BACTERIÓFAGOS PARA EL CONTROL DE BIOFILMS

Dr. Eduardo de Mello Volotão

Ministério da Saúde
Fundação Oswaldo Cruz
INSTITUTO OSWALDO CRUZ

Ministerio
de Educación
y Cultura

iibce
INSTITUTO DE INVESTIGACIONES
BIOLÓGICAS CLEMENTE ESTABLE

Ecología

Ecología

Interacciones entre organismos y medio ambiente

Ecología Microbiana - Virus

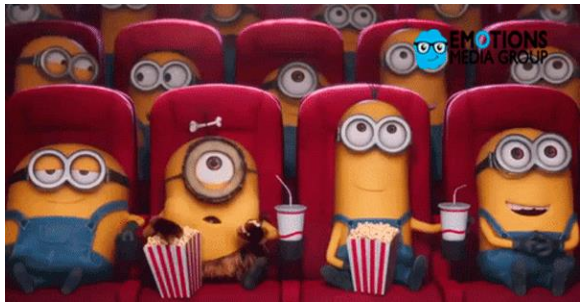
Qué son los virus?

Qué son los virus?

- Son microorganismos que se replican siempre dentro de células vivas;

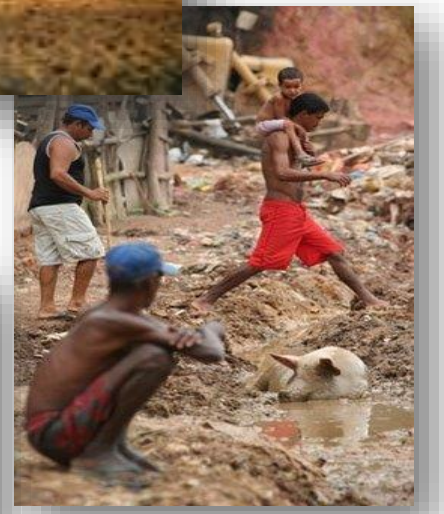
- Utilizan (en mayor o menor grado) el sistema de síntesis de las células;

- Inducir la diferenciación celular, la síntesis de proteínas y son capaces de transferir el genoma viral a otras células.



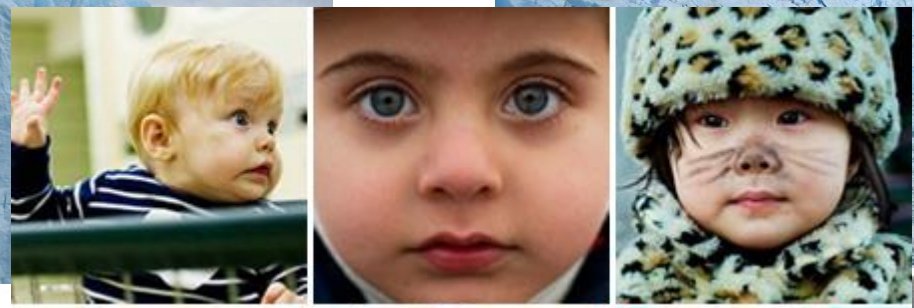
Historia de la Virología

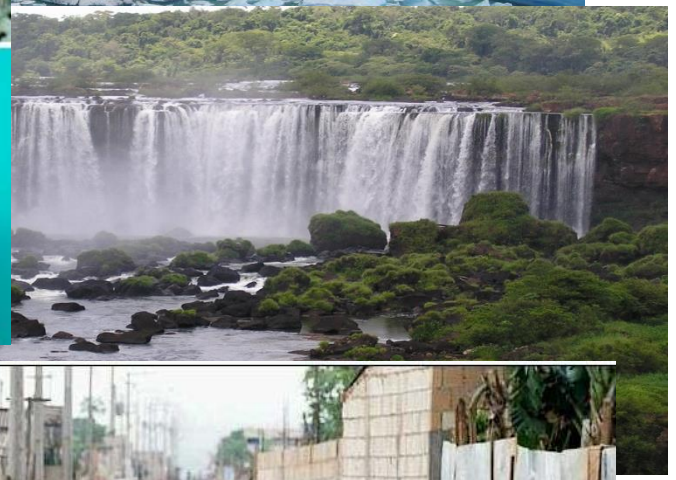
Temas ambientales, culturales, sociales, económicos, sanitarios y de salud.

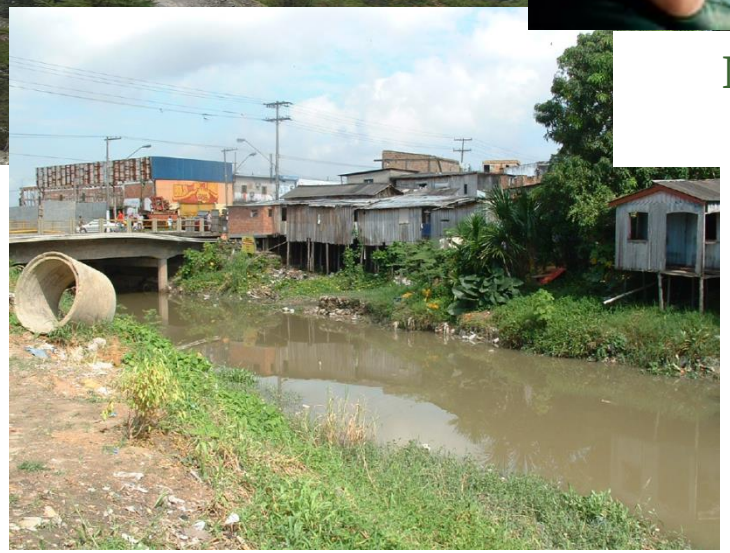


laboratoriodegeografia.blogspot.co

http://g1.globo.com/Noticias/Mundo/foto/0,,17724557-FMM,00.jpg



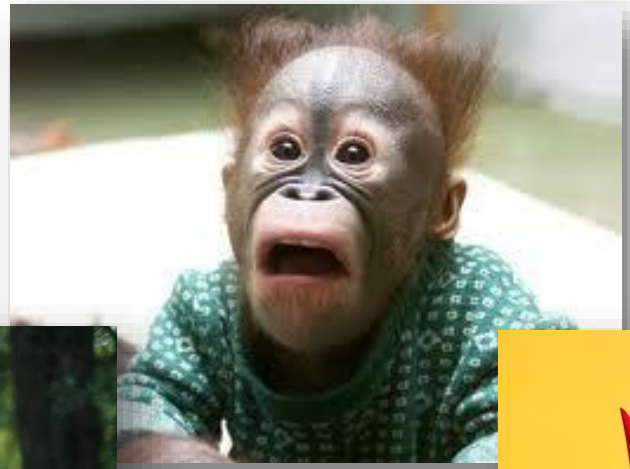


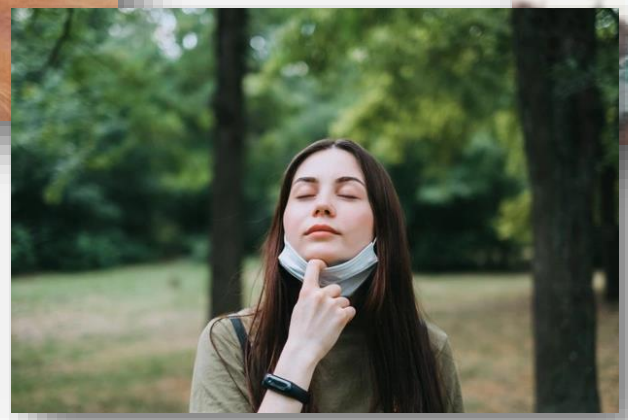


Mondo globalizado con CONTRASTES

Económicos
Sociales
Ambientales
VÍRUS ?

Vivimos y prosperamos en una nube de virus.





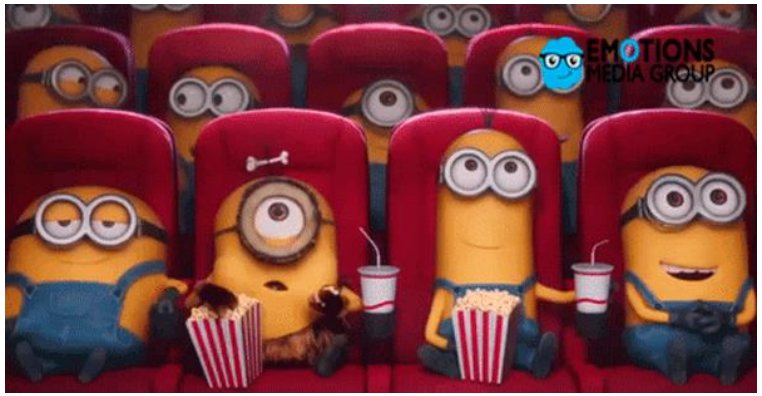
¿Qué están haciendo estos genomas allí?

La Virología es fascinante

• Los virus son una parte importante del ecosistema e infectan a todos los seres vivos.

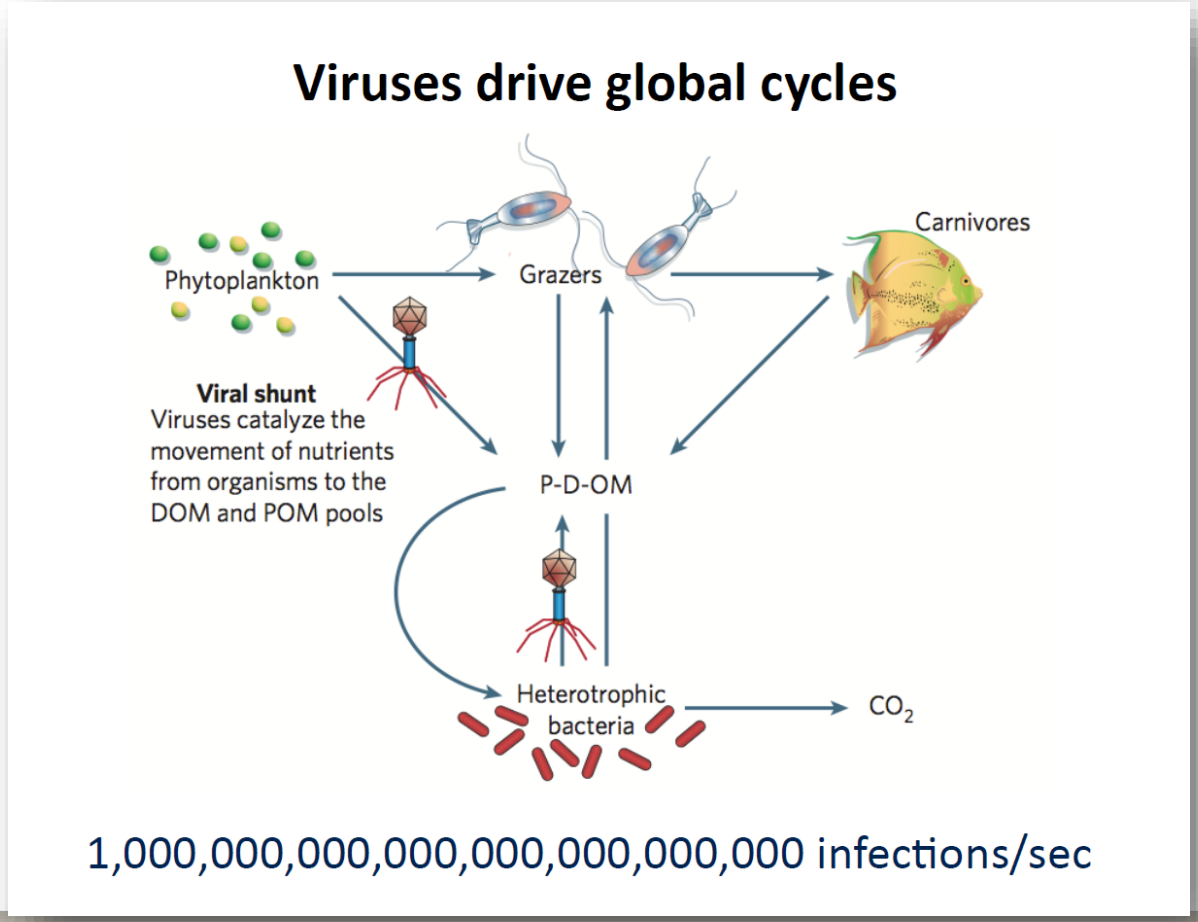
• Sin embargo, para las personas comunes, los virus son "malas noticias envueltas en alguna proteína".

Créame, los virus pueden hacer mucho más que causar enfermedades.



La cantidad de virus que nos golpean es asombrosa

- 10^{31} partículas de bacteriófagos en el suministro de agua del mundo.

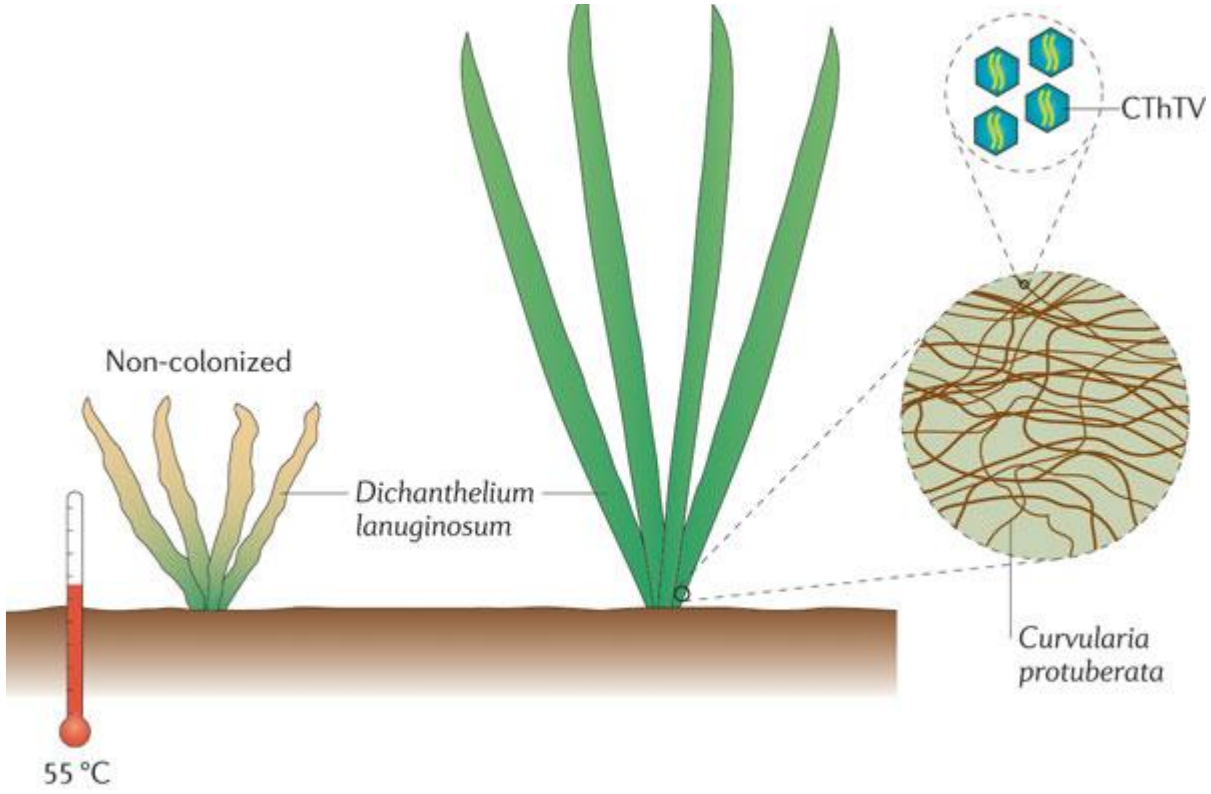


¿Por qué estudiar virus?

Existen innumerables partículas de virus con una diversidad sorprendente:

- Tamaño del genoma, naturaleza y topología
- Partículas extrañas
- Estrategias de codificación increíbles
- Tropismo de tejidos / células
- Grados de patogénesis de benignos a letales

Virus buenos



The panic grass *Dichanthelium lanuginosum* is found in geothermal soils in Yellowstone National Park, USA, where it can grow at soil temperatures >50 °C. The plant requires a fungal endophyte, *Curvularia protuberata*, to survive at this temperature. In turn, the fungus requires a virus, Curvularia thermal tolerance virus (CThTV), to confer this thermotolerance effect.

Virus buenos

Europe PMC Funders Group
Author Manuscript
Nature. Author manuscript; available in PMC 2015 June 04.

Published in final edited form as:
Nature. 2014 December 4; 516(7529): 94–98. doi:10.1038/nature13960.

An enteric virus can replace the beneficial function of commensal bacteria

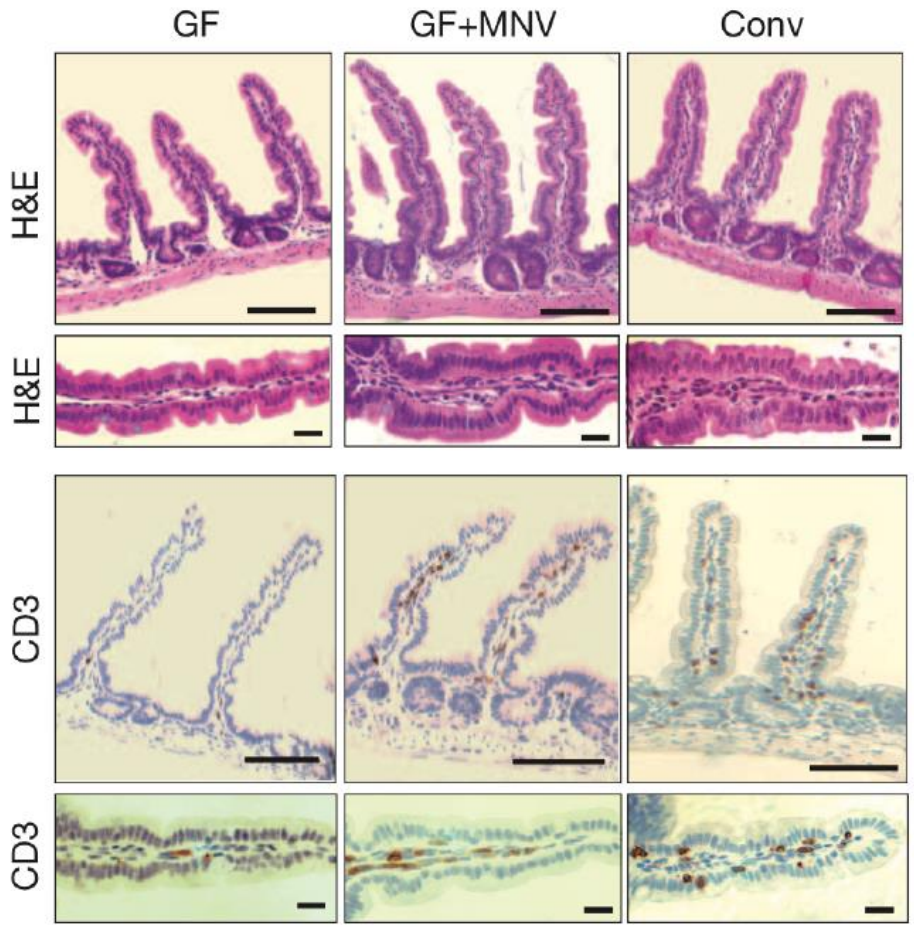
Elisabeth Kernbauer[1,2], **Yi Ding**[3], and **Ken Cadwell**[1,2]

[1]Kimmel Center for Biology and Medicine at the Skirball Institute, New York University School of Medicine, New York, NY 10016, USA

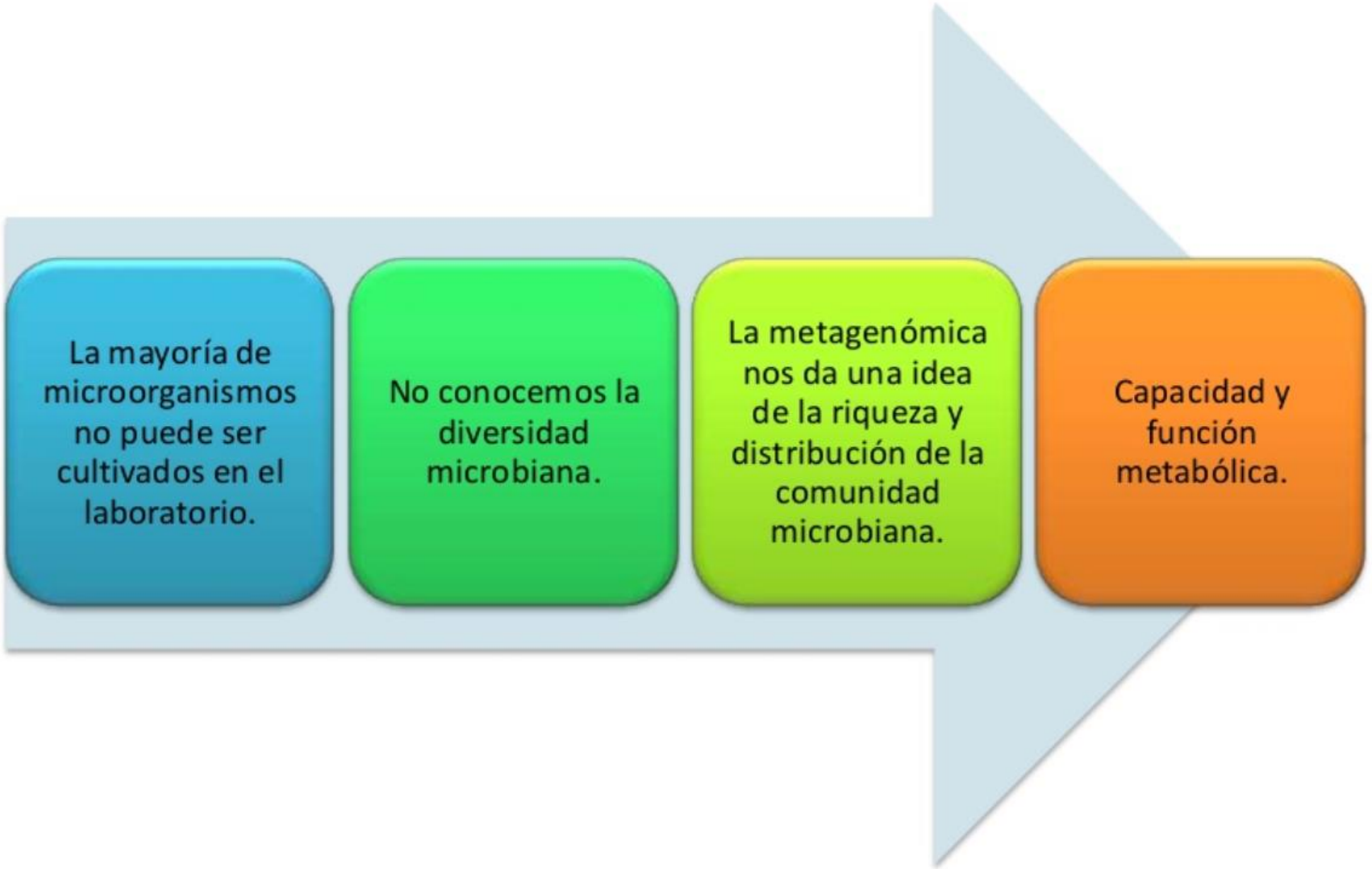
[2]Department of Microbiology, New York University School of Medicine, New York, NY 10016, USA

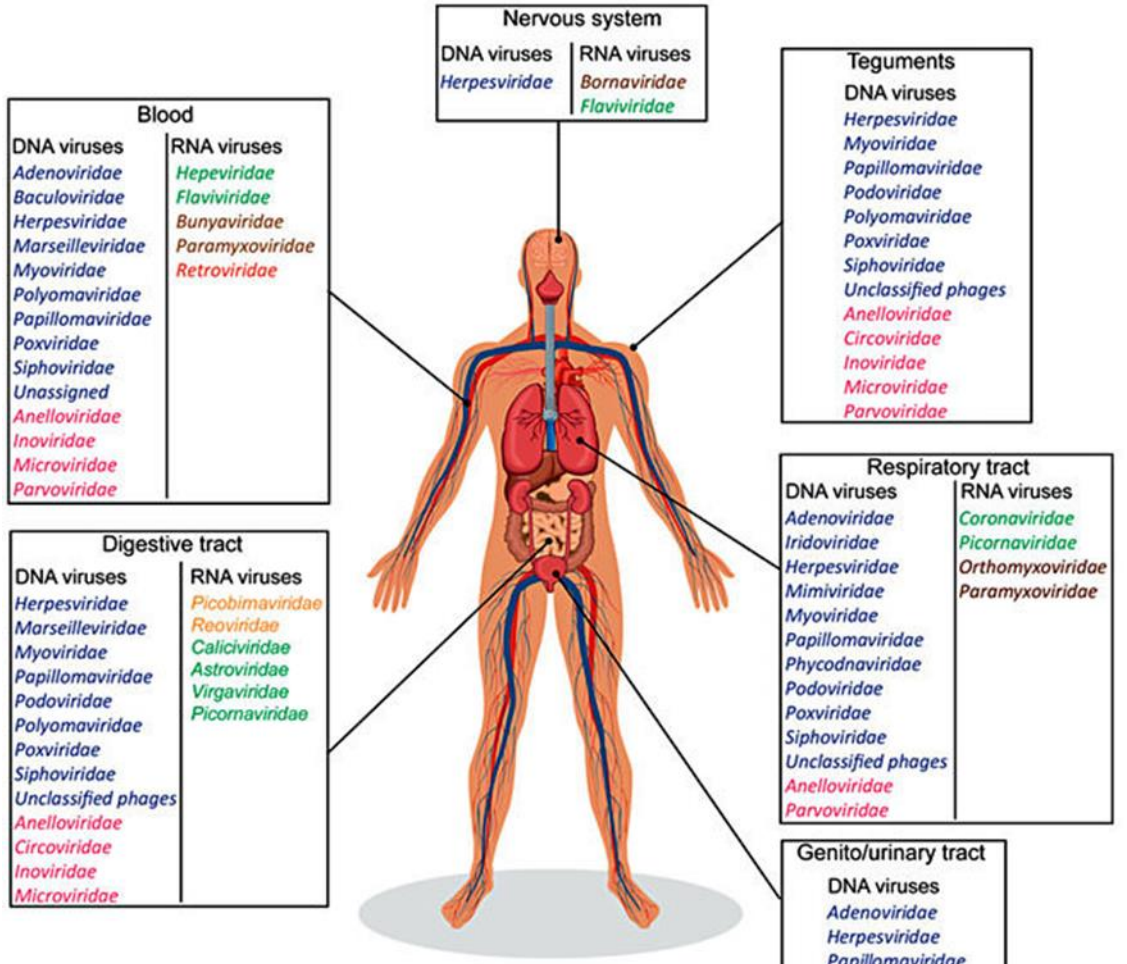
[3]New York Presbyterian Hospital, New York, NY 10065, USA

An enteric virus can replace the beneficial function of commensal bacteria

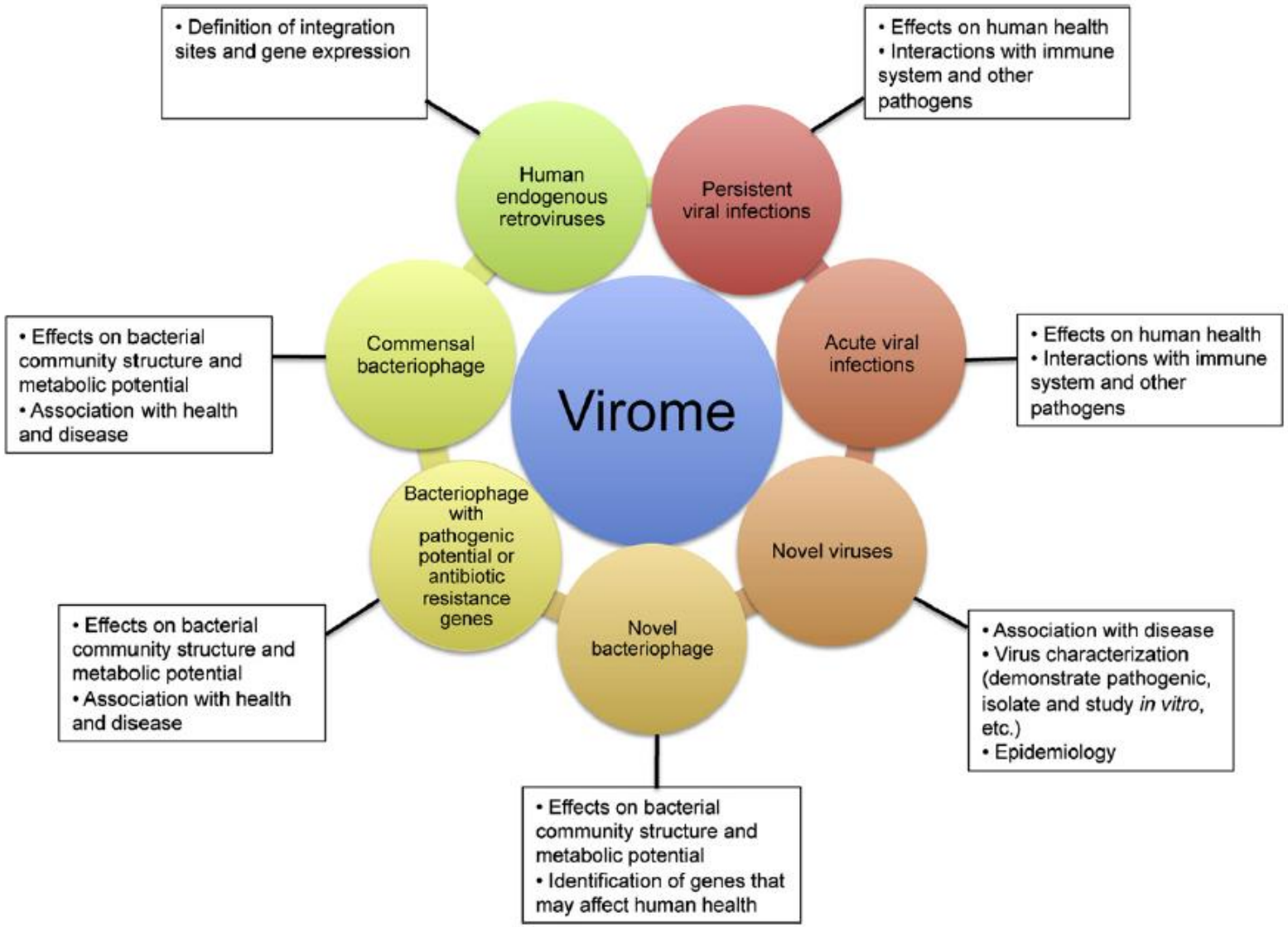


Metagenómica


La mayoría de microorganismos no puede ser cultivados en el laboratorio.
No conocemos la diversidad microbiana.
La metagenómica nos da una idea de la riqueza y distribución de la comunidad microbiana.
Capacidad y función metabólica.



Viroma Humano

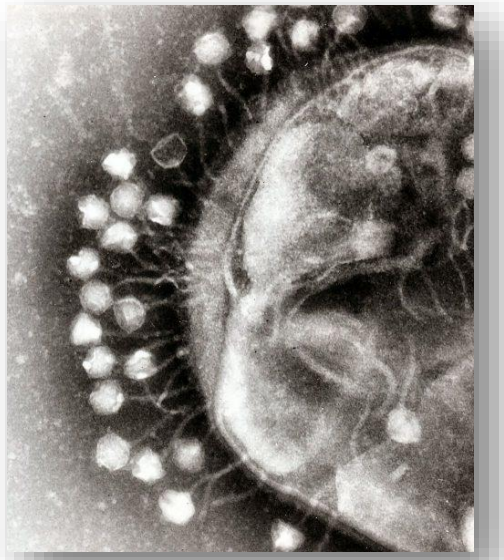

• Definition of integration sites and gene expression
Human endogenous retroviruses
• Effects on human health
• Interactions with immune system and other pathogens
Persistent viral infections
• Effects on bacterial community structure and metabolic potential
• Association with health and disease
Commensal bacteriophage
Virome
Acute viral infections
• Effects on human health
• Interactions with immune system and other pathogens
Bacteriophage with pathogenic potential or antibiotic resistance genes
Novel viruses
• Effects on bacterial community structure and metabolic potential
• Association with health and disease
Novel bacteriophage
• Association with disease
• Virus characterization (demonstrate pathogenic, isolate and study *in vitro*, etc.)
• Epidemiology
• Effects on bacterial community structure and metabolic potential
• Identification of genes that may affect human health

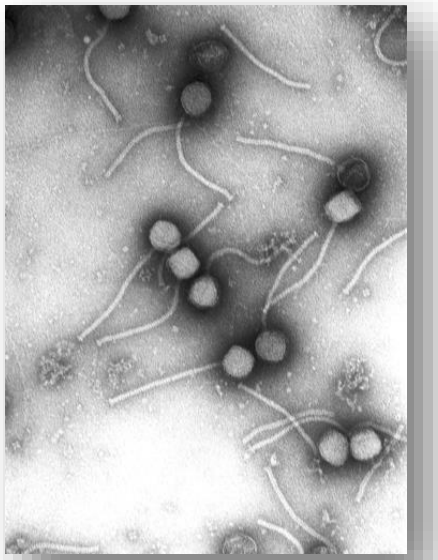
Histórico

Los **bacteriófagos** (también llamados **fagos**, del griego φαγητόν *faguētón*, 'alimento', 'ingestión') son virus que infectan exclusivamente a los organismos procariotas (bacterias y arqueas).

Frederick Twort
(1877–1950)

Félix d`Herelle
(1873–1949)



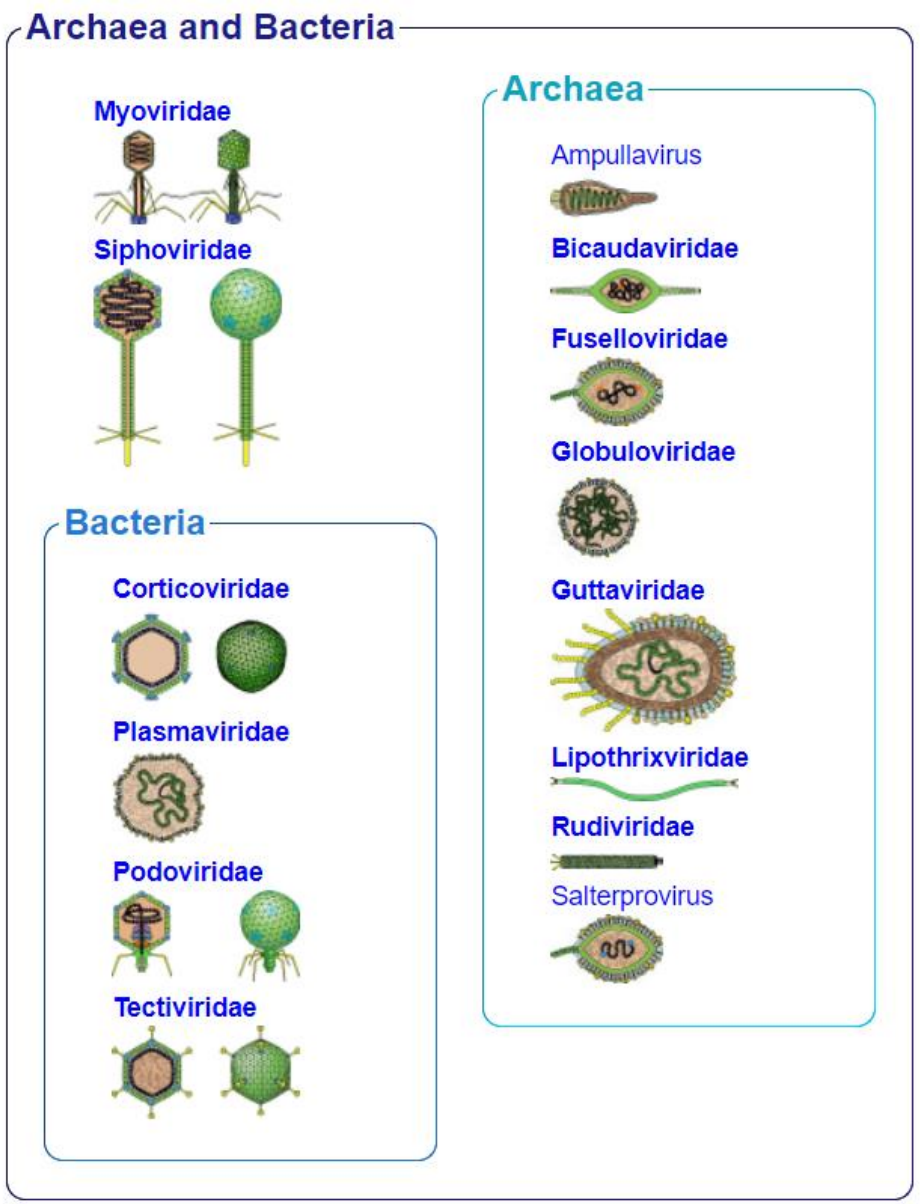


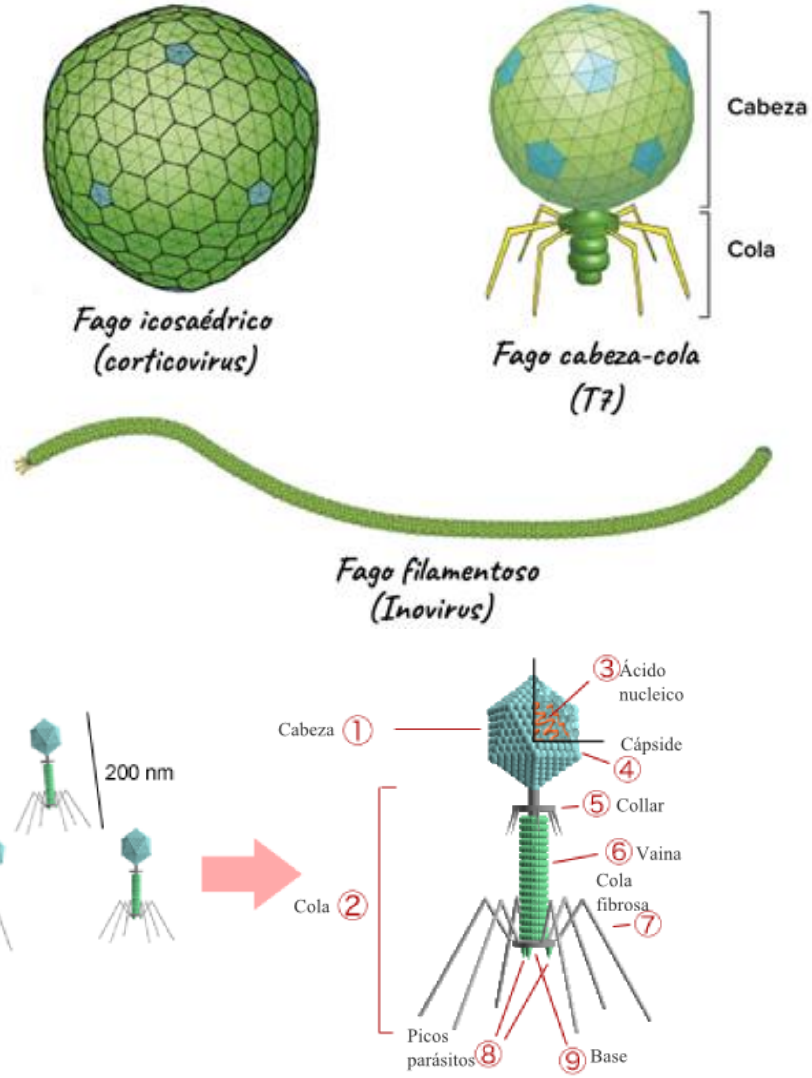
d'Herelle F. Sur un microbe invisible antagoniste des bacilles dysente´riques. Comptes rendus de l'Acade´mie des Sciences–Series D. 1917; 165:373–375

Características

- Un bacteriófago (fago), es un virus que infecta a las bacterias (procariotos .
- Como otros tipos de virus, los bacteriófagos varían mucho en su forma y material genético.
- Los genomas de fagos pueden constar de ADN o ARN, y pueden contener de 5000 a 500 000 genes.
- La cápside de un bacteriófago puede ser icosaédrica, filamentosa o en forma cabeza-cola.

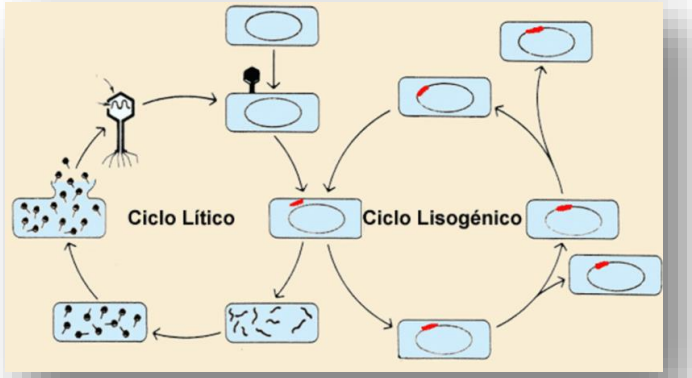
Bacteriófagos

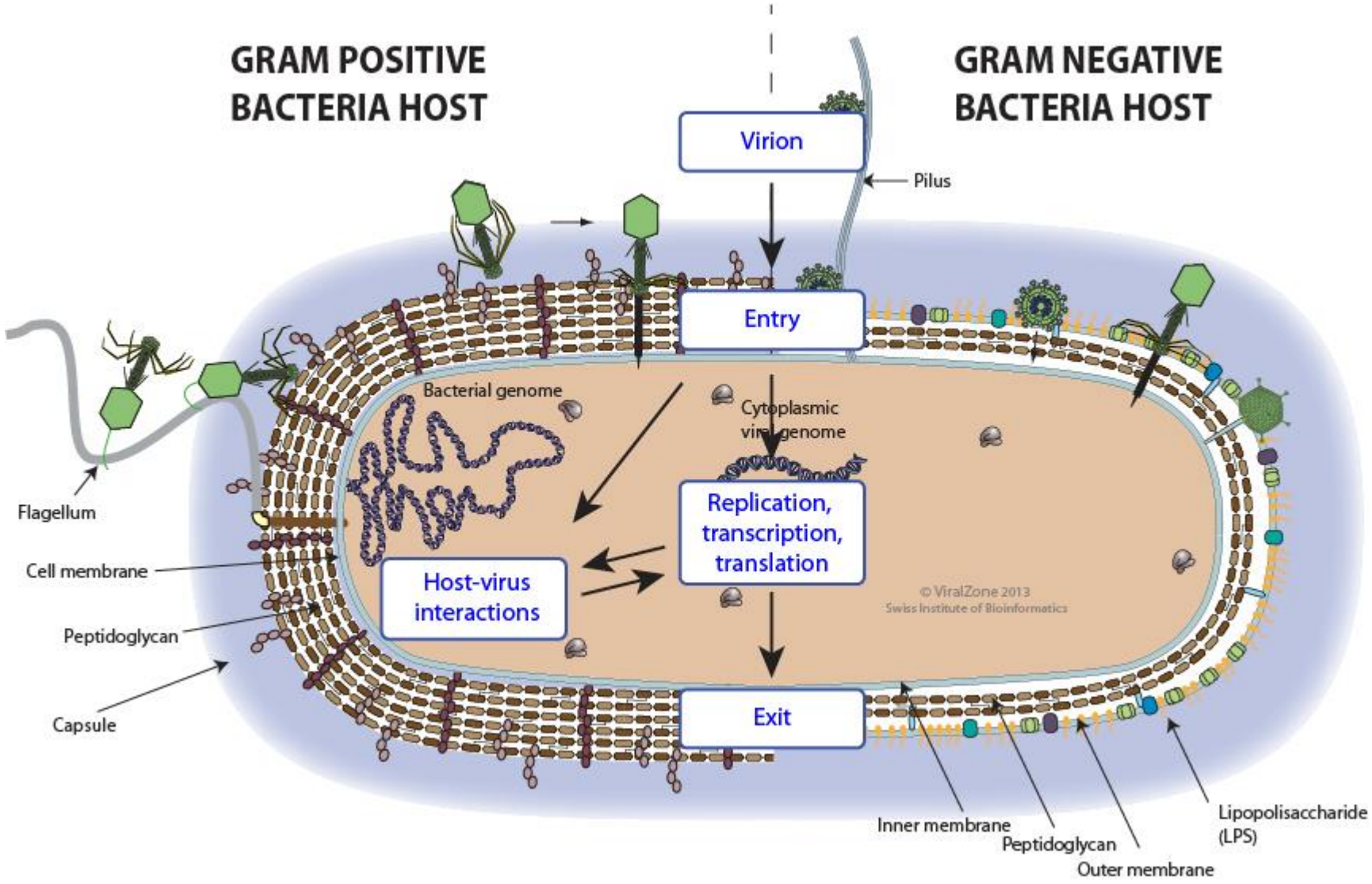




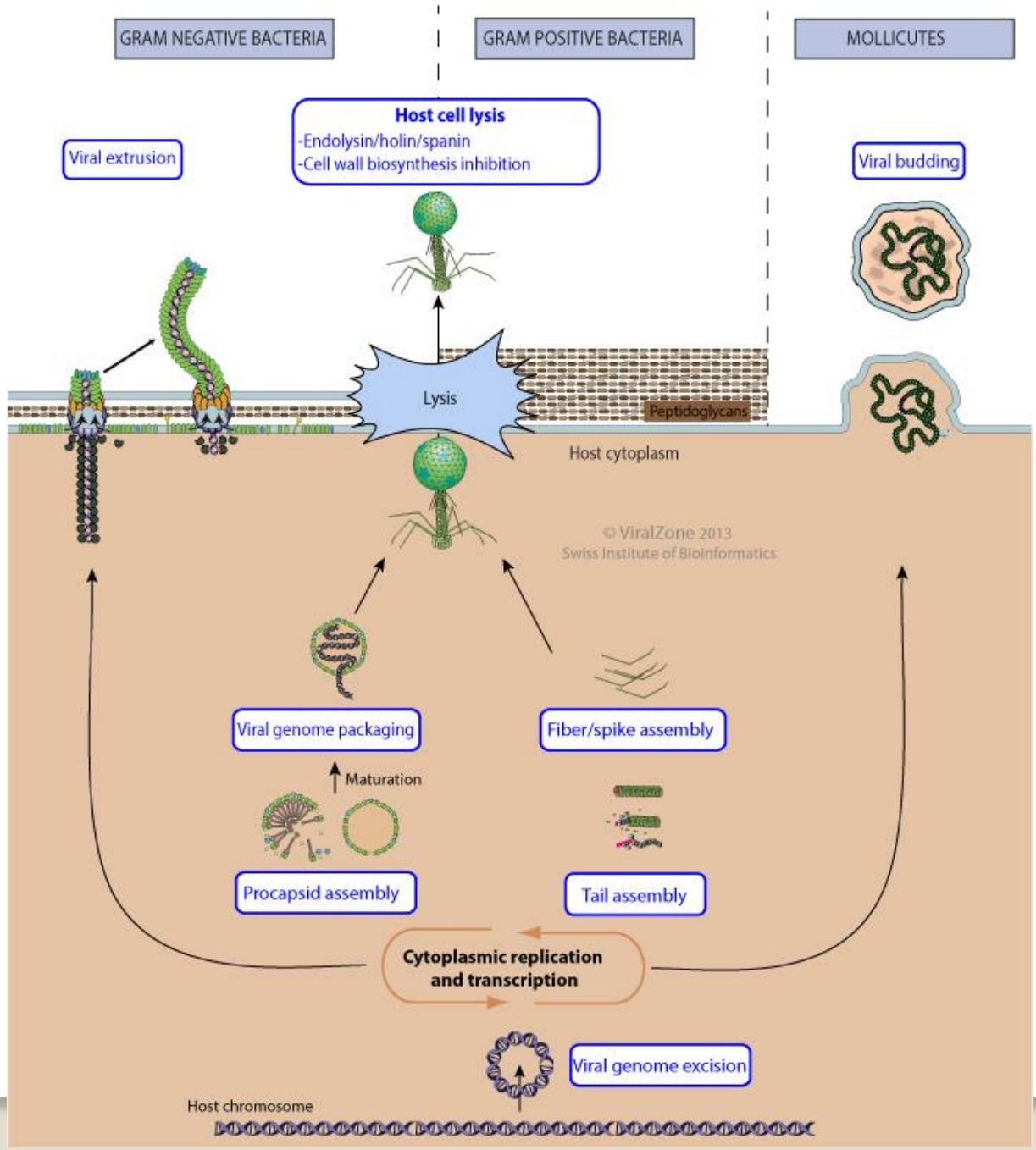
Infecciones por bacteriófagos

- Los bacteriófagos, como otros virus, deben infectar a una célula hospedera para que sea reproducido. **(ciclo de vida del fago).**
- Algunos fagos solo pueden reproducirse por medio de un ciclo de vida lítico, en el cual lisan y matan a las células infectadas.
- Otros fagos pueden alternar entre un ciclo de vida lítico y un ciclo de vida lisogénico, donde no matan a la célula infectada, sino que se copian junto con el ADN del hospedero cada vez que se divide la célula.

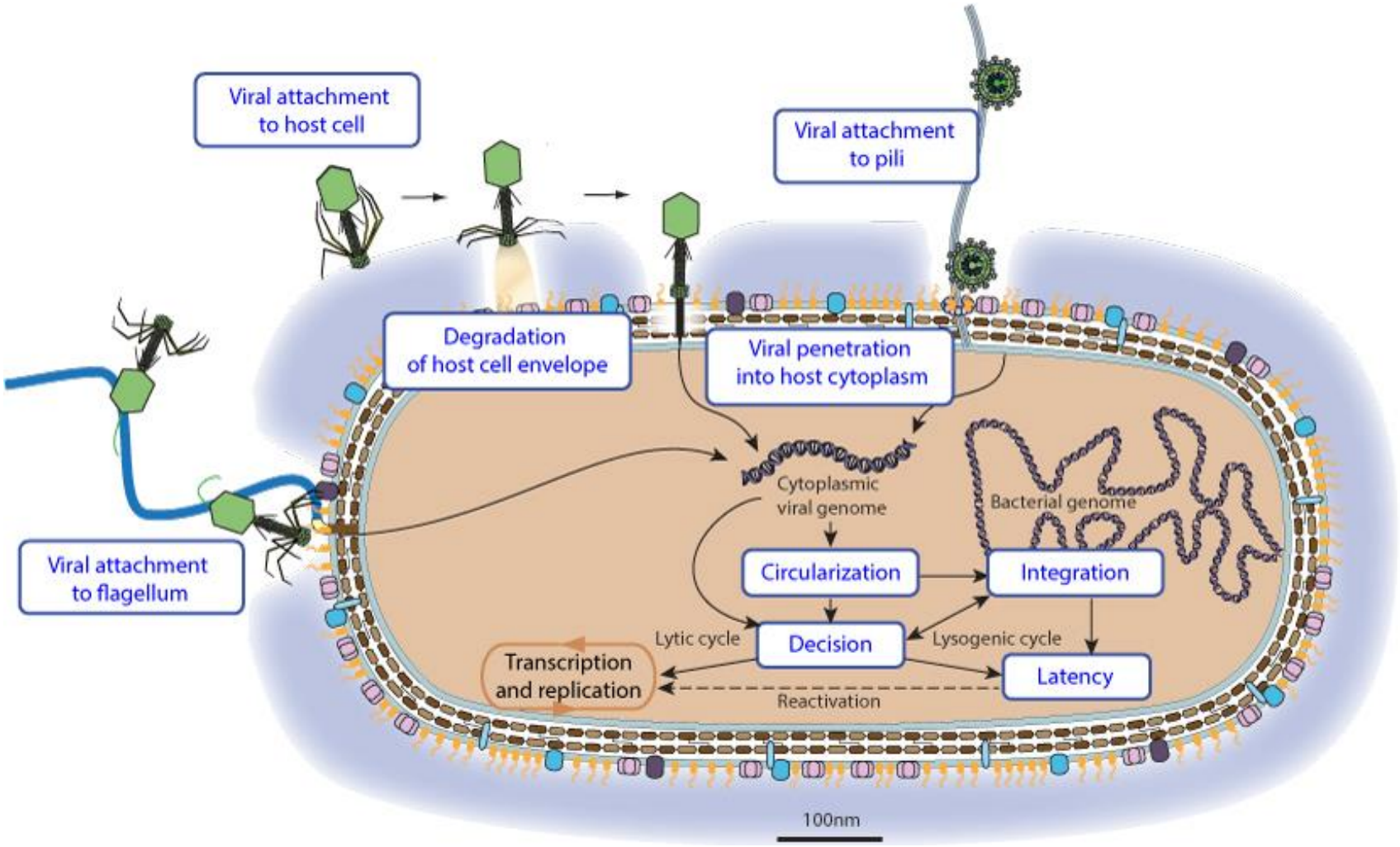



GRAM POSITIVE
BACTERIA HOST
GRAM NEGATIVE
BACTERIA HOST
Virion
Pilus
Entry
Bacterial genome
Cytoplasmic
viral genome
Replication,
transcription,
translation
Host-virus
interactions
Exit
Flagellum
Cell membrane
Peptidoglycan
Capsule
© ViralZone 2013
Swiss Institute of Bioinformatics
Inner membrane
Peptidoglycan
Outer membrane
Lipopolisaccharide
(LPS)

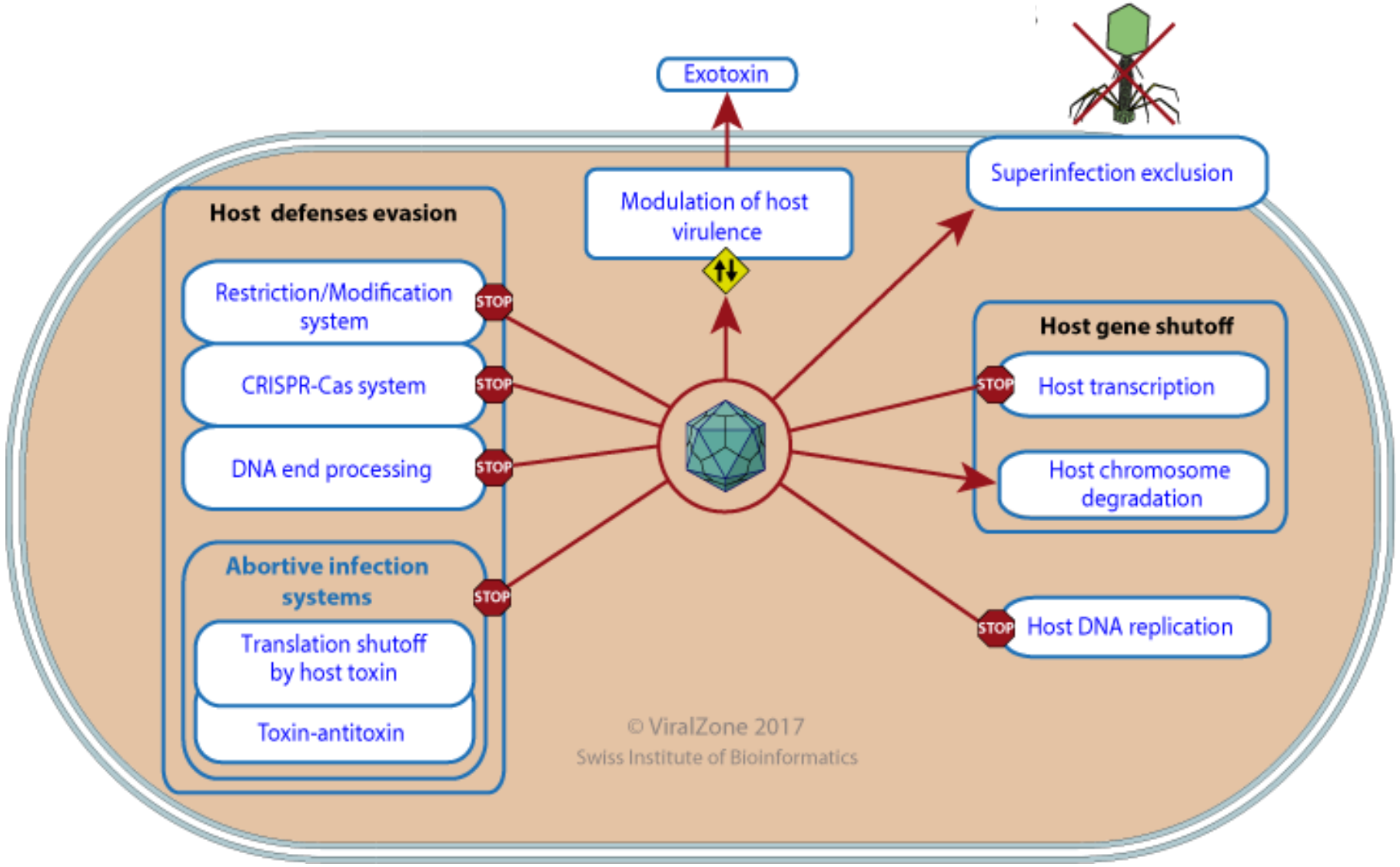
Ciclo lítico



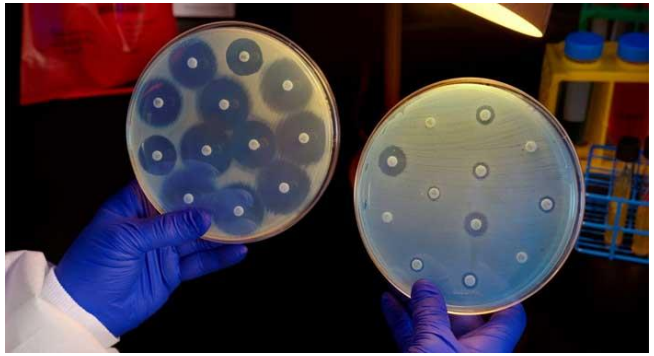
Ciclo lítico o lisogénico



Interacciones virus - Bacteria



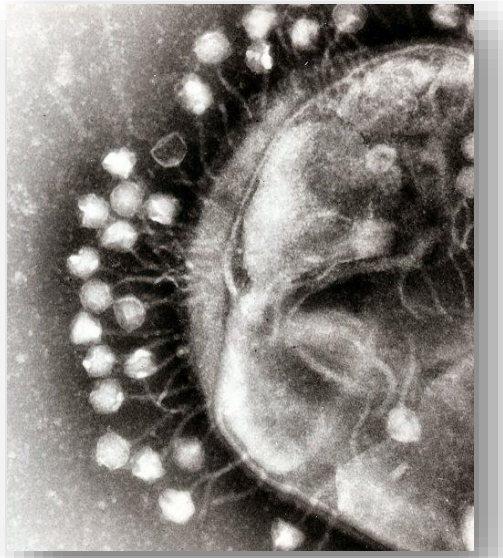
Problema



Solución

Frederick Twort
(1877–1950)

Félix d`Herelle
(1873–1949)



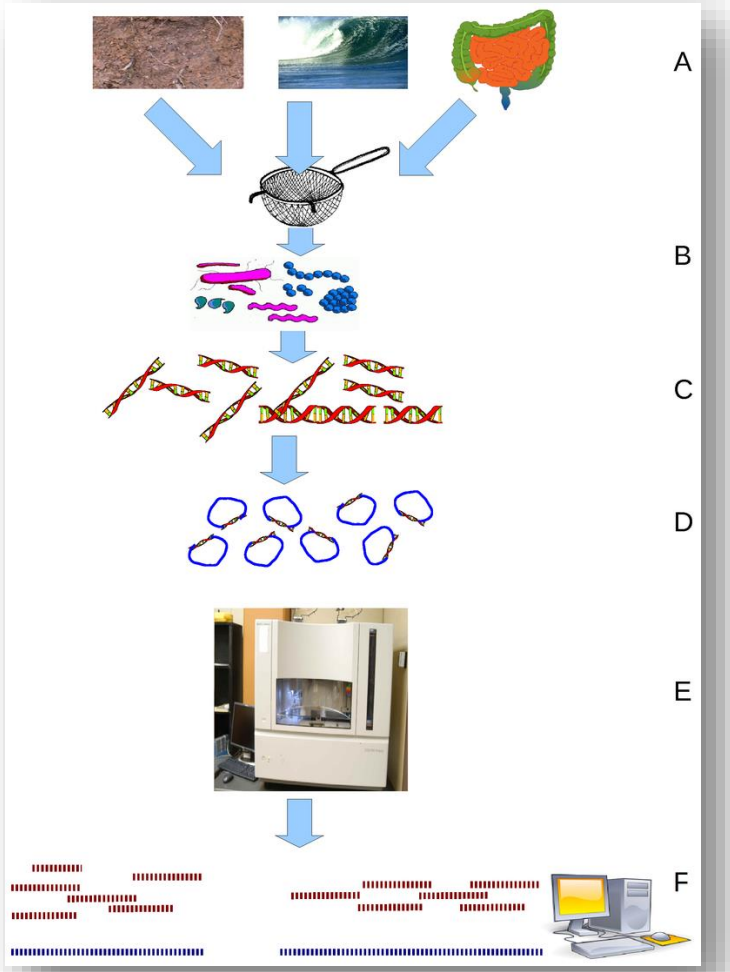
Problema/solución

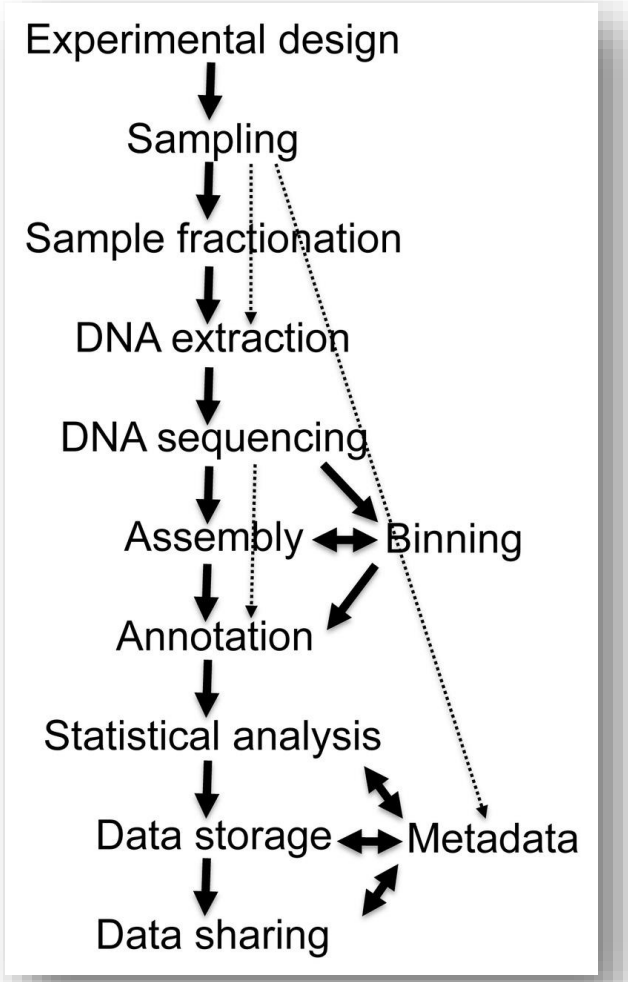
Dr. Alberto M. R. Dávila (davila@fiocruz.br) – Laboratório de Biologia Computacional e Sistemas, IOC

Dra. Ana Paula Assef (anapdca@ioc.fiocruz.br) – Laboratório de Pesquisa em Infecção Hospitalar, IOC

Dr. Eduardo de Mello Volotão (volotao@ioc.fiocruz.br) - Laboratório de Virologia Comparada e Ambiental, IOC

Proyecto de innovación





Resultados

Aguas residuales del hospital (Rio de Janeiro Brasil)

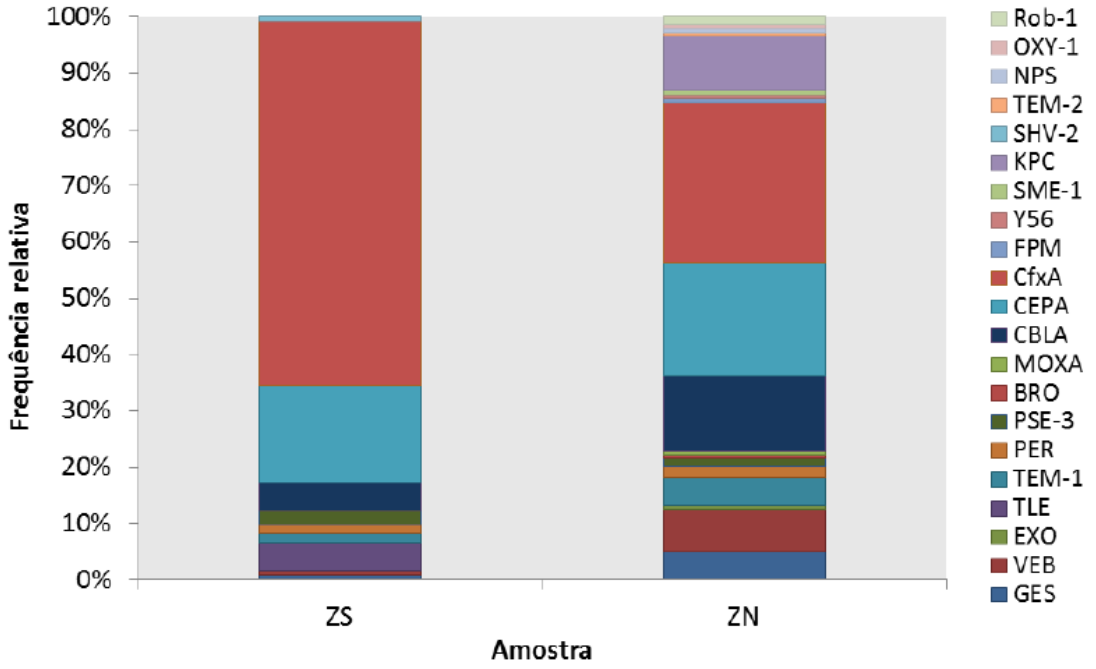


Figura 5.7 Frequência relativa das subclasses das β-lactamases classe A presentes nas amostras de esgotos hospitalares ZS (Zona Sul) e ZN (Zona Norte) classificadas a partir da base de dados ARDB.

Resultados

Aguas residuales del hospital (Rio de Janeiro Brasil)

Organism (VirNoG)	Annotation (UniProt)	Virus host
Enterobacteria phage P2	Replication gene A protein	Enterobacteriaceae [TaxID: 543]
Organism (VirNoG)	Annotation (UniProt)	Virus host
Pseudomonas phage phikZ	PHIKZ214	Pseudomonas aeruginosa [TaxID: 287]
Enterococcus phage phiEF24C	Ribonucleoside-diphosphate reductase	Enterococcus faecalis (Streptococcus faecalis) [TaxID: 1351]
Organism (VirNoG)	Annotation (UniProt)	Virus host
Vibrio phage KVP40	Putative uncharacterized protein	Vibrio parahaemolyticus [TaxID: 670]
Organism (VirNoG)	Annotation (UniProt)	Virus host
Bordetella phage BPP-1	Probable portal protein	Bordetella bronchiseptica (Alcaligenes bronchisepticus) [TaxID: 518]
Salmonella phage Vil	RIIA protector from prophage-induced early lysis	Salmonella typhi [TaxID: 90370]
Human immunodeficiency virus 1	Gag-Pol polyprotein	Homo sapiens (Human) [TaxID: 9606]
Haemophilus phage HP1	Capsid assembly scaffolding protein	Haemophilus [TaxID: 724]
Staphylococcus phage Twort	ORF021	Staphylococcus phage Twort [TaxID: 55510]
Enterobacteria phage P2	Endolysin	Enterobacteriaceae [TaxID: 543]
Salmonella phage Felix O1	Lysozyme	Salmonella [TaxID: 590]
Burkholderia phage BcepMu	Gp29	Burkholderia cenocepacia [TaxID: 216591]
Enterobacteria phage Phieco32	Thymidylate synthase thyX/thy1	Escherichia coli [TaxID: 562]
Clostridium phage phiCD119	Methyltransferase	Clostridioides difficile (Peptoclostridium difficile) [TaxID: 1496]
Halomonas phage phiHAP-1	DNA adenine methyltransferase	Halomonas aquamarina [TaxID: 77097]
Lactococcus phage c2	Recombination protein	Lactococcus (lactic streptococci) [TaxID: 1357]
Clostridium phage phiCD119	Putative uncharacterized protein	Clostridioides difficile (Peptoclostridium difficile) [TaxID: 1496]
Bacillus phage SP01	Probable portal protein	Bacillus subtilis [TaxID: 1423]
Haemophilus phage HP1	Probable portal protein	Haemophilus [TaxID: 724]
Enterobacteria phage P2	Baseplate protein J	Enterobacteriaceae [TaxID: 543]
Halomonas phage phiHAP-1	Putative baseplate assembly protein J	Halomonas aquamarina [TaxID: 77097]

Resultados

Aguas residuales del hospital (Rio de Janeiro Brasil)

Organism (VirNoG)	Annotation (UniProt)	Virus host
Bordetella phage BPP-1	Probable portal protein	Bordetella bronchiseptica (Alcaligenes bronchisepticus) [TaxID: 518]
Salmonella phage Vil	Gp61 DNA primase subunit	Salmonella typhi [TaxID: 90370]
Vibrio phage KVP40	dTMP (Thymidylate) synthase	Vibrio parahaemolyticus [TaxID: 670]
Pseudomonas phage phikZ	PHIKZ235	Pseudomonas aeruginosa [TaxID: 287]
Pseudomonas phage LUZ24	Putative uncharacterized protein gp40	Pseudomonas aeruginosa [TaxID: 287]
Staphylococcus phage Twort	ORF052	Staphylococcus phage Twort [TaxID: 55510]
Enterobacteria phage P1	DNA-invertase	Enterobacteriaceae [TaxID: 543]
Organism (VirNoG)	Annotation (UniProt)	Virus host
Vibrio phage KVP40	DenV Endonuclease V	Vibrio parahaemolyticus [TaxID: 670]
Bordetella phage BPP-1	Repressor protein cI	Bordetella bronchiseptica (Alcaligenes bronchisepticus) [TaxID: 518]
Bacillus phage SP01	Gp31.2	Bacillus subtilis [TaxID: 1423]
Enterobacteria phage T5	Putative H-N-H-endonuclease P-TflIX	Escherichia coli [TaxID: 562]
Salmonella phage Felix O1	Putative uncharacterized protein	Salmonella [TaxID: 590]
Enterobacteria phage T7	Protein 7.7	Escherichia coli [TaxID: 562]
Pseudomonas phage LUZ24	Putative uncharacterized protein gp40	Pseudomonas aeruginosa [TaxID: 287]
Enterobacteria phage T4 sensu lato	aracterized 17.5 kDa protein in tk-vs intergenic r	Escherichia coli [TaxID: 562]
Enterobacteria phage Phieco32	Appr-1-p processing enzyme family	Escherichia coli [TaxID: 562]
Chlamydia phage 1	Capsid protein VP1	Chlamydophila psittaci (Chlamydia psittaci) [TaxID: 83554]
Lactococcus phage c2	Recombination protein	Lactococcus (lactic streptococci) [TaxID: 1357]
Mouse mammary tumor virus	Gag-Pro-Pol polyprotein	Mus musculus (Mouse) [TaxID: 10090]
Vibrio phage KVP40	RIIB Protector from prophage-induced early lysis	Vibrio parahaemolyticus [TaxID: 670]
Salmonella phage epsilon15	Structural protein	Salmonella anatum [TaxID: 58712]
Staphylococcus phage Twort	ORF063	Staphylococcus phage Twort [TaxID: 55510]
Burkholderia phage BcepMu	Gp50	Burkholderia cenocepacia [TaxID: 216591]
Halomonas phage phiHAP-1	Putative baseplate assembly protein J	Halomonas aquamarina [TaxID: 77097]
Mycobacterium phage Bxz1	Gp137	Mycobacterium smegmatis [TaxID: 1772]
		Mycobacterium vaccae [TaxID: 1810]

Metodología

Área de estudio y coleta de muestras
(Aguas residuales hospitalar e de lagunas)

Filtragem (0.8, 0.45 y 0.22 µm)

Aislamiento (Bacterias indicadoras)

Prueba de lisis (Bacterias patógenas)

Secuenciación

Análisis Computacionales

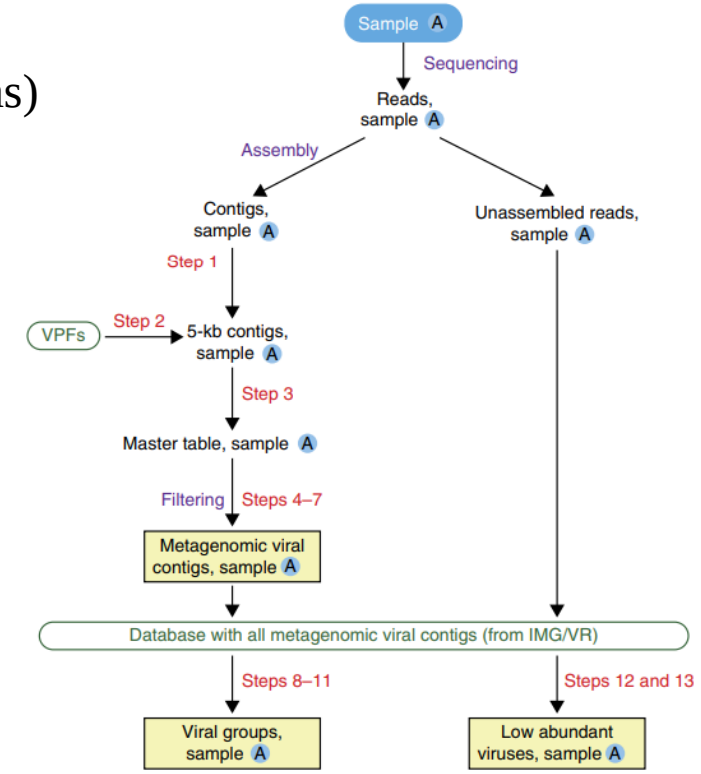
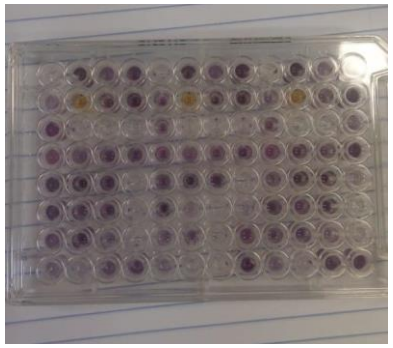
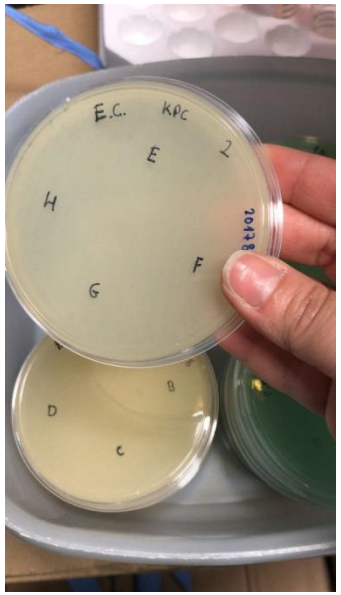


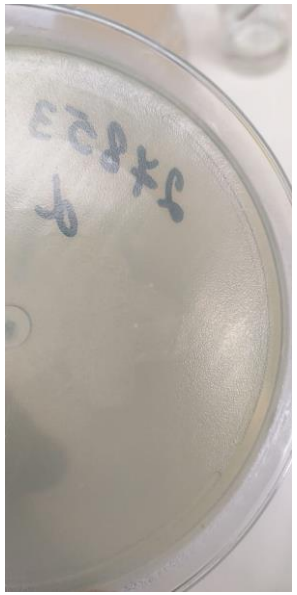
Figure 1 | Overview of the computational workflow. General pipeline of the protocol, showing the different steps required for the detection of abundant and low-abundant metagenomic viral contigs, as well as their classification into viral groups. Viral protein family models (VPFs) and all metagenomic viral contigs from IMG/VR are available through the aforementioned FTP site.

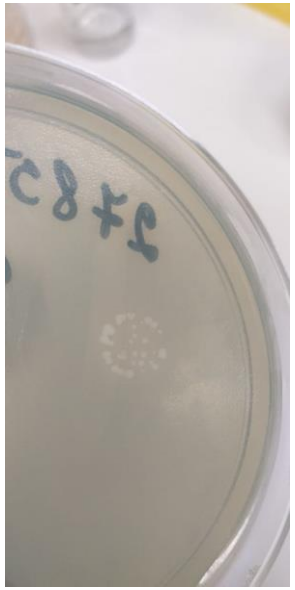
Metodología y resultados

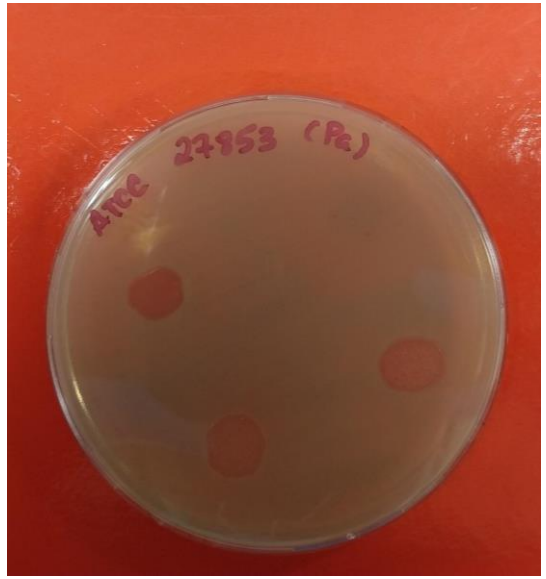
Metodología y resultados











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*

Rebekah M. Dedrick[1,4], Carlos A. Guerrero-Bustamante[1,4], Rebecca A. Garlena[1], Daniel A. Russell[1], Katrina Ford[2], Kathryn Harris[2], Kimberly C. Gilmour[2], James Soothill[2], Deborah Jacobs-Sera[1], Robert T. Schooley[3], Graham F. Hatfull[1*] and Helen Spencer[2*]

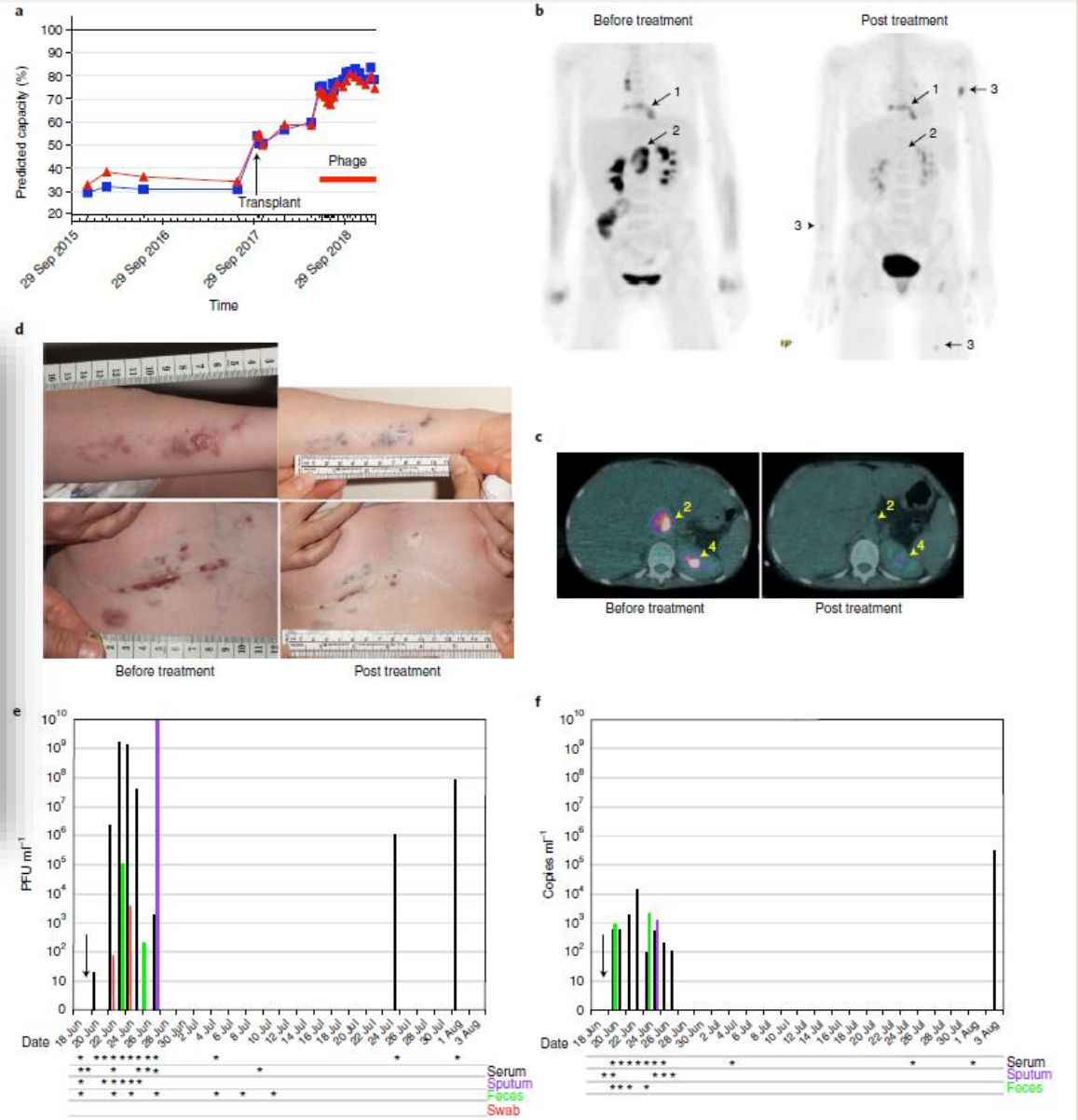


Fig. 1 | Patient status before and after phage treatment. a, Lung function as percent predicted FEV1 (blue) and forced vital capacity (FVC; red). **b**,**c**, Whole-body (**b**) and cross-section (**c**) PET-CT scans 12 weeks before and 6 weeks post phage treatment. Arrows show (1) the sternal area and surrounding soft tissue, (2) abdominal lymph nodes at the porta hepatis, and (3) skin nodules. Arrow 4 indicates normal kidney excretion. **d**, Upper and lower panels show the patient's left arm and sternal wound, respectively, immediately prior to and 6 months after phage treatment. **e**,**f**, Phage titers by plaque assay (**e**) or dPCR (**f**) following phage administration (vertical arrow). Serum (black bars), sputum (purple bars), feces (green bars), and wound swab (red bars) were tested on the dates indicated (asterisks).

frontiers in Microbiology

PERSPECTIVE
published: 08 September 2016
doi: 10.3389/fmicb.2016.01352

More Is Better: Selecting for Broad Host Range Bacteriophages

*Alexa Ross, Samantha Ward and Paul Hyman**

Department of Biology and Toxicology, Ashland University, Ashland, OH, USA

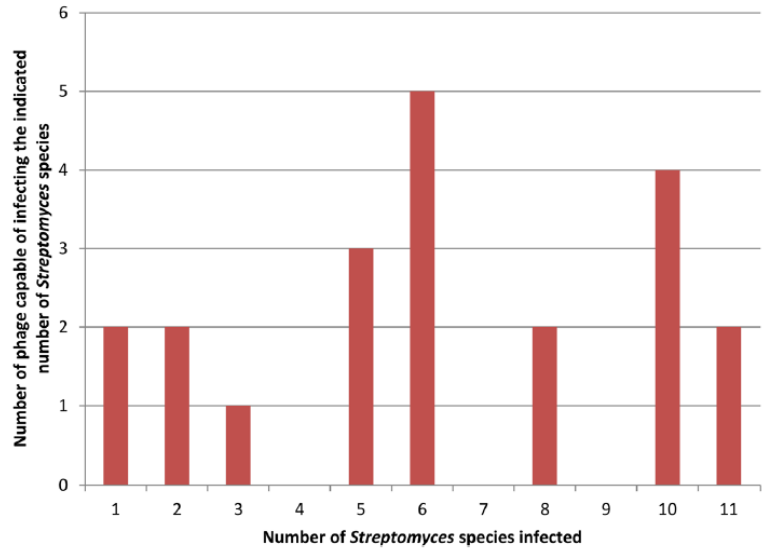


FIGURE 1 | Distribution of host range breadths of *Streptomyces* temperate phages. Data for this figure is taken from Table 3 of Greene and Goldberg (1985). Twenty-one distinct phages were tested on 11 different host strains. In this figure both clear and turbid plaques (as indicated in the original results) are combined to indicate host susceptibility to a phage.

antibiotics

MDPI

Article

Bystander Phage Therapy: Inducing Host-Associated Bacteria to Produce Antimicrobial Toxins against the Pathogen Using Phages

T. Scott Brady [1], Christopher P. Fajardo [1], Bryan D. Merrill [1], Jared A. Hilton [1], Kiel A. Graves [1], Dennis L. Eggett [2] and Sandra Hope [1,*]

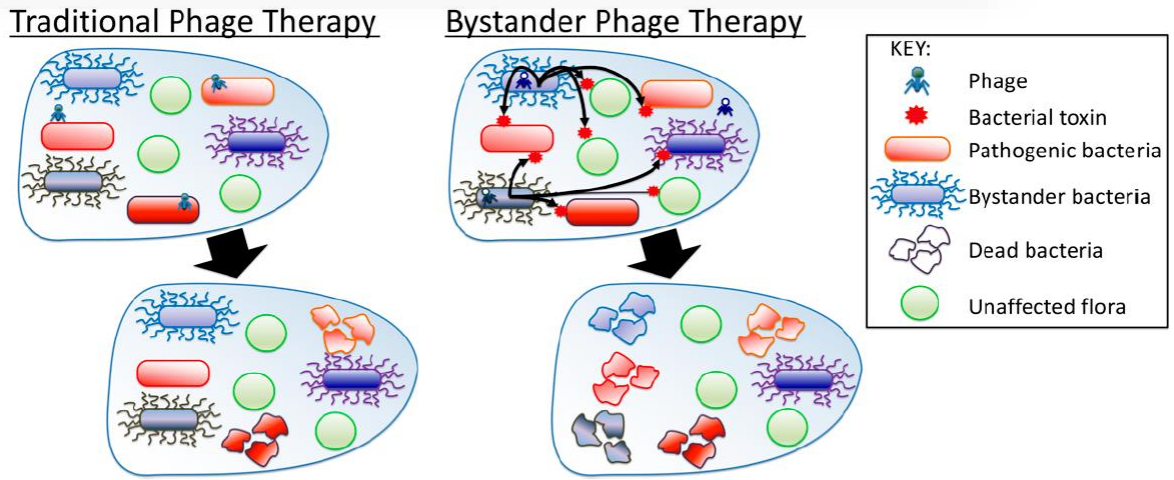
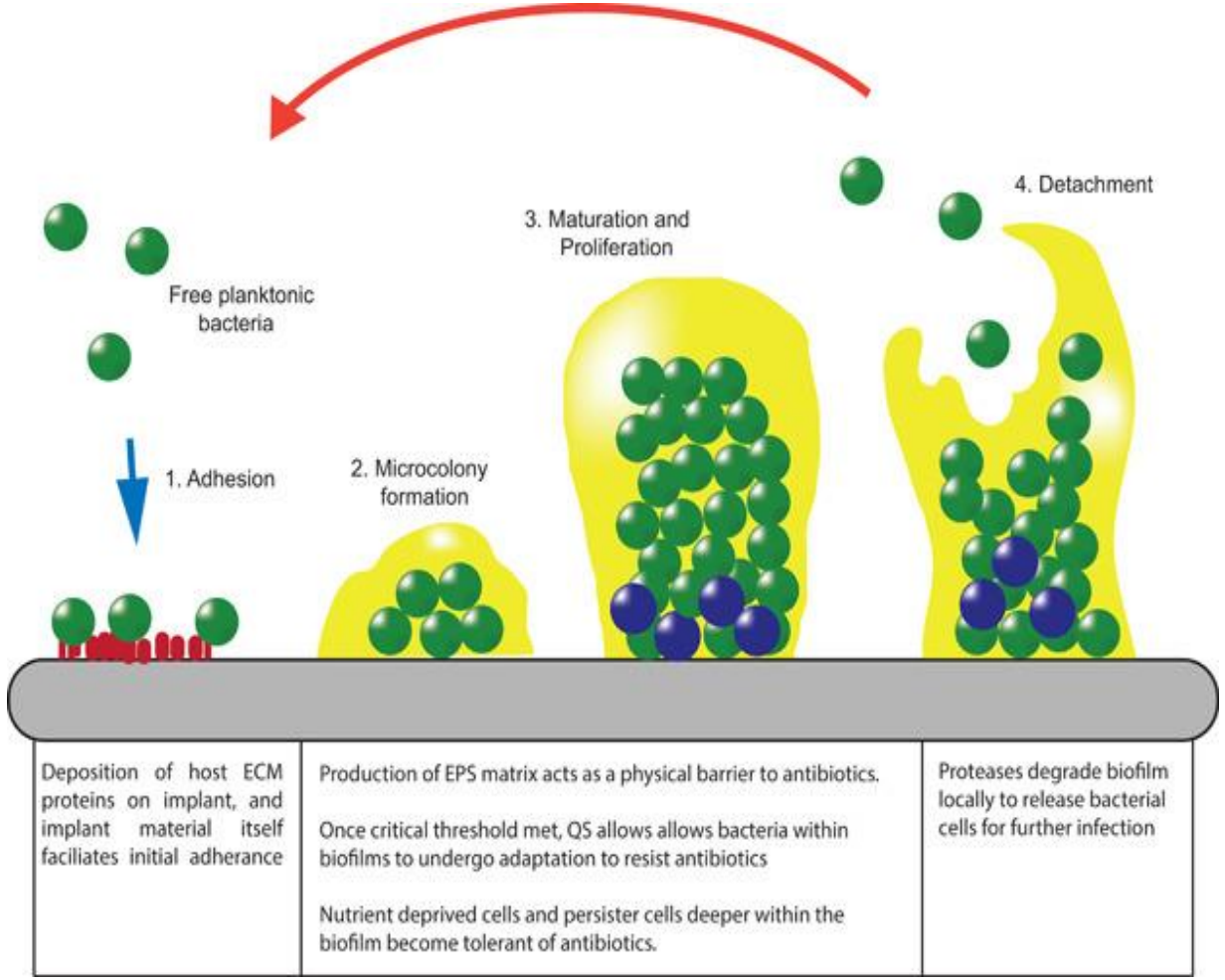


Figure 5. Mechanism of pathogen killing using phage therapy versus bystander phage therapy. In traditional phage therapy, phages against a pathogenic bacterium bind and lyse come bacterial strains, but may leave others unscathed (Left Panel). In Bystander Phage Therapy, phages against a bystander induce the bystander to make a toxin that kills all versions of the pathogenic bacteria while leaving an untouched population of itself that was not infected by phages (Right Panel).

Current review—The rise of bacteriophage as a unique therapeutic platform in treating peri-prosthetic joint infections



Journal of Orthopaedic Research, Volume: 36, Issue: 4, Pages: 1051-1060, First published: 02 October 2017, DOI: (10.1002/jor.23755)

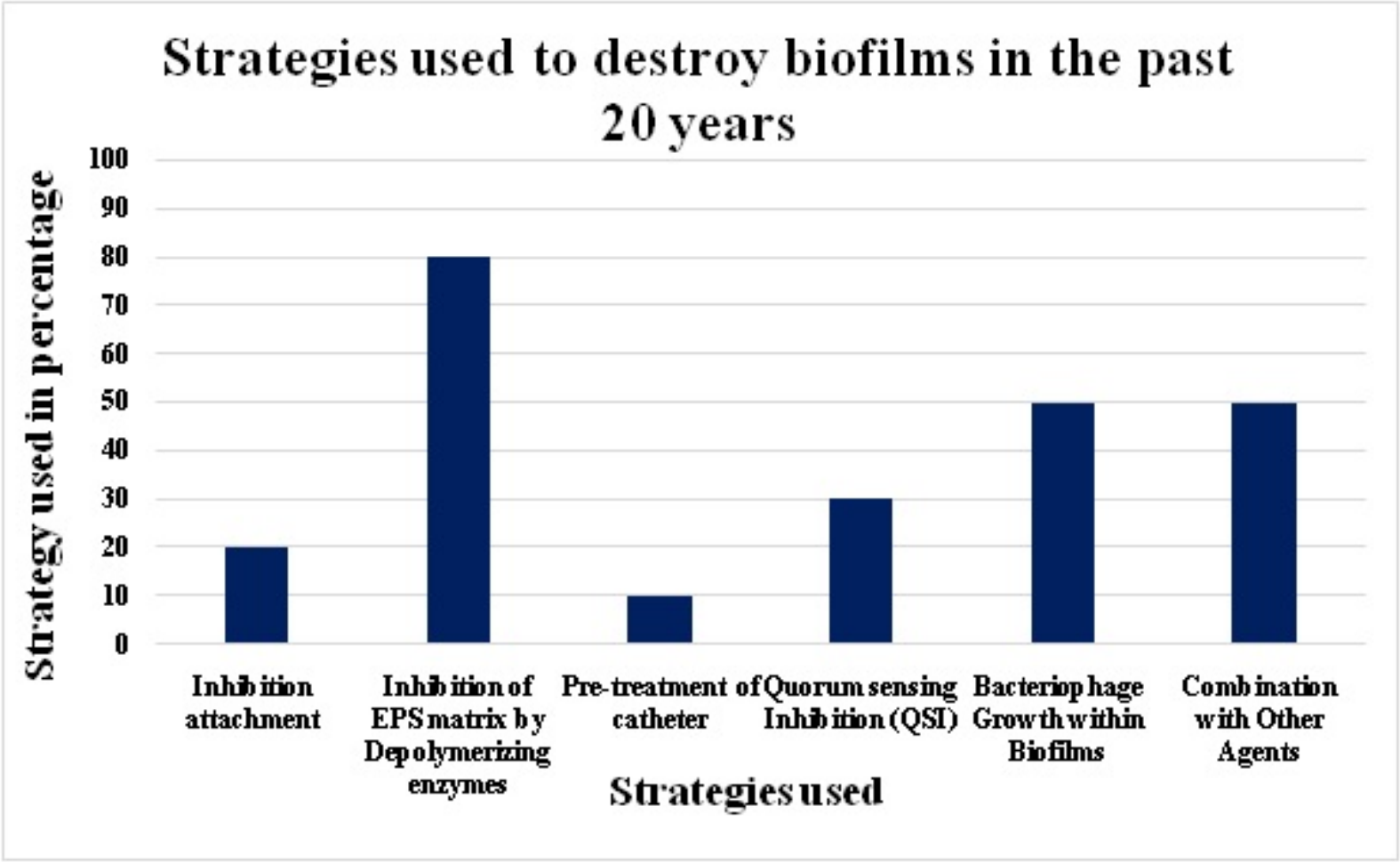
Table 3 Partial summary of more modern clinical treatment of infected wounds

Authors	Year	Bacterial species	Type of infection	Degree of success	Comments
Fish et al. [138, 139]	2016, 2018	*S. aureus*	Diabetic toe ulcers	100%	Of 7 infections treated
Miedzybrodzki et al. [140]	2012	Various	Various	37%	Of 30 "soft-tissue infections" treated
Rhoads et al. [141]	2009	*E. coli*, *P. aeruginosa*, *S. aureus*	Venous leg ulcers	0%	Of 39 treated; this was a phase I trial using well-characterized phages rather than phages for which previous efficacy had been indicated
Marza et al. [142]	2006	*P. aeruginosa*	Burn	100%	Of 1 treated, with success indicated by skin graft take
Jikia et al. [143]	2005	*S. aureus*	Radiation burn	100%	Of 2 treated with a phage-impregnated artificial skin (PhagoBioDerm)
Markoishvili et al. [144]	2002	Various	Venous stasis ulcers, poorly healing wounds	70%	Of 96 treated, with success indicated as complete healing
Weber-Dąbrowska et al. [145]	2000	Various	Bedsores	81%	Of 16 treated, showing full recovery
Weber-Dąbrowska et al. [145]	2000	Various	Burns	100%	Of 49 treated, showing marked improvement (14%) or better (86%)
Weber-Dąbrowska et al. [145]	2000	Various	Postoperative	100%	Of 35 treated, showing marked improvement (17%) or better (83%)
Weber-Dąbrowska et al. [145]	2000	Various	Varicose ulcers	88%	Of 77 treated, showing marked improvement (27%) or better (61%)
Ślopek et al. [146]	1987	Various	Various	85%	Of 72 treated (49 + 23), with the rest showing only transient improvement

Biofilm Attenuation by Bacteriophages

Manal Mohammed Alkhulaifi

King Saud University, College of Science, Department of Botany and Microbiology,
Box Office: 55670, 11544 Riyadh, Saudi Arabia.

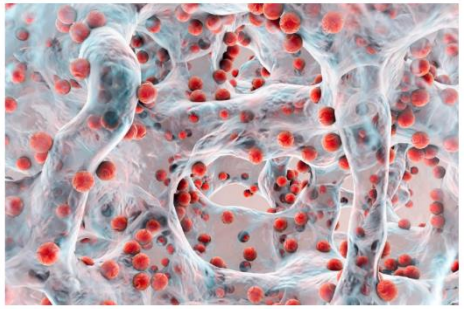


BETELGEUX
CHRISTEYNS FOOD HYGIENE

¿QUIÉNES SOMOS? ARTÍCULOS

22 SEPTIEMBRE, 2017

Bacteriófagos para el control de biofilms en la industria alimentaria



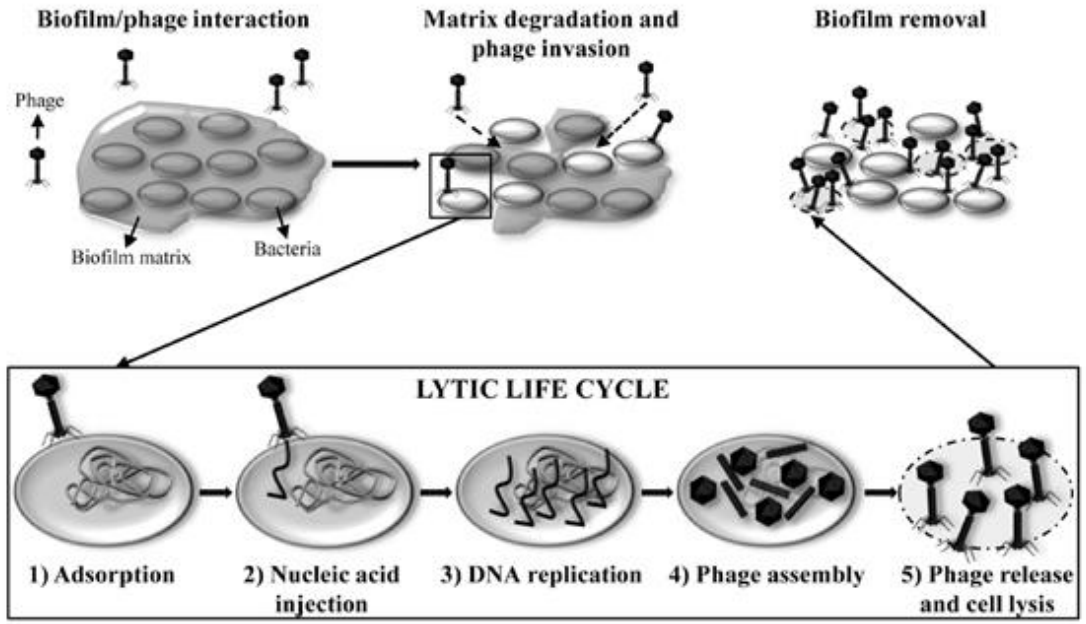
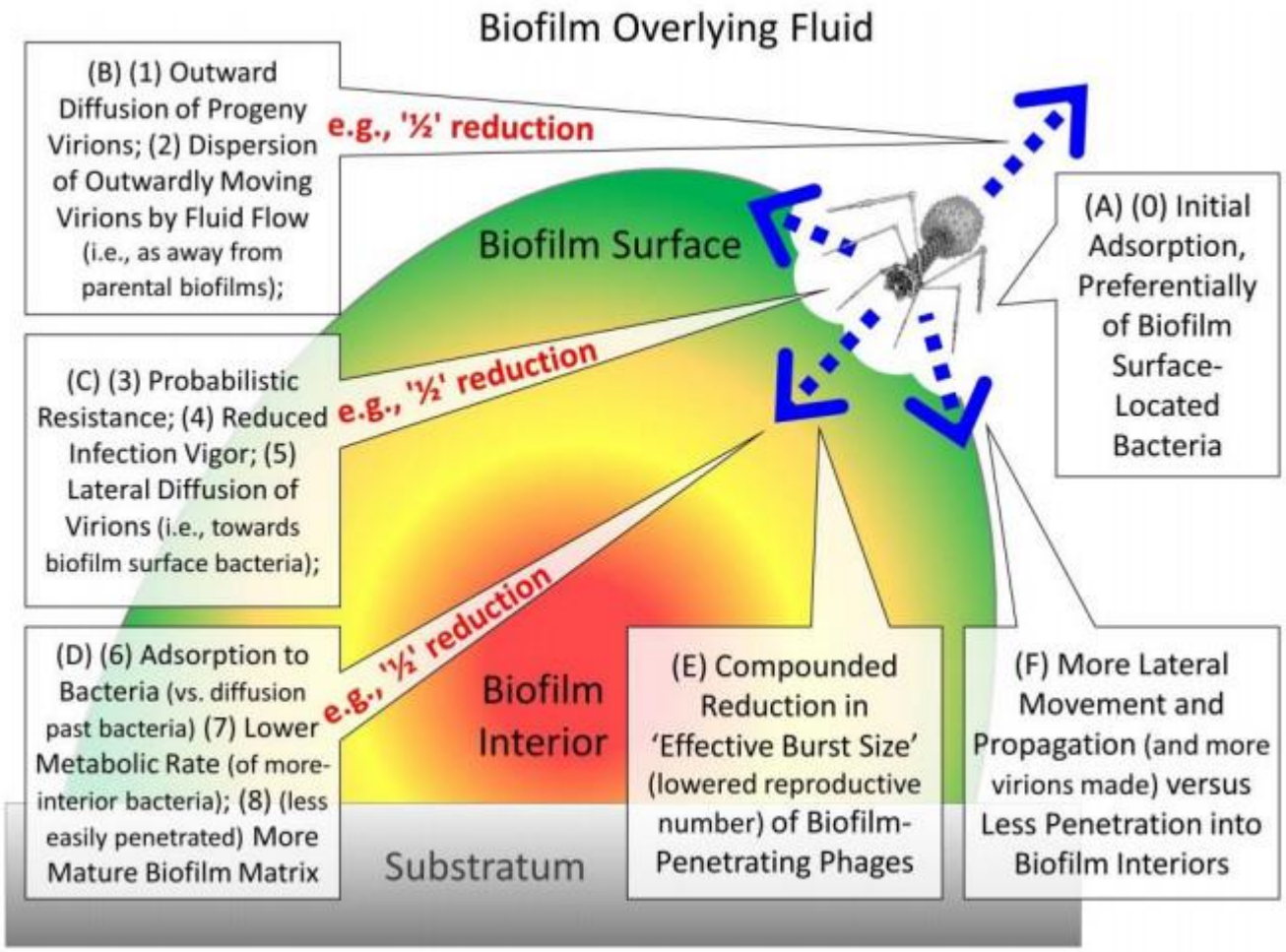


Figura 1. Ciclo lítico de los fagos en el interior de un biofilm. Extraído de [5] (Creative Commons Attribution License).



Stephen T. Abedon. Phage "delay" towards enhancing bacterial escape from biofilms: a more comprehensive way of viewing resistance to bacteriophages[J]. AIMS Microbiology, 2017, 3(2): 186-226. doi: 10.3934/microbiol.2017.2.186 shu

From: Bacteriophage therapy against *Pseudomonas aeruginosa* biofilms: a review

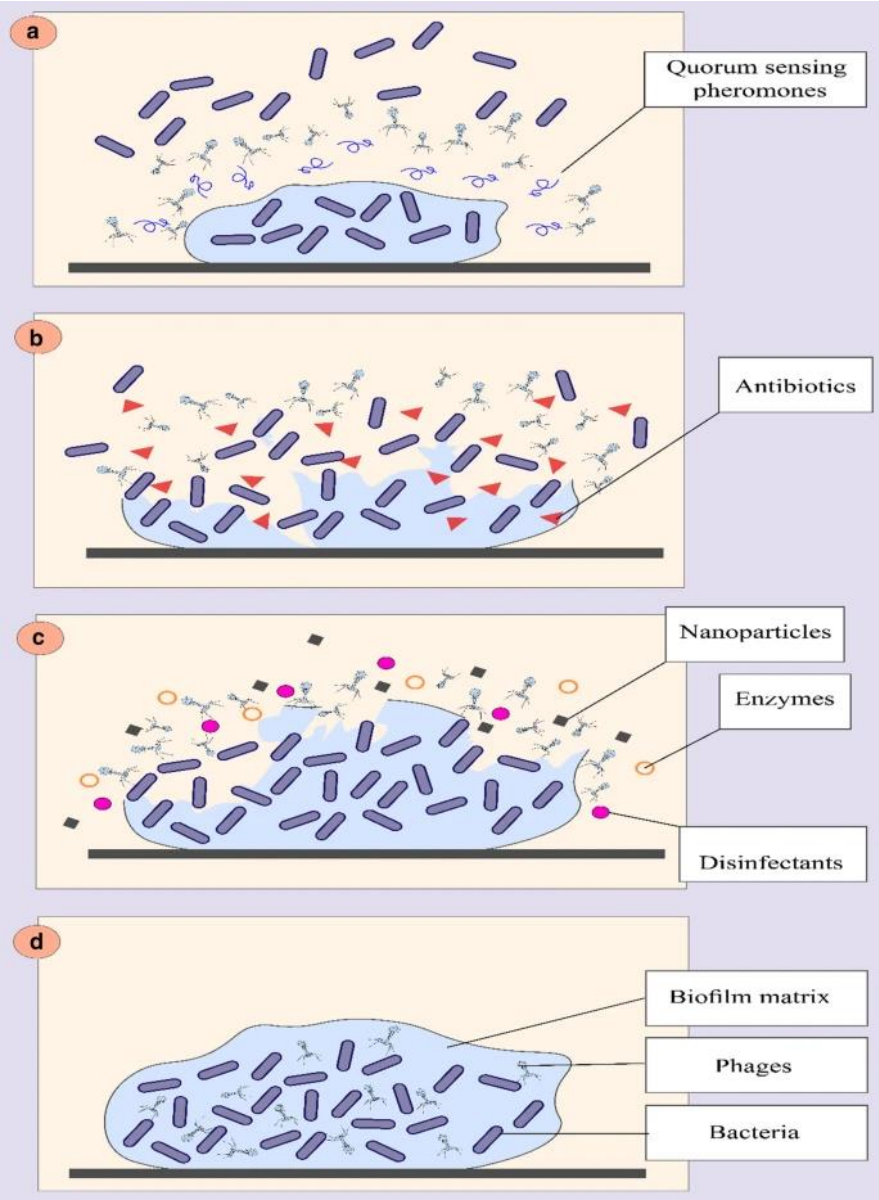
First author and year	Species	Type of phage	Experimental results	References
Liyuan Mi (2019)	*P. aeruginosa* 1193	Lytic IME180 phage depolymerase	This phage enzyme degraded *P. aeruginosa* exopolysaccharide, enhanced bactericidal activity mediated by serum complement proteins in vitro, and disrupt the bacterial biofilm	[50]
Yangyijun Guo (2019)	*P. aeruginosa* PAO1	vB_PaeM_SCUT-S1 and vB_PaeM_SCUT-S2	These two phages inhibited the growth of bacterium at low multiplicity of infection levels, had good performance both on preventing biofilm formation and eradicating preformed biofilms	[51]
Tomasz Olszak (2017)	*P. aeruginosa* PAO1	O-specific polysaccharide lyase from the phage LKA1	This enzyme reduced *P. aeruginosa* virulence, sensitized this bacterium to serum complement activity, and caused biofilm degradation	[52]
Diana R. Alves (2016)	*P. aeruginosa* PAO1	A cocktail of six specific phage	After 4 h of biofilm contact with the phage suspension (MOI 10), more than 95% of biofilm biomass was eliminated, and 48 h after adding the phage cocktail in the flow biofilm model, the biofilm was dispersed	[53]
Muafia Shafique (2017)	A hospital isolate of *P. aeruginosa*	JHP	This phage reduced biofilm biomass from 2 to 4.5 logs (60–90%) and reduced bacterial load that highlights its potential to prevent biofilm formation from indwelling medical devices	[54]
Ruoting Pei (2014)	*P. aeruginosa* PAO1	Engineered T7 bacteriophage that encode lactonase enzyme	This phage lyses bacteria and expressed quorum-quenching enzymes that inhibited biofilm formation	[40]
A. Phee (2013)	*P. aeruginosa* PA14	JBD4 and JBD44a	These phages significantly reduced the mean percentage of biofilm biomass in 24 and 96-h grown on microplates, but in 24 and 96-h *P. aeruginosa* PA14 biofilms in a root canal model, phage therapy did not affect biofilm inhibition	[55]
Katarzyna Danis-Wlodarczyk (2015)	*P. aeruginosa* PAO1	Bacteriophages KTN6 and KT28	Both of these bacteriophages reduced colony-forming units (70–90%) in 24 h to 72 h *P. aeruginosa* PAO1 biofilm cultures, reduced the secretion of pyocyanin, and pyoverdin, and increased diffusion rate through the biofilm matrix	[56]
Susan M. Lehman (2014)	Clinical *P. aeruginosa* and *Proteus mirabilis*	Novel phages	Phage pretreatment reduced *P. aeruginosa* and Proteus mirabilis biofilm counts by 4 log10 CFU/cm2 and 2 log10 CFU/cm2, respectively, so it is reported that pretreatment of a hydrogel urinary catheter with a phage cocktail can significantly reduce mixed-species biofilm formation by clinically relevant bacteria	[57]
Diana Pires (2011)	*P. aeruginosa* PAO1 and ATCC 10,145	PhiIBB-PAA2 and phiIBB-PAP21),	Both phages after 2 h of infection reduced approximately 1–2 log the biofilm population, and the reduction was further enhanced after 6 h of biofilm infection. *P. aeruginosa* PAO1 showed resistance to phiIBB-PAP21, while phage phiIB-PAA2 for *P. aeruginosa* ATCC10145 continued to destroy biofilm cells, even after 24 h of infection	[58]
P. Knezevic (2011)	*P. aeruginosa* ATCC 9027	δ, J-1, σ-1 and 001A	Phages δ and 001A inhibited bacterial growth and biofilm formation for more than a half at all MOIs, but σ-1 significantly inhibited bacterial growth only at very high MOIs and had no effect on biofilm formation	[59]
Matthew K. Kay (2011)	*P. aeruginosa* PAO1	*Escherichia coli* bacteriophage _W60 and *P. aeruginosa* bacteriophage PB-1	In mixed-species biofilm communities, both of bacterium maintained stable cell populations in the presence of one or both phages	[60]
Weiling Fu (2009)	*P. aeruginosa* M4	*P. aeruginosa* phage M4 and five-phage cocktail from a larger library of *P. aeruginosa* phages	The pretreatment of catheters with phage reduced viable biofilm count by 2.84 log10, and the pretreatment of catheters with the cocktail of phage reduced the 48-h mean biofilm cell density by 99.9%	[61]

Chegini, Z., Khoshbayan, A., Taati Moghadam, M. *et al.* Bacteriophage therapy against *Pseudomonas aeruginosa* biofilms: a review. *Ann Clin Microbiol Antimicrob* **19,** 45 (2020). https://doi.org/10.1186/s12941-020-00389-5

Biofilm forming bacteria	Bacterial Properties	Phage	Outcome	References
Acinetobacter baumannii	XDR *A. baumannii*	Phage AB1801	This phage inhibited biofilm formation and reduced preformed biofilms in a dose-dependent manner	[70]
	MDR *A. baumannii*	Phage lysin PlyF307	Treatment with PlyF307 was able to significantly reduce planktonic and biofilm of *A. baumannii*, both in vitro and in vivo	[71]
	A. baumannii strain AIIMS 7	Lytic bacteriophageAB7-IBB1	The phage affected *A. baumannii* biofilm formation on an abiotic (polystyrene) and biotic (human embryonic kidney 293 cell line) surface	[72]
	Clinical isolate of *A. baumannii* strain AIIMS 7	Phage AB7-IBB2	The phage could inhibit *A. baumannii* biofilm formation and disrupt preformed biofilm as well	[73]
Klebsiella pneumoniae	P DR *K. pneumonia* UA168	The phage KP168	After 48 h of co-cultivation of this phage and the host bacteria at each MOI, the inhibition rates of biofilm were similar, with an average of about 45%	[74]
	MDR *K. pneumonia*	Depolymerase Encoded by Bacteriophage SH-KP152226	This enzyme showed specific enzymatic activities in the depolymerization of the *K. pneumoniae* capsule and was able to significantly inhibit biofilm formation and/or degrade formed biofilms	[75]
	An environmental isolate of *K. pneumoniae* ShA2 strain	TSK1 bacteriophage	Post-treatment with TSK1 against different age *K. pneumoniae* biofilms reduced 85–100% biofilm biomass. Pre-treatment of TSK1 bacteriophage against the biofilm of *K. pneumoniae* reduced > 99% biomass in the initial 24 h of incubation	[76]
	MDR *K. pneumoniae* KP/01	Bacteriophage ZCKP1	This phage reduced bacterial counts and biofilm biomass (> 50%) when applied at a high multiplicity of infection (50 PFU/CFU)	[77]
	A clinical strain of *K. pneumoniae*	Bacteriophage Z	Phage Z reduced biofilm biomass twofold and threefold after 24 and 48 h, respectively	[78]
Staphylococcus aureus	MRSA	UPMK_1 and UPMK_2 phages	Both bacteriophages were able to destroy biofilms using their lytic enzymes	[79]
	MRSA and MSSA	Bacteriophage CSA13	This bacteriophage removed over 78% and 93% of MSSA and MRSA biofilms in an experimental setting, respectively	[80]
	MRSA ATCC 43,300	Bacteriophage Sb-1	This phage showed a synergistic effect with antibiotics on eradicating MRSA biofilm, direct killing activity on ≈ 5 × 105 CFU/mL persisters cells, and degraded MRSA polysaccharide matrix	[81]
Escherichia coli	*E. coli* MG1655 and MDR UPEC strain 390G7	Bacteriophage vB_EcoP-EG1	vB_EcoP-EG1eliminated biofilm of these bacteria. The median biofilm biomass reduction was about 60% and 50% for *E. coli* MG1655 and for clinical isolate 390G7 after 24 h, respectively	[82]
	E. coli TG1	T3 bacteriophage	T3 at lower bacteriophage titers (10^3 PFU/ml) inhibited the production of biofilm	[83]
	E. coli 30	vB_EcoM-UFV017 (EcoM017)	This phage reduced the bacterial growth and the quantity of biofilm formed by *E. coli* in 90.0% and 87.5%, respectively	[84]
Enterococcus faecalis	*E. faecalis* clinical strains	vB_EfaH_EF1TV	This phage infected *E. faecalis* and degraded biofilm formed by this bacterium	[85]
	VRE *E. faecalis*	Vancomycin-phage EFLK1	This phage, in combination with vancomycin, was synergistically effective against VRE planktonic and biofilm cultures	[86]
	E. faecalis and *Enterococcus* clinical isolates	vB_EfaS-Zip and vB_EfaP-Max	The cocktail of these phages reduced 2 and 1 log CFU/mL *E. faecalis* load in biofilms formed in the wound after 3 and 6 h of treatment, respectively, and significantly reduced cell concentration in dual-species biofilm	[87]

MDR, Multi-drug resistant; PDR, Pan-drug resistant; MRSA, Methicillin-resistant *S. aureus*; MSSA, Methicillin-susceptible *S. aureus*; VRE, Vancomycin-resistant Enterococcus, UPEC: Uropathogenic *E. coli*

Chegini, Z., Khoshbayan, A., Taati Moghadam, M. *et al.* Bacteriophage therapy against *Pseudomonas aeruginosa* biofilms: a review. *Ann Clin Microbiol Antimicrob* **19,** 45 (2020). https://doi.org/10.1186/s12941-020-00389-5



Anti-biofilm mechanisms of bacteriophages.

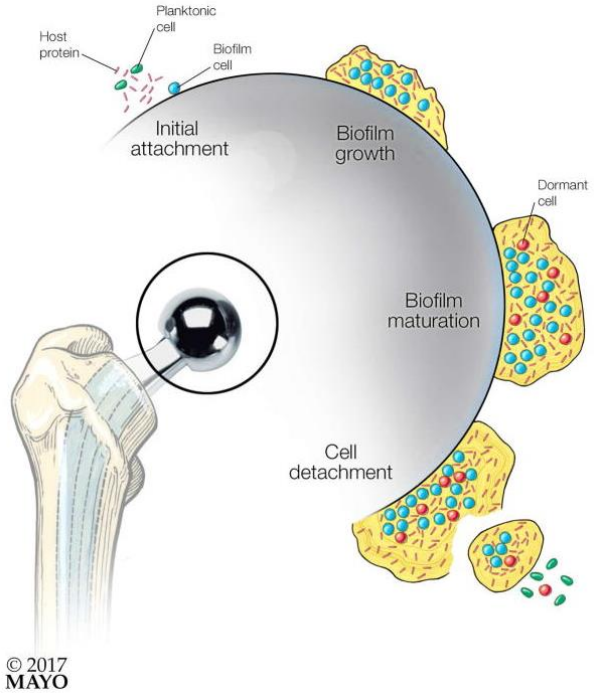
a Bacteriophages inhibit biofilm formation by inhibiting quorum sensing and reducing cellular communication.

b Combined treatments with sequential application of phage and antibiotics have a killing efficacy on *P. aeruginosa* biofilm.

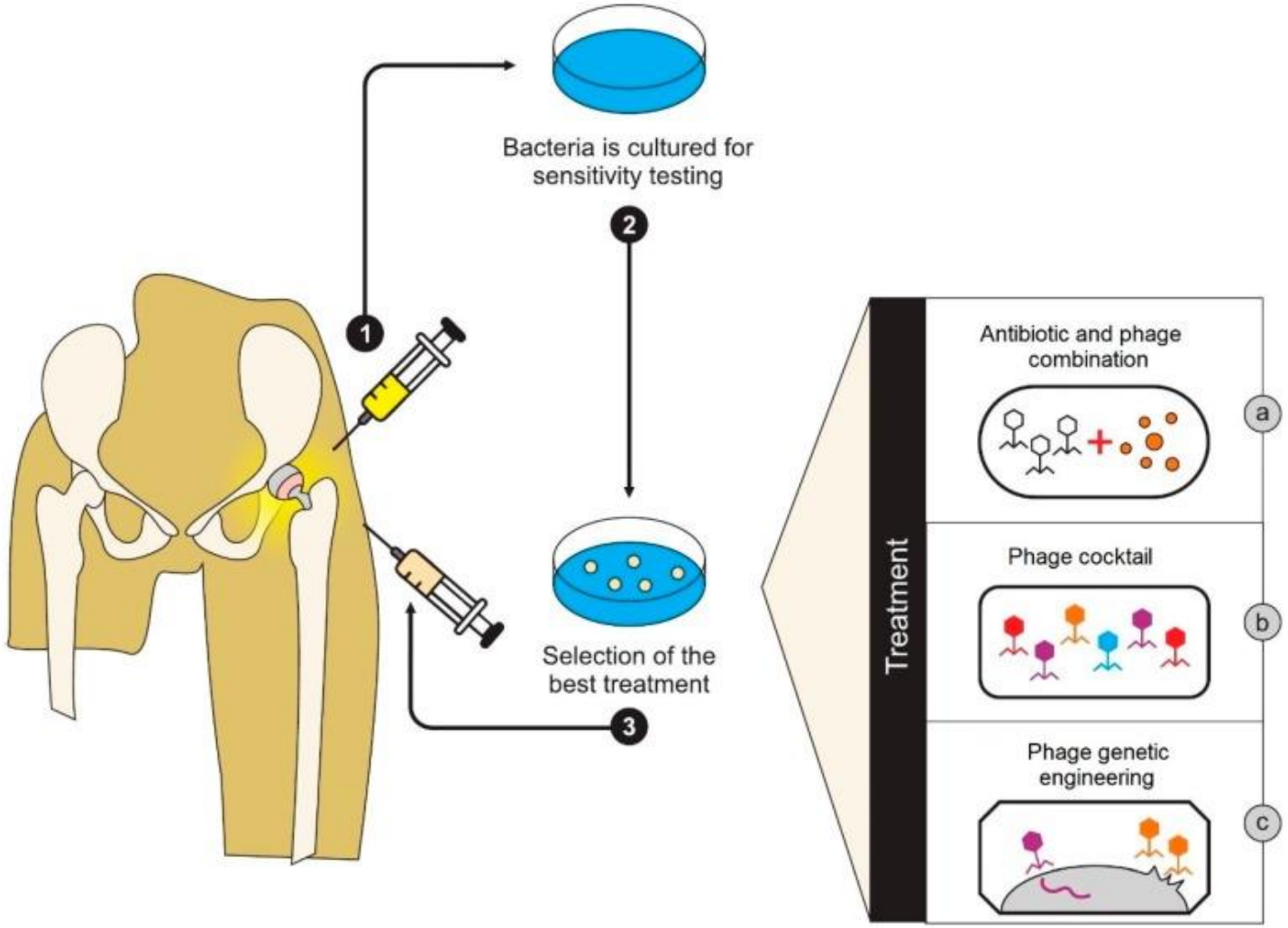
c Combined use of bacteriophages with molecules with anti-biofilm properties can help biofilm destruction.

d Bacteriophages can penetrate the inner layers of the biofilm through the biofilm void spaces without destroying the external matrix and replicate in the deeper-layer of biofilm

Chegini, Z., Khoshbayan, A., Taati Moghadam, M. *et al.* Bacteriophage therapy against *Pseudomonas aeruginosa* biofilms: a review. *Ann Clin Microbiol Antimicrob* **19,** 45 (2020). https://doi.org/10.1186/s12941-020-00389-5



Wi YM, Patel R. Disease Clinics of North America. 2018 Dec;32(4):915-929. DOI: 10.1016/j.idc.2018.06.009.



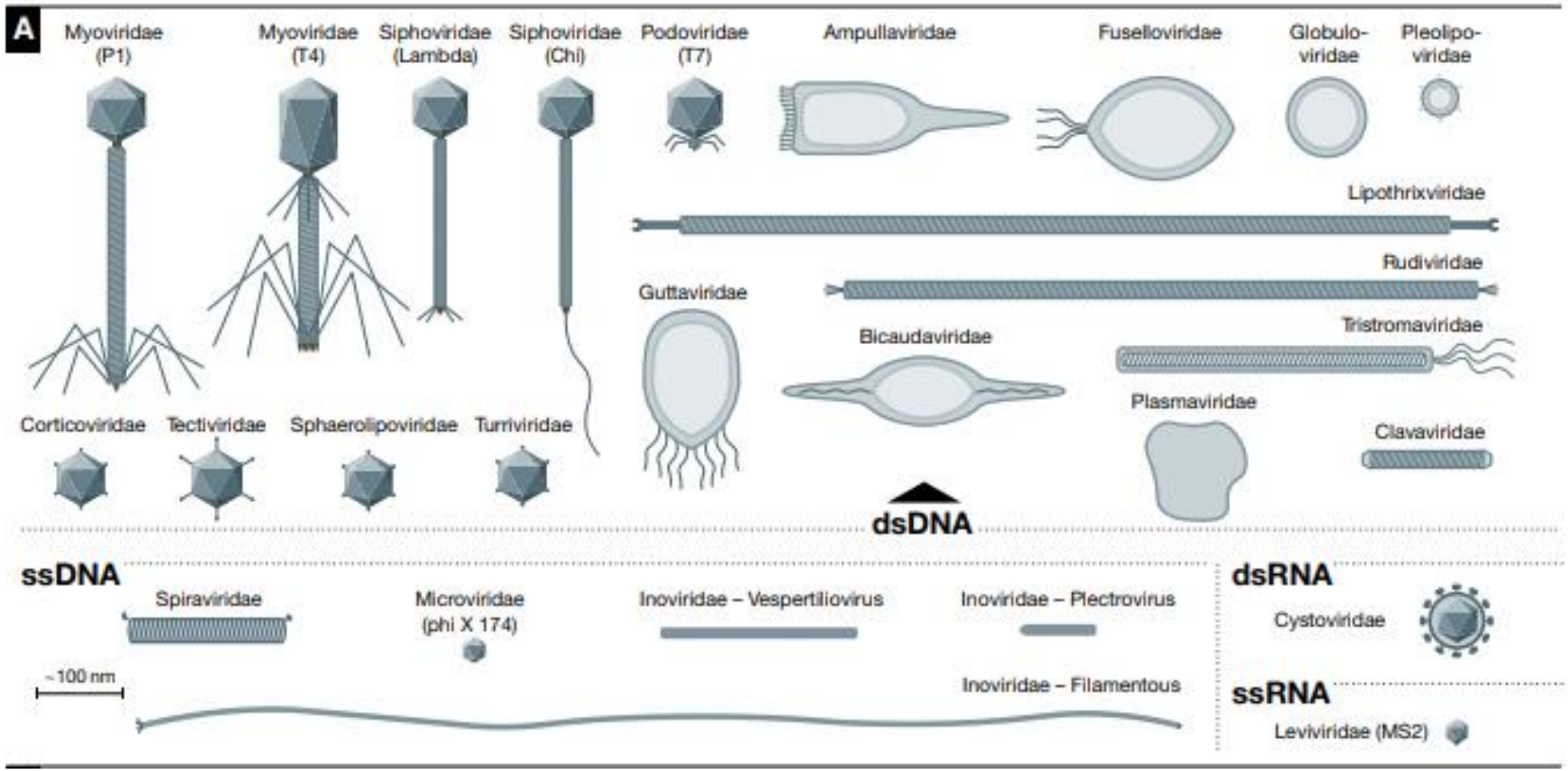
Romero-Calle D, Guimarães Benevides R, Góes-Neto A, Billington C. Bacteriophages as Alternatives to Antibiotics in Clinical Care. Antibiotics. 2019 Sep;8(3). DOI: 10.3390/antibiotics8030138. PMID: 31487893; PMCID: PMC6784059.

Review

EMBO reports

Filamentous phages: masters of a microbial sharing economy

Iain D Hay[1,*] & Trevor Lithgow[2,**]

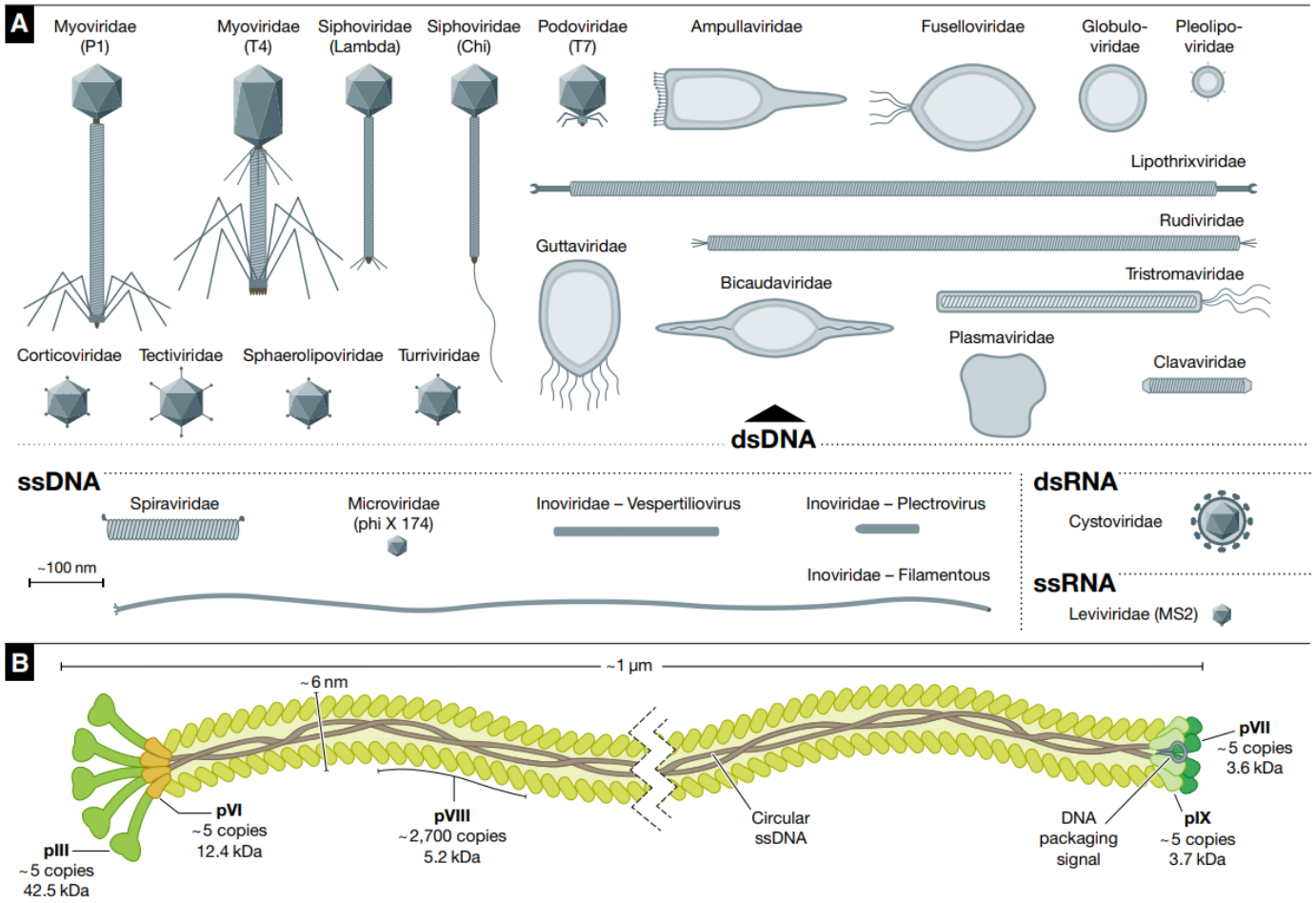


Review

EMBO reports

Filamentous phages: masters of a microbial sharing economy

Iain D Hay[1,*] & Trevor Lithgow[2,**]

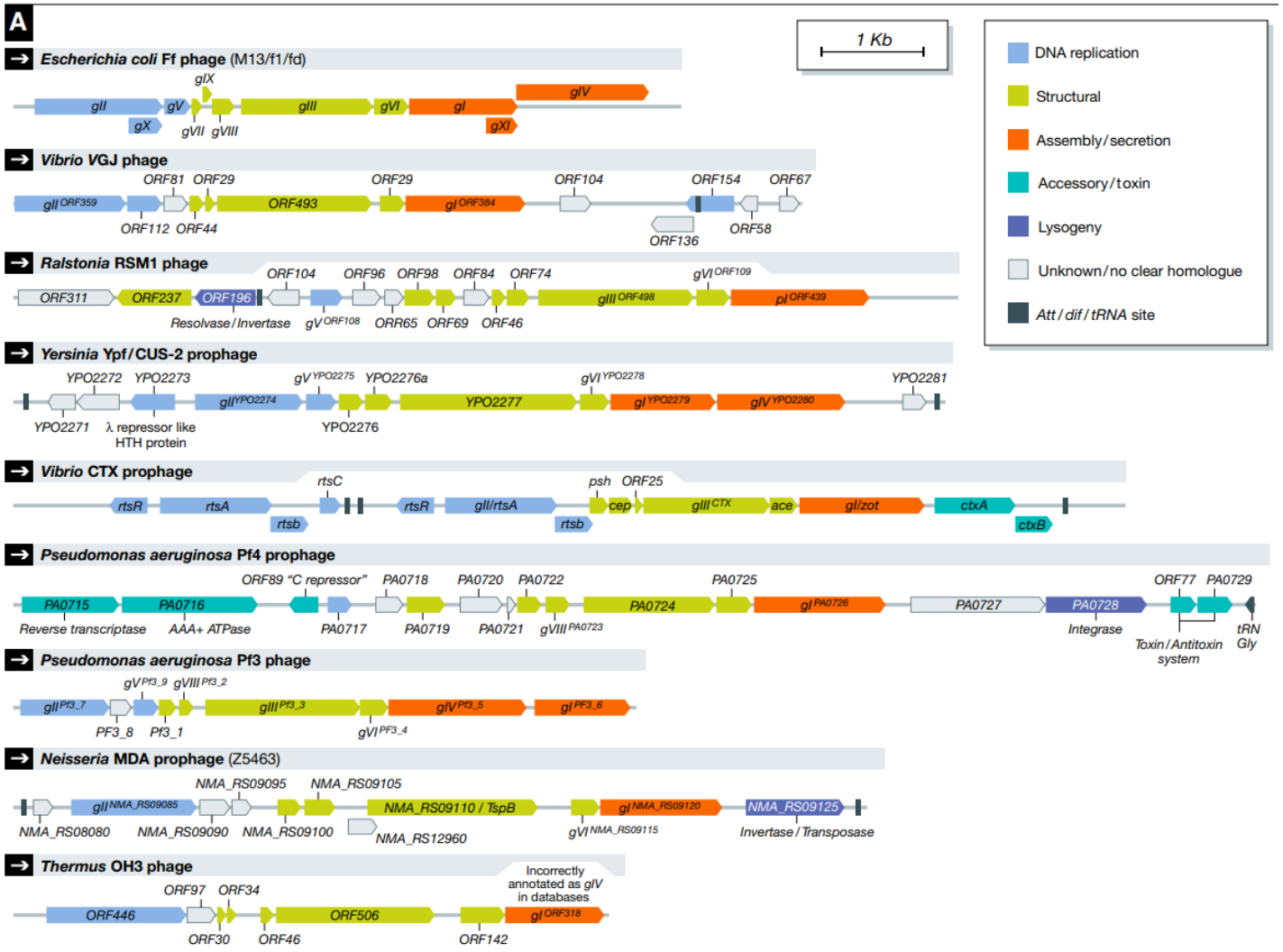


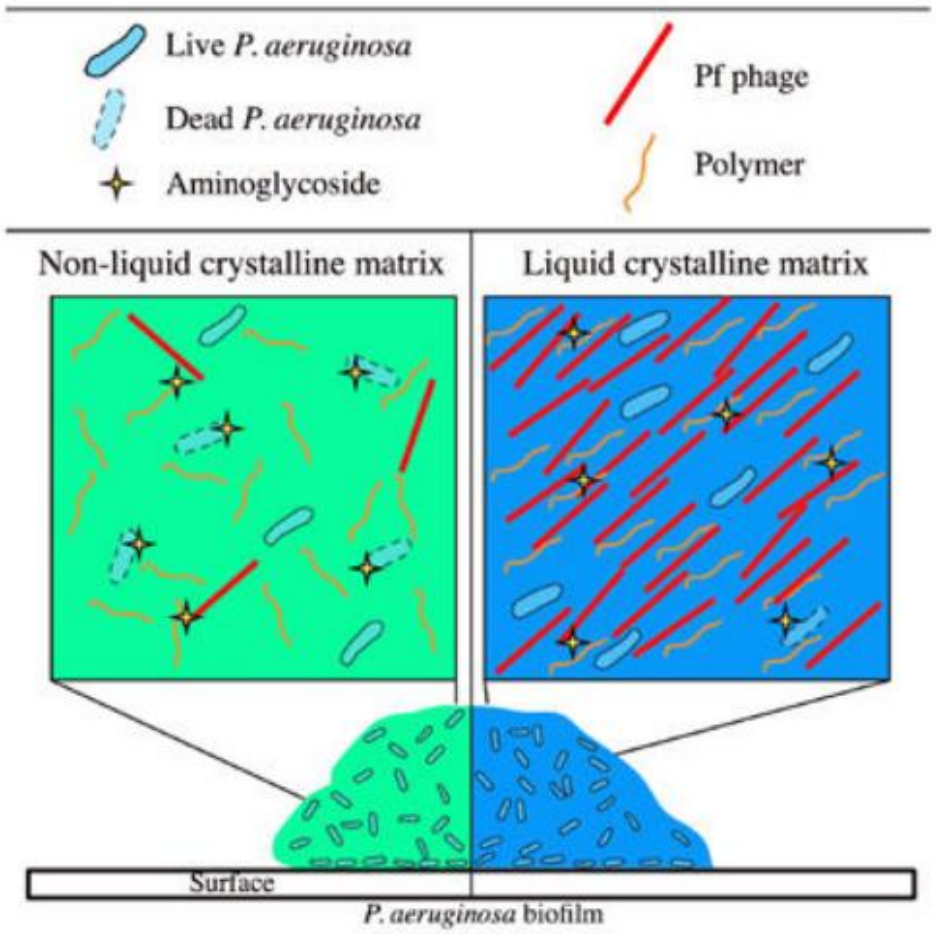
Review

EMBO reports

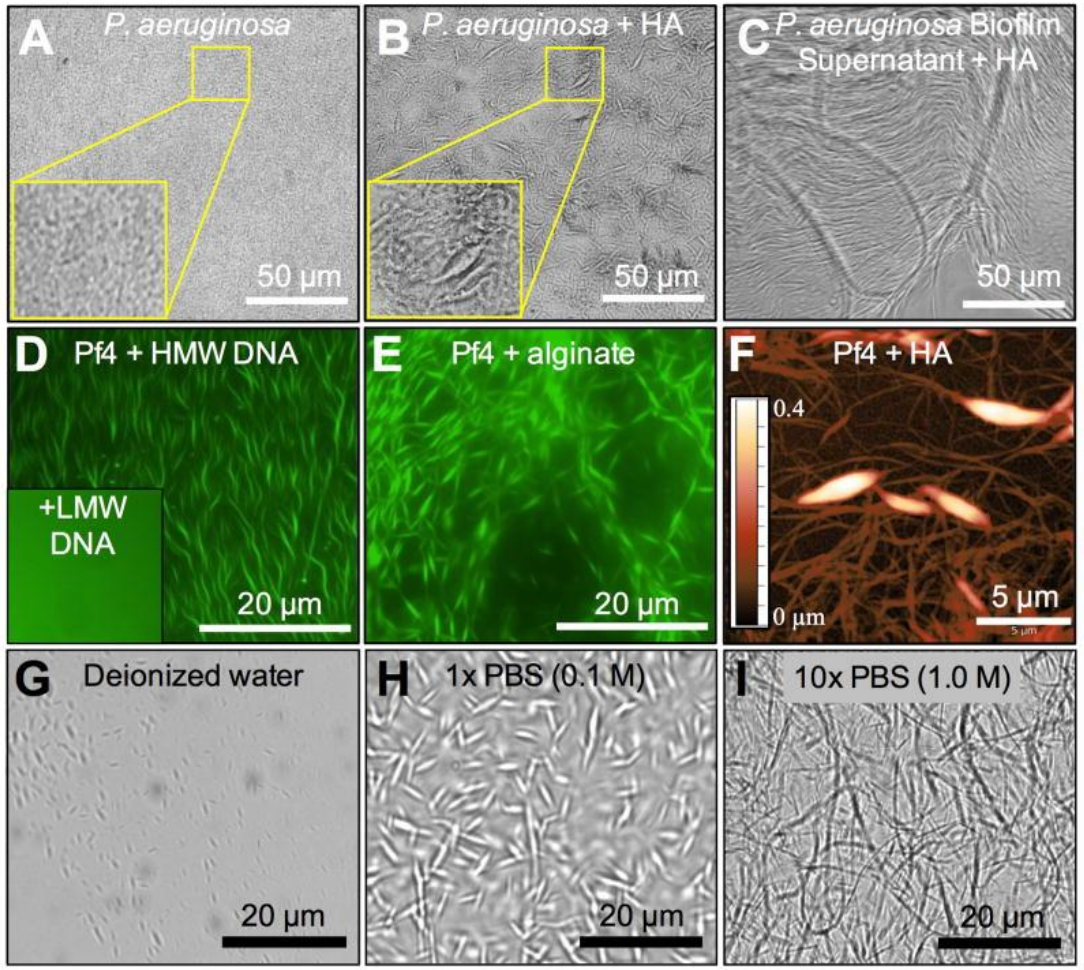
Filamentous phages: masters of a microbial sharing economy

Iain D Hay[1,*] & Trevor Lithgow[2,**]





Secor, Patrick R et al. “Filamentous Bacteriophage Promote Biofilm Assembly and Function.” Cell host & microbe vol. 18,5 (2015): 549-59. doi:10.1016/j.chom.2015.10.013



The Filamentous Phage Pf4 Interacts With Host and Microbial Polymers To Spontaneously Assemble Higher Order Structures

(A) P. aeruginosa forms a flat confluent biofilm in vitro.

(B) P. aeruginosa supplemented with 5 mg/ml HA forms morphologically complex biofilms in vitro.

(C) The addition of P. aeruginosa biofilm supernatant to HA (5 mg/ml) results in the spontaneous formation of higher order structures.

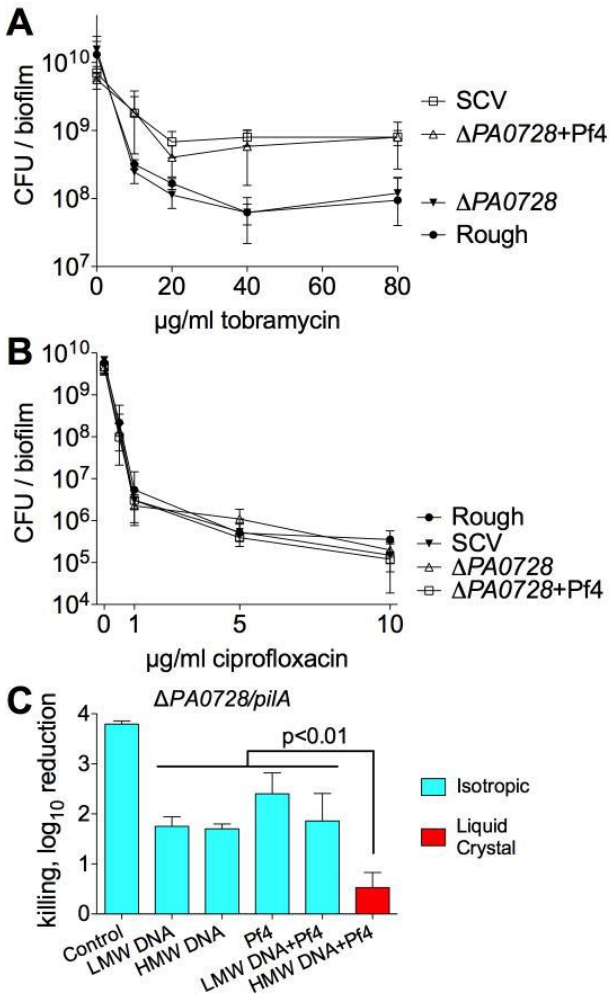
(D) Purified, fluorescently labeled Pf4 (green, 8.8 × 109 PFU/ml) mixed with 5 mg/ml DNA 2 kbp in size (HMW) forms large, interwoven structures while DNA <0.3 kbp in size (LMW) does not (inset).

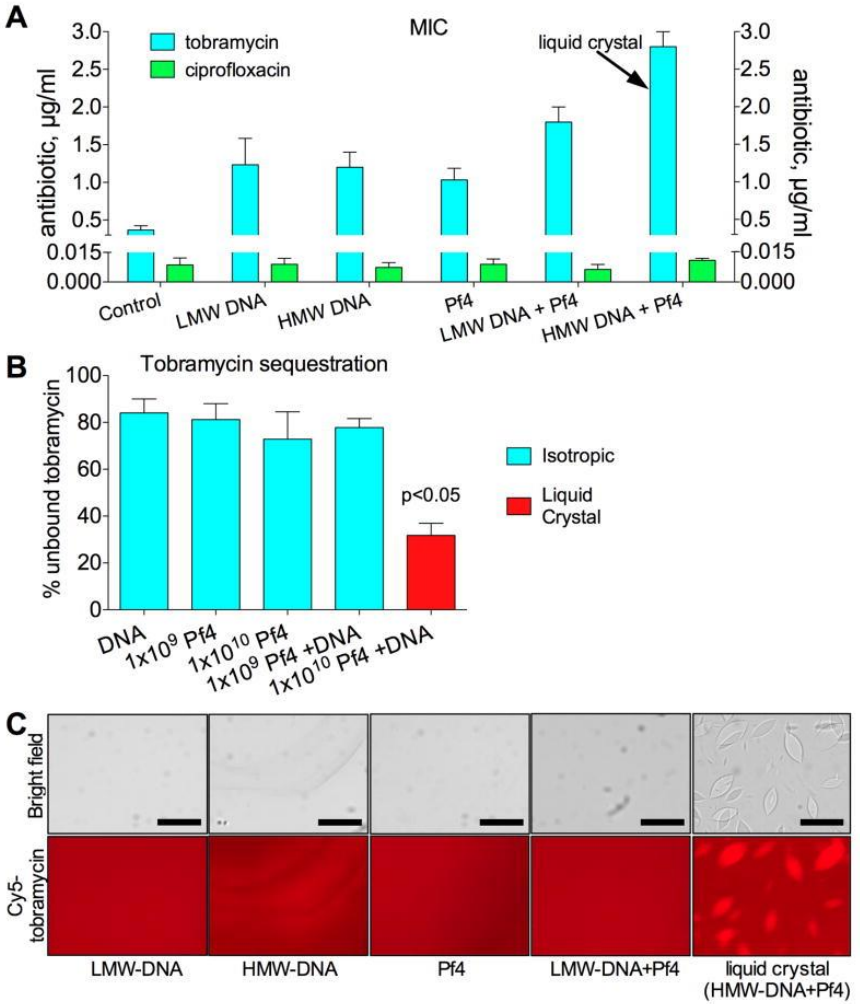
(E) Purified, fluorescently labeled Pf4 (green, 8.8 × 109 PFU/ml) mixed with 5 mg/ml alginate forms large, interwoven structures.

(F) Visualization of structures formed from Pf4 and HA by AFM semi-contact topography. The color scale indicates height.

(G-I) Pf4 (8.8 × 109 PFU/ml) and HA (5 mg/ml) were suspended in: DI water, 1× PBS, or 10× PBS.

Secor, Patrick R et al. “Filamentous Bacteriophage Promote Biofilm Assembly and Function.” Cell host & microbe vol. 18,5 (2015): 549-59. doi:10.1016/j.chom.2015.10.013





Secor, Patrick R et al. "Filamentous Bacteriophage Promote Biofilm Assembly and Function." Cell host & microbe vol. 18,5 (2015): 549-59. doi:10.1016/j.chom.2015.10.013

microbial cell
The journal for unicellular biology and human disease

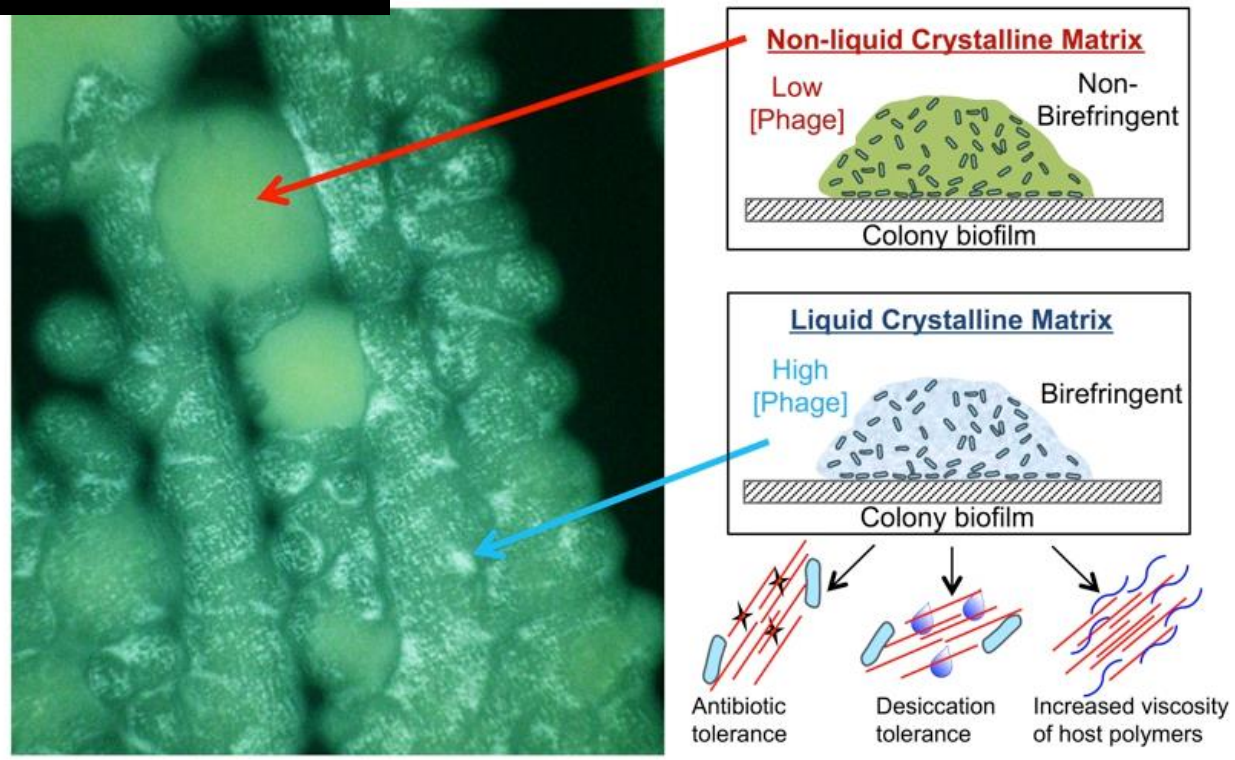


FIGURE 2: Pf phages organize the *P. aeruginosa* biofilm matrix into a liquid crystal.

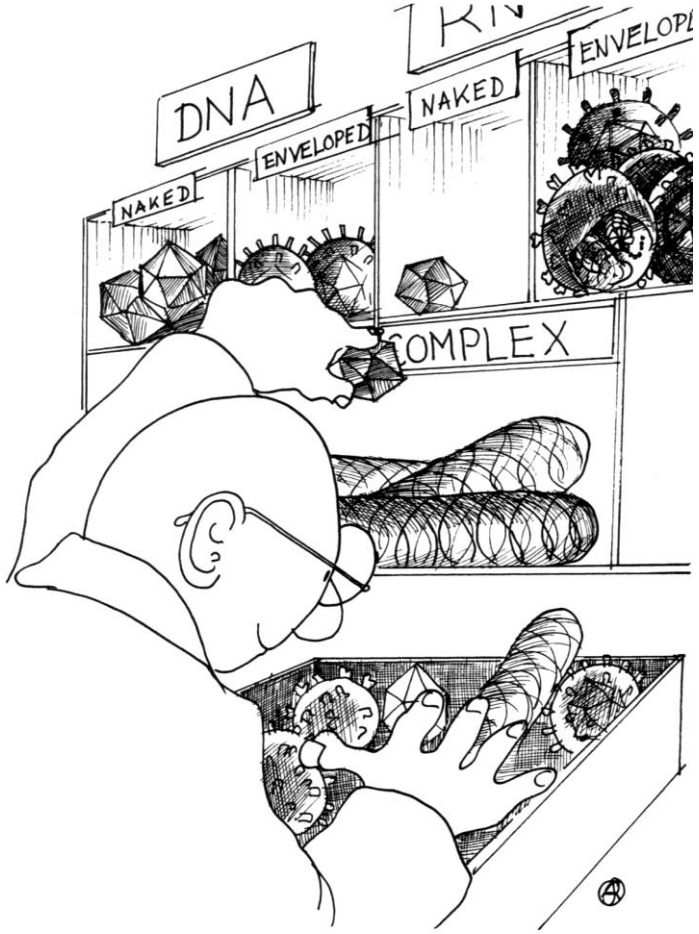
The birefringence of the liquid crystalline biofilm matrix can be visualized by placing colony biofilms on an agar pad between crossed polarizing lenses. The liquid crystalline matrix can change the polarization of light allowing it to pass through both polarizing lenses. Thus, non-liquid crystalline biofilms appear opaque (red arrow) while liquid crystalline biofilms appear bright (blue arrow). The organization of the biofilm matrix into a liquid crystal enhances adhesion, antibiotic tolerance, and desiccation survival. Further, Pf phage can increase the viscosity of host polymers such as mucin and DNA.

Copyright © 2021 by Shared Science Publishers OG · ISSN (online) 2311-2638
Legal Notice · Privacy Statement · Terms of Use · Contact · Site powered by WordPress

el Futuro.....

.....Conocimiento

El futuro.....



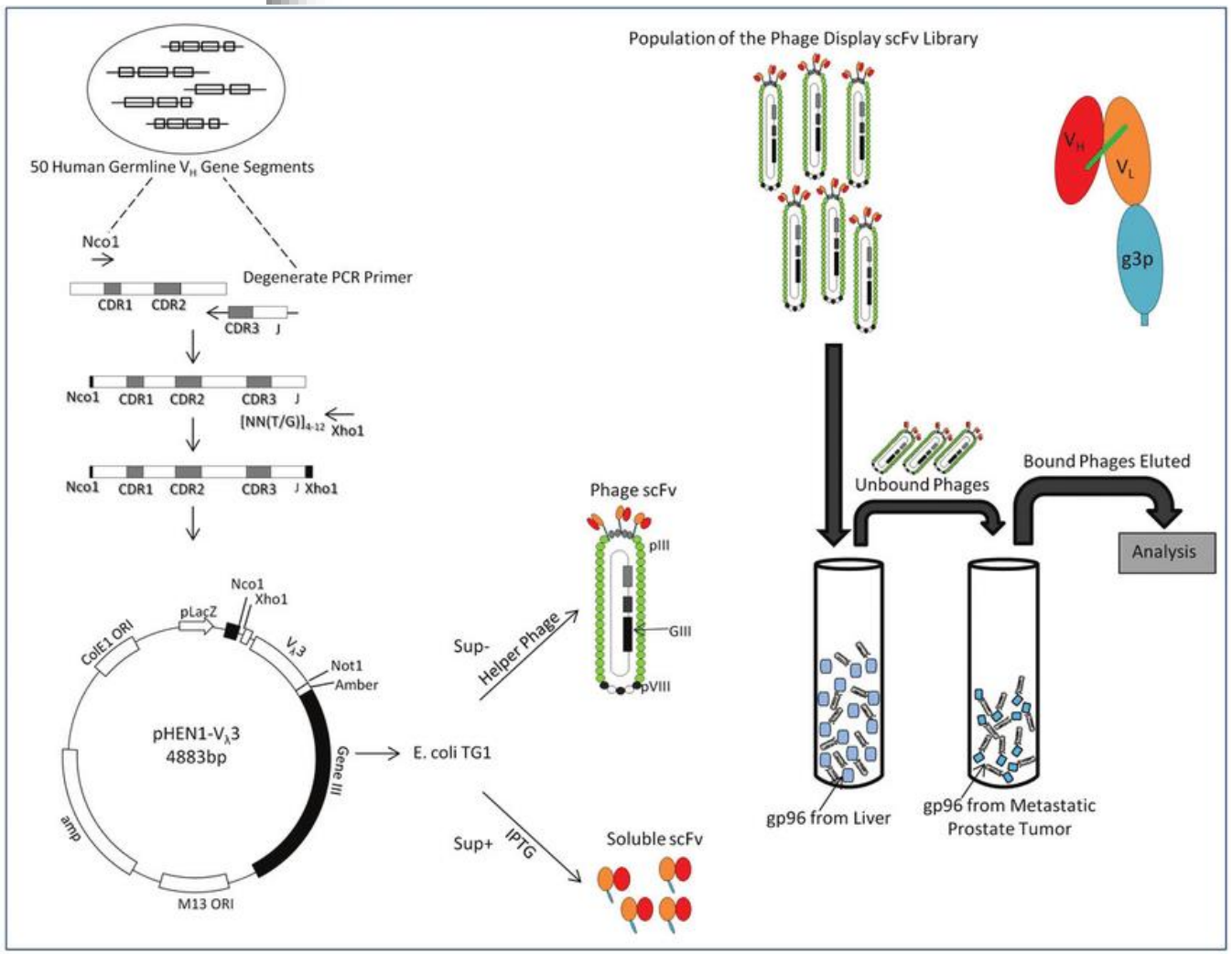
CLASSIFIED MATERIAL

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/302485562

Cancer Vaccines: Bench to Bedside

Article · January 2016

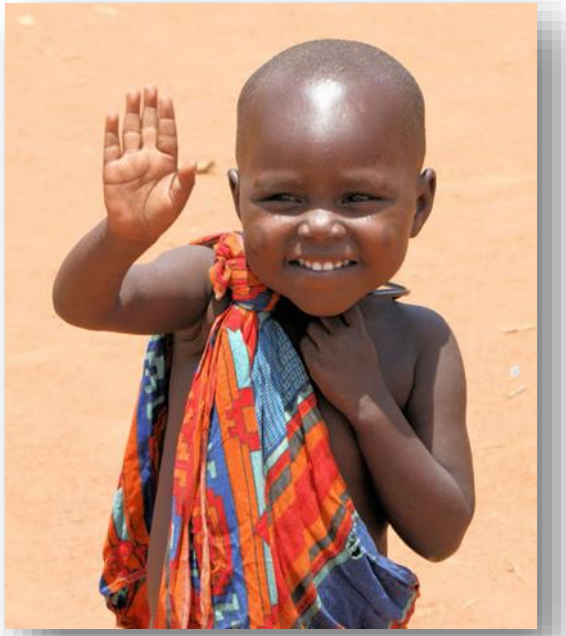
DOI: 10.13052/ijts2246-8765.2016.003



Consideraciones finales

- Conocimiento
- Funciones
- Preguntas y respuestas
- Aplicaciones

Gracias



Prof. Eduardo de Mello Volotão
volotas@gmail.com

Ministério da Saúde
Fundação Oswaldo Cruz
INSTITUTO OSWALDO CRUZ

Ministerio
de Educación
y Cultura

iibce
INSTITUTO DE INVESTIGACIONES BIOLÓGICAS CLEMENTE ESTABLE