ESCMID MANAGING INFECTIONS PROMOTING SCIENCE

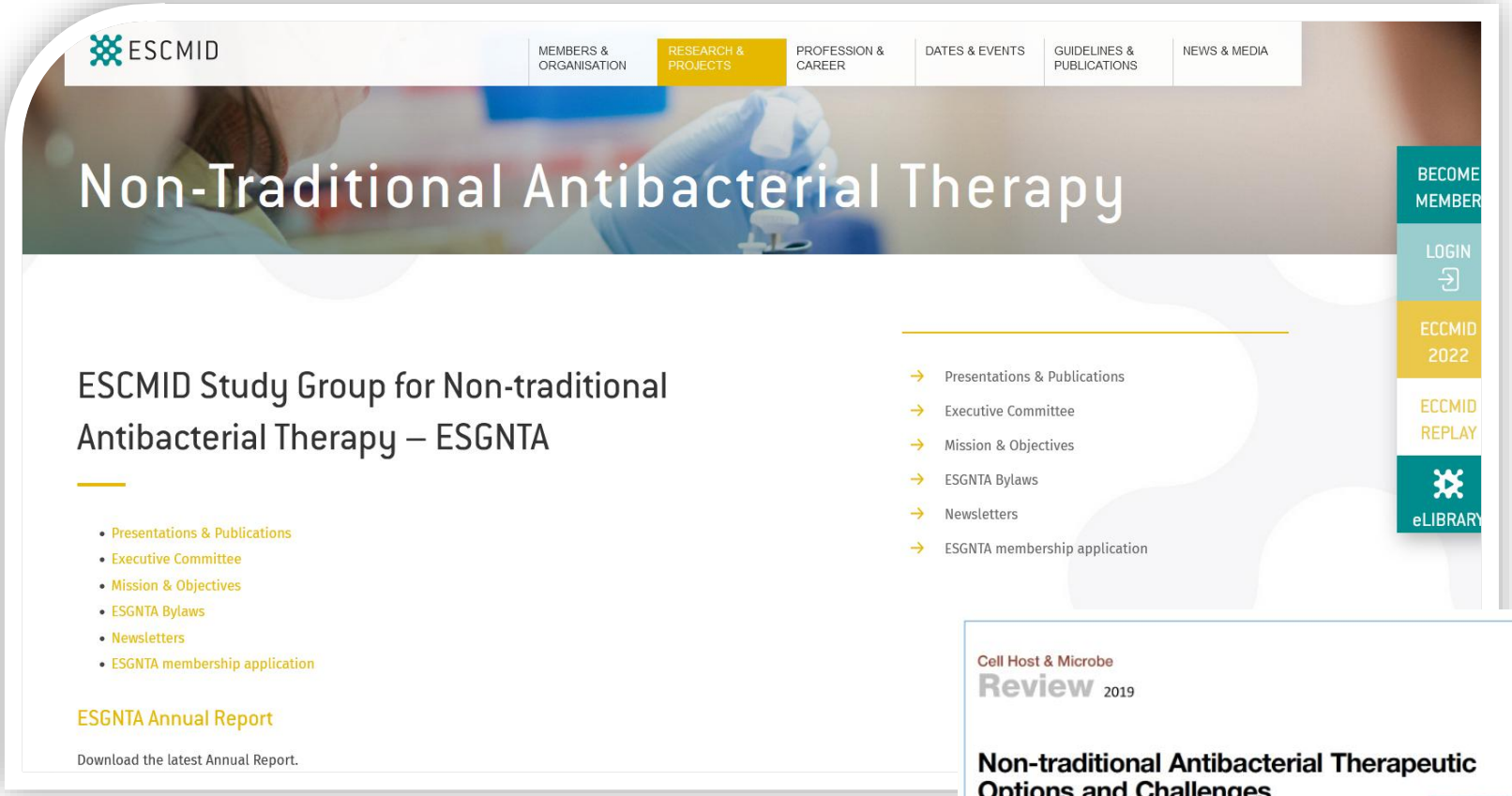
ESCMID Study Group for Non-traditional Antibacterial Therapy – ESGNTA

Traitements non antibiotiques des infections bactériennes

Dr Bleibtreu Alexandre

S^vce Maladies Infectieuses Pitié Salpêtrière

AP-HP Sorbonne Université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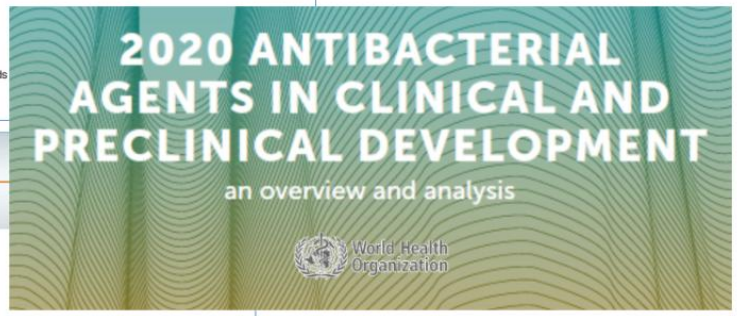
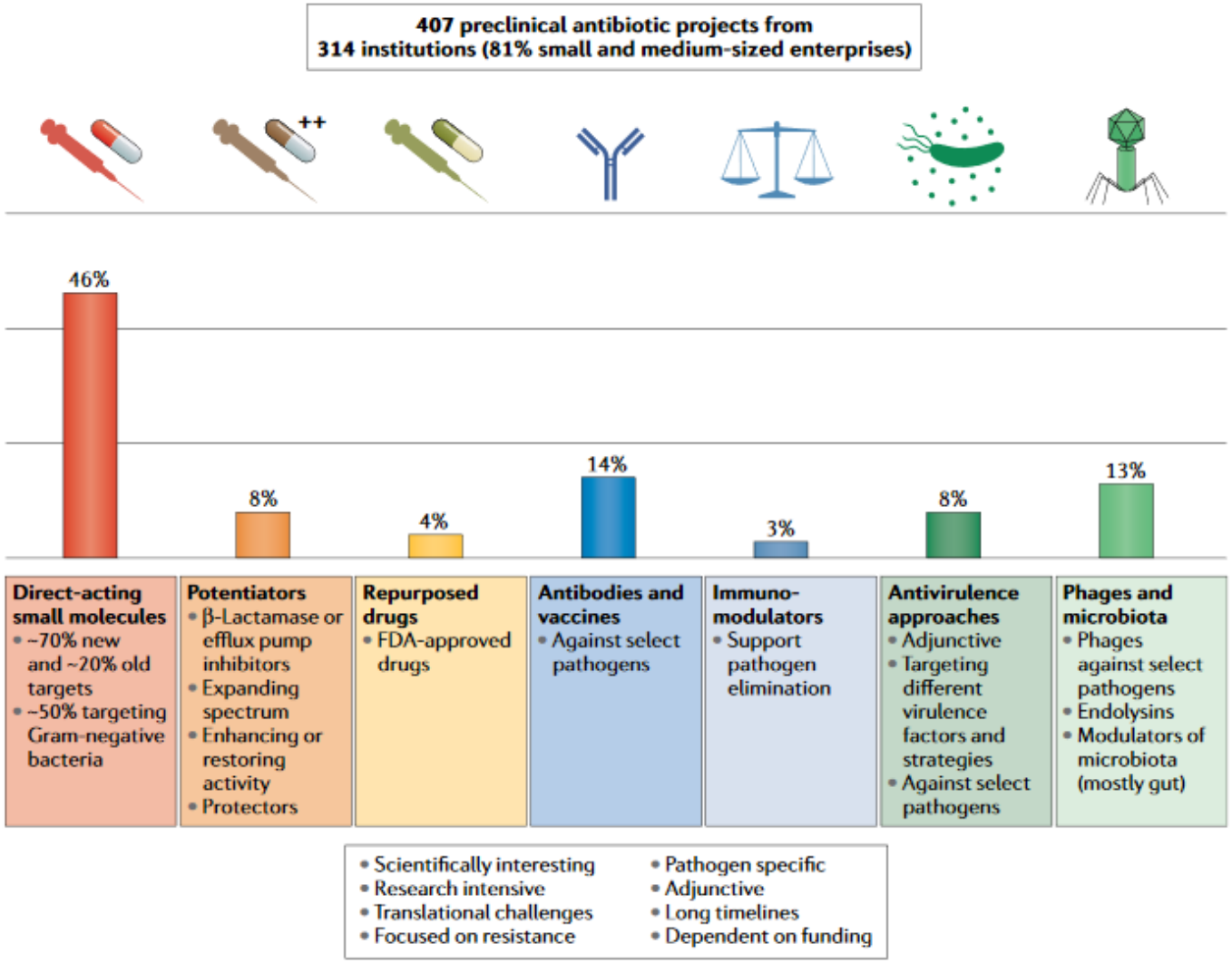
Cell Host & Microbe
Review 2019
CellPress
Non-traditional Antibacterial Therapeutic Options and Challenges
Ursula Theuretzbacher and Laura J.V. Piddock
Centre for Anti-Infective Agents, Vienna, Austria
Institute of Microbiology and Infection, University of Birmingham, Birmingham, West Midlands
Correspondence: l.j.v.piddock@bham.ac.uk
https://doi.org/10.1016/j.chom.2019.06.004


2020 ANTIBACTERIAL AGENTS IN CLINICAL AND PRECLINICAL DEVELOPMENT
an overview and analysis
World Health Organization

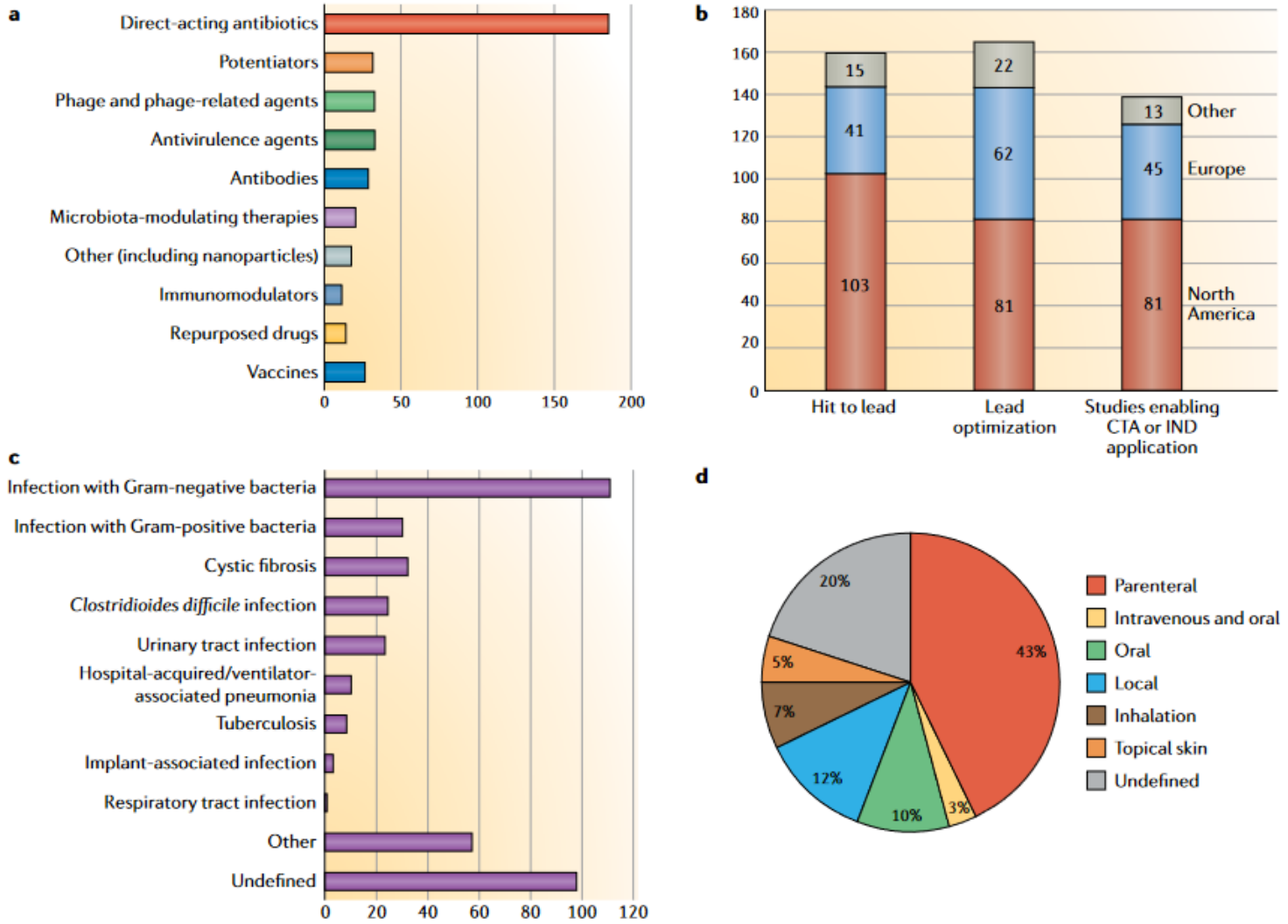

nature COMMUNICATIONS
NATURE COMMUNICATIONS | (2019)10:3416
PERSPECTIVE
https://doi.org/10.1038/s41467-019-11303-9
OPEN
Designing development programs for non-traditional antibacterial agents
John H. Rex, Holly Fernandez Lynch, I. Glenn Cohen, Jonathan J. Darrow & Kevin Outterson

Quels types de nouveaux traitements

- Ac monoclonaux
- Phages
- Transplantation de microbiote
- Bactéries Interférentes
- Molécules naturelles
- Vaccins
- Molécules anti-virulence



La moitié des projets de développement concerne des molécules à action directe



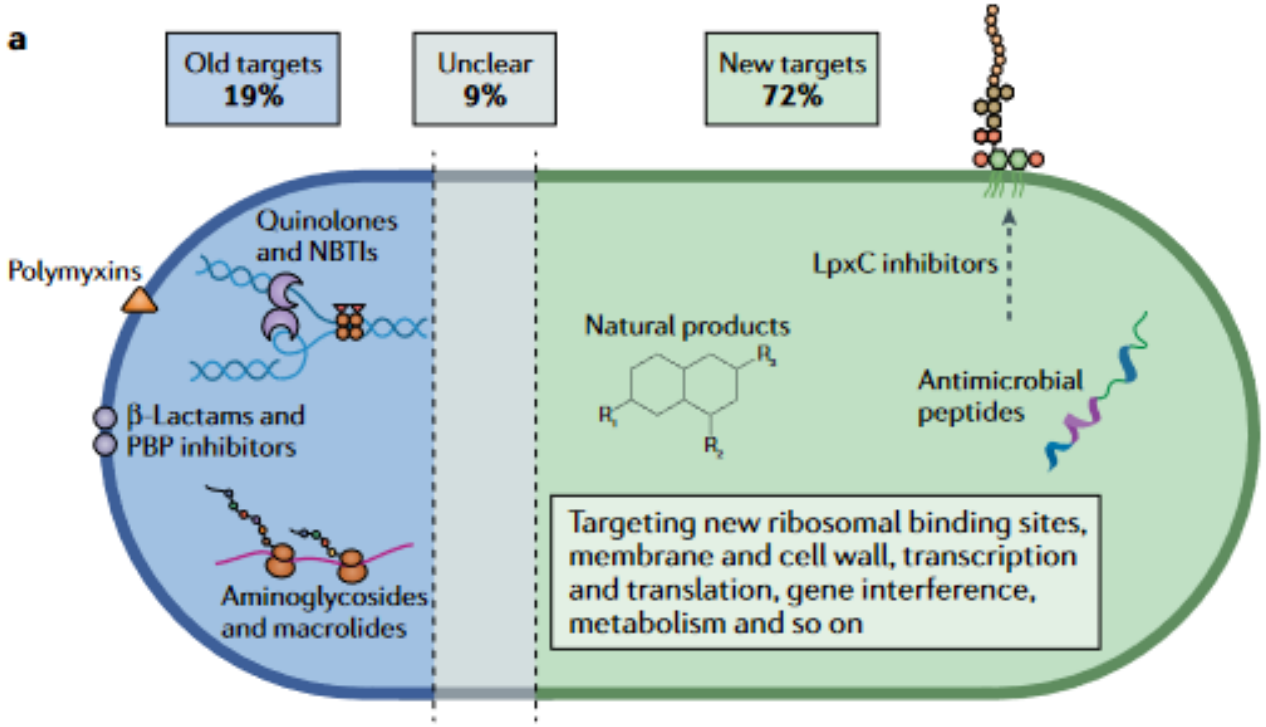
PMID: **31745331**

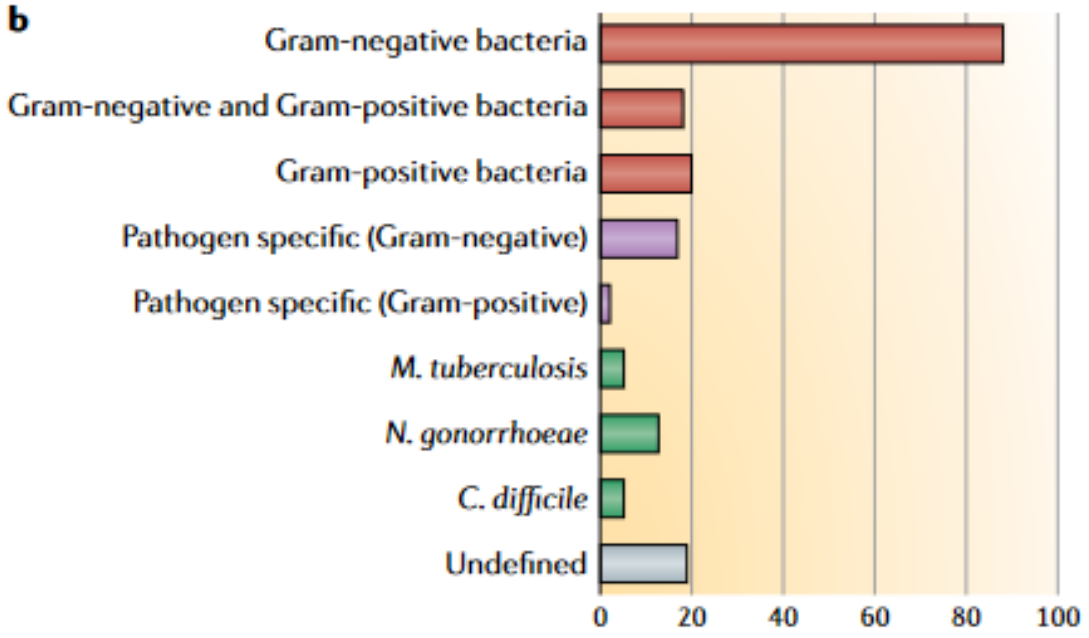
Molécules à action directe

19% nouveaux ATB ou optimisation de familles d'ATB déjà existantes
72% concernent de nouvelles cibles
- ribosomes
- membrane cellulaire
- Paroi
- interférence
- Métabolisme

Recherche surtout centrée sur BGN ++++

PMID: **31745331**





Anticorps moncolonaux ciblant des bactéries

Nom	Espèce	Cible	Indication	Phase	Laboratoire
Tosatoxumab (AR301)	*S. aureus*	α-toxine	Adjuvant ttt VAP	Phase 3	Aridis
Sevratoxumab (MEDI4893)	*S. aureus*	α-toxine	Prévention VAP	Phase 2	Medimmune
514G3	*S. aureus*	Protéine A	Adjuvant ttt BSI	Phase 2	XBiotech
ASN-100	*S. aureus*	AT + 5 leucocidines		Phase 2	Arsansis
RG7861	*S. aureus*	Paroi + rifamycine		Phase 1	Roche
MEDI3902	*P. aeruginosa*	T3SS PcrV + Psl	Adjuvant ttt VAP	Phase 2	Medimmune
AR101	*P. aeruginosa*	Alginate	Adjuvant ttt VAP	Phase 2	Aridis
ASN-4	*E. coli*	LPS		Préclinique	Arsansis
ASN-5	*K. pneumoniae*	O-Ag		Préclinique	Arsansis
AR401-mAb	*A. baumannii*		BSI	Préclinique	Aridis
VXD-003	*A. baumannii*			Préclinique	VaxDyn
PolyCAb	*C. difficile*			Phase 1	Micropharm
Cd-ISTAb	*C. difficile*			Préclinique	BioTherapeutics

Diapo F. Valour Cours d'Automne 2021

Zurawski et al, Antibiotics 2020 – Theuretzbacher et al, Cell Host Microbe 2019

Un cocktail de 3 Mab diminue l'infection sur prothèse à SARM

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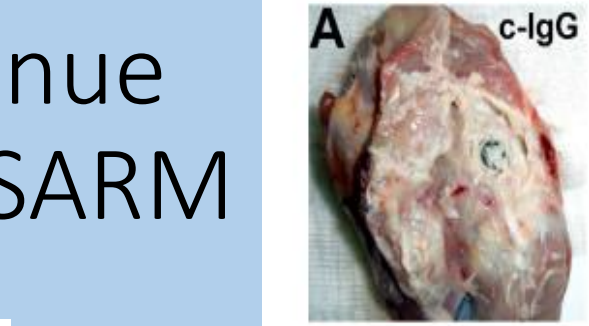
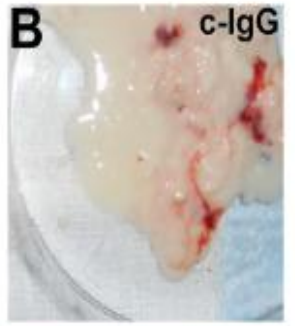
EXPERIMENTAL THERAPEUTICS

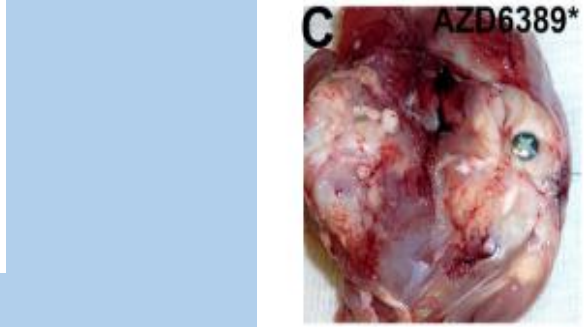
Multimechanistic Monoclonal Antibody Combination Targeting Key *Staphylococcus aureus* Virulence Determinants in a Rabbit Model of Prosthetic Joint Infection

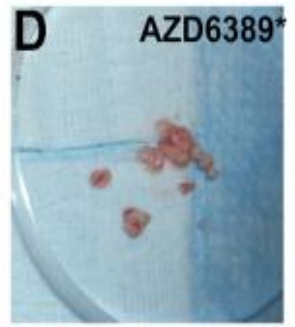
Yanjie Mao,[a,b]* Florent Valour,[a,c,d]* Nhu T. Q. Nguyen,[a] Thien M. N. Doan,[a] Holly Koelkebeck,[e] Christopher Richardson,[f] Lily I. Cheng,[a] Bret R. Sellman,[f] Christine Tkaczyk,[f] Binh An Diep[a]

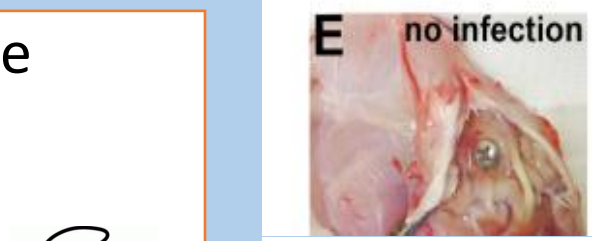
- Modèle animal d'infection de prothèse articulaire à SARM
- Randomisation Ig-poly *vs.* AZD6389
  - α-hemolysin
  - cytotoxines (LukSF/LukED/HlgAB/HlgCB)
  - Clumping factor A
- Administration 12h avant injection de SARM

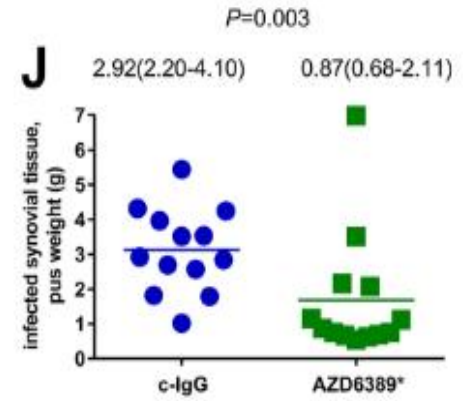


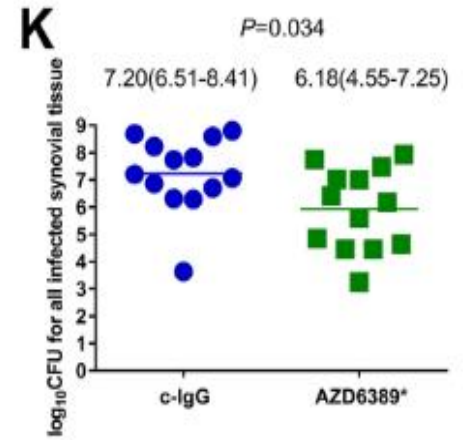


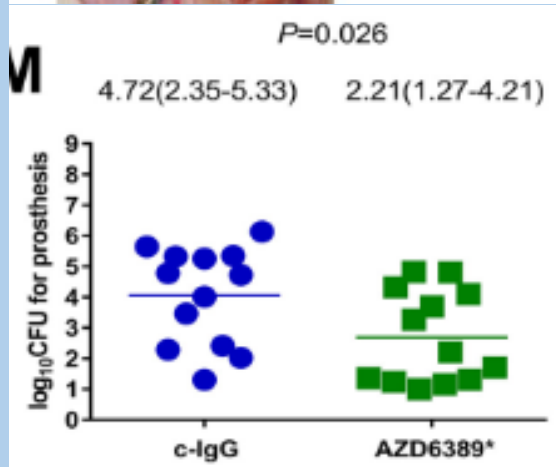


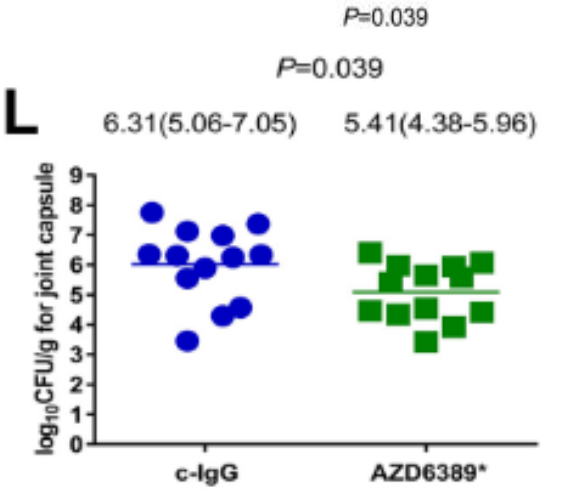






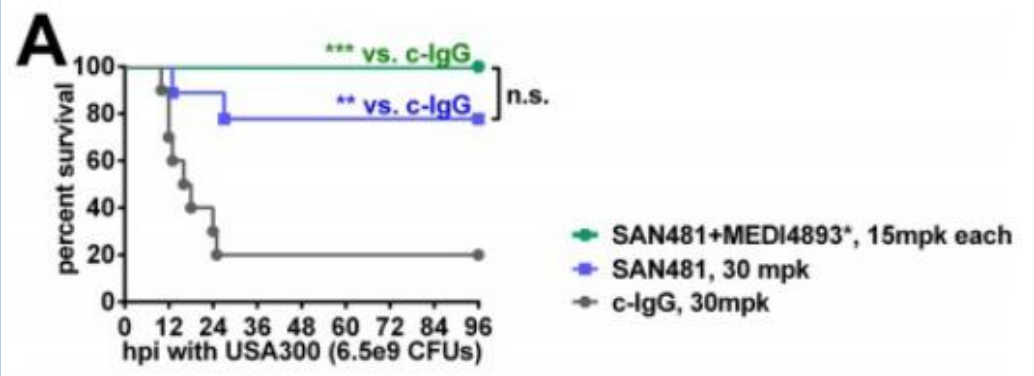


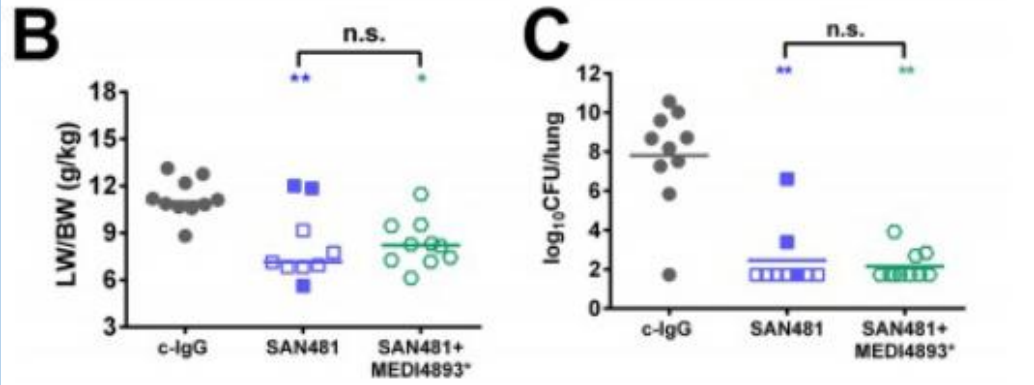


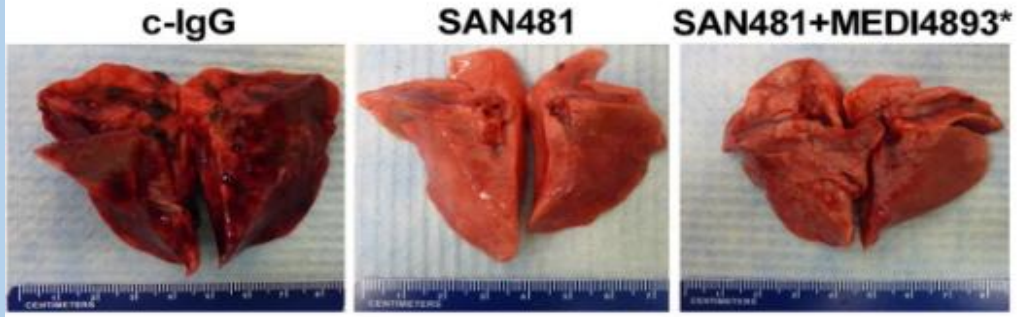


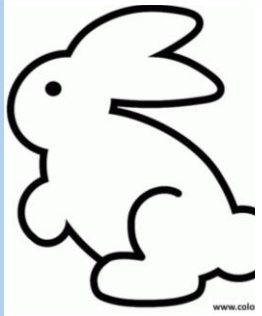
Une prophylaxie par Mab diminue la mortalité de la PAVM à SARM chez le lapin

- Modèle animal de PAVM à S. aureus
- Randomisation Ig-poly *vs.* MEDI4893*+/- SAN481
- Administration 24h avant injection de SARM en intratrachéal
- ½ Vie Mab ≈ 80j









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EXPERIMENTAL THERAPEUTICS

Protective Efficacy of Monoclonal Antibodies Neutralizing Alpha-Hemolysin and Bicomponent Leukocidins in a Rabbit Model of *Staphylococcus aureus* Necrotizing Pneumonia

Trang T. T. Vu,[a] Nhu T. Q. Nguyen,[a] Vuvi G. Tran,[a] Emmanuelle Gras,[a,b] Yanjie Mao,[a,c] David H. Jung,[a] Christine Tkaczyk,[d] Bret R. Sellman,[d] Binh An Diep[a]

Suvratoxumab (Astra-Zeneca)

Anticorps monoclonal anti-lysine α de *S. aureus*.

Phase 2
Patients ventilés + en PCR sur aspiration trachéale à *S. aureus*

Incidence des pneumopathies à *S. aureus* à J30 : Suvratoxumab 1 injection vs PCB

	Placebo group (n=100)	Suvratoxumab 5000 mg group (n=96)	Percentage relative risk reduction (90% CI)*	Absolute risk reduction	p value*
Incidence of *S aureus* pneumonia	26 (26%)	17 (18%)	31·9 (−7·5 to 56·8)	8·3	0·17
Incidence of all-cause pneumonia	30 (30%)	20 (21%)	30·6 (−4·9 to 54·0)	9·2	0·15
Incidence of all-cause pneumonia or death	42 (42%)	31 (32%)	23·1 (−4·9 to 43·6)	9·7	0·16

Data are n (%), unless otherwise specified. All endpoints were adjudicated by an endpoint adjudication committee. *S aureus=Staphylococcus aureus*. * Relative risk reduction (suvratoxumab *vs* placebo), 90% CIs, and p values were calculated by modified Poisson regression analysis with robust variance.

Table 2: **Primary and key exploratory efficacy results at 30 days in the modified intention-to-treat population**

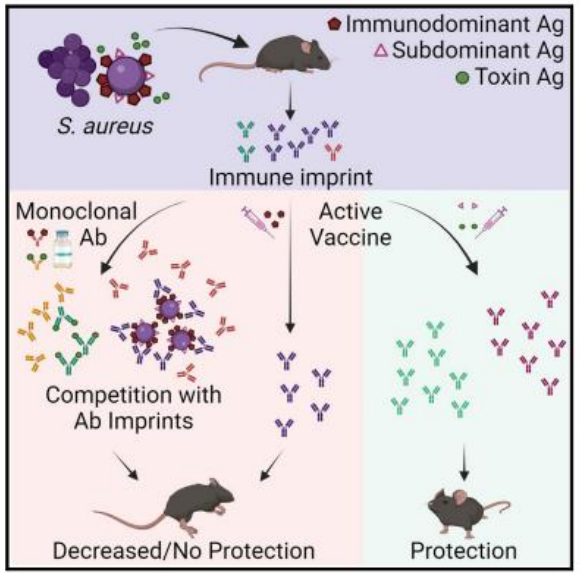
François B *et al.* Lancet Infect Dis 2021

Cell Reports Medicine

Article

The characteristics of pre-existing humoral imprint determine efficacy of *S. aureus* vaccines and support alternative vaccine approaches

Graphical abstract



Authors

J.R. Caldera, Chih-Ming Tsai, Desmond Trieu, ..., Xin Du, Brian Lin, George Y. Liu

Correspondence

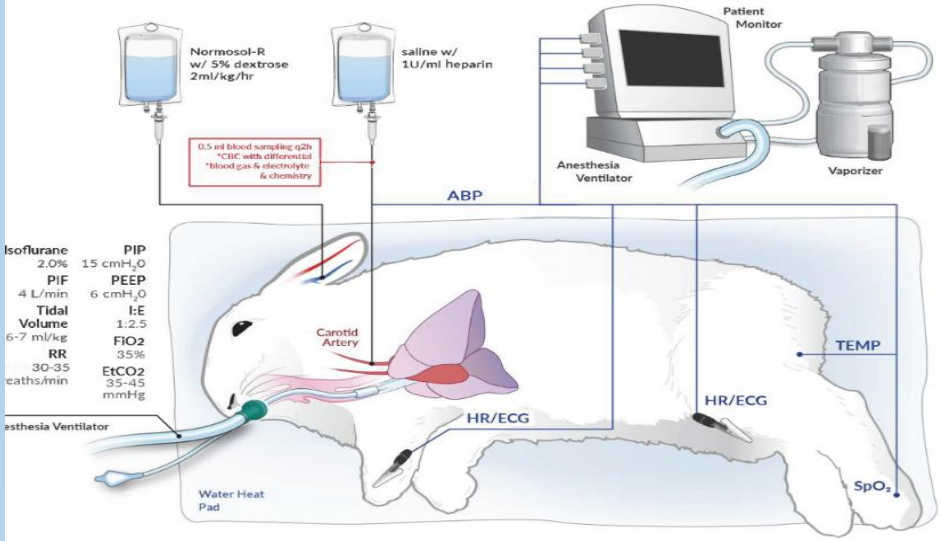
gyliu@ucsd.edu

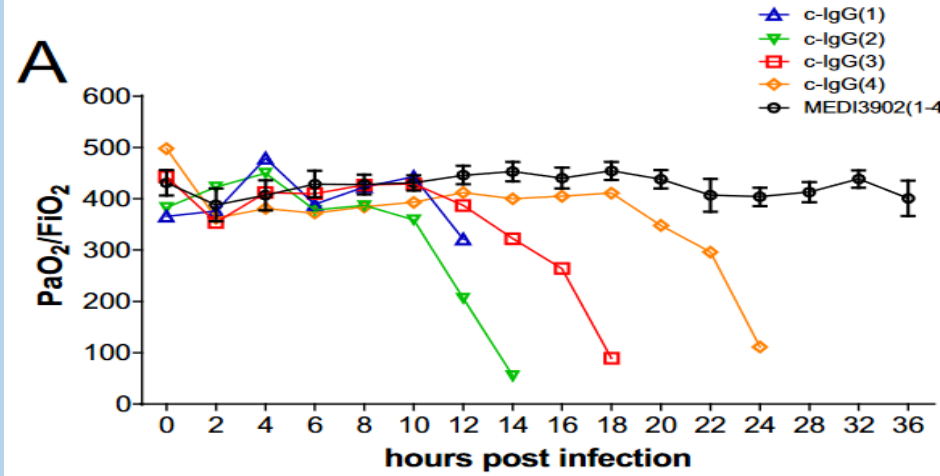
In brief

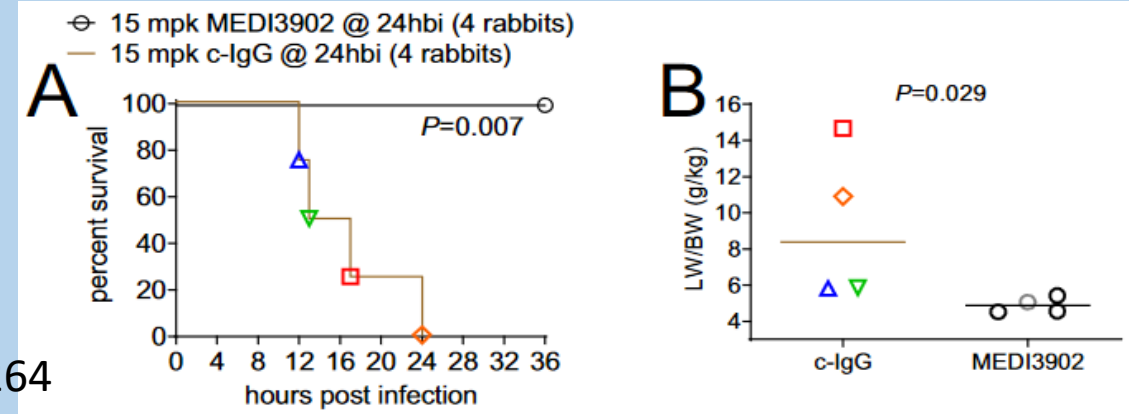
There has been no successful vaccine against *S. aureus* after approximately 30 human trials. Humans are exposed to *S. aureus* early on in life. Caldera et al. show that the type of antigen target and the titer of pre-existing antibodies can predict the outcome of staphylococcal vaccines in pathogen-exposed mice.

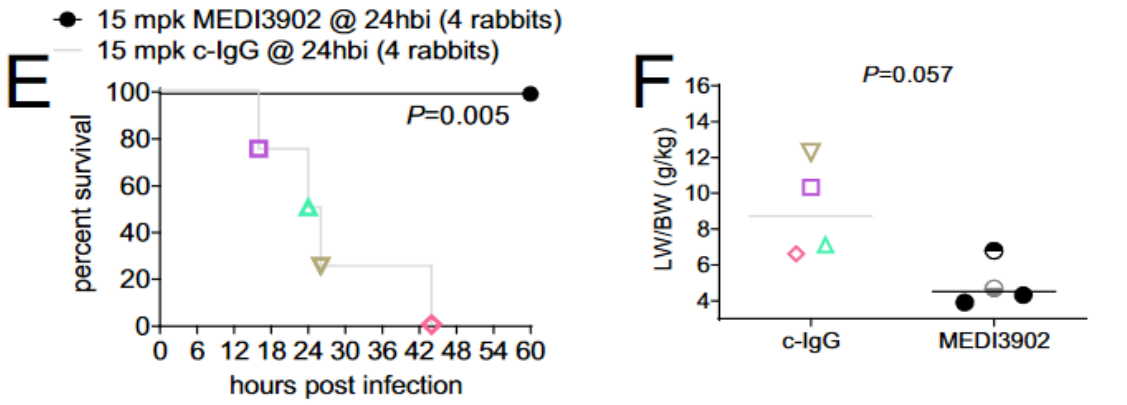
Prophylaxie par Mab réduit la mortalité de la PAVM à *P. aeruginosa* du lapin

- Modèle animal de PAVM à *P. aeruginosa*
- Randomisation Ig-poly *vs.* MEDI3902
- Administration 24h avant injection de P. aeruginosa en intratrachéal
- Sacrifice à H36 ou H60
- N'empèche pas la bactériémie



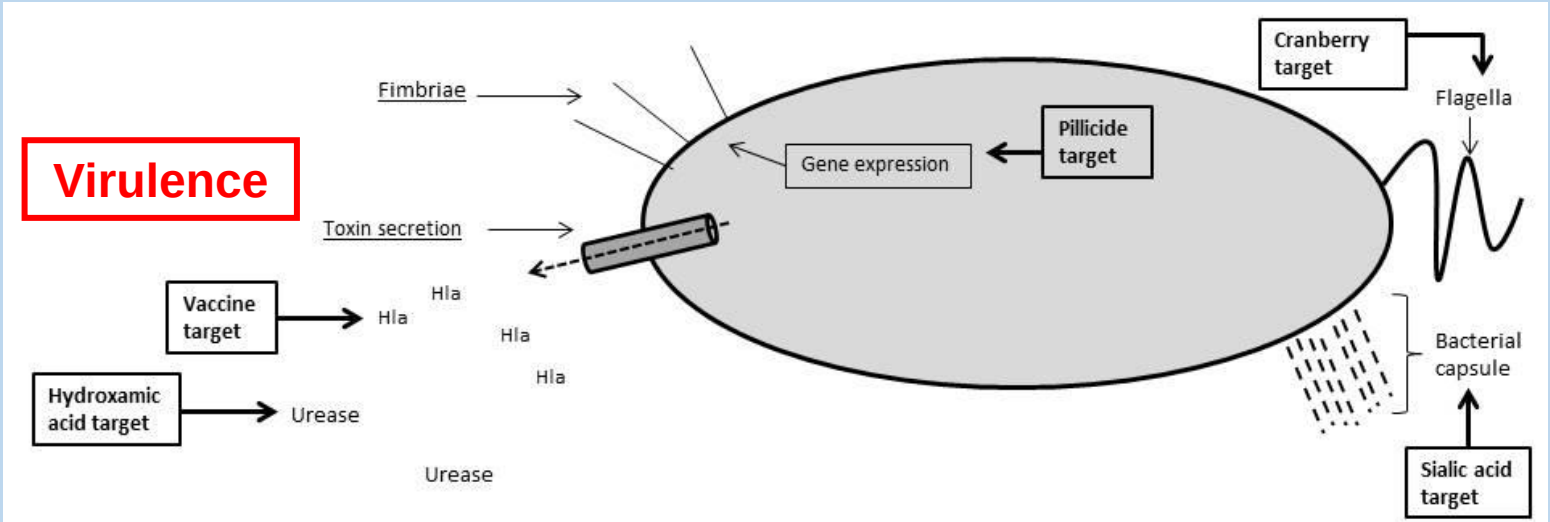


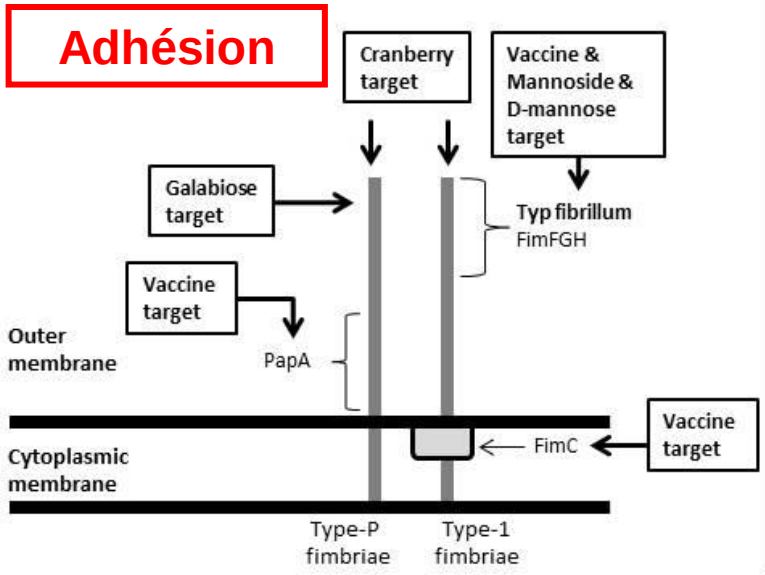


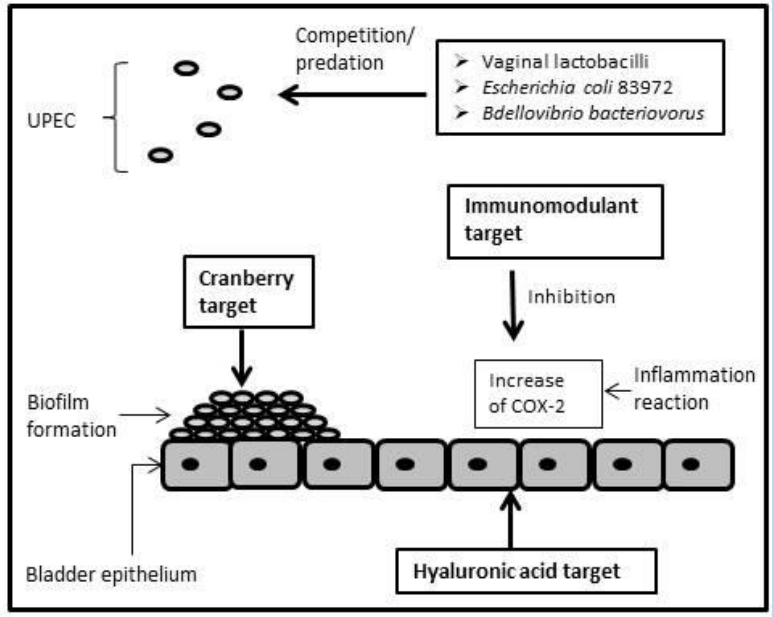


PMID: 34902264

Thérapeutiques non antibiotiques







D'après Ranfaing

Exemples d' options préventives dans les IUR

- **Vitamine C**>> pas d'intérêt démontré
- **Methenamine**>> Non recommandé, pas de preuve suffisante.
- **D Mannose** >> pas de preuves suffisantes

- **Instillations de nitrate d'argent >>** Pas d'efficacité démontré
- **Herbologie traditionnelle chinoise** >> Pas de données (toxicité ?)

D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial

Bojana Kranjčec · Dino Papeš · Silvio Altarac

World J Urol (2014) 32:79–84

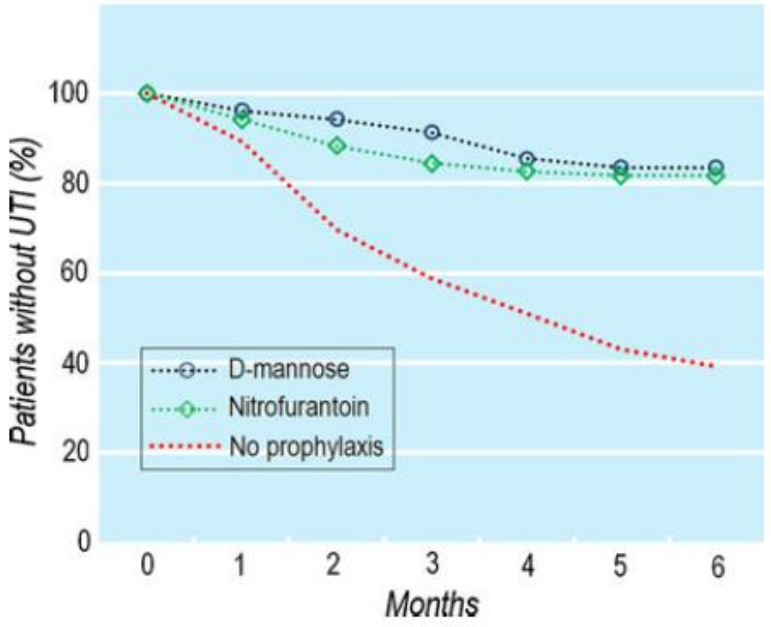
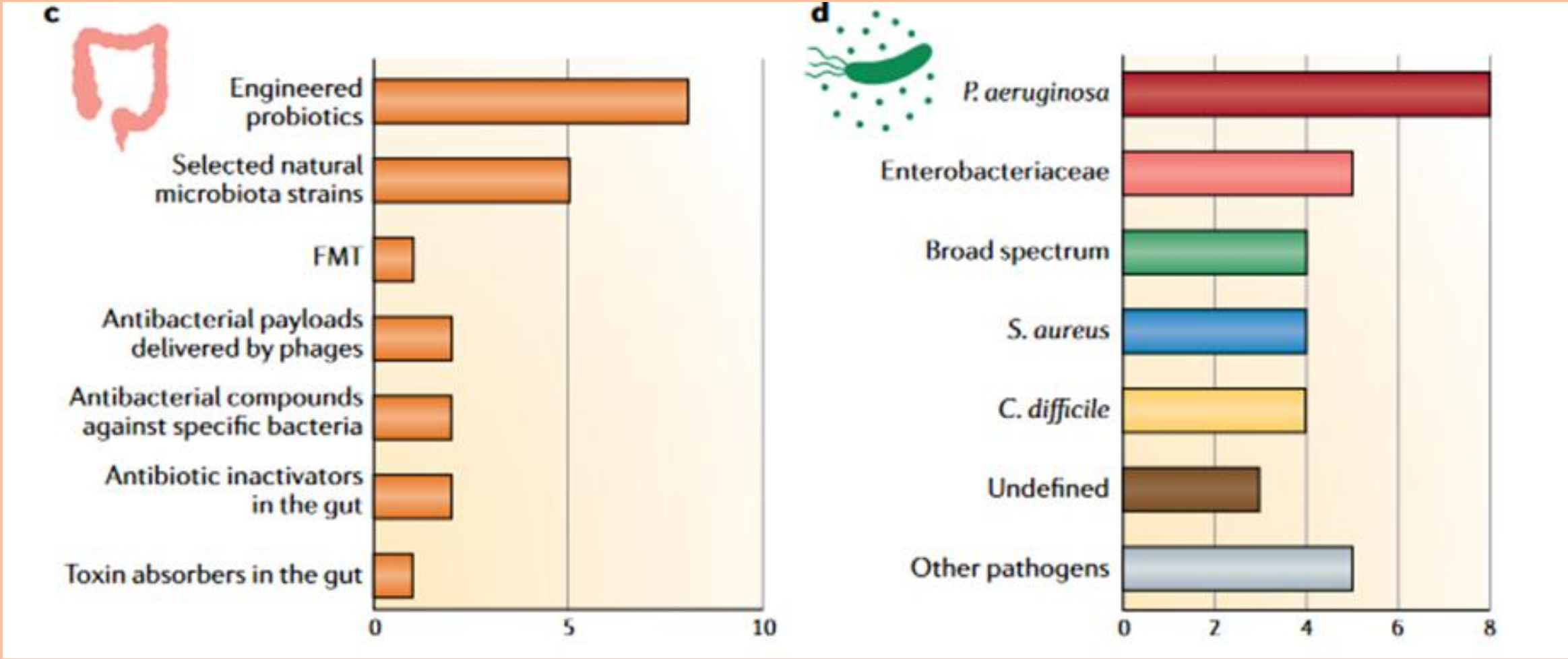


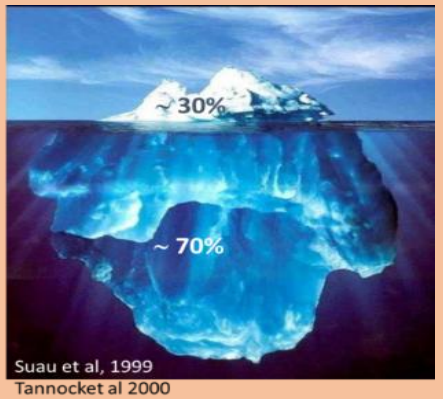
Fig. 2 Kaplan–Meier plot showing the percentage of patients remaining cystitis-free during the 6-month clinical trial period

TMF ET PRODUITS ISSUS DU MICROBIOTE



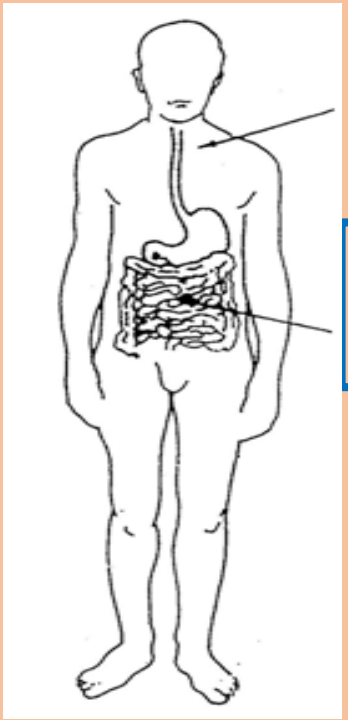
Le microbiote intestinal

- Ecosystème complexe avec 400 à 1200 espèces (<30% cultivables)
- Variabilité inter-individuelle +++ malgré un noyau conservé
- Un partenaire à part entière:
  ~ 30-100 gènes procaryote / 1 gène eucaryote



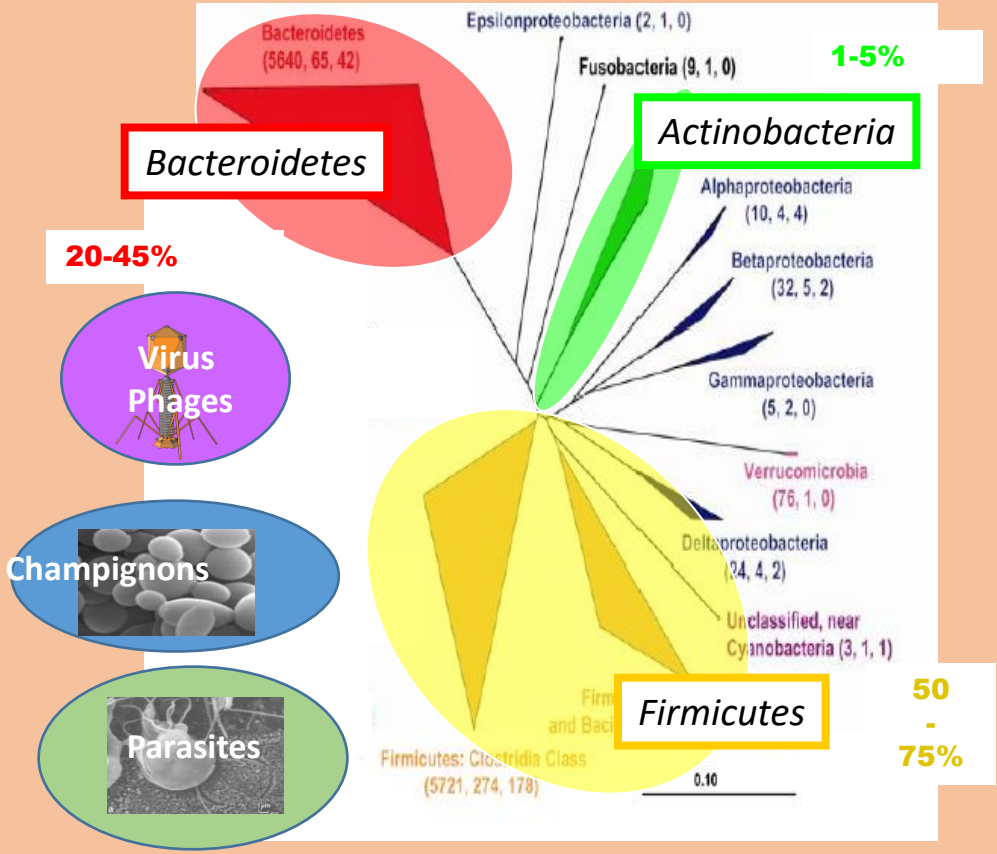
Cultivable

Non cultivable



humain: 10^{13} cellules

Tractus digestif
10^{13} à 10^{14} bactéries
>10^{11} bactéries/g



(adapté de Eckburg al., 2005)

Historique de la transplantation fécale

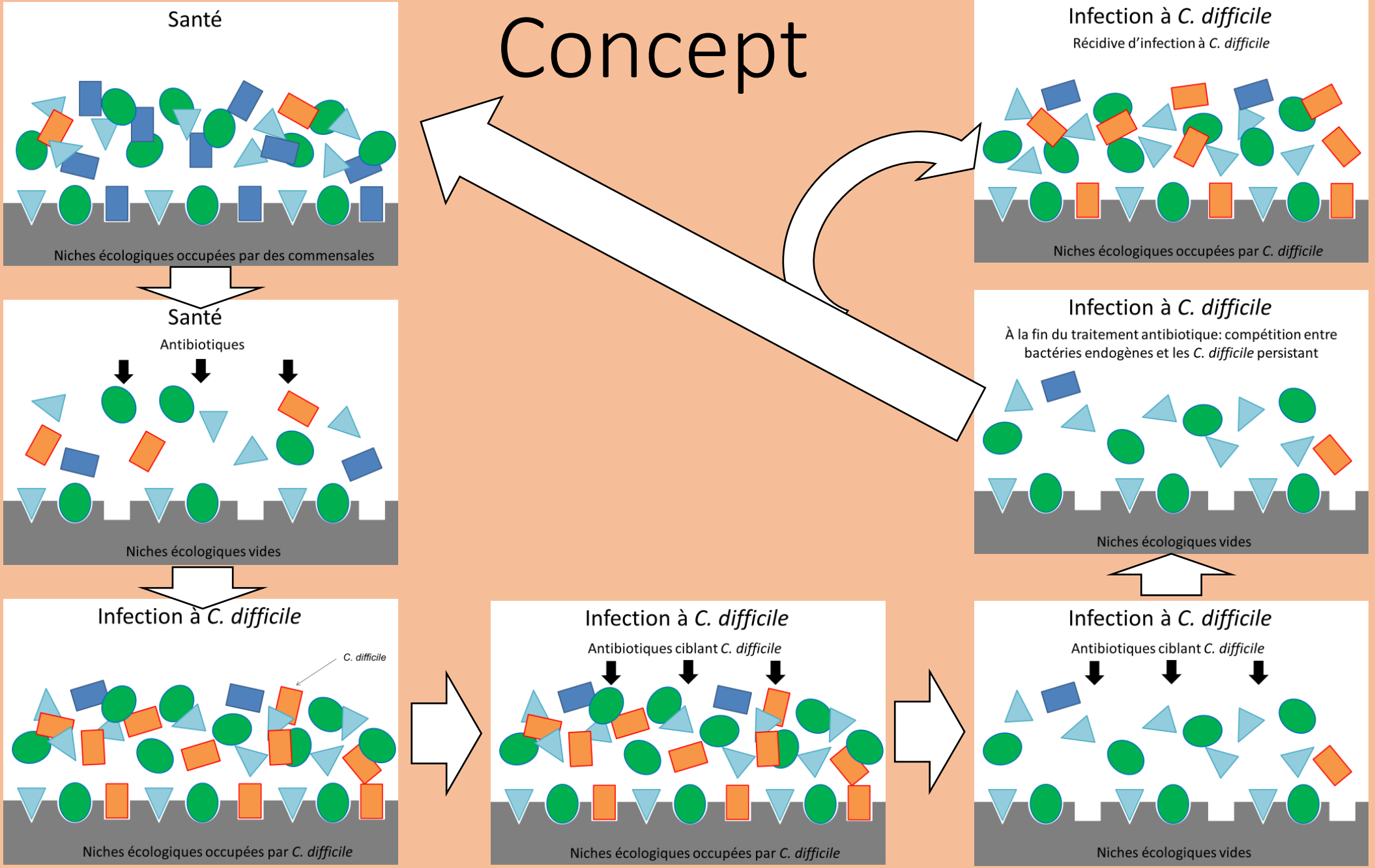
- V^{e} siècle en Chine (Ge Hong)
  - ⇨ administration de suspensions fécales humaines par voie orale à des patients souffrant d diarrhées sévères → résultats +++

- XVI^{e} siècle en Chine (Li Shezenet)
  - ⇨ série d'utilisation de suspensions fécales =« soupe jaune » pour le traitement de diarrhées sévères, fièvre, douleurs abdominales, vomissements et même constipation

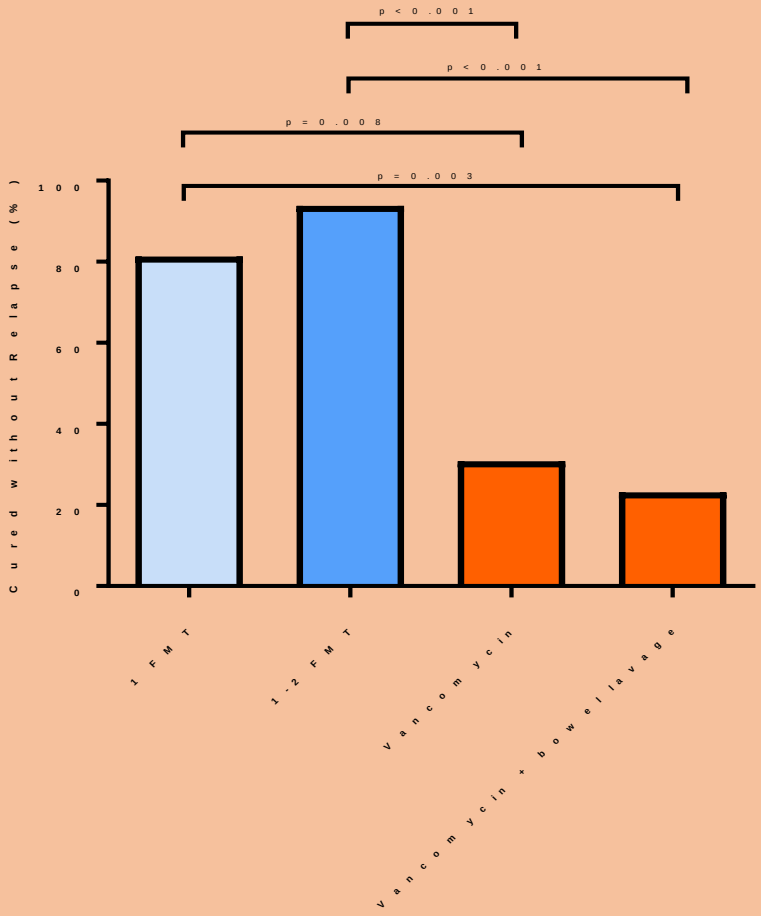
- Chez les Bédouins
  - ⇨ tradition de coprophagie basée sur l'utilisation de selles de chameaux comme remède contre la dysenterie (repris par des soldats stationnés en Afrique du Nord pendant la 2ème guerre mondiale)

- Eisenman,1958 : 1ère publication de l'ère moderne
  - ⇨ guérison de 4 patients atteints de colite pseudo membraneuse sévère

Concept


Santé
Niches écologiques occupées par des commensales
Santé
Antibiotiques
Niches écologiques vides
Infection à C. difficile
C. difficile
Niches écologiques occupées par C. difficile
Infection à C. difficile
Antibiotiques ciblant C. difficile
Niches écologiques occupées par C. difficile
Infection à C. difficile
Antibiotiques ciblant C. difficile
Niches écologiques vides
Infection à C. difficile
À la fin du traitement antibiotique: compétition entre bactéries endogènes et les C. difficile persistant
Niches écologiques vides
Infection à C. difficile
Récidive d'infection à C. difficile
Niches écologiques occupées par C. difficile

1er essai randomisé contrôlé
ICD récidivante



Etude arrêtée après l'analyse intermédiaire

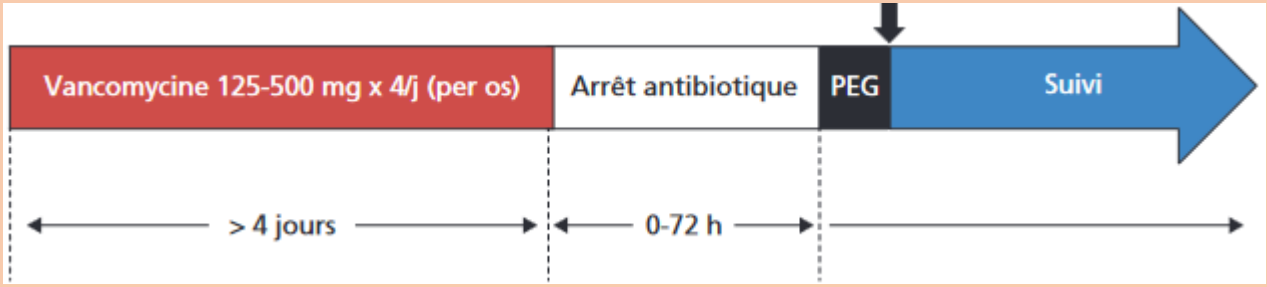
➔ Non éthique de continuer avec une telle différence entre les 2 groupes de traitement

Table 2. Adverse Events in 16 Patients in the Infusion Group.*

Adverse Event	On Day of Infusion of Donor Feces	During Follow-up
	no. of events	
Belching	3	0
Nausea	1	0
Vomiting	0	0
Abdominal cramps	5	0
Diarrhea	15	0
Constipation	0	3
Abdominal pain	2 (associated with cramping)	0
Infection	0	2†
Hospital admission	NA	1‡
Death	0	0
Other adverse event	1§	1‡

Van Nood et al. NEJoM 2013

Préparation du patient avant TMF



- Antibiothérapie d'au moins 4 jours *=> vancomycine PO ou fidaxomicine*
  - *pas de prise la veille au soir de la TMF*

- Préparation colique
  - *fin de la préparation au moins 6h avant le geste ou 3h avant si gélules*)

- Receveur à jeun à minuit la veille

Procédures d'administration (1)

- **<u>Voie orale (gélules)</u>:** possible en ambulatoire

  2 X 15 gélules à 24h d'intervalle

  Sous la surveillance d'une infirmière

  Délai maximal pour ingérer les gélules: 4h

- **<u>Voie haute:</u>** par SND ou SNG

  100 à 200ml d'une suspension à administrer par sonde entérale

  2 à 4 seringues ND, administration 50ml en 2 min (rinçage de la sonde à l'eau et sonde restée en place durant 30 min après)

Procédures d'administration (2)

- **Voie basse:**

Par voie rectale:

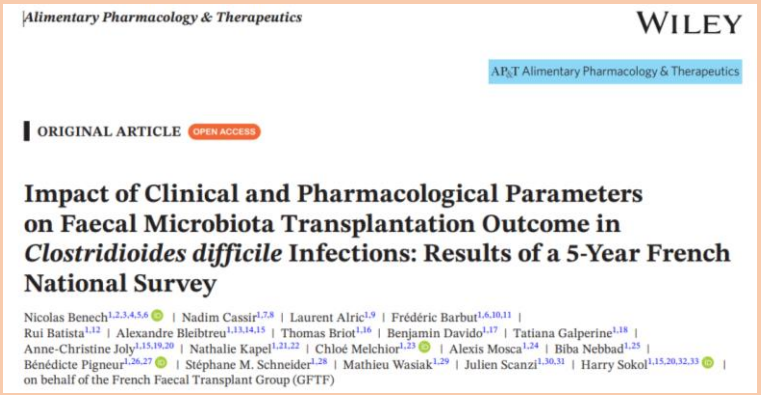
500 mL d'une suspension pour lavement rectal dans 1 poche à lavement (le patient doit rester allongé en décubitus latéral au minimum durant 2h après l'administration du lavement)

Par coloscopie:

200-300 mL d'une suspension : 4-6 seringues avec embout adaptable sur un canal opérateur de coloscope

Surveillance le jour de la TMF

- Surveillance clinique toutes les heures pendant **4h**
- Reprise d'une alimentation normale 4 heures après la TMF en l'absence de complications
- Surveillance sur la nuit en hospitalisation ou sortie à H+4 en fonction du contexte clinique (prise en charge HDJ)
- Fiche de suivi: notification si présence de nausées, fièvre, douleur



Alimentary Pharmacology & Therapeutics WILEY

APT Alimentary Pharmacology & Therapeutics

ORIGINAL ARTICLE OPEN ACCESS

Impact of Clinical and Pharmacological Parameters on Faecal Microbiota Transplantation Outcome in *Clostridioides difficile* Infections: Results of a 5-Year French National Survey

Nicolas Benech[1,2,3,4,5,6] | Nadim Cassir[1,7,8] | Laurent Alric[1,9] | Frédéric Barbut[1,6,10,11] | Rui Batista[1,12] | Alexandre Bleibtreu[1,13,14,15] | Thomas Briot[1,16] | Benjamin Davido[1,17] | Tatiana Galperine[1,18] | Anne-Christine Joly[1,15,19,20] | Nathalie Kapel[1,21,22] | Chloé Melchior[1,23] | Alexis Mosca[1,24] | Biba Nebbad[1,25] | Bénédicte Pigneur[1,26,27] | Stéphane M. Schneider[1,28] | Mathieu Wasiak[1,29] | Julien Scanzi[1,30,31] | Harry Sokol[1,15,20,32,33] | on behalf of the French Faecal Transplant Group (GFTF)

GFTF Groupe Français de Transplantation Fécale

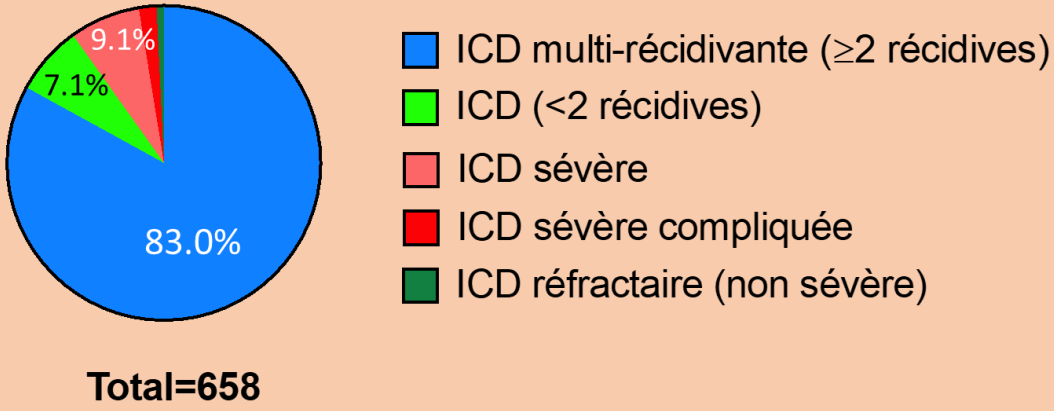
- Pas d'effet de la fidaxomicine pré-TMF
- Pas d'effet poids des selles
- Pas d'effet voie d'administration

France 2018-2022 :

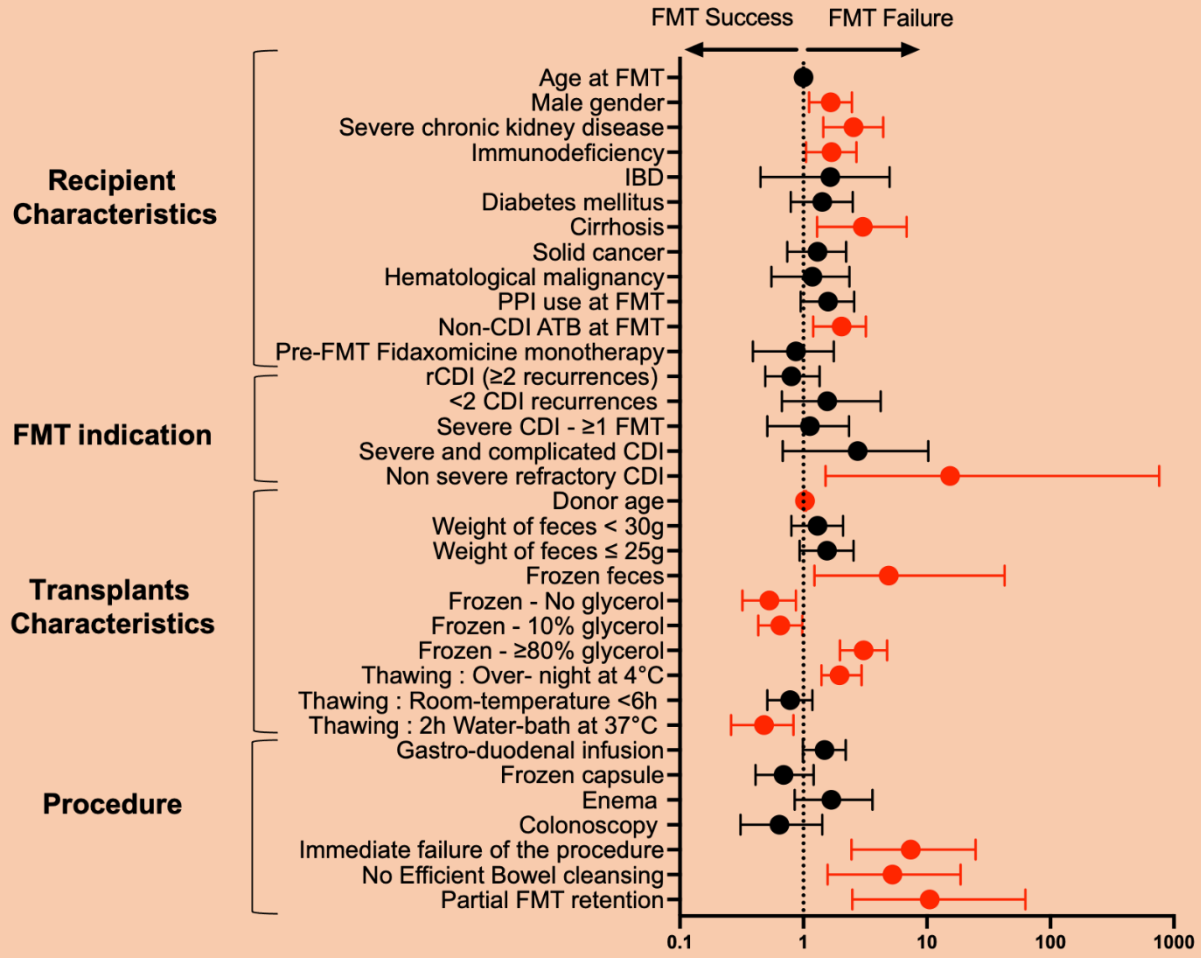
658 TMF pour 617 patients

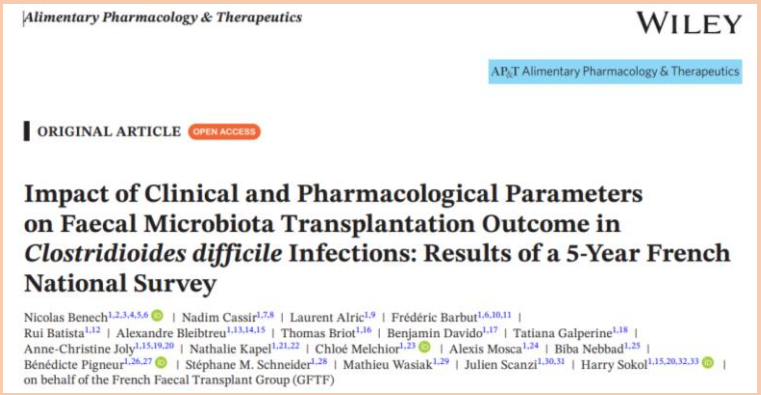
17 centres en 2018

- Indications:



Total=658





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GFTF Groupe Français de Transplantation Fécale

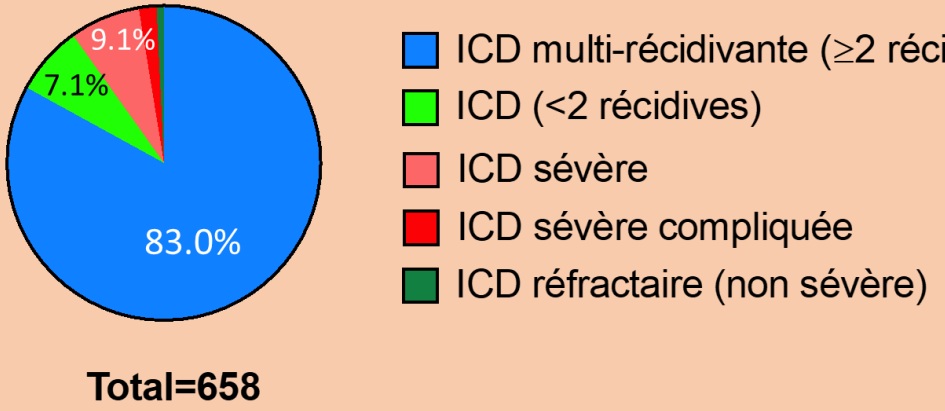
Analyse multivariée

France 2018-2022 :

658 TMF pour 617 patients

17 centres en 2018

- Indications:



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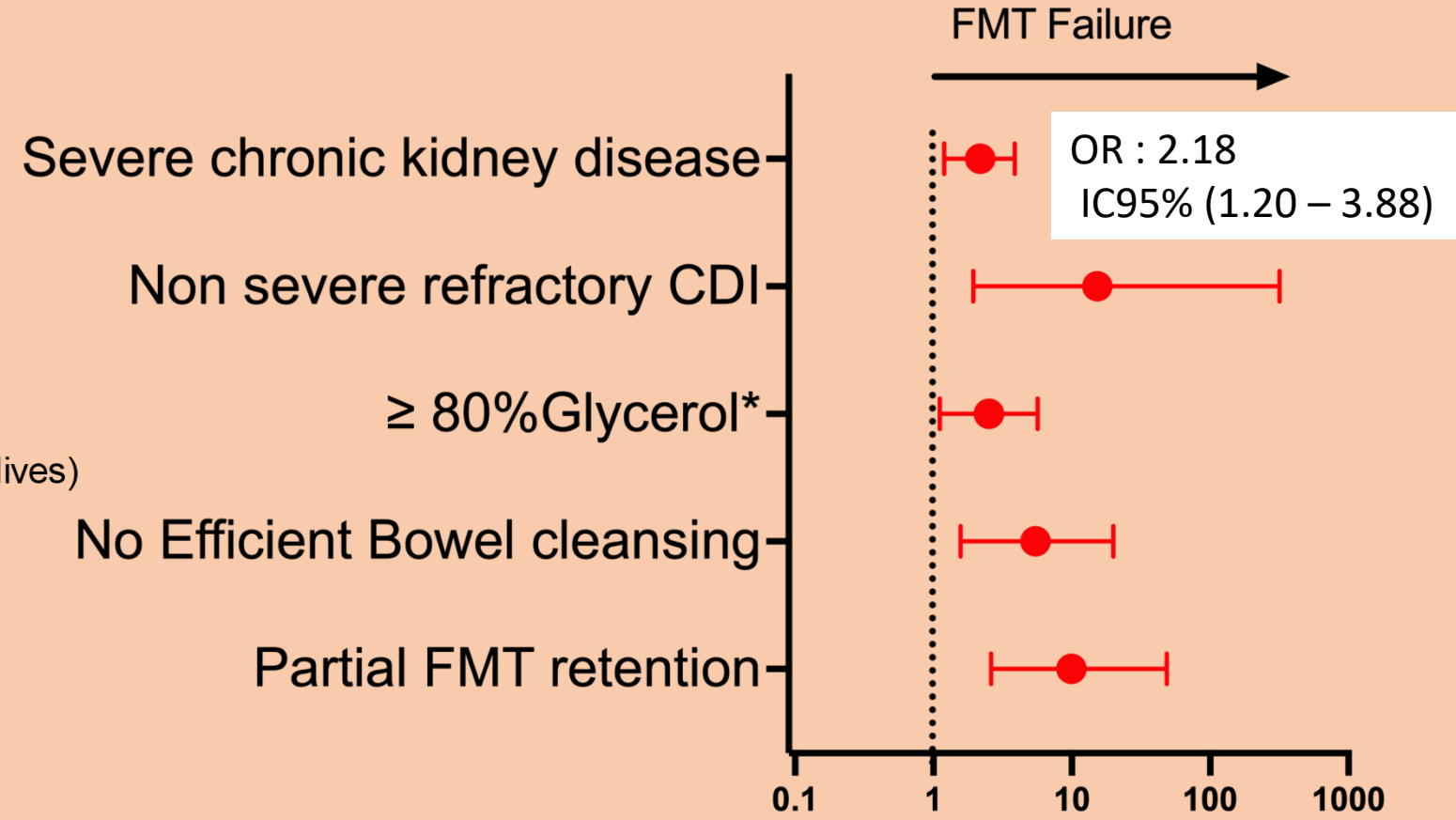


Régression logistique multiple

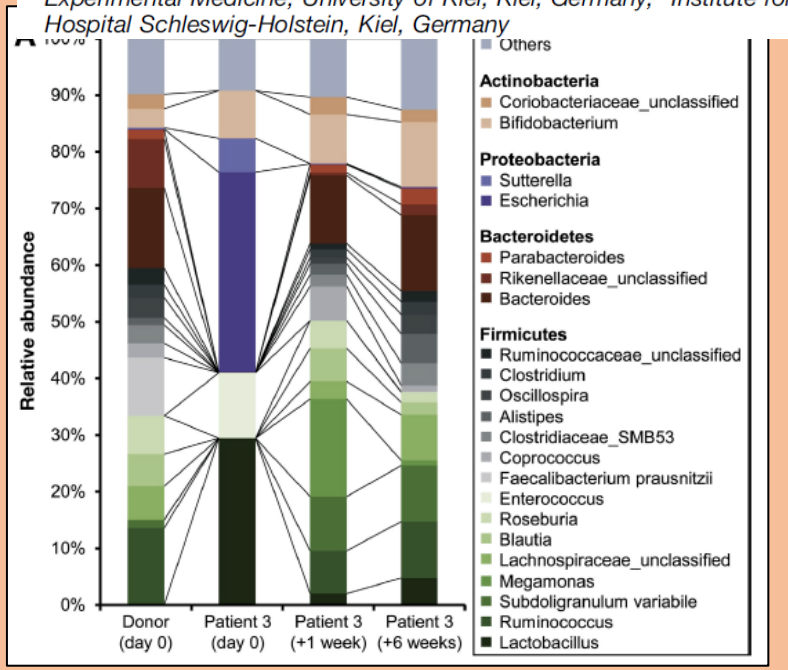
Le Microbiote ce n'est pas que des bactéries

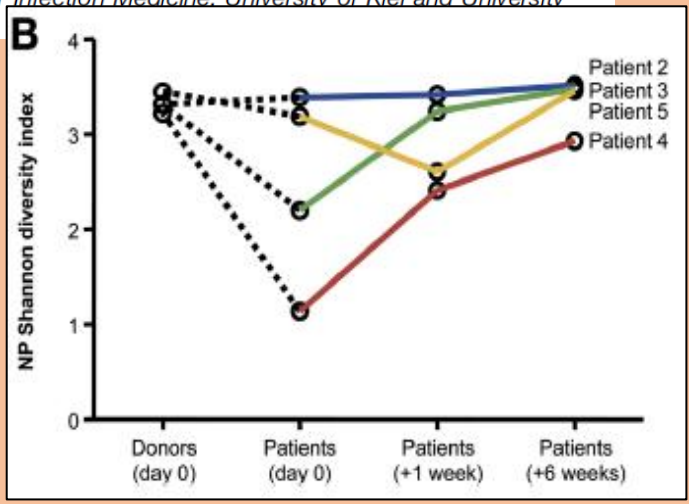
Efficacy of Sterile Fecal Filtrate Transfer for Treating Patients With *Clostridium difficile* Infection

Gastroenterology 2017;152:799–811

Stephan J. Ott,[1,*] **Georg H. Waetzig**,[2,*] **Ateequr Rehman**,[3,*] Jacqueline Moltzau-Anderson,[3,4] Richa Bharti,[3] Juris A. Grasis,[5] Liam Cassidy,[6] Andreas Tholey,[6] Helmut Fickenscher,[7] Dirk Seegert,[2] Philip Rosenstiel,[3,§] and Stefan Schreiber[1,3,§]

[1]Department of Internal Medicine I, University Hospital Schleswig-Holstein, Kiel, Germany; [2]CONARIS Research Institute AG, Kiel, Germany; [3]Institute of Clinical Molecular Biology, University of Kiel, Kiel, Germany; [4]Max Planck Institute for Evolutionary Biology, Plön, Germany; [5]Department of Biology, San Diego State University, San Diego, California; [6]Institute of Experimental Medicine, University of Kiel, Kiel, Germany; [7]Institute for Infection Medicine, University of Kiel and University Hospital Schleswig-Holstein, Kiel, Germany





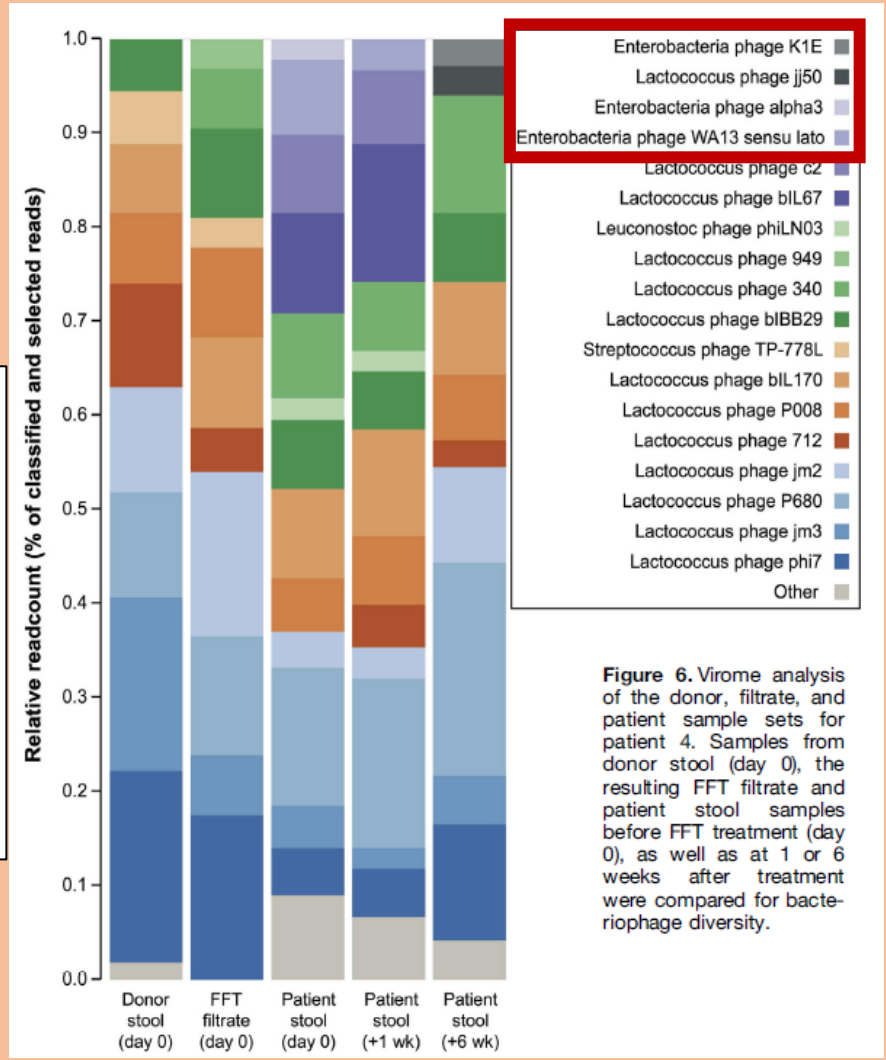
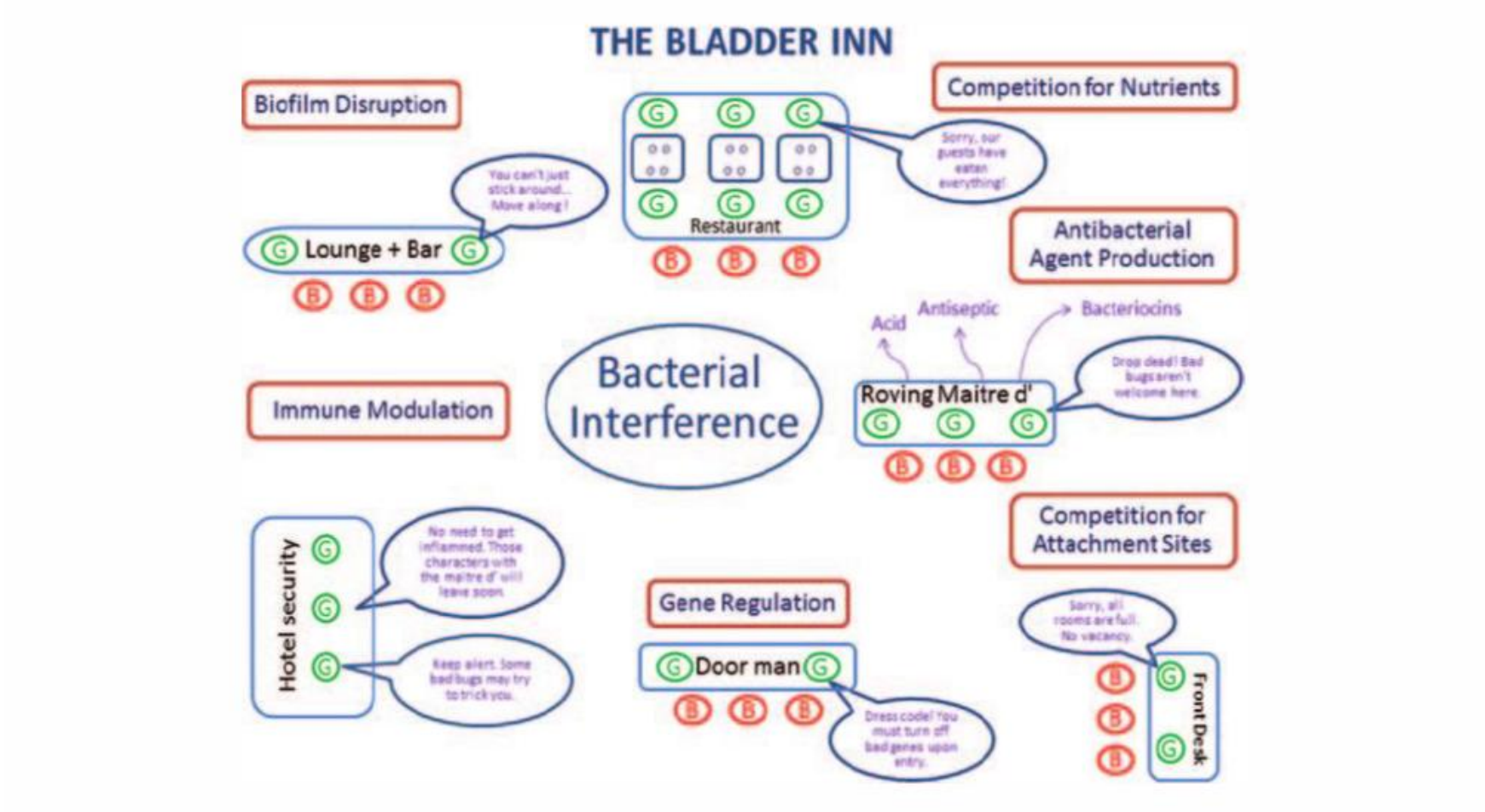


Figure 6. Virome analysis of the donor, filtrate, and patient sample sets for patient 4. Samples from donor stool (day 0), the resulting FFT filtrate and patient stool samples before FFT treatment (day 0), as well as at 1 or 6 weeks after treatment were compared for bacteriophage diversity.

Bacterial Interference for Prevention of Urinary Tract Infection

Rabih O. Darouiche[1,2,3,4] and Richard A. Hull[5]

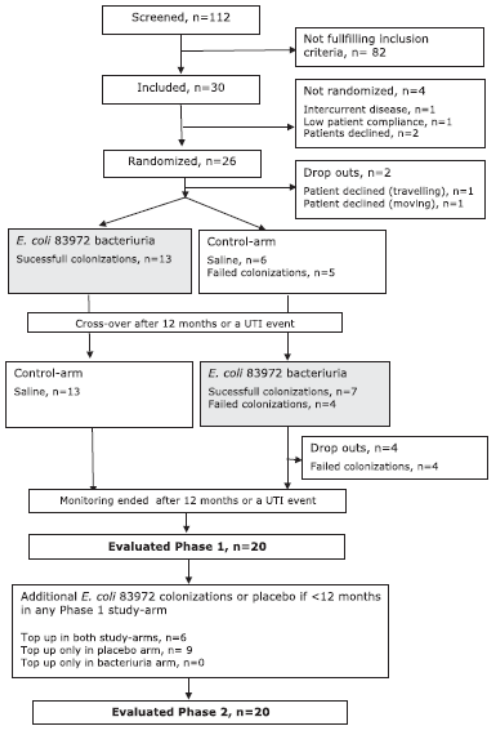


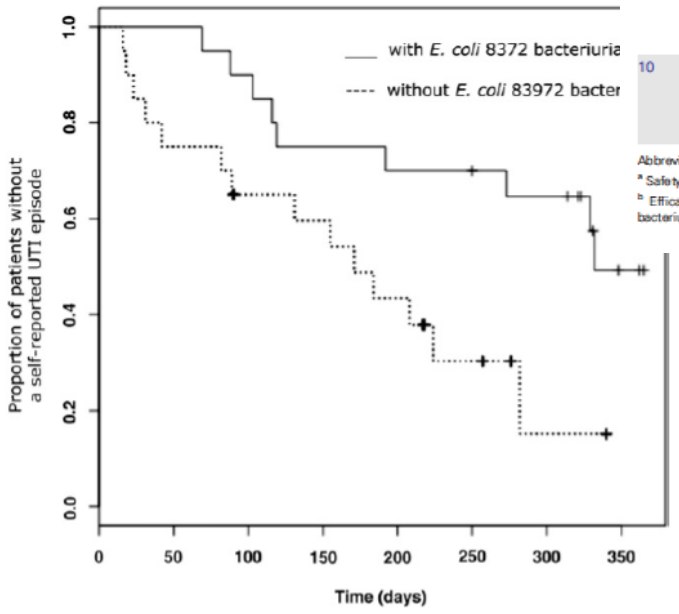
RO Darrouiche CID 2012

Bactéries Interférentes

Escherichia coli 83972 Bacteriuria Protects Against Recurrent Lower Urinary Tract Infections in Patients With Incomplete Bladder Emptying

Fredrik Sundén, Lars Håkansson, Eva Ljunggren and Björn Wullt*





The journal of urology 2010

Table 1. Clinical Trials Using *Escherichia coli* for Prevention of Urinary Tract Infection

Ref	Author/Year	*E. coli* Strain	Study Design	Enrolled Patients	Intervention	Reported Safety[a]	Reported Efficacy[b]
9	Darouiche 2011	HU2117	Randomized, placebo-controlled, double-blind	65	Bladder inoculation	Yes	Average no. of episodes of symptomatic UTI per patient-year was lower in the experimental group than in the control group (0.50 vs 1.68, $P = .02$).
37	Sundén 2010	83972	Crossover, placebo-controlled, double-blind	20	Bladder inoculation	Yes	The time to first symptomatic UTI was longer with than without *E. coli* 83972 bacteriuria (median 11.3 vs 5.7 mo, sign test $P = .013$). There were fewer reports during 1 year of symptomatic UTI with than without *E. coli* 83972 bacteriuria (13 vs 35 episodes; paired *t* test, $P = .009$, 95% CI: .31–1.89).
38	Prasad 2009	83972	Open-label, compared *E. coli* colonizers to historic control	13	Insertion of a coated bladder catheter for 3 d in patients practicing intermittent bladder catheterization	Yes	Lower rate of symptomatic UTI while colonized with *E. coli* 83972 than during prestudy period (0.77 vs 2.27 episodes per patient-year). Statistical comparison not provided.
39	Trautner 2007	HU2117	Open-label, compared *E. coli* recipients to historic control	12	Insertion of a coated bladder catheter for 28 d in patients with indwelling bladder catheters	Yes	Calculated rate of symptomatic UTI in the experimental group was lower than the reported historic rate in spinal cord–injured subjects with indwelling bladder catheters (0.15 vs 2.72 cases per 100 patient-days). Statistical comparison not provided.
15	Darouiche 2005	83972	Randomized, placebo-controlled, double-blind	27	Bladder inoculation	Yes	Mean number of symptomatic episodes of UTI per year was lower in experimental group than in control group (1.6 vs 3.5, $P = .036$).
16	Darouiche 2001	83972	Open-label, compared *E. coli* colonizers to noncolonizers and historic control	44	Bladder inoculation	Yes	A lower mean rate of symptomatic UTI in patients colonized with *E. coli* 83972 vs patients who could not be colonized (0.06 vs 1.80 episodes of UTI/patient-year, $P < .001$).
10	Hull 2000	83972	Open-label, compared *E. coli* colonizers to noncolonizers and historic control	21	Bladder inoculation	Yes	Mean rates of symptomatic UTI per patient-year were 0 in patients colonized with *E. coli* 83972 vs 3.1 in the same patients before colonization. Statistical comparison not provided.

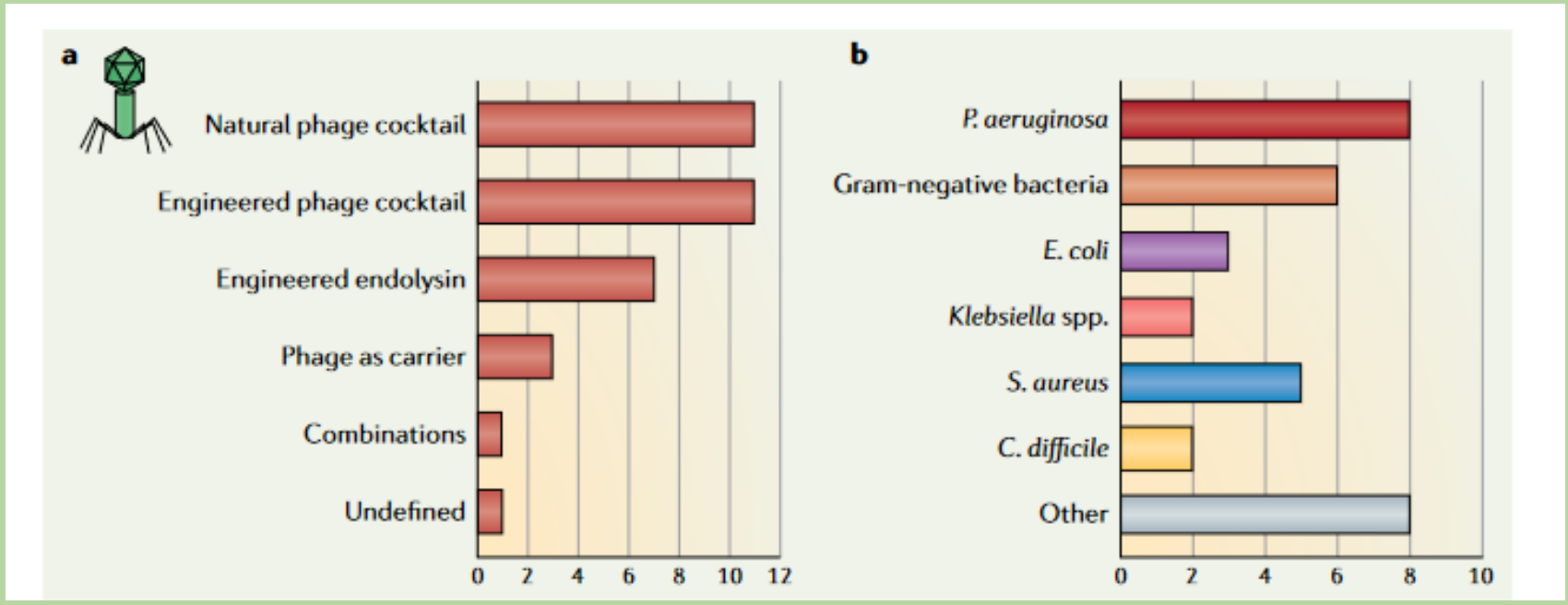
Abbreviations: CI, confidence interval; *E. coli*, *Escherichia coli*; UTI, urinary tract infection.

[a] Safety: Intervention is considered safe if inoculated *E. coli* strain does not cause symptomatic UTI.

[b] Efficacy: Intervention is considered efficacious if bladder colonization by the inoculated *E. coli* strain significantly reduces the incidence of symptomatic UTI as compared with persons or periods without bacteriuria due to the inoculated strain of *E. coli*.

Darouich & Hull, CID 2012

Phagothérapie



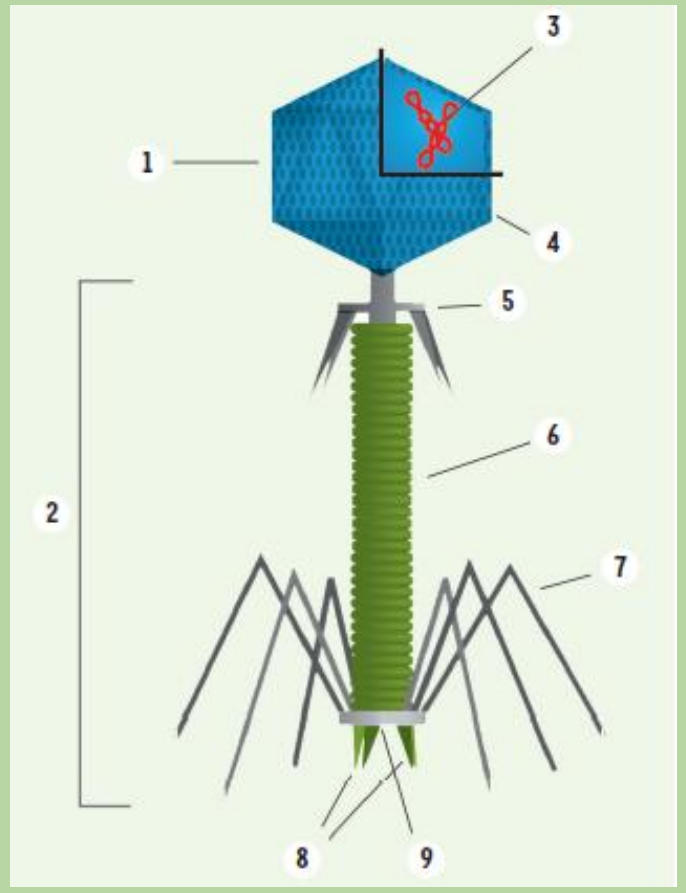
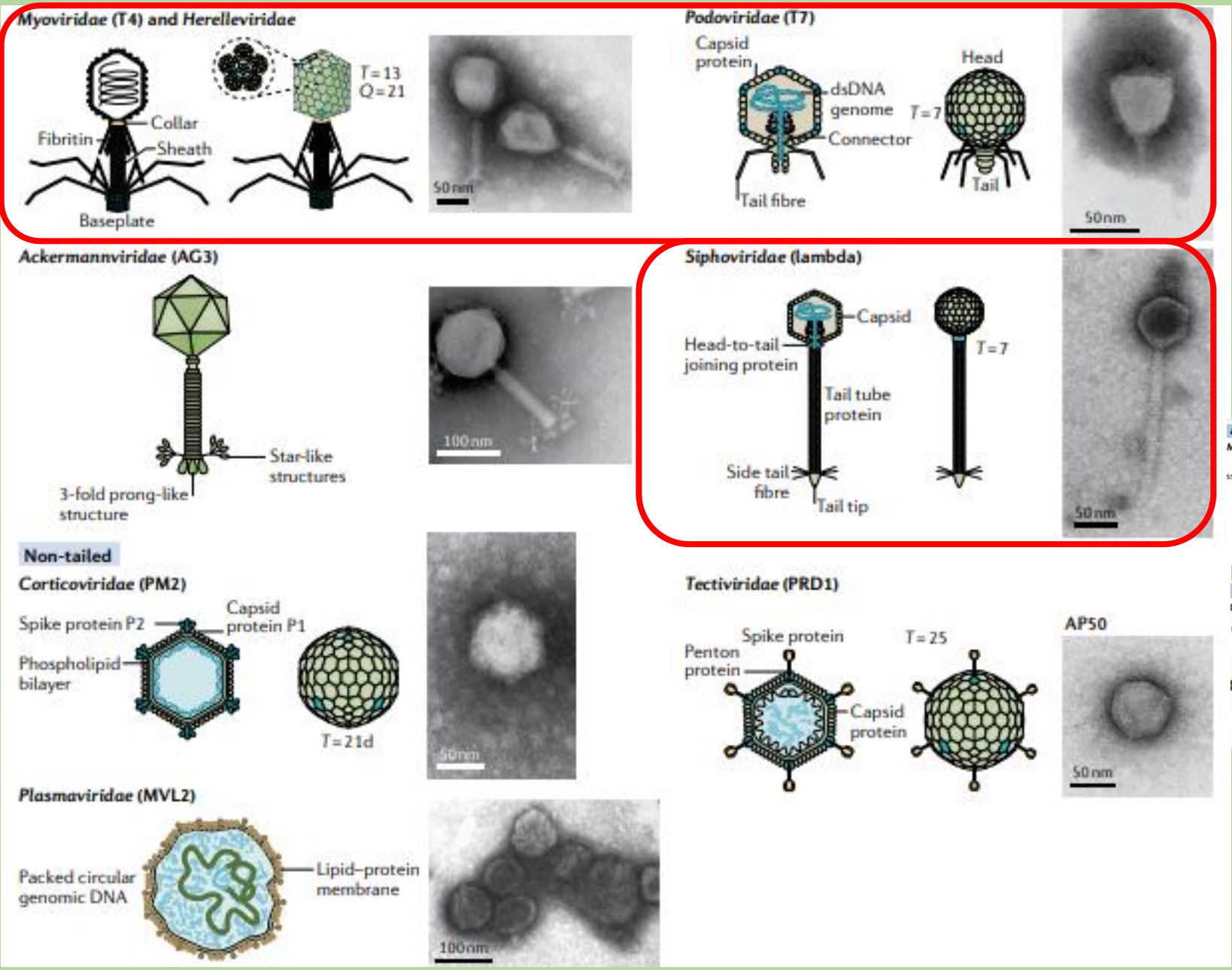


Figure 1. ***Structure du bactériophage T4.*** 1 : tête, 2 : queue, 3 : acide nucléique, 4 : capside, 5 : collier, 6 : gaine, 7 : fibres de queue, 8 : épines, 9 : plaque basale (d'après Y. Tambe, © Wiki-

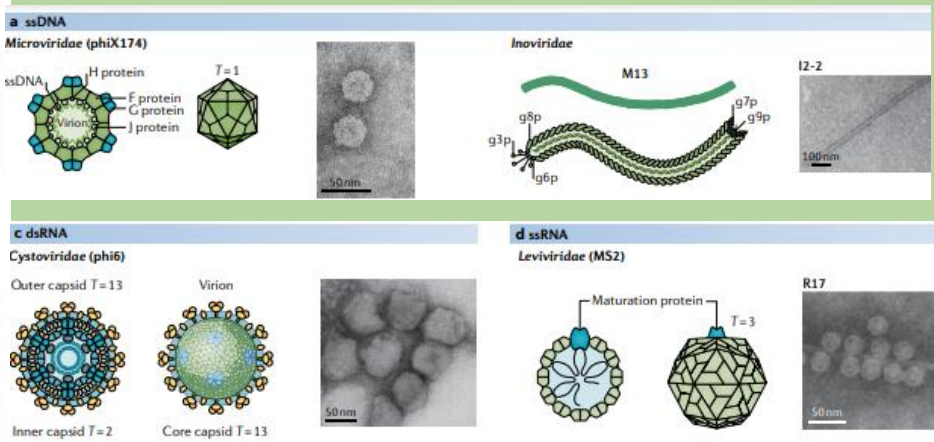
PMID: **31745331**

Dufour & Debarbieux 2018

Structure et classification



Majorité phages isolés:
queue + ADN double brin



Dion *et al* Nat rev 2020

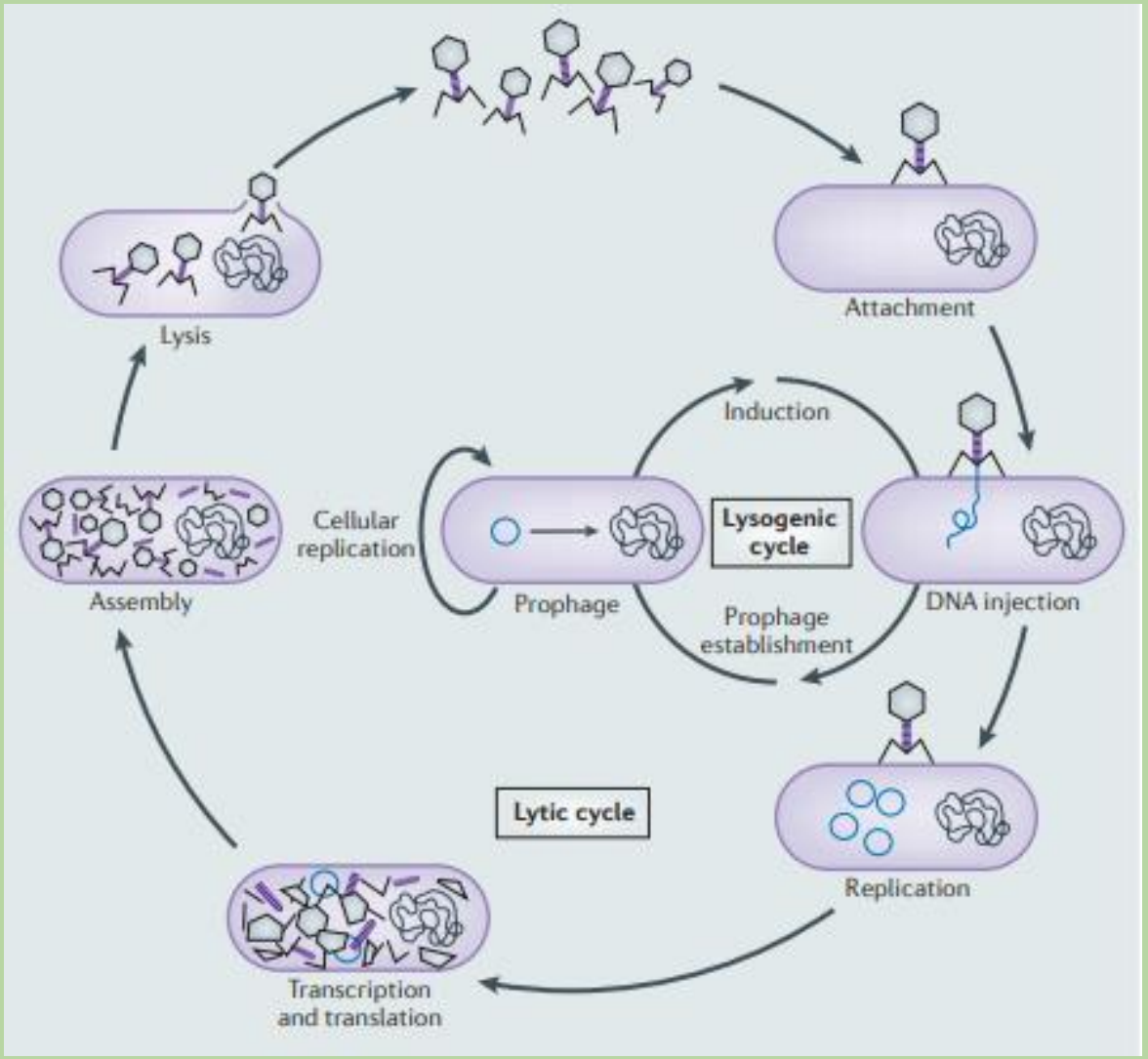
Les bactériophages : le cycle lytique

Cycle lytique

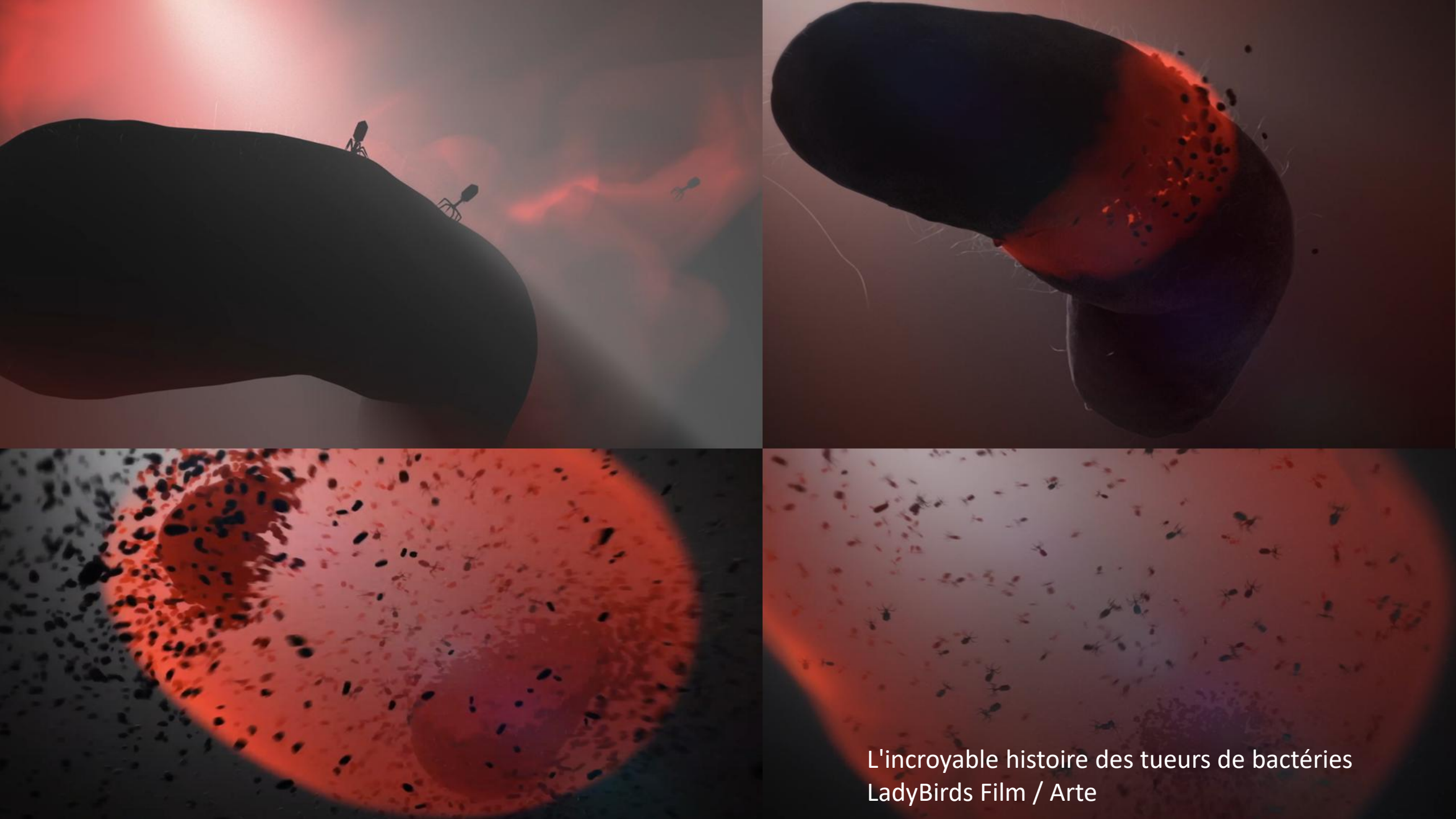
Interaction avec récepteurs
Adsorbtion
Injection génome (ADN +++)
Réplication
Assemblage nouvelles particules virales
Lyse bactérie

Cycle lysogénique (phages tempérés)

Intégration de l'ADN viral au chromosome
Prophage en dormance
Rôle dans l'évolution bactérienne (échange de matériel génétique)

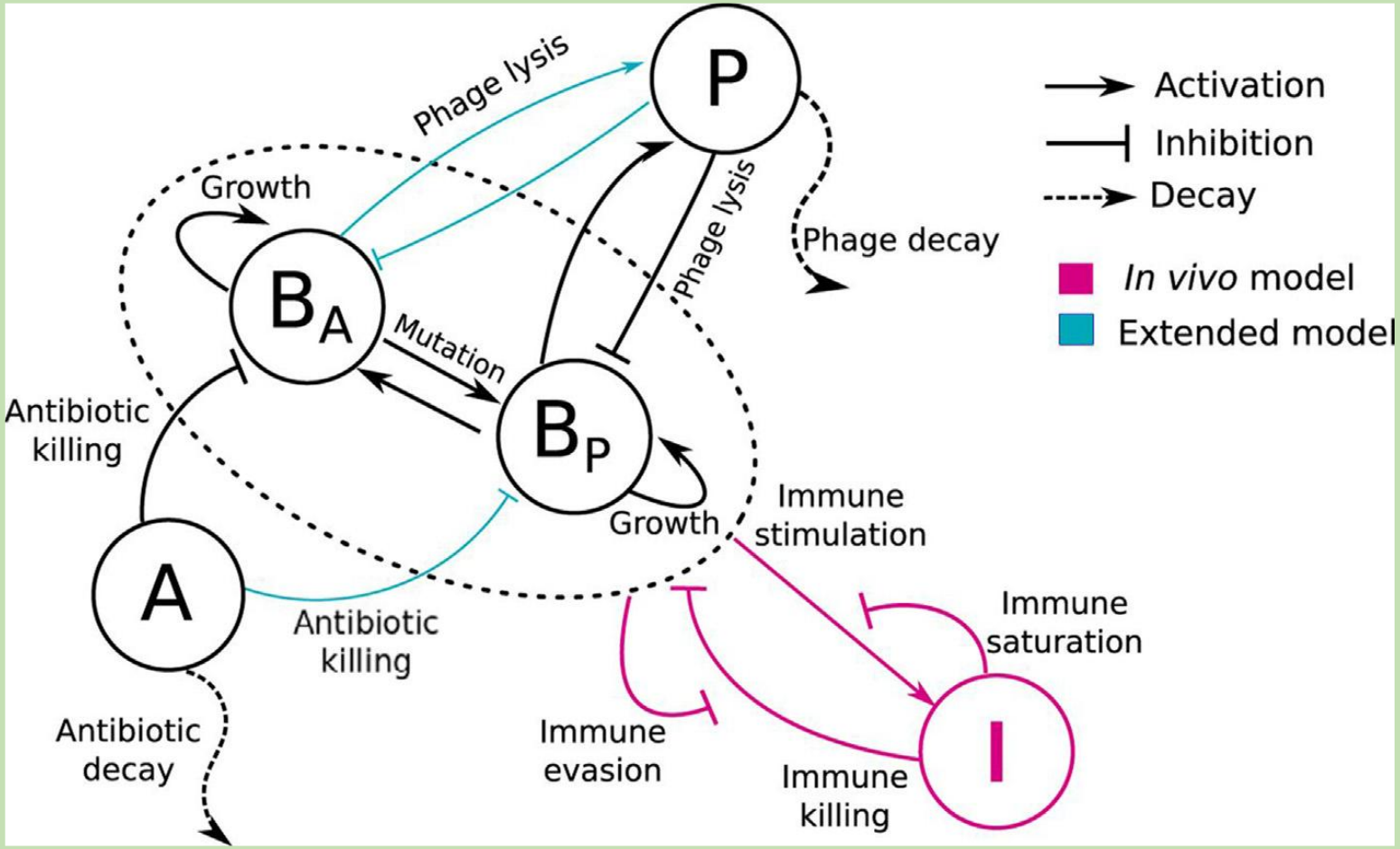


Salmond and Fineran Nat Rev Microbiol 2015



L'incroyable histoire des tueurs de bactéries
LadyBirds Film / Arte

Relations phages–antibiotiques c'est compliqué

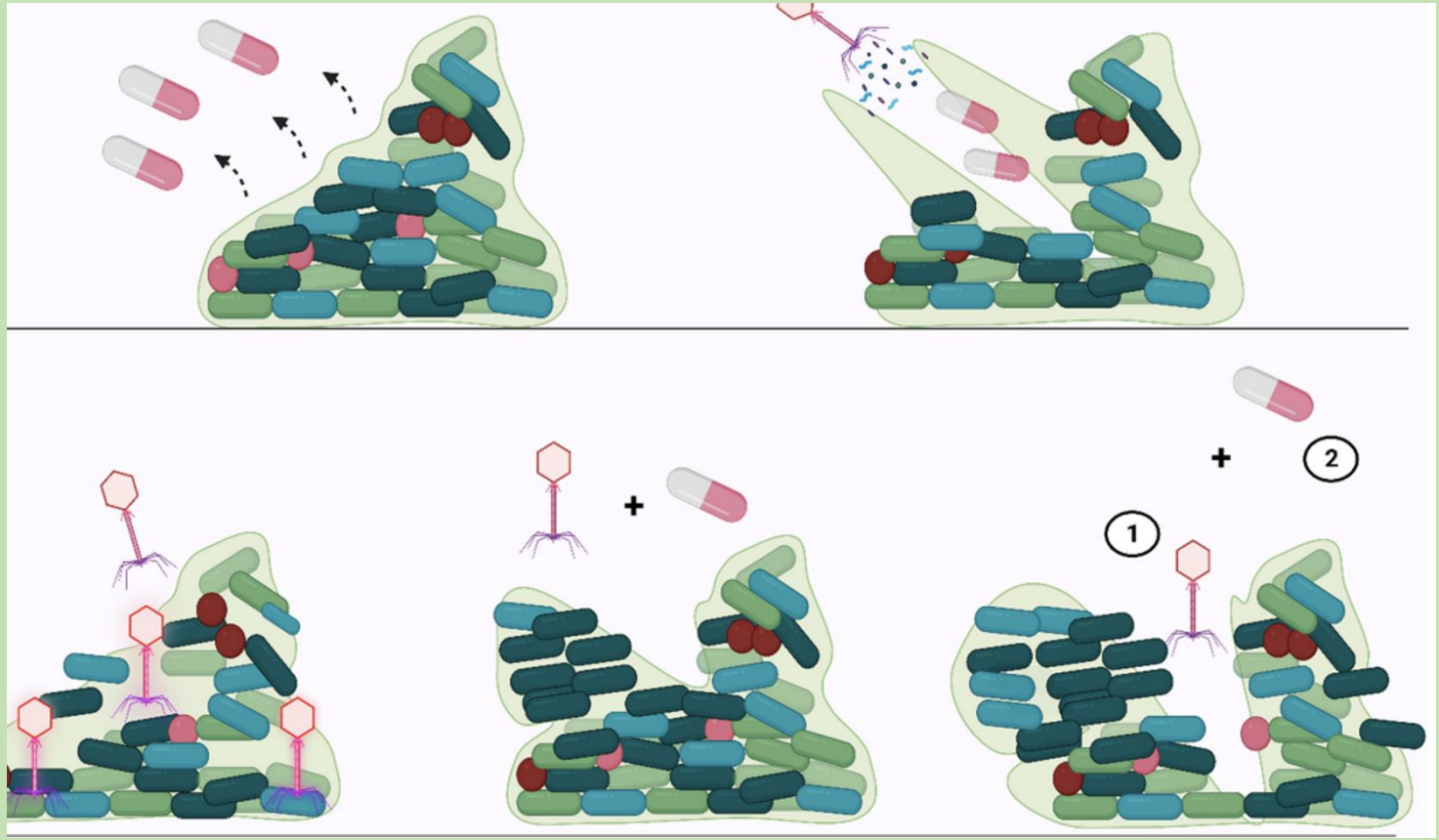


- Des synergies d'actions
- Des opportunités
- Des antagonismes
- Des notions de timing

Łusiak-Szelachowska et al. Journal of Biomedical Science (2022) 29:23.

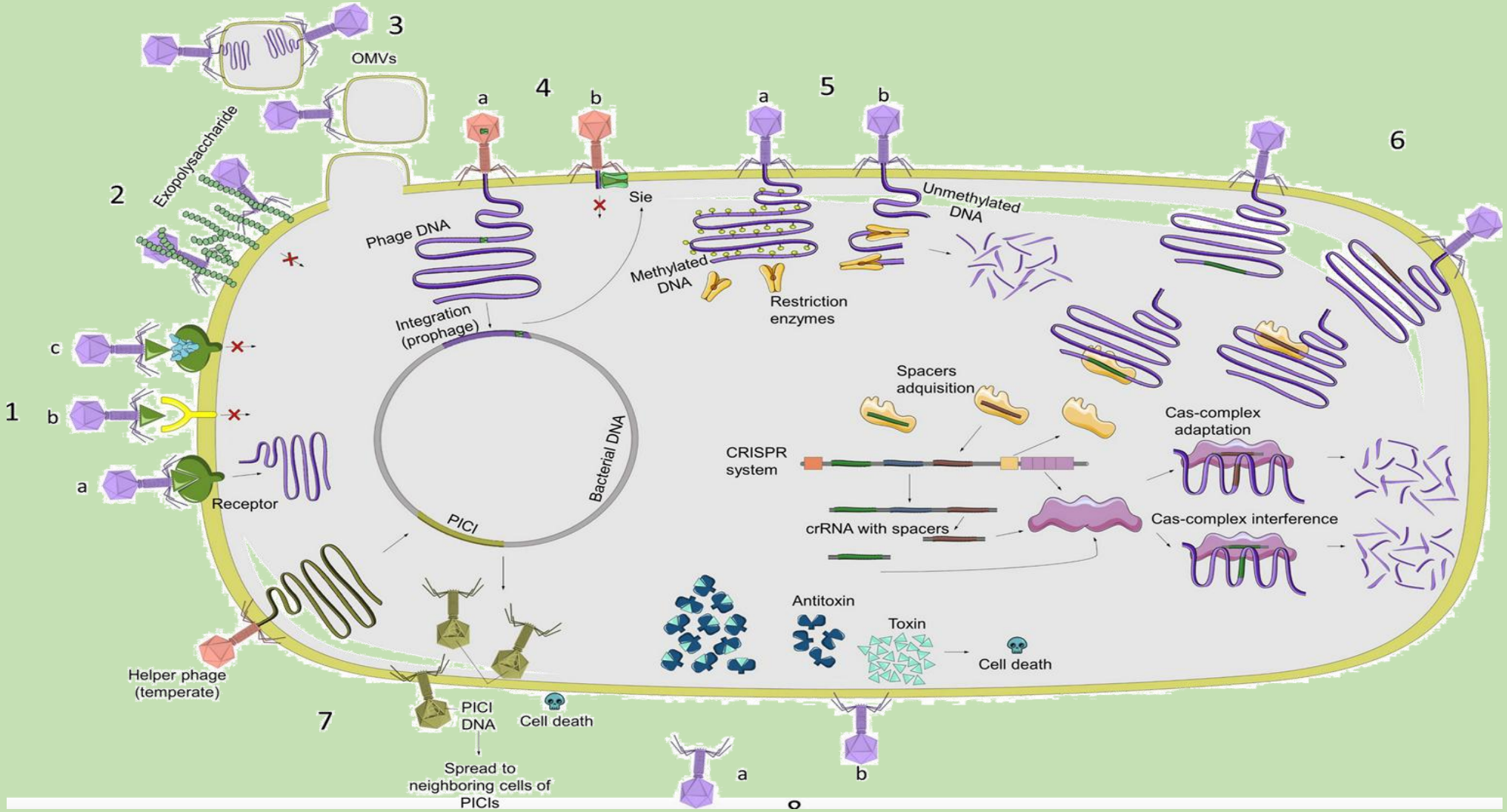
Biofilm et Phages

Activité dépolymérase : Fragilisation des biofilms bactériens



Rétablissement de l’accès aux bactéries par phages et antibiotiques

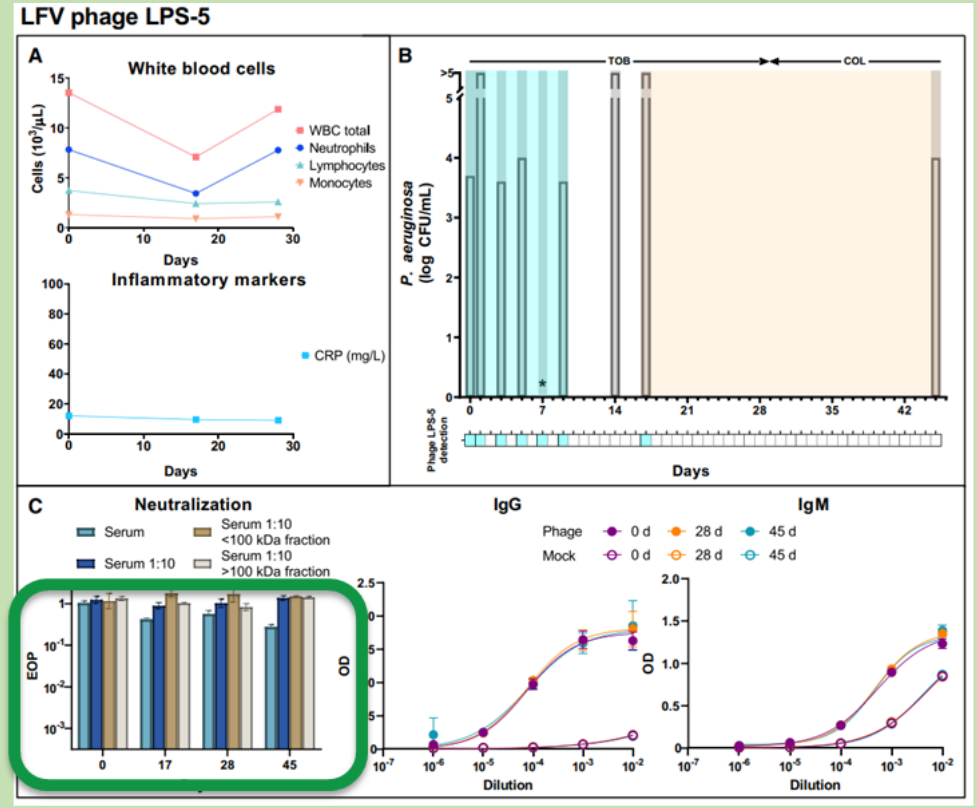
Mécanismes de résistances aux phages : Naturels et Acquis … comme les ATB

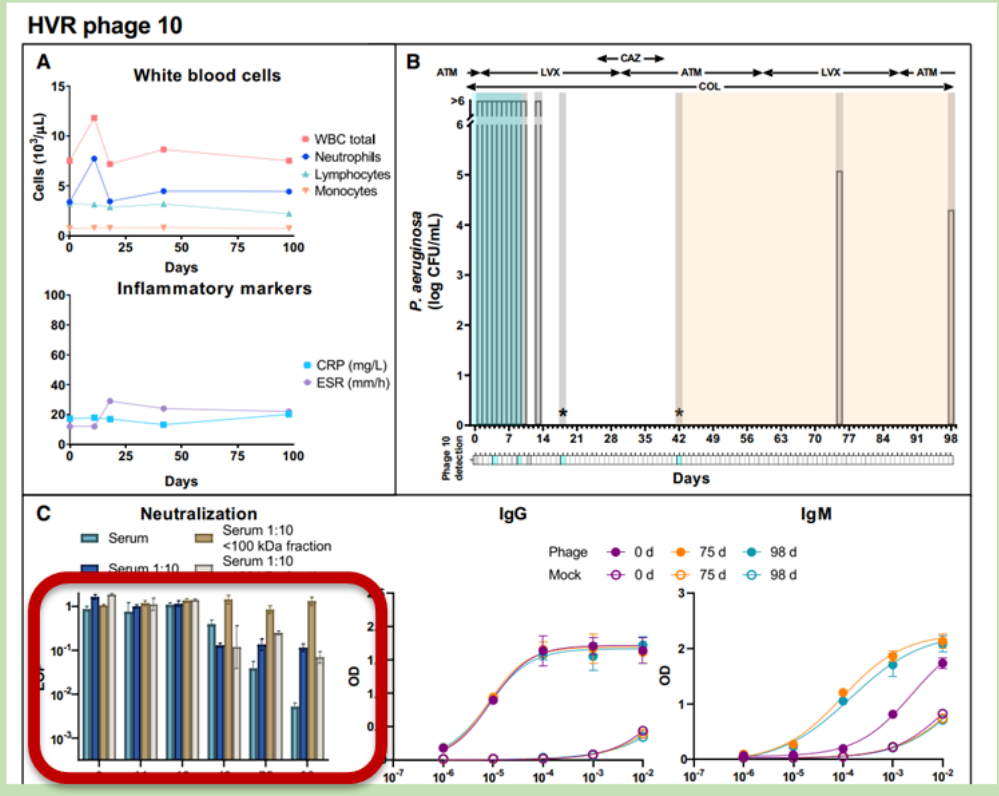


Impact des Ac Anti-Phages

- Ac chez patients non traités
- Ac Dans 20% des cas traités
- + d'AC par voie IV

- Pas de corrélation claire avec échec thérapeutique





Bernabe´ u-Gimeno et al., Med 5, 1096-1111 September 13, 2024

Problématique actuelle

Avoir des Phages

Isoler des Phages

Tester leur activité

Produire des phages

Proof of concept

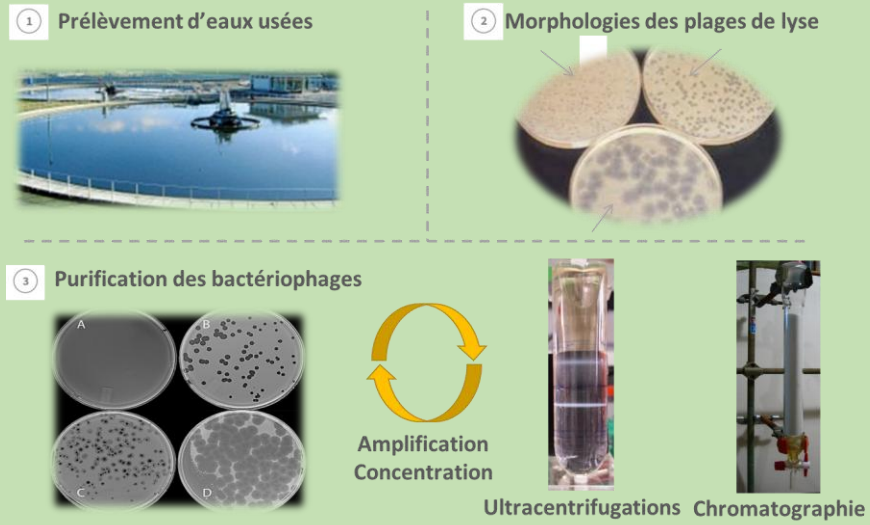
Cas compassionnels = impasse thérapeutique

Produire selon normes BPF

Prouver innocuité

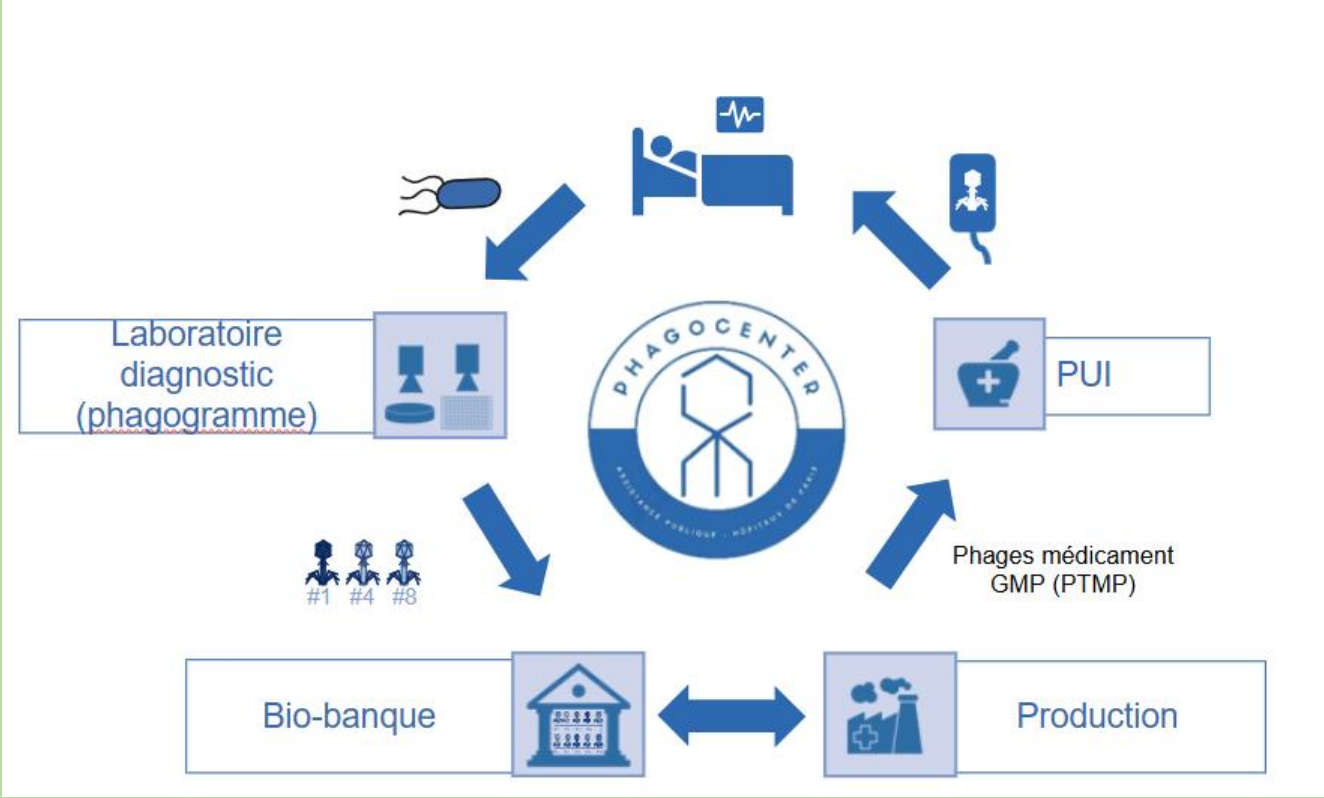
Essais cliniques

Prouver efficacité



Que faut-il pour avancer sur la phagothérapie

- Des Phages
- Des centres d’expertises
- Un travail collaboratif inter national
- Poser les bonnes indications
- Timing vis-à vis des ATB
- Des investissements
- Du temps, de la passion, de la rigueur scientifique
- Un peu de chance



Place des phages en 2024

Cas compassionnels

- >50 patients rapportés
- Probablement X5 ou X 10 réalisés

Terrain

- Mucovicidose, Transplanté pulmonaire, PAVM
- IOA complexe
- IPV complexe
- Endocardite complexe
- Abcès
- Brûlés
- infection cutanée chroniques

Bactéries

- SA, PA, AB, AX, NTM, KP, EC, BC

Indication

- Salvage therapy
- Pan Drug resistance

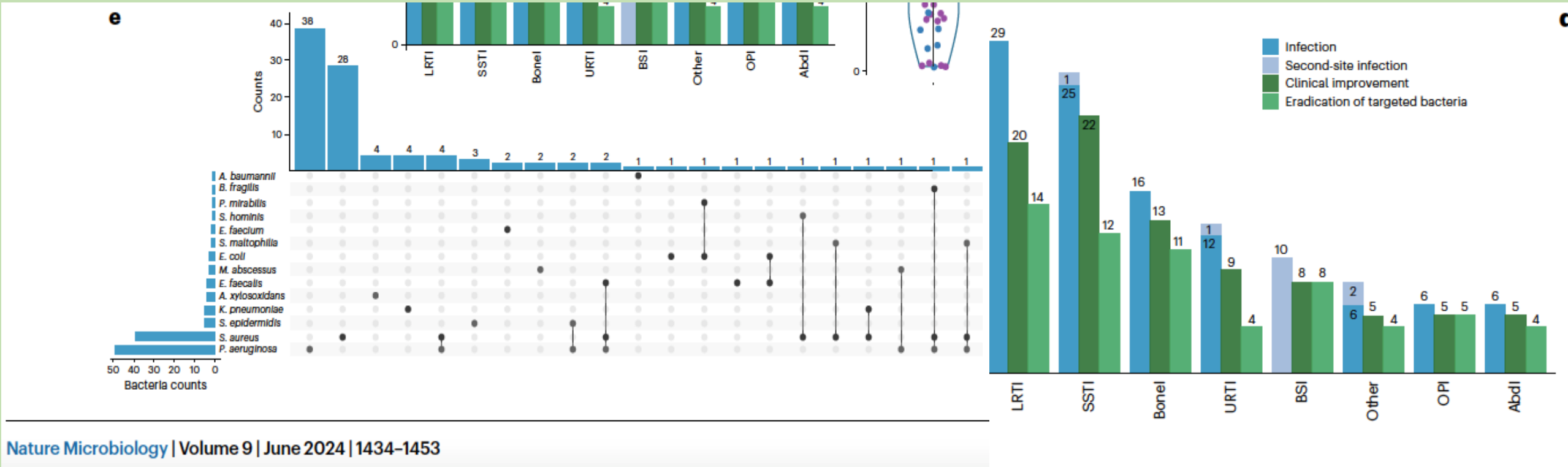
L'EXEMPLE BELGE

nature microbiology

Article

https://doi.org/10.1038/s41564-024-01705-x

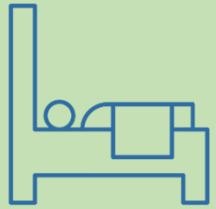
Personalized bacteriophage therapy outcomes for 100 consecutive cases: a multicentre, multinational, retrospective observational study



Nature Microbiology | Volume 9 | June 2024 | 1434–1453

Accès aux phages thérapeutiques 2024

Impasse thérapeutique

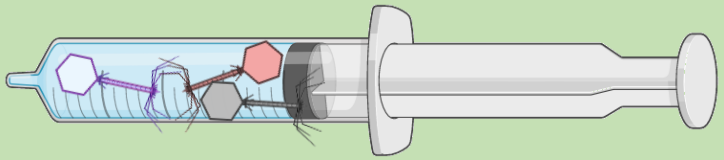


Administration au patient

4-10j

15-200 j

Préparation magistrale extemporanée



Envoi à la pharmacie à usage intérieure de l'hôpital du patient

Phages médicament – GMP
AAC ou AAP

Validation de l'indication et discussion du protocole d'administration
ANSM

Phagothérapie évoquée

S. aureus ou *P. aeruginosa*

Isolement souche bactérienne en cause chez le patient

Envoi de la souche à un phage provider

Phagogramme sur la souche bactérienne

Phagogramme sur la souche bactérienne

importation

Pleins de cas cliniques divers

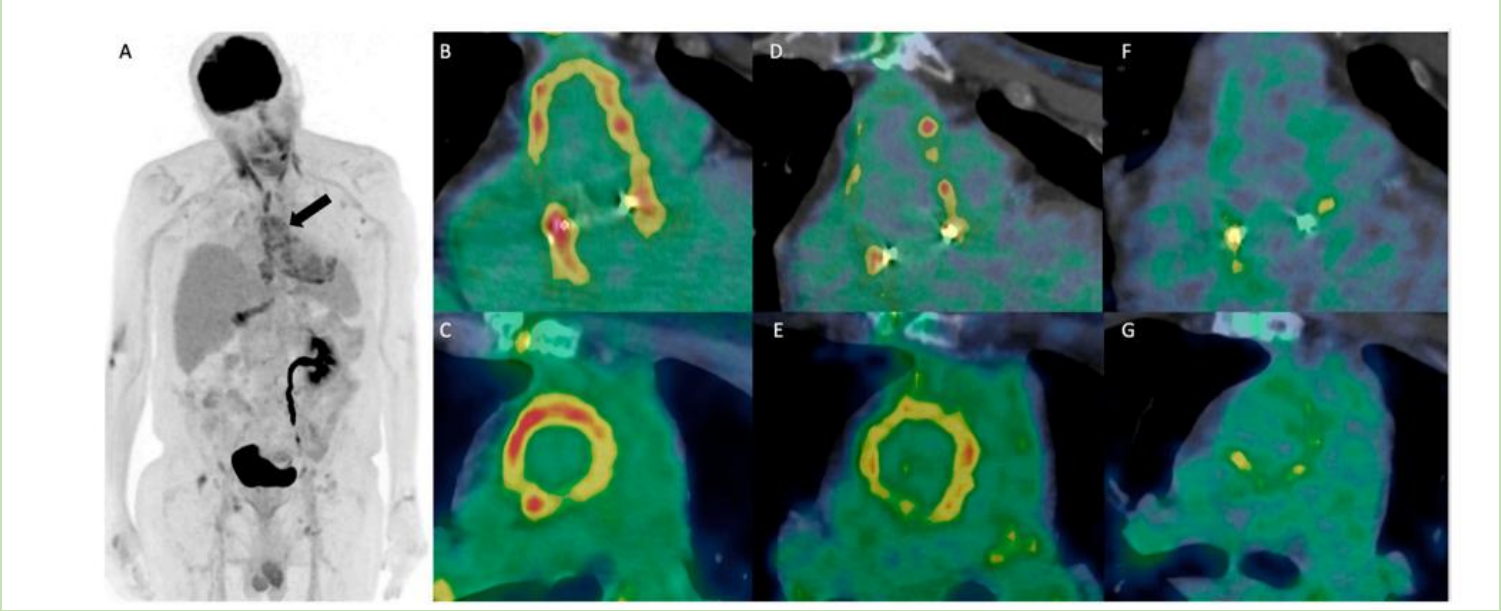
viruses

MDPI

Case Report

Phage Therapy as a Rescue Treatment for Recurrent *Pseudomonas aeruginosa* Bentall Infection

Victor Eiferman [1,*], Pierre-Adrien Vion [2] and Alexandre Bleibtreu [1]



Essai clinique en France en 2025

Académiques

Phagopied (Nimes) SA pied diabétique
Phagos (Bordeaux) SA Ostéite chronique
Pyophaneb (Paris) PA PAVM
Phagoscarpa (Melun) SA IPV

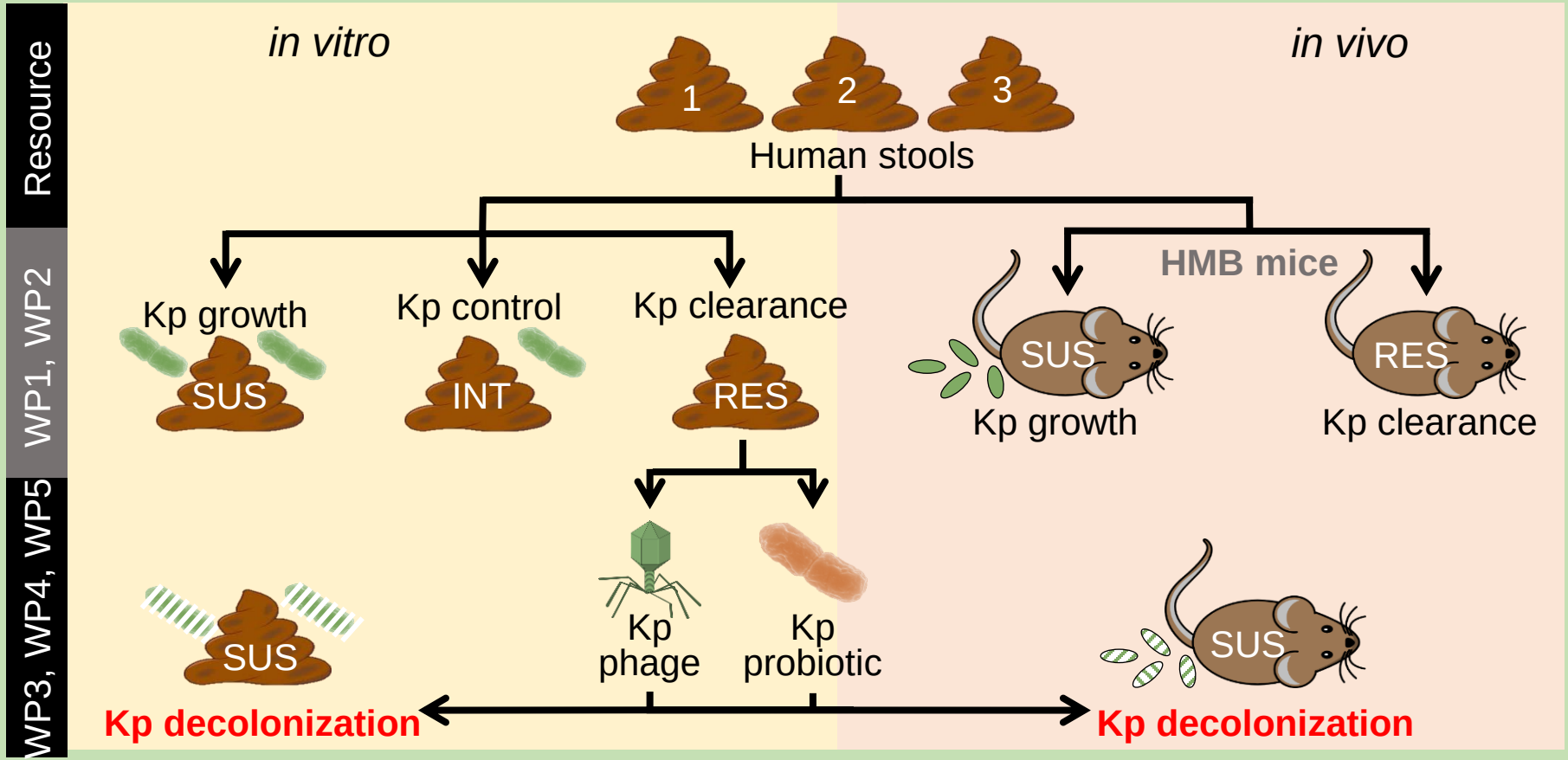
Industriels

Phage-endocardite (Phaxiam) EI à SA
GLORIA (Phaxiam) IPTG/TH SA

Décolonize

Promoting gut decolonization of multi-resistant *Klebsiella pneumoniae* via the microbiome

ANR franco-allemande (R. Tournebize, A. Bleibtreu, T. Strowig)



Lysines issues des phages

Name (synonym)	Phase	Antibiotic class	Route of administration (developer)	Expected activity against priority pathogens
CF-301 (exebacase)	3	Phage endolysin	iv (ContraFect)	*S. aureus*
SAL-200 (tonabacase)	2a	Phage endolysin	iv (iNtRON Biotechnology, Roivant Sciences)	*S. aureus*
PhageBank	1/2	Phage bank (process)	oral (Adaptive Phage Therapeutics and US Department of Defense)	*E. coli*, *K. pneumoniae*
LBP-EC01	1b	CRISPR-Cas3 enhanced phage	iv (Locus Bioscience)	*E. coli*, *K. pneumoniae*

Traitement adjuvant dans les bactériémies à *S. aureus*

Ajouter une lysine (exebacase) issue d'un phage anti *S. aureus* à de la Vanco améliore la survie

Combination Therapy With Lysin CF-301 and Antibiotic Is Superior to Antibiotic Alone for Treating Methicillin-Resistant *Staphylococcus aureus*–Induced Murine Bacteremia

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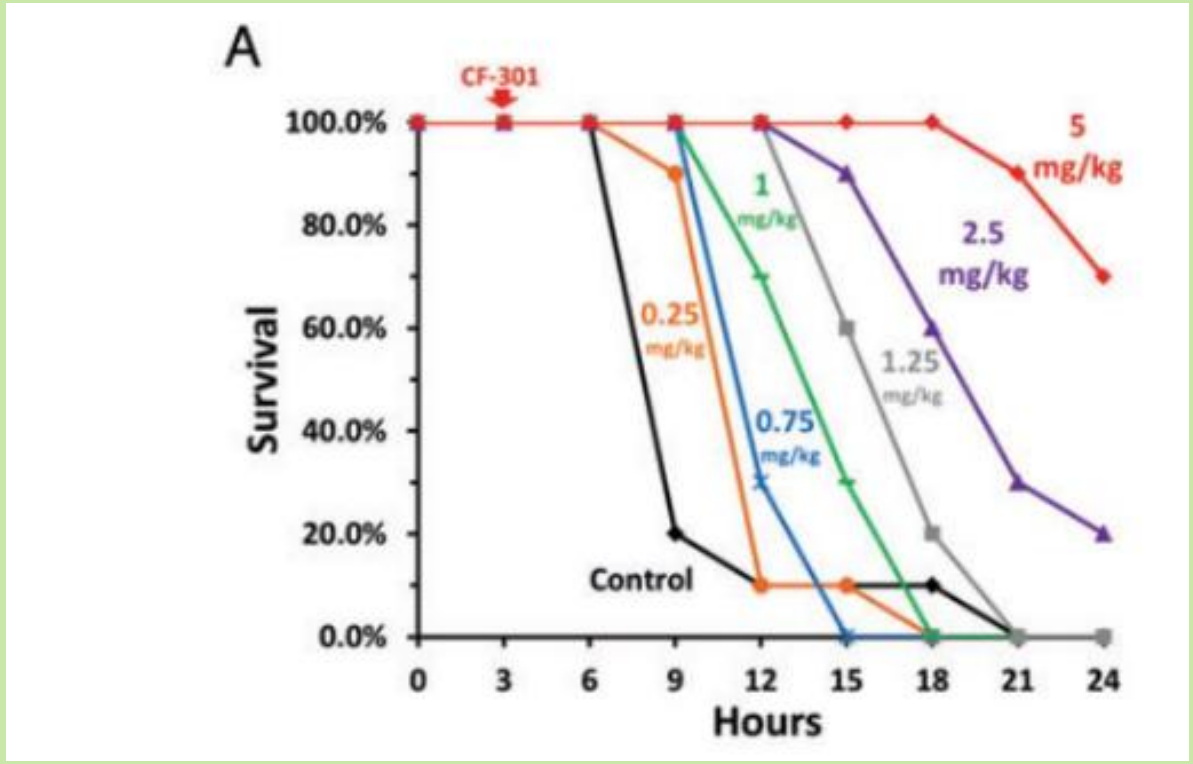
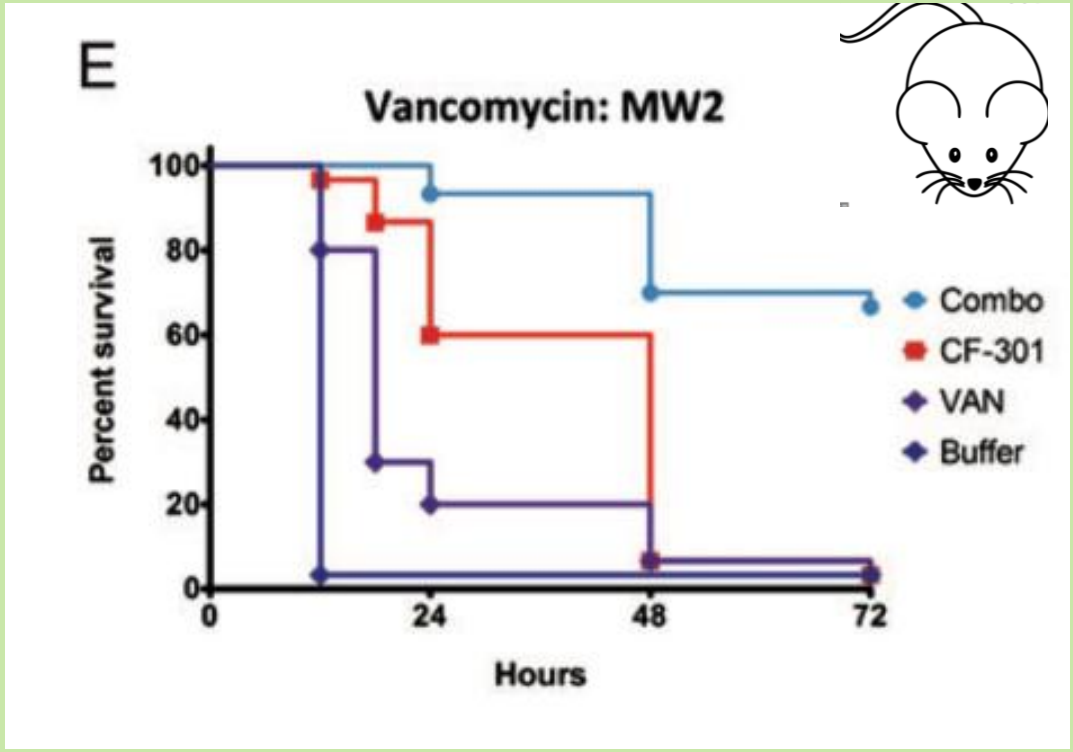


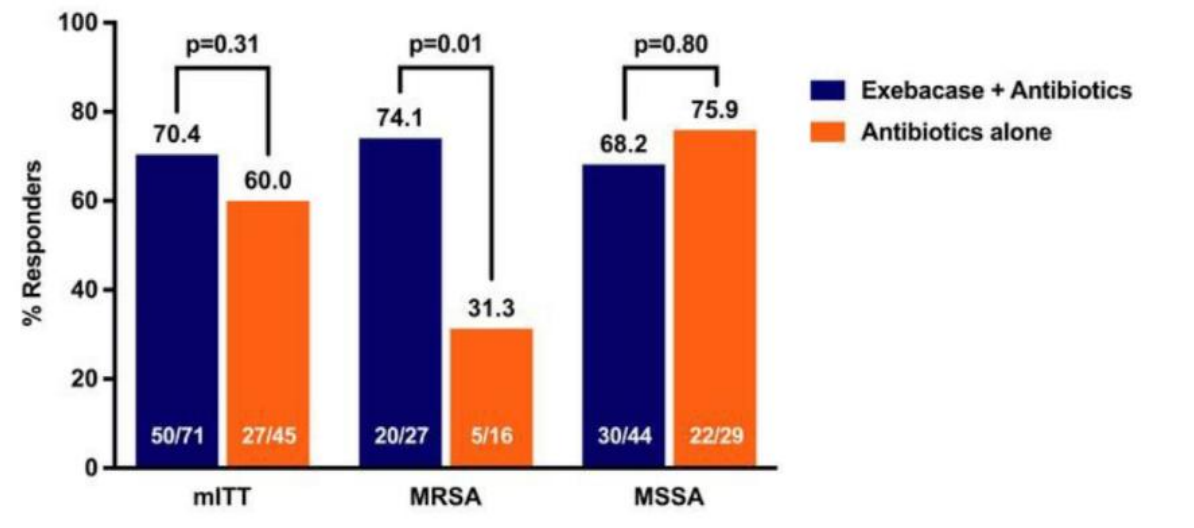
EFFET DOSE



SYNERGIE

1 dose de lysine anti-*S. aureus* (exebacase) améliore la réponse au traitement

Étude de supériorité 3 : 2 1 dose d'exebacase 0.25 mg/kg en perfusion de 2h vs. Placebo
Patient inclus dans les 72h suivant le diagnostic de bactériémie. 121
Bactériémie/endocardite à SAMS/SARM
ATB au choix du clinicien
CJP = réponse au ttt à J14



CLINICAL MEDICINE
The Journal of Clinical Investigation

Exebacase for patients with *Staphylococcus aureus* bloodstream infection and endocarditis

Vance G. Fowler Jr.,[1,2] Anita F. Das,[3] Joy Lipka-Diamond,[4] Raymond Schuch,[5] Roger Pomerantz,[5] Luis Jáuregui-Peredo,[6] Adam Bressler,[7] David Evans,[8] Gregory J. Moran,[9] Mark E. Rupp,[10] Robert Wise,[11] G. Ralph Corey,[1] Marcus Zervos,[12] Pamela S. Douglas,[1,2] and Cara Cassino[5]

Clinical Infectious Diseases
MAJOR ARTICLE

Exebacase in Addition to Standard-of-Care Antibiotics for *Staphylococcus aureus* Bloodstream Infections and Right-Sided Infective Endocarditis: A Phase 3, Superiority-Design, Placebo-Controlled, Randomized Clinical Trial (DISRUPT)

Pas de bénéfice à l'ajout d'exebacase

Table 5. Thirty-Day Survival and All-Cause Mortality Through Days 14, 30, and 60 Visit Windows (mITT Analysis Set)

	Overall Population		MRSA Population		MSSA Population	
	Exebacase + SoCA (N = 165) n (%)	SoCA Alone (N = 85) n (%)	Exebacase + SoCA (N = 64) n (%)	SoCA Alone (N = 33) n (%)	Exebacase + SoCA (N = 101) n (%)	SoCA Alone (N = 52) n (%)
30-day survival						
Died	18 (10.9)	7 (8.2)	13 (20.3)	3 (9.1)	5 (5.0)	4 (7.7)
Censored[a]	147 (89.1)	78 (91.8)	51 (79.7)	30 (90.9)	96 (95.0)	48 (92.3)
Alive at day 30	143 (86.7)	77 (90.6)	51 (79.7)	30 (90.9)	92 (91.1)	47 (90.4)
Unknown	4 (2.4)	1 (1.2)	0 (0.0)	0 (0.0)	4 (4.0)	1 (1.9)
KM estimates of survival probability at day 30 (95% CI)[b]	0.89 (0.83, 0.93)	0.92 (0.83, 0.96)	0.80 (0.68, 0.88)	0.91 (0.74, 0.97)	0.95 (0.88, 0.98)	0.92 (0.80, 0.97)
P[c]	.4784		.1424		.5003	
All-cause mortality[d]						
Day 14 (+1 d)	11 (6.7)	3 (3.5)	9 (14.1)	1 (3.0)	2 (2.0)	2 (3.8)
Day 30 (+4 d)	20 (12.1)	8 (9.4)	15 (23.4)	4 (12.1)	5 (5.0)	4 (7.7)
Day 60 (+7 d)	29 (17.6)	15 (17.6)	18 (28.1)	6 (18.2)	11 (10.9)	9 (17.3)

N = Number of patients in the microbiological intent-to-treat (mITT) analysis set as the denominator.

Abbreviations: CI, confidence interval; KM, Kaplan-Meier; MRSA/MSSA, methicillin-resistant/methicillin-sensitive *Staphylococcus aureus*; SoCA, standard of care.

[a]Patients were censored at the last known date alive on or before day 30.

[b]Two-sided 95% CIs were based on the log–log transformation.

[c]*P* was from log-rank test.

[d]All-cause mortality included deaths that occurred within the visit windows noted in the table.

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  - ATB de réserve/couteux J1
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Labo de Mycologie 1/ sem (Pr Piarroux)
Réunion Pharmacie (Dr Junot)
Quotidien pour les ATB, 1/sem pour les antifongiques
Staff Réa chir polyvalente 2/sem
Staff Réa neurochir

Merci

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ESCMID Study Group for Non-traditional Antibacterial Therapy – ESGNTA