Neue Horizonte

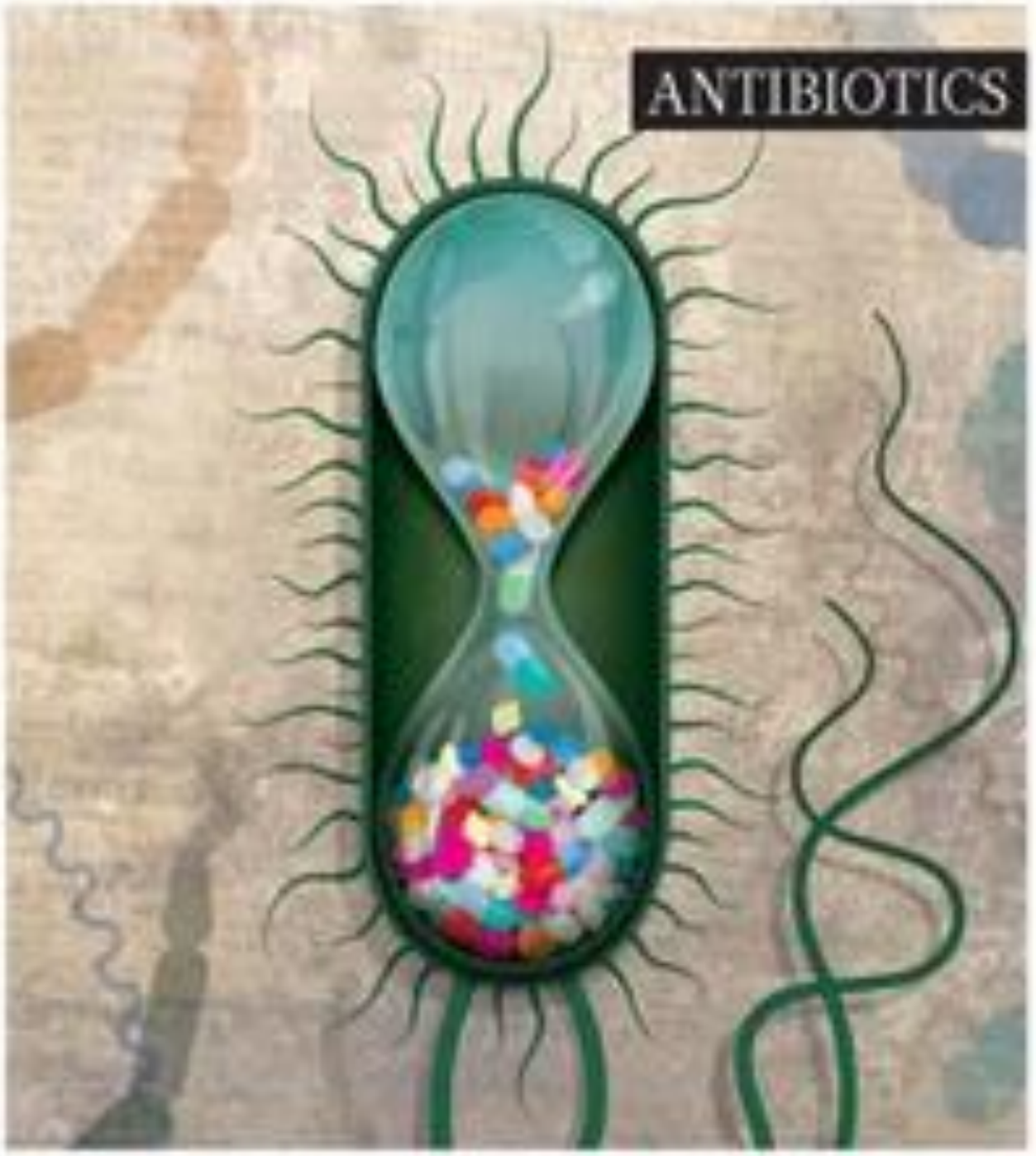
Ueberwindung von Antibiotikaresistenz

Thilo Köhler

Hôpitaux Universitaires Genève

UNIVERSITÉ DE GENÈVE

Trendtage Gesundheit Luzern, 25-26.3.2026



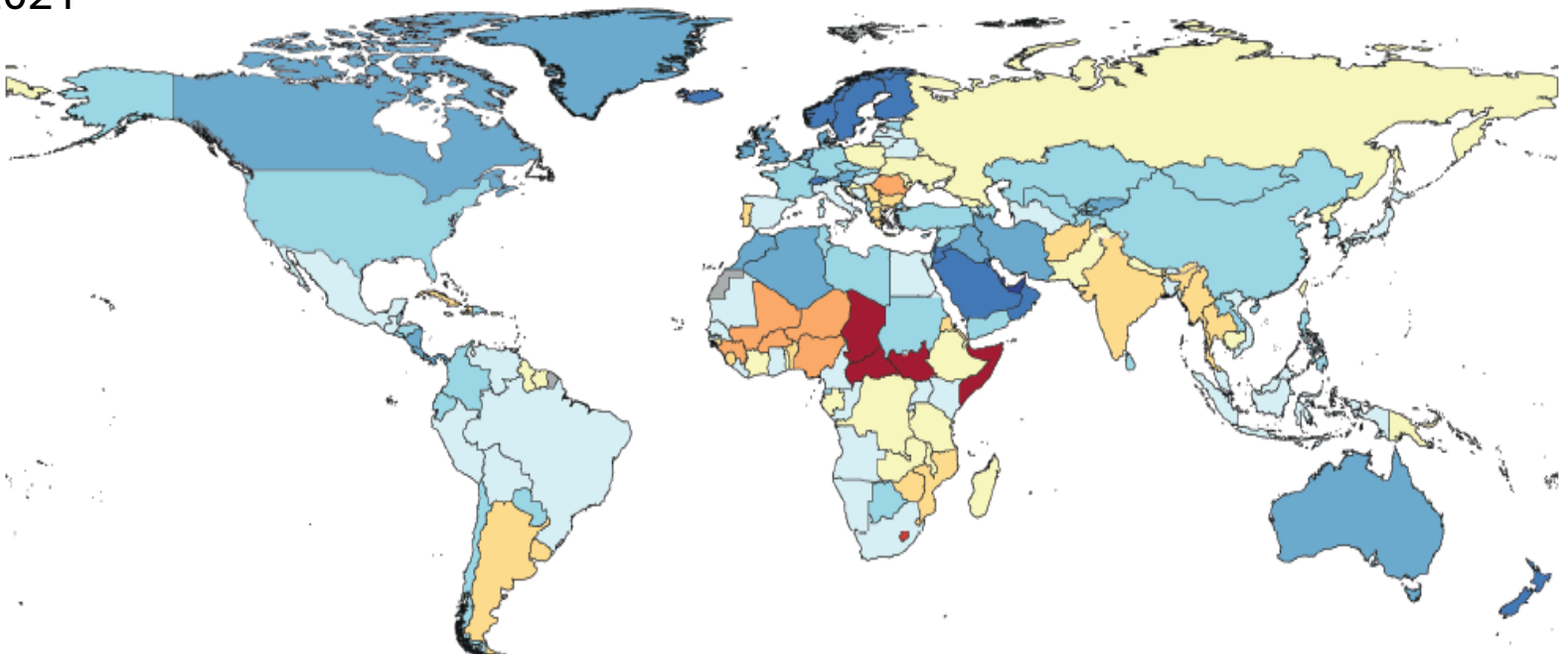
Antimicrobial resistance (AMR)

1.2 M deaths worldwide were directly attributable in 2019 to AMR

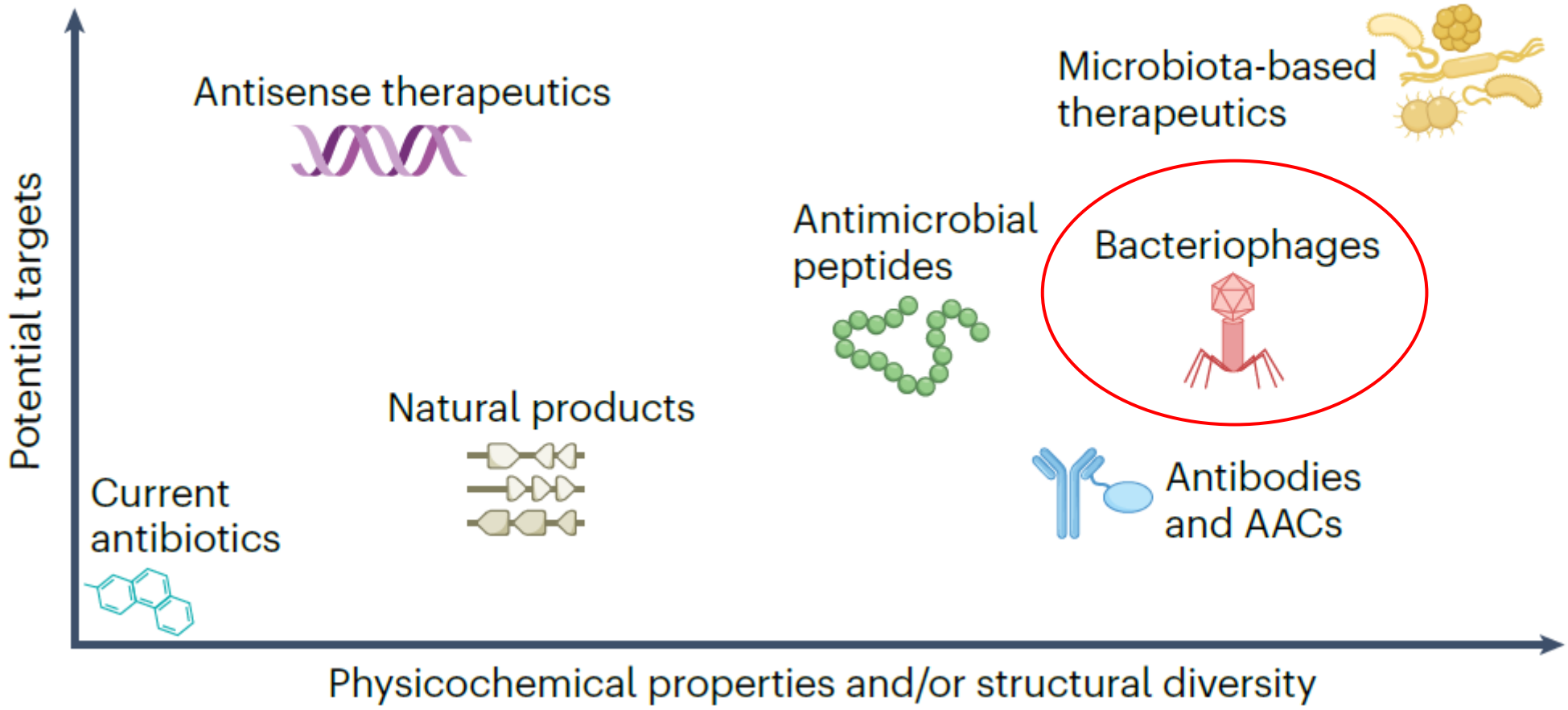
Numbers are expected to increase due to

- **lack of novel Ab classes**
- **increase of risk groups**
- **misuse in agriculture**

2021



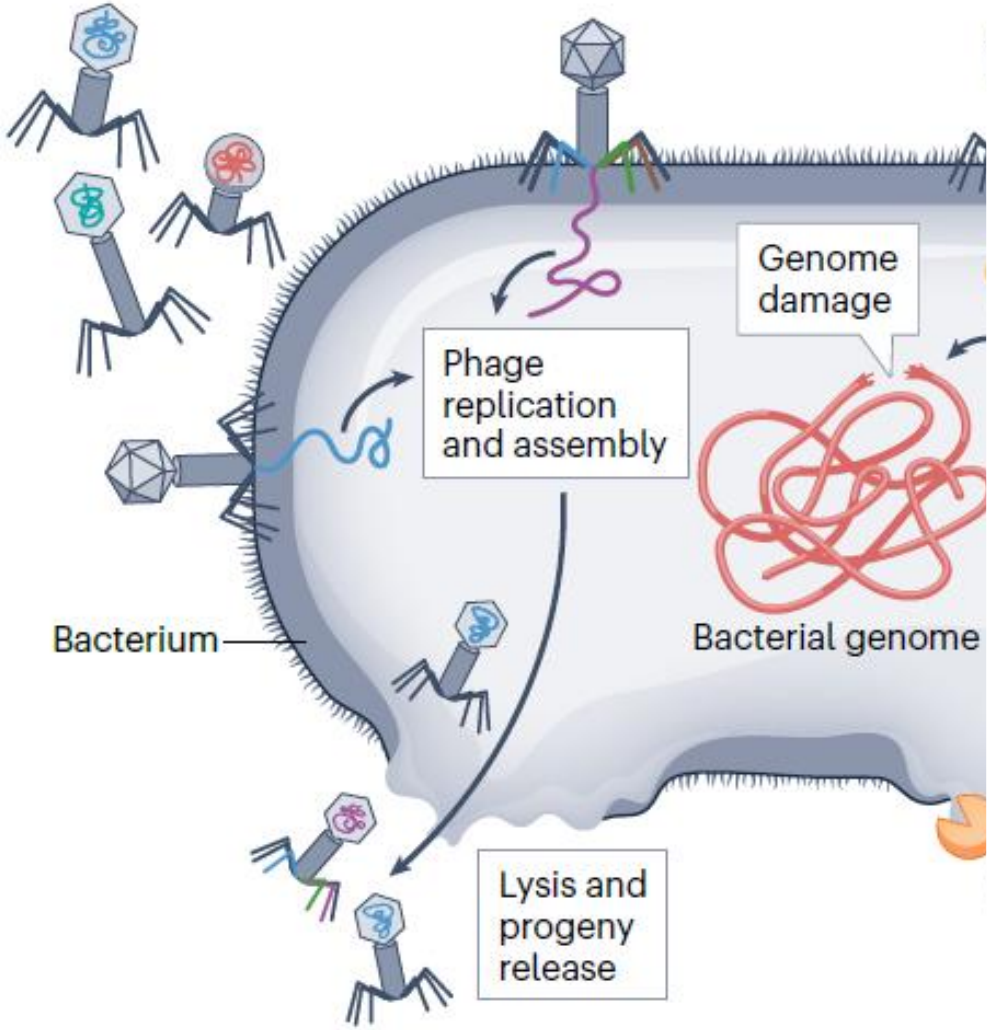
Alternatives to antibiotics



Nat Rev Microbiol., **2023**

Bacteriophages :
natural predators of bacteria

Bacteriophages:
personalized therapeutics

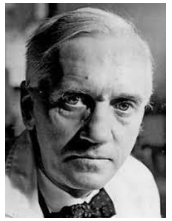


Nat Rev Microbiol., **2023**

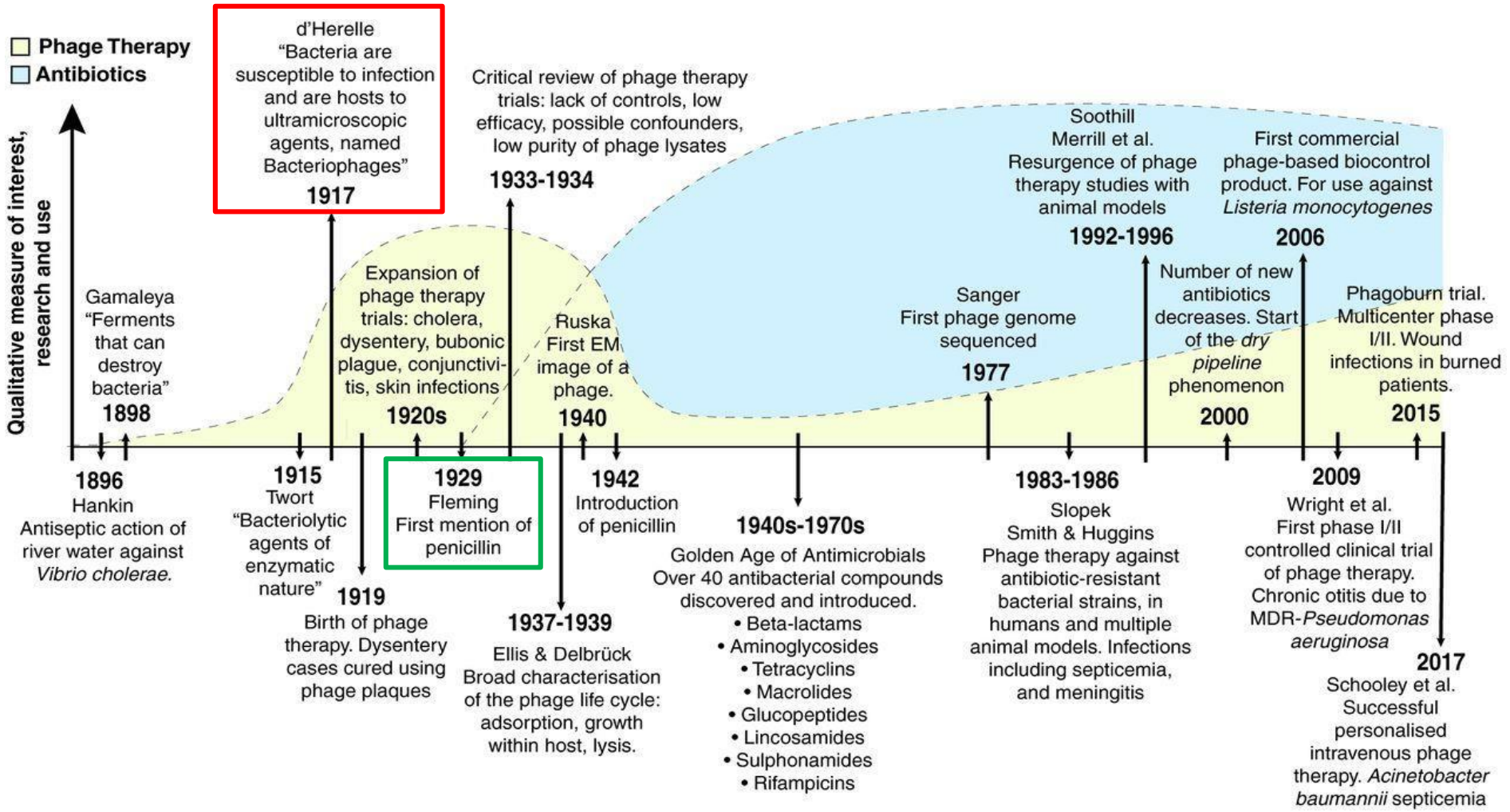
Phagotherapy and antibiotics discovery



F. d'Hérelle



A. Fleming

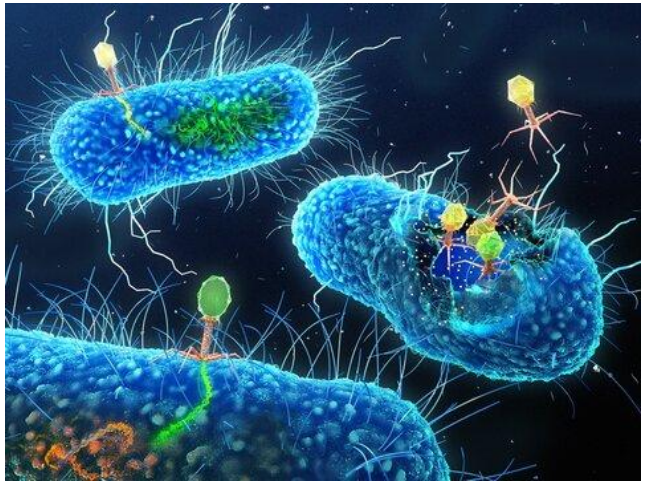


Clin Microb Rev **2019**;32:e00066-18

Advantages and limitations of phage therapy

Advantages

- phages active on **MDR bacteria** (and potentially on biofilm growing bacteria)
- strain specific and should thus **not affect the microbiota**
- phage replication is **self-limiting**
- application as highly **personalized medicine**



Limitations

- prior **isolation of bacterial isolate** required for phage screening
- risk for **transfer of antibiotic resistance** or virulence genes
- emergence of **resistance to phage**
- generation/presence of neutralizing **phage antibodies**

Viruses **2024**; 16:478

Applications for phage therapy in human medicine

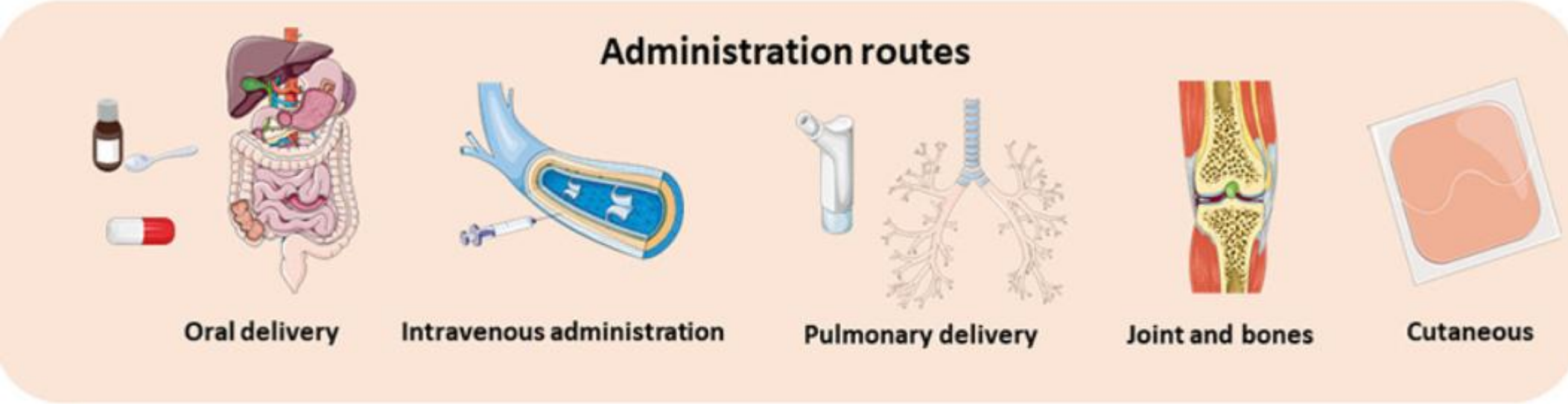


Systemic

Chronic lung infections
- COPD
- CF

Surgical device

Wound infections
- Burn-
- Chronic



Briot et al., J Contr Rel, 2022

Clinical efficacy of phage therapy

Case studies



100 consecutive phage therapies in Europe*

<u>Clinical outcome</u>:

Clinical improvement:	**77 %** (88/114)
Eradication of targeted bacteria:	**61 %** (65/106)
Clinical improvement w/o eradication:	**17 %** (18/106)

minor adverse effects in 7 patients

*All phages offered free of charge by QA Military Hospital, BEL

Nat. Microbiol., 2024

Clinical trials



Burn patients (*P. aeruginosa*)
multicenter study (F, BEL, CH)
Technical issue with phage titers

Lancet Infect Dis **2019**;19:35

Urinary tract infection (several bacteria)
Balgrist Hospital ZH (patients in Georgia)
Not superior to placebo irrigation

Lancet Infect Dis **2021**; 21:427

Acute diarrhea (*E. coli ETEC*)
Bangladesh
No benefit

EbioMedicine **2016**;4:124

Chronic otits (*P. aeruginosa*)
Clear benefit

Clin Otolaryngol **2009**;34:349

Failure likely due to non-target phages

The Geneva experience: personalized phage therapy



Hôpitaux Universitaires Genève

UNIVERSITÉ DE GENÈVE

- 41-year-old
- Kartagener's syndrome, tetraplegic due to traumatic C7-D1 fracture
- Chronic lung-colonization since 2018 by *Pseudomonas aeruginosa*
- Hospitalized at HUG in 2019
- 6 months on continuous iv antibiotic treatment
- Emergence of MDR *P. aeruginosa*

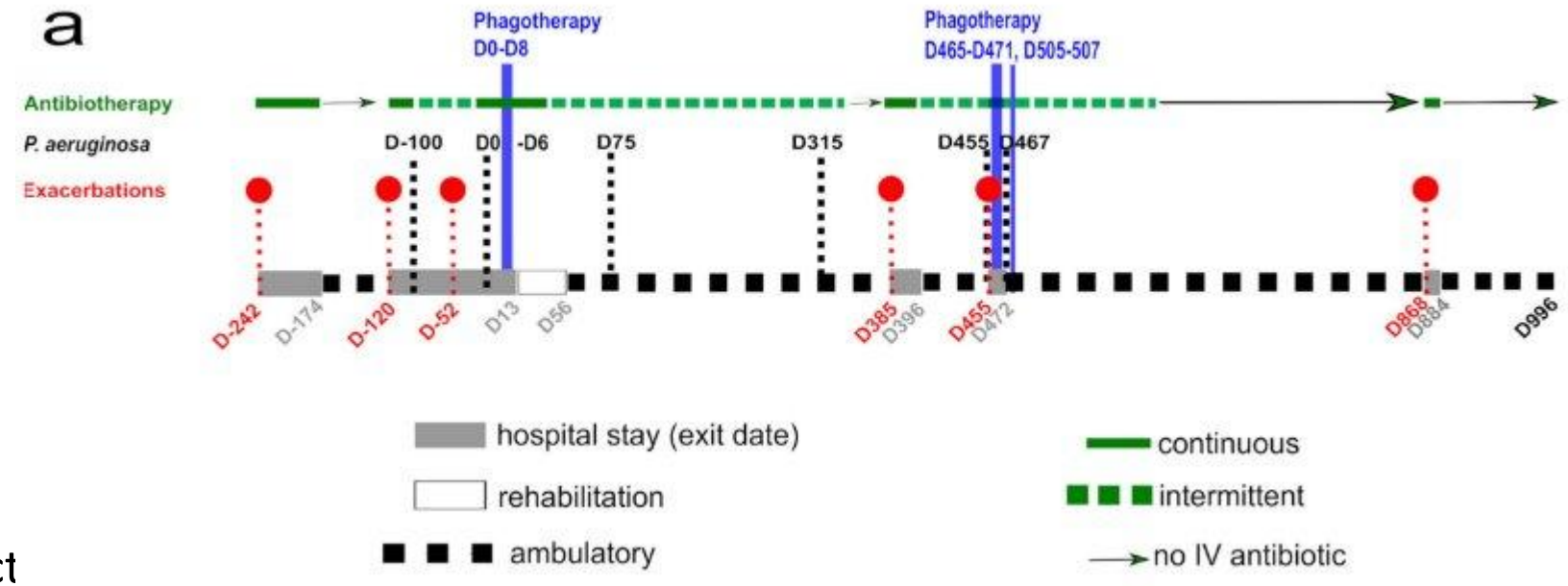
ANTIBIOGRAMMES	(1)x1 Pseudomonas aeruginosa
Piperacilline	RESIST.
Piperac.+tazob	>32 R
Ceftazidime	>16 R
Ceftazidime-Avibactam	4 .
Ceftolozane+tazobactam	8 R
Cefepime	>16 R
Ceftobiprole	>4 .
Imipenem	32 R
Meropeneme	32 R
Doripenem	>8 R
Ertap?nem	4 R
Aztreonam	RESIST.
Amikacine	>32 R
Gentamicine	RESIST.
Tobramycine	RESIST.
Ciprofloxacine	8 R
Levofloxacine	>8 R
Co-trimoxazole	2 R
Fosfomycine	>32 .
Tig?cycline	>4 R
Colistine	2 S

Personalized compassionate (experimental) phage treatment

Nat Commun **2023**; 14 :3629

Phage treatment and outcome





Outcome:

- rapid clinical improvement :
  - decreased sputum product
  - improved oxygen saturation
- left hospital after first phage therapy on intermittent iv antibiotics
- decrease of lung consolidations
- progressive stop of iv antibiotics
- resumed professional activity after 2nd phage therapy one year later

Nat Commun **2023**; 14 :3629

Hurdles and (regulatory) limitations

HEALTH AND HEALTHCARE SYSTEMS

This regulatory shift is unlocking alternatives to antibiotics in the fight against superbugs

Oct 30, 2025

Do you prefer your phage cocktail with or without GMP flavor ?



Classical antibiotic based thinking:

- Animal model > clinical phase 1-3 studies
- Single molecule with defined dosages
- GMP production is standard
- Defined administration protocol
- Drug monitoring possible



Acknowledgements

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Alexandre Luscher
Klara-Isabell Garbe

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Truong-Thanh Pham
Diego Andrey



ETH zürich

A. Harms

S. McCallin and the phage therapy group

and the patients for their support and confidence !

Yale University

B. Chan

FELIX BIOTECHNOLOGY

R. McBride

CHUV Centre hospitalier universitaire vaudois

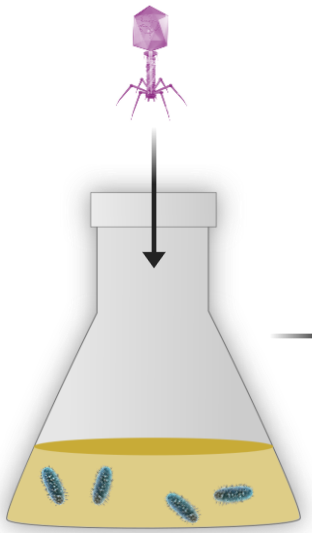
G. Resch

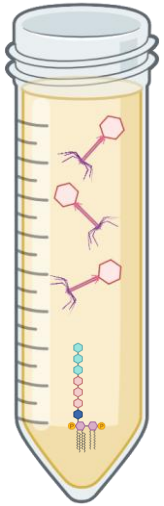
Queen Astrid Military Hospital

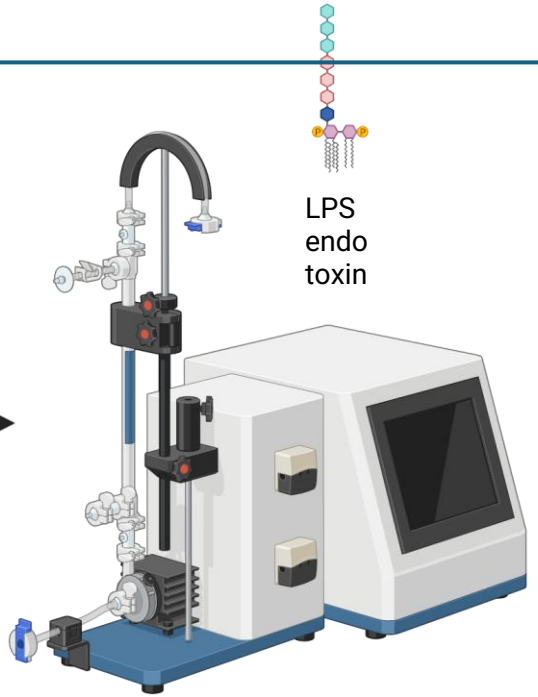
FNSNF
FONDS NATIONAL SUISSE DE LA RECHERCHE SCIENTIFIQUE

Phage production for therapies

Cell-based

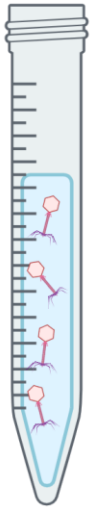


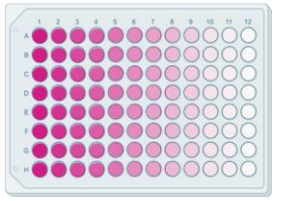




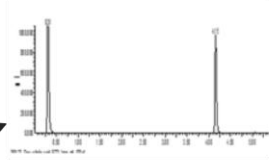
LPS
endo
toxin

Retentate





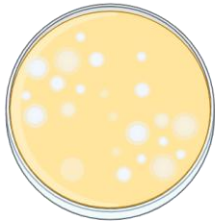
Endotoxin quantification kit



DOC measurement by
LC-QDa



Sterility test



Phage Titer

Cell-free









Search for lytic phage on patient's last available isolate

Hôpitaux Universitaires Genève



Centre hospitalier universitaire vaudois

G. Resch

PHAGE FUTURES EUROPE
Phage Therapy at Belgium's Queen Astrid Military Hospital
Phage Directory

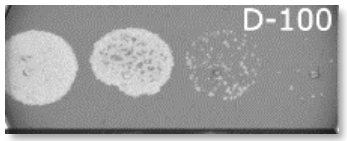
S. McCallin

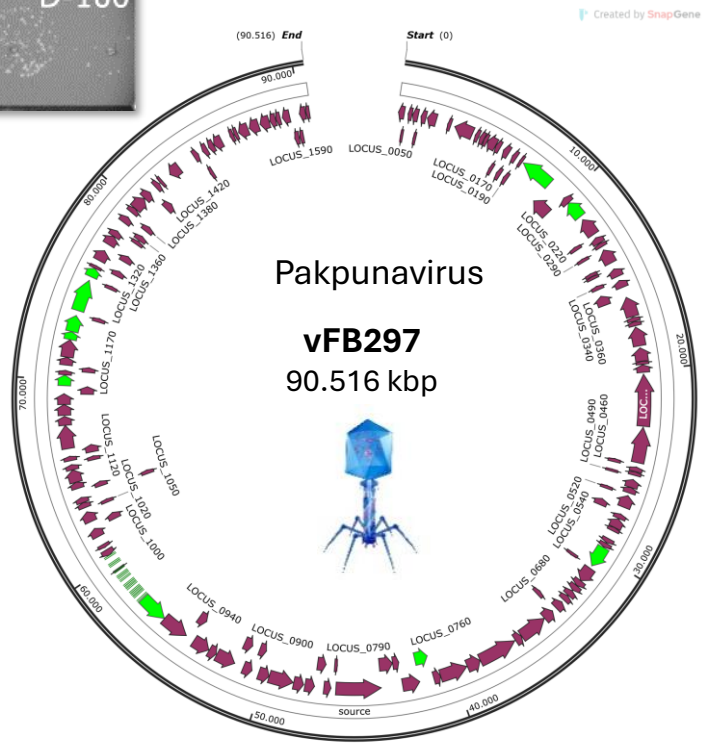
R. McBride

FELIX BIOTECHNOLOGY

Yale University

B. Chan





Nat Commun **2023**; 14 :3629

Host immune response to phage therapy



- Animal studies
  - Phages are subject to immune system clearance



- Phages do not replicate in human cells
  - $CD8^+$ T-cell response likely not significant



- Phagocytic cells process phage antigens
  - $CD4^+$ T-cell response leading to antibody production



- Preexisting phage-specific antibodies in patients never exposed to phages

JID **2023**; 227:311