

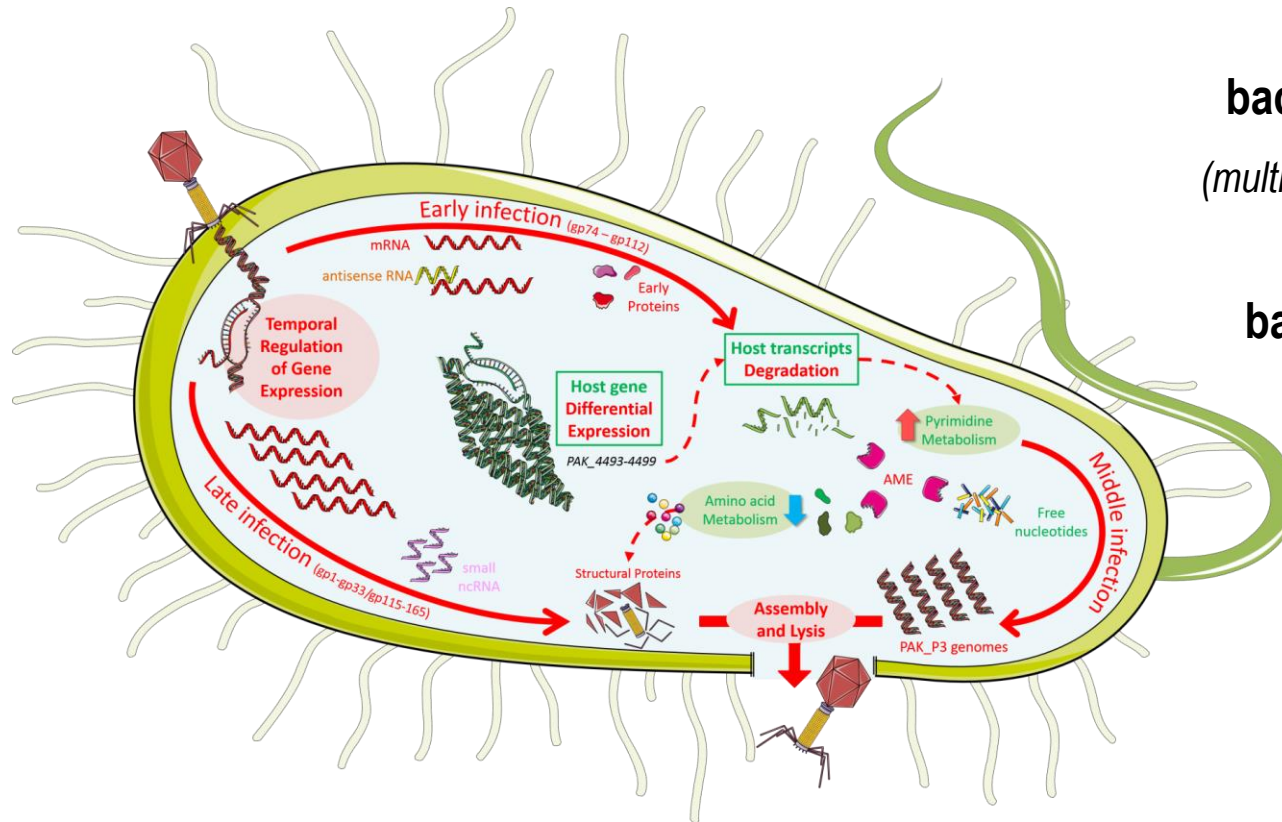
Phagothérapie : données pré-cliniques dans les infections pulmonaires

Laurent DEBARBIEUX

- **Je n'ai pas de conflits d'intérêt à déclarer à propos de cette présentation.**
- **Je respecte la charte éthique de mon employeur, l'Institut Pasteur.**

Bactériophages, virus mangeurs de bactéries

BUT
bacteria can fight back !
(multiple resistance mechanisms)
AND
bacteriophages too !!!



Phagothérapie, un traitement français oublié

The use of bacteriophages to kill pathogenic bacteria

Date: 1920's

Father: Félix d'Herelle (1873-1949)

Location: Institut Pasteur, Paris, France

Particular signs: first specific antibacterial treatment

1920's-1940's: world expansion (Brazil, Egypt, Georgia,...)

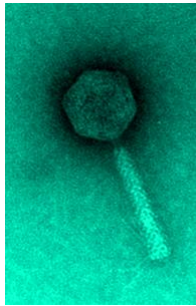
1950's-1990's: world decline (except Eastern Europe)



Phagothérapie d'infections pulmonaires aiguës

Our experimental parameters:

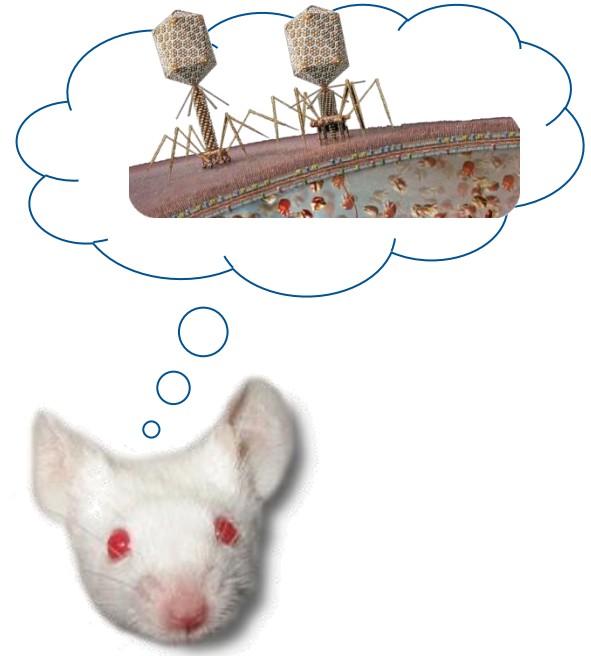
- clinical strains (bioluminescent) *P. aeruginosa* or *E. coli*
- virulent phages
- lethal infection for mice in 48-72h



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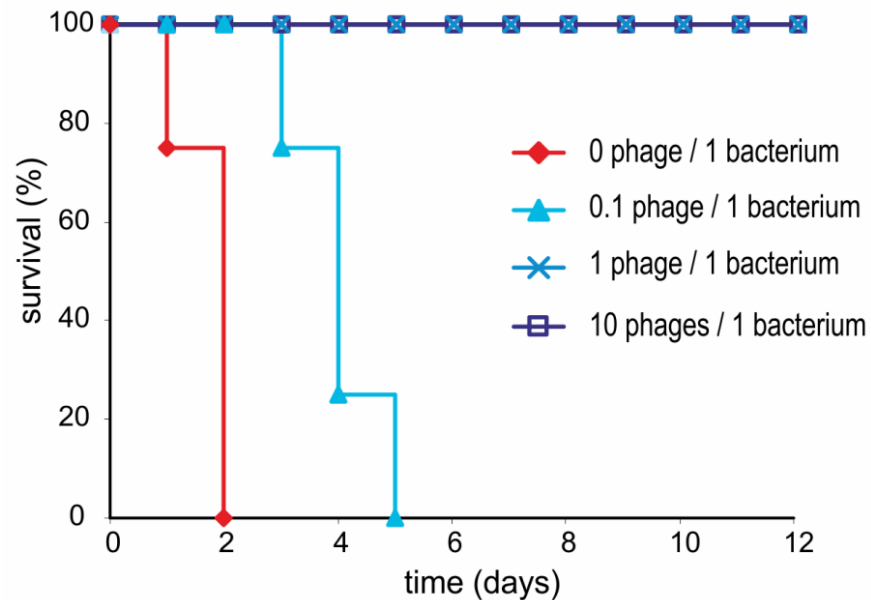
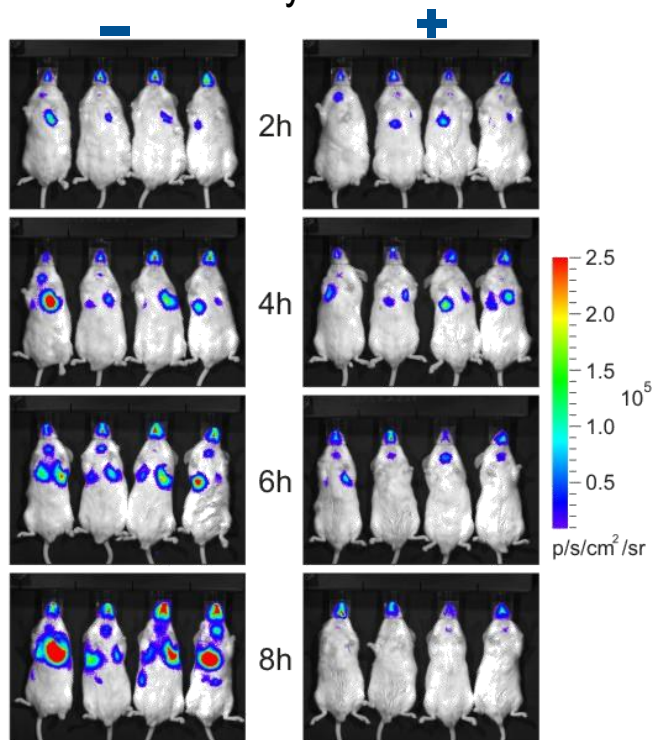
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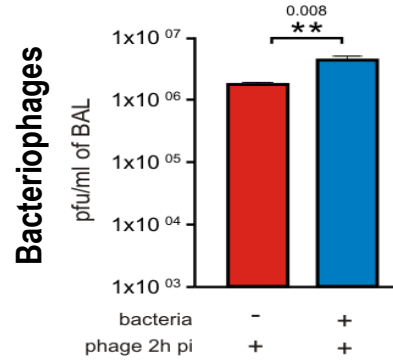
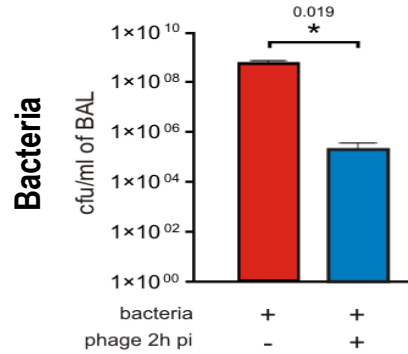
Kinetics of pulmonary phage therapy

Infection at time 0 by 1.0×10^7 bacteria

Treatment at H2
(1.0×10^8 pfu)

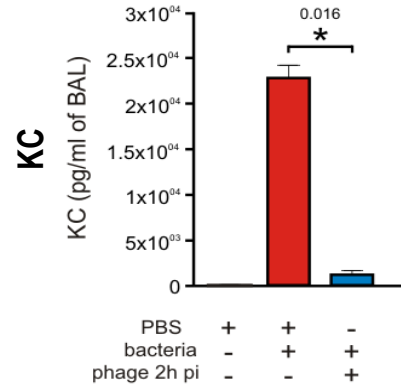
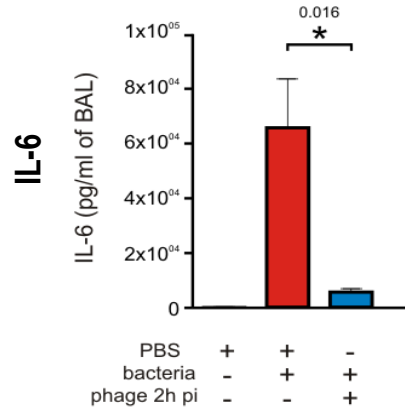


Lungs content 20H post-infection



Bacteria ↘

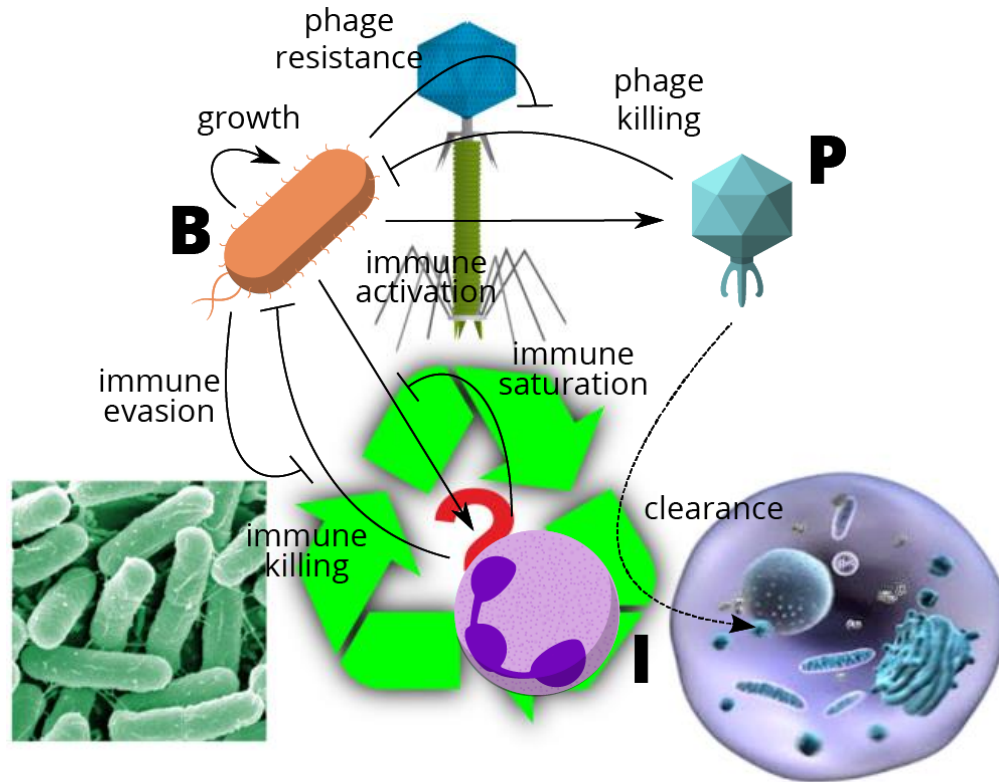
Bacteriophages ↗



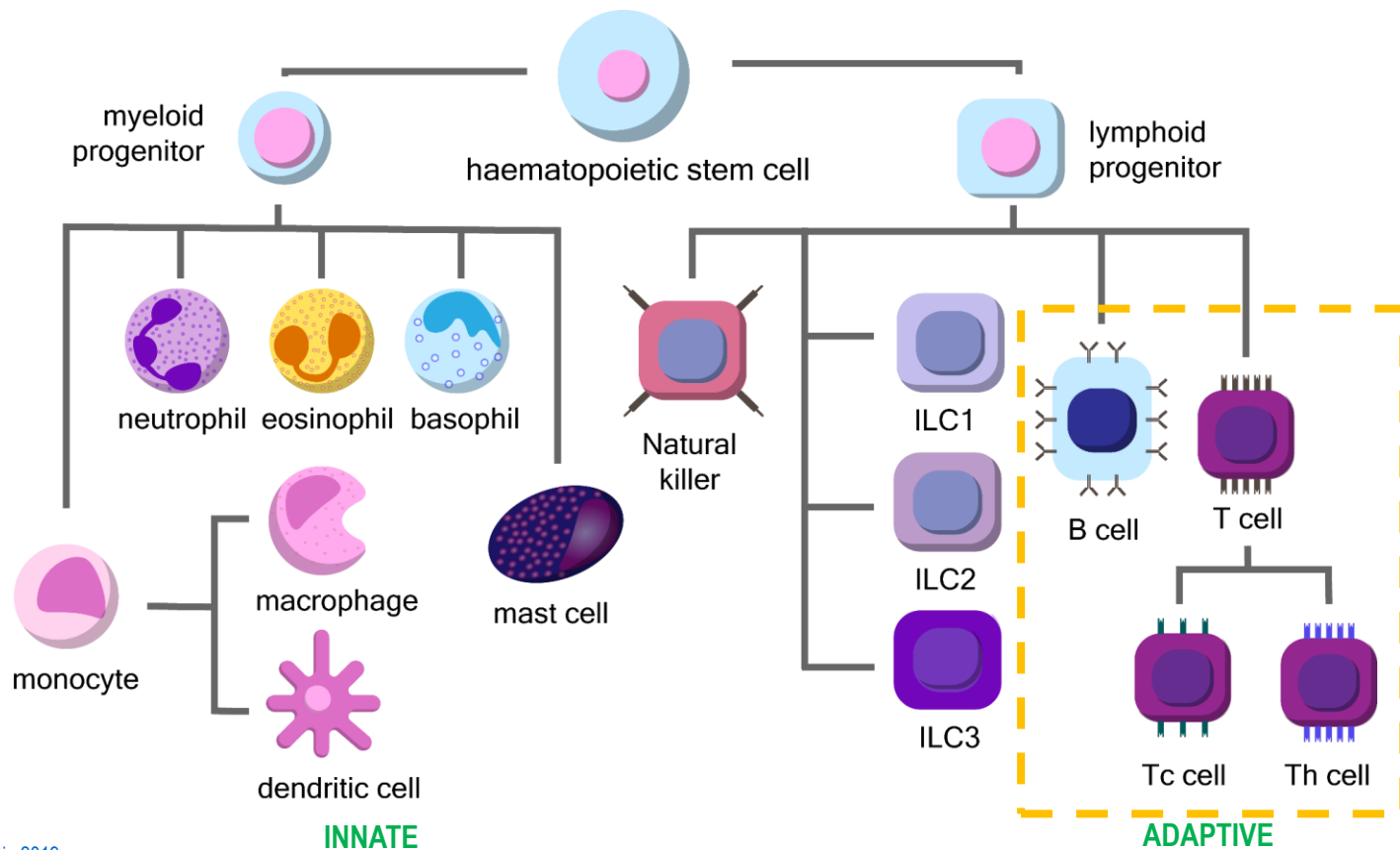
Inflammation ↘

Survival ↗

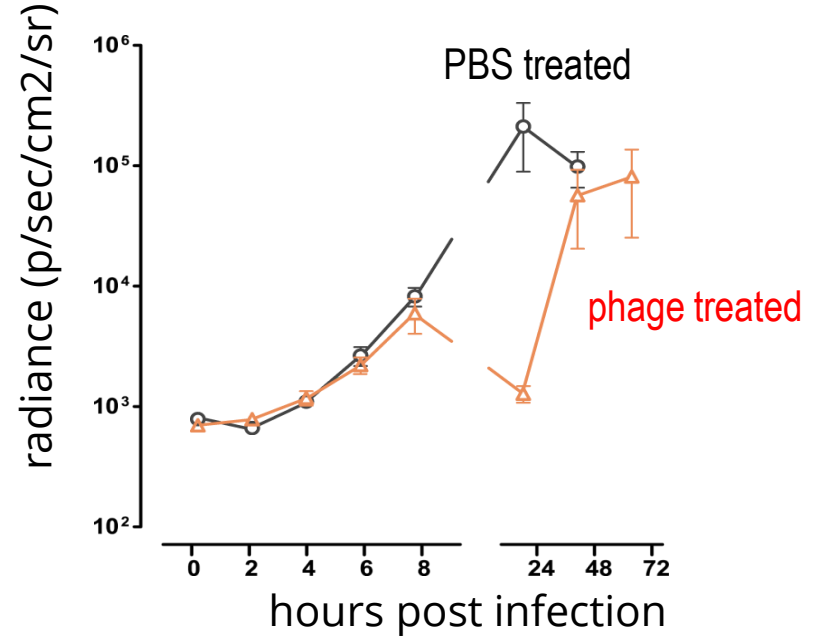
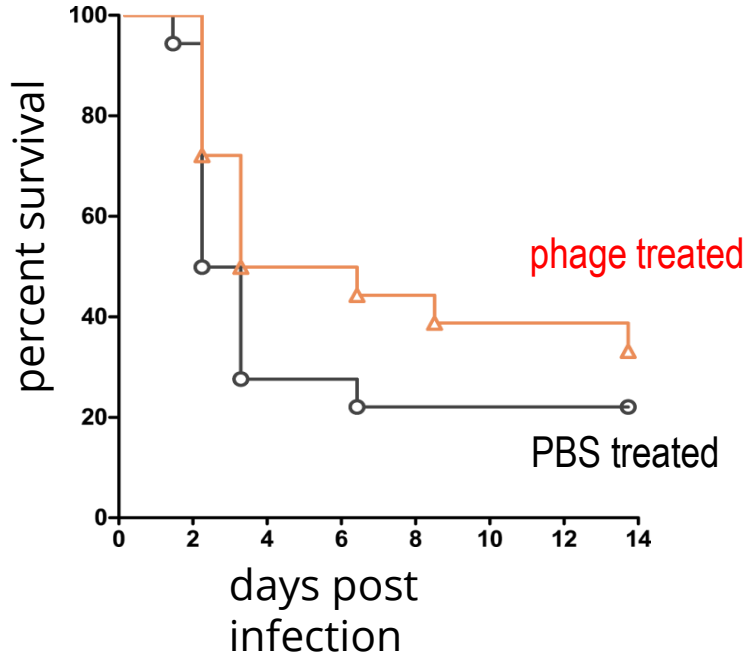
Are phages doing the job alone ?



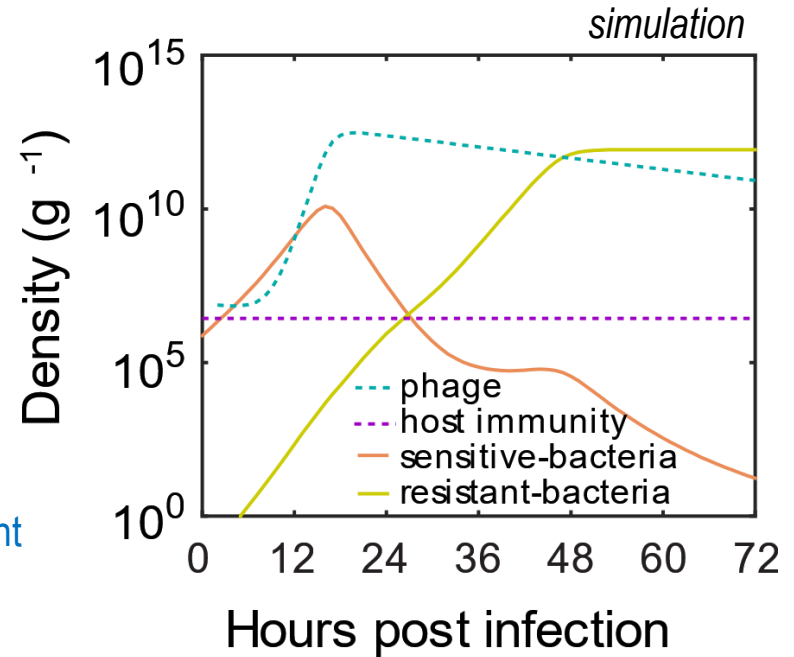
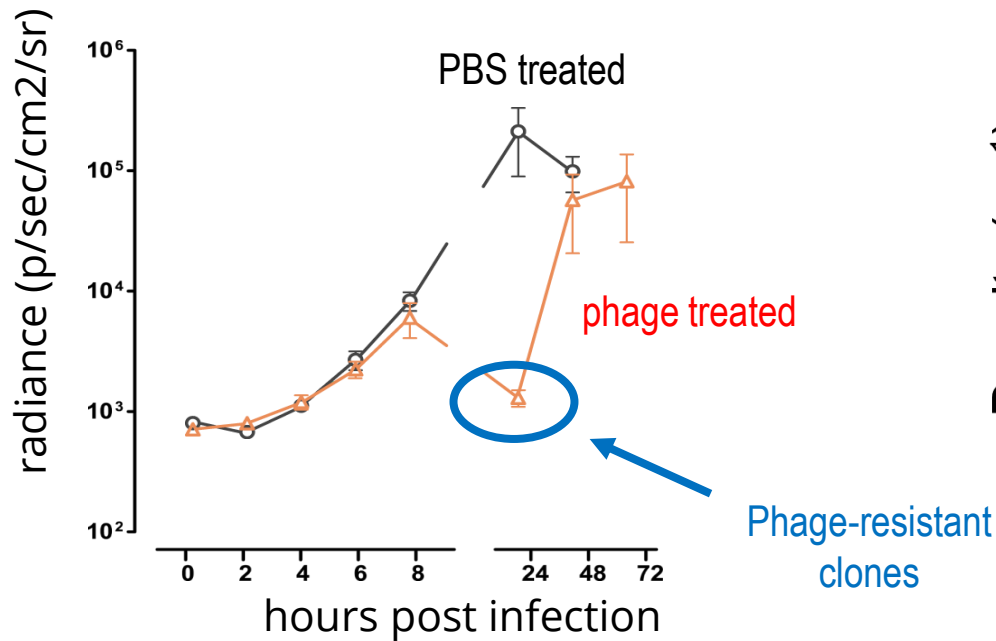
Is the immune system needed ?



Phage treatment failed in Myd88^{-/-} mice

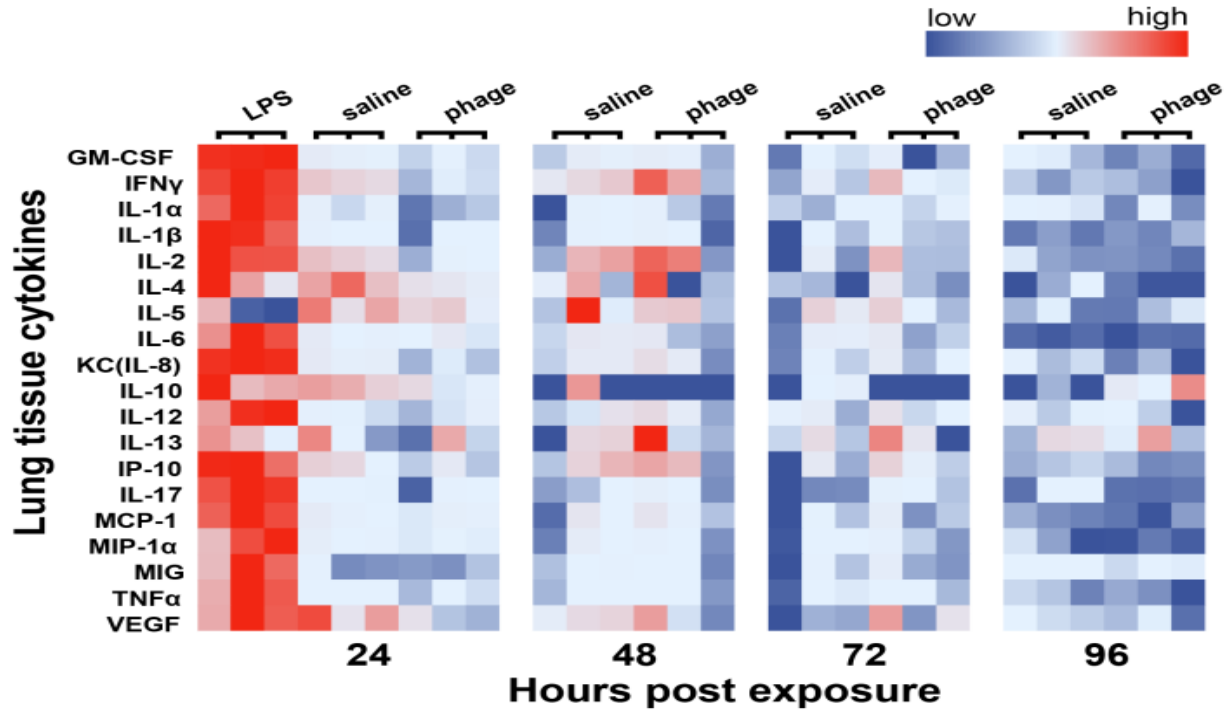


Failure is caused by phage-resistant bacteria



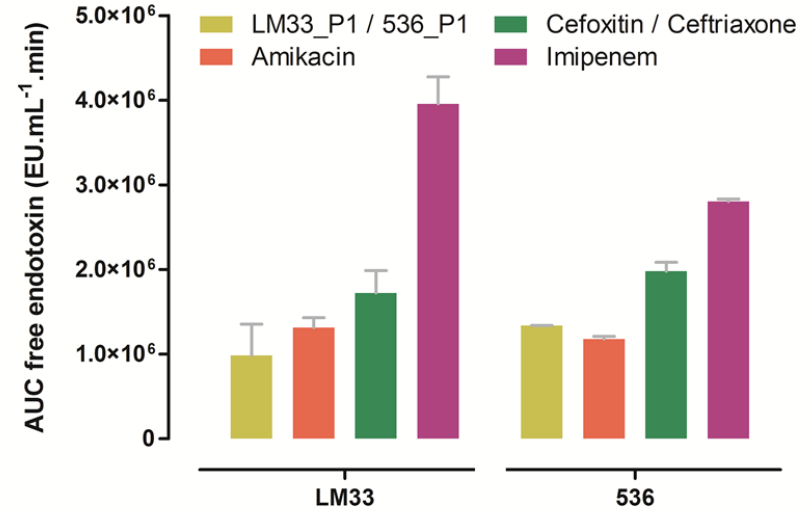
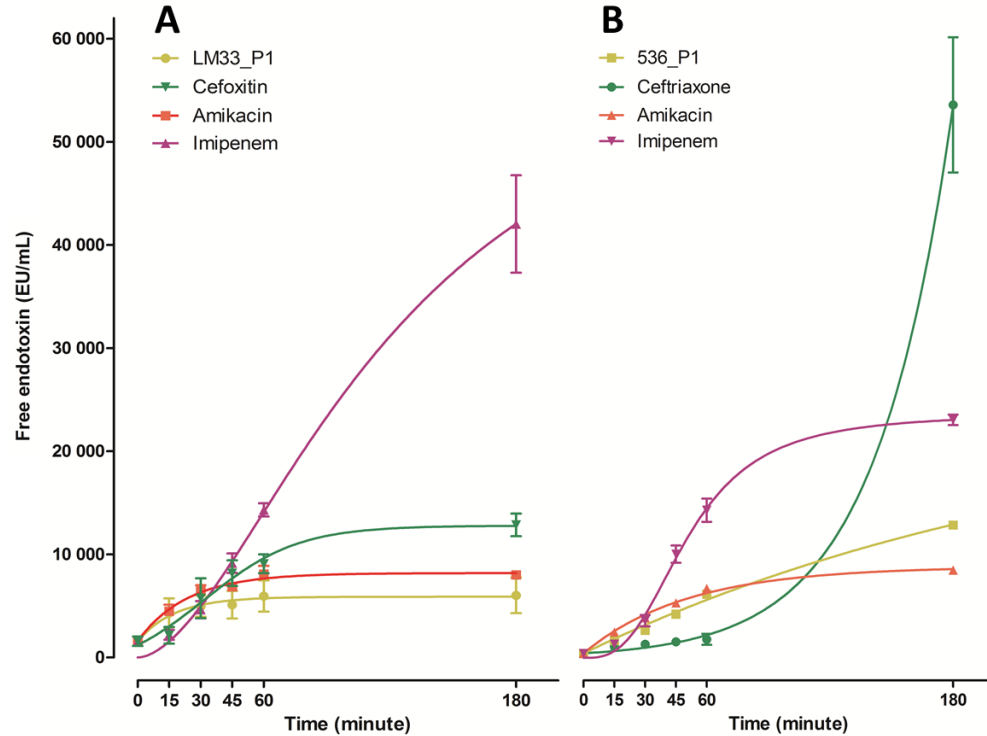
Phage therapy efficacy relies on immunophage synergy

Are phages safe ?



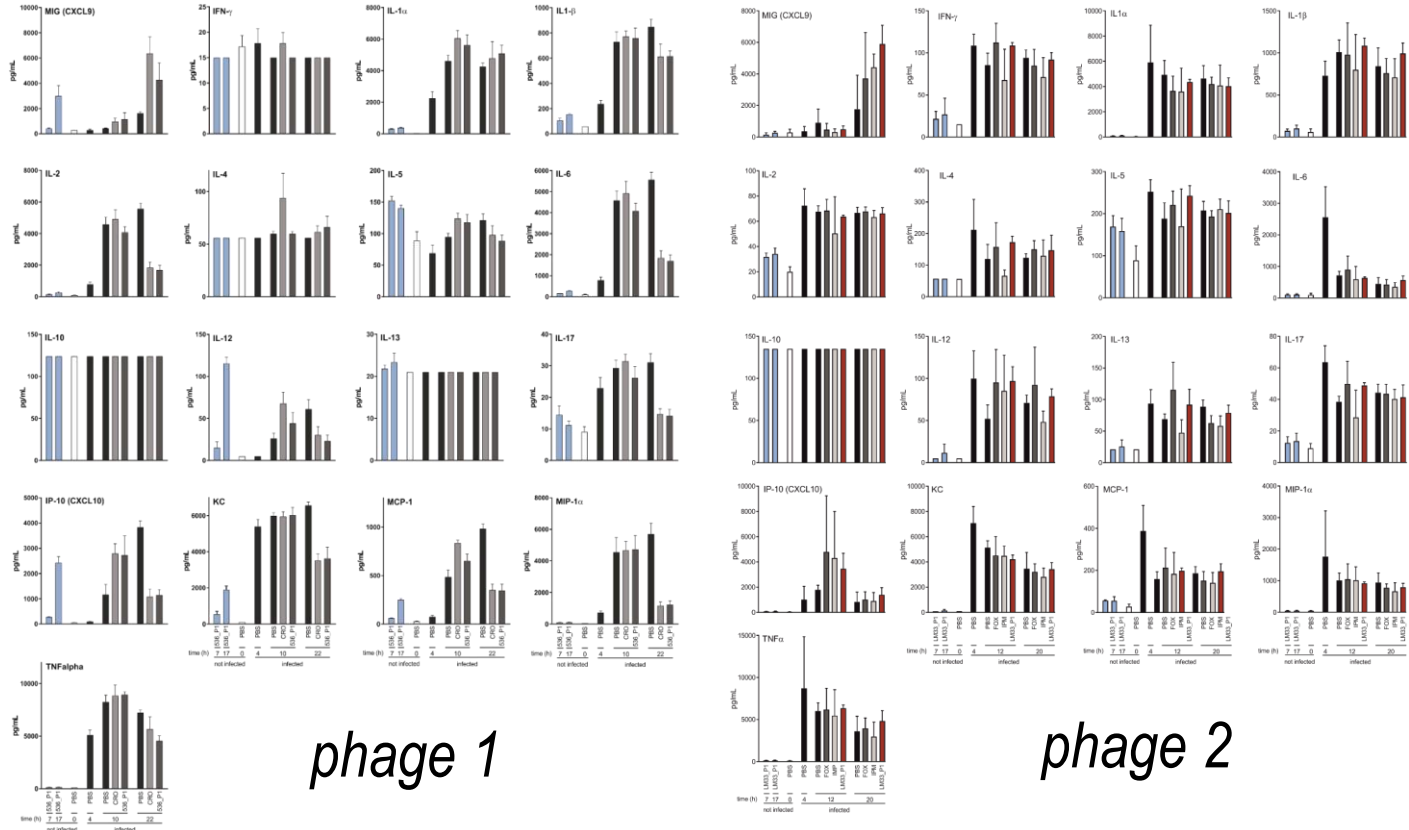
No induction of cytokines in lungs over time (10 times higher dose)

Phages release less endotoxins than β -lactams



Are phage treatments increasing cytokines ?

2 phages tested,
17 markers:
No specific signal



phage 1

phage 2

Compassionate treatments are increasing

BRIEF COMMUNICATION

<https://doi.org/10.1038/s41591-019-0437-z>

nature
medicine

Engineered bacteriophages for treatment of a patient with a disseminated drug-resistant *Mycobacterium abscessus*

Young teenager, CF, lung transplanted because of *M. abscessus* AR. After transplantation, *M. abscessus* comes back, then phages were administered IV 2/day during 3 months ! She is now back to school !!!

Host Bacterium Bacteriophage Interactions Team



Lorenzo CHAFFRINGEON (M2)

Raphaëlle DELATTRE (MD-PhD)

Quentin LAMY-BESNIER (PhD)

Mathieu De JODE (PhD)

Baptiste GABORIEAU (MD, M2)

Marta LOURENÇO (PhD)



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International Society for

Viruses of Microorganisms

www.isvm.org



Phages.fr

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Next Annual Meeting in GRENOBLE

October 8 and 9, 2019