Antibactériens non conventionnels

Tristan Ferry, MD, PhD

tristan.ferry@univ-lyon1.fr

Infectious and Tropical Diseases Unit, Croix-Rousse Hospital , Hospices Civils de Lyon, Claude Bernard Lyon1 University, Lyon
Centre International de Recherche en Infectiologie, CIRI, Inserm U1111, CNRS UMR5308, ENS de Lyon, UCBL1, Lyon, France
Centre de Référence des IOA complexes de Lyon (CRIOAc Lyon)

@FerryLyon

Two major issues, sometimes combined

AMR: Antimicrobial resistance

nature COMMUNICATIONS

NATURE COMMUNICATIONS | (2019)10:3416

PERSPECTIVE

https://doi.org/10.1038/s41467-019-11303-9 OPEN

Designing development programs for non-traditional antibacterial agents

John H. Rex[1,2], Holly Fernandez Lynch[3], I. Glenn Cohen[4,5], Jonathan J. Darrow[6] & Kevin Outterson[7]

Table 1 The wide range of non-traditional antimicrobial agents

Category	[b] products
Antibiotic-sequestering pro antibiotic-degrading enzym	es
Antibodies	s that produce the anthrax, diphtheria,
Bacteriophage (both wild-t engineered)	es
Host immune response mo (stimulating and immunosu	-CSF
Lysins	es
Metal chelation	es
Microbiome and probiotics	es

carriage of resistant or pathogenic bacteria (Narrow

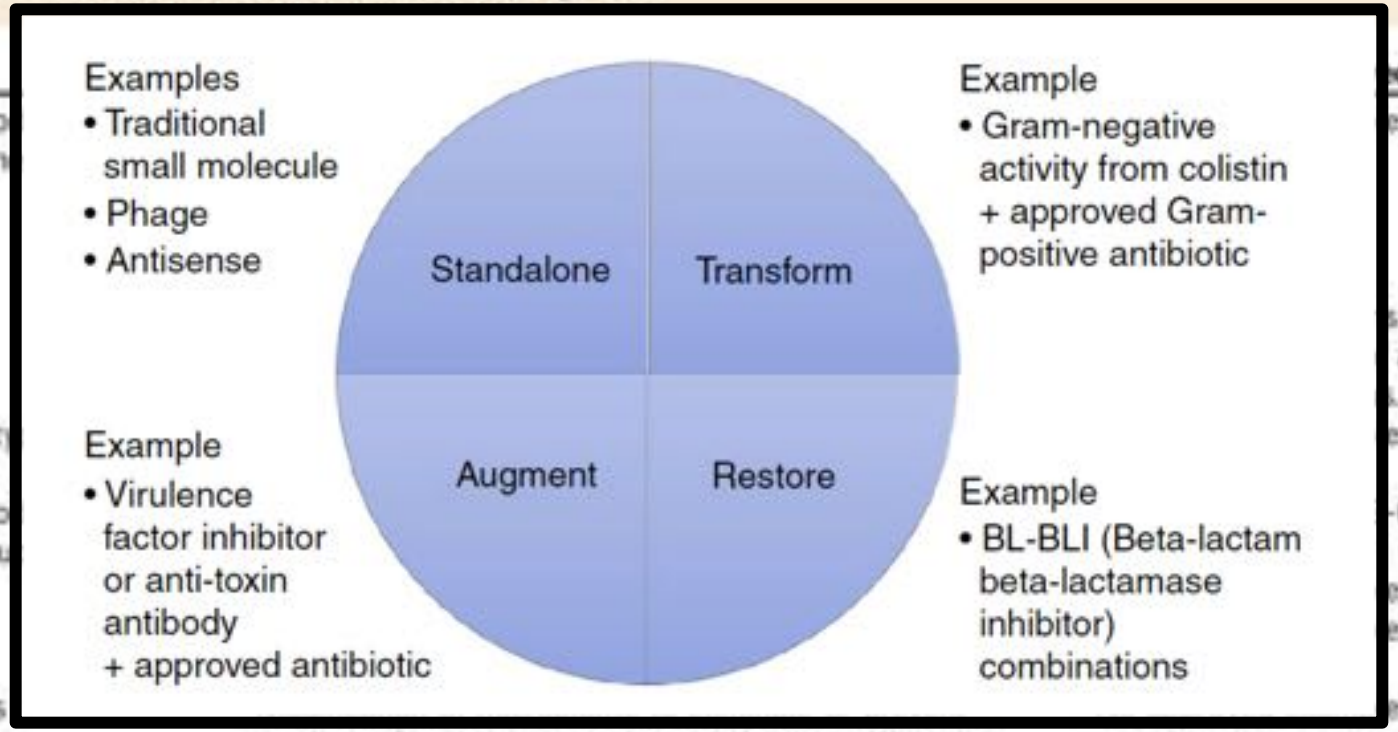


Table 3 Development options for the four categories

Design options	Would data from a non-inferiority study be adequate for approval?[a]	To what extent is a demonstration of superiority required for approval?[b]
Standalone	Yes	Optional
Transform	Yes	Optional
Augment	No	Required
Restore	Yes	Usually optional

[a]Is it possible to achieve initial approval by studying the product in a head-to-head non-inferiority study in which the novel product is compared with an existing agent in a usual drug resistance (UDR) setting where the comparator agent has retained activity?
[b]Recognizing the conflicting tension around use of superiority studies for approving new agents (see text), does demonstration of the value of the novel agent effectively require a superiority study?

Cell Host & Microbe
Review 2019

Non-traditional Antibacterial Therapeutic Options and Challenges

Ursula Theuretzbacher[1] and Laura J.V. Piddock[2,*]
[1]Centre for Anti-Infective Agents, Vienna, Austria
[2]Institute of Microbiology and Infection, University of Birmingham, Birmingham, West Midlands B15 2TT, UK
*Correspondence: l.j.v.piddock@bham.ac.uk
https://doi.org/10.1016/j.chom.2019.06.004

Anti-virulence approaches

Microbiome-Modifying Therapies

Phages and phage-related therapies

Anti-virulence approaches

Table 1. Monoclonal Antibodies in Clinical Development

Monoclonal Antibody, Company	Clinical Development	Anti-virulence Target	Indication
Suvratoxumab (MEDI4893), MedImmune	phase 2	*S. aureus* α-toxin	prevention of VAP caused by *S. aureus*
AR-301 (Salvecin, Tosatoxumab), Aridis	phase 3	*S. aureus* α-toxin	adjunctive therapy for VAP caused by *S. aureus*
MEDI3902, MedImmune	phase 2	*P. aeruginosa* T3SS needle-tip protein PcrV and Psl exopolysaccharide	prevention of VAP caused by *P. aeruginosa*
AR-105 (Aerucin), Aridis	phase 2	*P. aeruginosa* alginate	adjunctive treatment of VAP caused by *P. aeruginosa*
514G3, XBiotch	phase 1/2	*S. aureus* protein A	adjunctive treatment of bloodstream infections caused by *S. aureus*
ASN-100, Arsanis	phase 2	*S. aureus* α-toxin and five leukocidins	failed to prove its effectiveness in high-risk, mechanically ventilated patients with *S. aureus* pneumonia

For information about the status of R&D of antibodies, small molecules, and other approaches to new treatments, please see www.clinicaltrials.gov or the website of the developer organization.

Table 3. Current Approaches to Manipulate the Microbiome

Approach	Indication	Comments
Transfer of human intestinal microbiota	Prevention of recurrent CDI	FMT: Transfer of stool suspension from a donor via colonoscopy, enema, nasogastric routes or pills (Finch, Open Biome)
		Fecal microbiota suspension: standardized number of live bacteria from stool suspension from donors via enema or capsules, GMP produced (Rebiotix (Ferring))
		of lanta)
		s from donors via capsules (Seres)
Synthetic microbiota	Intestinal, dermatological (e.g., atopic dermatitis), lung conditions (e.g., CF)	Selected live bacteria producing specific metabolites or cocktail of secondary metabolites
		Selected live bacteria from skin microbiota (MatriSys Bio)
		Selected live bacteria for balancing the lung microbiota
Manipulating the metabolism of microbiota	–	Manipulating the metabolic balance through specific bacterial nutrients, e.g., Glycans (Kaleido)
Competition	Prevention of recurrent CDI, catheter-associated UTI	Non-toxinogenic *C. difficile* that is assumed to outcompete the toxic strain (Microbiotica)
		Apathogenic *E. coli* introduced into the bladder via catheter coating (Atterx)
Engineering probiotics to deliver antibacterial proteins	Various indications (Bäumler and Sperandio, 2016)	Engineered *Lactobacillus* to express bacteriocin against *P. aeruginosa* (inhaled, CF) and *C. difficile* (SciBac)
		Engineered *Lactobacillus* to express SagA protein that promotes tolerance to enteric infections including *C. difficile* infection (Rise Therapeutics)
		R-type bacteriocins against *C. difficile*
Prevention of disbalance of microbiome due to antibiotic therapy	Prevention of recurrent CDI	Hydrolyzing specific beta-lactam antibiotics in the gut (beta-lactamase, Synthetic Biologics, DaVolterra)
Decolonization of MDR Gram-negative pathogens in high-risk patients	Various indications	Decolonization of asymptomatic carriers with live bacteria (e.g., carriers of *C. difficile*, MDR Gram-negative pathogens in high-risk patients, *Salmonella* Typhi)

Microbiome-Modifying Therapies

Phages and phage-related therapies

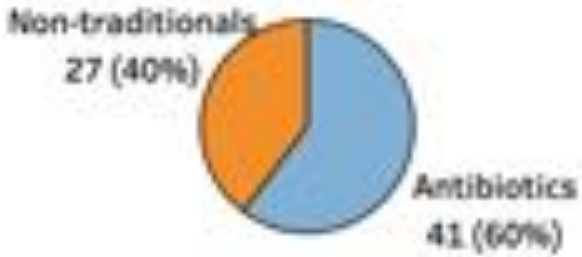
Table 4. Current Approaches Using Phages

Approach	Composition
Fixed phage cocktails	Fixed composition of lytic phages to achieve a broad host range of a bacterial species
Individualized phage cocktail	The lytic phages are stored individually in a phage bank with established QC. Only the most active phages based on rapid diagnostic tests are selected for an individual patient
Genetically engineered phages	Engineered phages with improved or specific characteristics
Genetically engineered non-replicating phages as vehicles	Engineered phages to express additionally antimicrobial peptides or protein toxins leading to rapid, nonlytic bacterial death. May deliver CRISPR-CAas3 genes directly into bacteria
Phage products, e.g., endolysins	Natural or recombinant cell wall hydrolyzing phage-based enzymes. Endolysins against *S. aureus* are in clinical development

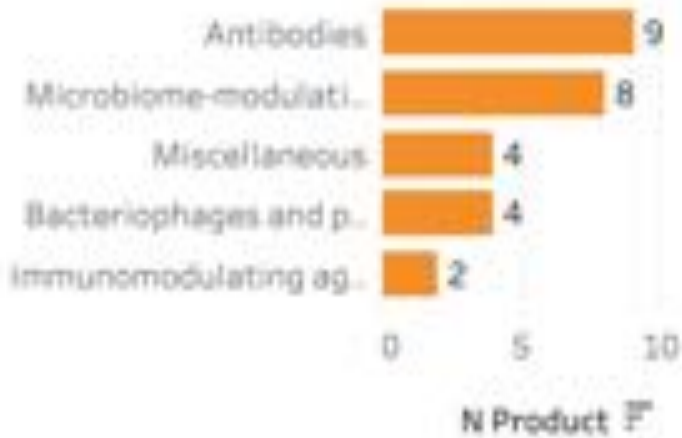
2020 ANTIBACTERIAL AGENTS IN CLINICAL AND PRECLINICAL DEVELOPMENT

an overview and analysis

A.1. Products by type



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



A.3. Products by pathogen category and phase

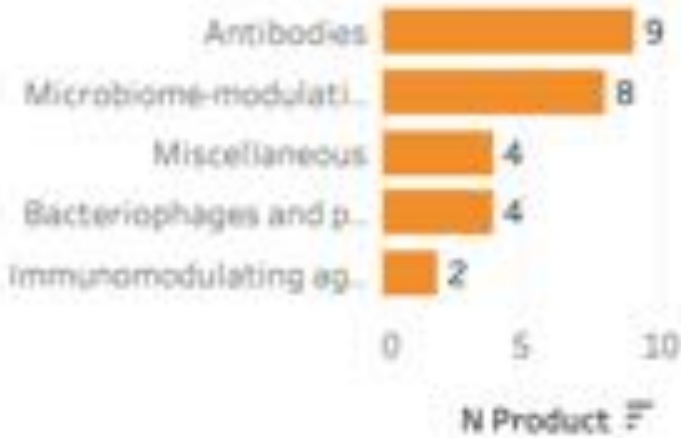
Pathogen category	Phase I	Phase II	Phase	Unkno..	Total
Priority pathogens	18	15	9	1	43
Mycobacterium tuberculosis	3	9			12
Clostridium difficile	3	8	2		13
Total	24	32	11	1	68

B. Expected activity against priority pathogens

	Critical priority pathogens					Other priority pathogens								
Active?	Acinetobac baumannii	Pseudomor aeruginosa	Enteroba..	All critical priority pathogens	Subtotal	Gram-positive priority p..	Neisseria gonnorhoe..	Helicobact pylori	Staphyloco aureus	Enterococc faecium	Streptococc pneumonia	Campyloba spp.	Subtotal	Total
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



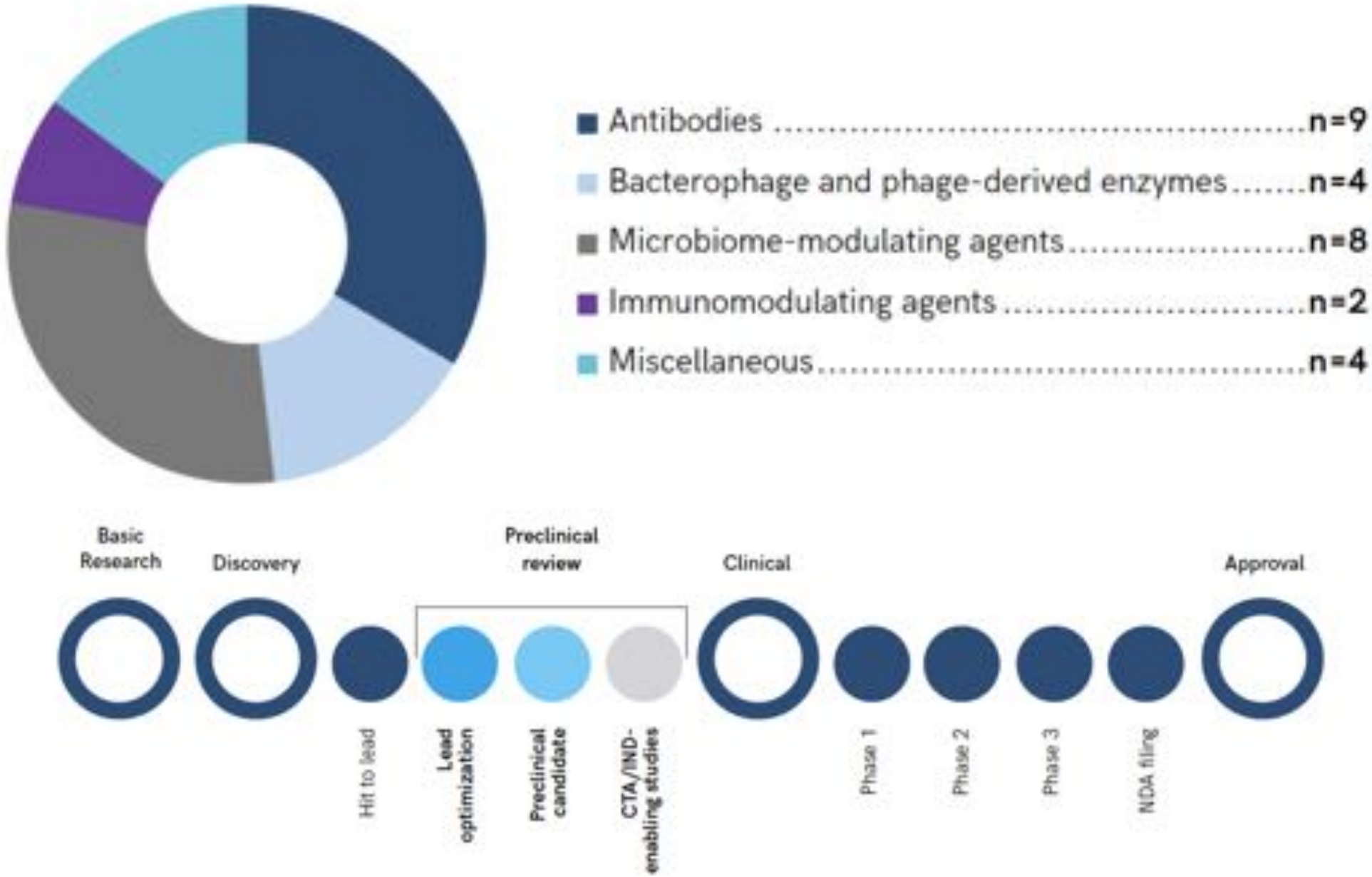
A.3. Products by pathogen category and phase

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

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

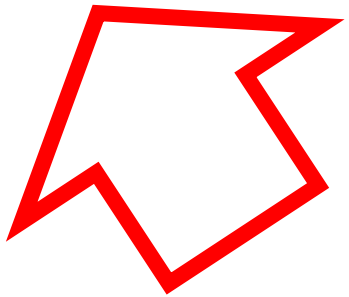
Fig. 7. Number of non-traditional antibacterials in the clinical pipeline.



Name (synonym)	Phase	Antibiotic class	Route of administration (developer)	Expected activity against priority pathogens
CF-301 (exebacase)	3	Phage endolysin	iv (ContraFect)	*S. aureus*
SAL-200 (tonabacase)	2a	Phage endolysin	iv (iNtRON Biotechnology, Roivant Sciences)	*S. aureus*
PhageBank	1/2	Phage bank (process)	oral (Adaptive Phage Therapeutics and US Department of Defense)	*E. coli*, *K. pneumoniae*
LBP-EC01	1b	CRISPR-Cas3 enhanced phage	iv (Locus Bioscience)	*E. coli*, *K. pneumoniae*

Traitement adjuvant dans les bactériémies à *S. aureus*

Name (synonym)	Phase	Antibiotic class	Route of administration (developer)	Expected activity against priority pathogens
CF-301 (exebacase)	3	Phage endolysin	iv (ContraFect)	*S. aureus*
SAL-200 (tonabacase)	2a	Phage endolysin	iv (iNtRON Biotechnology, Roivant Sciences)	*S. aureus*
PhageBank	1/2	Phage bank (process)	oral (Adaptive Phage Therapeutics and US Department of Defense)	*E. coli*, *K. pneumoniae*
LBP-EC01	1b	CRISPR-Cas3 enhanced phage	iv (Locus Bioscience)	*E. coli*, *K. pneumoniae*

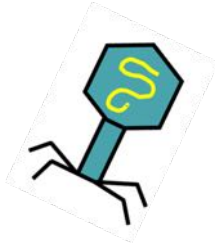


Traitement vs placebo dans les colonisations ou infections urinaires

Name (synonym)	Phase	Antibiotic class	Route of administration (developer)	Expected activity against priority pathogens
CF-301 (exebacase)	3	Phage endolysin	iv (ContraFect)	*S. aureus*
SAL-200 (tonabacase)	2a	Phage endolysin	iv (iNtRON Biotechnology, Roivant Sciences)	*S. aureus*
PhageBank	1/2	Phage bank (process)	oral (Adaptive Phage Therapeutics and US Department of Defense)	*E. coli*, *K. pneumoniae*
LBP-EC01	1b	CRISPR-Cas3 enhanced phage	iv (Locus Bioscience)	*E. coli*, *K. pneumoniae*
+				
Phagos (PHRC 2015)	1/2	Bacteriophage cocktail	Local (Pherecydes)	*S. aureus*
PhagoPied (PHRC 2015)	1/2	Bacteriophage cocktail	Local (Pherecydes)	*S. aureus*
PhagoDAIR	1/2	Bacteriophage cocktail	Local (Pherecydes)	*S. aureus*

What is a bacteriophage?

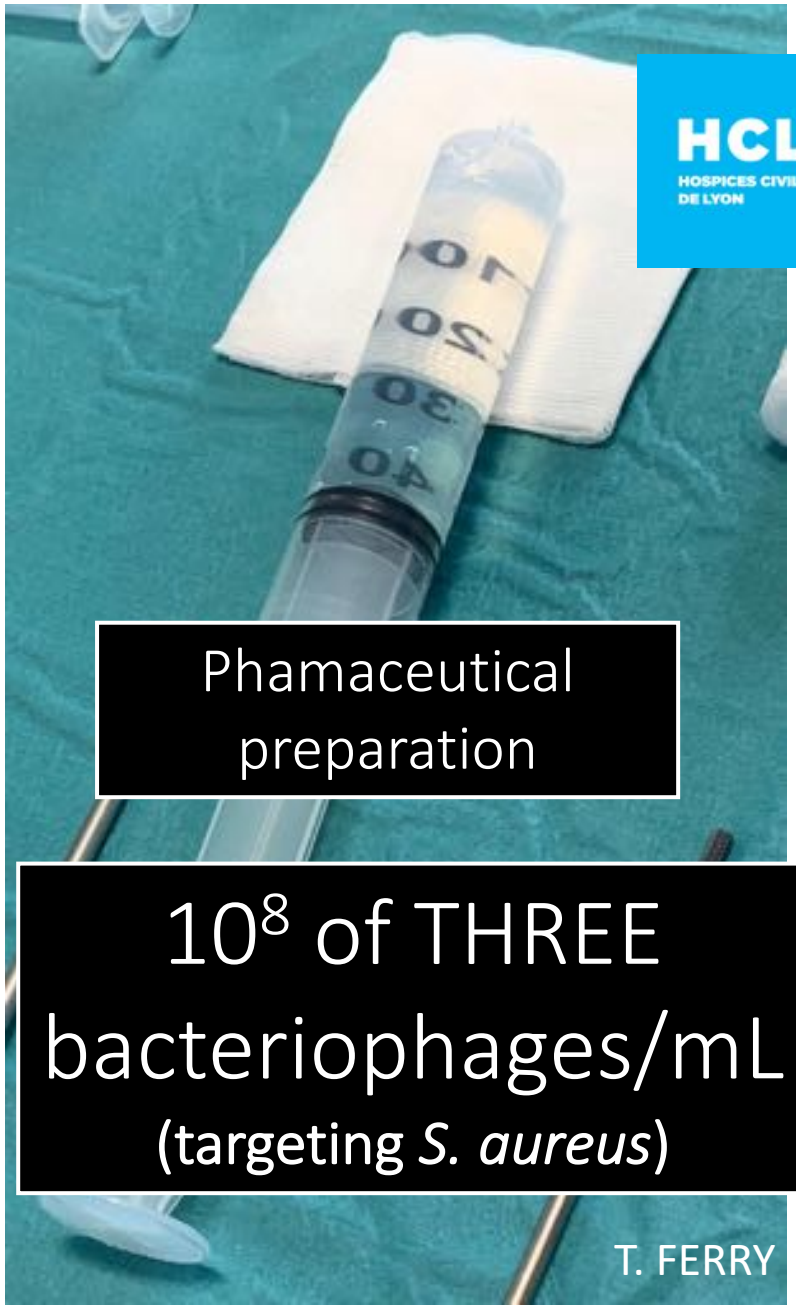
- Suffix –phage, *phagos* φαγεῖν (*phagein*), "to eat", "to devour"
- Viruses that infect ONLY bacteria
- Classification (*myoviridae, podoviridae, etc…)*
- A phage is specific to A TYPE of bacteria
- Largely abundant in the biosphere:
  10^{31} bacteriophages on the planet, more than every other organism
- Especially in marine environment, sea, lake, backwater, soil, animal and human stools, etc.



10 to 100 fold smaller than a bacteria

Translucent tap water

X million of ≠ Bactériophage<u>S</u> !!!
(targeting environmental bacteria)



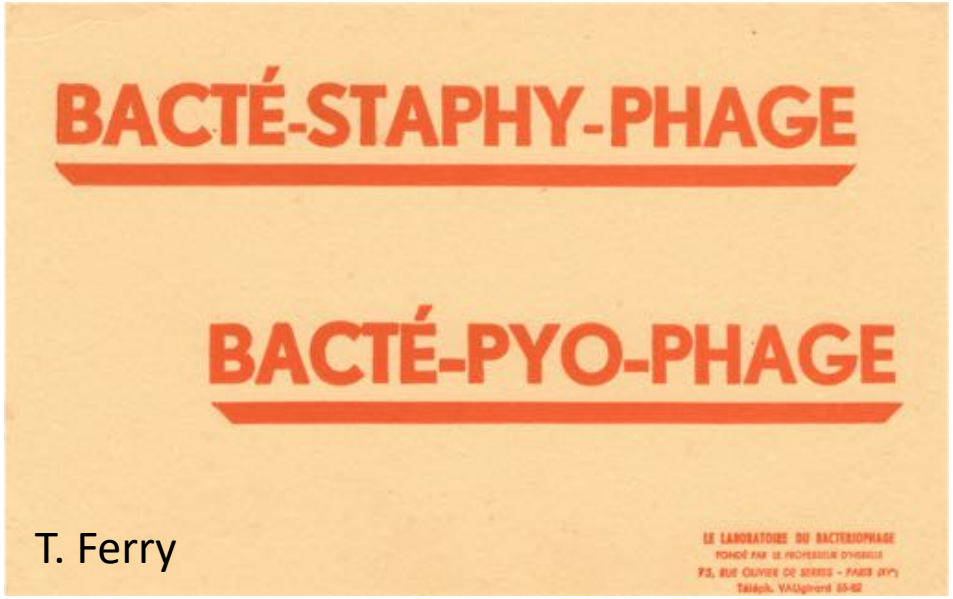
Phamaceutical preparation

10^8 of THREE bacteriophages/mL
(targeting *S. aureus*)

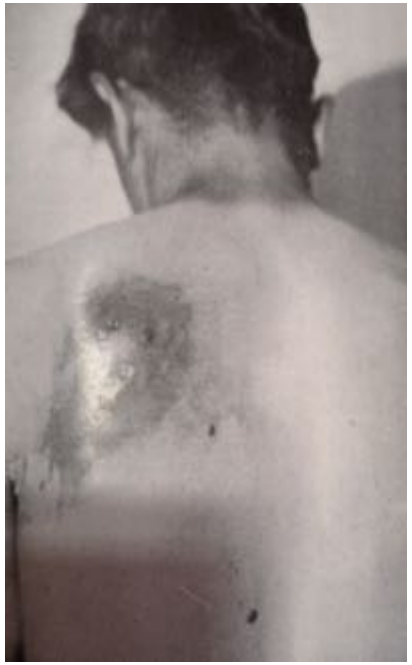
Story of phage Therapy

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**



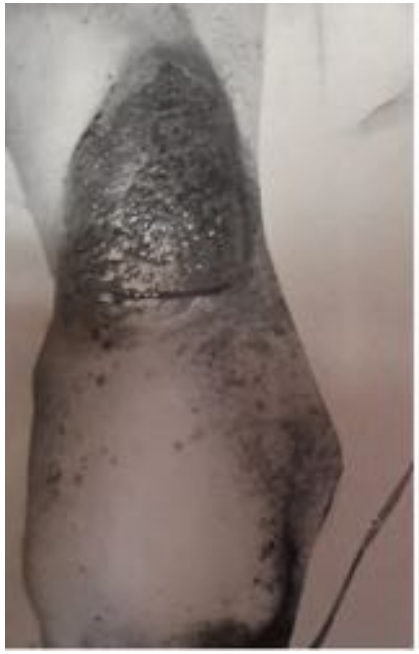
Ferry T. et al. Virologie 2020;24(1):49-56

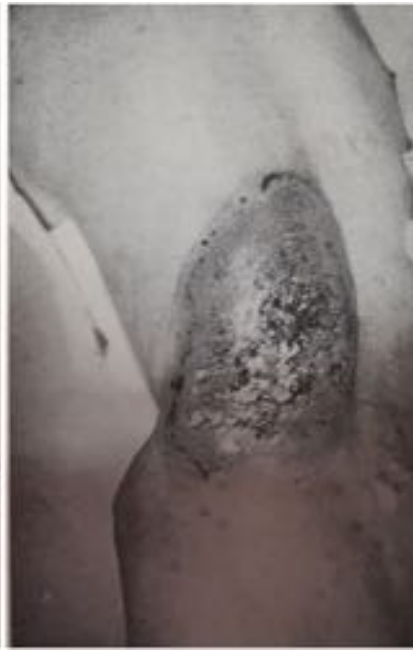


Story of phage Therapy in Lyon

Dr. Emile PESCE

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

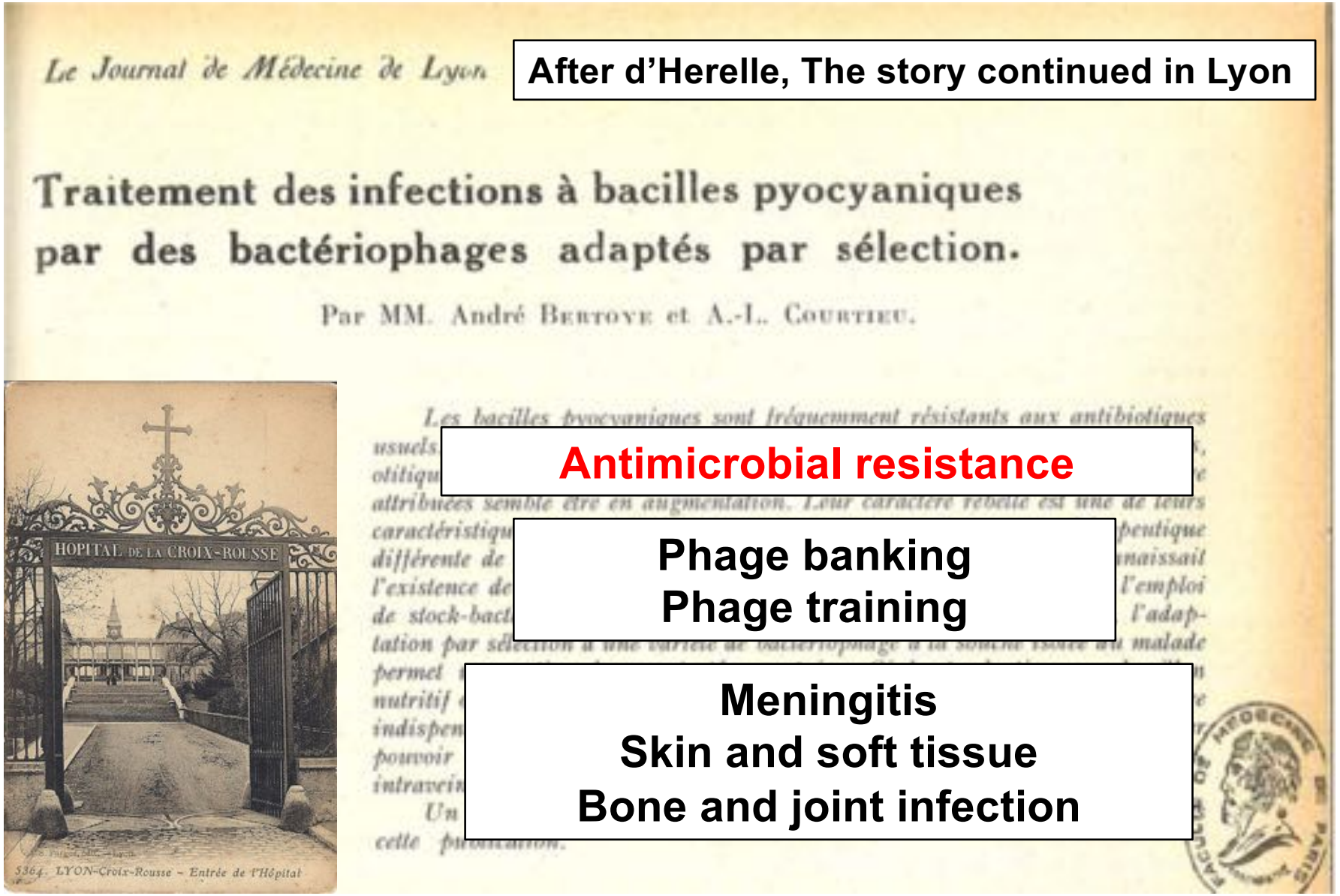




"Need for a microbiological analysis to select the phage, based on its activity on the patient's strain"

"If microbiological analysis could not be done, use fixed cocktail"

Archives from Ferry T.



After d'Herelle, The story continued in Lyon

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 traitée par un bactériophage adapté intrarachidien

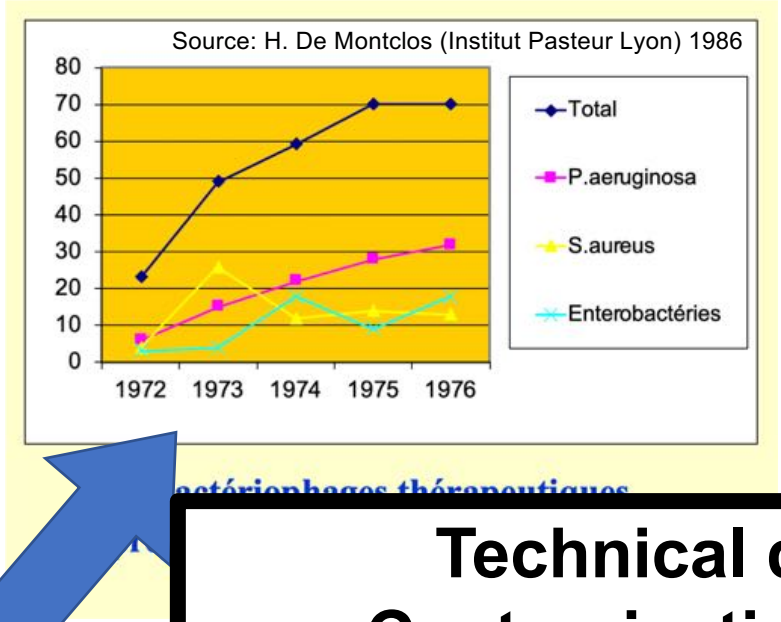
Par MM. P. SEDALLIAN, A. BERTOYE, J. GAUTHIER. J.-M. MULLER et A.-L. COURTIEU.

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

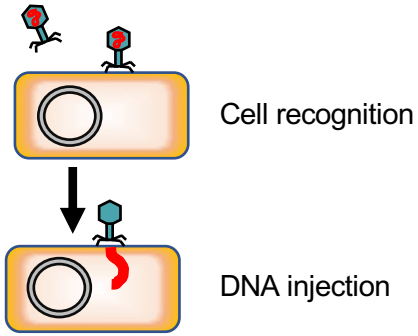
Technical development
Customisation of treatment
Academic multidisciplinary approach
70 patients/year!

Isolation of the isolates responsible for the infection

Infectious diseases clinic

HCL
HOSPICES CIVILS DE LYON

The phage life



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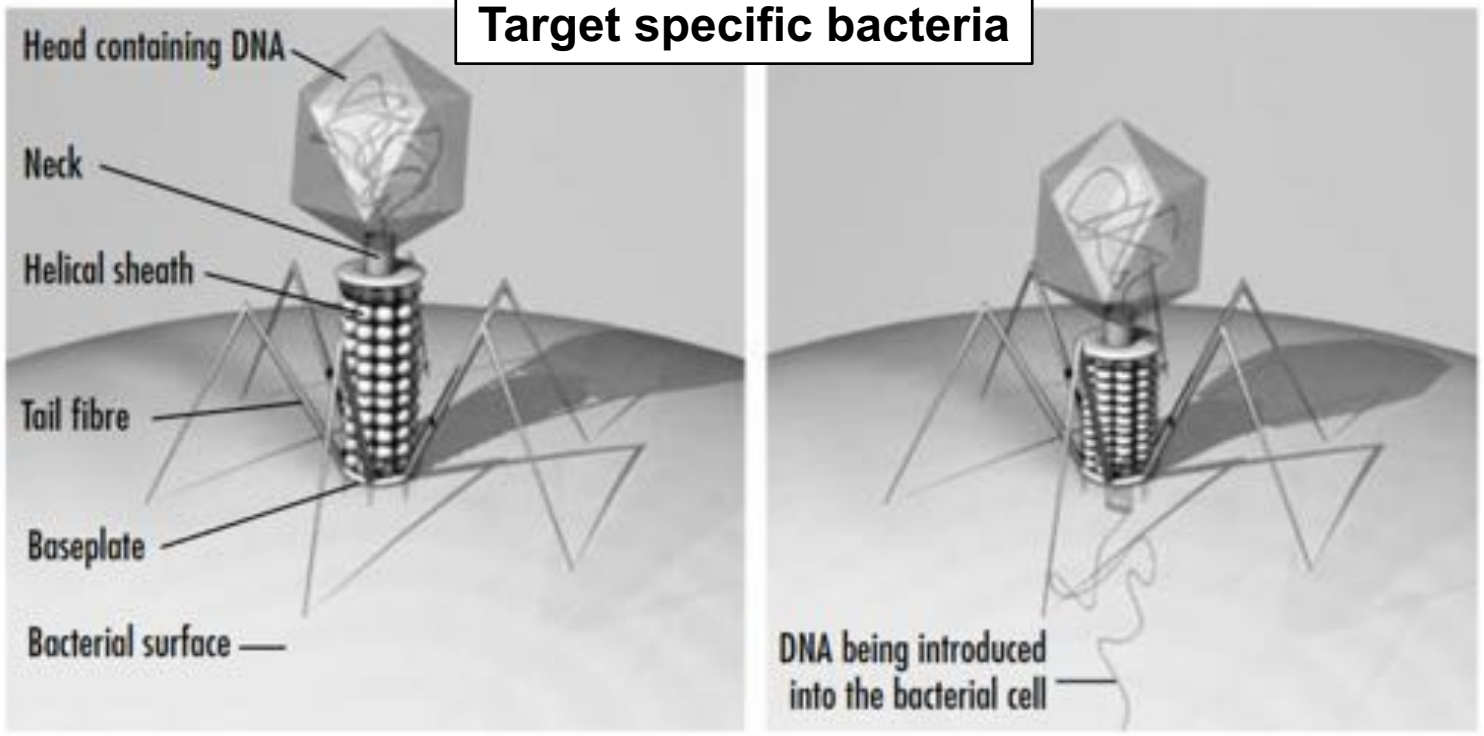
Virologie

2020;24(1):49-56

Environmental viruses
Target specific bacteria



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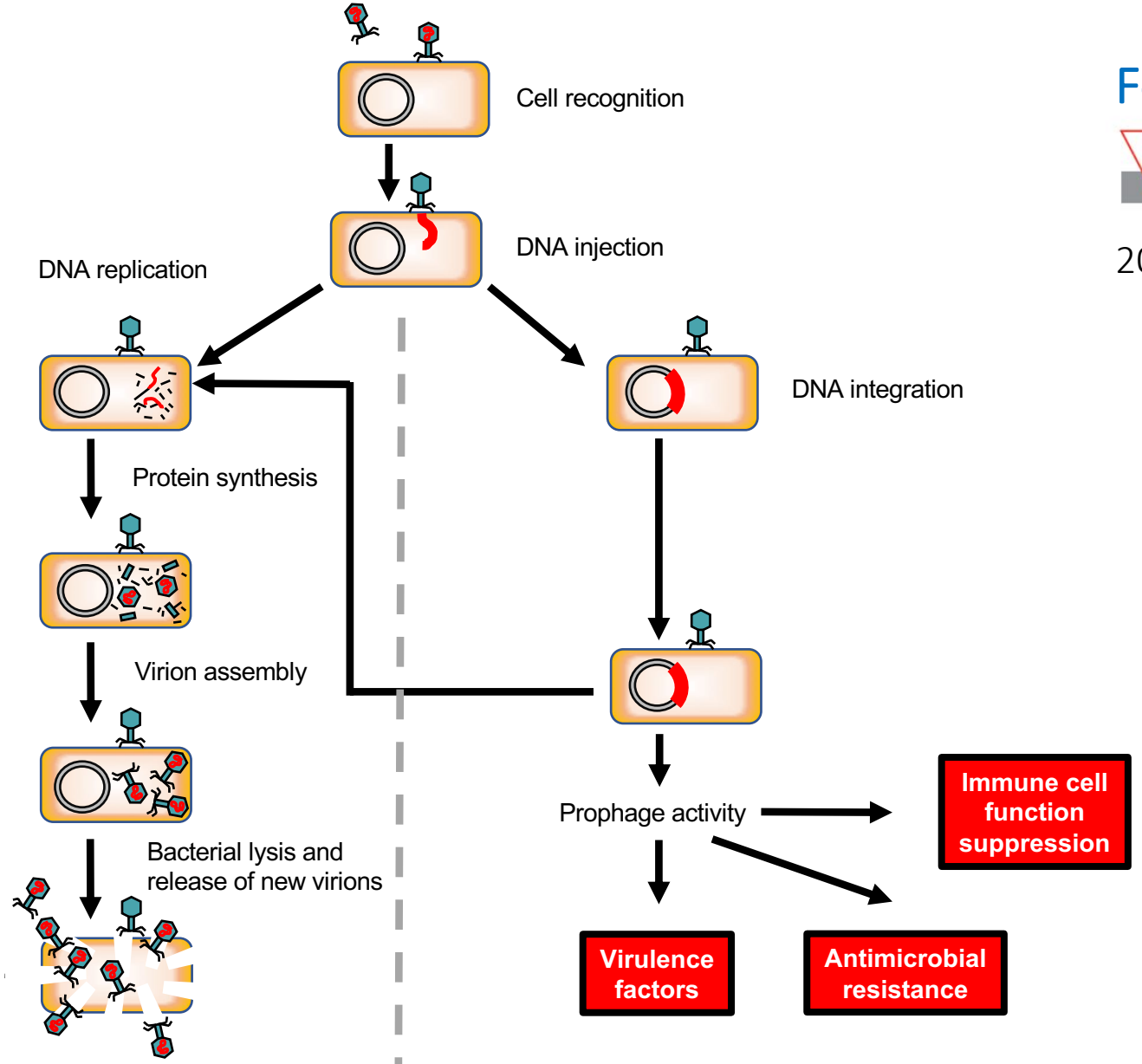

Lytic cycle

Self-maintained bacterial lysis

Lysogenic cycle

Bacterial genetic remodeling

The phage life

Ferry T. et al.

Virologie

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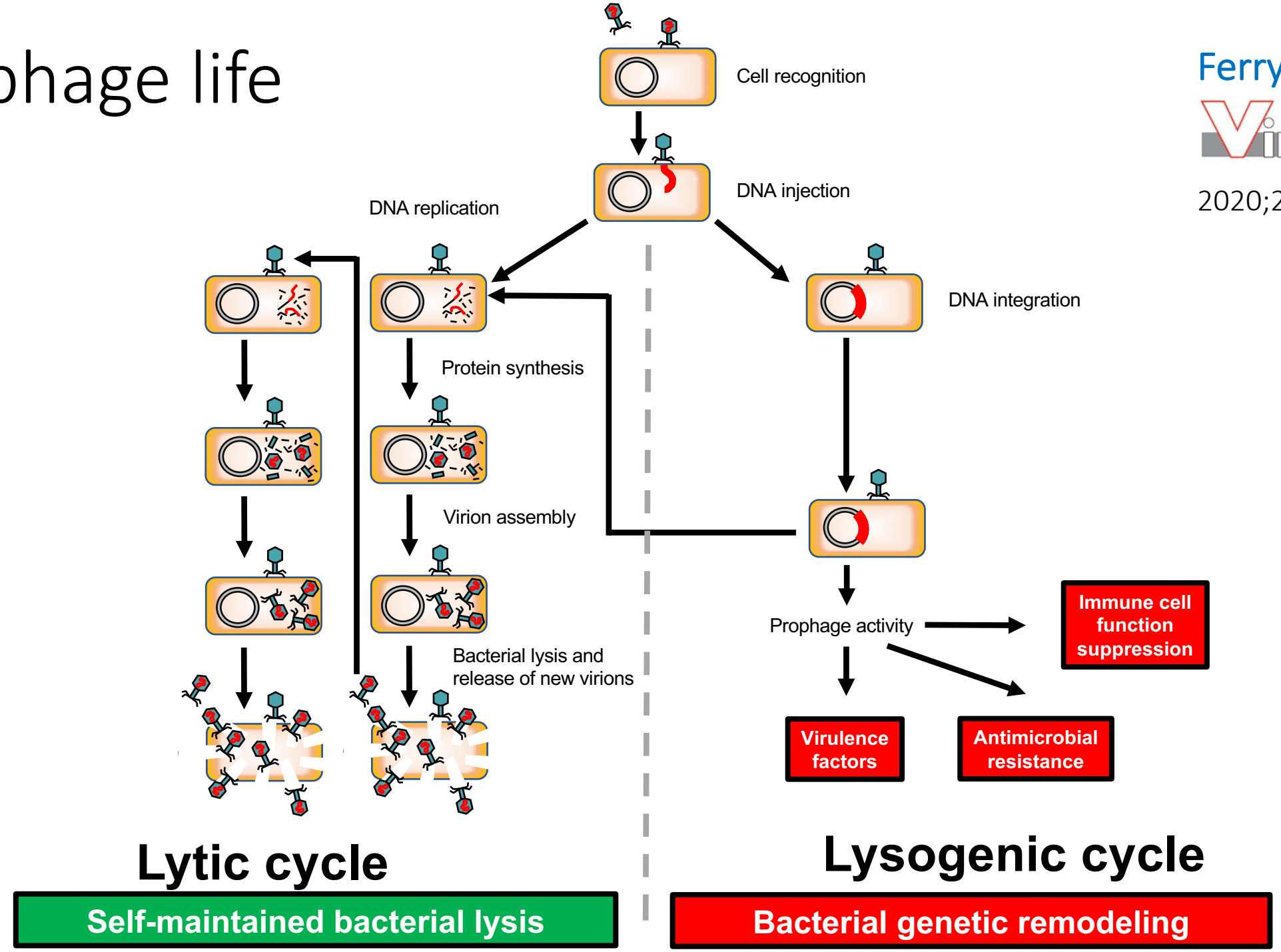

The phage life

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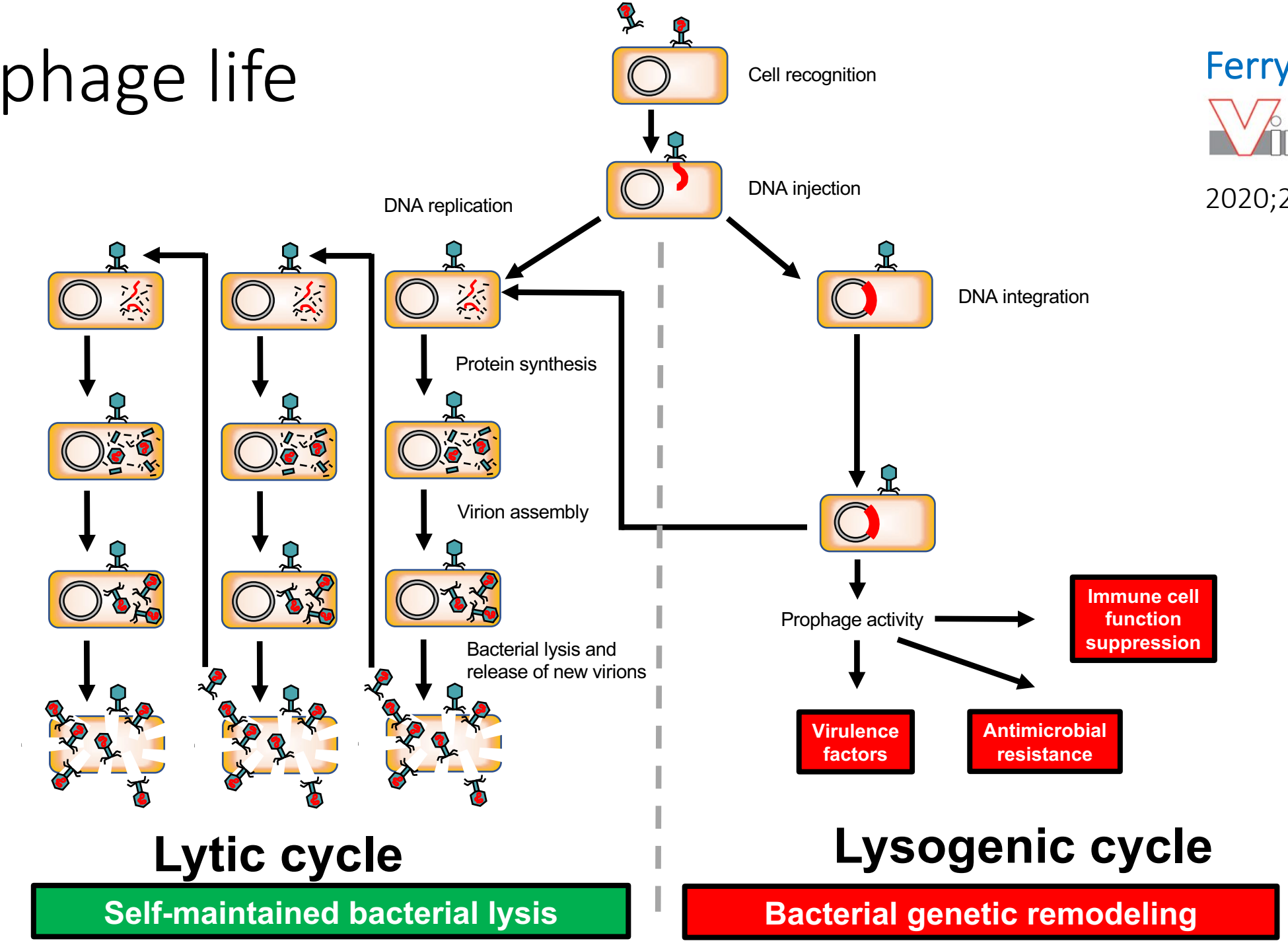
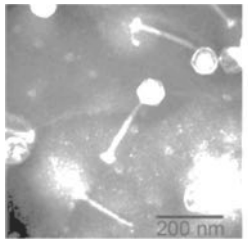


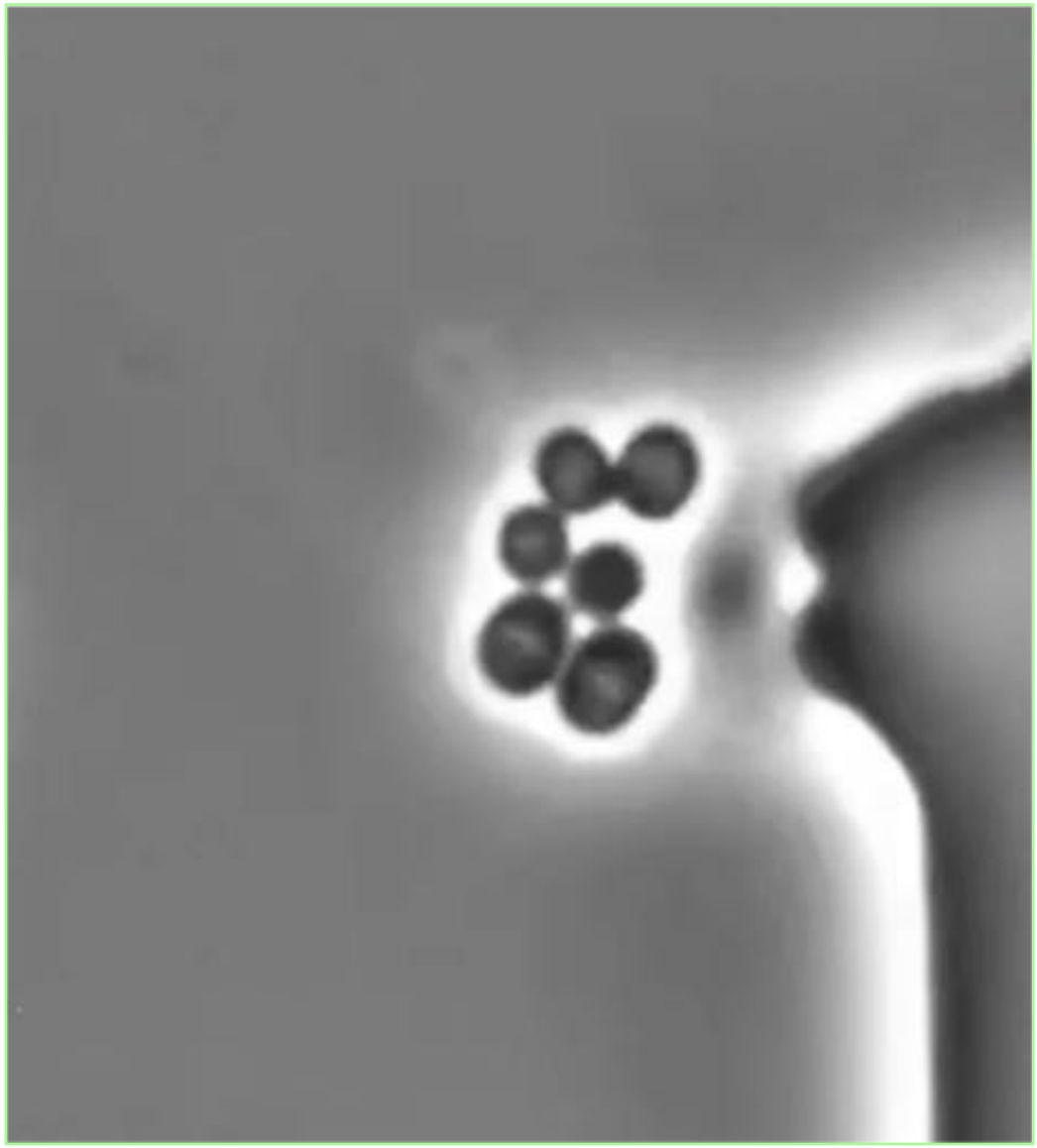
Only lytic phages have to be used

S. aureus being lysed by the Sa2 phage

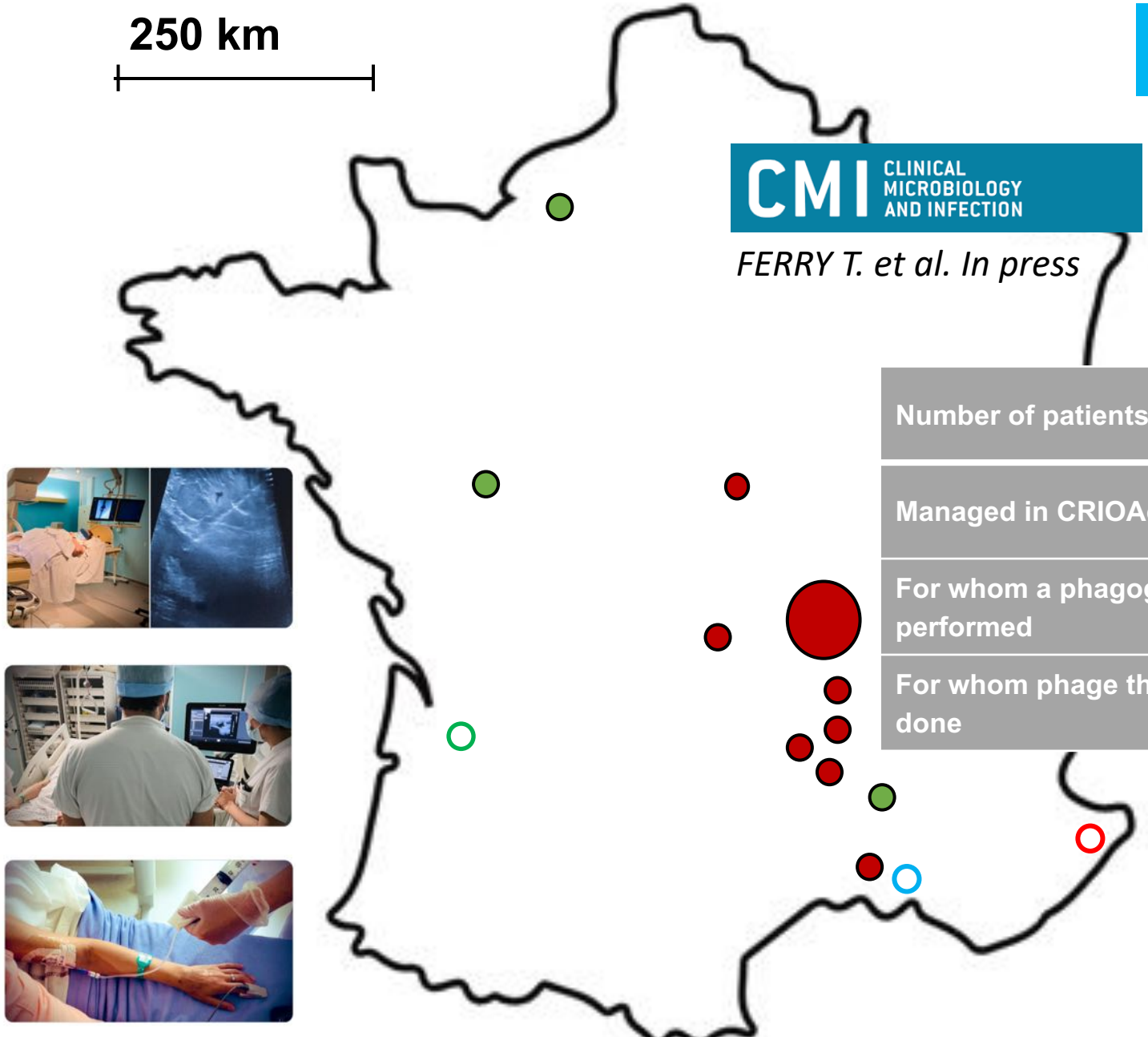


Bacterial DNA appeared in green

Courtesy Pascal Maguin
Luciano Marraffini Lab
THE ROCKEFELLER UNIVERSITY



Implementation of a Phage Therapy Center in a CRIOAc



CMI CLINICAL MICROBIOLOGY AND INFECTION

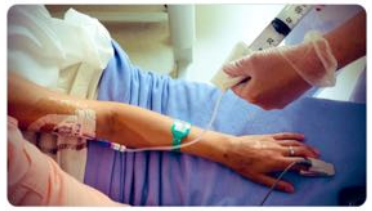
FERRY T. et al. In press

Number of patients	2017	2018	2019	2020	Total
Managed in CRIOAc Lyon	557	594	647	520	**2318**
For whom a phagogram was performed	7 (1.2%)	10 (1.7%)	17 (2.6%)	23 (4.4%)	**57 (2.4%)**
For whom phage therapy was done	4 (0.7%)	2 (0.3%)	8 (1.2%)	7 (1.3%)	**21 (0.9%)**

IOA Endocardite Pneumonies

Implementation of a Phage Therapy Center in a CRIOAc

250 km



CMI CLINICAL MICROBIOLOGY AND INFECTION

FERRY T. et al. In press

HCL PHAGE*in*LYON FONDATION HCL

Lyon 1 CRIOAc LYON ciri Centre International de Recherche en Infectiologie

29 patients traités aux HCL depuis 2017

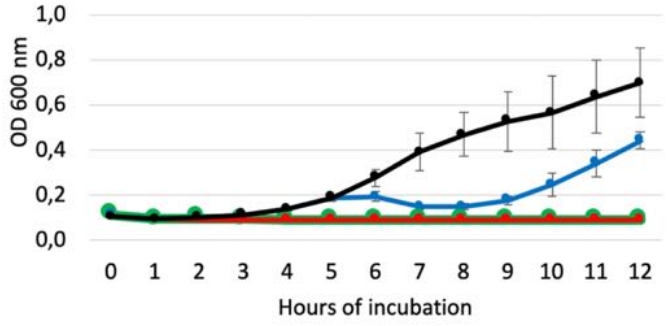
- 26 avec des phages de PHERECYDES PHARMA
- 3 avec des phages MHKA HMRA

- 26 **IOA** (dont **22 infections de prothèse**)
- 3 **endocardites**

+ 3 patients accompagnés et traités hors HCL

IOA **Endocardite** **Pneumonies**

PHAGE*in*LYON team



Phagogram
Selection of active bacteriophages

ID Clinic

HCL HOSPICES CIVILS DE LYON

CRIOAC LYON

ADJUVANT INNOVATIVE ANTI-INFECTIVE AGENTS
OPTIMAL SEPTIC SURGERY
TARGETED AND OPTIMAL ANTIMICROBIAL THERAPY
MULTIDISCIPLINAR MEETING

Surgery

HCL HOSPICES CIVILS DE LYON

Lab

HCL HOSPICES CIVILS DE LYON

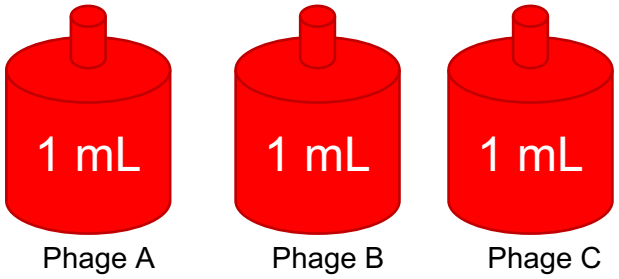
Under the supervision of

ansm
Agence nationale de sécurité du médicament et des produits de santé

French Health Authority

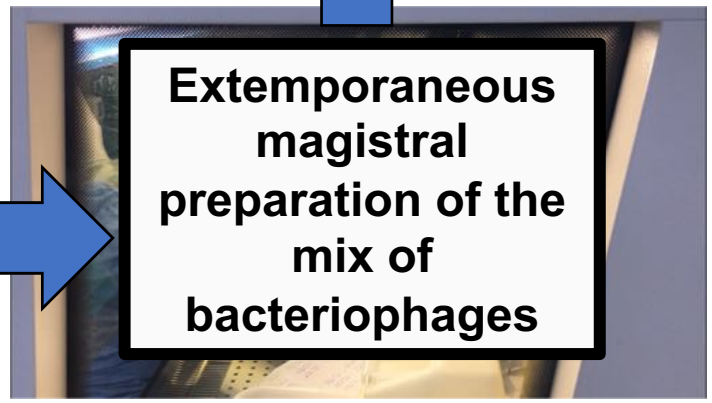
Active GMP

***S. aureus* Bactériophages**



Pharmacy

HCL HOSPICES CIVILS DE LYON



Extemporaneous magistral preparation of the mix of bacteriophages

Case series

Phage Therapy as Adjuvant to Conservative Surgery and Antibiotics to Salvage Patients With Relapsing *S. aureus* Prosthetic Knee Infection

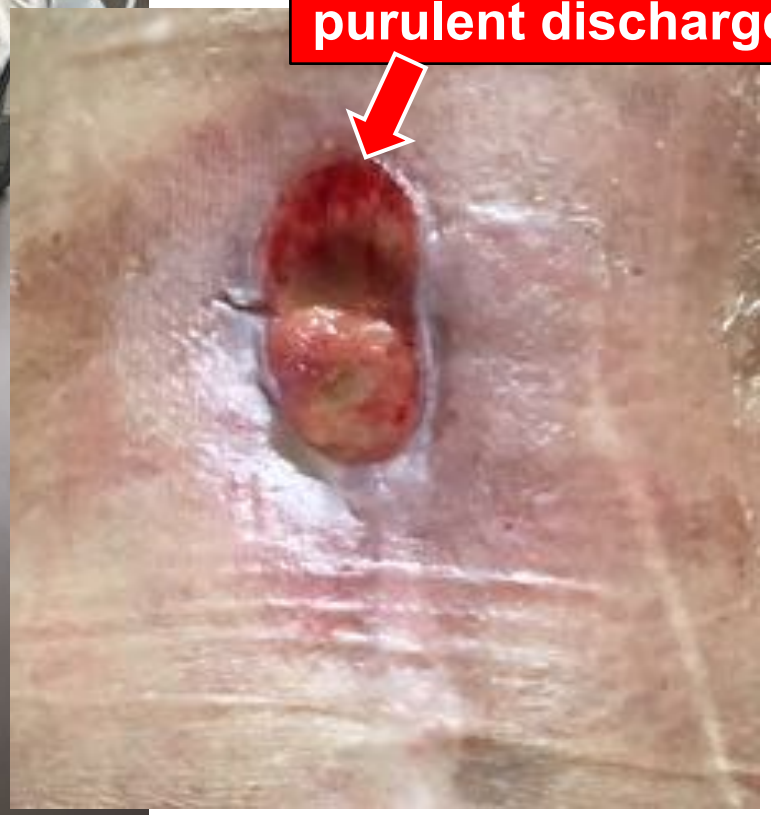
Tristan Ferry[1,2,3,4*], *Camille Kolenda*[2,3,4,5], *Cécile Batailler*[2,3,6], *Claude-Alexandre Gustave*[2,3,4,5], *Sébastien Lustig*[2,3,6], *Matthieu Malatray*[3,6], *Cindy Fevre*[7], *Jérôme Josse*[2,3,4,5], *Charlotte Petitjean*[7], *Christian Chidiac*[1,2,3,4], *Gilles Leboucher*[8] and *Frédéric Laurent*[2,3,4,5] *on behalf of the Lyon BJI Study group*

frontiers in Medicine

CASE REPORT
published: 16 November 2020
doi: 10.3389/fmed.2020.570572

#PhagoDAIR


Septic arthritis


Fistula and purulent discharge

“PhagoDAIR”

<u>One shot</u> peroperative phage application after “DAIR”

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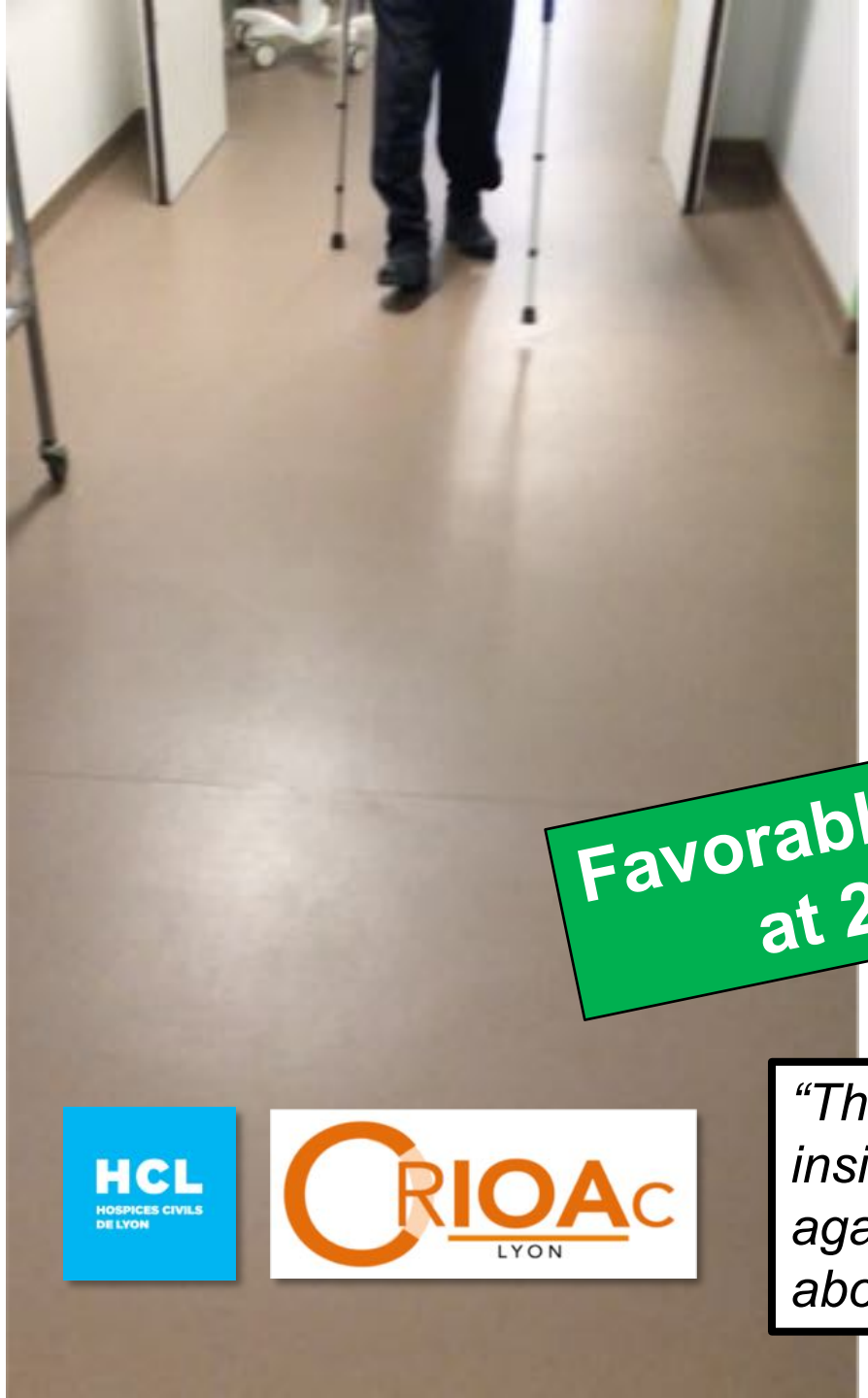
CRIOAc LYON



Favorable outcome at 2 years

“The bacteriophages saved my life, he insists. I never thought one day to walk again. And to say that doctors were talking about cutting my leg off!” R.N.

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T. Ferry et al.

CASE REPORT
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Lyon 1

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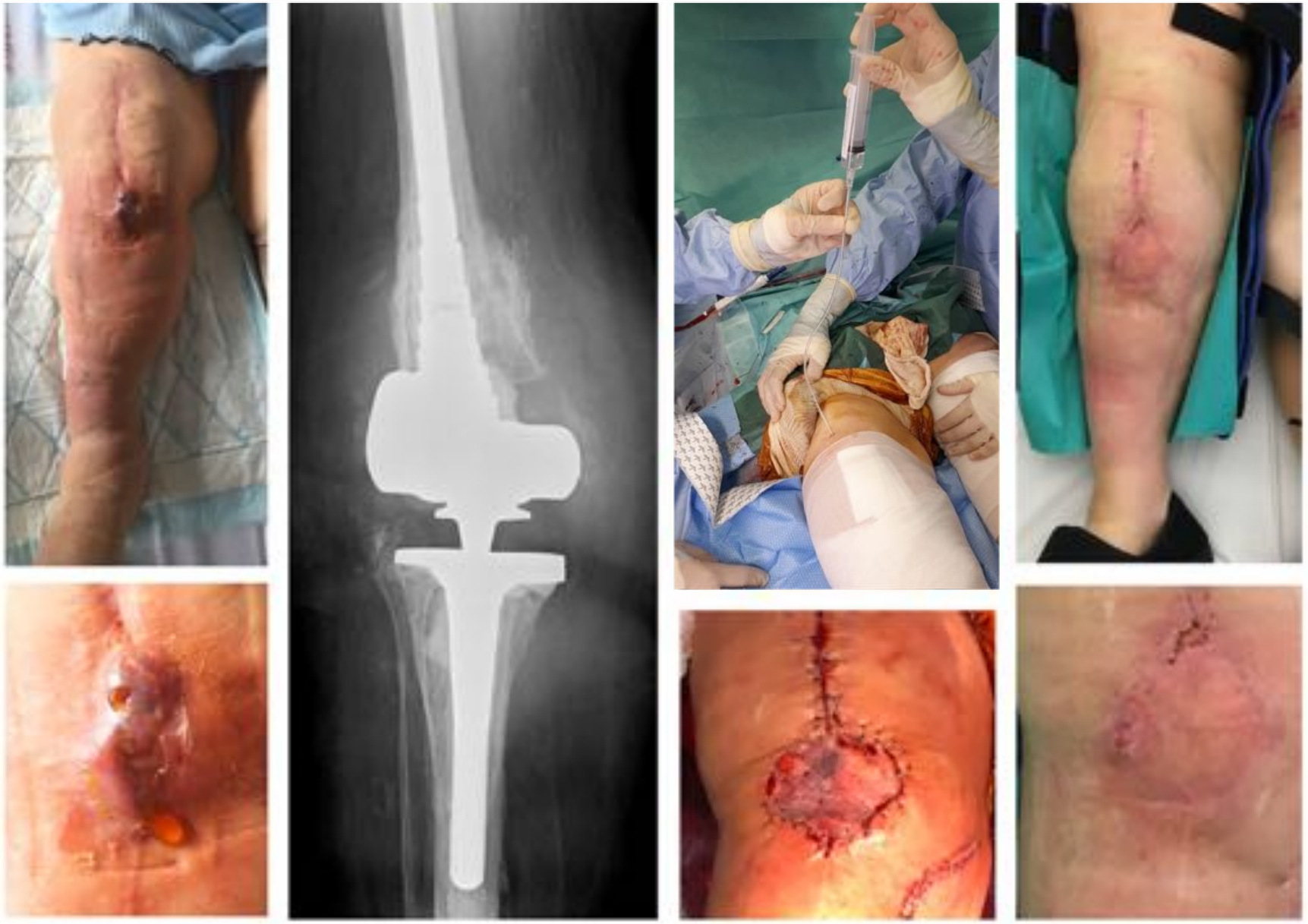

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T. Ferry et al.

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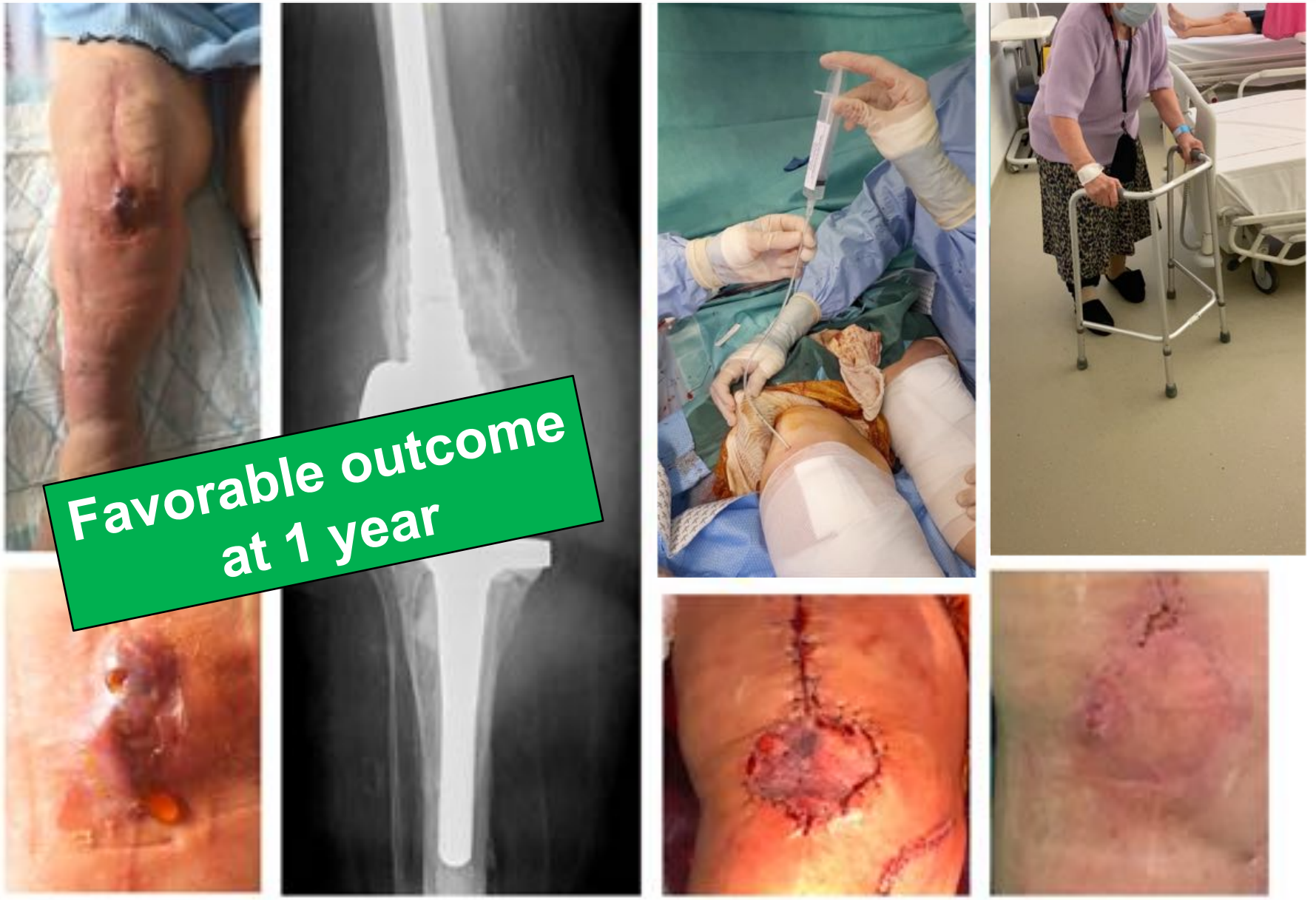
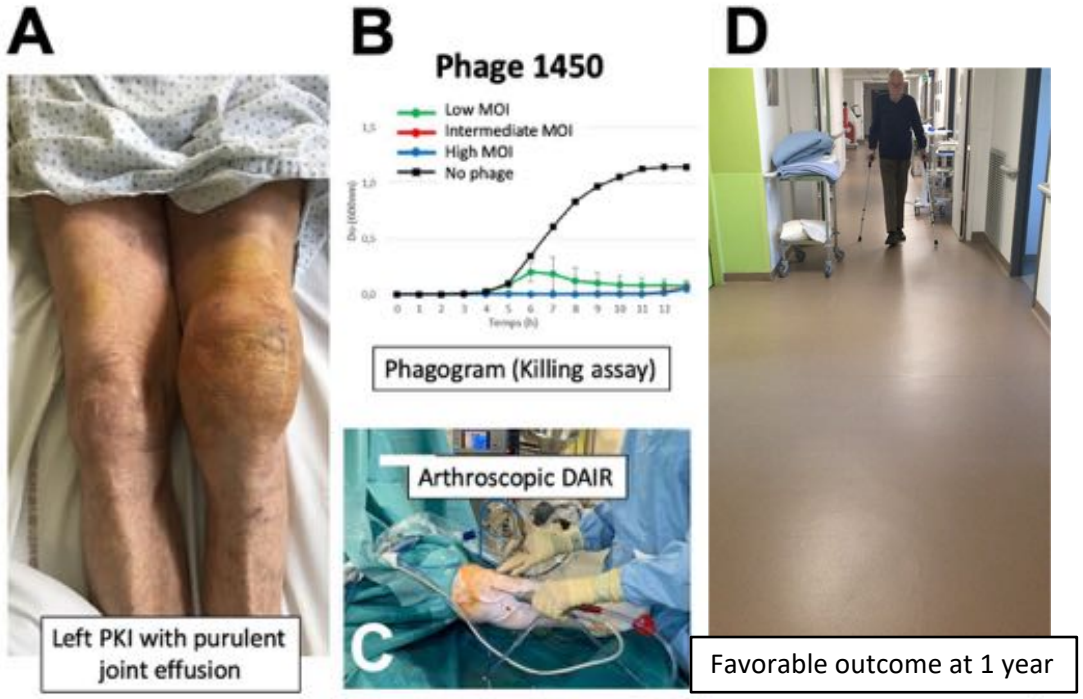


Arthroscopic "Debridement Antibiotics and Implant Retention" with phages to salvage *Pseudomonas aeruginosa* prosthetic knee infection

Phago DAIR



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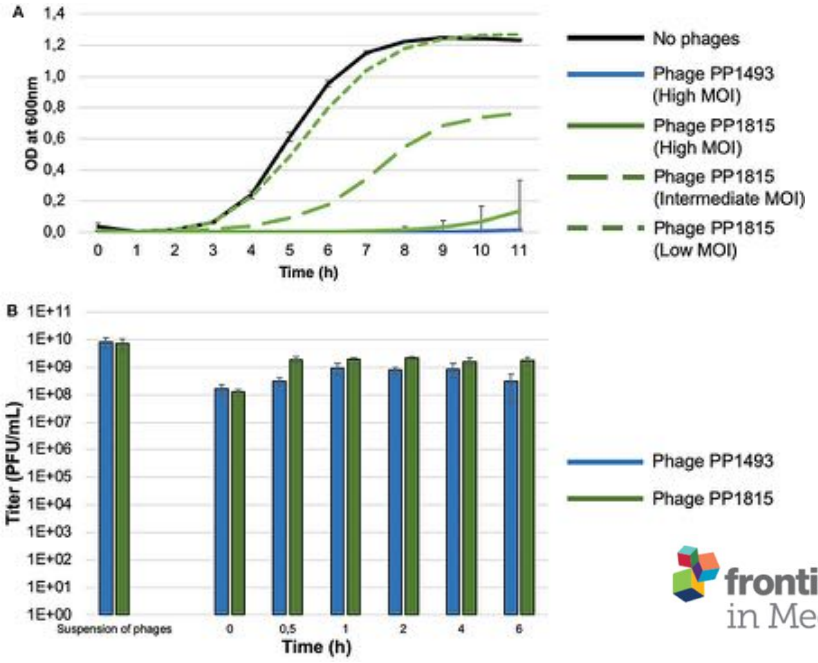
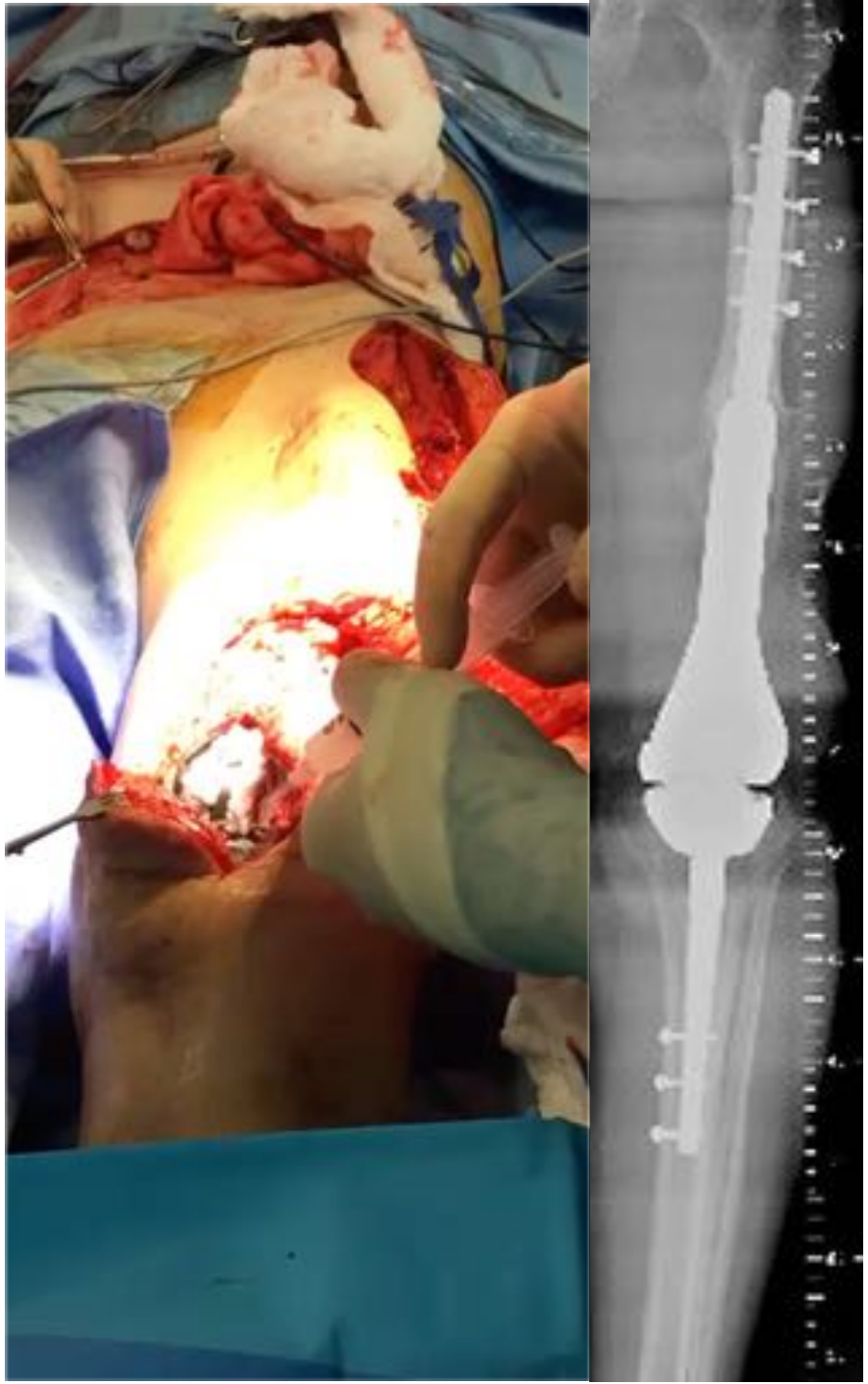
Conclusions: The **PhagoDAIR** procedure by **arthroscopy** has the potential to be used **as salvage therapy** for patients with *P. aeruginosa* relapsing PJI, in combination with suppressive antimicrobial therapy. **A Phase II clinical study deserves to be performed to confirm this hypothesis.**

The Potential Innovative Use of Bacteriophages Within the DAC® Hydrogel to Treat Patients With Knee Megaprosthesis Infection Requiring "Debridement Antibiotics and Implant Retention" and Soft Tissue Coverage as Salvage Therapy

Tristan Ferry[1,2,3,4], Cécile Batailler[2,3,5], Charlotte Petitjean[6], Joseph Chateau[7], Cindy Fevre[6], Emmanuel Forestier[8], Sophie Brosset[7], Gilles Leboucher[9], Camille Kolenda[2,3,4,10], Frédéric Laurent[2,3,4,10] and Sébastien Lustig[2,3,5] on behalf of the Lyon BJI Study Group*





Where to find phages for clinical use?

- Pherecydes Pharma

- Phage community

Under the supervision of

French Health Authority

?

Where to find phages for clinical use?

- Pherecydes Pharma

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Under the supervision of

French Health Authority

?

PHAG-ONE

MINISTÈRE DE L'ENSEIGNEMENT SUPÉRIEUR, DE LA RECHERCHE ET DE L'INNOVATION

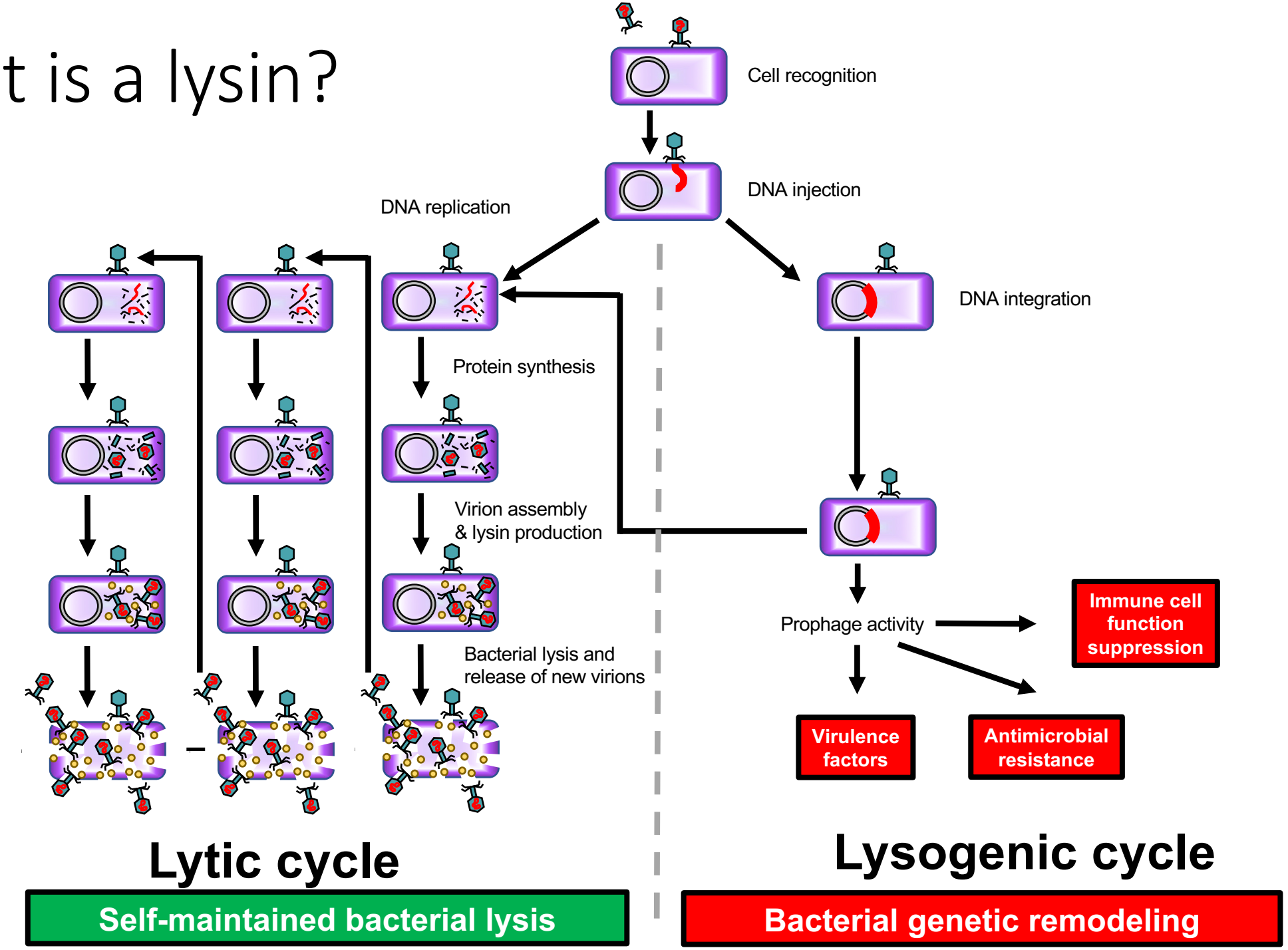
Liberté
Égalité
Fraternité

PHAGE*in*LYON

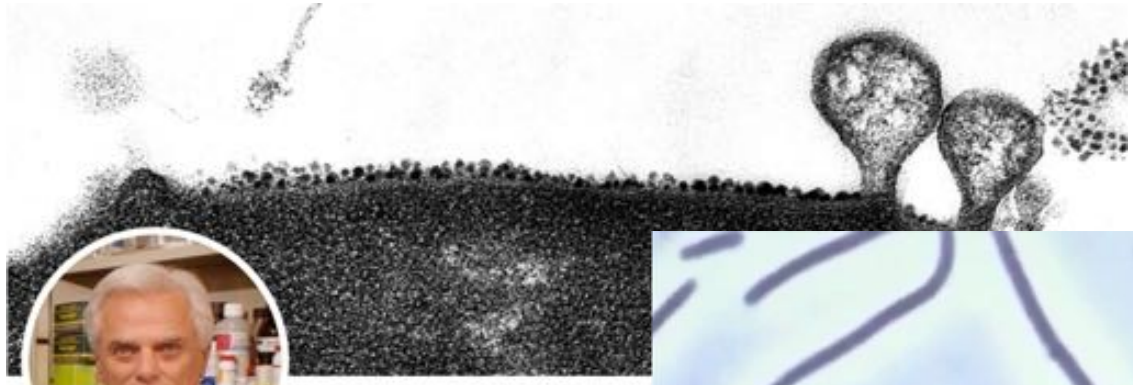
Purified **academic** phages
Usable in the next 5 years

FRI PHARM

What is a lysin?



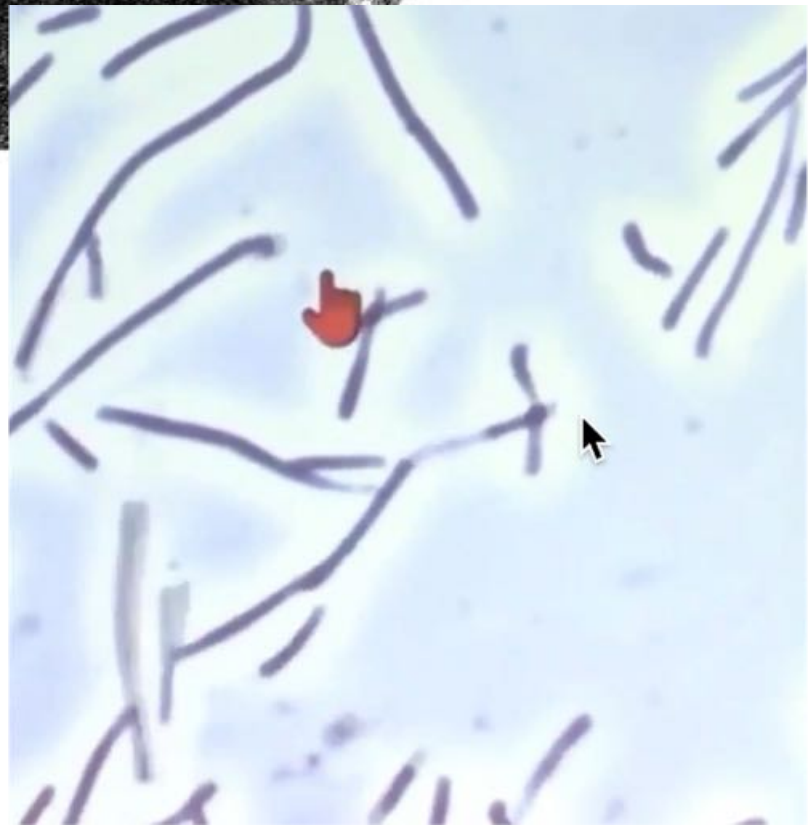
What is a lysin?



Vincent A Fischetti
@microbephage

Tristan Ferry Lyon University Hospitals
@FerryLyon

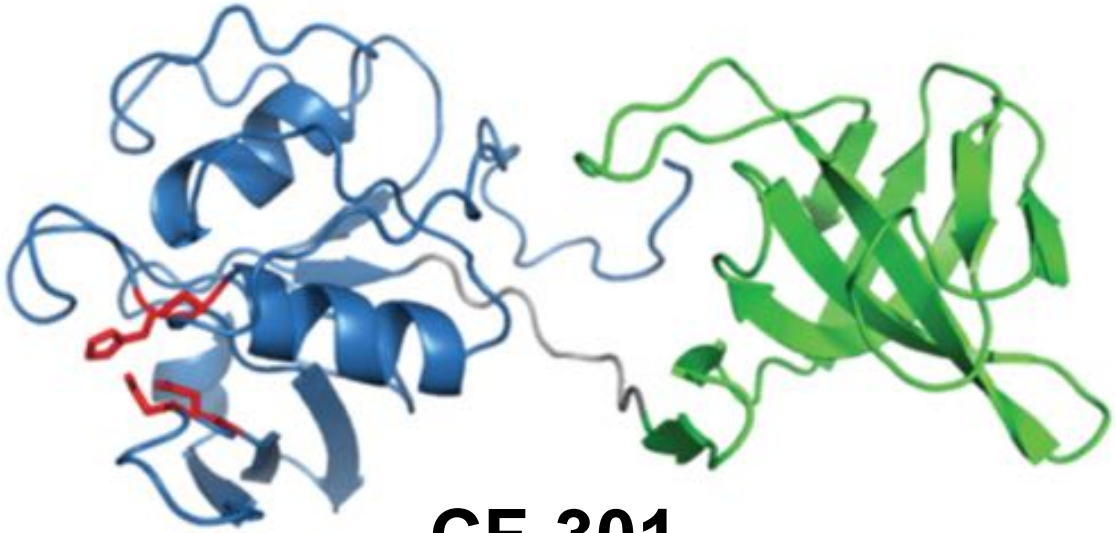
Incredible talk of Pr. Vincent A. Fischetti @microbephage @IDWeek2019 about the great potential of #bacteriophage #lysins to induce bacterial explosion... and disappearance! It's good to hear that he discovered lysins that are active against #multidrugresistant #ESKAPE pathogens!



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 Wittekind[1]

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



CF-301

CF-301 is a lysin from a *S. aureus* phage
Broader spectrum of activity: against *S. aureus*, but also against coagulase-negative staphylococci

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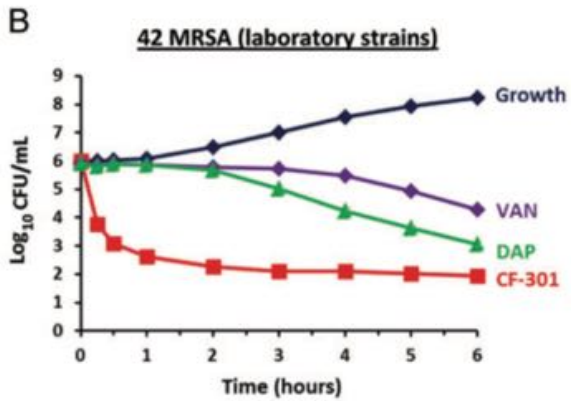
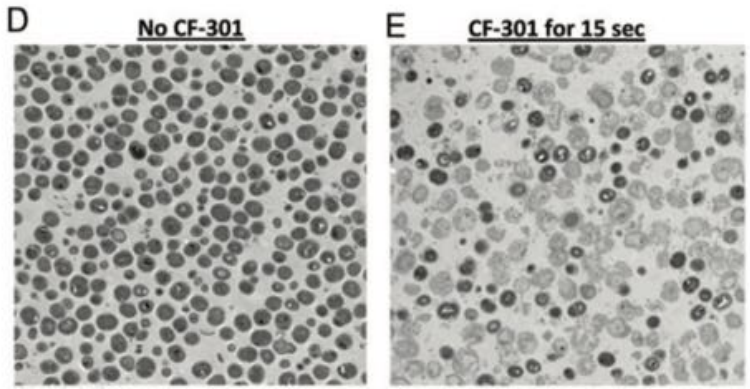
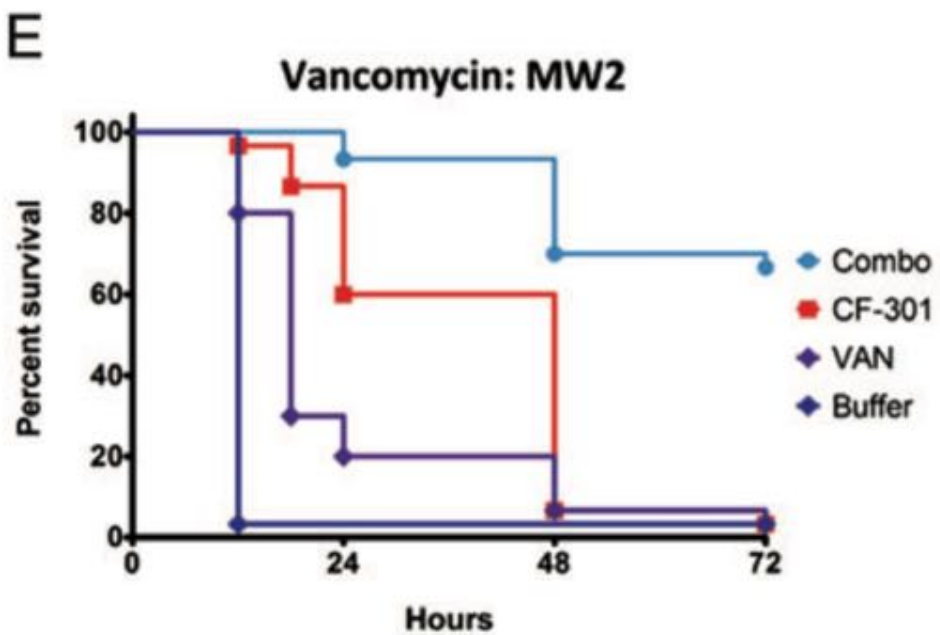






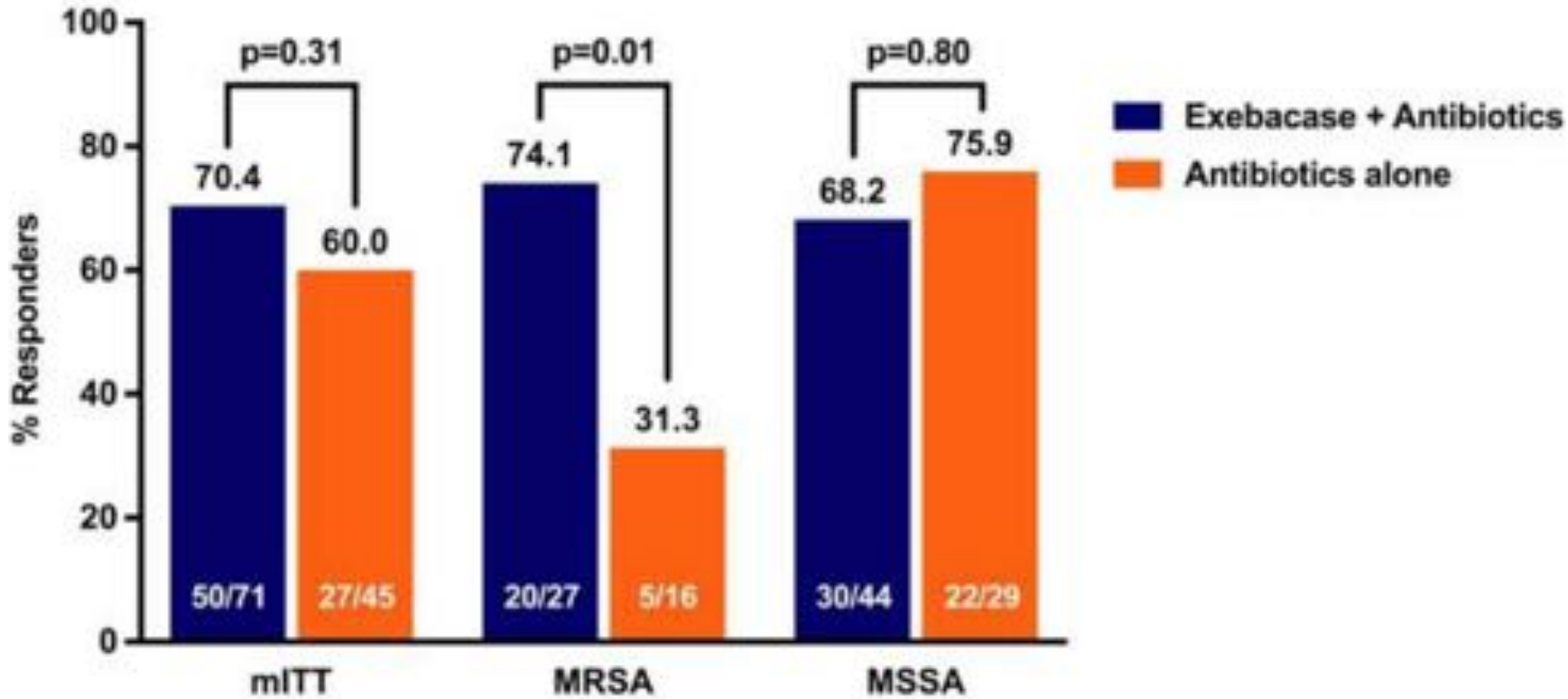
J Infect Dis 2014

The Journal of Clinical Investigation

2020

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 Cassino[5]



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

HCL
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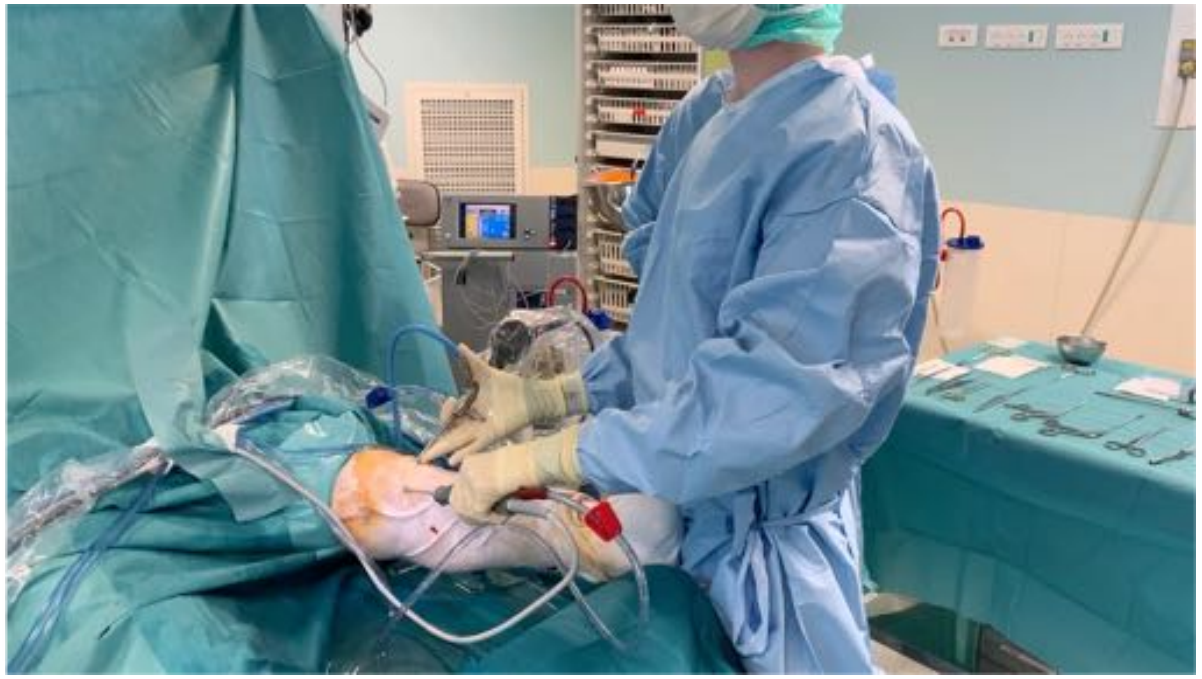

30th ECCMID
Paris, France
18 –21 April 2020

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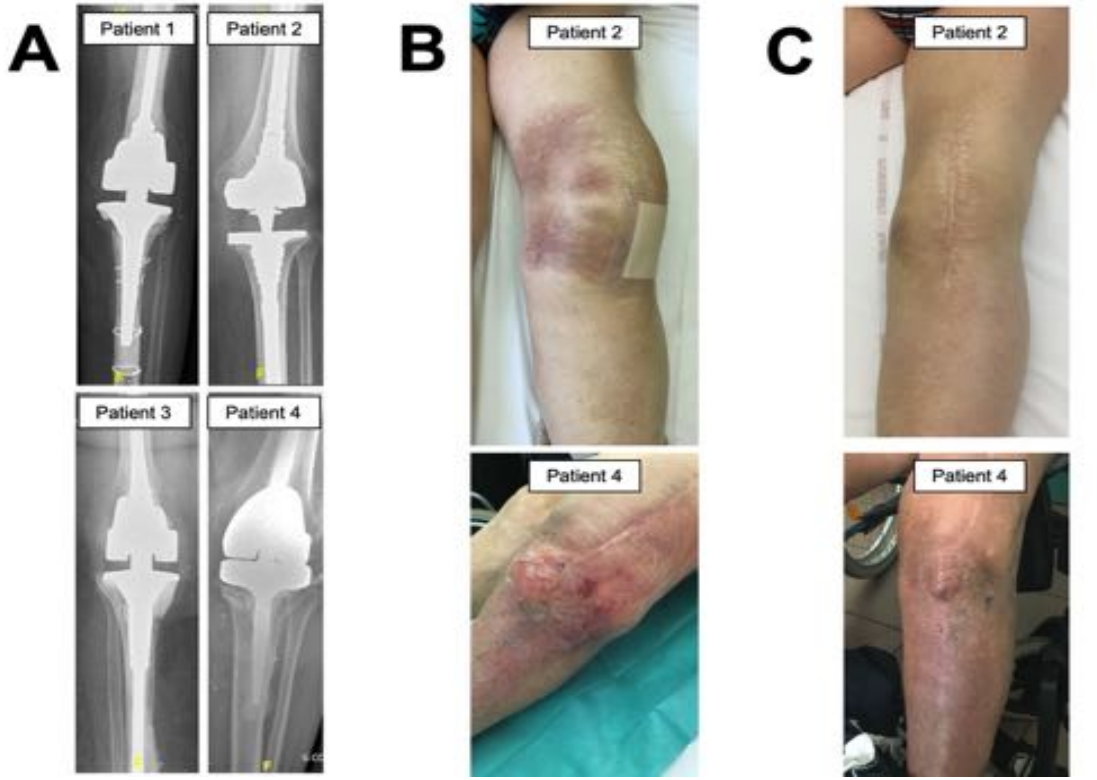
ContraFect

CRIOAc LYON

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.

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



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.

UC San Diego
School of Medicine

Center for Innovative Phage Applications and Therapeutics

In the Division of Infectious Diseases & Global Public Health

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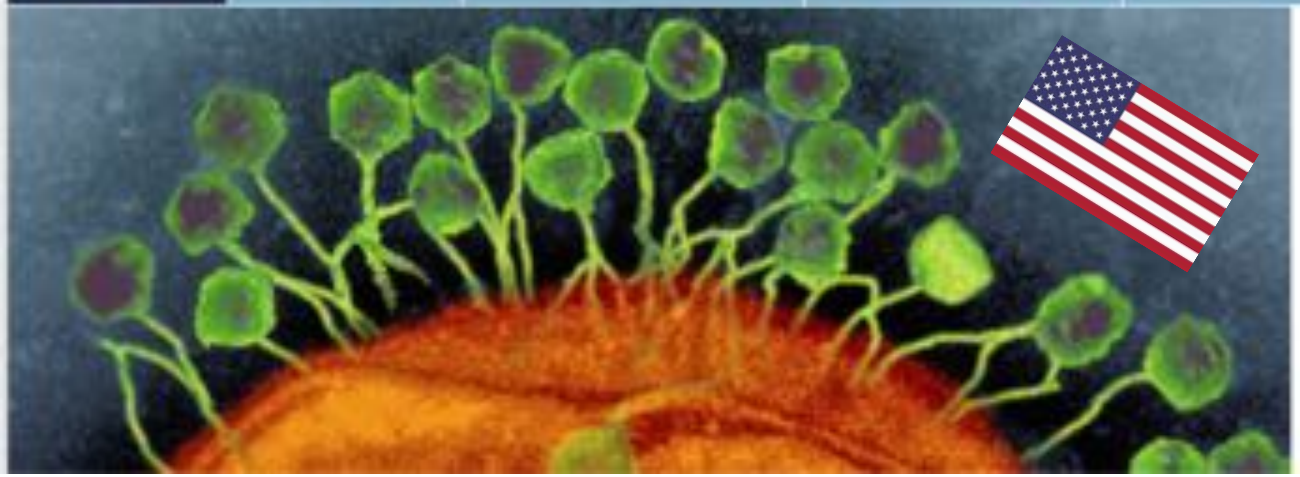

Welcome to IPATH

Center for Innovative Phage Applications and Therapeutics

We are the first dedicated phage therapy center in North America, bringing innovative research and clinical practice to the field of medicine. Join us on our journey and witness a revolutionary wave of solutions to combat antibiotic resistance.

Open Forum Infectious Diseases

MAJOR ARTICLE

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]

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

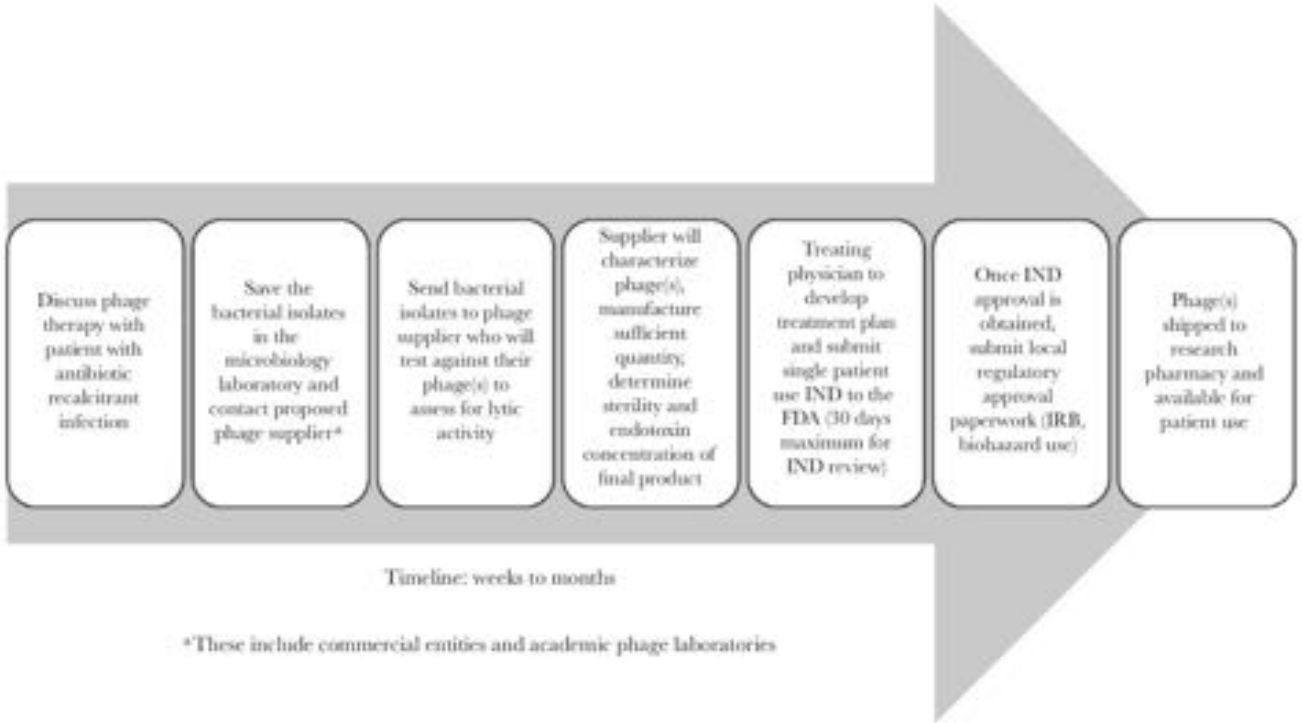

Figure 2. Timeline of the process to initiate bacteriophage therapy for a patient on a compassionate use basis in the United States. Abbreviations: FDA, Food and Drug Administration; IND, Investigational New Drug; IRB, institutional review board.

Open Forum Infectious Diseases

MAJOR ARTICLE

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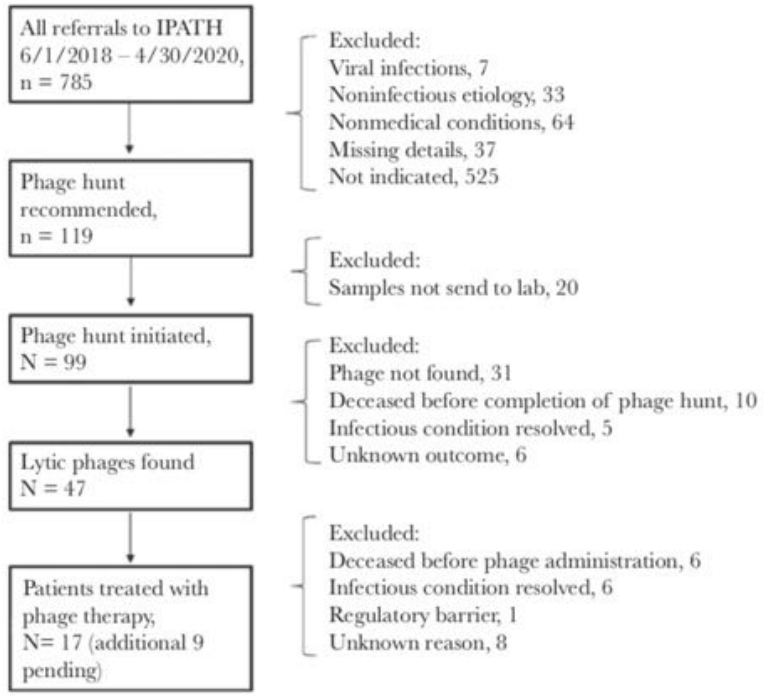
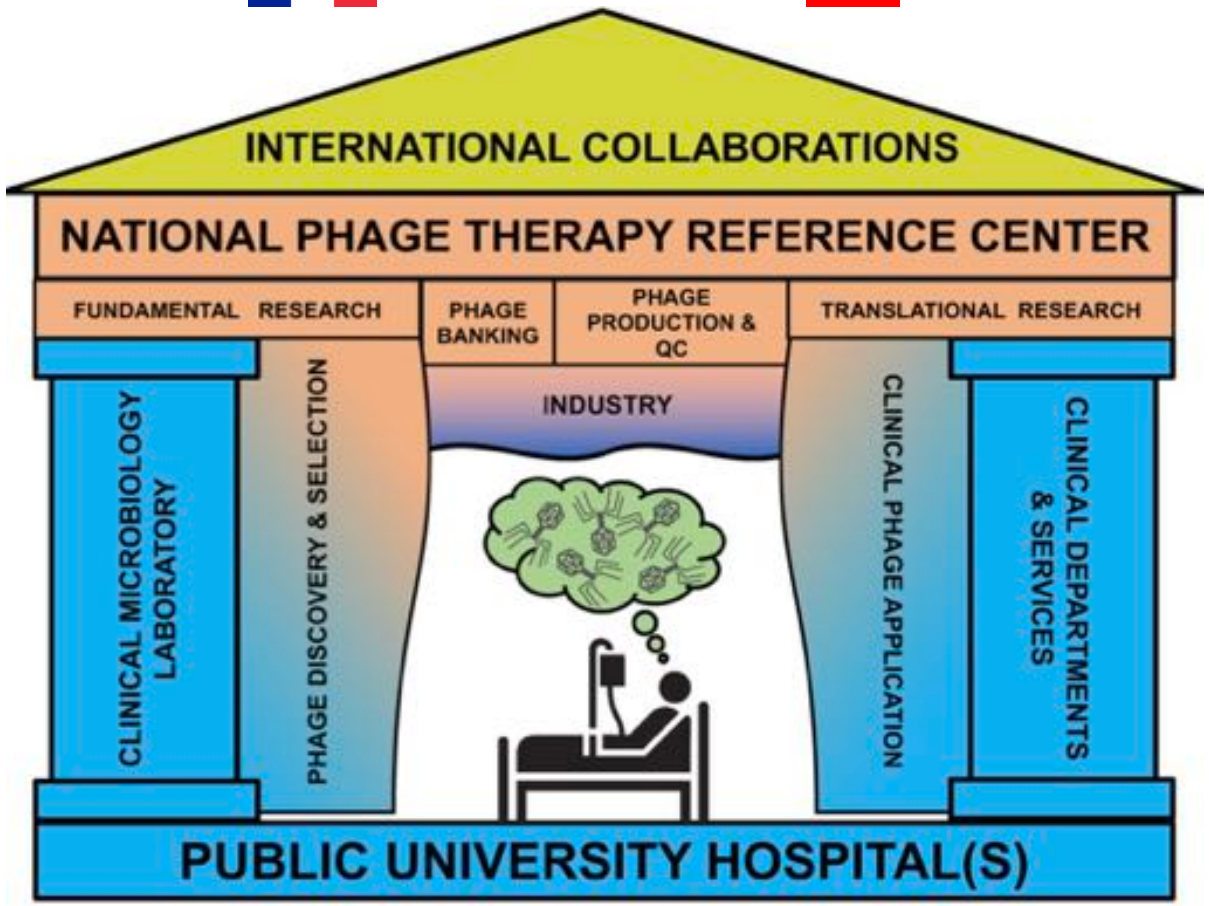


Figure 1. Flowchart depicting outcome of all bacteriophage therapy requests at the Center for Innovative Phage Applications and Therapeutics. Abbreviation: IPATH, Center for Innovative Phage Applications and Therapeutics.

REVIEW ARTICLE

Recent progress toward the implementation of phage therapy in Western medicine

Jean-Paul Pirnay[1,†], Tristan Ferry[2,3,†] and Grégory Resch[4,*,†]



FEMS Microbiology Reviews
2021

ESGNTA

ESCMID STUDY GROUP FOR NON-TRADITIONAL ANTIBACTERIAL THERAPY

European Society of Clinical Microbiology and Infectious Diseases

Inauguration Committee Members

Prof. Ran NIR-PAZ
Hadassah-Hebrew University Medical Center
Clinical Microbiology and infectious Diseases
Israël

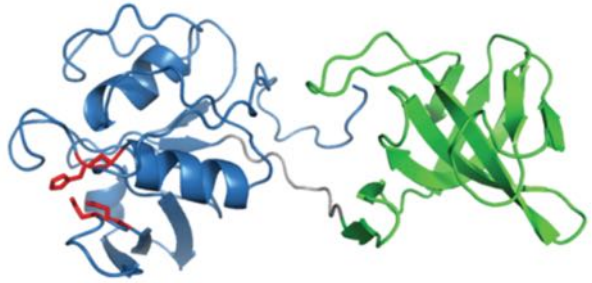
Prof. Tristan FERRY
Hospices Civils de Lyon
Infectious Diseases
France

Prof. Patrick SOENTJENS
Department of Clinical Sciences
Institute of Tropical Medicine, Antwerp
Belgium

Prof. Zuzanna DRULIS-KAWA
University of Wroclaw
Department of Pathogen Biology and Immunology
Poland

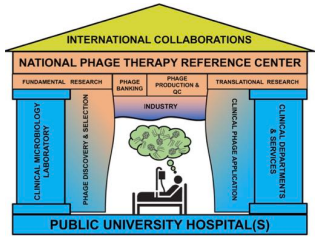
Prof. Joana AZEREDO
Universidade do Minho
Engenharia Biológica
Portugal

Conclusion



- Real potential for **non-traditional antibacterial therapies**
- **Distinguish:**
  - Anti-virulence approaches
  - Immunomodulators
  - Microbiome-Modifying Therapies
  - Phages
  - Phage-related therapies (Lysins)
- **Phages** have a **real potential** in prosthetic-joint infection
  - Need for **EMA positioning about the status of phages**
  - Need for **industrial and academic developement** of therapeutic phages (discovery, banking, susceptibility testing) in connection with health care authorities
  - Need for creation of nation-wide **reference centers** dedicated to phage therapy
  - Need to **perform clinical trials** to evaluate the ability of these innovations to improve the outcome
- **Lysins** are evaluated in *S. aureus* bacteremia, but could be also active against coagulase-negative staphylococci
  - Has also antibiofilm activities (as bacteriophages)
  - Has to follow the classical way of a drug

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



2.0

ansm
Agence nationale de sécurité du médicament et des produits de santé

PÉTITION EN FAVEUR DE LA RENAISSANCE DE LA BACTERIOPHAGIE THERAPEUTIQUE

Frappé par le désarroi des malades se trouvant, depuis plusieurs mois, dans l'impossibilité de trouver en pharmacie les ampoules de Bactériophage qui leur avaient été prescrites ou bien de renouveler la provision que les plus prévoyants d'entre eux avaient constituée pour surmonter victorieusement, dès le prime début, tout assaut microbien, j'ai pensé que la SOCIETE DES AMIS DE FELIX D'HERELLE se devait de mettre la puissance de son autorité au service de ces doléances qui m'étaient exprimées pour contribuer à redonner à la Phagothérapie tous les moyens d'expression dont la prestigieuse découv
toujours, car aucune
préparer son malade
la production naturel
« guérison naturelle
mencement du milieu
Ce sont ces races qu
sont inconnues, sélect
les pharmacies.

J'ai donc résol
lieu, à convier :

— Vous, mes MAIT
le plus grand b

— Vous, MALADES o
vos proches ou vos amis, des succès remportés au cours des applications thérapeutiques du Phénomène de Bactériophagie ;

— Vous, MEMBRES DE LA SOCIETE DES AMIS DE FELIX D'HERELLE qui vous êtes groupés pour pouvoir, par le soutien de chacun, assurer la pérennité de l'œuvre exceptionnelle de ce grand savant qui, venu de Montréal, a offert à la France la gloire attachée à la découverte d'un phénomène naturel dont le microscope électronique, fait unique dans la Science, a confirmé dans ses moindres détails la réalité que la méthode expérimentale seule avait permis de dévoiler :

à signer l'attestation ci-contre pour influencer par le nombre des signataires les milieux scientifiques aptes à relever le flambeau qui est tombé par suite de la défaillance du Laboratoire qui avait été fondé par d'Hérelle en 1928 et qui a permis, au cours des 50 années qui suivirent, la mise au point d'un traitement d'une efficacité jamais égalée par sa qualité, sa constance et sa parfaite innocuité : LA PHAGOTHERAPIE. Cette défaillance est d'autant plus catastrophique que, d'une part, ce Laboratoire était le seul à assurer la préparation des différentes races de Bactériophage qui sont indispensables à la pratique médicale et chirurgicale dans le domaine de toute la pathologie infectieuse et que, d'autre part, le phénomène de Bactériophagie qui est reproduit dans un but thérapeutique ne peut être remplacé par aucune spécialité pharmaceutique puisque, seul de tous les traitements, il est l'expression d'un phénomène de la nature. L'arrêt de ce Labo-

ratoire a pour conséquence inéluctable d'entraîner dans sa chute la pratique d'une méthode thérapeutique qui a fait ses preuves dans tous les domaines depuis 1917, date à laquelle le phénomène de Bactériophagie fut révélé au monde du haut de la tribune de l'Académie des Sciences.

C'est donc un devoir pour la SOCIETE DES AMIS DE FELIX D'HERELLE, dont la mission est d'assurer la défense de l'œuvre du Pr d'Hérelle contre toute manœuvre dirigée directement ou indirectement contre elle, que d'appuyer de son influence toutes initiatives généreuses qui sont disposées à œuvrer dans ce sens. Plus les voix seront nombreuses, plus elles auront chance d'être entendues.

Disciples convaincus de la Bactériophagie, venez tous à nous en nous offrant le poids de votre signature.

Dr A. RAIGA-CLEMENCEAU

.....

.....

.....

la campagne entre-
de promouvoir une
Bactériophage, et
us, notamment par
moi-même apprécié

servations complémentaires (facultatives, mais éminemment souhaitées) .....

.....

.....

Date : Signature :

Cette attestation, sans être séparée de la pétition, est à renvoyer au Dr Raiga-Clemenceau, Secrétaire Général de la SOCIETE DES AMIS DE FELIX D'HERELLE,

11, rue Boissière - 75116 PARIS

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 Pouderoux, 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, 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 Boussel, Jean-Baptiste Pialat, Isabelle Morelec;

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

Clinical research assistant and database manager– Eugénie Mabrut

Lyon 1

CRIOAc LYON

ciri Centre International de Recherche en Infectiologie

HCL HOSPICES CIVILS DE LYON

Croix-Rousse Hospital

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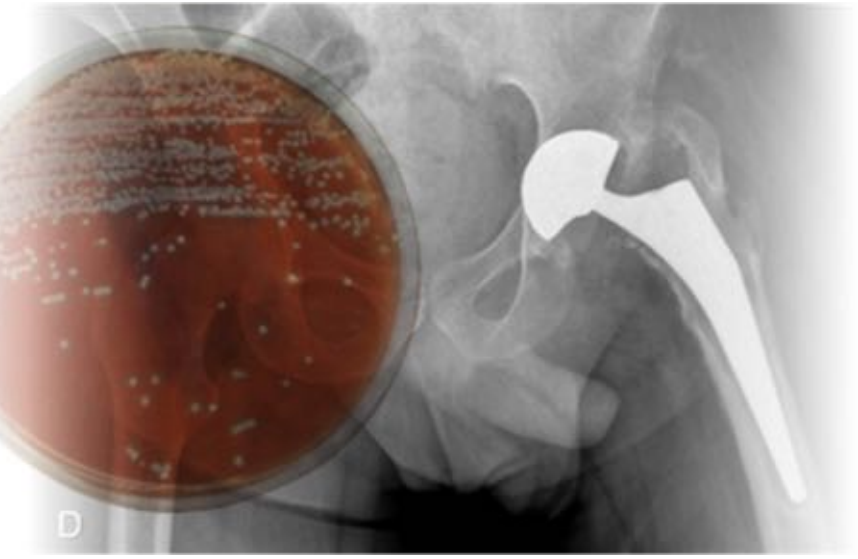

- Published cases
- Open acces studies in pdf
- All thesis in pdf
- All recommendations
- **Newsletter**

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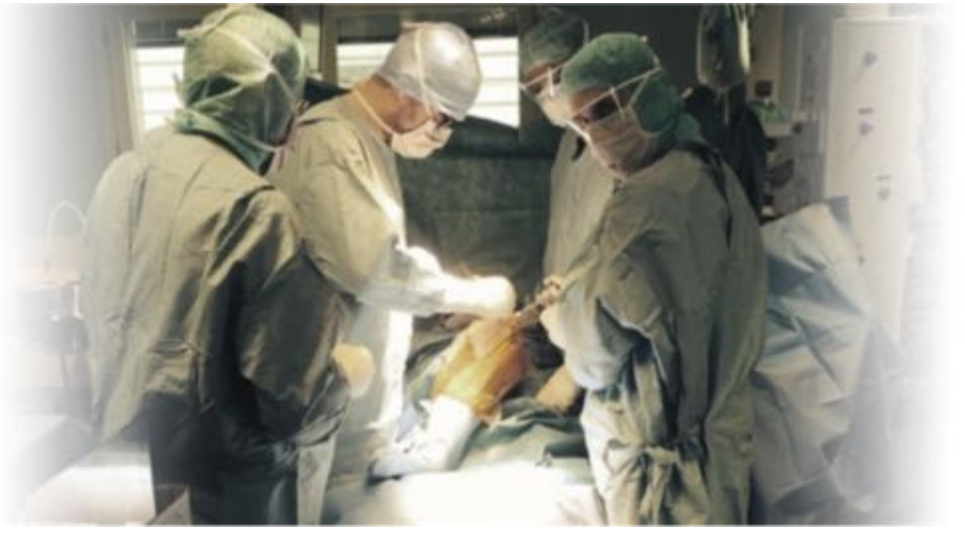

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PRÉSENTIEL
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