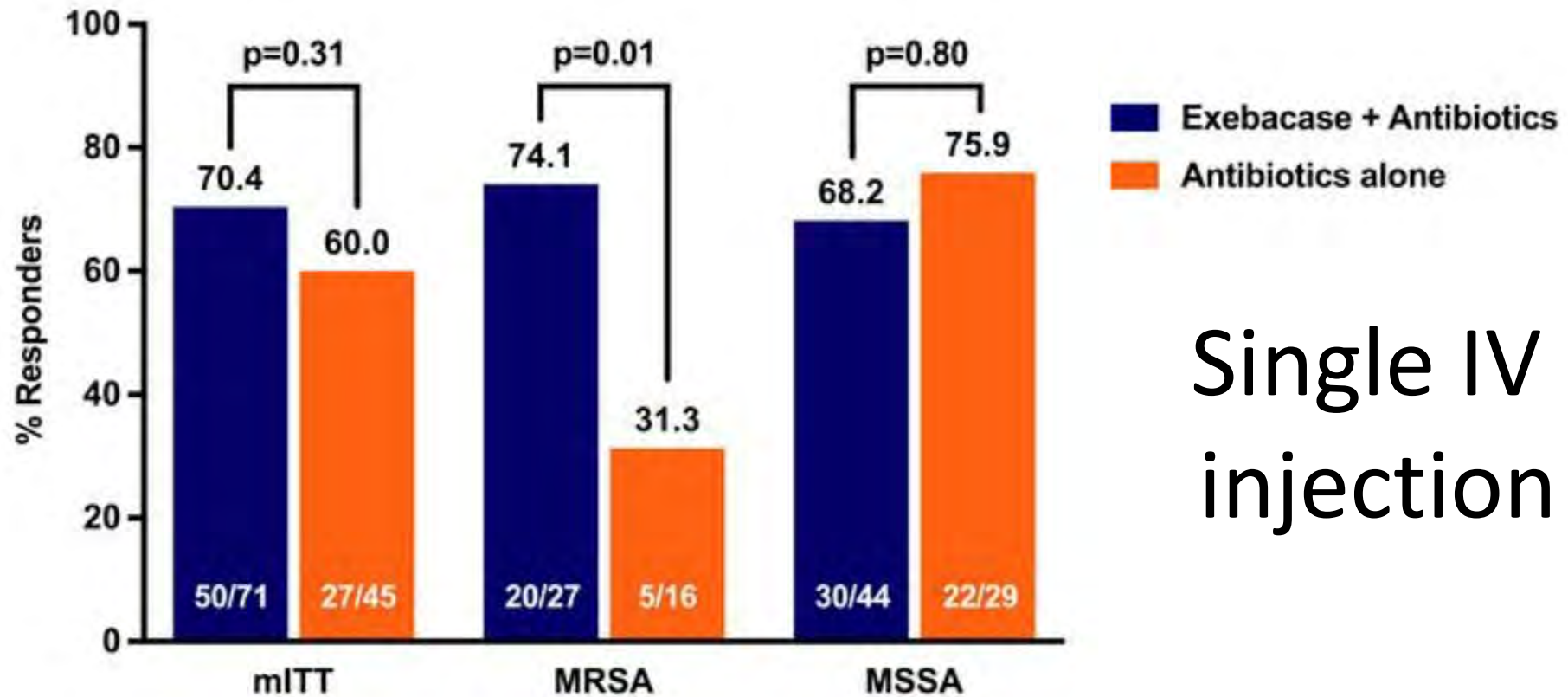
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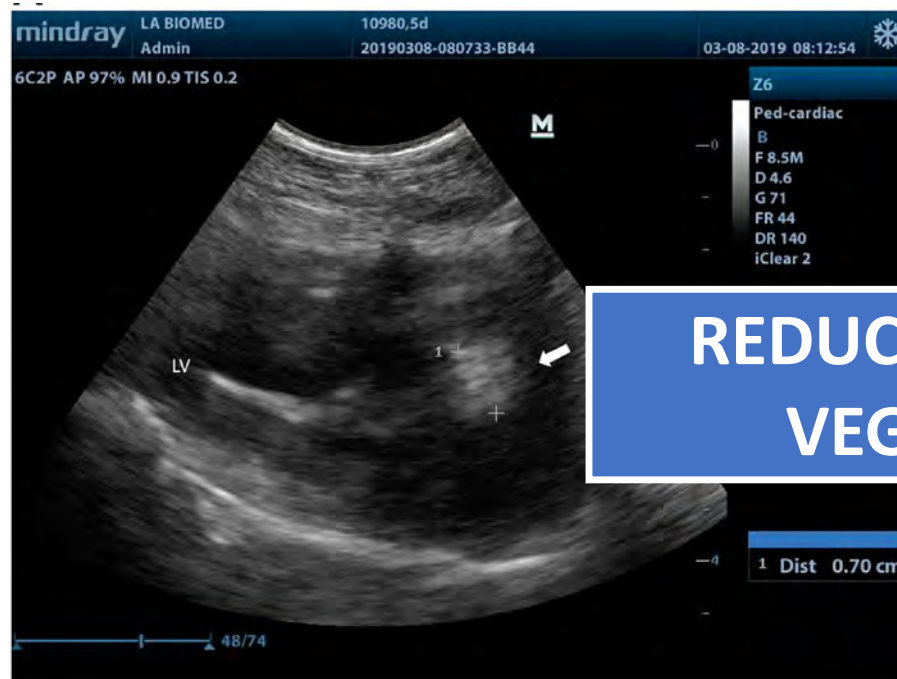
Exebacase for patients with *Staphylococcus aureus* bloodstream infection and endocarditis

Vance G. Fowler Jr.,^{1,2} Anita F. Das,³ Joy Lipka-Diamond,⁴ Raymond Schuch,⁵ Roger Pomerantz,⁵ Luis Jáuregui-Peredo,⁶ Adam Bressler,⁷ David Evans,⁸ Gregory J. Moran,⁹ Mark E. Rupp,¹⁰ Robert Wise,¹¹ G. Ralph Corey,¹ Marcus Zervos,¹² Pamela S. Douglas,^{1,2} and Cara Cassino⁵

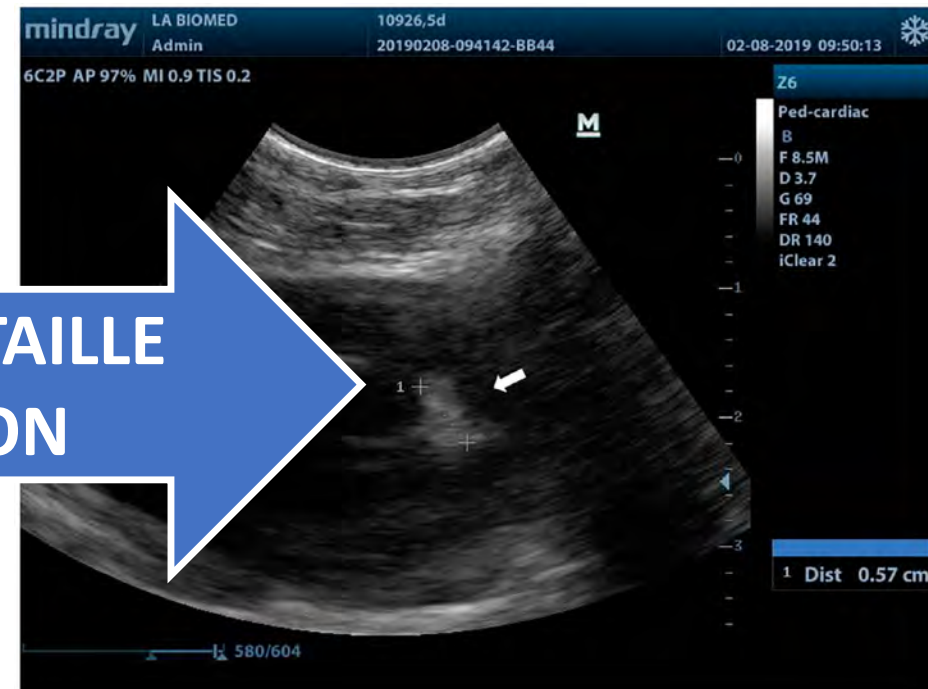


Effect of the Lysin Exebacase on Cardiac Vegetation Progression in a Rabbit Model of Methicillin-Resistant *Staphylococcus aureus* Endocarditis as Determined by Echocardiography


Sonia U. Shah,^{a,b,c} Yan Q. Xiong,^{b,c} Wessam Abdelhady,^b James Iwaz,^a Youngju Pak,^{b,c}  Raymond Schuch,^d Cara Cassino,^d Dario Lehoux,^d Arnold S. Bayer^{b,c}

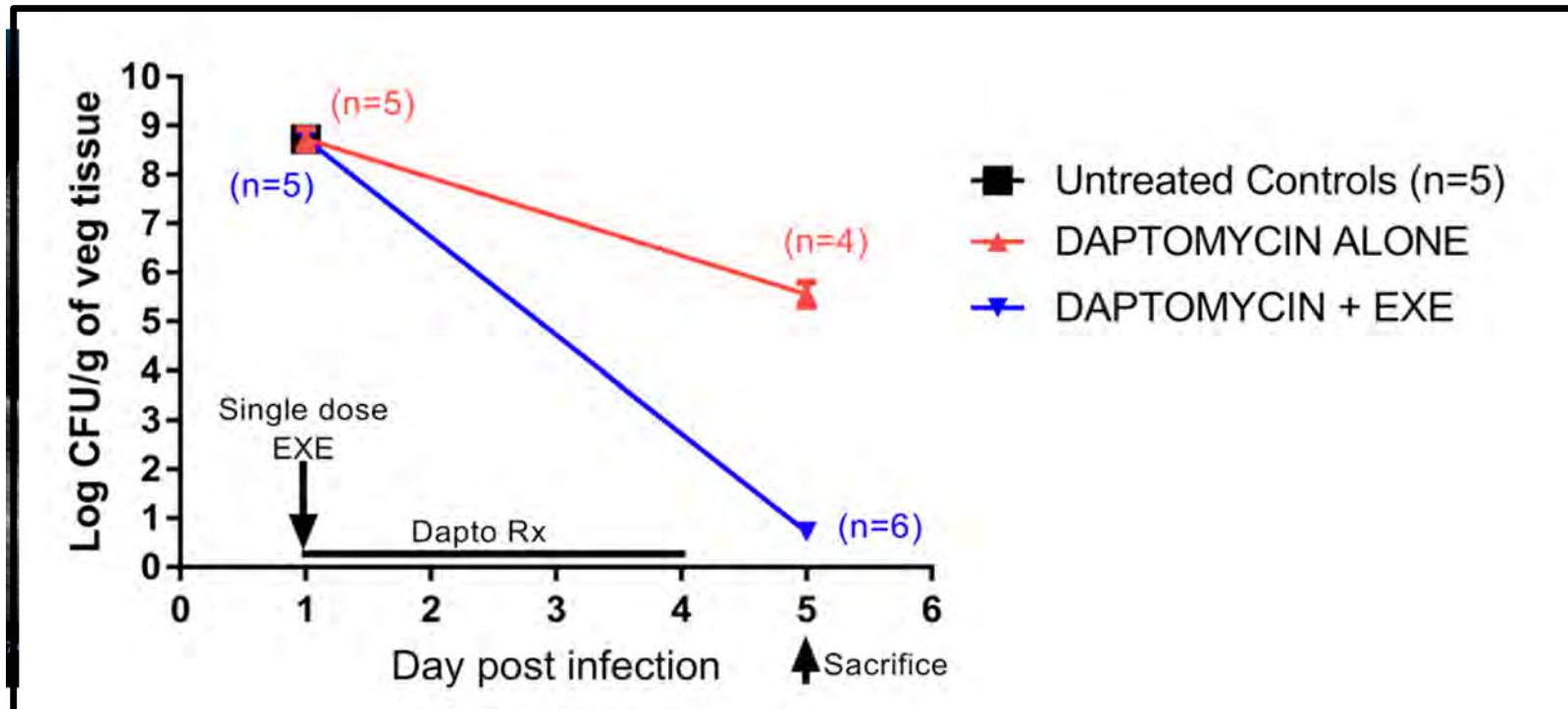
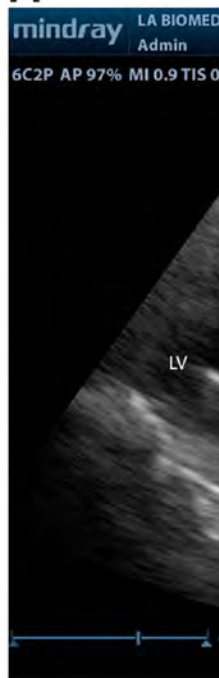


**REDUCTION TAILLE
VEGETATION**



Effect of the Lysin Exebacase on Cardiac Vegetation Progression in a Rabbit Model of Methicillin-Resistant *Staphylococcus aureus* Endocarditis as Determined by Echocardiography

Sonia U. Shah,^{a,b,c} Yan Q. Xiong,^{b,c} Wessam Abdelhady,^b James Iwaz,^a Youngju Pak,^{b,c}  Raymond Schuch,^d Cara Cassino,^d Dario Lehoux,^d Arnold S. Bayer^{b,c}



CONTRAFECT PROVIDES UPDATE FROM THE FUTILITY ANALYSIS OF THE PHASE 3 DISRUPT STUDY OF EXEBACASE

Enrollment in the trial was stopped following a review of the pre-specified, interim futility analysis by the independent Data Safety Monitoring Board (DSMB). The DSMB recommended the trial be stopped because the conditional power of the trial was below the pre-specified threshold for futility as per the DSMB charter. No safety concerns were noted by the DSMB.

“The unprecedented clinical response in the placebo arm of this study, which is nearly double the response rate observed in our Phase 2 study of exebacase and in comparable Phase 3 studies of daptomycin and fosfomycin, coupled with the conduct of the study during the **COVID pandemic**, leaves us with trial results that are uninterpretable”

Arthroscopic debridement, antibiotic and implant retention (DAIR) with local administration of Exebacase (Lysin CF-301) (LysinDAIR) followed by suppressive tedizolid as salvage therapy in elderly patients for relapsing multidrug-resistant *Staphylococcus epidermidis* prosthetic knee infection



30th
ECCMID

Paris, France
18 –21 April 2020

 frontiers
in Medicine

 CRIOAc
LYON

ContraFect



Conclusions: Exebacase has the potential to be used as salvage therapy during arthroscopic DAIR in patients with relapsing MDR *S. epidermidis* PKI, to improve the efficacy of suppressive antibiotics, and to avoid considerable loss of function.

Antibacterial properties of a pre-formulated recombinant phage endolysin, SAL-1

Soo Youn Jun^a, Gi Mo Jung^a, Seong Jun Yoon^a, Myoung-Don Oh^b, Yun-Jaie Choi^c, Woo Jong Lee^d, Joon-Chan Kong^d, Jae Goo Seol^a, Sang Hyeon Kang^{a,*}

^a iNtRON Biotechnology, Inc., Room 903, JungAng Induspia V, 138-6, Sangdaewon-dong, Jungwon-gu, Seongnam-si, Gyeonggi-do 462-120, Republic of Korea

^b Department of Internal Medicine, Seoul National University College of Medicine, Seoul 110-799, Republic of Korea

^c Laboratory of Animal Cell Biotechnology, Department of Agricultural Biotechnology, Seoul National University, Seoul 151-742, Republic of Korea

^d Biomedical Technology Center, Korea Institute of Industrial Technology, Yeongcheon-si, Gyeongsangbuk-do 770-200, Republic of Korea

Phase I (healthy volunteers)
Jun SY et al. AAC 2017

Phase IIa (*S. aureus* bacteremia)
NCT03089697

N-Rephasin®

SAL200

containing phage
endolysin SAL-1

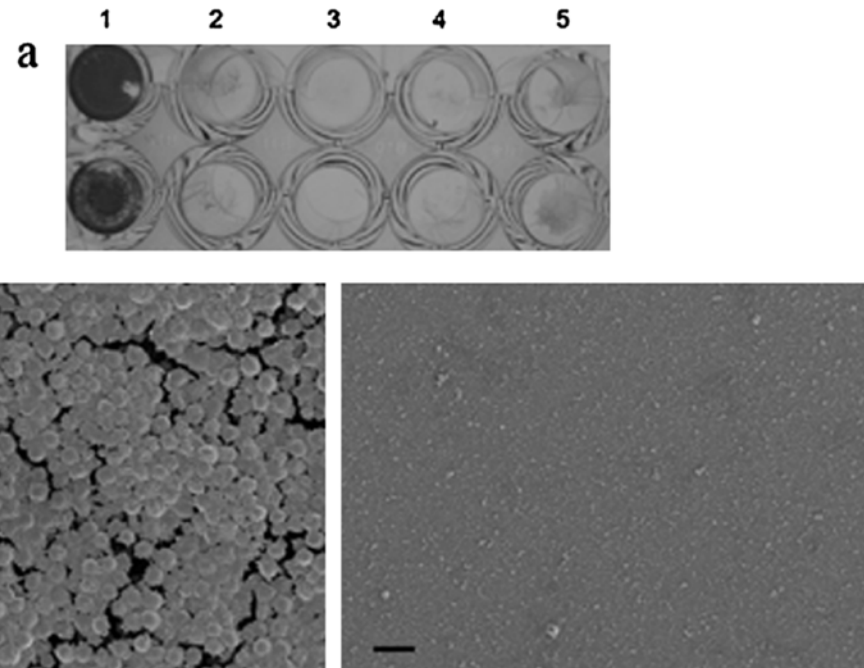


Fig. 2. Examination of the *Staphylococcus aureus* biofilm removal activity of SAL200. Biofilms of *S. aureus* SA1 were treated with SAL200 and biofilm removal was examined by (a) safranin staining and (b) scanning electron microscopy. (a) Well 1, negative control (basal buffer); well 2, SAL200 (10 $\mu\text{g}/\text{mL}$ SAL-1); well 3, SAL200 (20 $\mu\text{g}/\text{mL}$ SAL-1); well 4, SAL200 (40 $\mu\text{g}/\text{mL}$ SAL-1); and well 5, SAL200 (80 $\mu\text{g}/\text{mL}$ SAL-1). The experiment was performed in duplicate in two rows of a 96-well microplate. Dark staining indicates a biofilm that was maintained after the attempted disruption treatment, and light or no staining indicates successful removal of the biofilm. (b) *Staphylococcus aureus* SA1 biofilms treated with basal buffer (left) and with SAL200 (10 $\mu\text{g}/\text{mL}$ SAL-1) (right). Magnification, $\times 10\,000$; scale bar, 2 μm .

ERAdicate *S.aureus* in Patients With Bacteremia and Endocarditis (ERASE)

An Open-Label, Multiple-Ascending Dose, Multicenter Study to Evaluate the **Safety, Tolerability, and Pharmacokinetics of LSVT-1701 (SAL200)** as an Add-on to Standard of Care Antibiotics for the Treatment of Complicated Methicillin-Sensitive and -Resistant ***Staphylococcus aureus* Bacteremia Including Left- and Right-sided Infective Endocarditis**

Recruitment Status ⓘ : Withdrawn (business decision before FPFV; not related to any safety concerns)

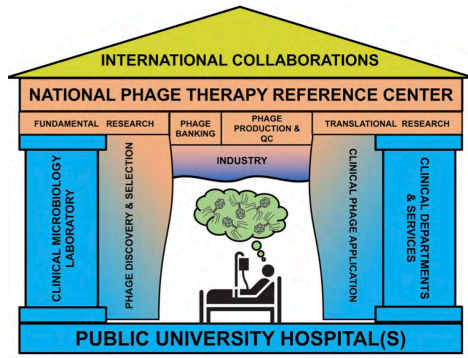
First Posted ⓘ : April 14, 2022

Last Update Posted ⓘ : June 30, 2022

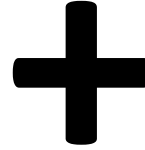
ClinicalTrials.gov Identifier: NCT05329168



iNtRON
BIOTECHNOLOGY



Phage therapy center



Referral center complex BJI



Phages from the industry
 Phages from academic
 Lysins from the industry

Dedicated referral activity
 Significant number of patients
 Relevant clinical situations



Significant level of Scientific evidence

Disruptive approach

Individual patient benefit



Implementation of a Phage Therapy Center in a CRIOAc

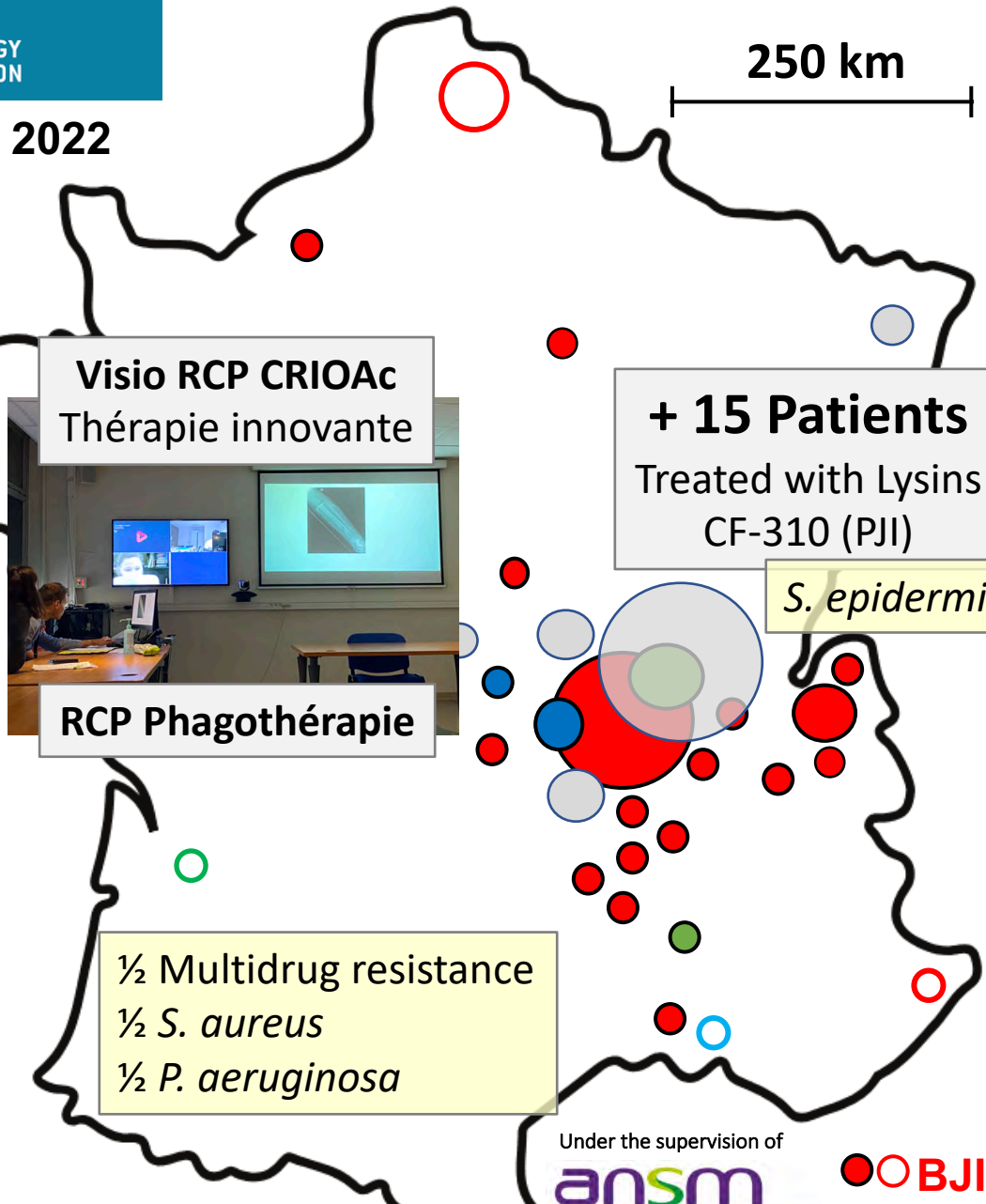
CMI CLINICAL MICROBIOLOGY AND INFECTION

FERRY T. *et al.* 2022

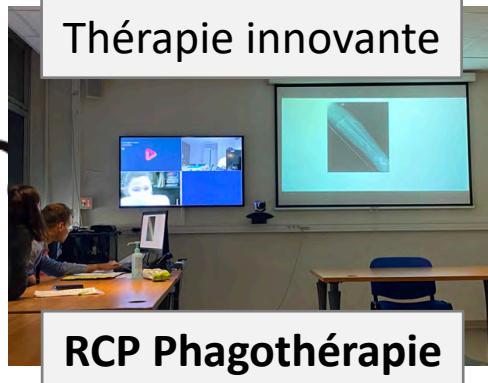
Updated



Clinic **PHAGEin LYON**



Visio RCP CRIOAc
Thérapie innovante



RCP Phagothérapie

+ 15 Patients
Treated with Lysins
CF-310 (PJI)

S. epidermidis

½ Multidrug resistance
½ *S. aureus*
½ *P. aeruginosa*

Under the supervision of **ansm**
Agence nationale de sécurité du médicament

53 patients in Lyon since 2017
~80% of the whole patients treated in France



- 50 with phages from **PHERECYDES PHARMA**
- 3 with phages from **MHKA HMRA**



- 42 **BJI** (including 34 **PJI**)
- 8 **endocarditis/vascular graft/ cardiac electronic device infection**
- 3 **lung infections** (VAP + bacteremia, pneumonia in lung graft bronchiectasia, cystic fibrosis exacerbation)



+ 11 patients managed outside Lyon ○
including 1 in and 1 in

●○ **BJI** ●○ **Endocarditis** ●○ **Pneumonia** ●○ **Burn**

P Bone and joint infections: Lyon becomes the national expert center for phage therapy HCR.REFERENCE-IOA@chu-lyon.fr

The reference center for complex bone and joint infections, based at the Hospices Civils de Lyon, will centralize all requests concerning this last resort treatment, using viruses against resistant bacteria.

Le Progrès - 23 Feb. 2023 at 17:51 | updated 23 Feb. 2023 at 18:08 - Reading time: 2 min



National online
multidisciplinary meetings



Dedicated to innovative
anti-infective therapies

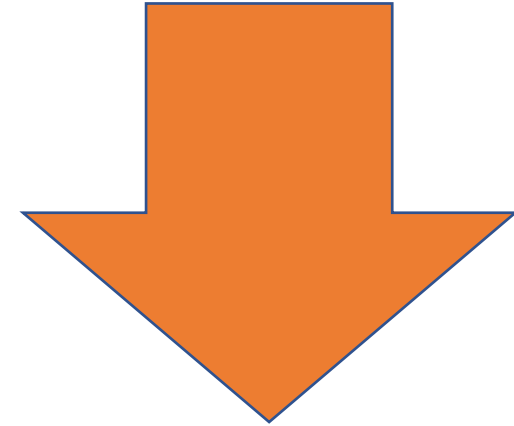


<https://www.chu-lyon.fr/phagothérapie-bacteriophage>



Les HCL

Offre de soins



[Accueil](#) > [Fiches Santé](#) > [Phagothérapie \(Bactériophage\)](#)

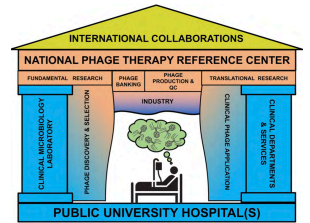
Phagothérapie (Bactériophage)

La phagothérapie consiste à produire des bactériophages spécifiques et à les utiliser pour une infection bactérienne.

- **Vous êtes professionnel de santé** et souhaitez faire une demande d'avis pour un patient, les demandes d'avis s'effectuent via la [messagerie sécurisée de santé MonSisra](#).
- **Vous êtes patient** et souhaitez faire une demande d'avis, [compléter le formulaire de demande sur myHCL](#).

Conclusion

- Les **bactériophages** et les **lysines de phages** sont des **thérapies anti-bactériennes non traditionnelles**
- La phagothérapie est une **thérapie innovante et réémergente**
- Indications paraissant pertinentes : infections **pulmonaires**, **endocardites** sur prothèse valvulaire, IOAc dont les infections de **prothèse articulaire**
- En **ADJUVANT** à l'antibiothérapie (et potentiellement la chirurgie)
- Modalités d'administration doivent être **personnalisées** en fonction de l'expérience clinique, des phages à disposition et de la présentation clinique
- Création d'une **mission nationale « CRIOAc thérapie innovante »**
 - Pour valider les **indications pertinentes** de phages/lysines dans les IOA
 - Pour orienter les prises en charge vers les **essais thérapeutiques**
 - Ou enfin pour **orienter et accompagner** le recours à des phages en « compassionnel » (nécessité d'une mission nationale « **RCP Phagothérapie** » pour préciser les modalités)
- Poser les jalons d'un **centre national de phagothérapie**
- Conception et réalisation d'**essais thérapeutiques**



Vendredi 6 Octobre - Thématique N° 27 – Recherche en Infectiologie, Ethique
Coordination : Vincent LE MOING - Eric DELAPORTE

Streaming	Conférence N° 1 - Réglementation de la recherche clinique	Nathalie GASTELLIER - Renarci
	Conférence N°2 – Organisation de la recherche en maladies infectieuses en France	Pr. Vincent LE MOING - Montpellier
	Conférence N° 3 – Exemple de recherche translationnelle : la phagothérapie	Pr. Tristan FERRY - Lyon
	Conférence N° 4 – Recherche en contexte d'urgence pandémique	Pr. Florence ADER - Lyon

Lyon BJI Study group



Coordinator: Tristan Ferry

Infectious Diseases Specialists – Tristan Ferry, Florent Valour, Thomas Perpoint, Florence Ader, Sandrine Roux, Agathe Becker, Claire Triffault-Fillit, Anne Conrad, Cécile Poudroux, Pierre Chauvelot, Paul Chabert, Johanna Lippman, Evelyne Braun

Surgeons – Sébastien Lustig, Elvire Servien, Cécile Batailler, Stanislas Gunst, Axel Schmidt, Elliot Sappey-Marinier, Quentin Ode, Michel-Henry Fessy, Anthony Viste, Jean-Luc Besse, Philippe Chaudier, Lucie Louboutin, Adrien Van Haecke, Marcelle Mercier, Vincent Belgaid, Aram Gazarian, Arnaud Walch, Antoine Bertani, Frédéric Rongieras, Sébastien Martres, Franck Trouillet, Cédric Barrey, Ali Mojallal, Sophie Brosset, Camille Hanriat, Hélène Person, Samuel Prive, Philippe Céruse, Carine Fuchsmann, Arnaud Gleizal;

Anesthesiologists – Frédéric Aubrun, Mikhail Dziadzko, Caroline Macabéo, Dana Patrascu;

Microbiologists – Frederic Laurent, Laetitia Beraud, Tiphaine Roussel-Gaillard, Céline Dupieux, Camille Kolenda, Jérôme Josse;

Imaging – Fabien Craighero, Loic Bousel, Jean-Baptiste Pialat, Isabelle Morelec;

PK/PD specialists – Michel Tod, Marie-Claude Gagnieu, Sylvain Goutelle;

Clinical research assistant and database manager– Eugénie Mabrut

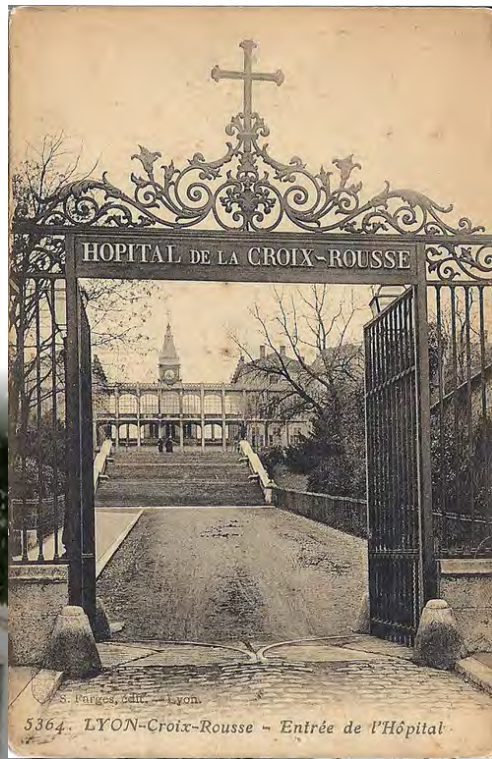
PHAGE_{in}LYON Clinic

Coordinator: Tristan Ferry

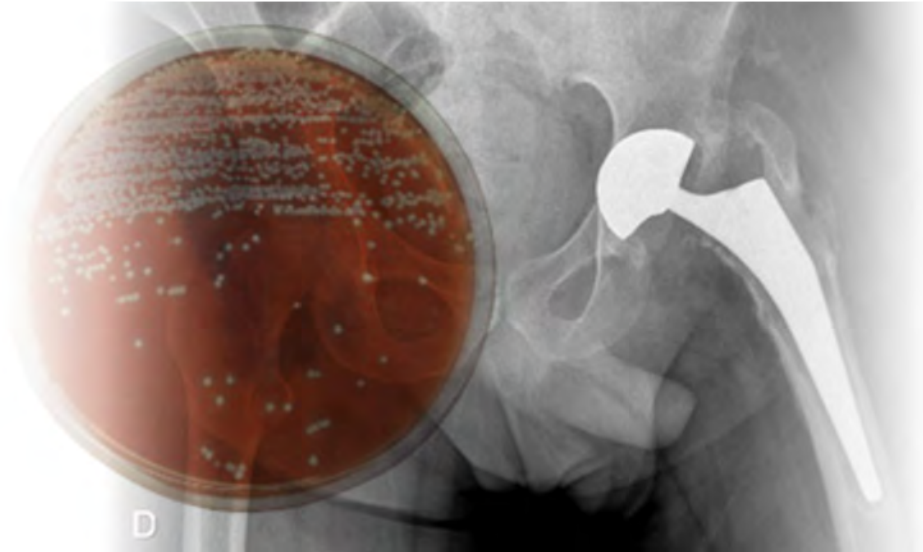
Tristan Ferry, Myrtille Le Bouar, Gilles Leboucher, Thomas Briot, Camille Kolenda, Tiphaine Roussel-Gaillard, Karine Dallosto



Croix-Rousse Hospital



<http://www.crioac-lyon.fr>



- Published cases
- Open acces studies in pdf
- All thesis in pdf
- All recommendations
- **Newsletter**



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