VIRUSES TO FIGHT AGAINST BACTERIA!?

BACTERIOPHAGES AND PHAGE THERAPY

GREGORY RESCH

CENTER FOR RESERCH AND INNOVATION IN CLINICAL PHARMACEUTICAL SCIENCES (CRISP)
LAUSANNE UNIVERSITY HOSPITAL (CHUV)

GREGORY.RESCH@CHUV.CH

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

BACTERIOPHAGES
FUNDAMENTALS

BACTERIOPHAGES?

Félix d'Hérelle
1917

Coccobacillus acridiorium

LE COCCOBACILLE DES SAUTERELLES

par F. D'HERELLE

I

LES SAUTERELLES

Historique. — De tout temps, les sauterelles ont été considérées comme un véritable fléau. Tous les pays tropicaux et subtropicaux en souffrent périodiquement, et si, maintenant, grâce à la facilité des échanges, la faim et son cortège obligé d'épidémies peut être évitée, les pertes matérielles sont souvent très élevées, se chiffrant parfois à plusieurs centaines de millions.

La Bible, les historiens grecs, latins et arabes nous ont conservé le souvenir d'un grand nombre d'invasions suivies de

1914. Annales de l'Institut Pasteur

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

TITRATION OF A PHAGE SUSPENSION
DOUBLE-LAYER ASSAY (DLA)

SOFT AGAR
PHAGE @ ≠ DILUTIONS
+ SUSCEPTIBLE STRAIN

SOLIDIFIED GROWTH MEDIUM

TITRATION OF A PHAGE SUSPENSION
DOUBLE-LAYER ASSAY (DLA)

SOFT AGAR
PHAGE @ ≠ DILUTIONS
+ SUSCEPTIBLE STRAIN

SOLIDIFIED GROWTH MEDIUM

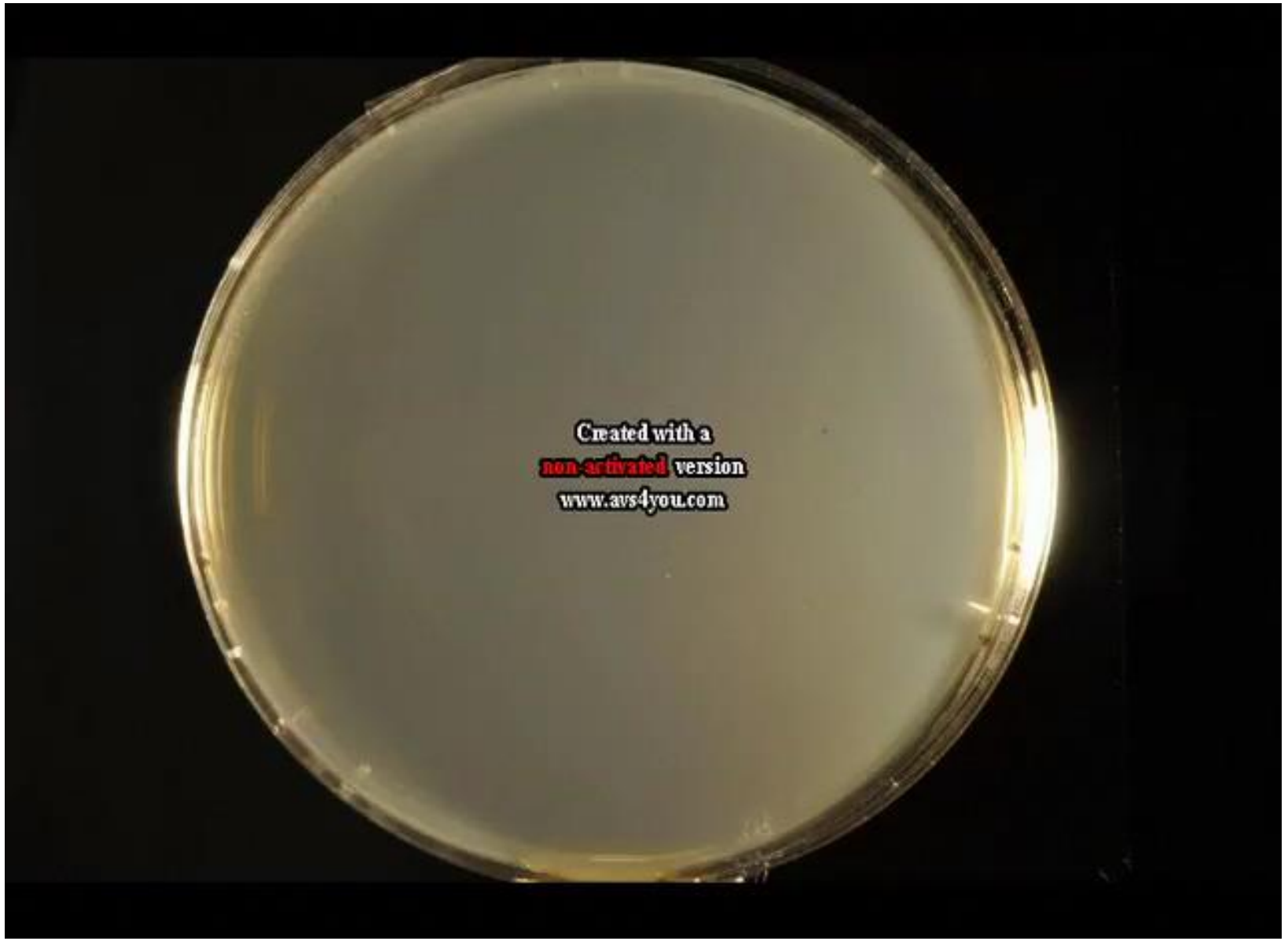
41 PFU x 10 (100µL DEPOSITED) = 410 PFU/mL
x 10^8 (DILUTION FACTOR) = **4.1x10^{10} PHAGES/mL**

PFU, Plaque Forming Unit

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

THE ANTIBACTERIAL POWER OF PHAGES

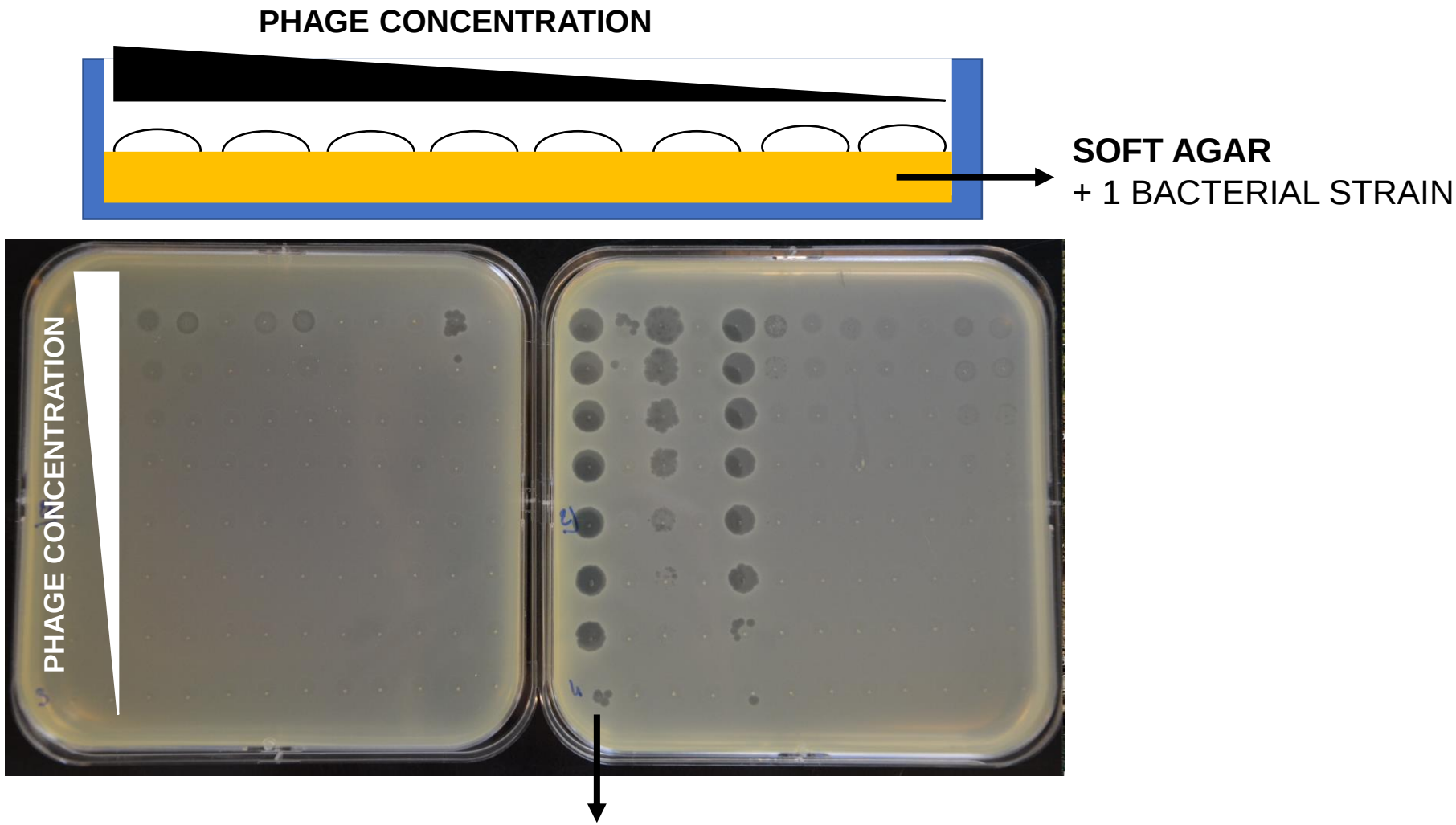


ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

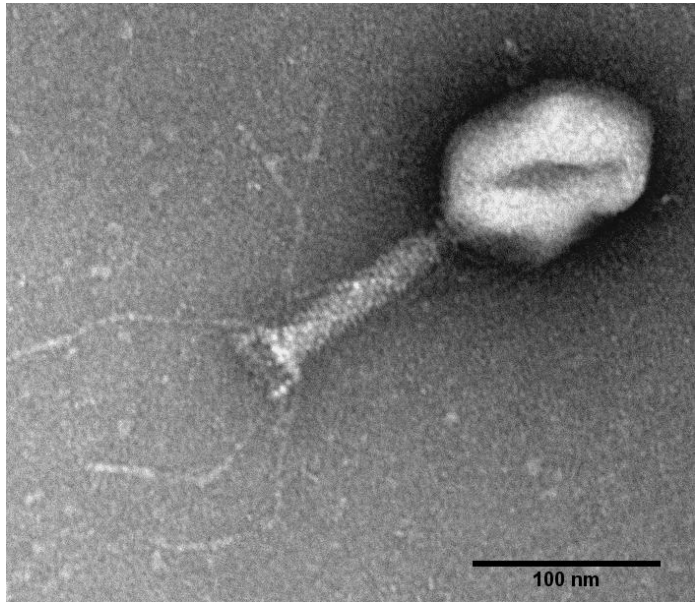
TITRATION OF A PHAGE SUSPENSION
DILUTED DROP TEST (DDT) – PHAGOGRAM (SOLID)

TITRATION OF A PHAGE SUSPENSION
DILUTED DROP TEST (DDT) – PHAGOGRAM (SOLID)



SO PHAGES ARE

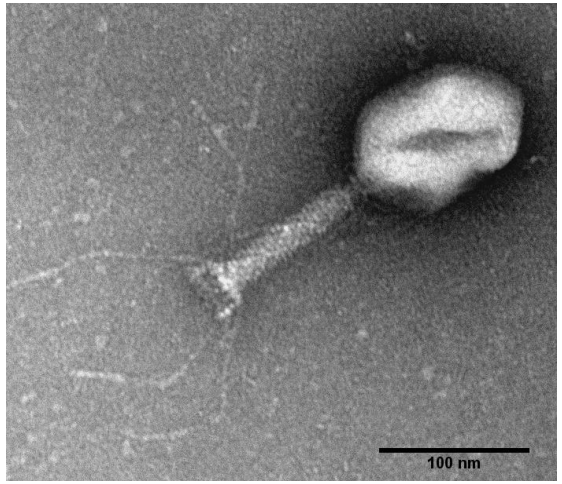
- BACTERIAL VIRUSES



AND HAVE

- HIGH SPECIES AND STRAIN SPECIFICITY

PHAGES ARE UBIQUITOUS



- 10^{31} PHAGES ON EARTH = MOST ABUNDANT BIOLOGICAL ENTITY
- $10^{15\text{-}16}$ IN A HUMAN BODY
- 10^{6}/ML IN SURFACE WATERS
- EVERYWHERE THERE ARE BACTERIA!
- MEAN SIZE = 100nm

PHAGES HAVE DIFFERENT SHAPES

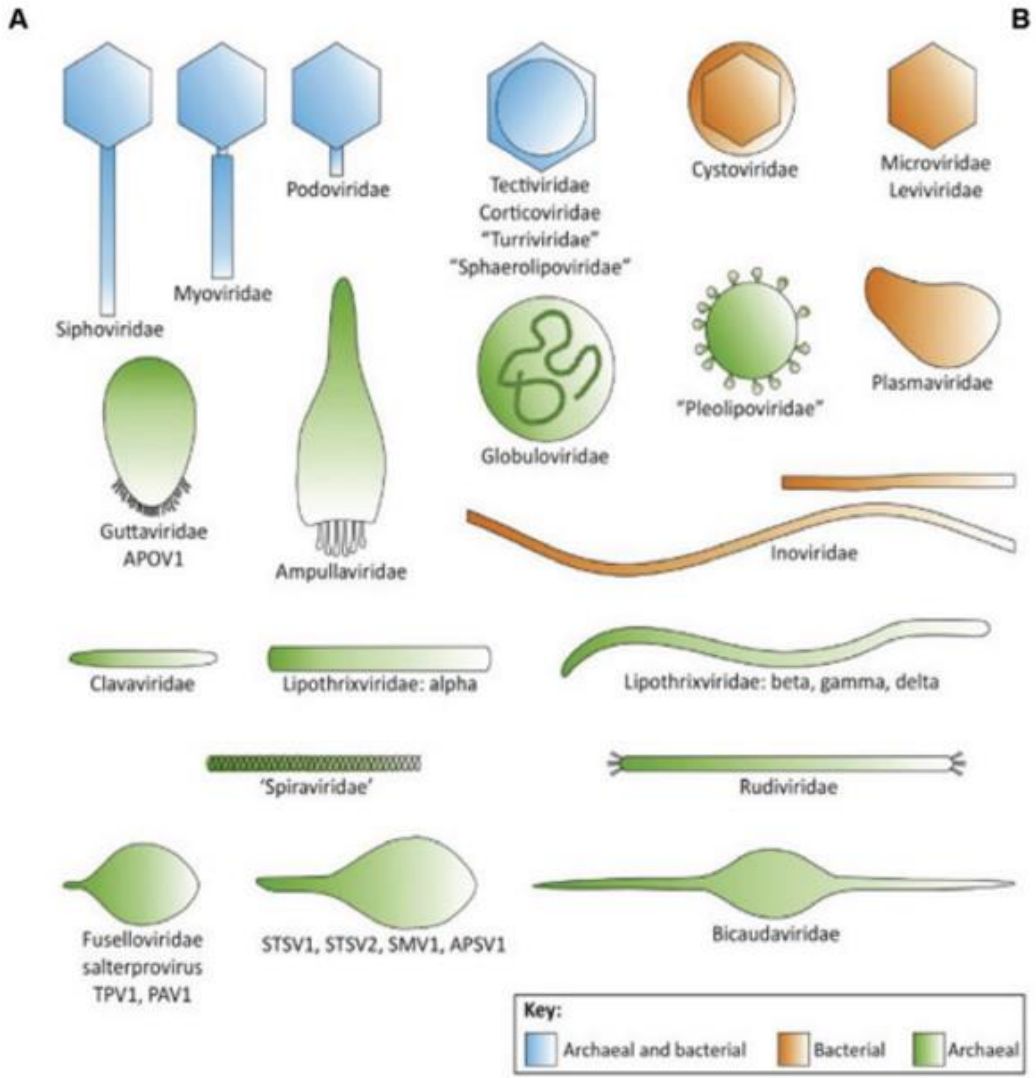


Figure 1.
(A) Representation of prokaryote bacteriophage morphotypes

Bacteriophages: Their Structural Organisation and Function
DOI: http://dx.doi.org/10.5772/intechopen.85484

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PHAGES HAVE DIFFERENT SHAPES

>95% OF PHAGES OBSERVED (>10'000) = *Caudovirales*

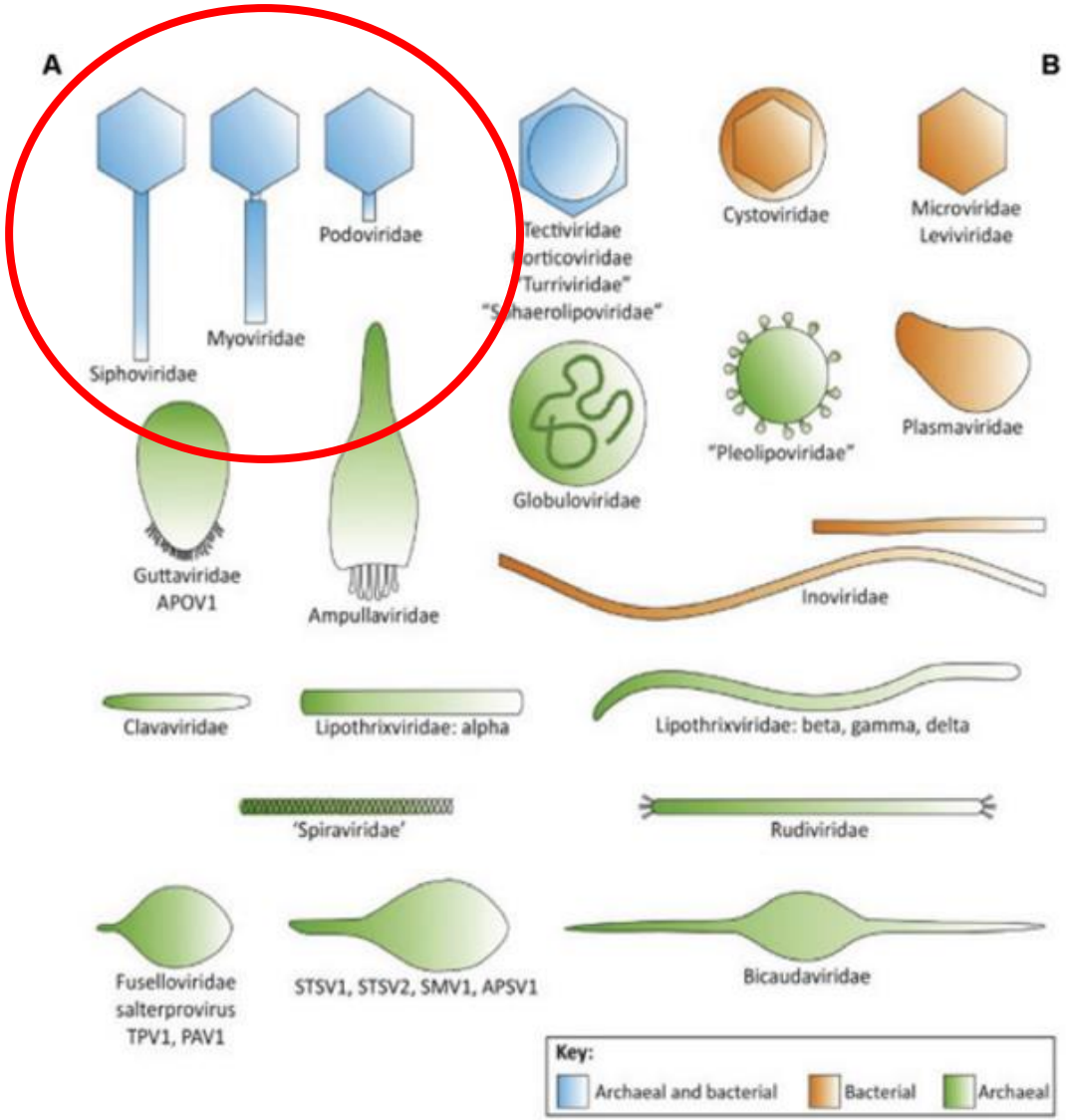


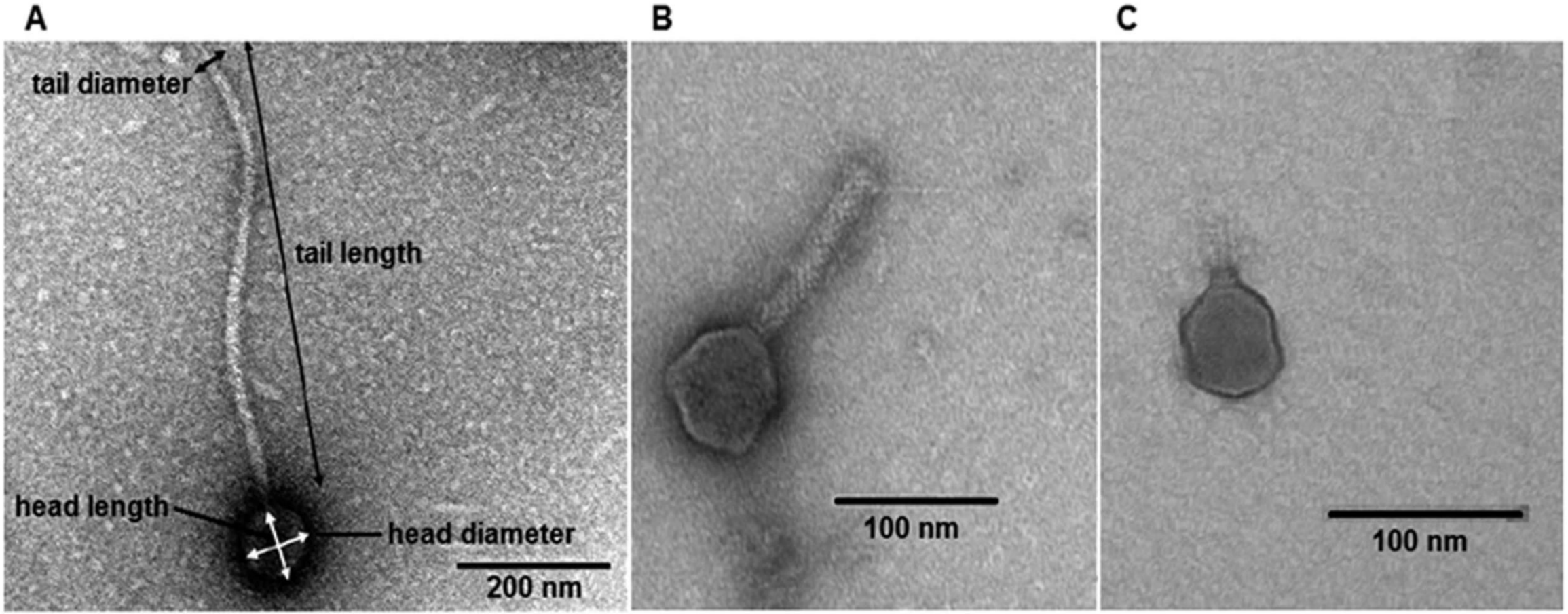
Figure 1.
(A) Representation of prokaryote bacteriophage morphotypes

Bacteriophages: Their Structural Organisation and Function
DOI: http://dx.doi.org/10.5772/intechopen.85484

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

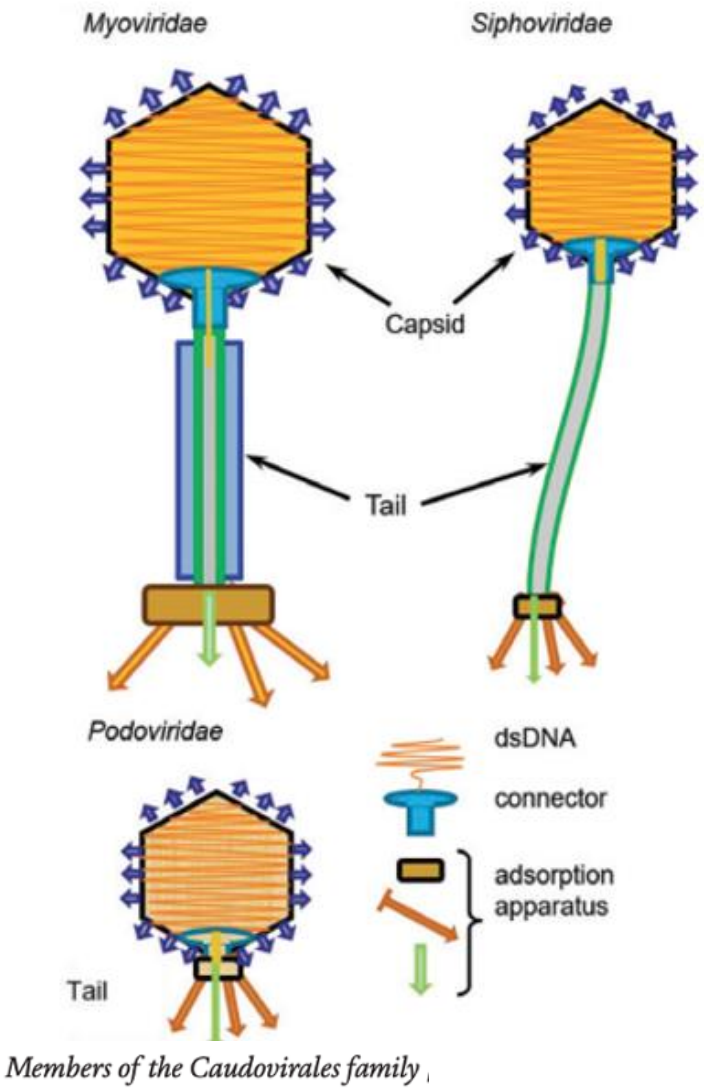
PHAGES HAVE DIFFERENT SHAPES



Examples of diversity of phage virions from the collection (**A** – *Siphoviride*, **B** –*Myoviridae*, **C** – *Podoviridae*).

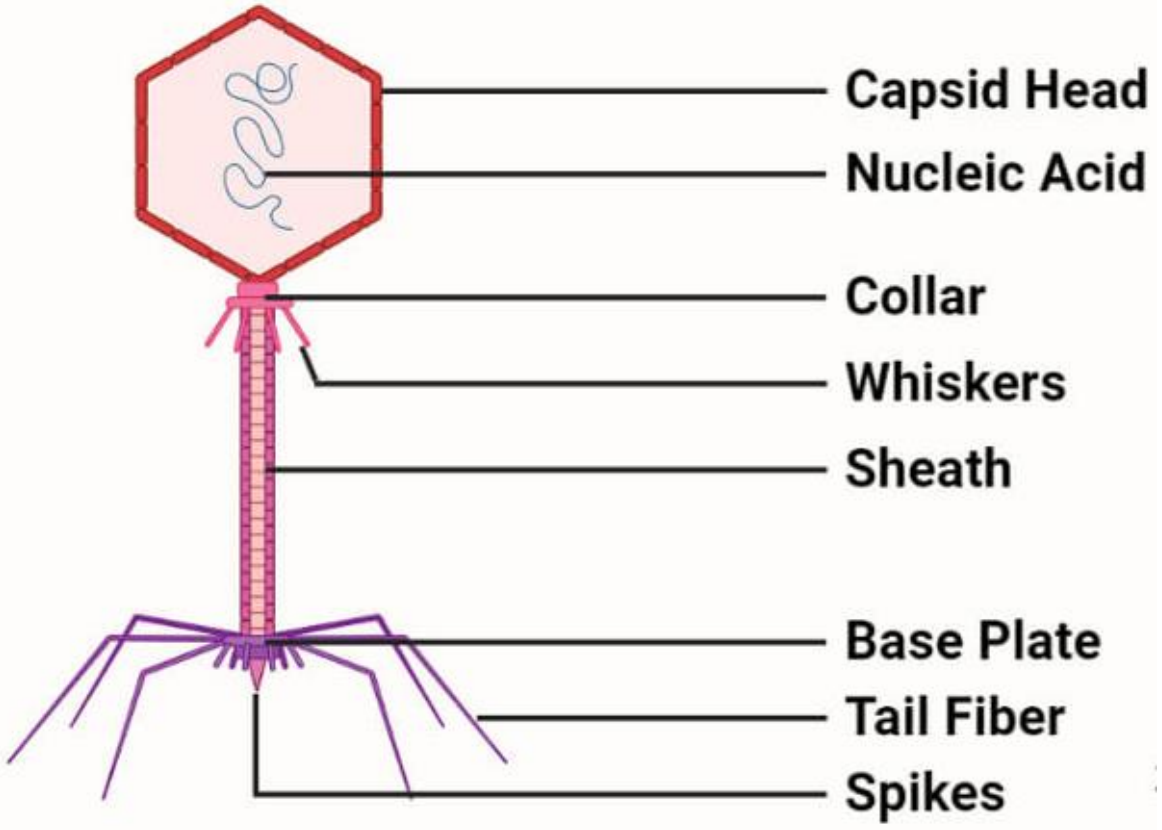
Jurczak-Kurek A. et al. 2016. Sci. Rep. 6, 34338.

COLIPHAGE T4 AS MODEL SYSTEM



Members of the Caudovirales family

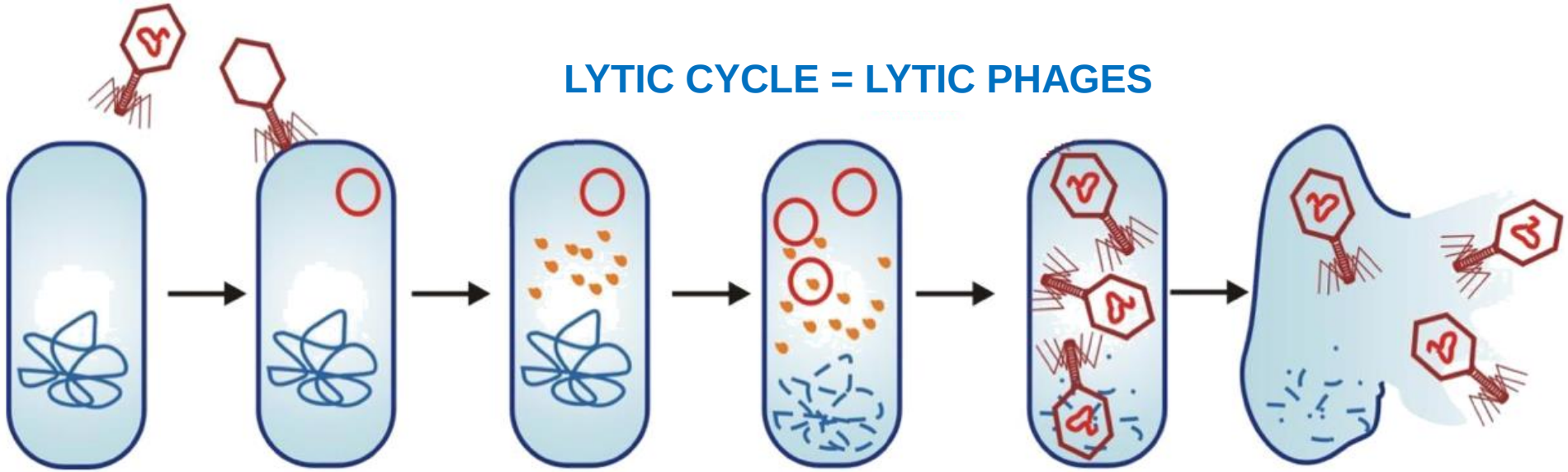
Bacteriophages: Their Structural Organisation and Function
DOI: http://dx.doi.org/10.5772/intechopen.85484



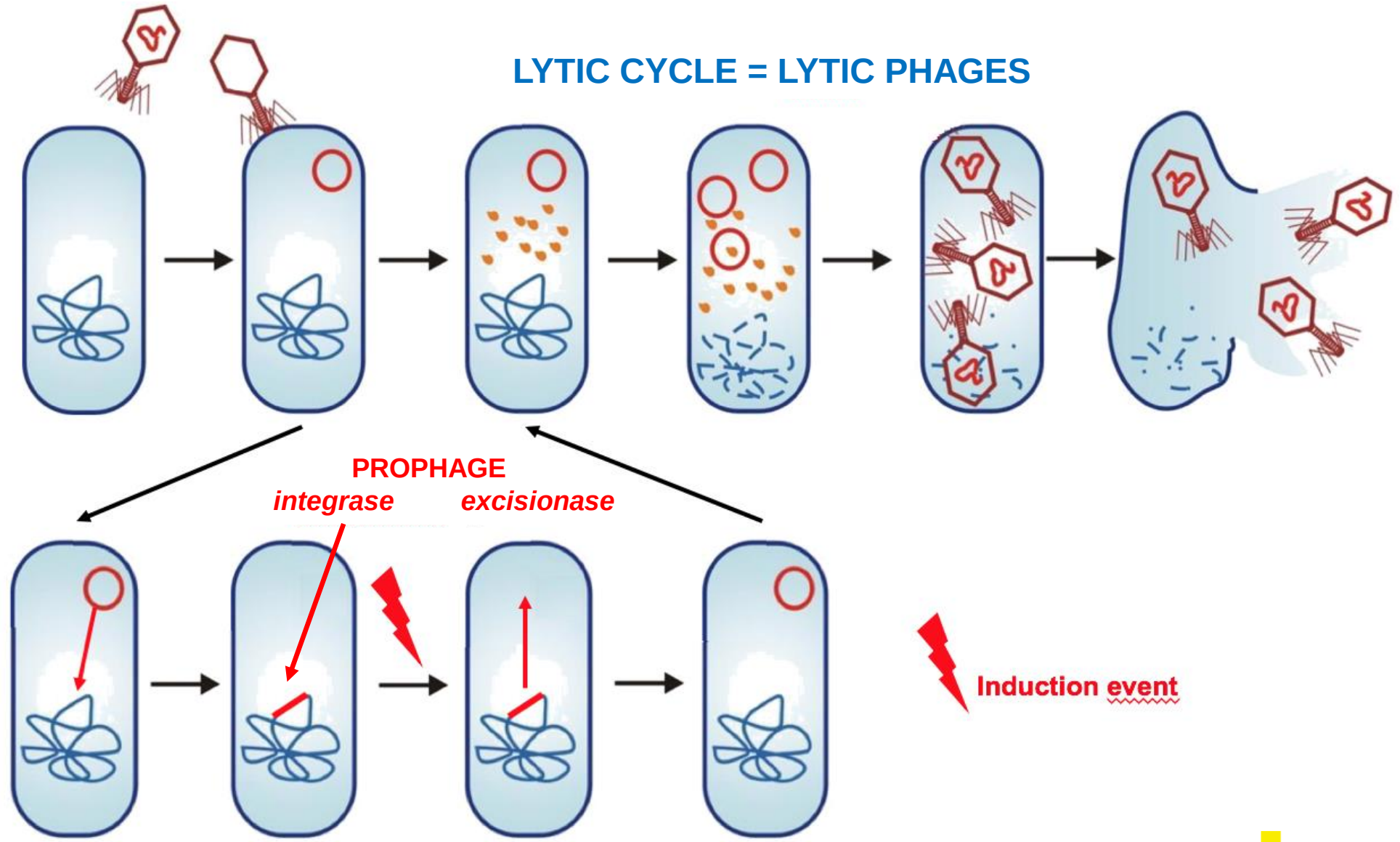
adapté de https://microbenotes.com/bacteriophage/

PHAGES LIFE CYCLES

LYTIC CYCLE



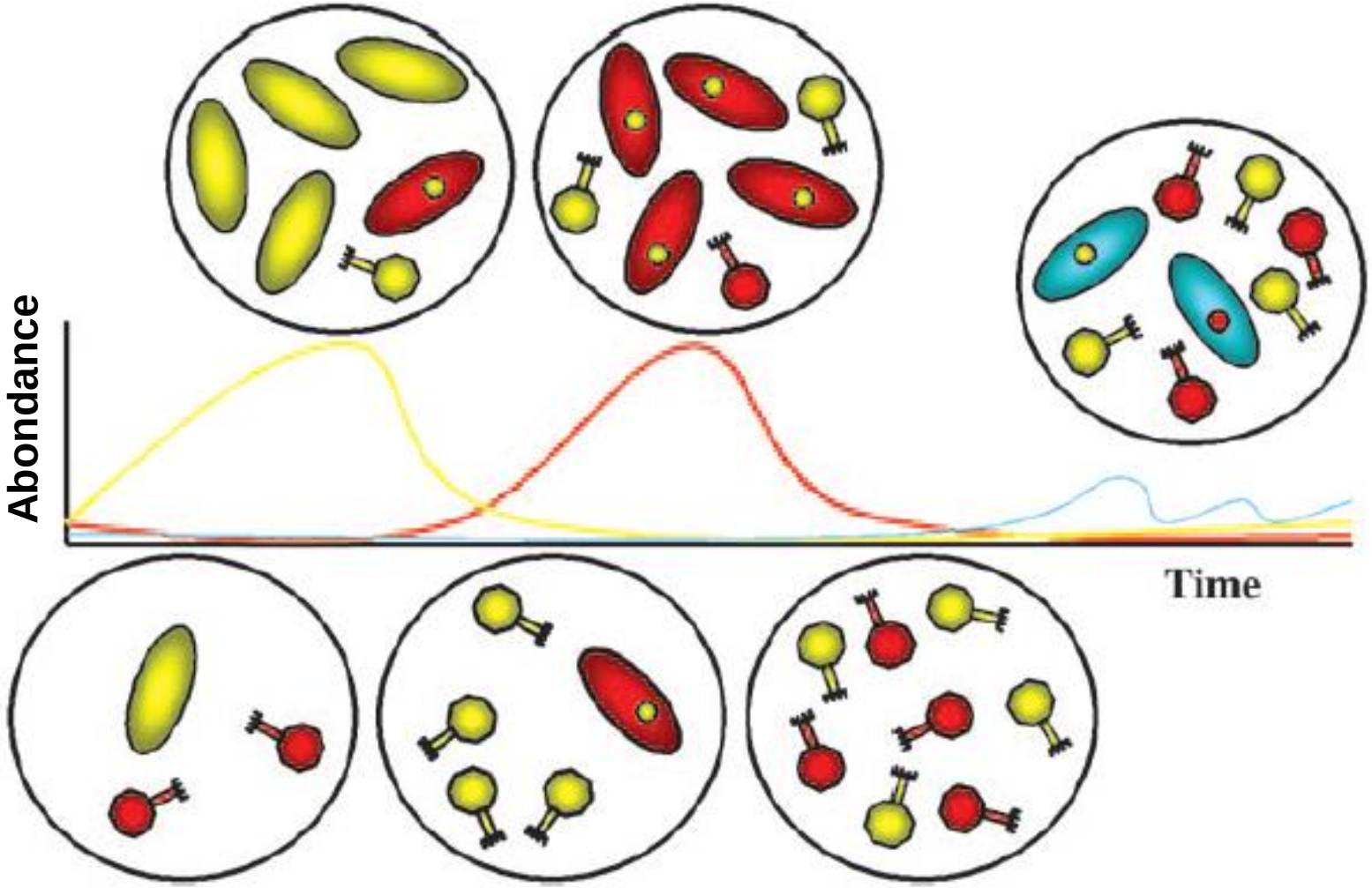
PHAGES LIFE CYCLES
LYTIC CYCLE AND LYSOGENIC CYCLE



LYSOGENIC CYCLE = LYSOGENIC OR TEMPERATE PHAGES

DYNAMICS OF PHAGES-BACTERIA INTERACTION

CO-EVOLUTION



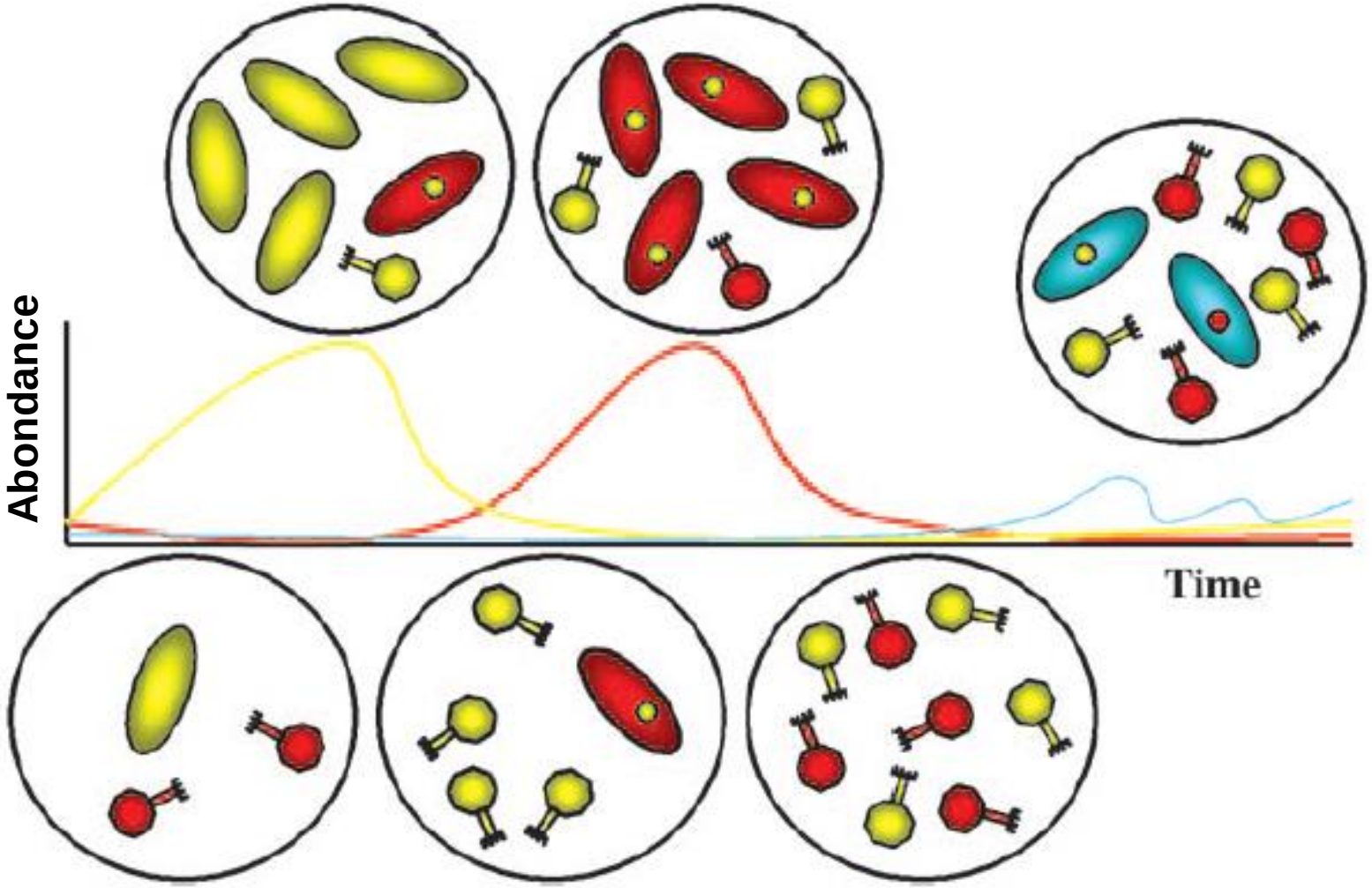
Faruque SM et al., PNAS, 2005 102 :6119–24

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

DYNAMICS OF PHAGES-BACTERIA INTERACTION

CO-EVOLUTION



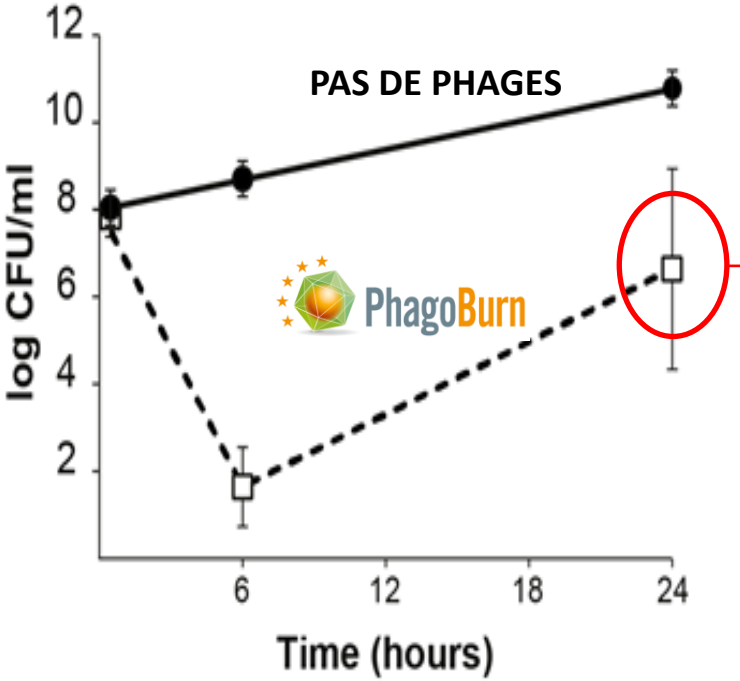
« KILL THE WINNER »

Faruque SM et al., PNAS, 2005 102 :6119–24

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

HOW DO BACTERIA RESIST TO PHAGES?
THE MAIN MECHANISM IN *PSEUDOMONAS AERUGINOSA*

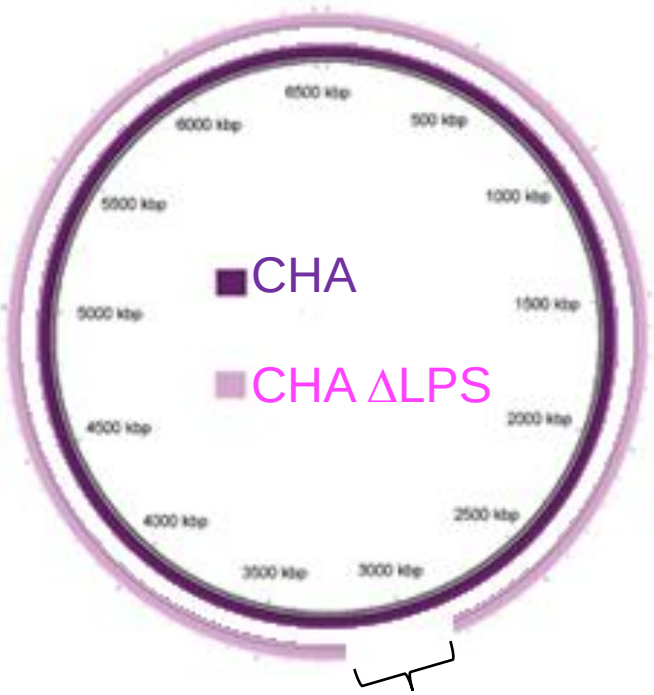


Oechslin F. et al., JID. 2017; 215(5):703-12

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

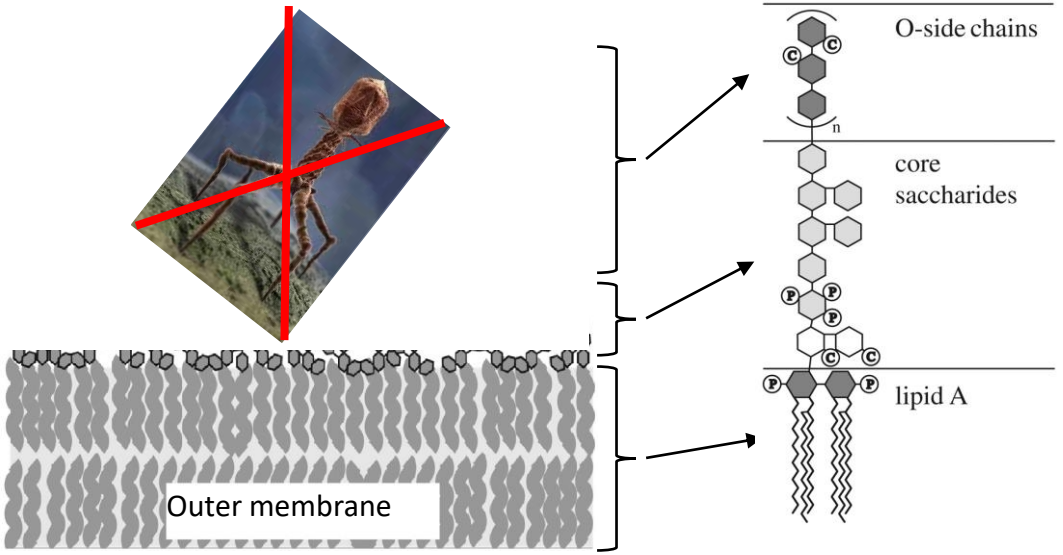
CHUV

HOW DO BACTERIA RESIST TO PHAGES?
THE MAIN MECHANISM IN *PSEUDOMONAS AERUGINOSA*

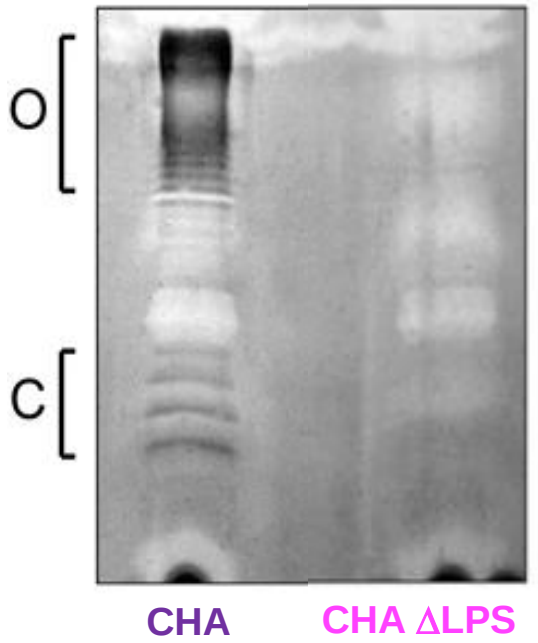


250kb
Δ*galU*

CHA ΔLPS



adapted from Schneck et al. 2009. J. R. Soc. Interface. Oct. 6;6: Suppl. 5:S671-8.

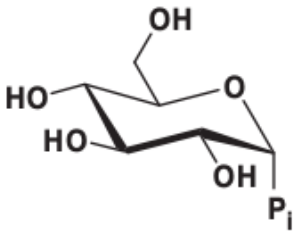


Oechslin F. et al., JID. 2017; 215(5):703-12

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

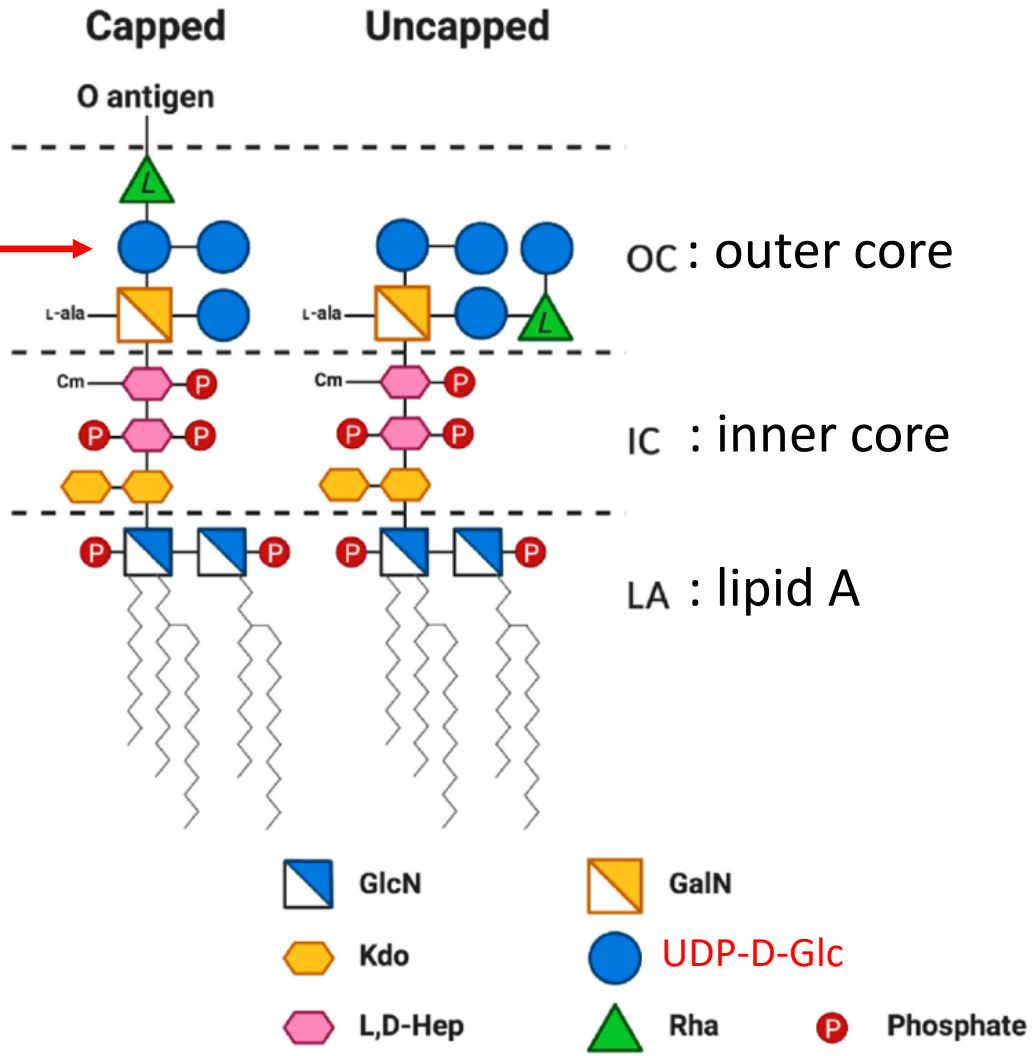
HOW DO BACTERIA RESIST TO PHAGES?
THE MAIN MECHANISM IN *PSEUDOMONAS AERUGINOSA*

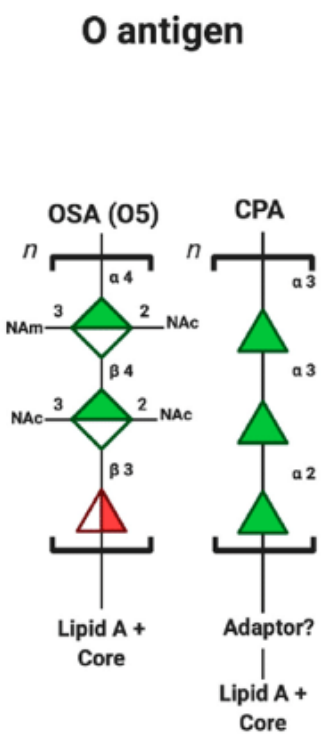


Glc-1-phosphate

GalU

+ UTP





Huszczynshi SM. et al., Pathognes 2020; 9(6).

PHAGE THERAPY

1919: FIRST HUMAN TREATMENTS

- 5 CHILDREN SUFFERING FORM DYSENTERY (HOPITAL NECKER, PARIS)
  - ➢ NOT PUBLISHED

1920-1950 : THE GOLDEN AGE

- **150 PUBLICATIONS/YEAR (SUCCESSES AND FAILURES)**

  - TYPHOID FEVER (*S. enterica typhi* et *paratyphi*)
  - UTI (*E. coli*)
  - DYSENTERY (*Shigella*)
  - PESTIS (*Y. pestis*)
  - CHOLERA (*V. cholerae*)
  - *S. aureus AND S. pneumoniae INFECTIONS*

1923 : ELIAVA INSTITUTE, TBILISSI, GEORGIA

- >3000 PATIENTS/YEAR
- IMPRESSIVE SUCCESS RATES

1949 : PHAGE THERAPY AT CHUV!

UNIVERSITÉ DE LAUSANNE - FACULTÉ DE MÉDECINE

La thérapeutique des staphylococcies par le bactériophage

Thèse

présentée à la Faculté de Médecine de l'Université de Lausanne
pour l'obtention du grade de docteur en médecine

par

JEAN-PIERRE FEIHL
Médecin diplômé de la Confédération suisse

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

1949 : PHAGE THERAPY AT CHUV!

Statistique

Maladies	Nombre de cas	Traités avec succès	Traités sans succès
Plaies infectées	4	4	
Phlegmons	7	6	1
Hidrosadénites	6	5	1
Sycosis à staphylocoque	2	2	
Mastites aiguës	8	7	1
Furoncles	16	12	4
Furoncles de la lèvre sup. et nez	10	9	1
Otites externes	4	3	1
Anthrax	5	4	1
Orgelets	9	8	1
Panaris	5	4	1
Septicémie	1		1
Totaux	77	64	13

Proportion des cas traités avec succès exprimée en pour cent : 83 %.

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

LATE 50’S - EARLY 60’s : THE DECLINE

IN WESTERN COUNTRIES

IN EASTERN COUNTRIES

Iron curtain

ELIAVA Institute

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

LATE 90's – EARLY 21ST CENTURY : THE RENEWED INTEREST IN THE WEST

THE ANTIBIOTIC RESISTANCE CRISIS

"Then there is the danger that the ignorant man may easily under-dose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant."

A. Fleming. Nobel Lecture, Dec. 11, 1945

LATE 90's – EARLY 21ST CENTURY : THE RENEWED INTEREST IN THE WEST
THE ANTIBIOTIC RESISTANCE CRISIS

"Then there is the danger that the ignorant man may easily under-dose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant."

A. Fleming. Nobel Lecture, Dec. 11, 1945

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

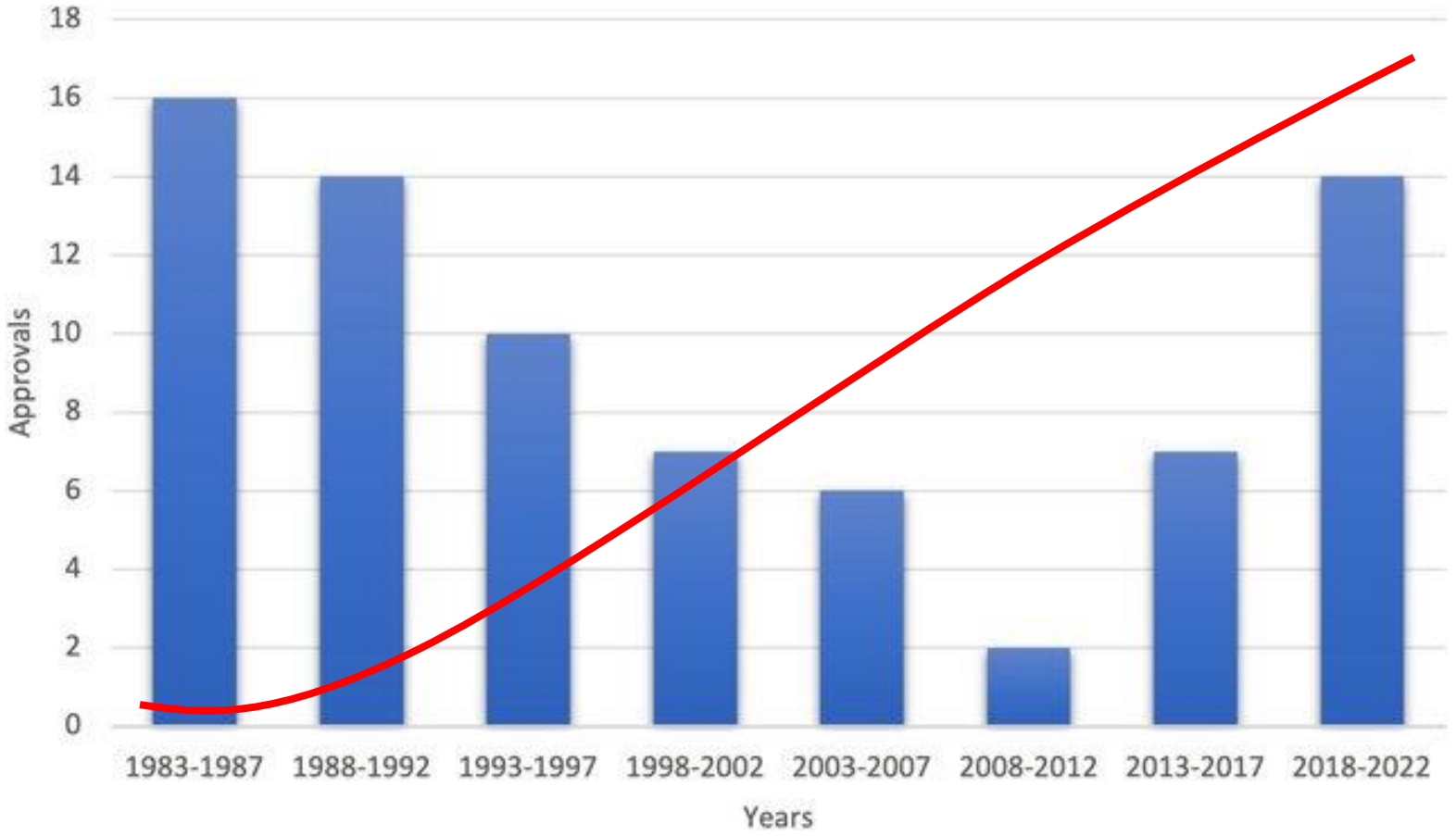
LATE 90's – EARLY 21ST CENTURY : THE RENEWED INTEREST IN THE WEST
THE ANTIBIOTIC RESISTANCE CRISIS

"Then there is the danger that the ignorant man may easily under-dose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant."
A. Fleming. Nobel Lecture, Dec. 11, 1945

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE
CHUV

LATE 90's – EARLY 21ST CENTURY : THE RENEWED INTEREST IN THE WEST

THE ANTIBIOTIC RESISTANCE CRISIS



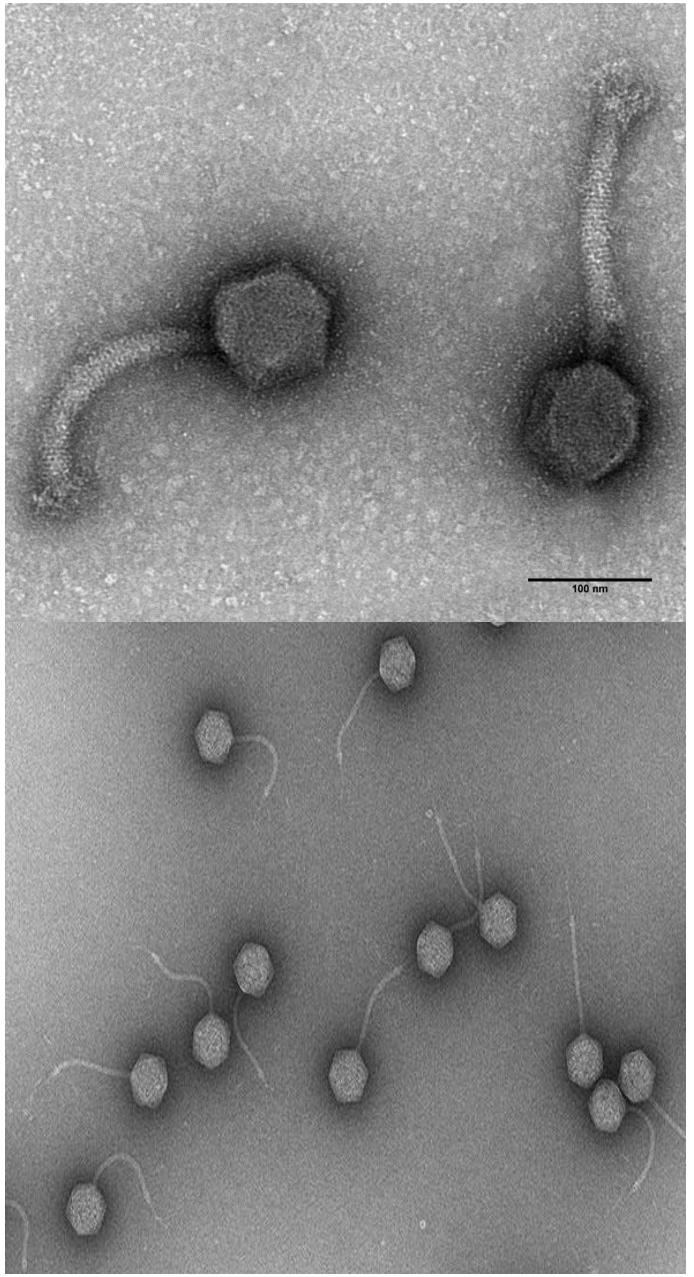
Chen et al., Arch. Microbiol., (2023) 205:336

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

AND… WE REMEMBERED THE PHAGES!

- NATURAL BACTERIAL VIRUSES
- **HIGHLY SPECIFIC = SPARE THE MICROBIOME**
- **KILL MDR BACTERIAL STRAINS**
- **SYNERGISE WITH ANTIBIOTICS**



MDR; MULTI-DRUG RESISTANT

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

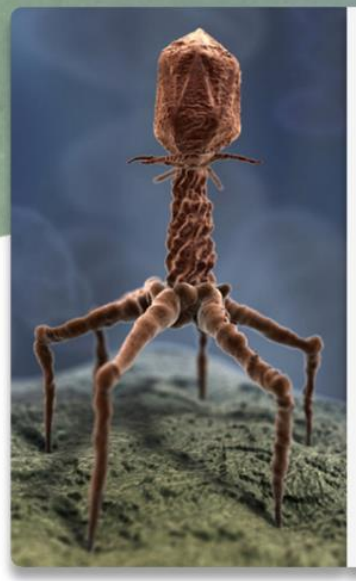
PHAGE THERAPY «TOURISM» TO EASTERN COUNTRIES INCREASED

Phage Rx

HOME GET HELP ABOUT PHAGES ABOUT US CONTACT US

BACTERIOPHAGES

TOOLS TO COMBAT ANTIBIOTIC RESISTANT BACT



The word **phage** is from the Greek 'phagos', meaning to eat. When combined to form the word **bacteriophage** it describes the organisms that eat bacteria. Bacteriophages occur naturally and their only known food source is the specific bacterial strains upon which they prey. When isolated and reproduced bacteriophages form an effective tool to destroy bacteria.

CAN WE HELP YOU?

Phage Rx has teamed with the Eliava Phage Therapy Center in Tbilisi, Georgia to provide therapy for chronic and acute infections. With decades of experience Eliava specialists have developed protocols for treatment of many common, yet difficult to treat infections including those listed below.

- Skin and soft tissue infections
- Ear, Nose and Throat infections
- Bone and Joint infections
- Respiratory infections
- Eye infections
- Bacterial Infections of the Oral Cavity
- Urinary tract infections
- Gastrointestinal conditions
- Gynecological Bacterial disorders

HTTP://PHAGERX.COM

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PHAGES ARE BIOLOGICAL MEDICINES AND SHOULD BE EVALUATED ACCORDING TO THE GOOD PRACTICES STANDARDS (GXP: GMP, GCP)

GMP; GOOD MANUFACTURING PRACTICES
GCP; GOOD CLINICAL PRACTICES

CURRENT STATUS

- **THROUGHOUT THE WORLD**
  - >1700 CLINICAL CASES PUBLISHED (COMPASIONNATE USE)
  - >20 RANDOMIZED CLINICAL TRIALS ENROLLING

    IN USA, FRANCE, BELGIUM, DANEMARK, CZECH REPUBLIC, CHINA, ISRAËL, IRAN (CLINICALTRIALS.GOV)

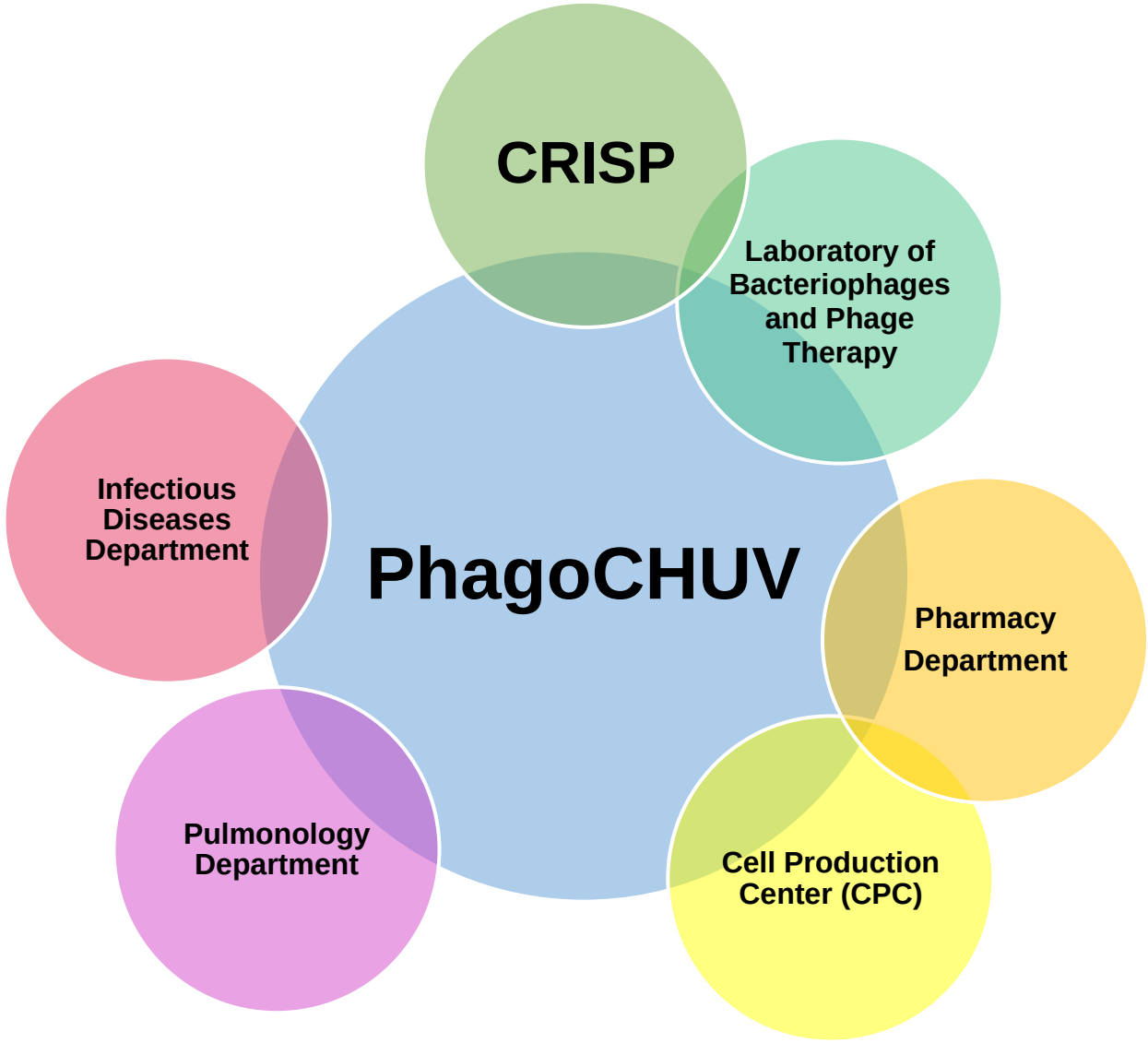
- **CHUV/UNIL (MARCH 2021) : PhagoCHUV**
  - COMPASSIONATE USE PROGRAM

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PhagoCHUV - ORGANISATION

- MULTIDISCIPLINARY PROGRAM
- CHUV STRATEGIC PLAN SINCE 2019



ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PhagoCHUV
GATHERING A PHAGE BANK

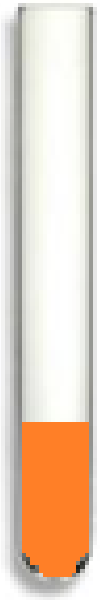
??

SEWAGE WATER

FILTRATION

PATIENT STRAIN

LIQUID CULTURE



SOFT AGAR

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PhagoCHUV
GATHERING A PHAGE BANK

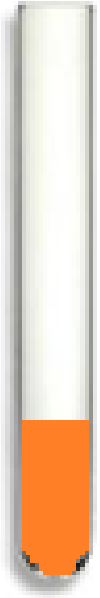
WASTEWATER TREATMENT PLAN

SEWAGE WATER

FILTRATION

PATIENT STRAIN

LIQUID CULTURE

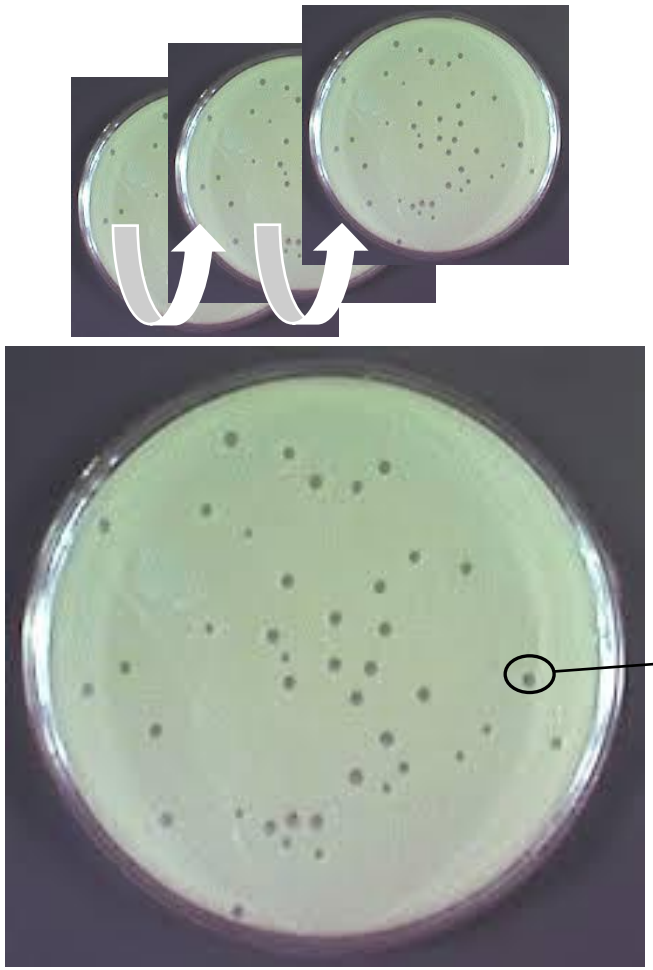


SOFT AGAR

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PhagoCHUV
GATHERING A PHAGE BANK



1 PFU = 1 PHAGE
PATIENT STRAIN
GROWTH MEDIUM

CENTRIFUGATION
FILTRATION

PHAGE COLLECTION IDENTIFIED, TITERED AND TRACEABLE

PFU; PLAQUE FORMING UNITS

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PhagoCHUV
PHAGE IDENTIFICATION

- **PHAGOGRAM** = HOST RANGE

- **PHAGE GENOME SEQUENCING**
  - INCLUSION CRITERIA
    - LYTIC PHAGE = NO GENE CODING FOR INTEGRASES/RECOMBINASES
    - NO GENE CODING FOR KNOWN VIRULENCE FACTOR
    - NO GENE CODING FOR KNOWN ANTIBIOTIC RESISTANCE DETERMINANTS

- **DEEP ANALYSIS OF THE BIOLOGICAL MATERIAL (THE PHAGE)**

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE
CHUV

PhagoCHUV

CURRENT STATE OF THE CHUV PHAGE COLLECTION

Family	*Pae*	*Eco*	*Aba*	*Kpn*	*Sau*	Total
Ackermannviridae	0	0	0	2	0	2
Autographiridae	4	7	3	9	0	23
Drexlerviridae	0	1	0	5	0	6
Herelleviridae	0	0	0	0	11	4
Myoviridae	45	10	7	3	0	65
Podoviridae	39	3	9	3	4	57
Siphoviridae	5	6	2	2	3	18
Unclassified	1	0	3	0	12	4
Total	**94**	**27**	**24**	**24**	**30**	**199**

STRAIN *Pae* MUCO (2023, N=51)

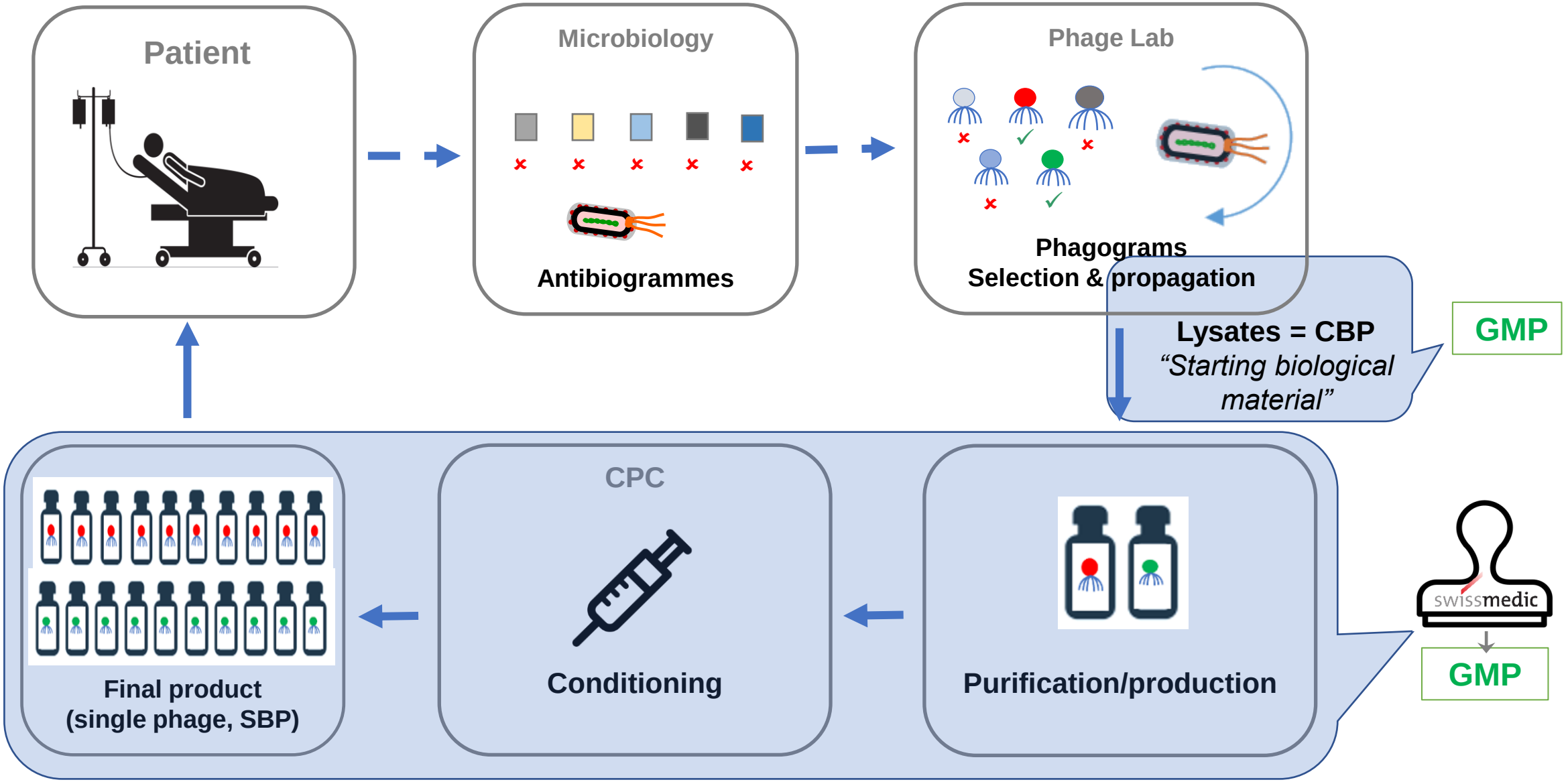
PER PHAGE COVERAGE: 0-28 STRAINS

NON-COVERED STRAINS = 9

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PhagoCHUV – PERSONALIZED PHAGE THERAPY



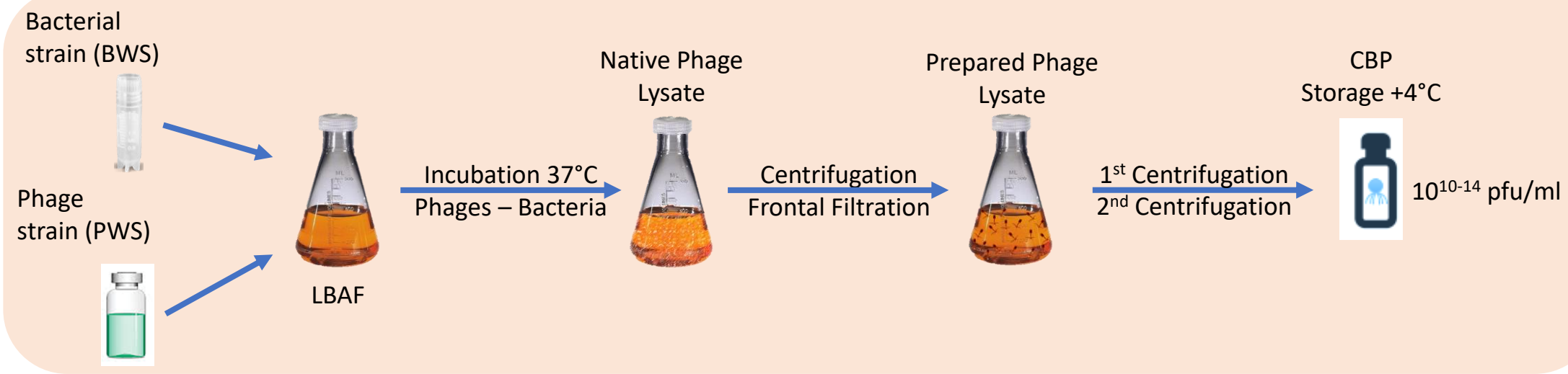
GMP, Good Manufacturing Practices; CBP, Concentrate of BacterioPhages;
SBP, Suspension of BacterioPhages, CPC, Cell Production Center

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PhagoCHUV – MANUFACTURING OF THERAPEUTIC PHAGE SUSPENSIONS

Laboratory of bacteriophages

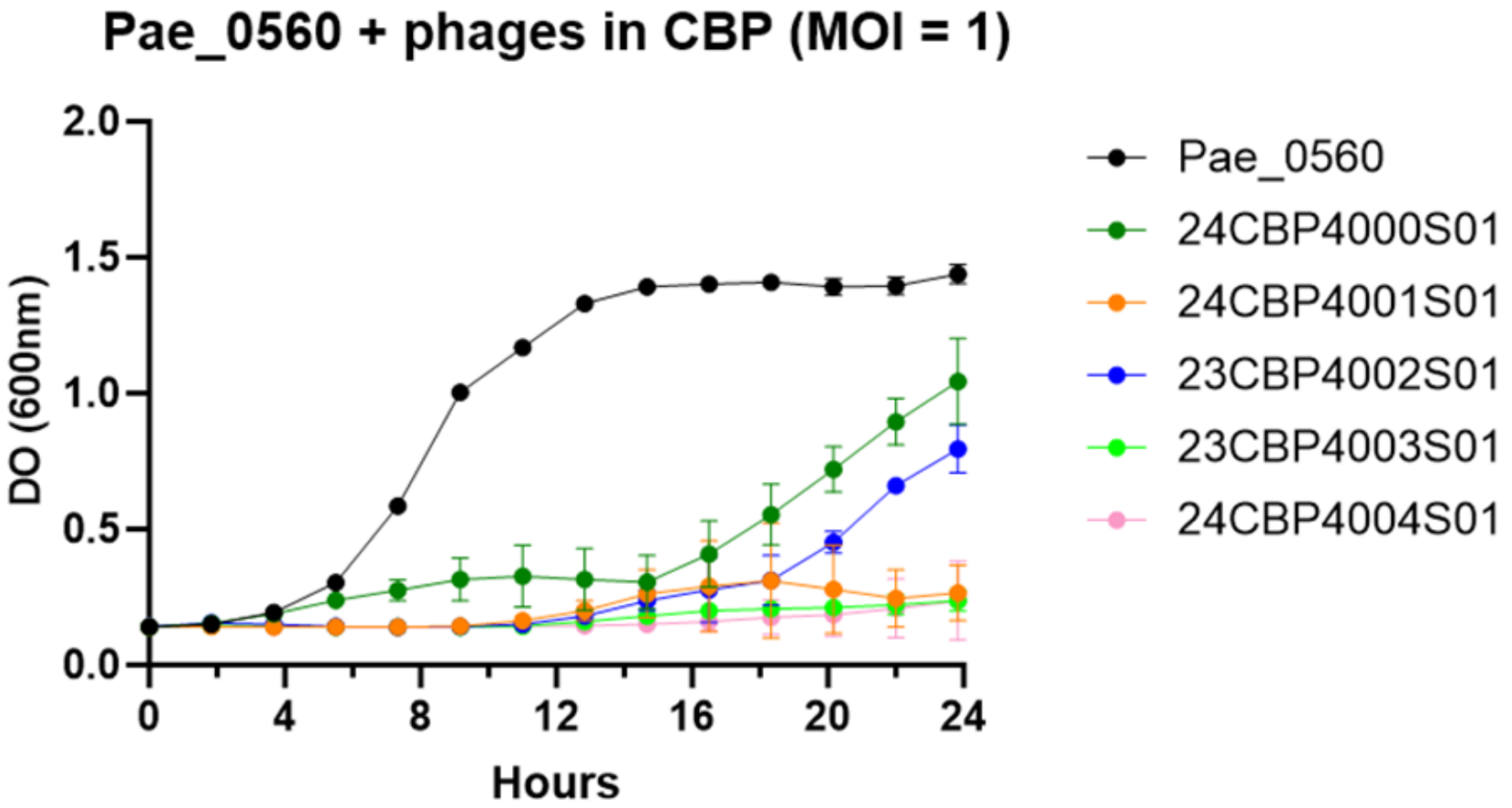


LBAF, LB animal free; CBP; Concentrate of BacterioPhages; SBP, Suspension of BacterioPhages

PhagoCHUV – PHAGE SELECTION

PHAGOGRAM IN TURBIDITY ASSAY

ON DEMAND



	C4000	C4001	C4002	C4003	C4004
Pae_0560	I	S	I	S	S

MOI, Multiplicity Of Infection = ratio phages/bacteria

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

PhagoCHUV – MANUFACTURING OF THERAPEUTIC PHAGE SUSPENSIONS

Laboratory of bacteriophages

Cell Production Center (CPC)

ON DEMAND

CBP stored → Dilution / Filtration → **CBP diluted** ($2x10^{8-9}$ pfu/mL)

Delivery to CPC

- Endotoxin ≤ 350 EU/ml → Dilution / Filtration
- Endotoxin > 350 EU/ml → 2nd Purification / Dilution + Filtration

48 Flacons SBP

1 ml/flask – 10^{8-9} pfu/ml
IV if Endotoxin ≤ 175 EU/ml

Delivery to the clinic

SWISSMEDIC AUTORISATION FOR PHAGE MANUFACTURE : 23/06/2023

WORLD FIRST!

Swissmedic Swiss Agency for Therapeutic Products

CERTIFICATE NUMBER: ***GMPE-CH-1004487***

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

Issued under the provisions of the Mutual Recognition Agreement between the European Union and ***Switzerland***.

The competent authority of Switzerland confirms the following:
The manufacturer: ***Centre Hospitalier Universitaire Vaudois***
Site address: ***Chemin Des Croisettes 22, Epalinges, 1066, Switzerland***
OMS Organisation Id. / OMS Location Id.: ***ORG-100025536 / LOC-100052444***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2023-02-09*** , it is considered that it complies with

The Good Manufacturing Practice requirements referred to in the Agreement of Mutual Recognition between the European Union and ***Switzerland***

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. This certificate is valid only when presented with all pages and both Parts 1 and 2.

The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

Part 2

Human Medicinal Products
Human Investigational Medicinal Products
Veterinary Medicinal Products

1 MANUFACTURING OPERATIONS	
1.3	**Biological medicinal products (list of product types)**
	1.3.1 Biological medicinal products (list of product types) 1.3.1.8 Other: Filtered and conditioned phages(en)
	1.3.2 Batch Certification (list of product types) 1.3.2.8 Other: Filtered and conditioned phages(en)
1.5	**Packaging**
	1.5.1 Primary Packaging 1.5.1.5 Liquids for external use 1.5.1.6 Liquids for internal use
	1.5.2 Secondary packaging
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility *1.6.3 Chemical/Physical*

Manufacture of active substance. Names of substances subject to inspection:
SWISSMEDIC LIST OF APIS, SEE 4 ACTIVE SUBSTANCES(en)
4. Other Activities - Active Substances:
Phage-CHUV

Online EudraGMDP, Ref key: 163584 Issuance Date 2023-06-23 Signatory: Confidential

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

TREATMENT OF PATIENTS AT CHUV

SINCE 02/2024

- 8 treatments administered to 4 patients (2 CF and 2 osteoarticular infections).
- Autorised by the Cantonal Pharmacist.
- Administration by inhalation (CF) or IV+locally (osteoarticular infections).
- No side effects.
- No recurrent osteoarticular infection after >1 year (cure).
- CF patients: improvement of quality of life, increase of the interval between hospital stays (from 4 to 6 weeks).
- Future planned treatments : 1xDecember 2025 and 1xJanuary 2026 (CF)

FEW MODERN RCTs THAT FAILED TO DEMONSTRATE SUPERIORITY OF PHAGE THERAPY

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 Jennes, Jean Paul Pirnay, Yok-Ai Que, Gregory Resch, Anne Françoise Rousseau, François Ravat, Hervé Carsin, Ronan Le Floch, Jean Vivien Schaal, Charles Soler, Cindy Fevre, Isabelle Arnaud, Laurent Bretaudeau, Jérôme Gabard

Summary

Background Wound infections are the main cause of sepsis in patients with burns and increase burn-related morbidity and mortality. Bacteriophages, natural bacterial viruses, are being considered as an alternative therapy to treat infections caused by multidrug-resistant bacteria. We aimed to compare the efficacy and tolerability of a cocktail of lytic anti-*Pseudomonas aeruginosa* bacteriophages with standard of care for patients with burns.

Lancet Infect Dis 2019; 19: 35-45
Published Online October 3, 2018
http://dx.doi.org/10.1016/S1473-3099(18)30482-1

EBioMedicine 4 (2016) 124–137

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Research Paper

Oral Phage Therapy of Acute Bacterial Diarrhea With Two Coliphage Preparations: A Randomized Trial in Children From Bangladesh

Shafiqul Alam Sarker [a], Shamima Sultana [a], Gloria Reuteler [b], Deborah Moine [c], Patrick Descombes [c], Florence Charton [b], Gilles Bourdin [b], Shawna McCallin [b], Catherine Ngom-Bru [b], Tara Neville [b], Mahmuda Akter [a], Sayeeda Huq [a], Firdausi Qadri [a], Kaisar Talukdar [a], Mohamed Kassam [c], Michèle Delley [b], Chloe Loiseau [b], Ying Deng [b], Sahar El Aidy [b], Bernard Berger [b], Harald Brüssow [b,*]

[a] *International Centre for Diarrheal Diseases Research, Bangladesh (icddr,b), 68 Shaheed Tajuddin Ahmed Sharani, Mohakhali, Dhaka 1212, Bangladesh,*
[b] *Nestlé Research Centre, Nestec Ltd., Vers-chez-les-Blanc, CH-1000 Lausanne 26, Switzerland*
[c] *Nestlé Institute of Health Science, EPFL Innovation Park, CH-1015 Lausanne, Switzerland*

Intravesical bacteriophages for treating urinary tract infections in patients undergoing transurethral resection of the prostate: a randomised, placebo-controlled, double-blind clinical trial

Lorenz Leitner, Aleksandre Ujmajuridze, Nina Chanishvili, Marina Goderdzishvili, Irina Chkonia, Sophia Rigvava, Archil Chkhotua, Giorgi Changashvili, Shawna McCallin, Marc P Schneider, Martina D Liechti, Ulrich Mehnert, Lucas M Bachmann, Wilbert Sybesma, Thomas M Kessler

Summary

Background Urinary tract infections (UTIs) are among the most prevalent microbial diseases and their financial burden on society is substantial. In the context of increasing antibiotic resistance, finding alternative treatments for UTIs is a top priority. We aimed to determine whether intravesical bacteriophage therapy with a commercial bacteriophage cocktail is effective in treating UTI.

Lancet Infect Dis 2021; 21: 427-36
Published Online September 16, 2020
https://doi.org/10.1016/S1473-3099(20)30330-3

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

FEW MODERN RCTs THAT SUCCEEDED TO DEMONSTRATE EFFICACY OF PHAGE THERAPY

nature communications

Article

https://doi.org/10.1038/s41467-025-60598-4

Phage therapy with nebulized cocktail BX004-A for chronic *Pseudomonas aeruginosa* infections in cystic fibrosis: a randomized first-in-human trial

Received: 24 August 2024

Accepted: 29 May 2025

Published online: 01 July 2025

Check for updates

A list of authors and their affiliations appears at the end of the paper

Cystic fibrosis is a monogenetic disease complicated by recurrent bacterial lung infections that require chronic antibiotics. *Pseudomonas aeruginosa* is an increasingly antibiotic-resistant pathogen associated with cystic fibrosis mor-

BiomX

Source: *BiomX*

March 31, 2025 06:30 ET

BiomX Announces Positive Topline Results from Phase 2 Trial Evaluating BX211 for the Treatment of Diabetic Foot Osteomyelitis (DFO)

- *BX211 was safe and well-tolerated*
- *BX211 produced sustained and statistically significant[1] Percent Area Reduction (PAR) of ulcer size* (p = 0.046 at week 12; p=0.052 at week 13), *with a separation from placebo starting at week 7 and a difference greater than 40% by week 10*
- *Compared to placebo, BX211 also produced statistically significant[1] improvements in both ulcer depth at week 13 (in patients with ulcer depth defined as bone at baseline) (p=0.048), and in reducing the expansion of ulcer area (p=0.017).*
- *BiomX is planning for a Phase 2/3 trial of BX211, pending U.S. Food and Drug Administration (FDA) feedback*

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

WHAT'S NEXT?

European Commission

CALL KEY DATA

TESTING SAFETY AND EFFICACY OF PHAGE THERAPY FOR THE TREATMENT OF ANTIBIOTIC-RESISTANT BACTERIAL INFECTIONS

FUNDING PROGRAM	Horizon Europe: Cluster 1 - Health
CALL NUMBER	HORIZON-HLTH-2025-01-DISEASE-01
DEADLINES	**Opening** 22.05.2025 **Deadline** 16.09.2025 17:00
FUNDING RATE	100%
CALL BUDGET	€ 45,000,000.00
ESTIMATED EU CONTRIBUTION PER PROJECT	€ 15,000,000.00

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

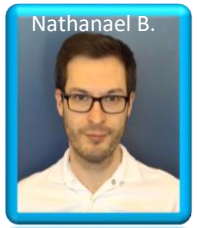
THIS WAS POSSIBLE

@ the Lab

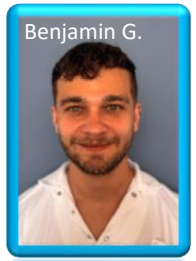
Quality Control

Head of QC

Quality Insurance



Responsable AQ



Production

Head of Prod.

Logistic

ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

WITH A HUGE NETWORK OF COMPETENCES

CRISP

Pre. Chantal Csajka

Unité des affaires réglementaires

Mme Jeanne-Pascale Simon

Service de pneumologie

Pr. Christophe von Garnier

Pre. Angela Koutsokera

Dre. Georgia Mitropoulou

Dr. Sylvain Blanchon

Service des maladies infectieuses

Pr. Benoît Guery

Service de Pharmacie

Pr. Farshid Sadeghipour

Dr. Laurent Carrez

ISPSO3
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

WITH A HUGE NETWORK OF COMPETENCES

Microbiology Institute (IMUL)

Pre. Claire Bertelli

Dr. Trestan Pillonel

Dre. Alessia Carrara

Dr. Damien Jacquot

Mme Maria Senra-Ortiz

Pr. Gilbert Greub

Proteomic Facility (PAF)

Pr. Manfredo Quadroni

Dr. Patrice Waridel

Mme Séverine Lorrain

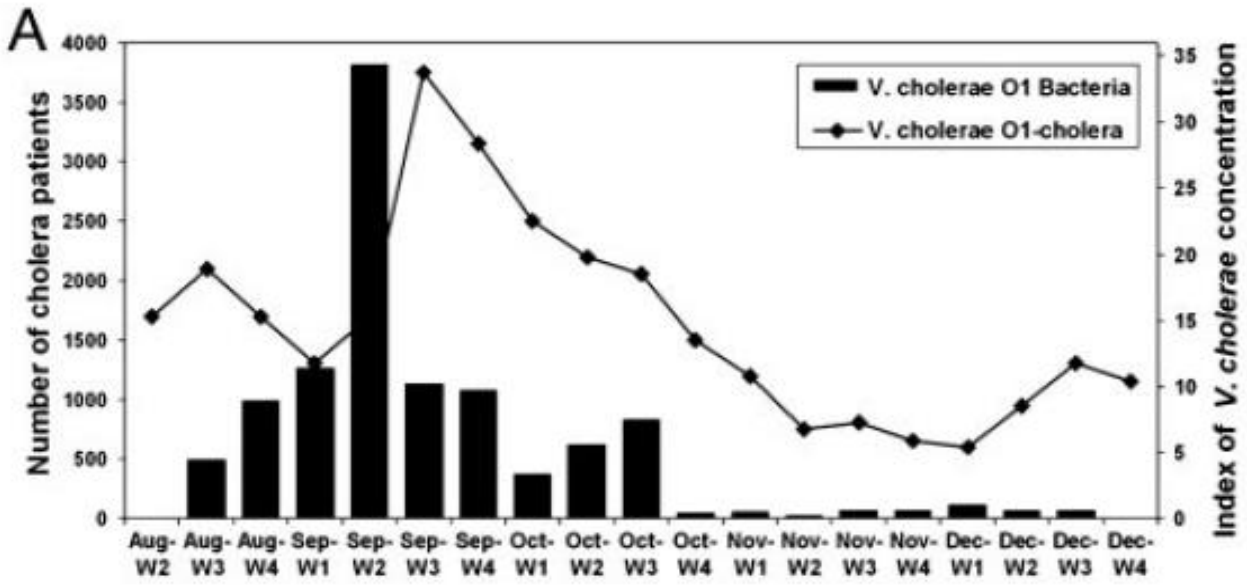
ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV


CHUV
THANKS FOR YOUR ATTENTION!

DYNAMICS OF PHAGES-BACTERIA INTERACTION

BACTERIA IN PATIENT STOOL



Faruque SM et al., PNAS, 2005 102 :6119–24

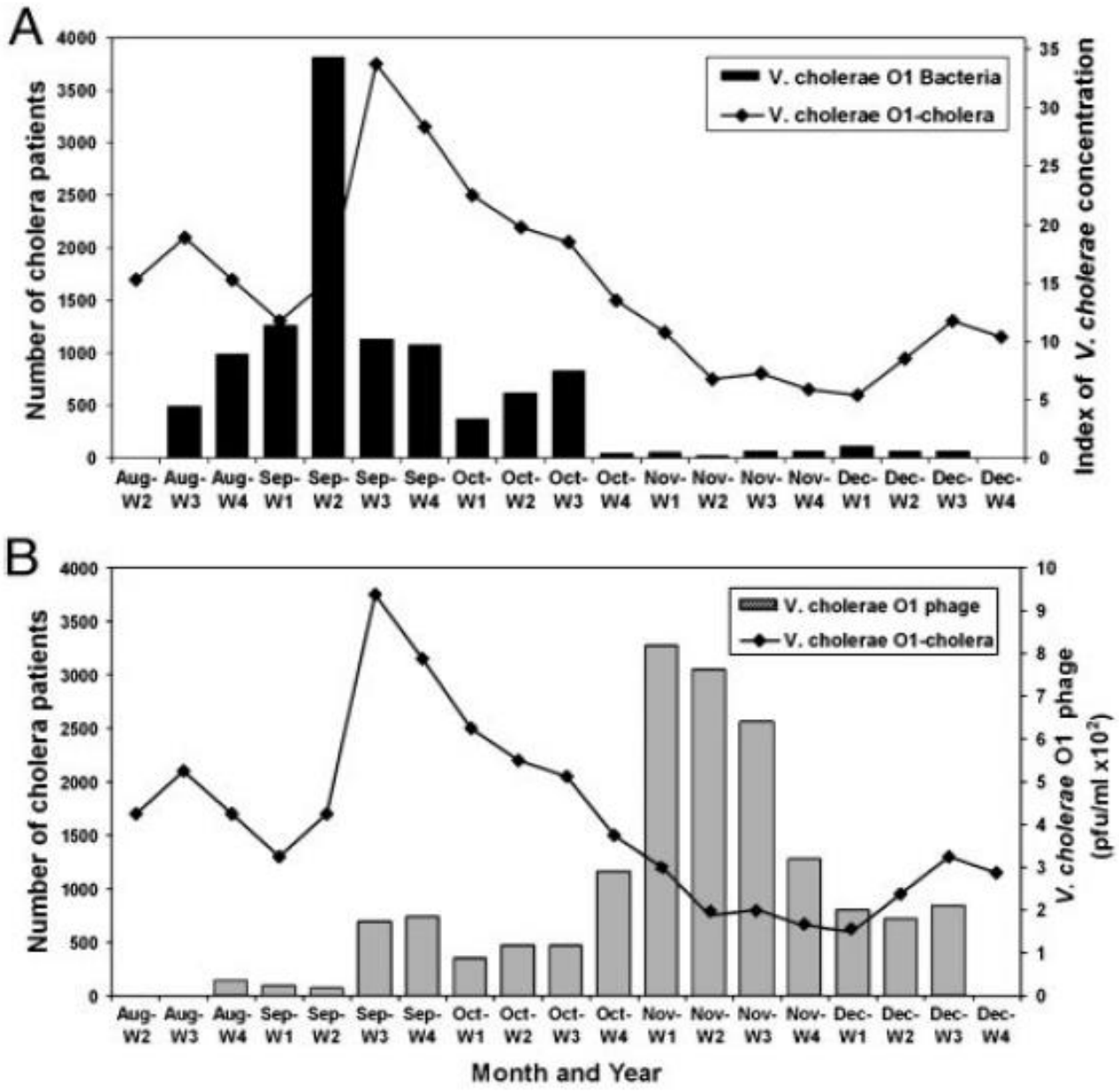
ISPSO
INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV

DYNAMICS OF PHAGES-BACTERIA INTERACTION

BACTERIA IN PATIENT STOOL

PHAGES IN PATIENT STOOL



Faruque SM et al., PNAS, 2005 102 :6119–24

ISPSO INSTITUT DES SCIENCES PHARMACEUTIQUES DE SUISSE OCCIDENTALE

CHUV