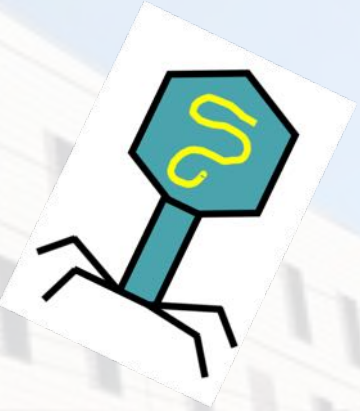
# infections osteoarticulaires, bactériophages et thérapie phagique :

## Histoire et perspectives



**Pr. Tristan Ferry**
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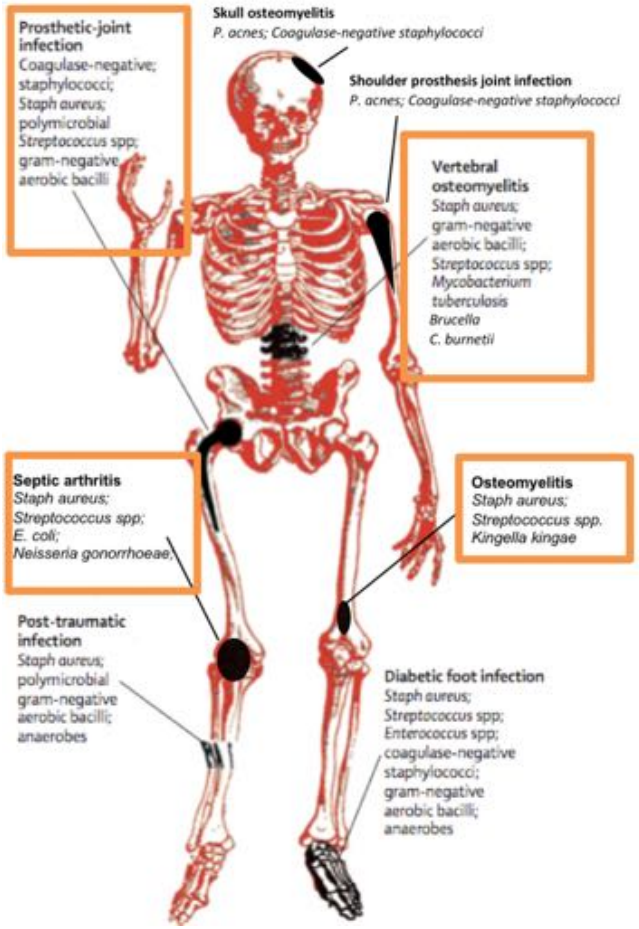
Claude Bernard Lyon1 University, Lyon

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

# Les infections ostéoarticulaires




*Lew et al. NEJM 1997*

- Infections **hétérogènes**
- Epidémiologie bactérienne **variable**
- Incidence '**faible'**
- Différentes **stratégies**
- **La stratégie** et **les comorbidités** influencent le **pronostic**
- **Pourcentage de succès faible** dans certaines situations cliniques
- **Coût considérable** (individuel et collectif)

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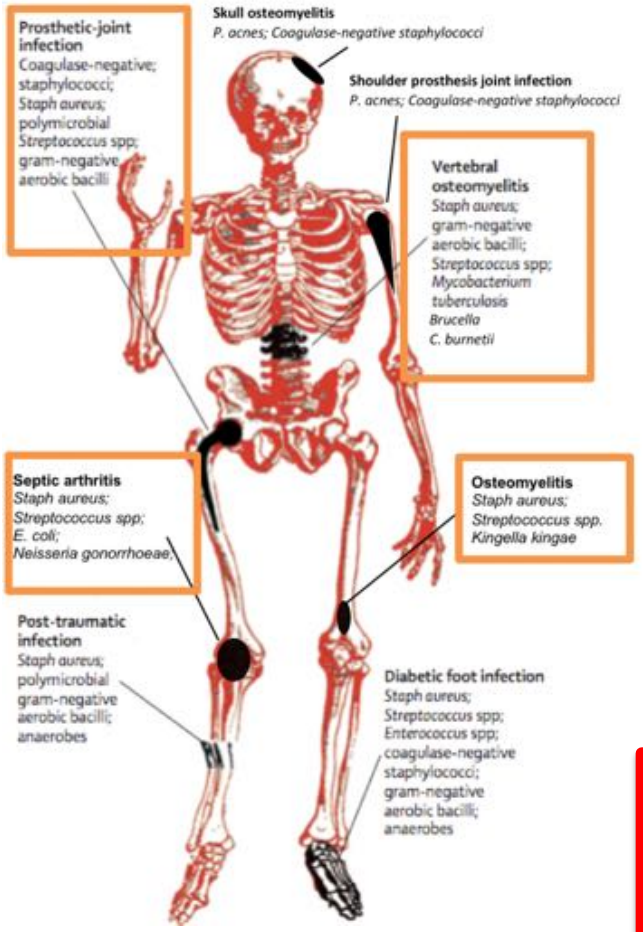


Lew et al. *NEJM 1997*

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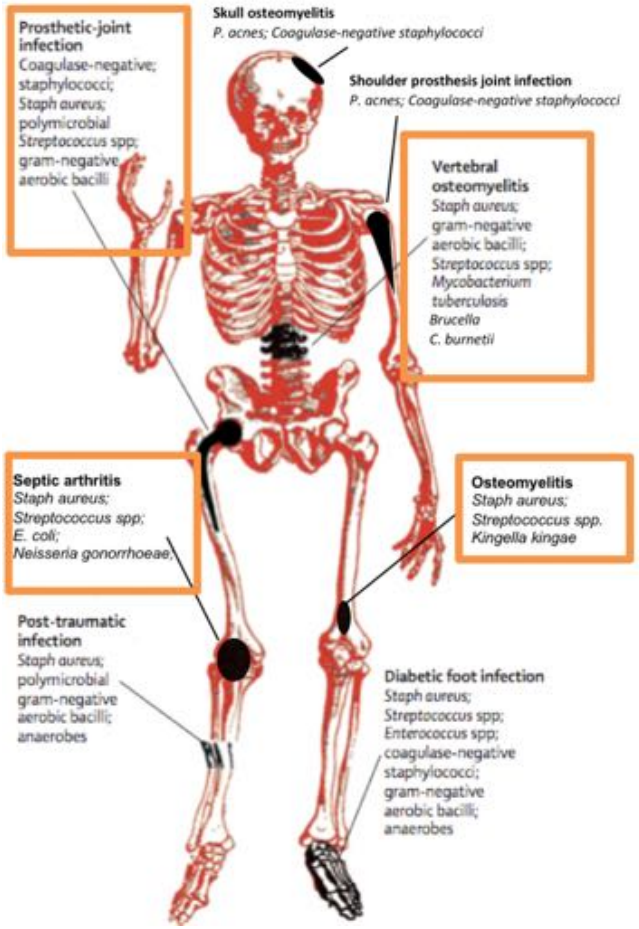
- **Peu d'essai clinique**
- **Peu de molécules anti-infectieuses approuvée**

# Les infections ostéoarticulaires

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NIH U.S. National Library of Medicine

ClinicalTrials.gov

- **Osteomyelitis: 68**
- **Prosthetic-joint infection: 47**
- Meningitis: 348
- Urinary tract infection: 492
- Tuberculosis: 915
- Influenza: 2’152

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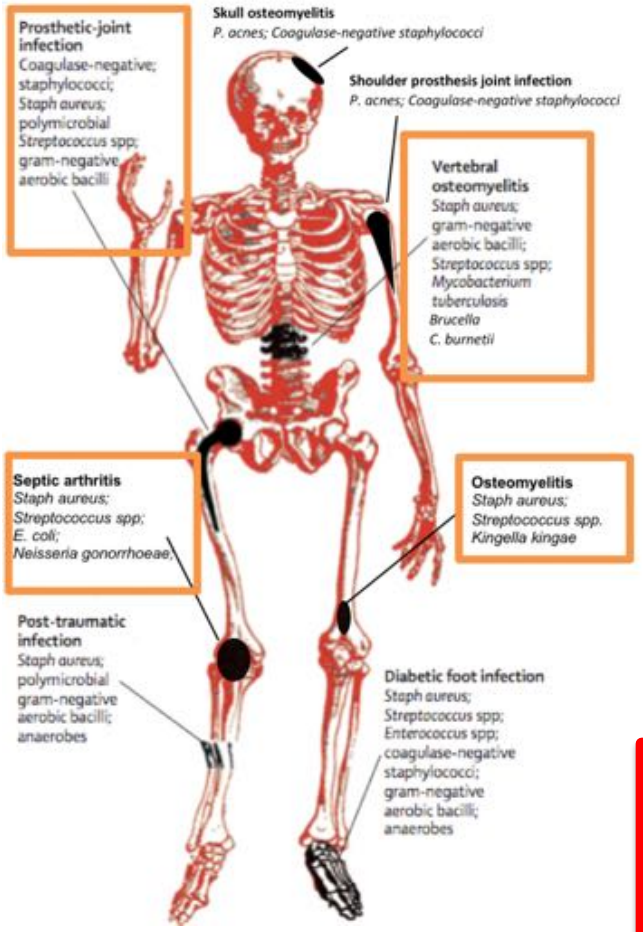


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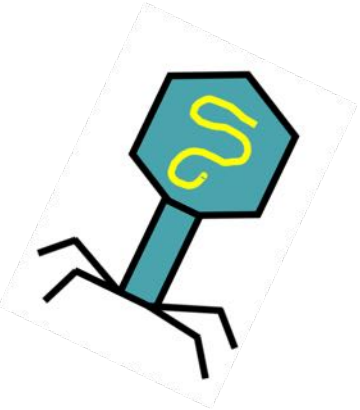
**Les IOA :**
**Maladies infectieuses négligées des pays industrialisés**

# 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.

# Marine viruses — major players in the global ecosystem

*Curtis A. Suttle*

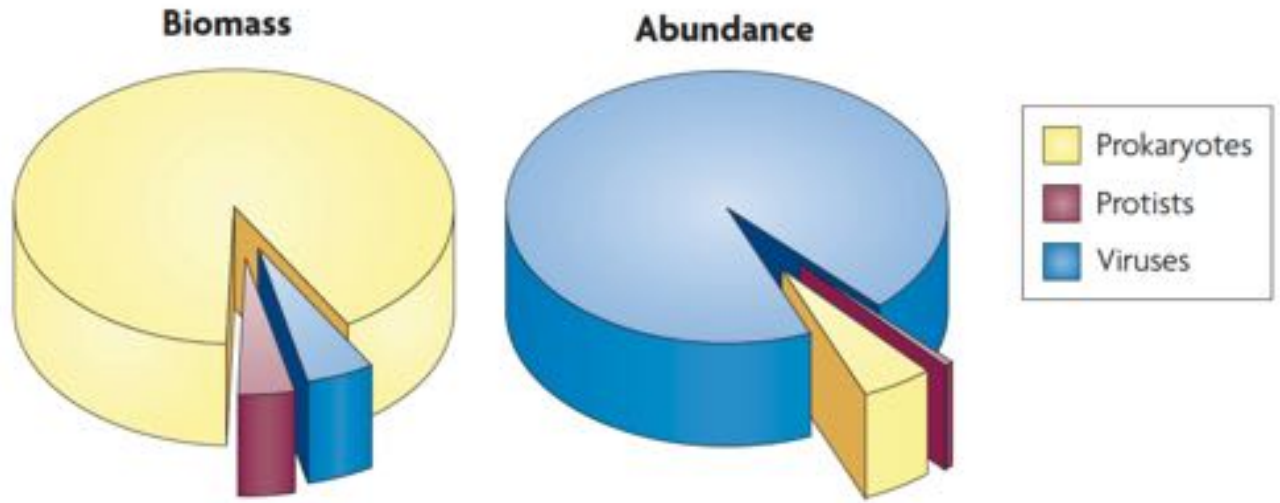
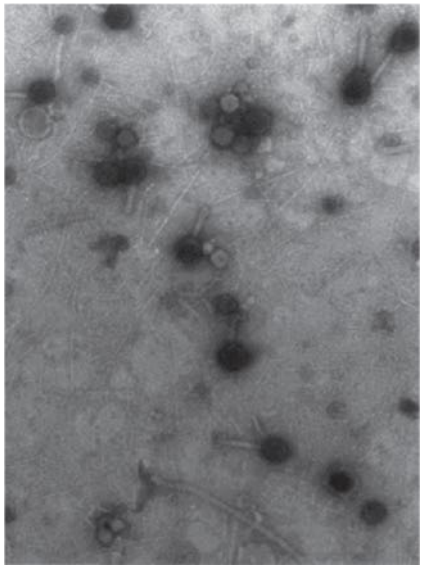



Figure 1 | **Relative biomass and abundances of prokaryotes, protists and viruses.**



***Probing this vast reservoir of genetic and biological diversity continues to yield exciting discoveries.***

*Nature Review Microbiology* 2007

# Self-limiting nature of seasonal cholera epidemics: Role of host-mediated amplification of phage

Shah M. Faruque*†, M. Johirul Islam*, Qazi Shafi Ahmad*, A. S. G. Faruque*, David A. Sack*, G. Balakrish Nair*, and John J. Mekalanos‡

Proc Natl Acad Sci U S A. 2005

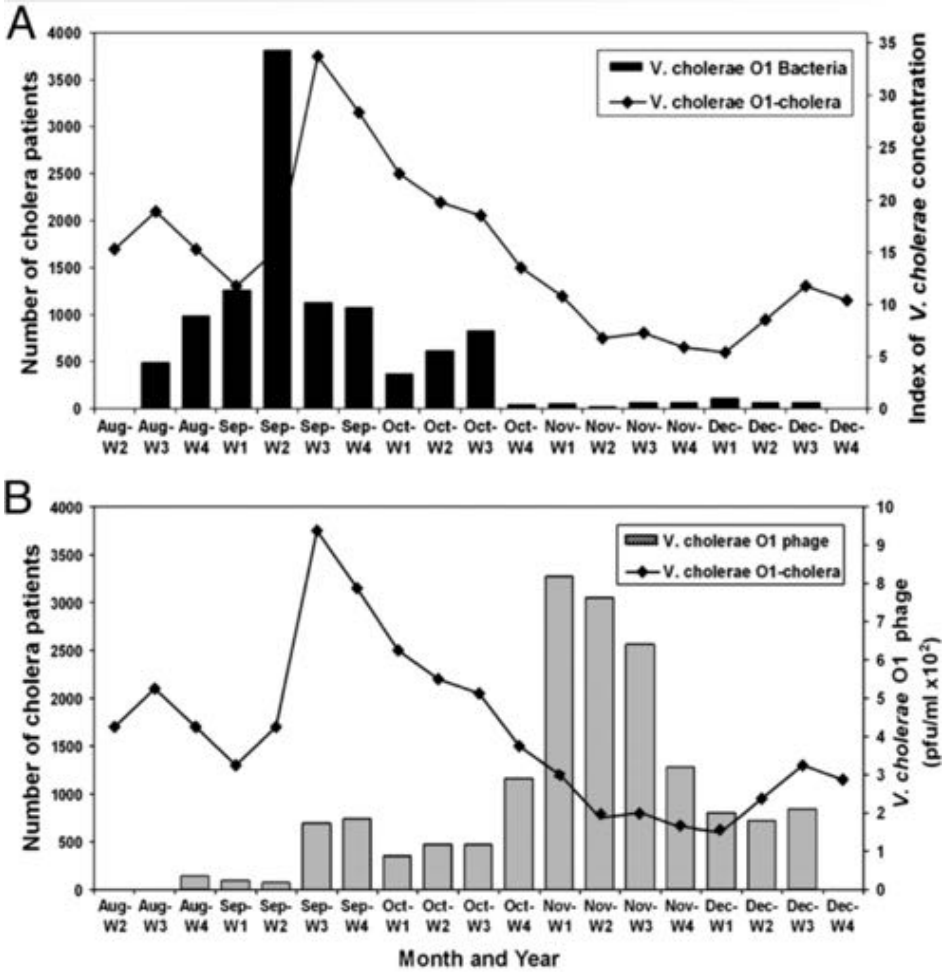




Fig. 1. Map of Dhaka showing the environmental sampling sites (●) and the location of the ICDDRB cholera hospital at the center of the city.

Bangladesh

10 to 100 fold smaller than a bacteria

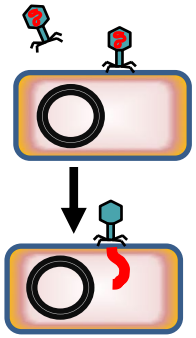
Translucent tap water

**X million** of ≠ Bactériophage**S** !!!
**(targeting environmental bacteria)**


Phamaceutical preparation

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

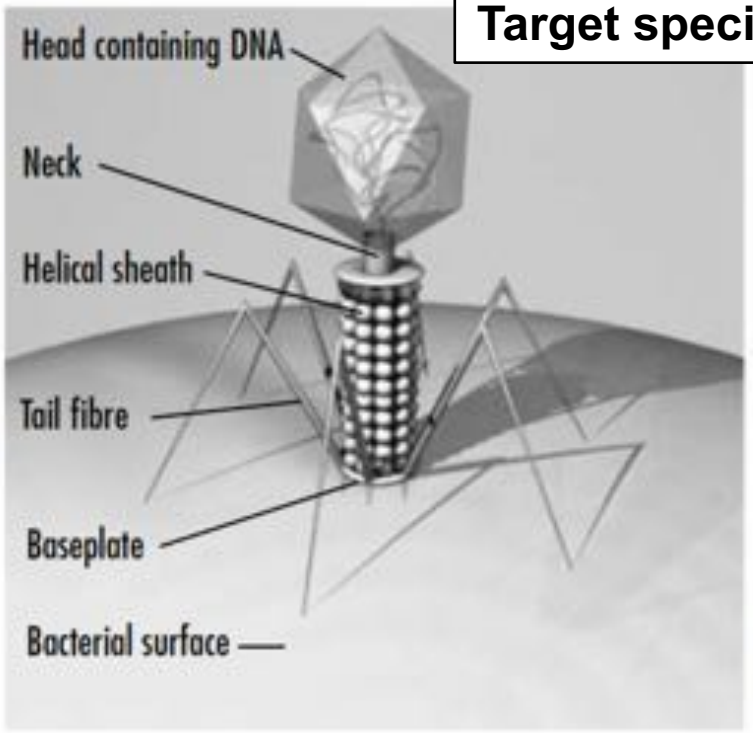
Ferry T.

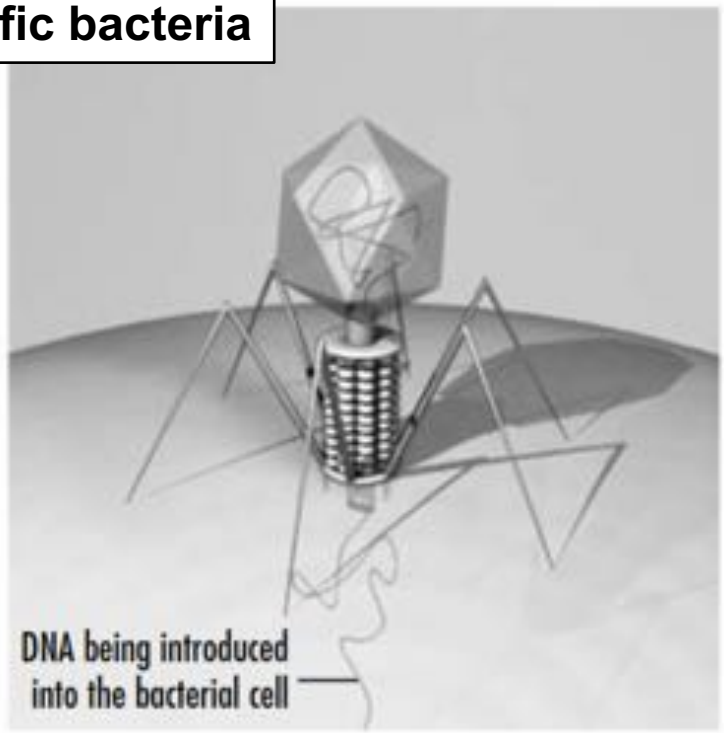


Cell recognition

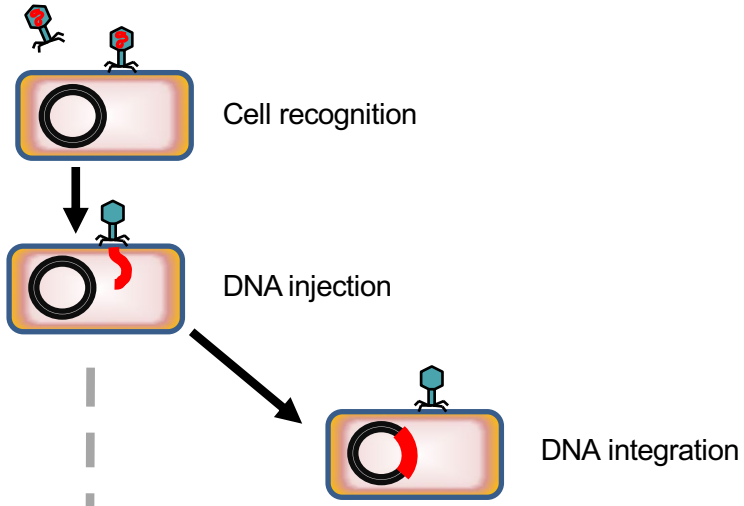
DNA injection

**Environmental viruses**
**Target specific bacteria**



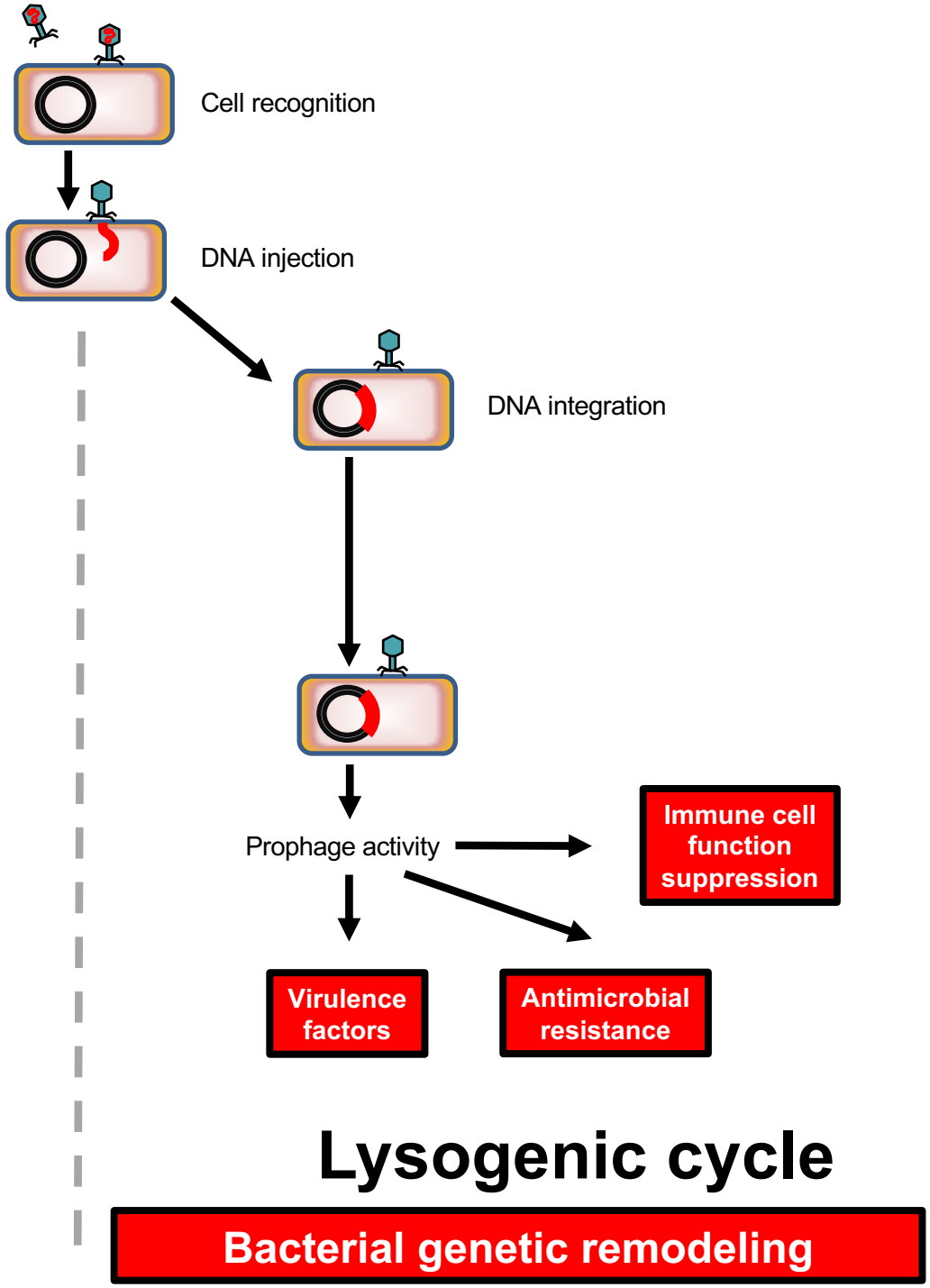
Ferry T.




# Lysogenic cycle

**Bacterial genetic remodeling**

Ferry T.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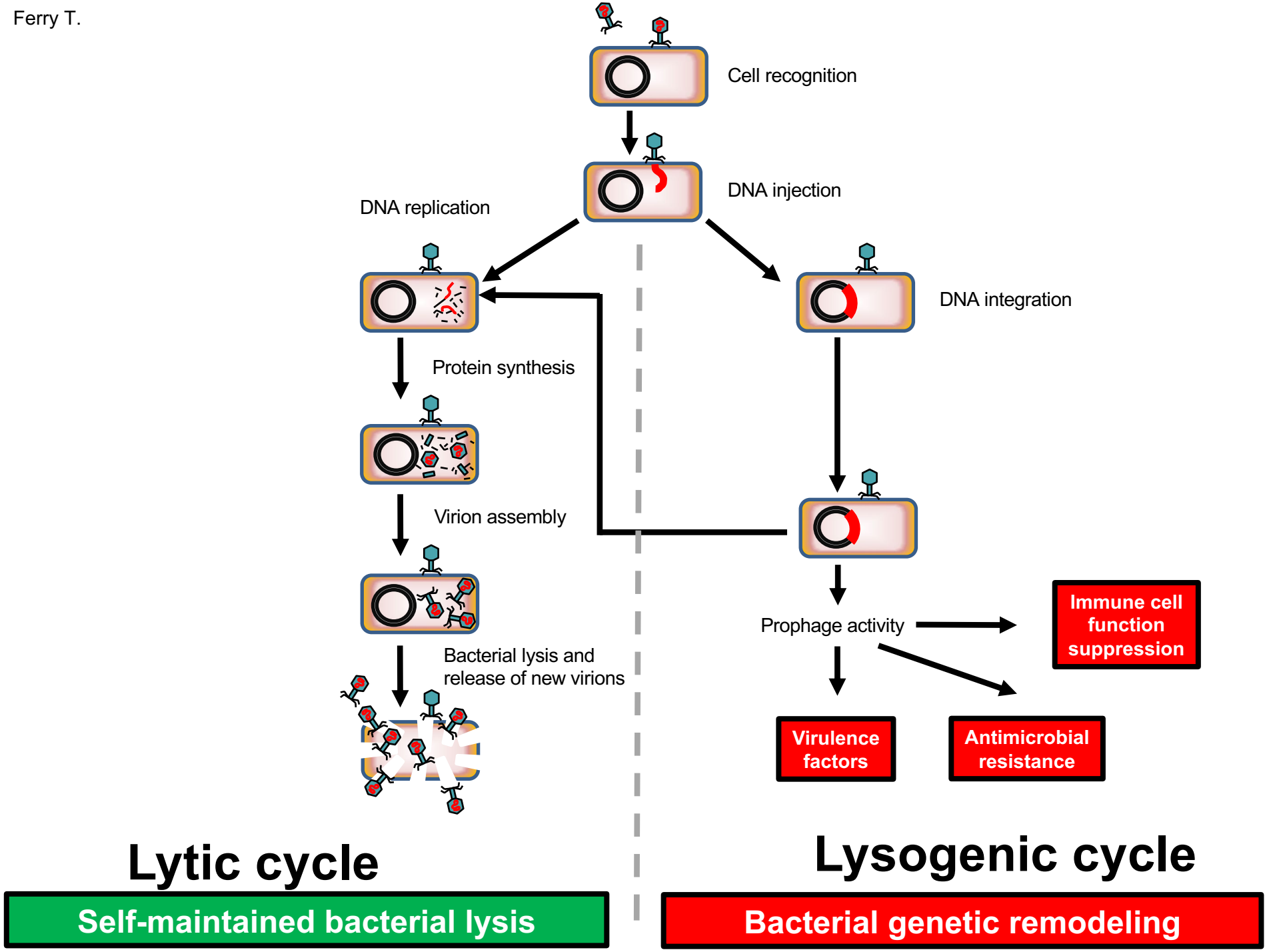
DNA injection
DNA integration
Prophage activity
Immune cell function suppression
Virulence factors
Antimicrobial resistance
Lysogenic cycle
Bacterial genetic remodeling

Ferry T.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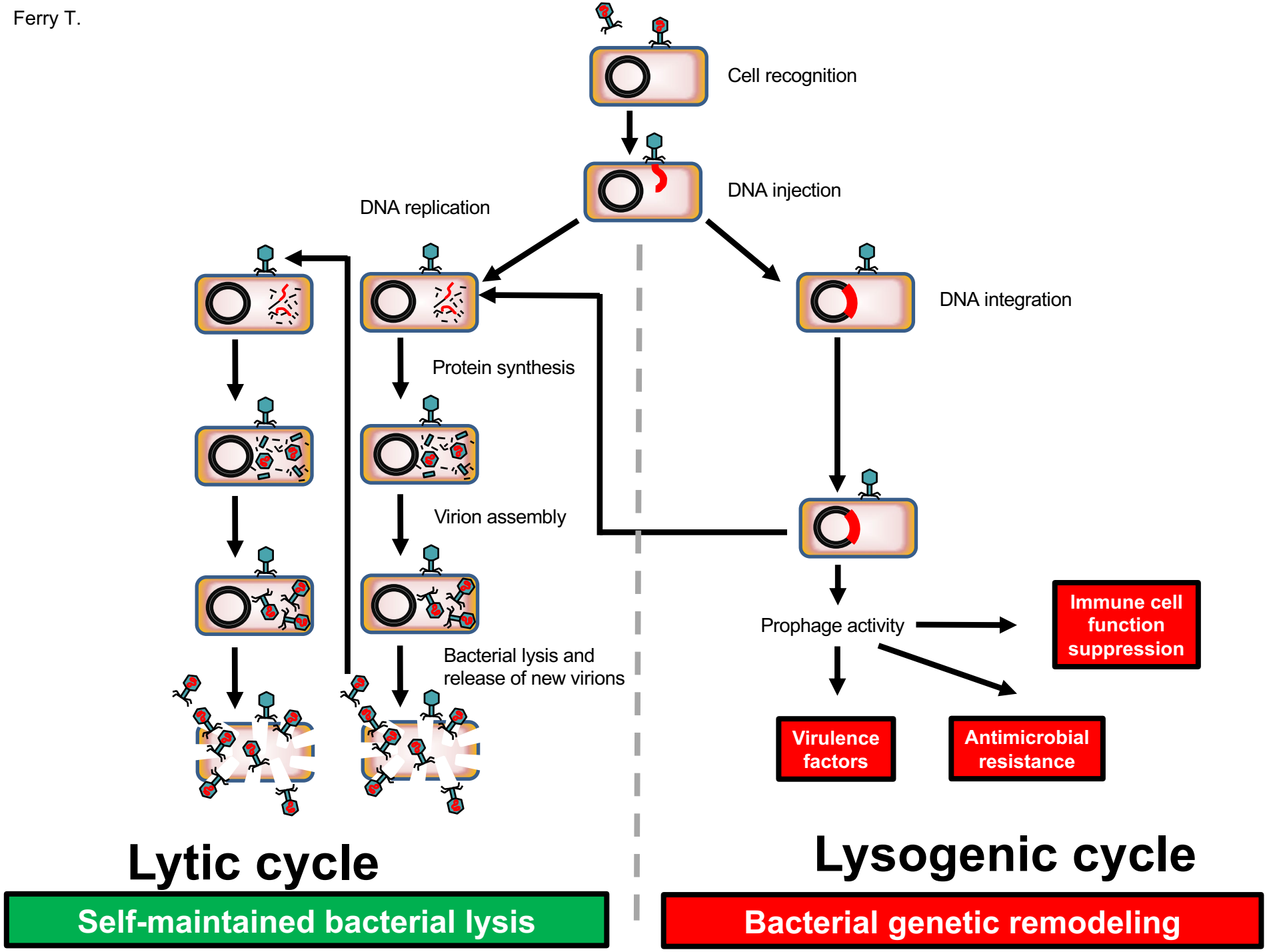
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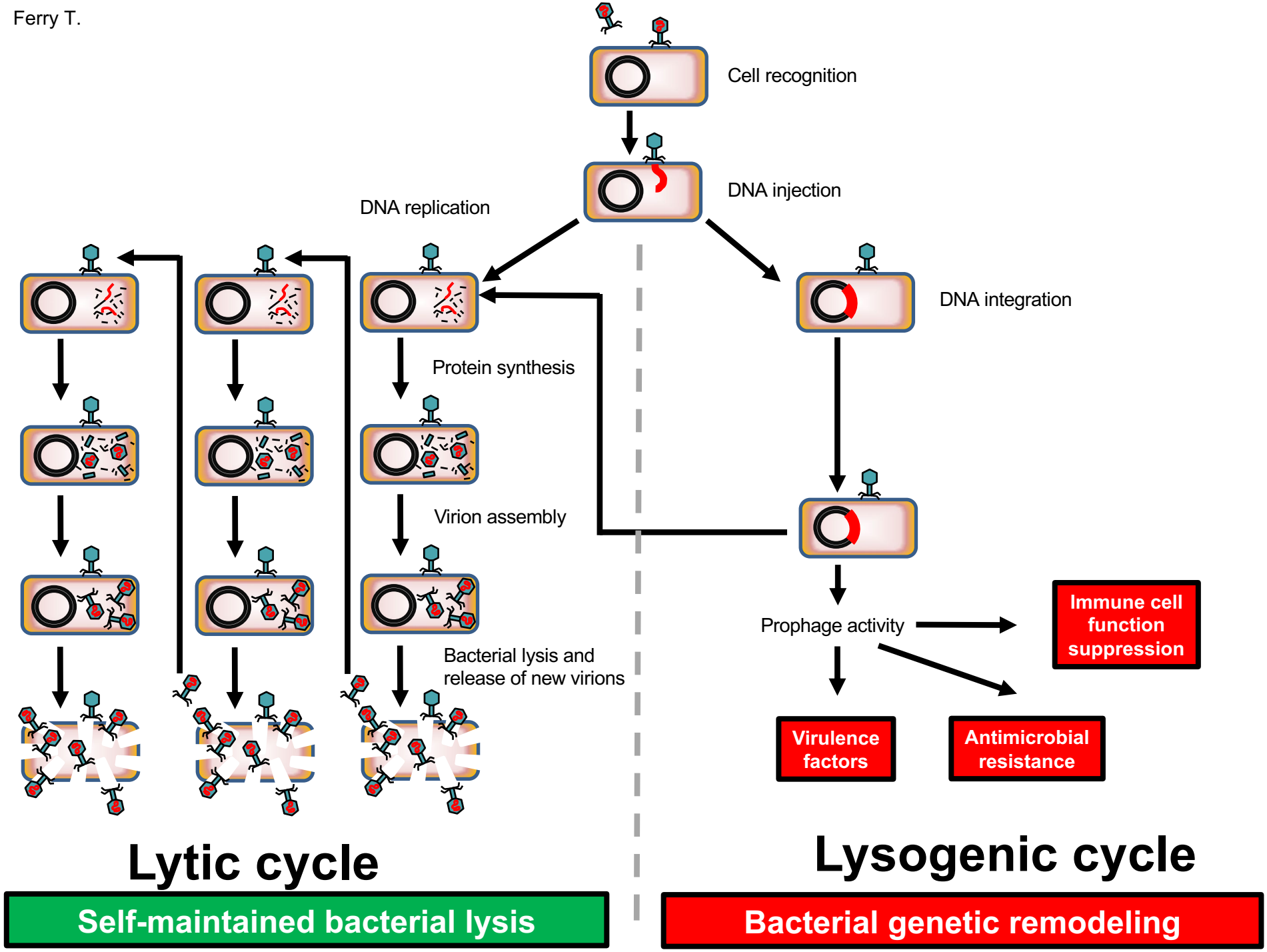
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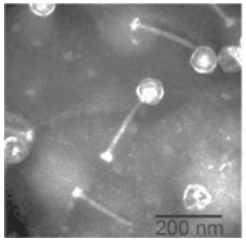
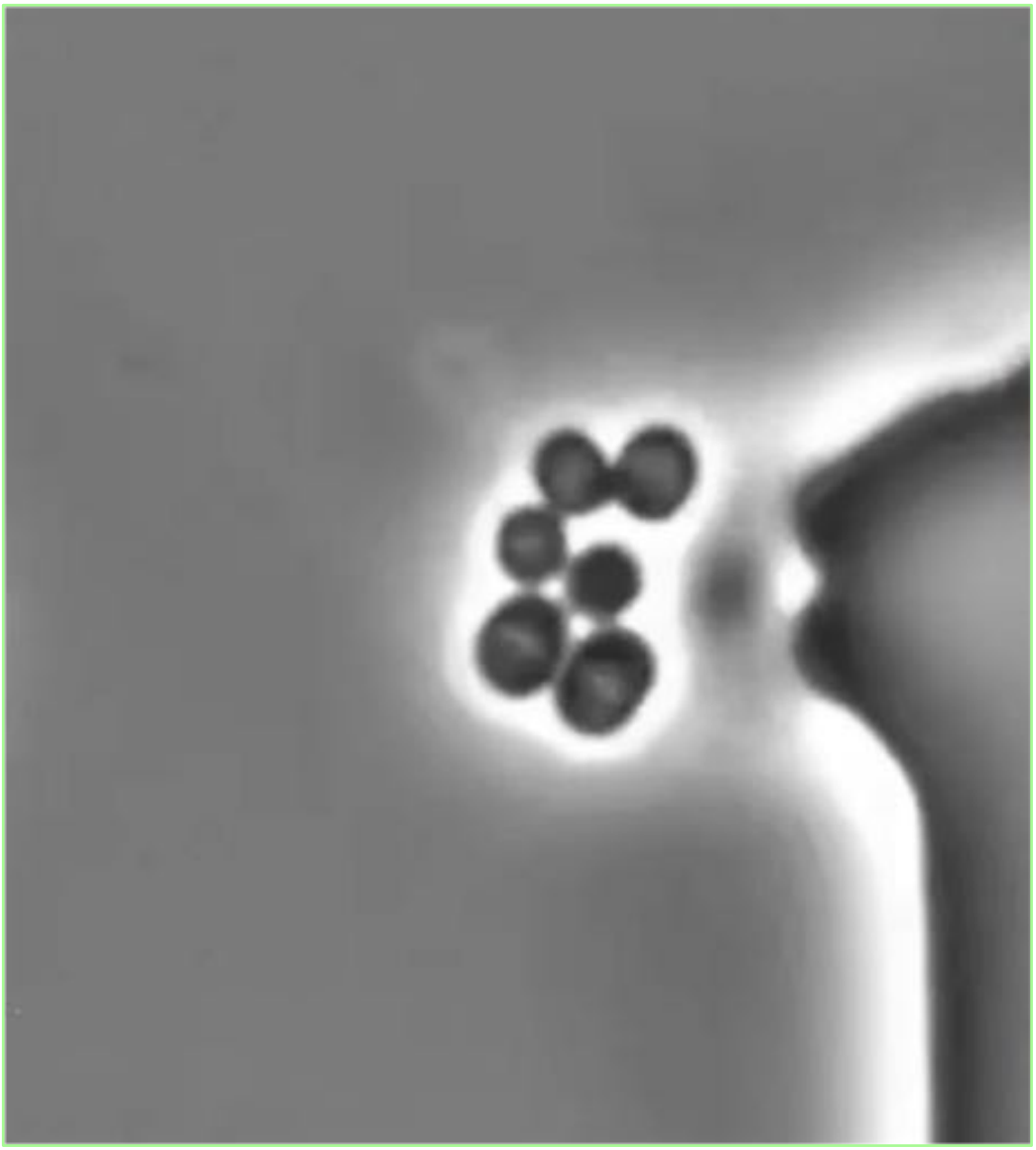
# A clear antibacterial activity!

## *S. aureus* being lysed by the Sa2 phage




Bacterial DNA appeared in green



Courtesy Pascal Maguin
Luciano Marraffini Lab
THE ROCKEFELLER UNIVERSITY

# History of phage therapy

- **Felix d'Herelle**
- Institut Pasteur, Paris

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- He founded **Eliava institute in Georgia** and the **"Laboratoire Français des Bactériophages"** in Paris

# History of phage therapy

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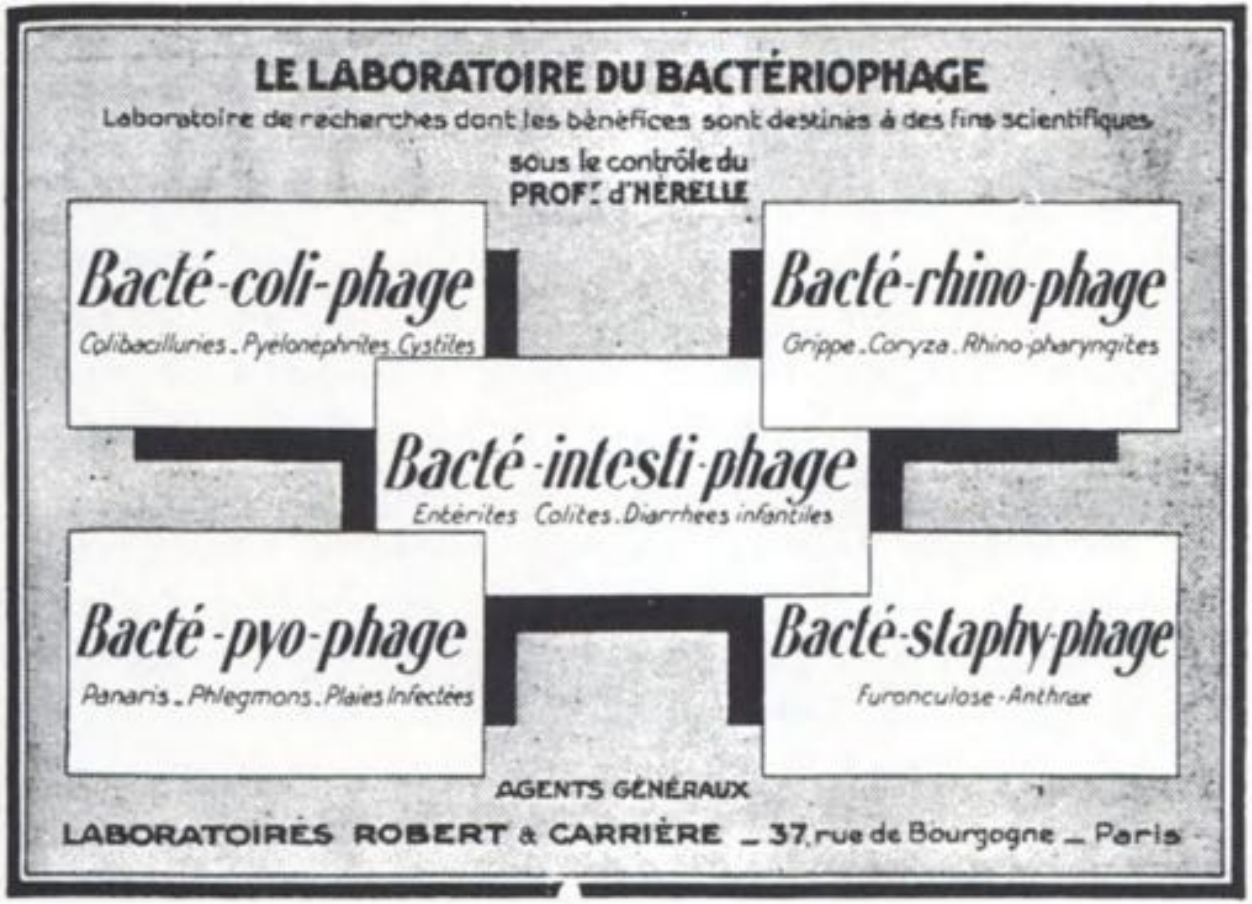


und

usly

**<u>orgia</u>**

and the **<u>“Laboratoire Français des Bactériophages”</u>** in Paris

# Lessons to be learned of phage therapy of the 20th century

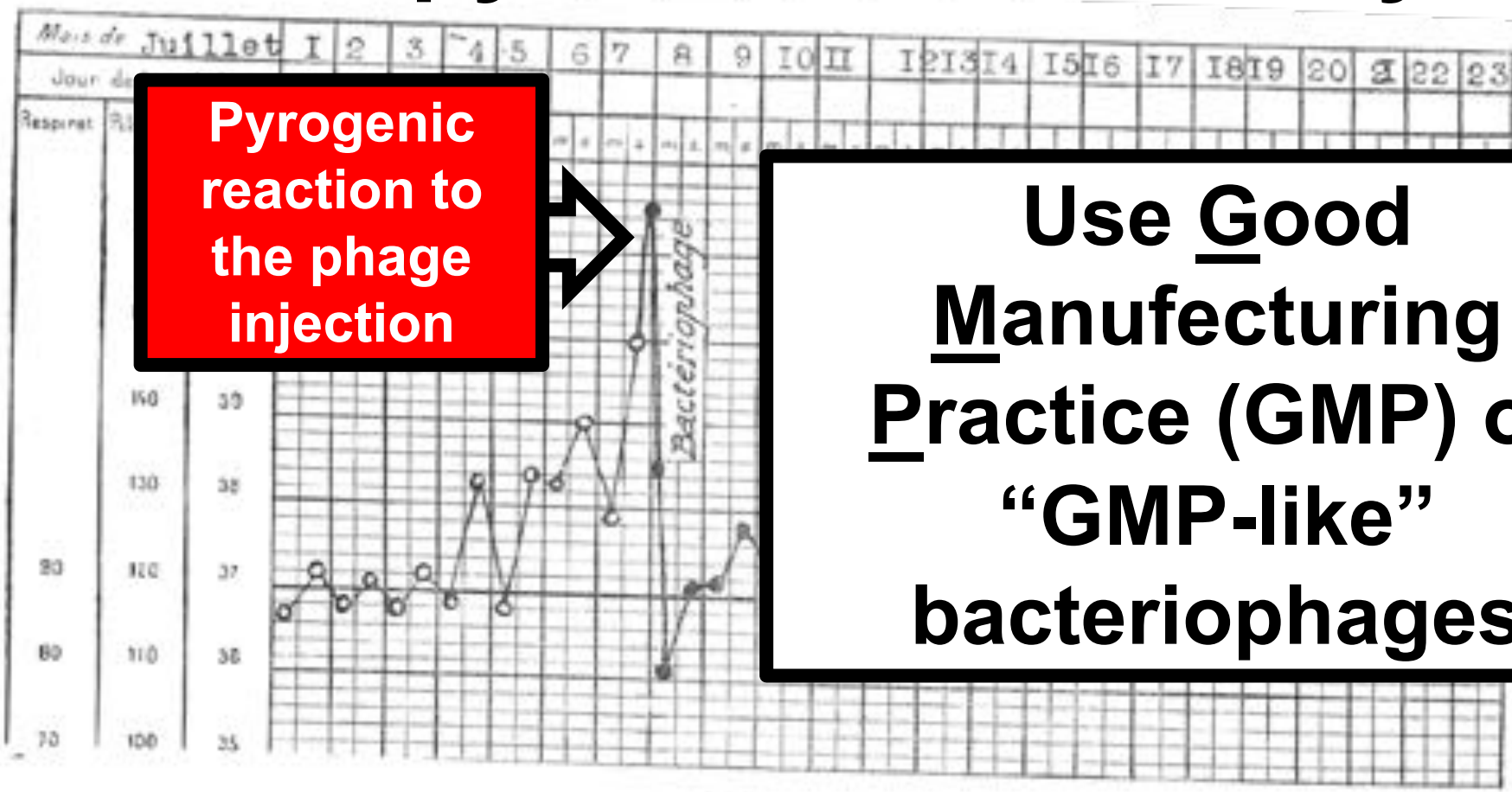


Fig. 1.

Obs. 841, Mme D..., 7, 8 Juillet 1930. Septicémie à staphylocoque.

o—o—o Température avant
●—●—● Température après
} l'injection intra-veineuse de Bactériophage.

**Pyrogenic reaction to the phage injection**

**Use Good Manufecturing Practice (GMP) or "GMP-like" bacteriophages**

Docteur André RAIGA

*Ancien Interne lauréat des Hôpitaux*
*Ex-Chef de Clinique chirurgicale à la Faculté*

. . .

*At the stage of bone necrosis,* ***it will only succeed in stopping the progression of the infection****, but* ***it will be able to do nothing against the dead bone deprived of circulation; this bone will become sequestered and the lesion is no longer a matter of surgery.*** *To do otherwise is to commit, in my opinion, an error of therapeutic indication.*

Au stade de nécrose osseuse, il ne réussira plus qu'à cnrayer la progression de l'infection, mais il nc pourra plus rien contre l'os que la mort a privé de circulation ; cet os va se séquestrer et la lésion ne relève plus maintenant que de la chirurgie. Agir autrement c'est commettre, à mon sens, une erreur d'indication thérapeutique.

1961

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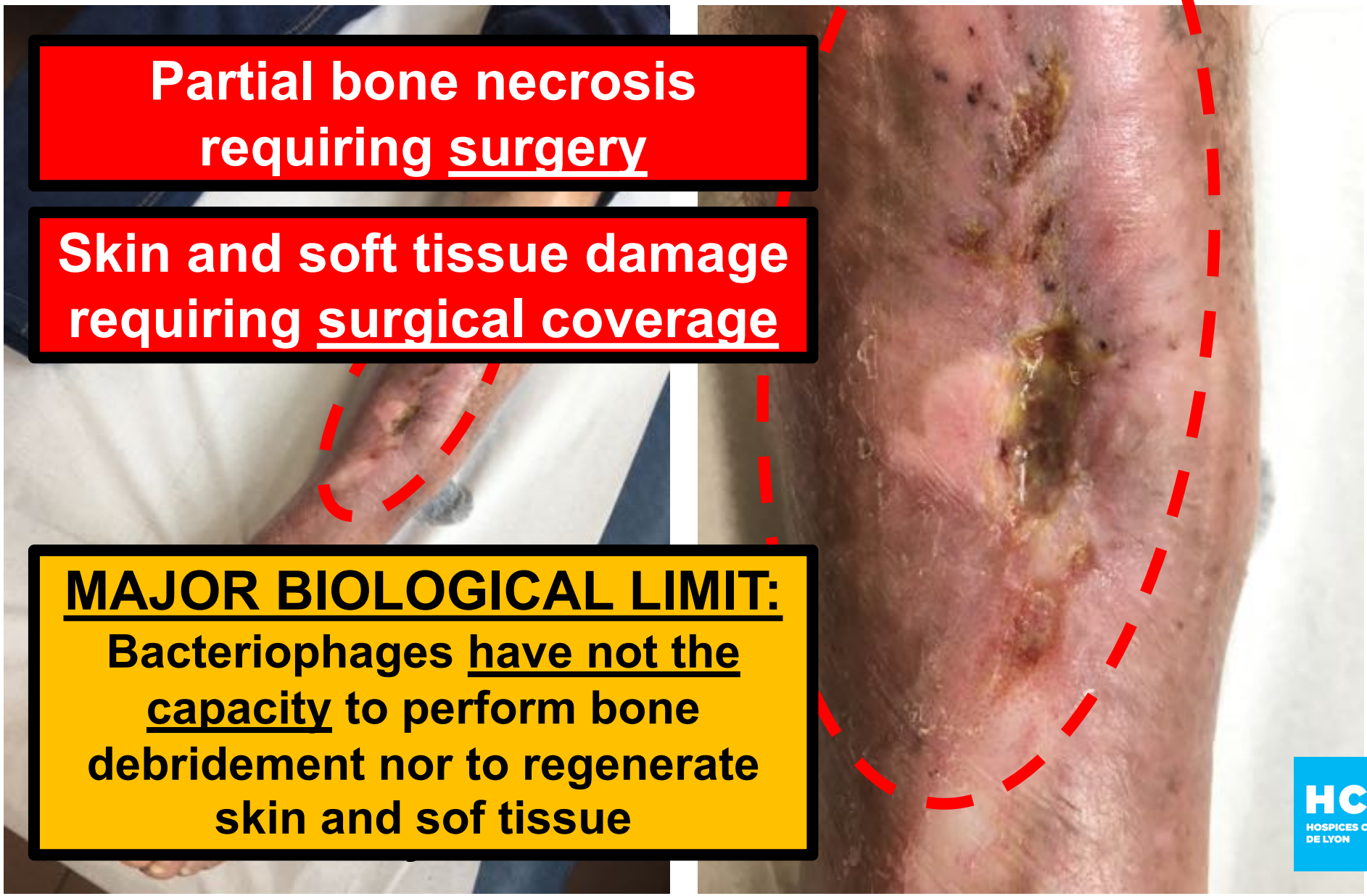



Patient with a relapsing infection after Phage therapy in Tbilissi

*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. Cepen... cutanées, otitiques, bron... leur être attribuées semble être en augmentation. Leur caractère rebelle est une de leurs caractéristiques. I... thérapeutique différente de celle... n connaissait l'existence de bact... Mais l'emploi de stock-bactériop... ntre, l'adaptation par sélection... permet une actio... sur bouillon nutritif ordinaire... est par contre indispensable de... in dilué pour pouvoir l'introdu... arachidienne intraveineuse, in...*

*Un certain n... pportés dan... cette publication.*

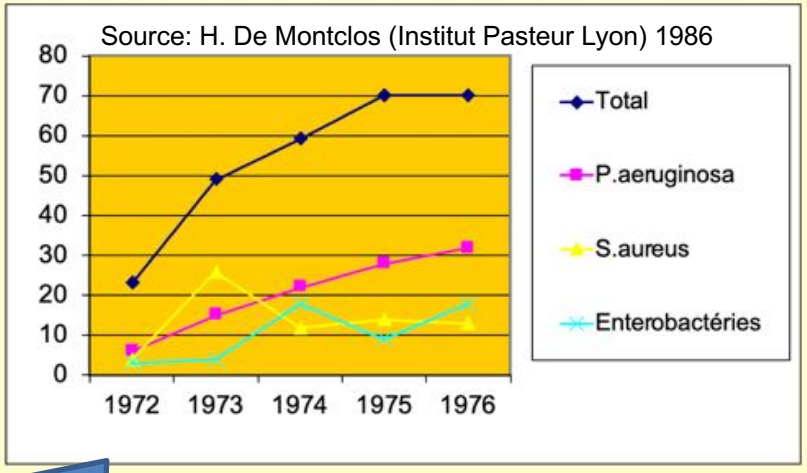
**Antimicrobial resistance**

**Phage banking**
**Phage training**

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

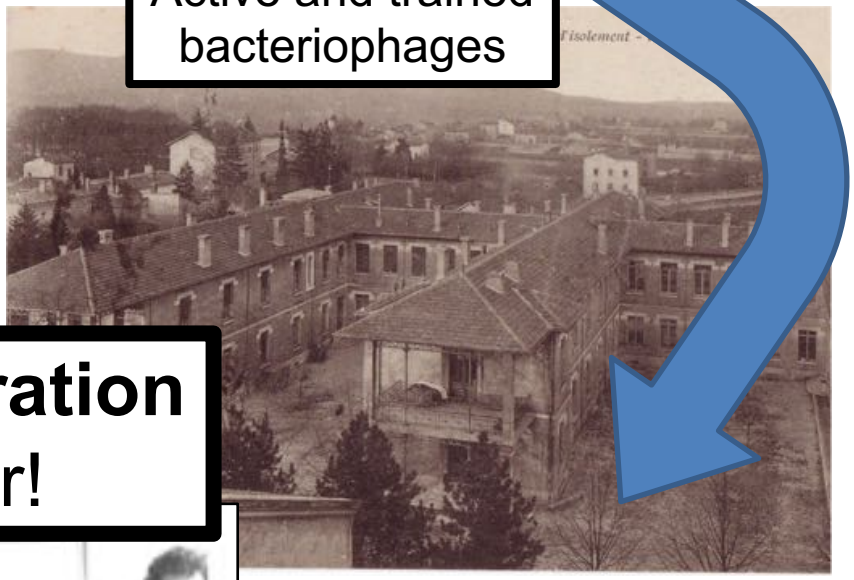
**Clinique des Maladies Infectieuses, Hôpital de la Croix-Rousse**
**Hospices Civils de Lyon**

1958-1960



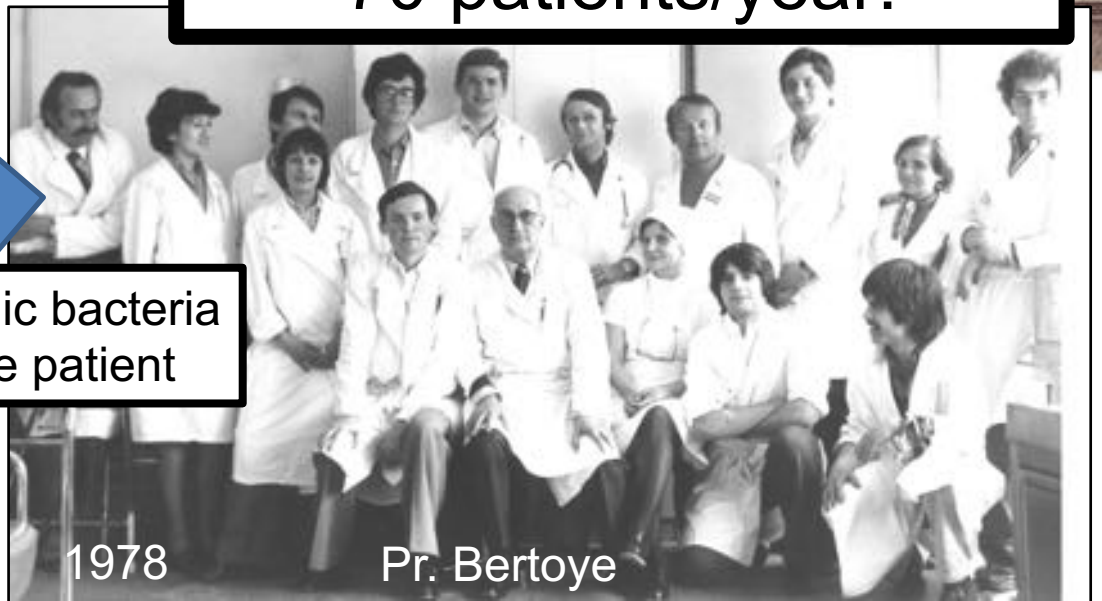

# Institut Pasteur Lyon

Active and trained bacteriophages



**Academic collaboration**
70 patients/year!

Pathogenic bacteria from the patient

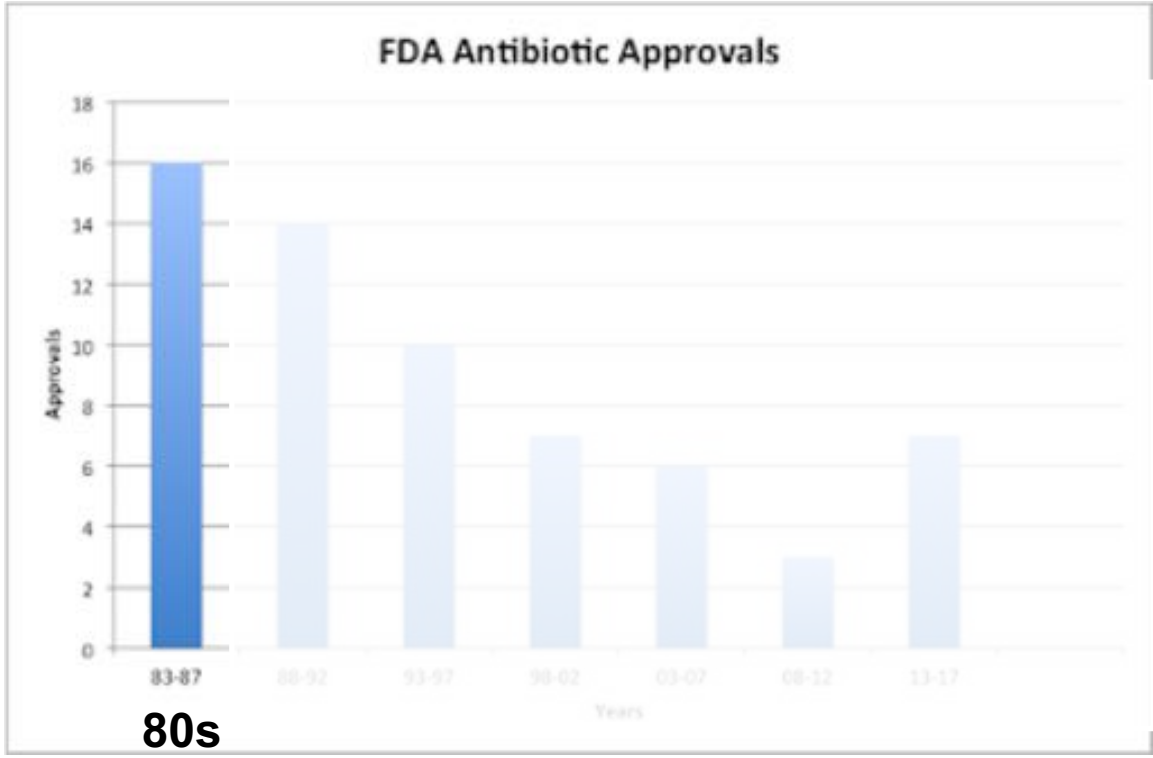



# Infectious Disease clinic

HCL
HOSPICES CIVILS DE LYON

# Large production of antibiotics in 1970-1980 killed the phage therapy

- **Industrial** production
- **Large** spectrum
- **Bactericidal** activity
- Oral and IV
- **Systemic diffusion** to the infected site
- Numerous **different kinds of families**, with different mechanism of action




80s

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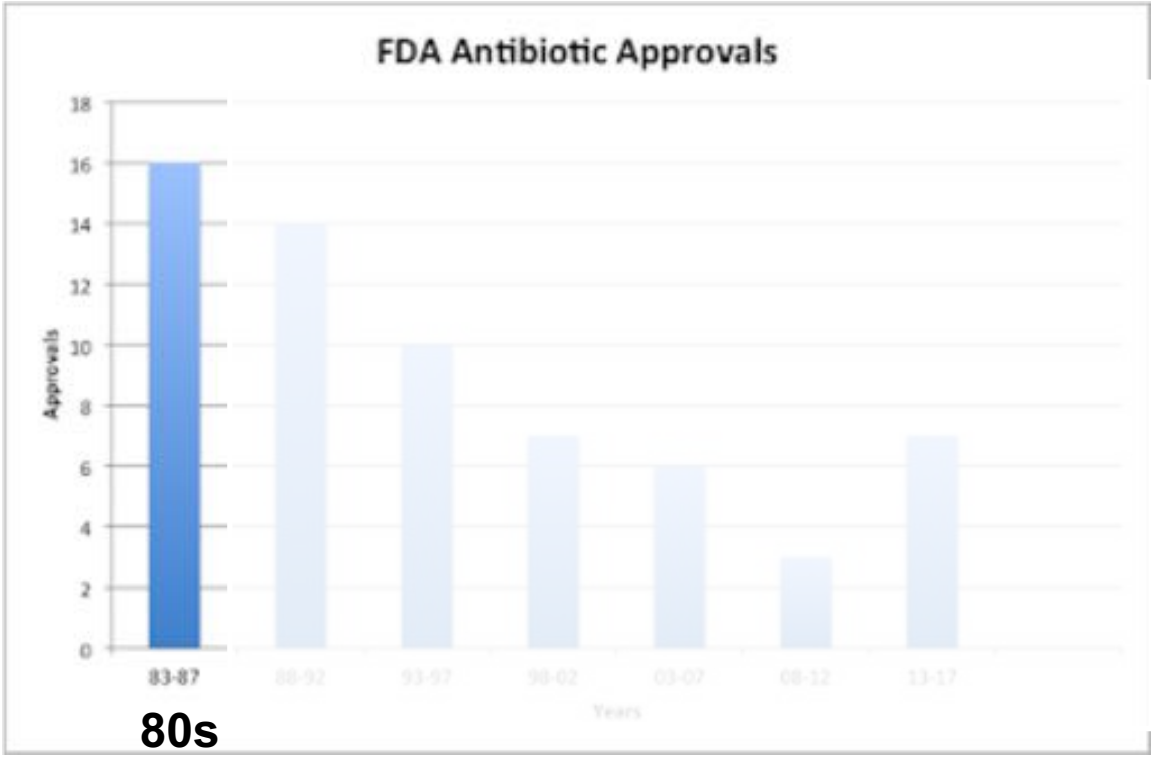
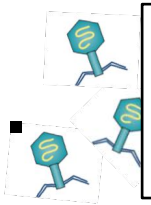



**80s**

**VS.**



**Complex virus-based personalized treatment without clear industrial process, not considered as a drug**

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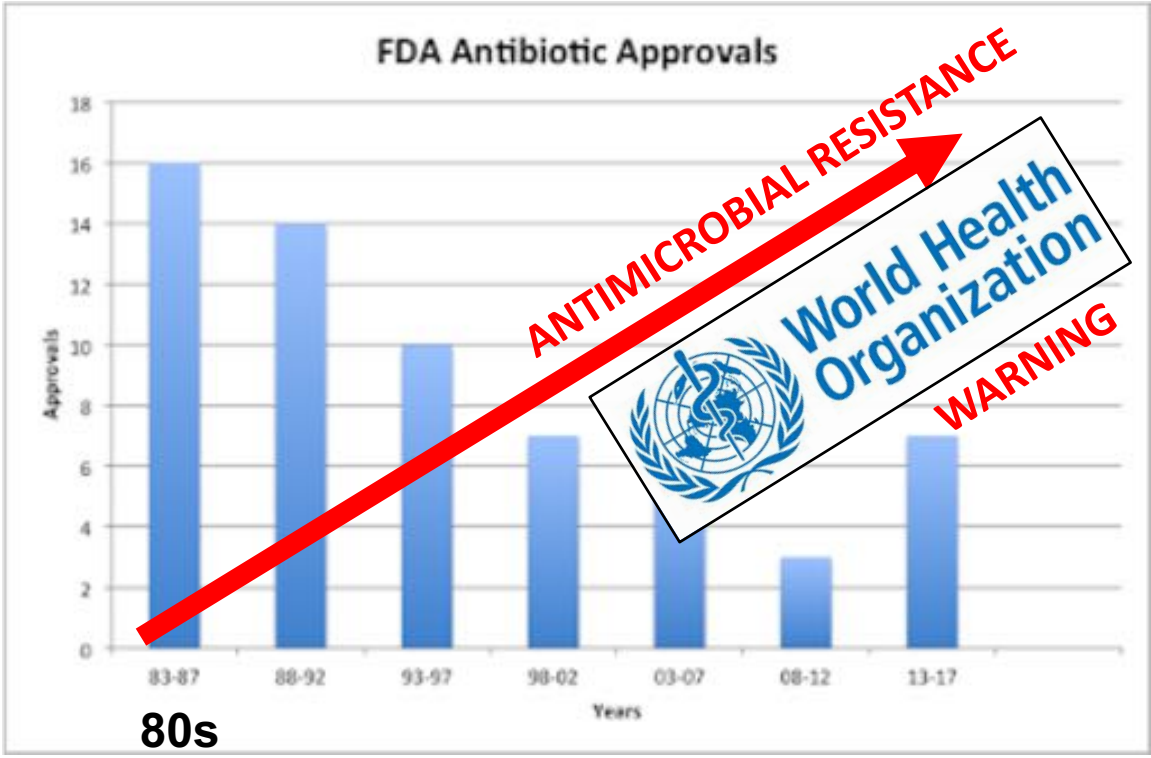


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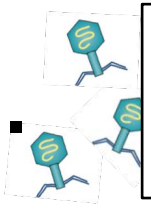

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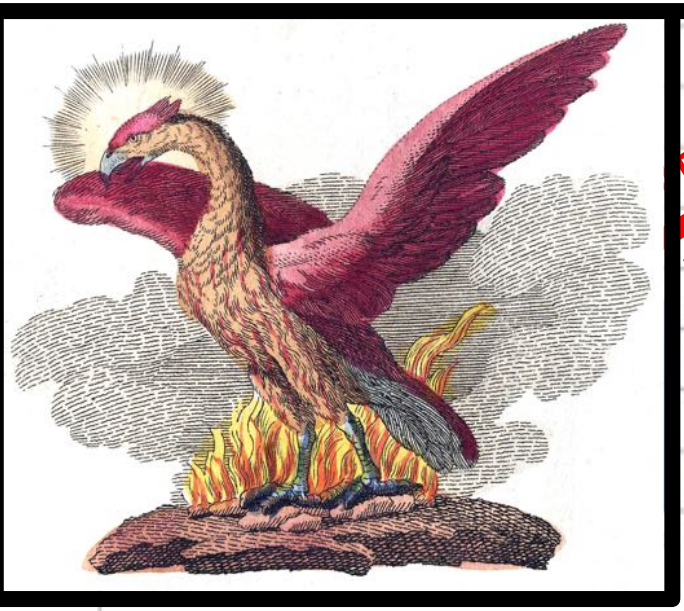
**Phages as the Phoenix?**



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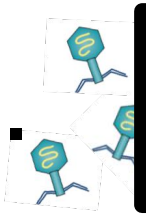
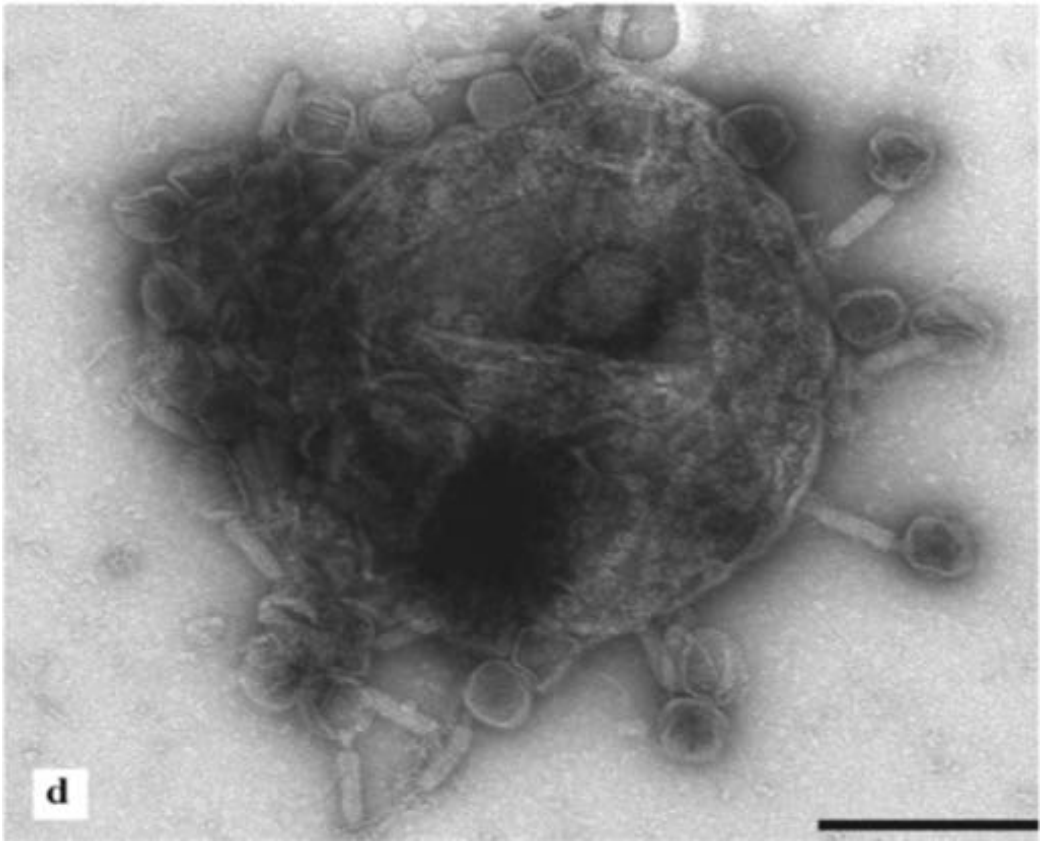


**Complex virus-based personalized treatment without clear industrial process, not considered as a drug**

# Cocktails produced in 2020 by the Eliava Institute

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


Bacteriophage ISP (*Myoviridae*)



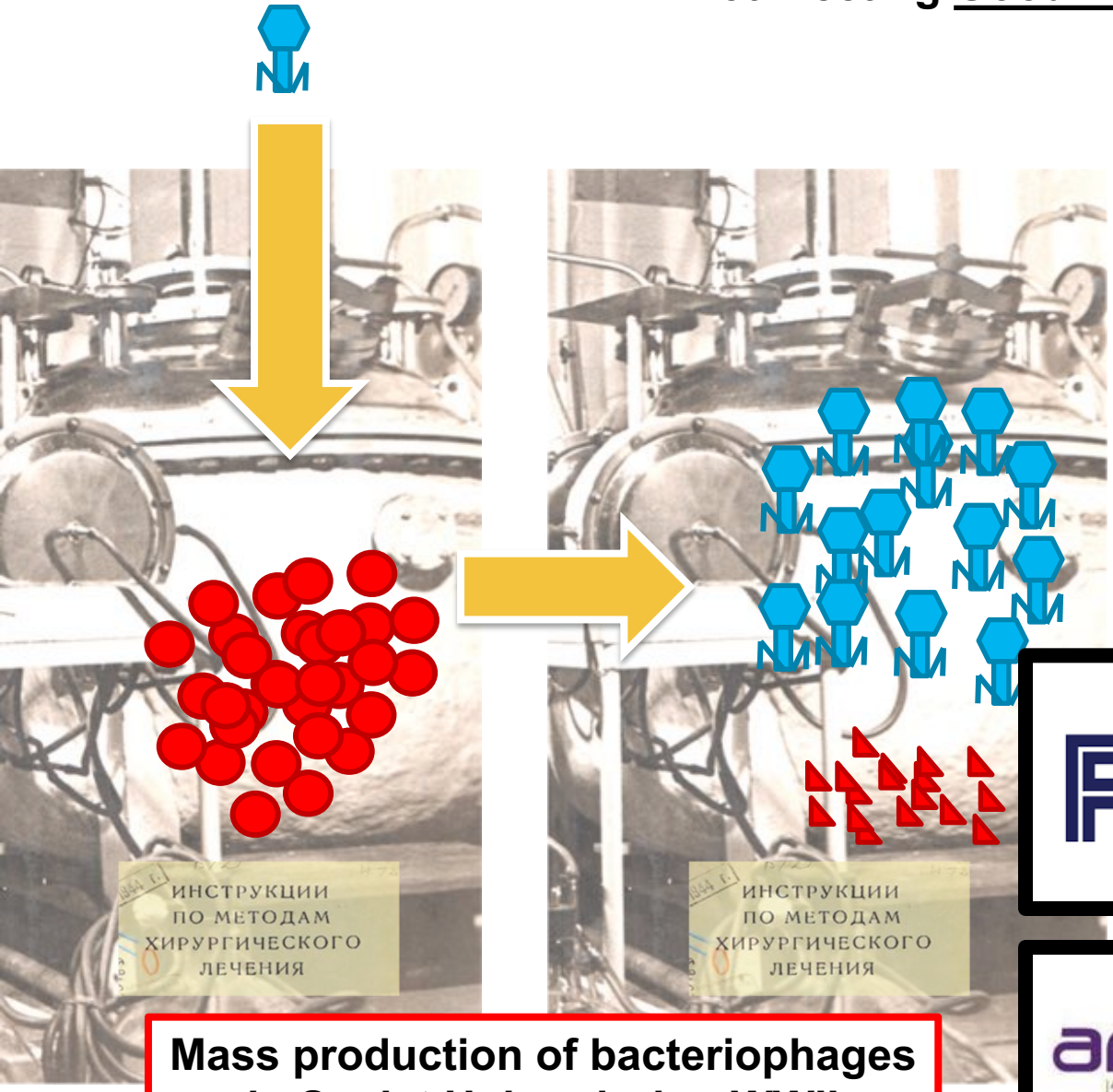

Merabishvili et al. PloS ONE 2009

**T. Ferry. *The story of Phage therapy***

Not meeting Good Manufacturing Practices (GMP)

Pyrogenic Bacterial remnant?

$10^6$ phages/mL




Mass production of bacteriophages in Soviet Union during WWII

T. Ferry. *The story of Phage therapy*

FDA

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

AMPLIPHI BIOSCIENCES CORPORATION
ARMATA PHARMACEUTICALS
PHERECYDES PHARMA

GMP

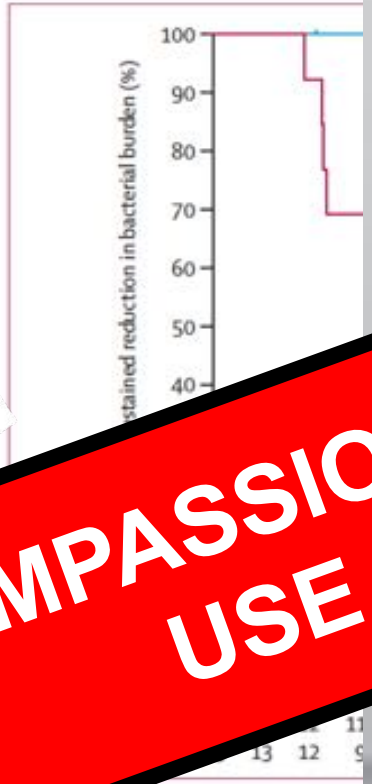
APPROVED

FOR

CLINICAL TRIALS

# Efficacy and tolerability of a cocktail of bacteriophages to treat burn wounds infected by *Pseudomonas aeruginosa* (PhagoBurn): a randomised, controlled, double-blind phase 1/2 trial

Patrick Jault, Thomas Leclerc, Serge J
Ronan Le Floch, Jean Vivien Schaal, C




2: Time to observe reduction
Kaplan-Meier analysis of median time
highest daily bacterial burden compared with day 0. HR=hazard ratio. PP1131=cocktail of 12 natural lytic anti-*Pseudomonas aeruginosa* bacteriophages.

COMPASSIONATE USE

osa

RECYDES
RMA

*Lancet Infect Dis* 2018























**<u>Phage discovery</u>**
**to find active bacteriophages against Staphylococci**

***Phages anti-S. aureus***

# REFERENCE CENTERS FOR THE MANAGEMENT OF BONE AND JOINT INFECTION

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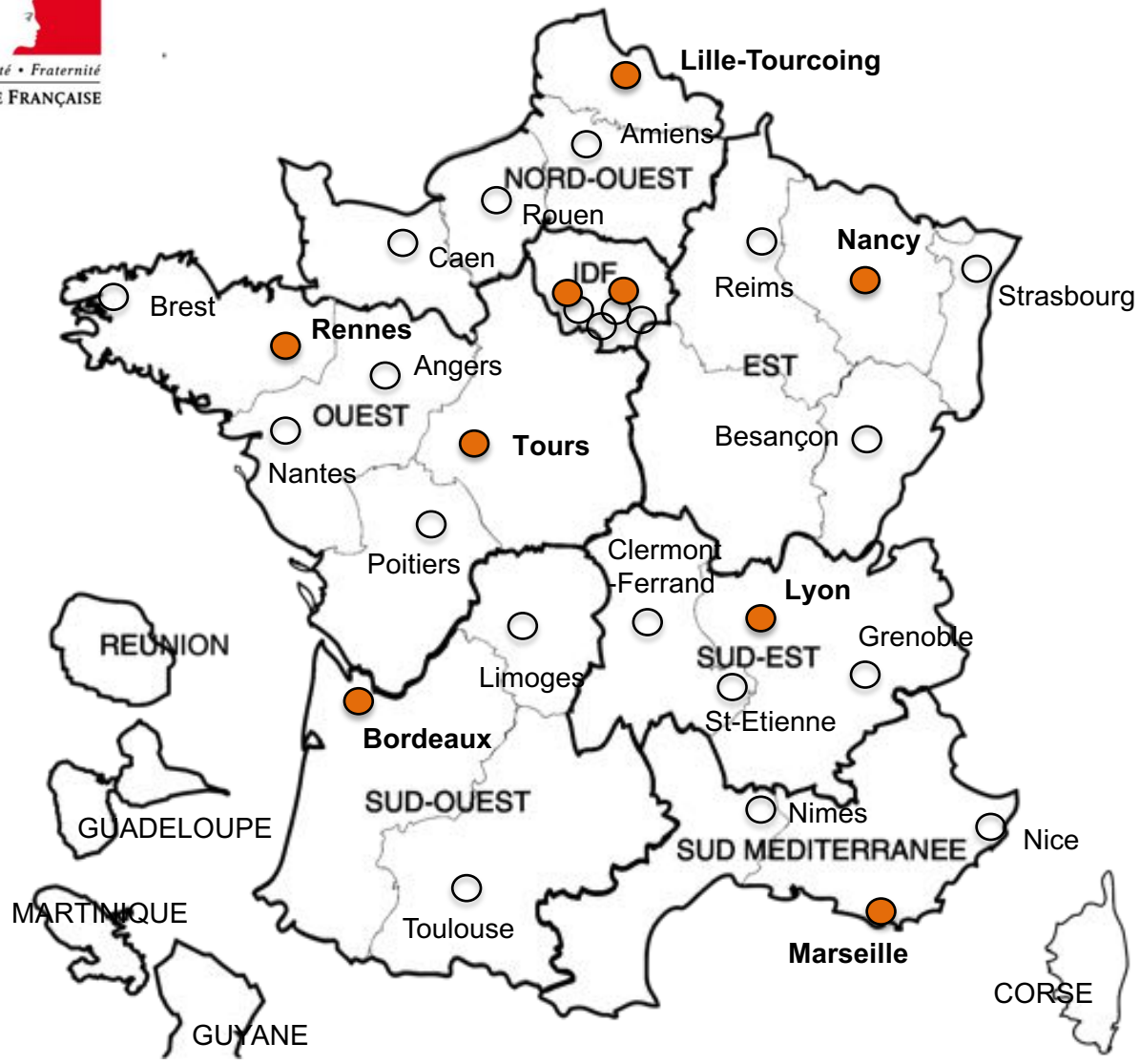
RÉPUBLIQUE FRANÇAISE




## "CRIOAc" Network

Adapted from Ferry T, et al. Orthop Traumatol Surg Res. 2019;105(1):185-190

# REFERENCE CENTERS FOR THE MANAGEMENT OF BONE AND JOINT INFECTION

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http://www.crioac-lyon.fr

@CrioacLyon

# CRIOAc Lyon


STAPHYLOCOQUES
Centre National de Référence



**Pr. Tristan Ferry**
MD, PhD
Infectiologist



**Pr. Sébastien Lustig**
MD, PhD
Orthopaedic surgeon



**Pr. Frédéric Laurent**
PharmD, PhD
Microbiologist

Lyon

IAI
BPN

Inserm

HCL
HOSPICES CIVILS DE LYON

CRB
Centre de Ressources Biologiques

ciri
Centre International de Recherche en Infectiologie

CRIOAc
LYON

- **Multidisciplinar management of the patient**
- **Better understanding of the pathophysiology of BJI**
- **Promotion of innovative treatments**

Adapted from Ferry T, et al. Orthop Traumatol Surg Res. 2019;105(1):185-190

# **Comité scientifique** des CRIOAc

Président : Pr. T. Ferry (Infectiologue, Lyon)
Pr. E. Senneville (Infectiologue, Lille-Tourcoing)
Pr. A. Stein (Infectiologue, Marseille)

Dr. S. Marmor (Orthopédiste, Paris)
Pr. E. Steindel (Orthopédiste, Brest)
Pr. D. Mainard (Orthopédiste, Strasbourg)

Dr. P. Bemer (Microbiologiste, Nantes)
Pr. V. Dubois (Microbiologiste, Bordeaux)

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RÉPUBLIQUE FRANÇAISE
MINISTÈRE DES SOLIDARITÉS ET DE LA SANTÉ

DIRECTION GÉNÉRALE DE L'OFFRE DE SOINS

Promotion de la recherche et de l'innovation

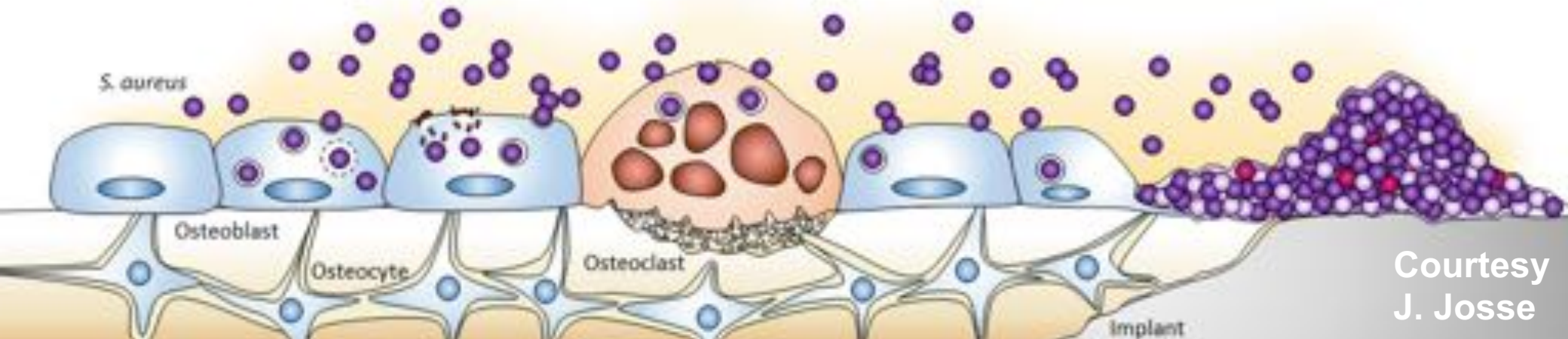
Centraliser les idées pour la réalisation de projets de recherche à l'échelle nationale

Expertise pluridisciplinaire

Utilisation du système d'information pour les études de faisabilité

# Persisters in chronic BJI

**"Bacterial cells that escape the effects of antibiotics without undergoing genetic change"**




Courtesy
J. Josse

# Persisters in chronic BJI

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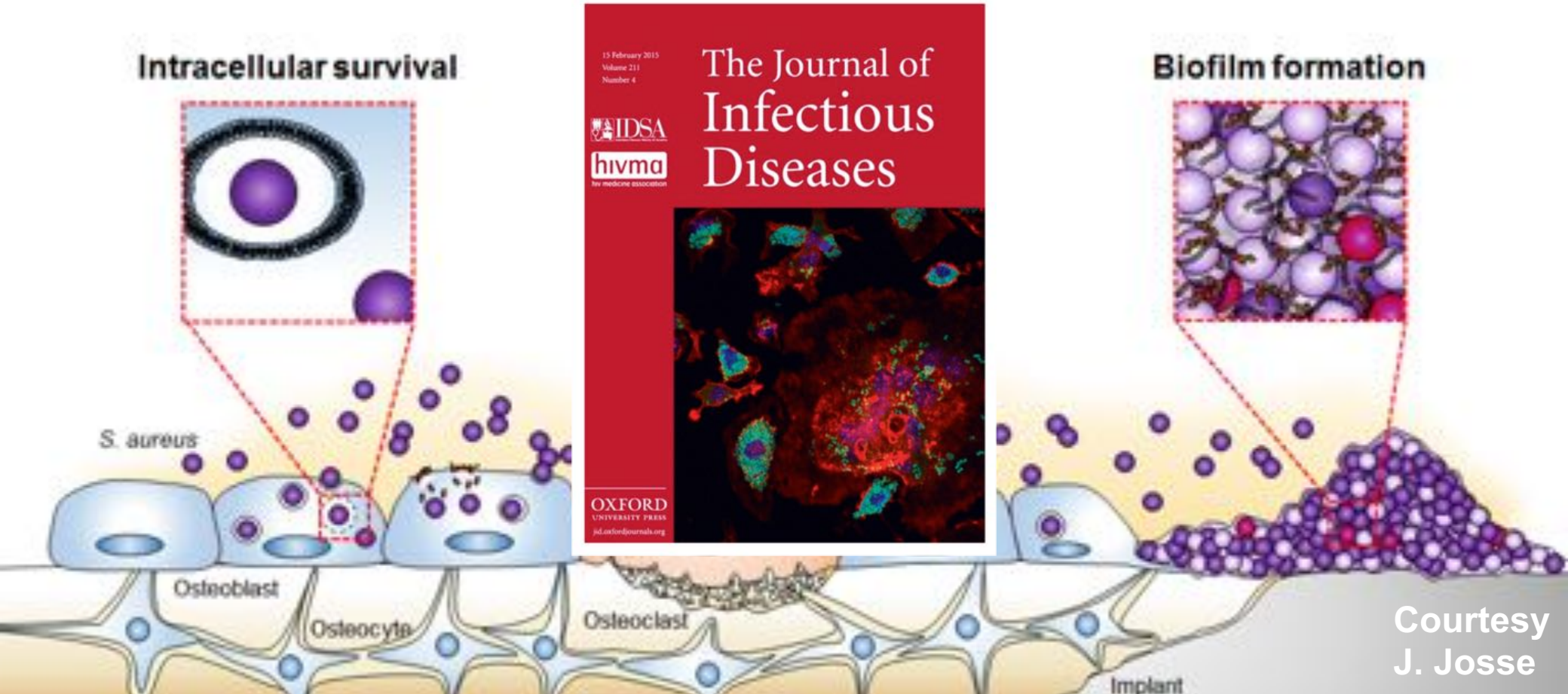

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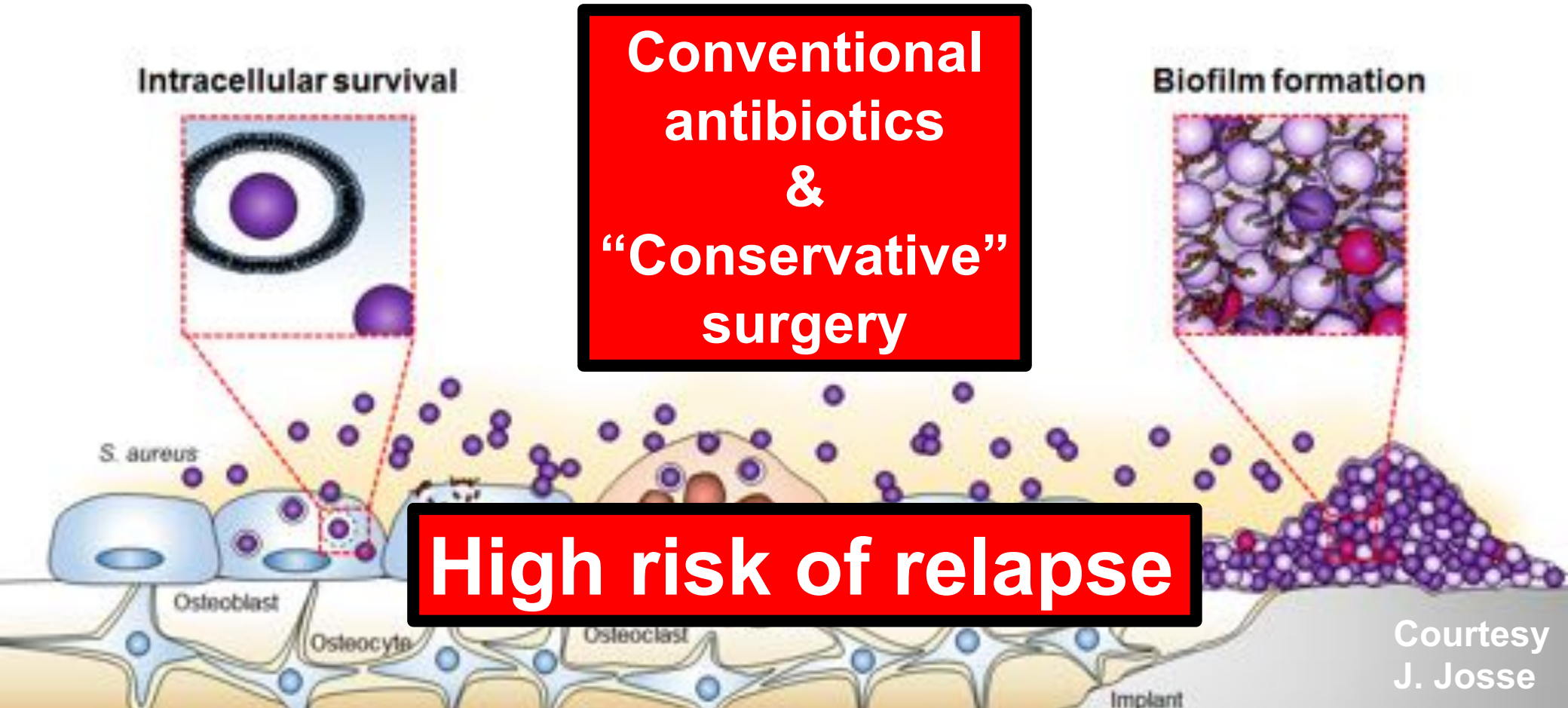

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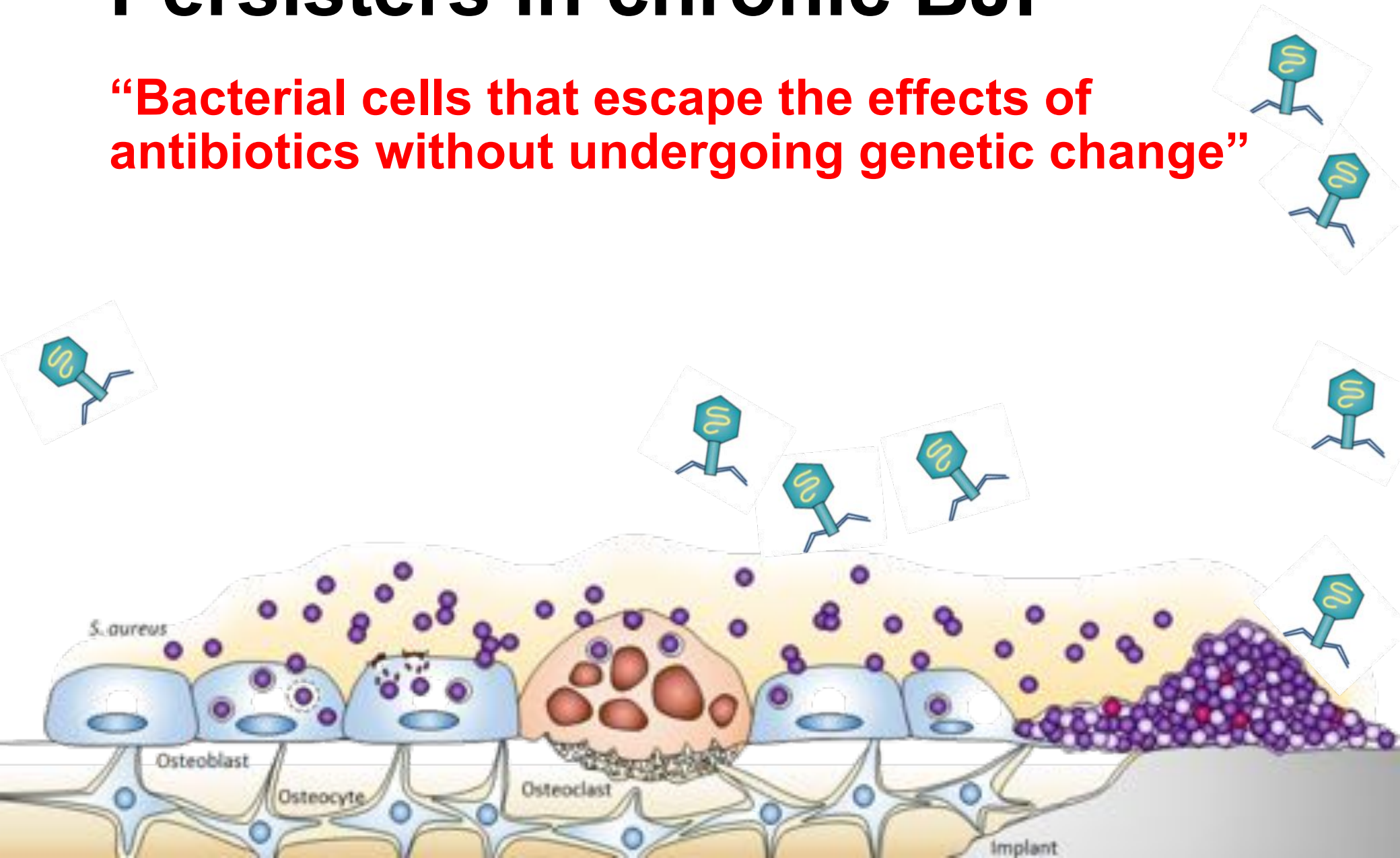
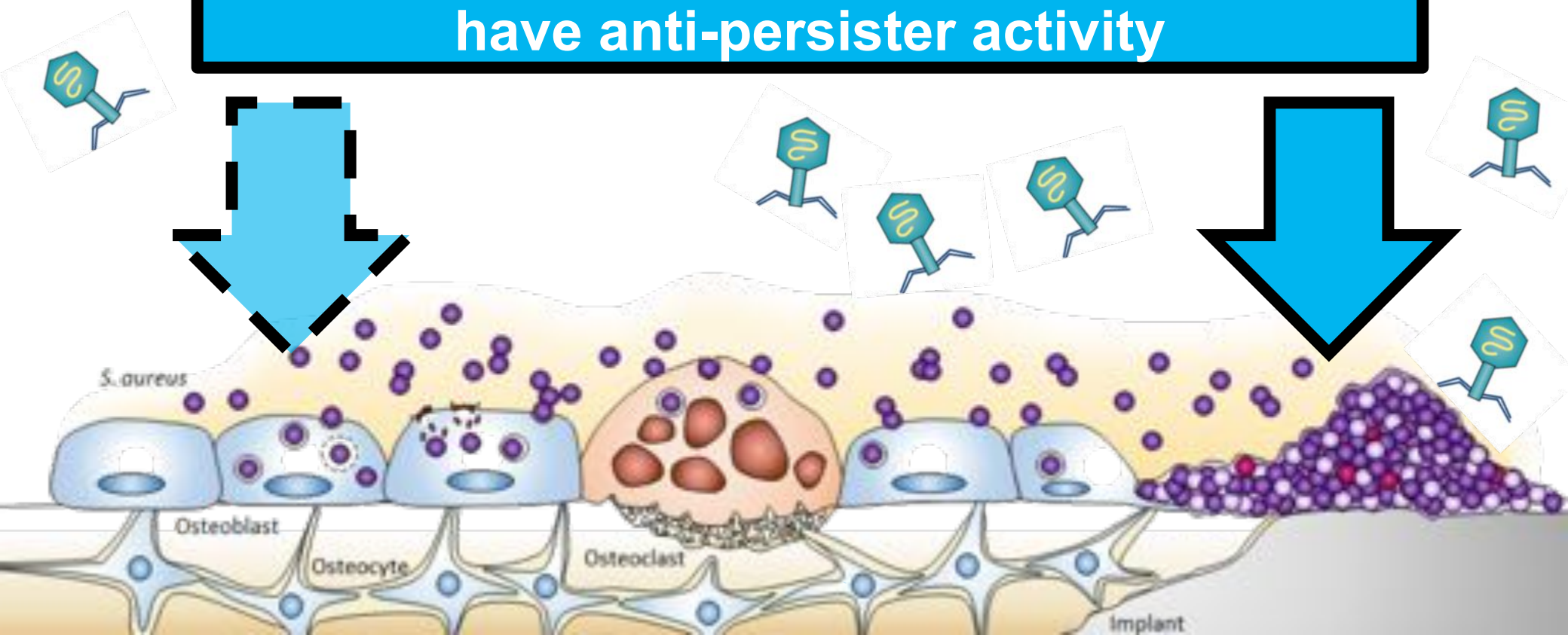


# Persisters in chronic BJI

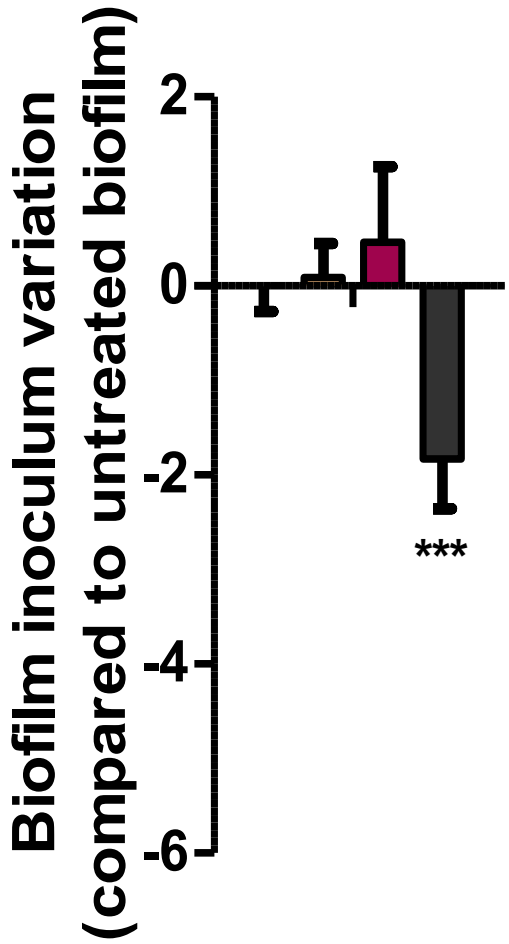
**"Bacterial cells that escape the effects of antibiotics without undergoing genetic change"**

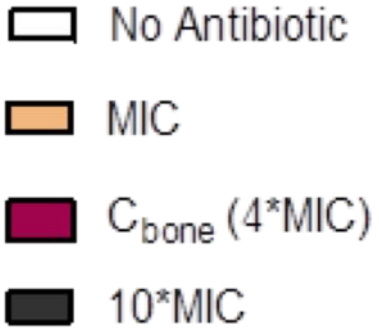
**Bacteriophages and lysins have anti-persister activity**



## C. Kolenda et al.

**vancomycin**



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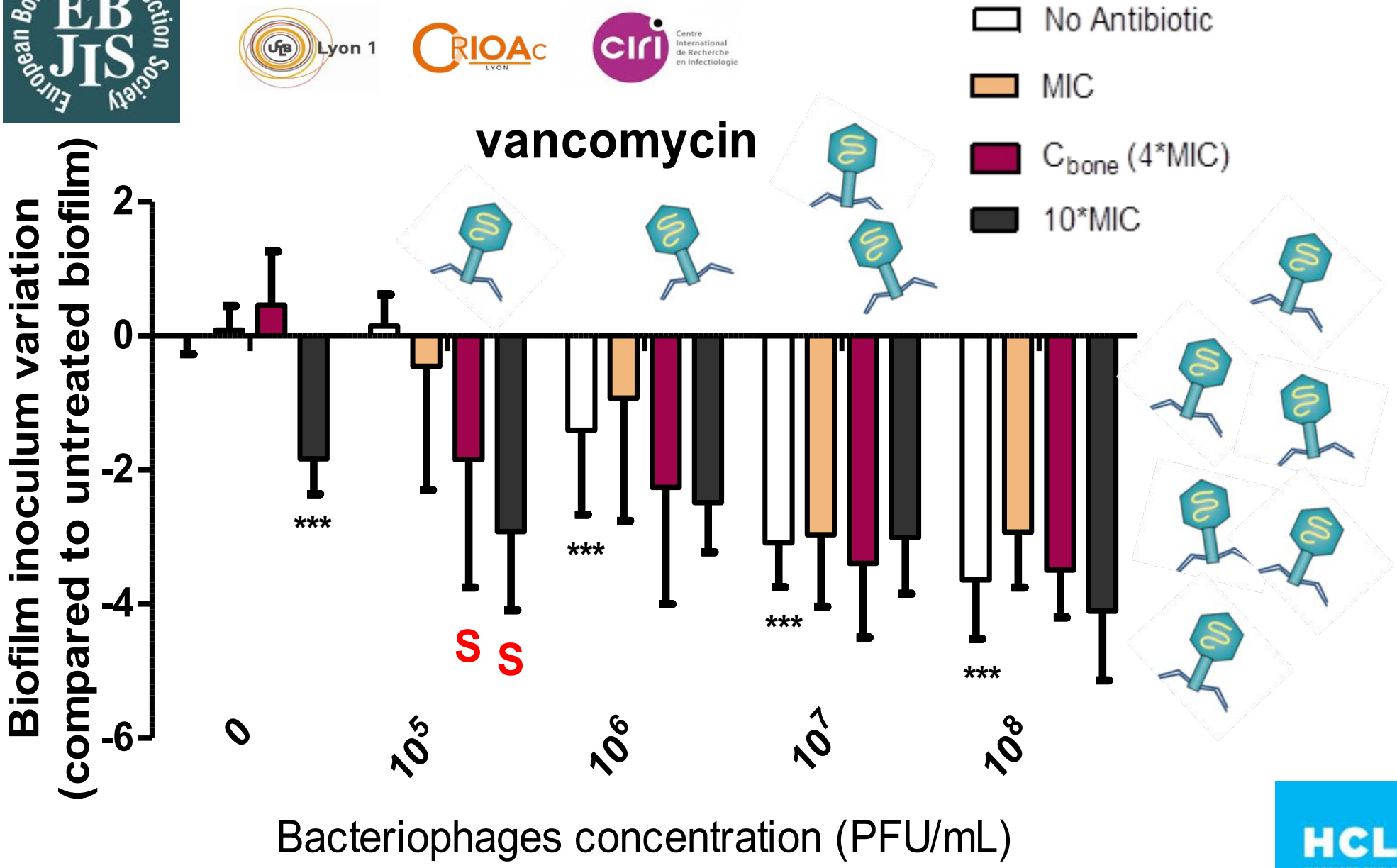


# Declaration of Helsinki

## Medical Research Involving Human Subjects

WORLD MEDICAL ASSOCIATION

WMA

Special Communication

World Medical Association Declaration of Helsinki
Ethical Principles for Medical Research
Involving Human Subjects

World Medical Association

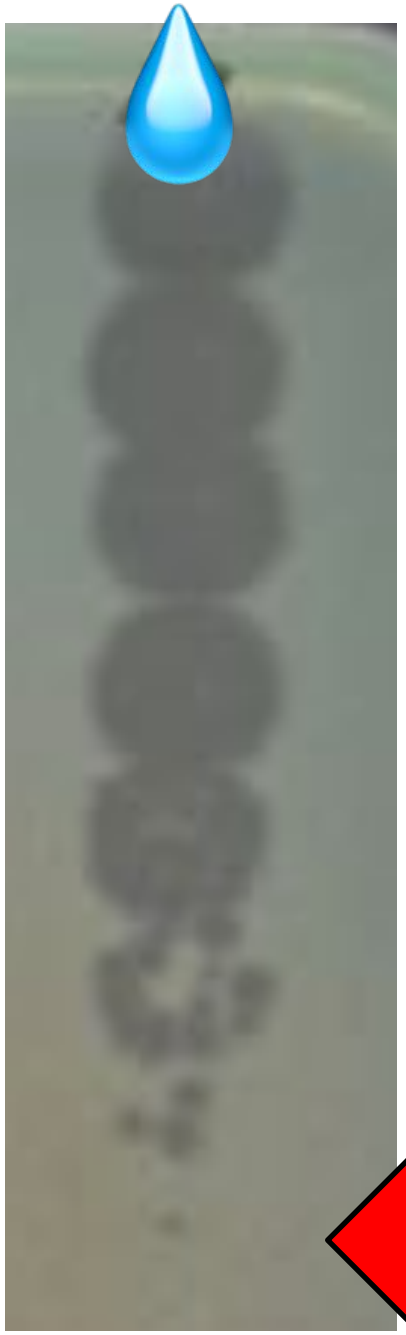
JAMA 2013

The Journal of the American Medical Association

- **Unproven Interventions in Clinical Practice**

- 37. In the treatment of an **individual patient**, **where proven interventions do not exist or other known interventions have been ineffective**, **the physician**, after seeking expert advice, **with informed consent from the patient** or a legally authorised representative, **may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health** or alleviating suffering.

In France: **compassionate** use,
**magistral preparation** by the hospital pharmacist



*Phage*

$10^{10}$

$10^{9}$

$10^{8}$

$10^{7}$

$10^{6}$

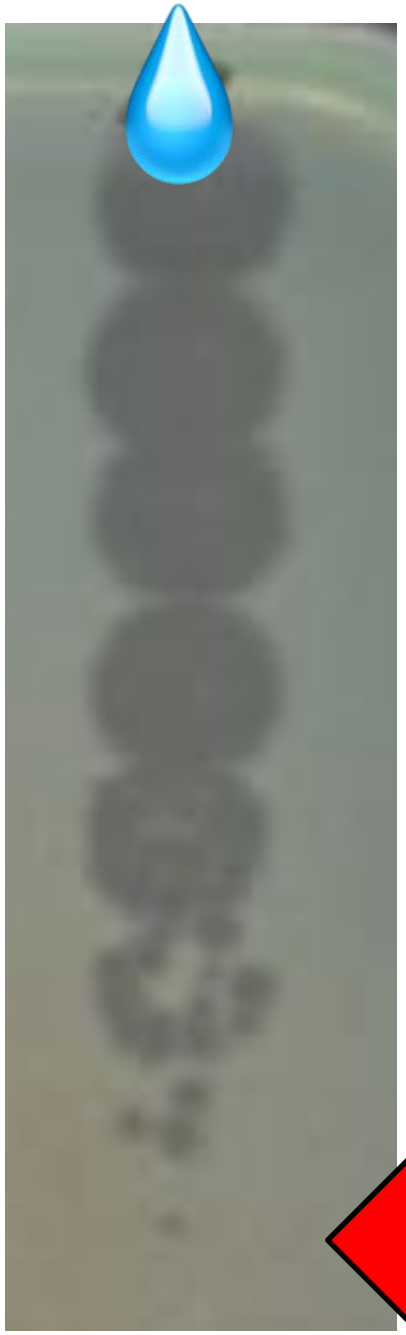
$10^{5}$

PFU/mL

**A clear antibacterial activity!**

# Phagogram

**_S. aureus_ culture on a gelosis**



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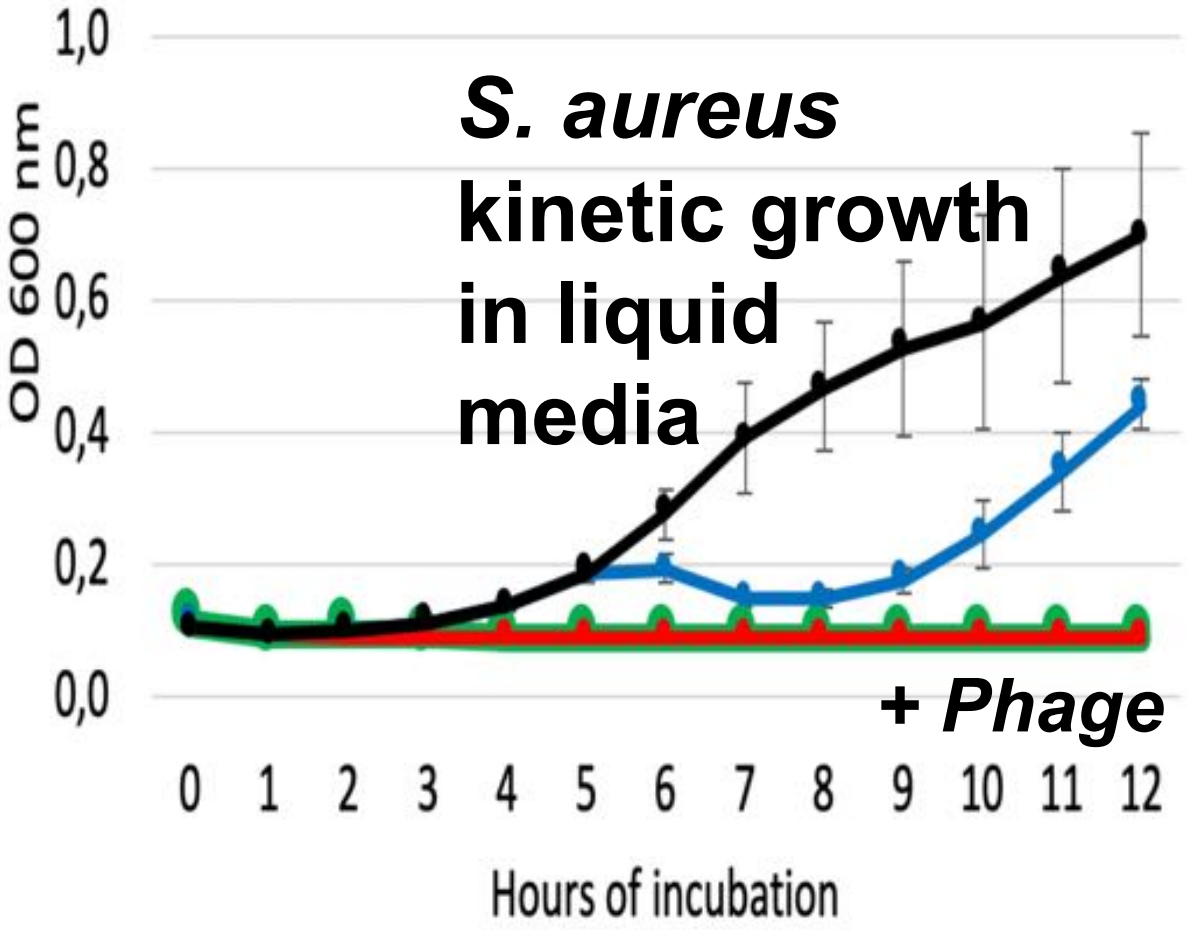


**S. aureus culture on a gelosis**

# Clinical case #4

80-year-old man

**<u>Relapsing MSSA</u>** prosthetic left knee infection (past revision)

**<u>Failure</u> under suppressive oral antimicrobial therapy**

Complex orthopaedic situation with past femoral fracture

Impossible to walk (painful knee)



Septic arthritis


Fistula and purulent discharge


HAL
HAL
HLP
HLP
FPR
FPR
FRA
FRA

# Clinical case #4

**Amputation**
**(but not feasible !) ?**


**<u>Doing nothing</u>**, but poor clinical situation with **<u>risk of complication and death</u>**

**<u>Conservative surgery</u>**
"Debridement And Implant Retention" (DAIR) + **<u>innovative approach to disrupt biofilm</u>** + suppressive antimicrobial therapy ?

# Lyon Phage team

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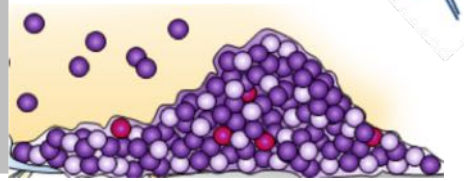
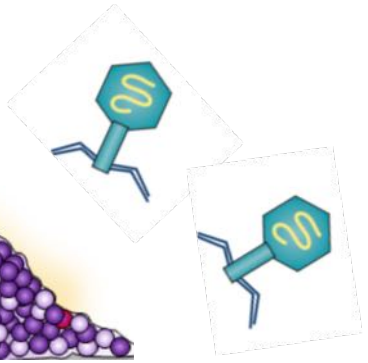
**Dr. Gilles Leboucher**
PharmD
Pharmacist





ID Clinic

HCL HOSPICES CIVILS DE LYON

CRIOAc LYON

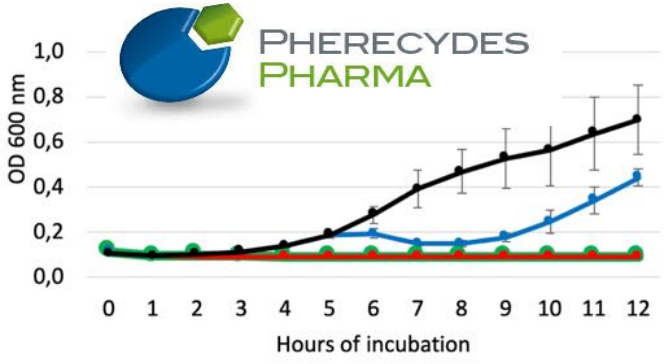
Surgery

HCL HOSPICES CIVILS DE LYON

Lab

HCL HOSPICES CIVILS DE LYON

PHERECYDES PHARMA




**Phagogram**
**Selection of active bacteriophages**

PHERECYDES PHARMA

**Active *S. aureus* Bactériophages**


Under the supervision of

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

French Health Authority

Pharmacy

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ID Clinic

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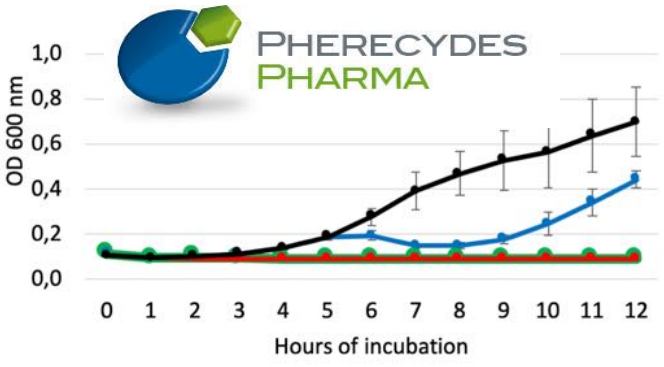


**Phagogram**
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**Active *S. aureus* Bactériophages**


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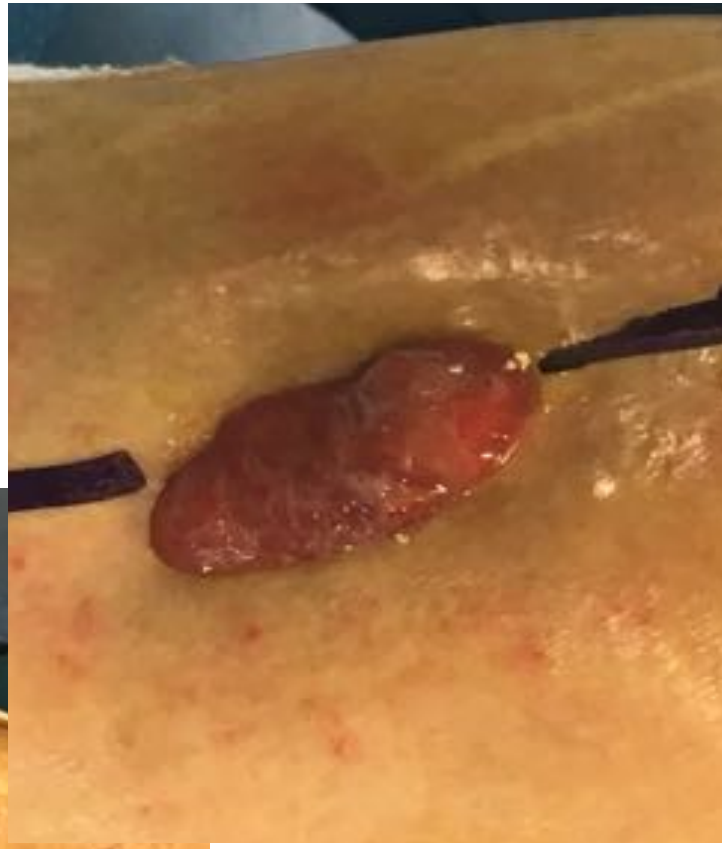
**Extemporaneous magistral preparation of the mix of bacteriophages**



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# “Debridement And Implant Retention” (DAIR)

# “PhagoDAIR”

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

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# Clinical case #4

**<u>Post-operative</u> antibiotics:**

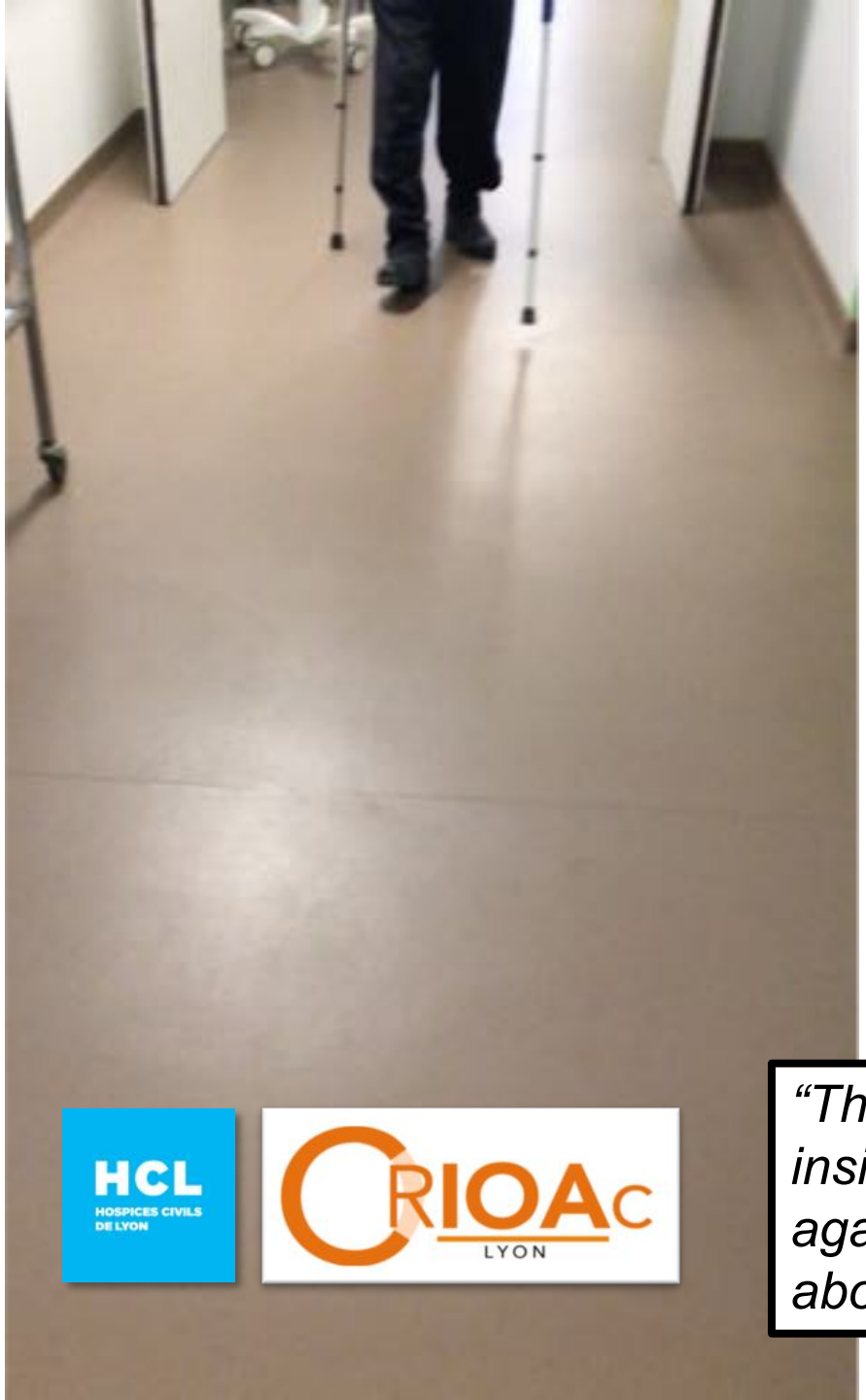
Daptomycin + Rifampin

**<u>At day 4</u> (only MSSA in all intraoperative samples):**

Levofloxacin + Rifampin

**<u>Then:</u>**

Cefalexin as suppressive antimicrobial therapy



*“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.

**‘Debridement And Implant Retention’ (DAIR) with local administration of personalized cocktail of bacteriophages (PhagoDAIR) followed by suppressive antibiotherapy as salvage therapy in patients with relapsing prosthetic knee infection**

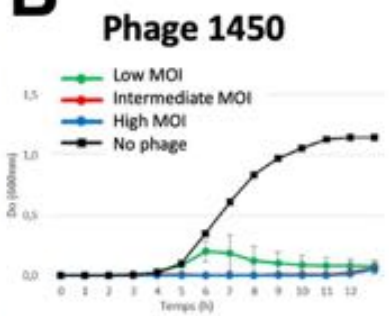
Phago DAIR

CRIOAc LYON

A

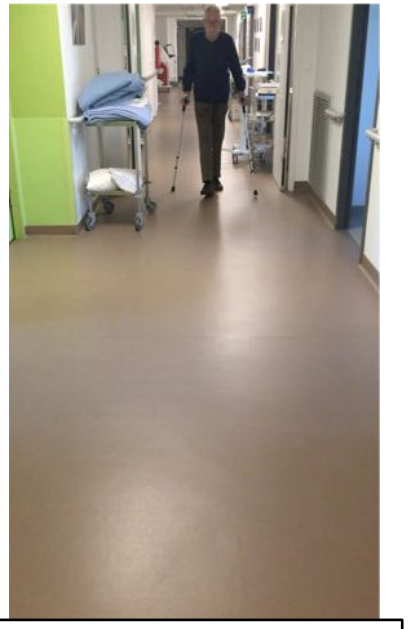
Left PKI with purulent joint effusion

B




Phagogram (Killing assay)


D



Favorable outcome at 1 year

30th ECCMID

Paris, France
18 –21 April 2020

PHERECYDES PHARMA

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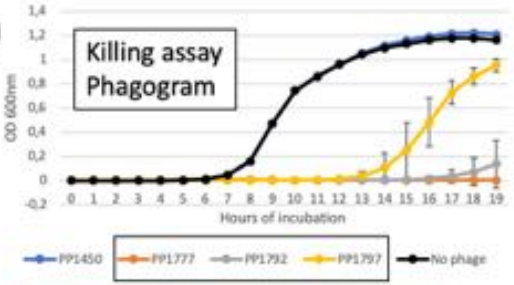
**Conclusions:** **Personalized bacteriophage therapy has the potential** to be used as salvage therapy during DAIR in patients with relapsing *S. aureus* and *P. aeruginosa* prosthetic knee infection, **to improve the efficacy of suppressive antibiotics, and to avoid considerable loss of function.**

# Ultrasound guided local administration of personalized cocktail of bacteriophages followed by suppressive antibiotherapy as salvage therapy in patients with relapsing total femur prosthesis infection





30th ECCMID
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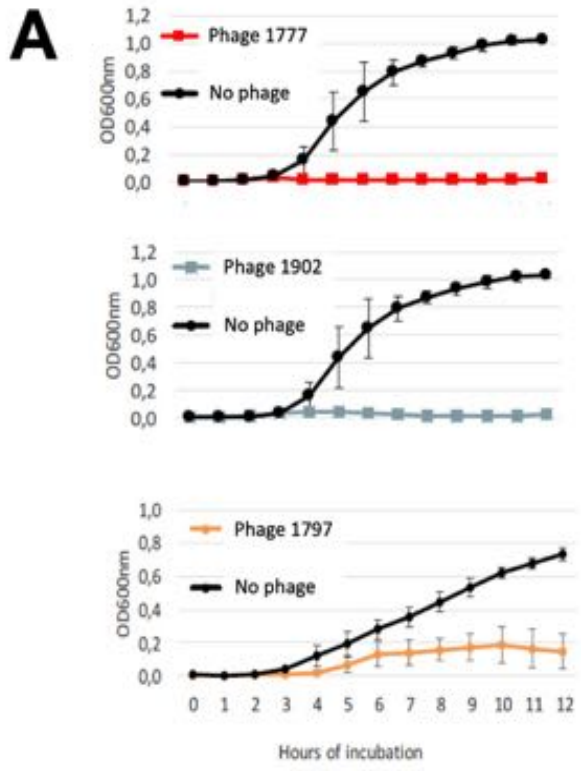
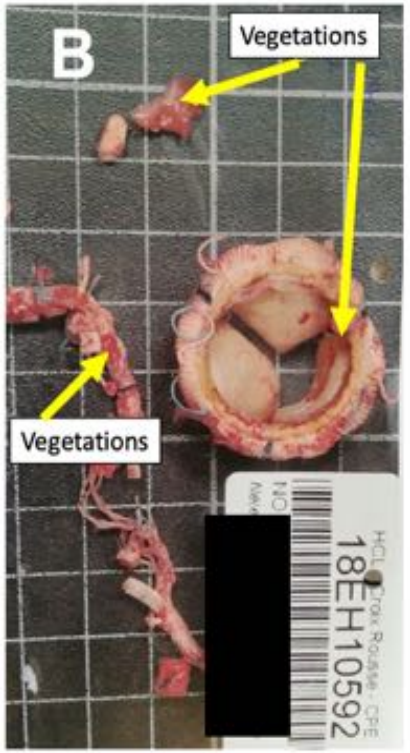
**Conclusions:** Ultrasound-guided local administration of personalized cocktail of GMP bacteriophages followed by suppressive antibiotherapy in patients with relapsing total femur PJI has the potential to be used as salvage therapy to control the infection and avoid disarticulation. Dramatic superinfection could be diagnosed at the time of phage administration.

# <u>Intravenous</u> administration of personalized cocktail of bacteriophages as salvage therapy in combination with ceftazidime/avibactam in patients with relapsing *P. aeruginosa* bacteremia: Lesson learned from two cases




30th ECCMID
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**Conclusions:** **The type of filter used for the magistral preparation and the duration of the perfusion influenced the phage titer, as the titer in the patient's blood.** Personalized GMP bacteriophage therapy has the potential to be used as salvage therapy of *P. aeruginosa* intravascular implant infections.

# Clinical case #5

74-year-old man

Melanoma treated with anti-PD1

Catheter-related ***P. aeruginosa*** **bacteriemia** in January 2018

Spinal pain summer 2018

**Spondylodiscitis** with **spinal abscess**

**Pandrug-resistant *P. aeruginosa* in culture!**

# Clinical case #5

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Catheter-related ***P. aeruginosa*** **bacteriemia** in January 2018

Spinal pain summer 2018

**Spondylodiscitis** with **spinal abscess**

**Pandrug-resistant *P. aeruginosa* in culture!**

| | *Pseudomonas aeruginosa* CMI (mg/l) |
|---|---|
| Ticarcilline + Ac. Clav | R (> 64) |
| Pipéracilline | R (> 64) |
| Pipéracilline + Tazobactam | R (> 64) |
| Ceftazidime | R (> 32) |
| Céfépime | R (> 32) |
| Aztréonam | R (> 32) |
| Imipénème | R (> 8) |
| Meropeneme | R (> 8) |
| Gentamicine | R (> 8) |
| Tobramycine | R (> 8) |
| Amikacine | R (> 32) |
| Ciprofloxacine | R (> 2) |
| Lévofloxacine | R (> 4) |
| Cotrimoxazole | R |
| Colistine | S (8) ⇨ R |
| Colistine (Etest) | S<br>E-test : 1 ⇨ R |
| Ceftolozane-tazobactam (Etest) | R<br>E-test : > 256 |
| Ceftazidime-Avibactam (Etest) | R<br>E-test : 64 |

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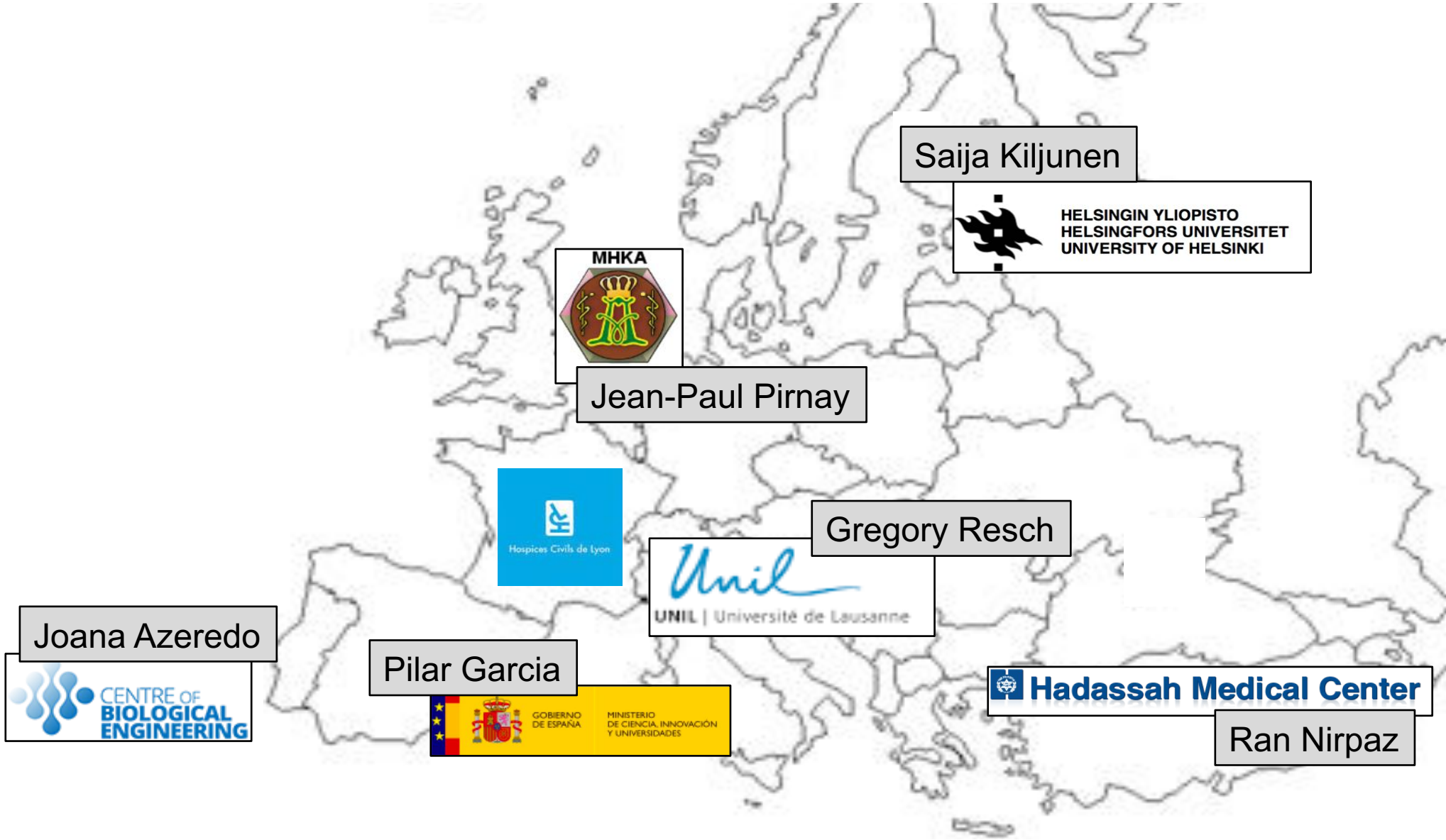
AMPLIPHI BIOSCIENCES CORPORATION

**The strain was also spontaneously resistant to GMP bacteriophages !!!**

# Potential European academic collaborations



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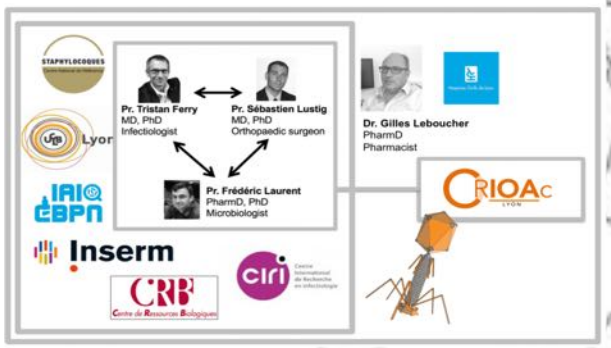
Agence nationale de sécurité du médicament et des produits de santé

French Health Authority

# Potential European academic collaborations

## Lyon Phage team

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# Potential European academic collaborations

MHKA

Jean-Paul Pirnay

Gregory Resch

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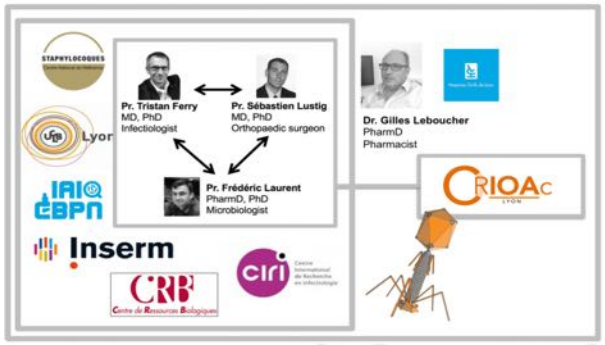


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# Potential European academic collaborations

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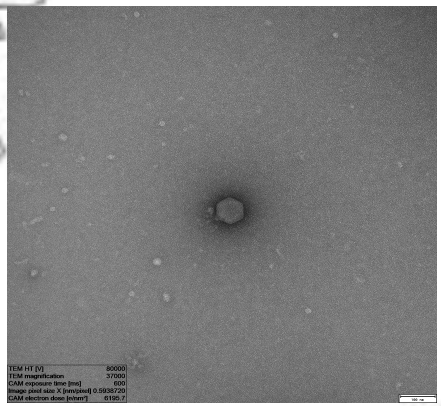

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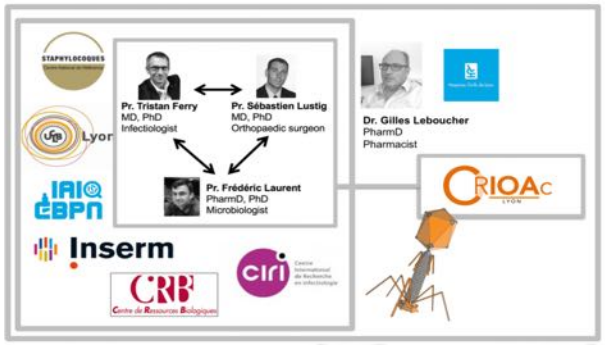
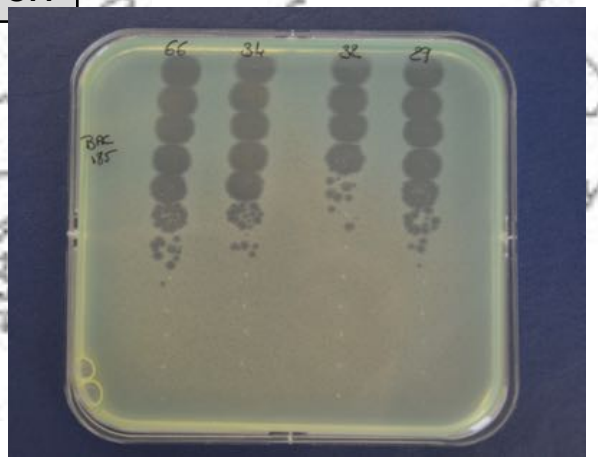



Hospices Civils de Lyon

Gregory Resch

UNIL | Université de [illegible]anne



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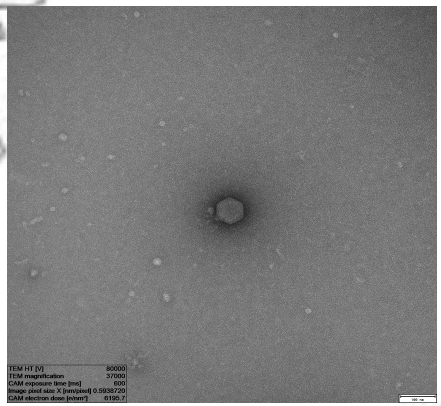

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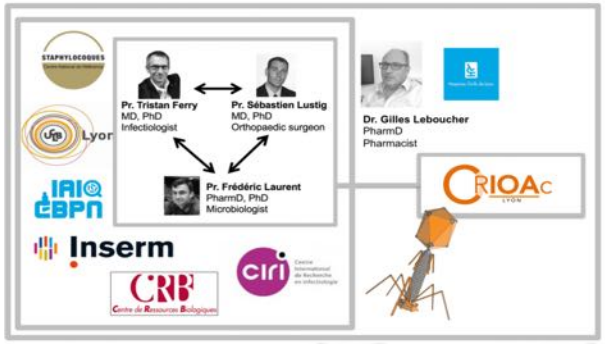


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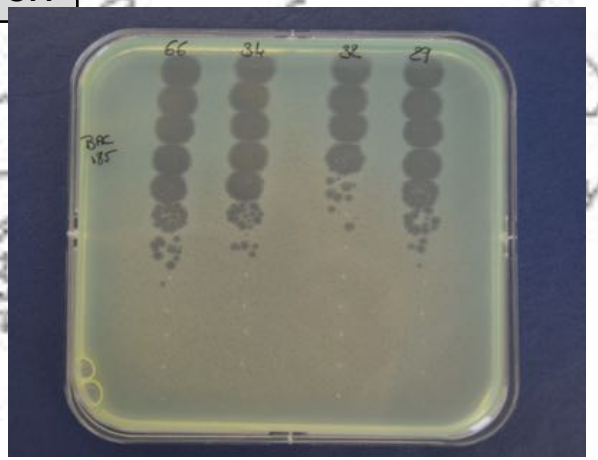

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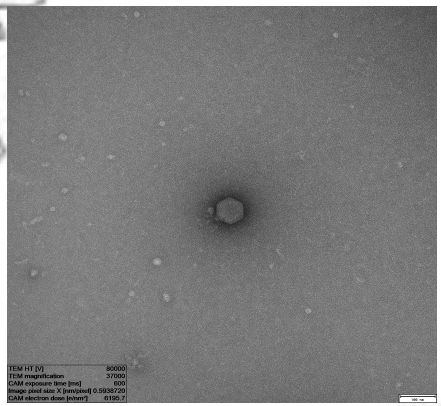

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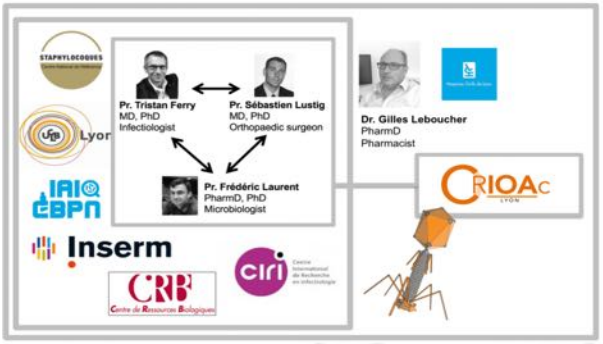


Hospices Civils de Lyon

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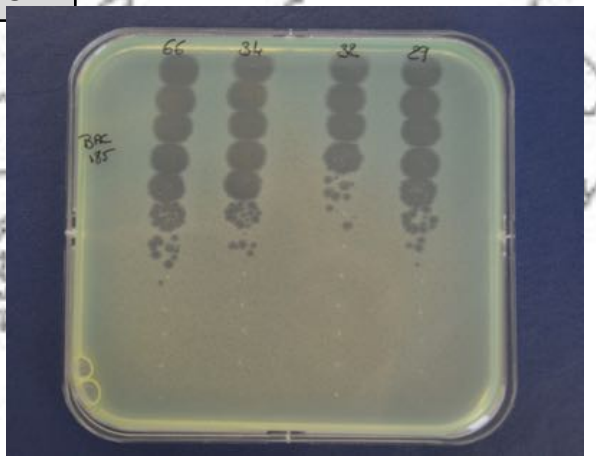
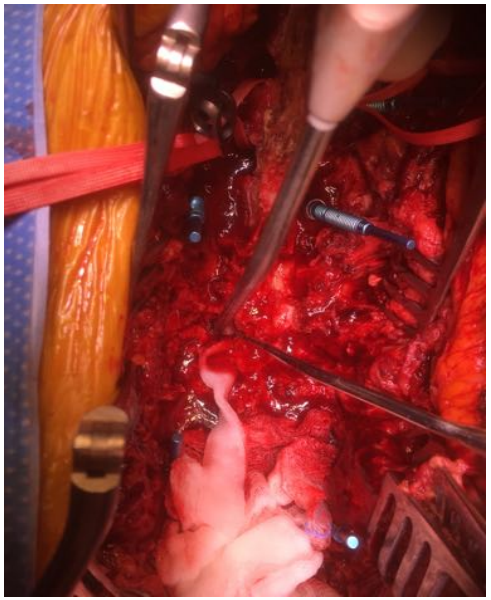
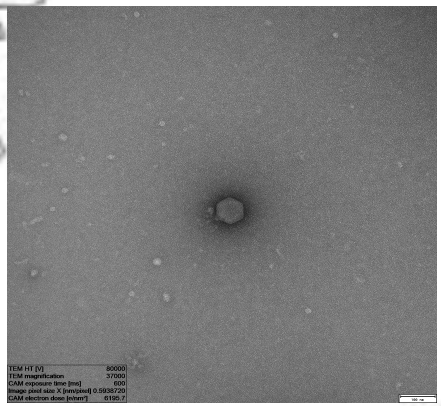


# Potential European academic collaborations

Under the supervision of

ansm
Agence nationale de sécurité du médicament et des produits de santé
French Health Authority

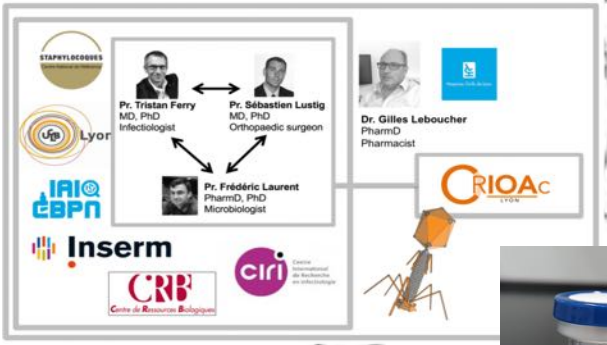




Lyon Phage tea

Jean-Paul Pirnay

Gregory Resch

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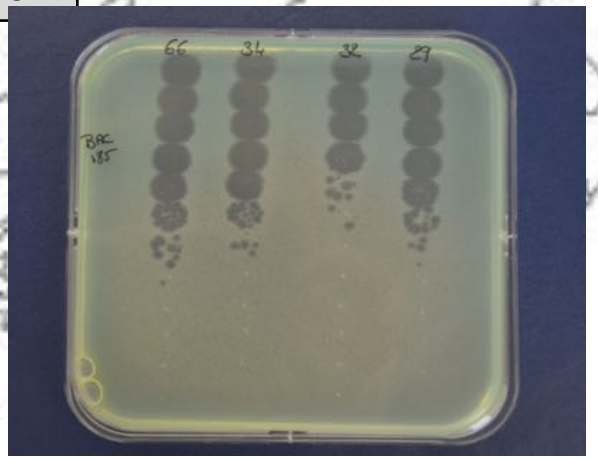
ATU



# Personalized production and administration of bacteriophages: lessons learned from a unique European academic collaboration to treat a patient with pandrug-resistant spinal *P. aeruginosa* infection

HCL HOSPICES CIVILS DE LYON

MHKA

HMRA

UNIL | Université de Lausanne

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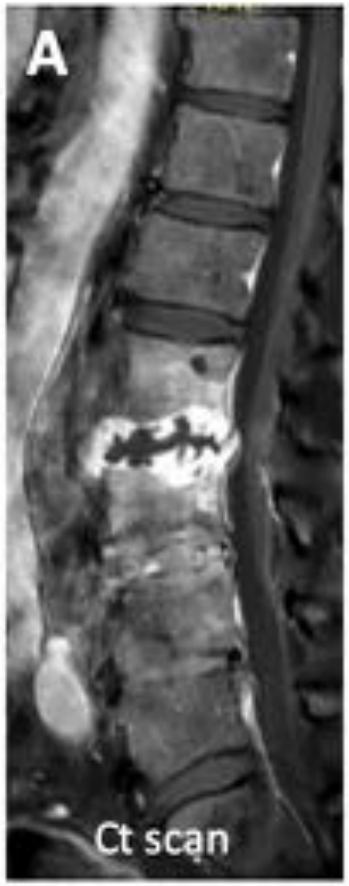


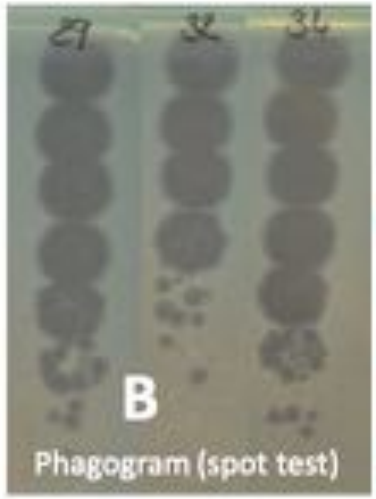


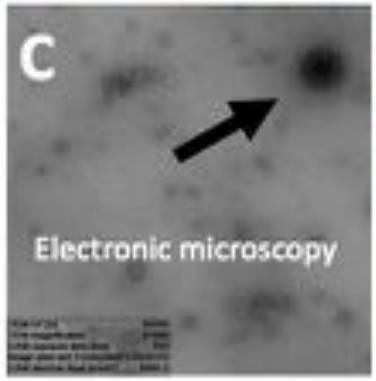


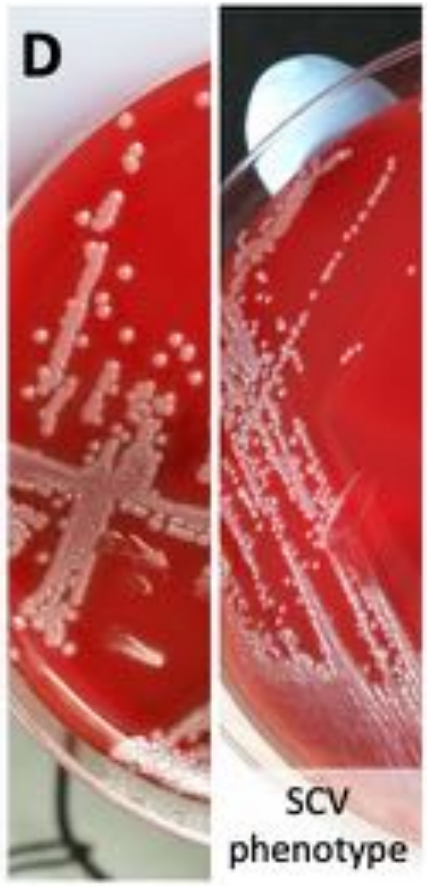


30th ECCMID

Paris, France
18 –21 April 2020

CRIOAc LYON

**Conclusions:** Personalized phage therapy is a potential adjunct treatment for patients with complex BJI due to pandrug-resistant bacteria. **In addition to industrial phages under development, academic collaborative research is crucial to develop personalized phage therapy.**

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# Implementation of a Phage Therapy Center in a CRIOAc




PHAGE*in*LYON

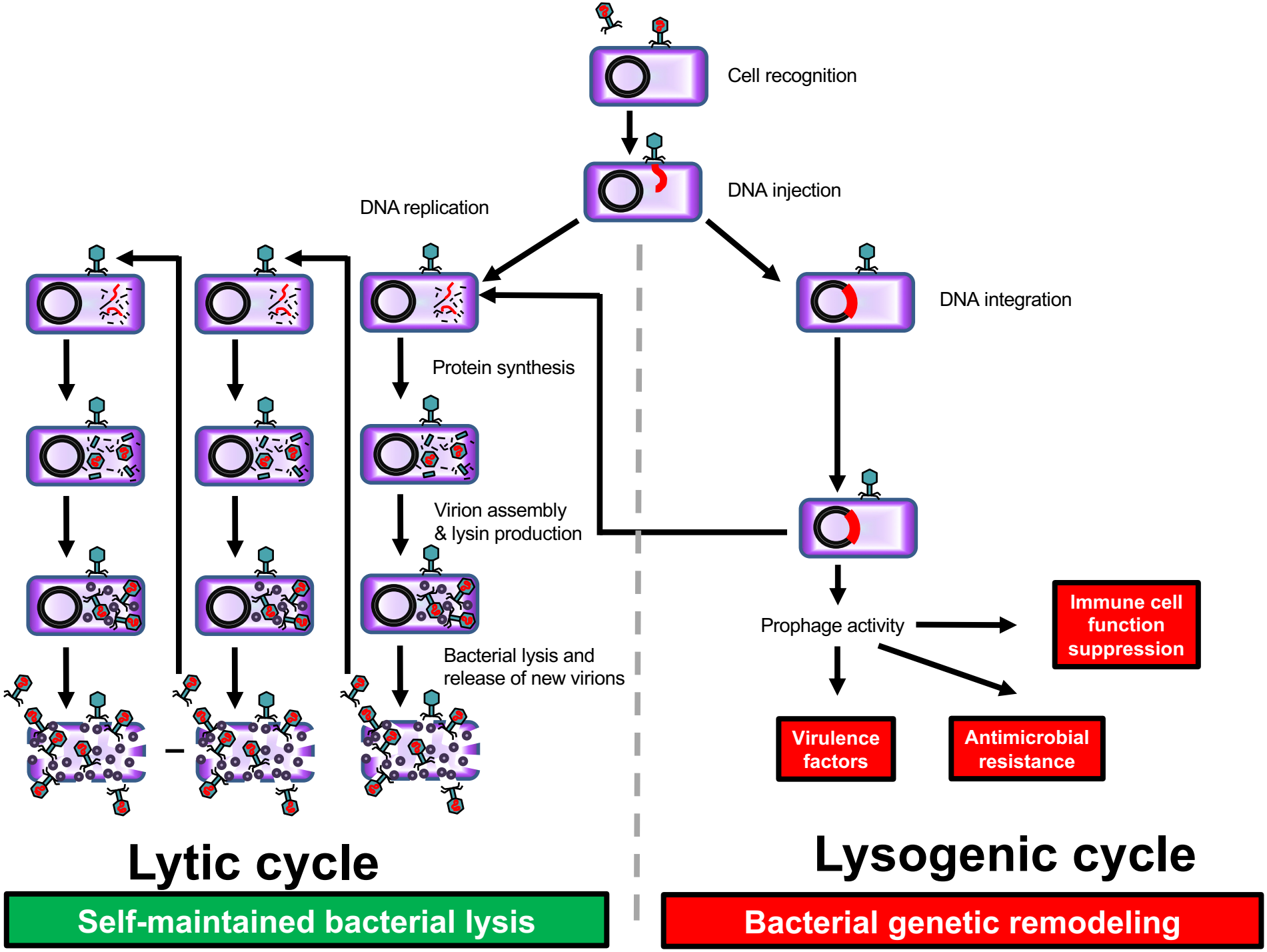
**30 patients in Lyon since 2017**

- 27 with phages from PHERECYDES PHARMA
- 3 with phages from MHKA HMRA

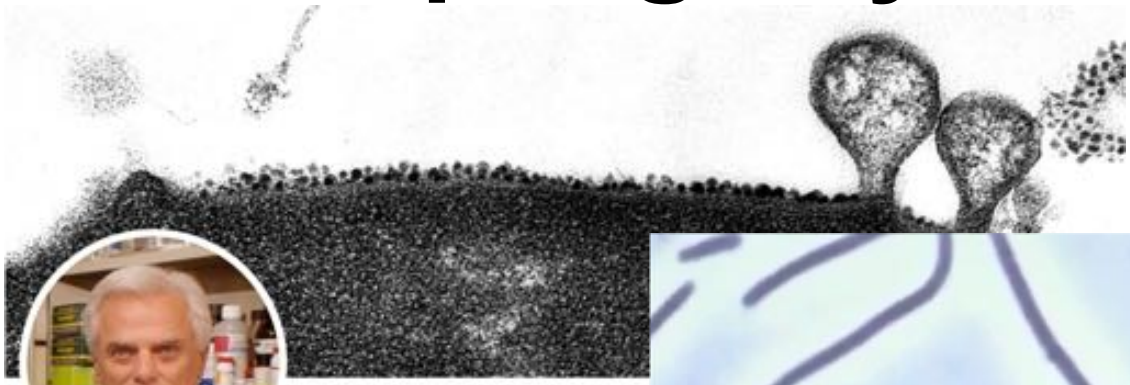
- 26 **BJI** (including **22 PJI**)
- 3 **endocarditis**
- 1 **PAVM bactériémique**

**+ 3 patients managed outside Lyon**

**BJI** **Endocarditis** **Pneumonia**


Cell recognition
DNA injection
DNA replication
DNA integration
Protein synthesis
Virion assembly
& lysin production
Bacterial lysis and
release of new virions
Prophage activity
Immune cell function suppression
Virulence factors
Antimicrobial resistance
Lytic cycle
Lysogenic cycle
Self-maintained bacterial lysis
Bacterial genetic remodeling

# Bacteriophage Lysins





**Vincent A Fischetti**
@microbephage

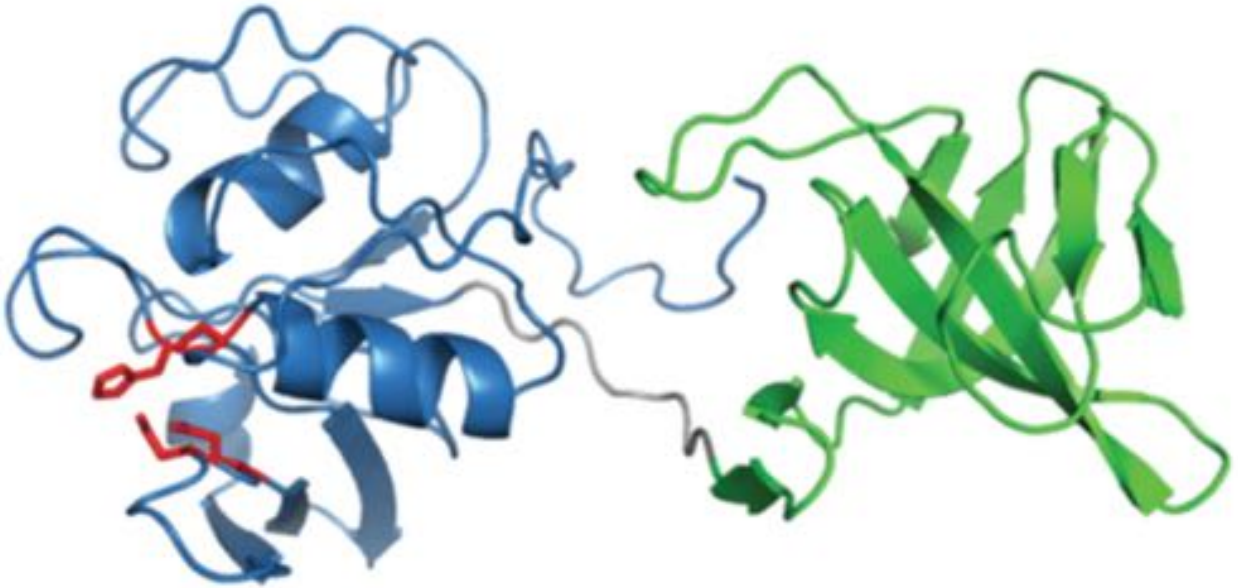
**Tristan Ferry Lyon University Hospitals**
@FerryLyon

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**

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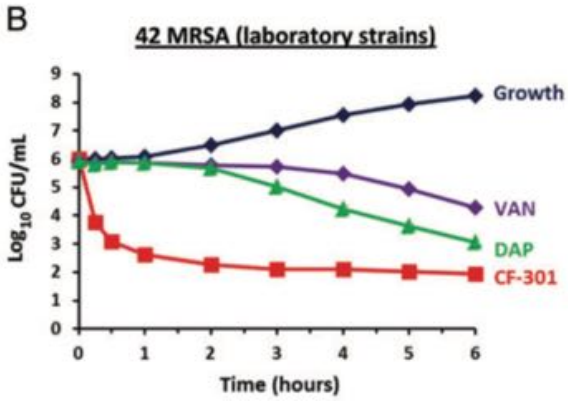


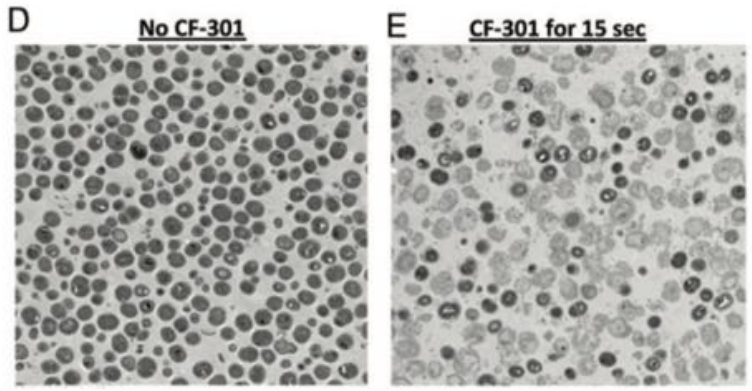


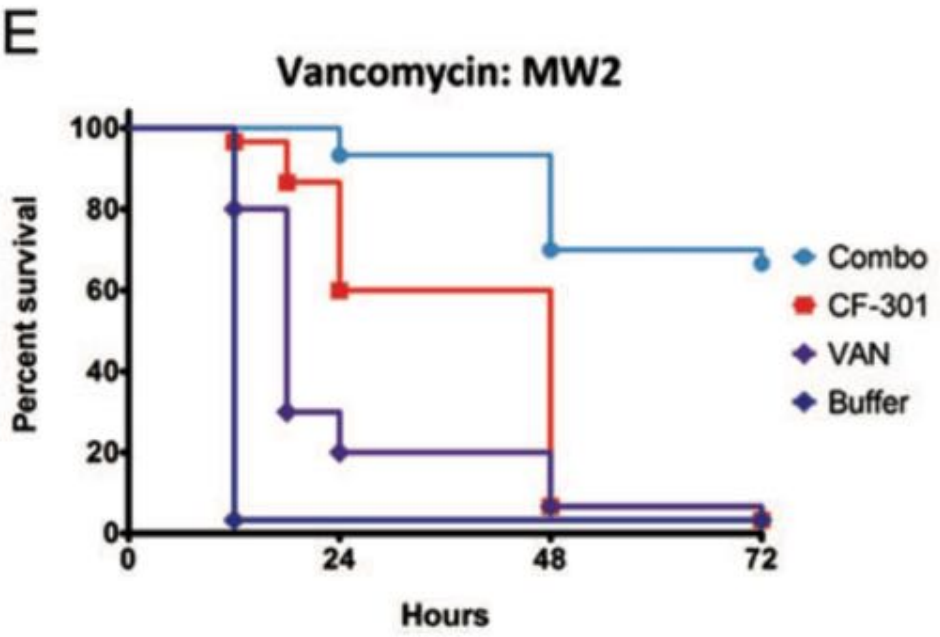


*J Infect Dis* 2014

**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**

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18 –21 April 2020

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**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.

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# Potential anti-Persisters

**Basic science > Pre-clinical > Clinical > Market approval > Marketing**

**New small molecules**

NH125 Nitroxoline TN-5 ADEP4S SAR2 2D-24 NCK-10 Piscidin p3 XF-73 SPI009 IDR1018 QAC-10 PLGP-0206

**New antibiotics or drugs derived from antibiotics**

ACH-702

TosufloxacinE HT61 C2DA

**Afabicin (FabI inhibitor)**

WLBU2 **Matrix-targeting agents or mAB**

**DSTA4637S**

Dispersin B Mucoid exopolysaccharide immune globulin

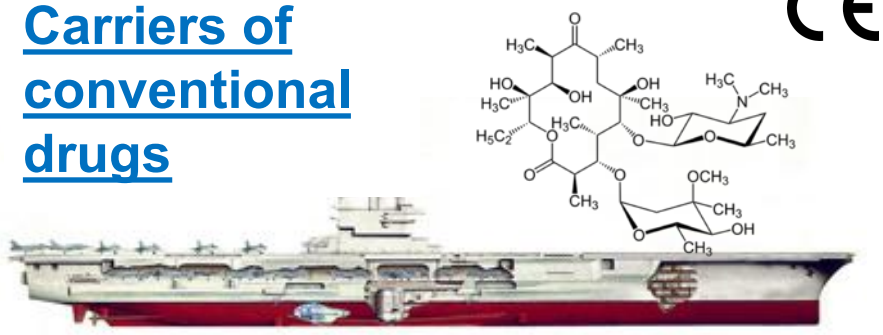
**Bacteriophage Lysins** LysK

**SAL200** **CF-301**

# Bacteriophages

**GMP-like Bacteriophages**

## Carriers of conventional drugs



**Local high doses and prolonged exposure**

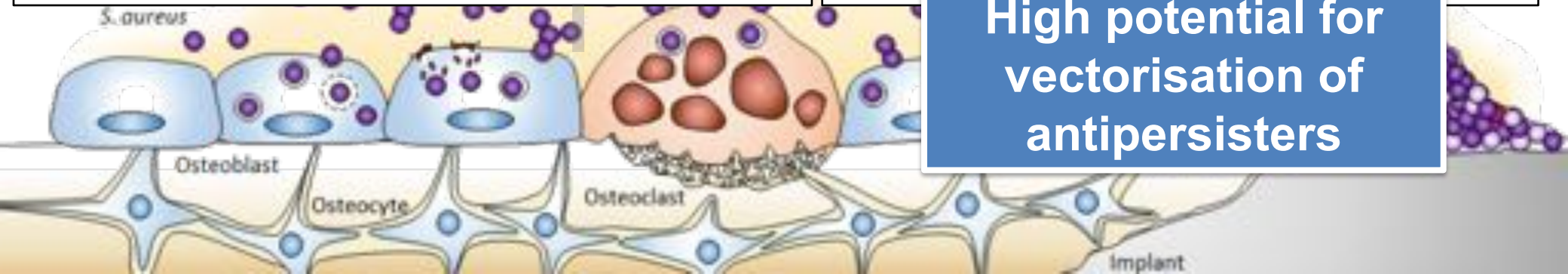
Nanotools

Liposomal carriers

**Antibiotic-loaded hydrogel**

**Antibiotic-loaded ceramic tailored implants**

**Antibiotic-loaded bone substitutes (CaSO4)**




**High potential for vectorisation of antipersisters**

# Conclusion

- Crucial need for (alternatives) **additional therapies to antibiotics** to maximize clinical success in complex bacterial infections

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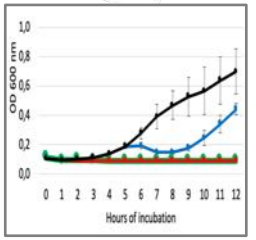

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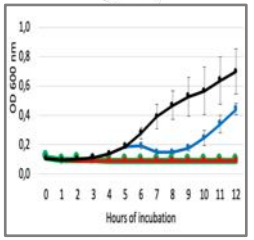
- **Need for national phage therapy center(s)**


Agence nationale de sécurité du médicament et des produits de santé

# Lyon BJI Study group

**Coordinator: Tristan Ferry**

**Infectious Diseases Specialists** – Tristan Ferry, Florent Valour, Thomas Perpoint, Florence Ader, Sandrine Roux, Claire Triffault-Filit, Agathe Becker, Anne Conrad, Marielle Perry, Cécile Pouderoux, Nicolas Benech, Pierre Chauvelot, Johanna Lippman, Evelyne Braun, Christian Chidiac

**Surgeons – Sébastien Lustig**, Elvire Servien, Cécile Batailler, Stanislas Gunst, Axel Schimdt, Matthieu Malatray, Eliott Sappey-Marinier, Michel-Henry Fessy, Anthony Viste, Jean-Luc Besse, Philippe Chaudier, Lucie Louboutin, Quentin Ode, Adrien Van Haecke, Marcelle Mercier, Vincent Belgaid, Arnaud Walch, Sébastien Martres, Franck Trouillet, Cédric Barrey, Ali Mojallal, Sophie Brosset, Camille Hanriat, Hélène Person

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

**Nuclear Medicine** – Isabelle Morelec, Marc Janier, Francesco Giammarile

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

**Clinical Research Assistant –** Eugénie Mabrut

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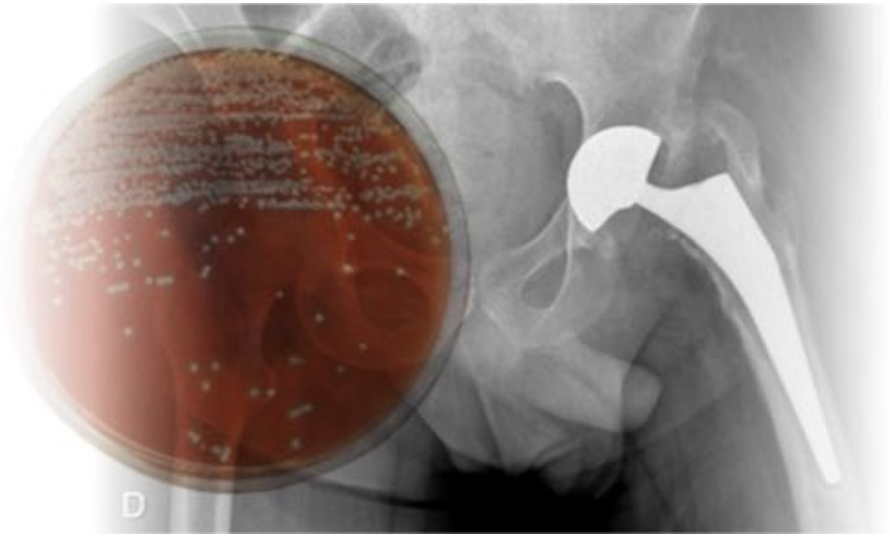
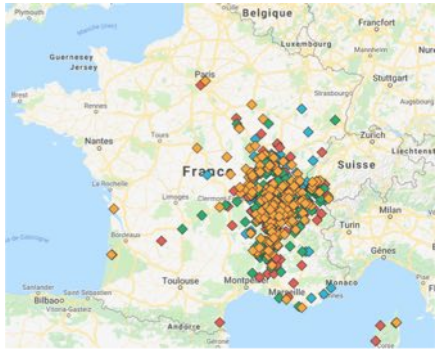


- Published cases
- Open acces studies in pdf
- All thesis in pdf
- All recommendations
- **Newsletter**

YouTube

@CrioacLyon

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