

# Physiopathologie des infections osseuses chroniques (biofilm, persistance intra-cellulaire)

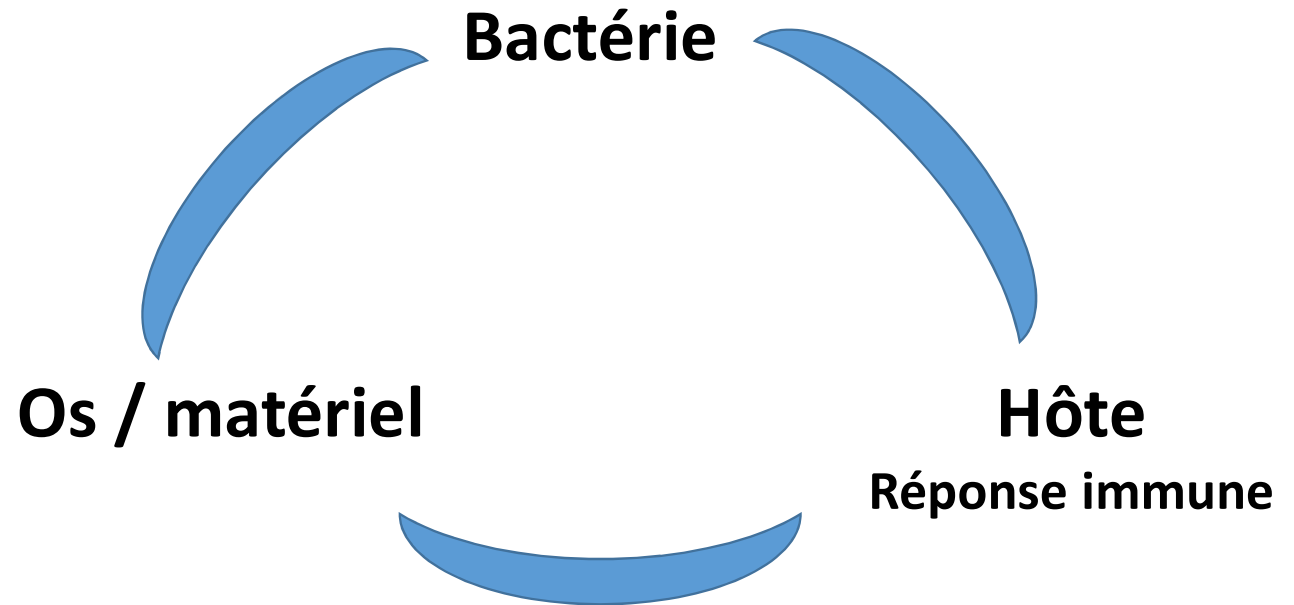
JP Bru

Maladies Infectieuses

Centre Hospitalier Annecy Genevois



Inoculation  
Infection aiguë  
Destruction osseuse  
Persistance bactérienne





Inoculation  
Infection aiguë  
Destruction osseuse  
Persistance bactérienne

Comportement bactérien

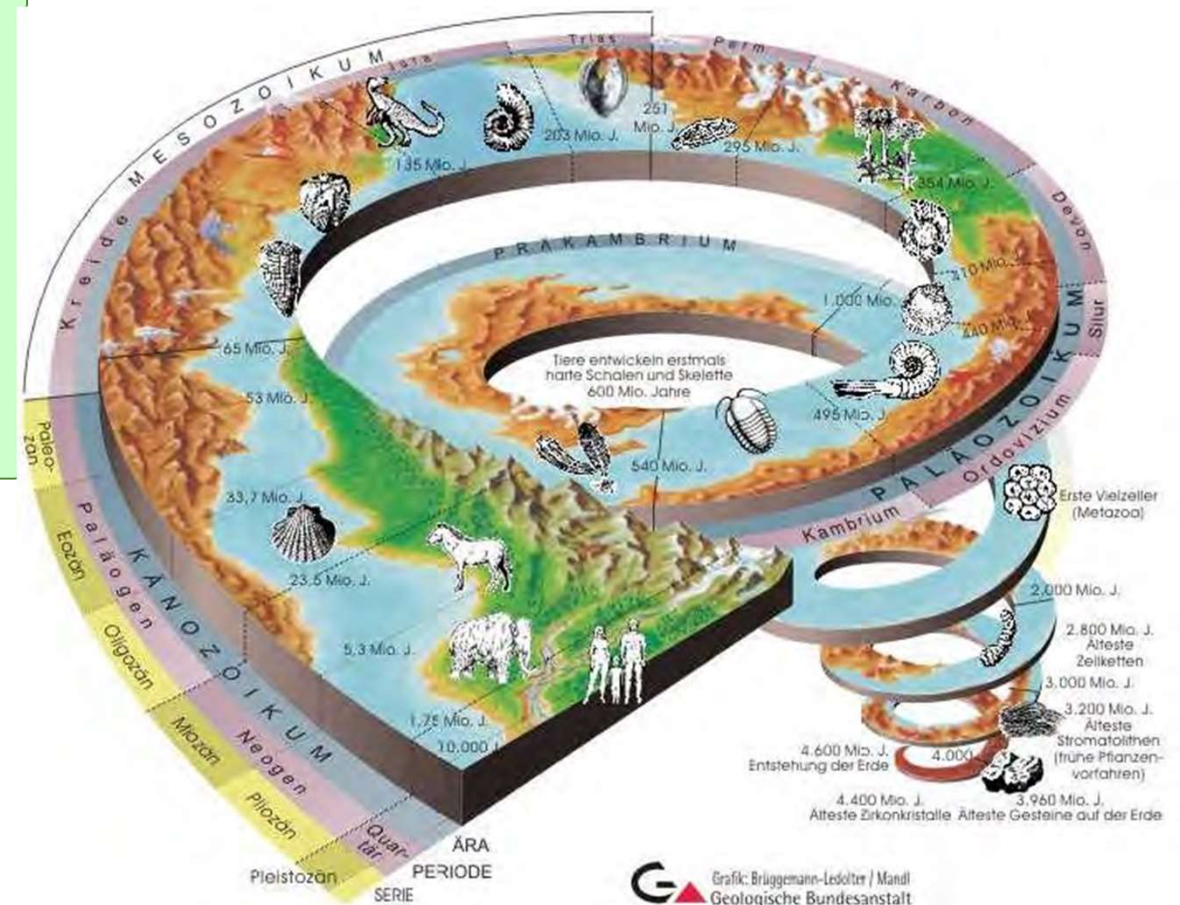


Conséquences pour  
infections osseuses / sur matériel  
(évolutives et thérapeutiques)

1/ Adh rence et  
organisations bact riennes

2/ Variants microcolonies

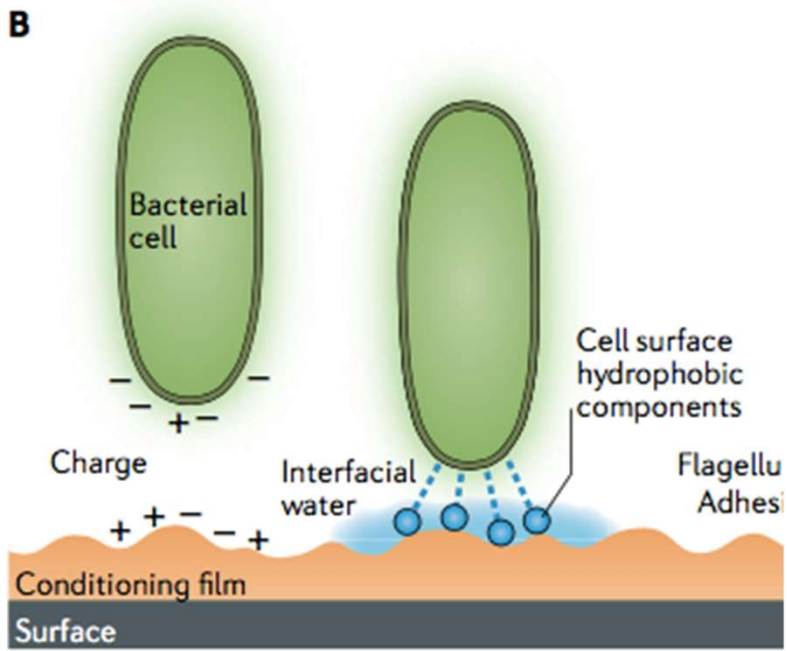
3/ Persistance intra cellulaire



Microcolonies forming biofilm identified :

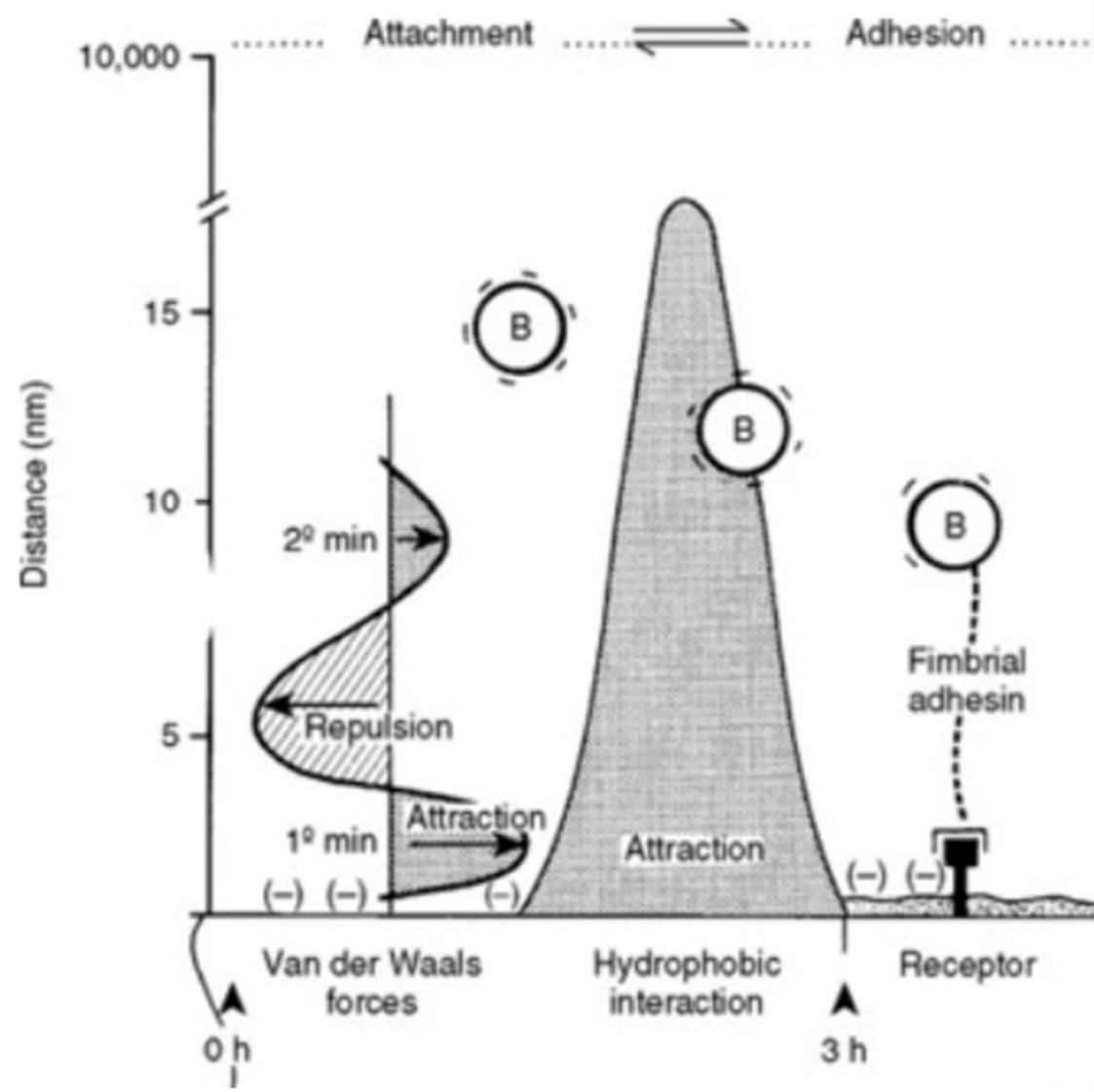
- 3.3–3.4 billion years South African Kornberg formation
- 3.2-billion years deep-sea hydrothermal rocks of the Pilbara Craton, Australia

# Adhérence

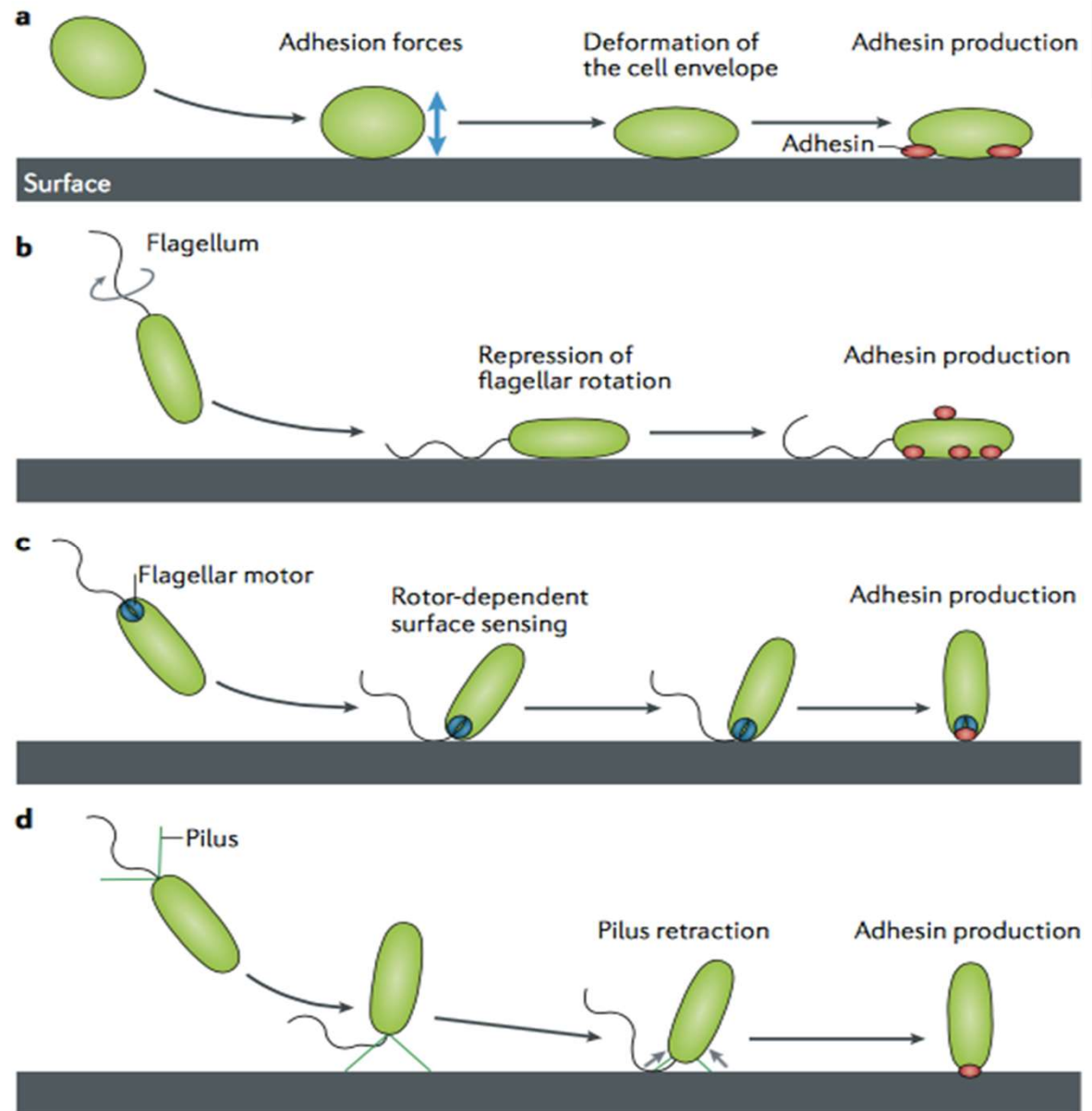


Cécile Berne NATURE Reviews | Microbiology  
 volume 16 | OCTOBER 2018 | 617

Gristina AG: Science 237:1588-1595, 1987



# Adh rence



C cile Berne  
NATURE Reviews | Microbiology  
volume 16 | OCTOBER 2018 | 617

# Adhérence & organisation bactérienne

INFECTION AND IMMUNITY, July 1982, p. 318-326  
0019-9567/82/070318-09\$02.00/0

Vol. 37, No. 1

## Adherence of Slime-Producing Strains of *Staphylococcus epidermidis* to Smooth Surfaces

GORDON D. CHRISTENSEN,<sup>1\*</sup> W. ANDREW SIMPSON,<sup>1,2</sup> ALAN L. BISNO,<sup>1</sup> AND EDWIN H. BEACHEY<sup>1,2</sup>

320 CHRISTENSEN ET AL.

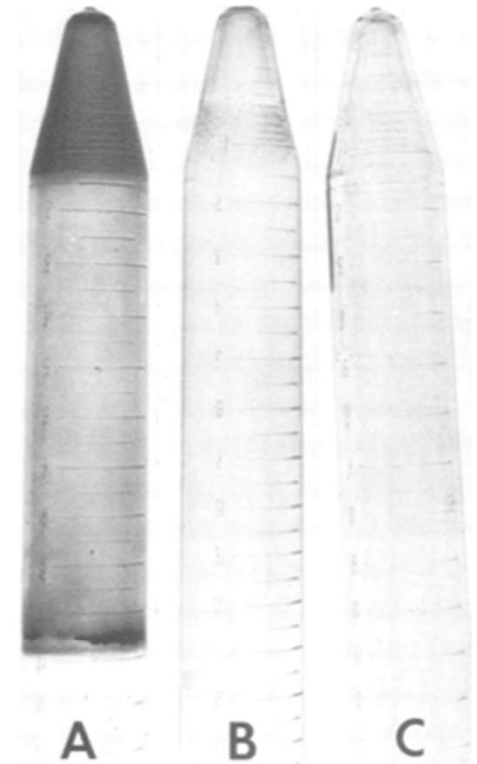
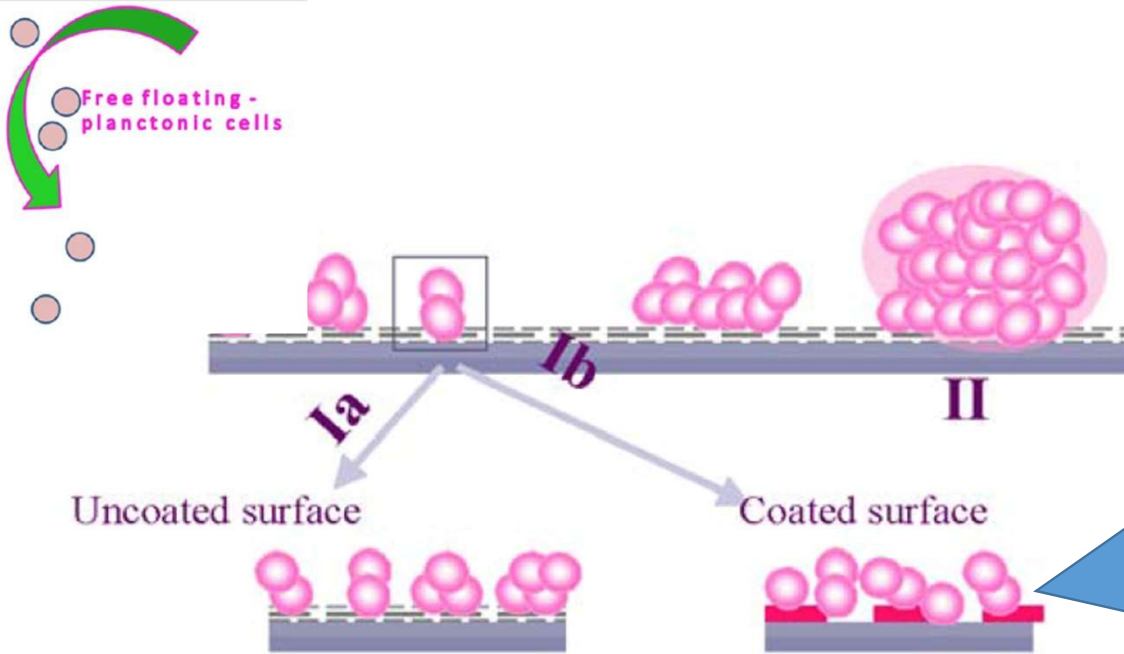


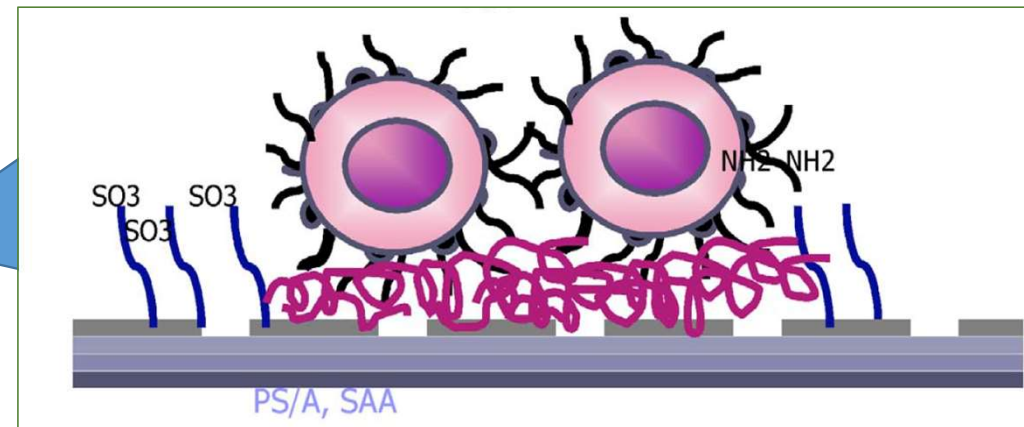
FIG. 1. Adherence of *S. epidermidis* grown in broth to the walls of plastic test tubes. The test tubes were emptied and stained with trypan blue. (A) Strong slime-producing strain in TSB; (B) weak slime-producing strain in TSB; (C) strong slime-producing strain grown in saccharide-free basal medium.

# Adhérence & organisation bactérienne



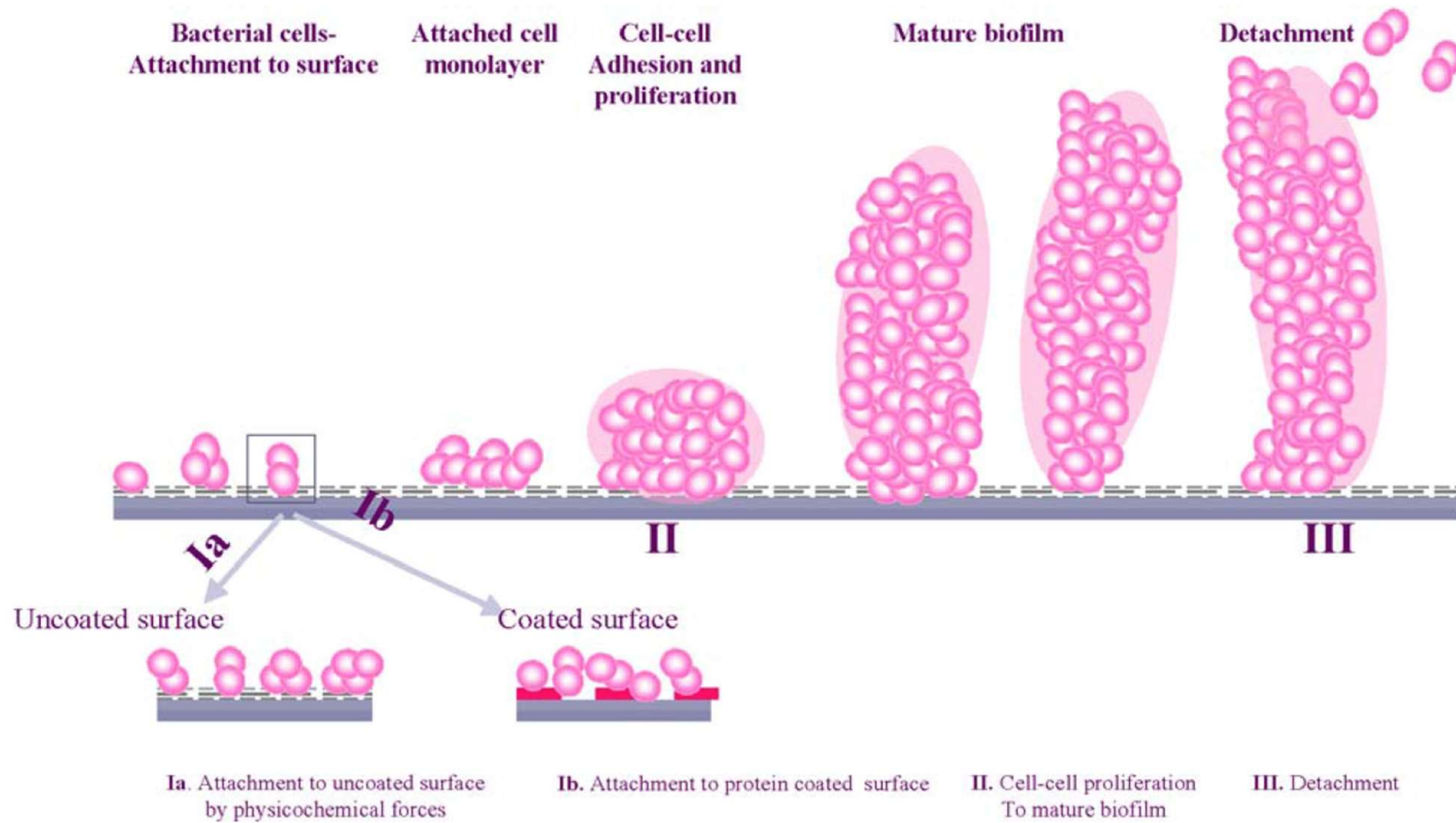
Interaction hydrophobique  
Forces électrostatiques  
Forces de Van der Waals

Fibrinogène  
facteur de Willbrand  
Plaquettes prothrombine





# Formation du biofilm

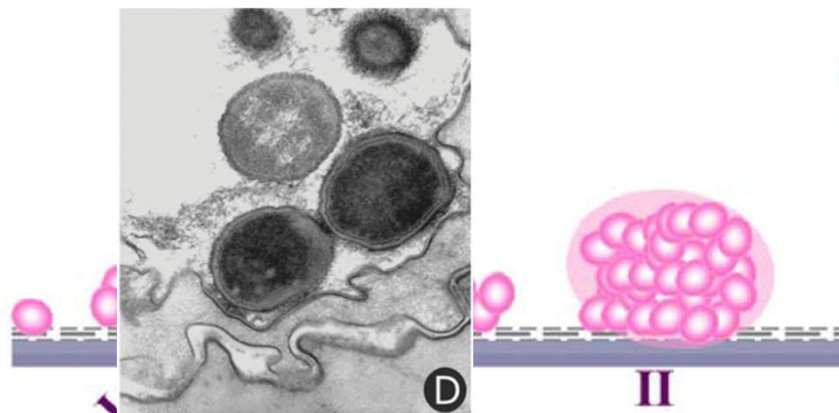


# Formation du biofilm

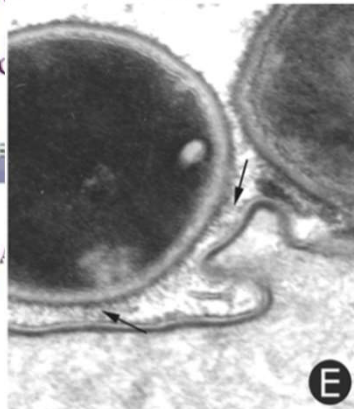
Bacterial cells-  
Attachment to surface

Attached cell  
monolayer

Cell-cell  
Adhesion and  
proliferation



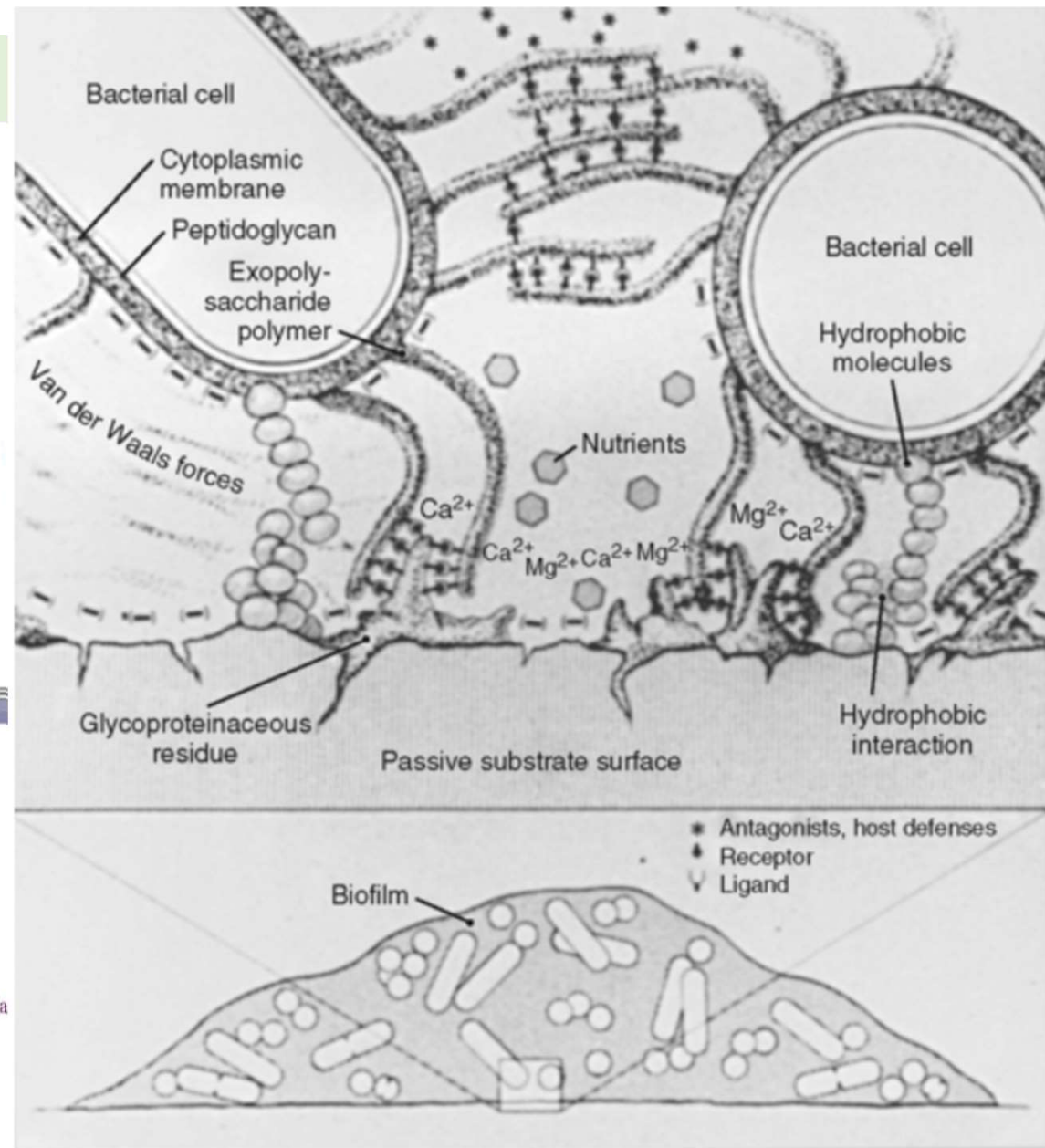
Uncoated surface

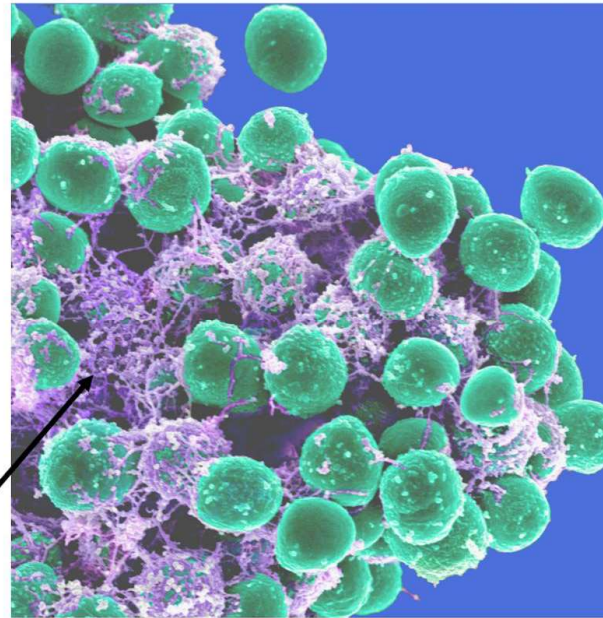
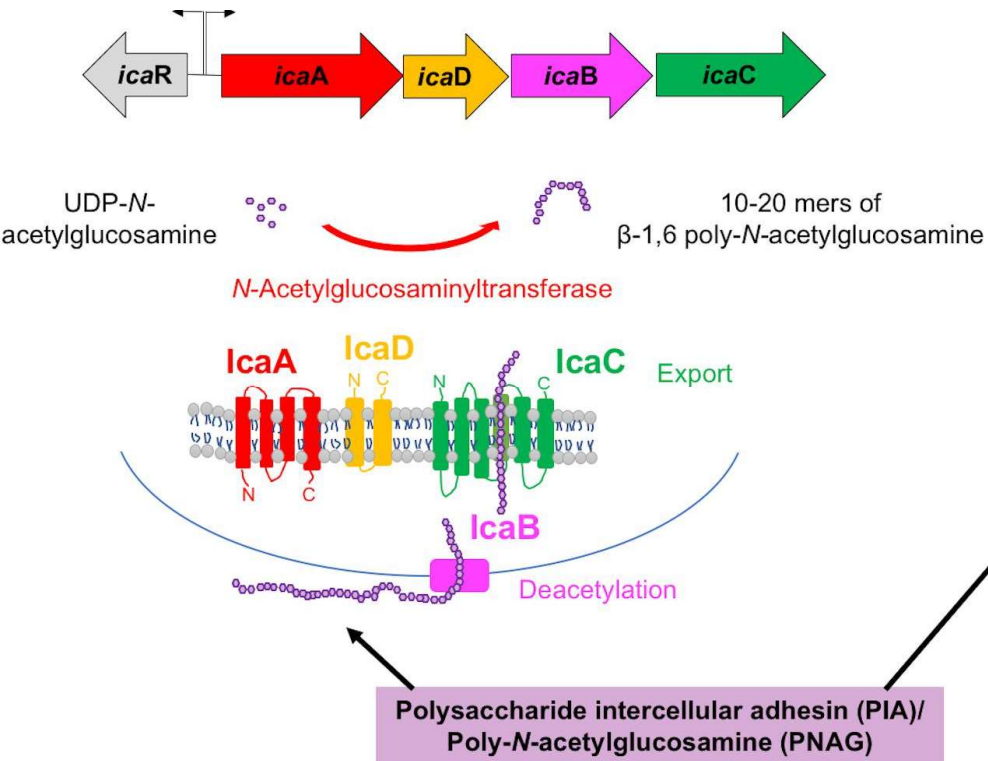


Coated surface



Ib. Attachment to protein coating



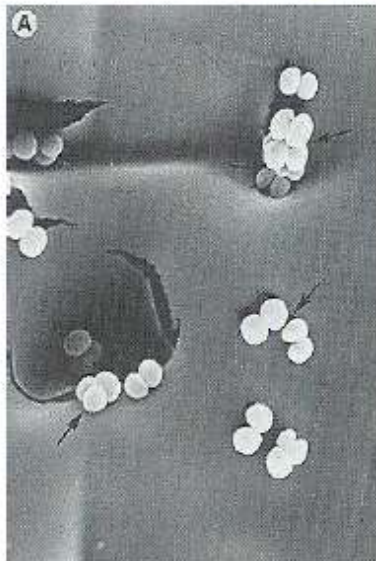


Matrice du biofilm

polysaccharide intercellular adhesion (PIA) exopolysaccharide, proteins such as accumulation-associated protein (Aap) extracellular matrix binding protein (Embp), teichoic acids, extracellular DNA (eDNA). Channels in the biofilm are formed by Phenol-soluble modulins (PSMs).

# Formation d'un biofilm

## Etapes de la colonisation du matériel par *S. epidermidis*



**2 h**

Fixation des staph sur des irrégularités à la surface du matériel



**4 h**

Début de fabrication du "slime"



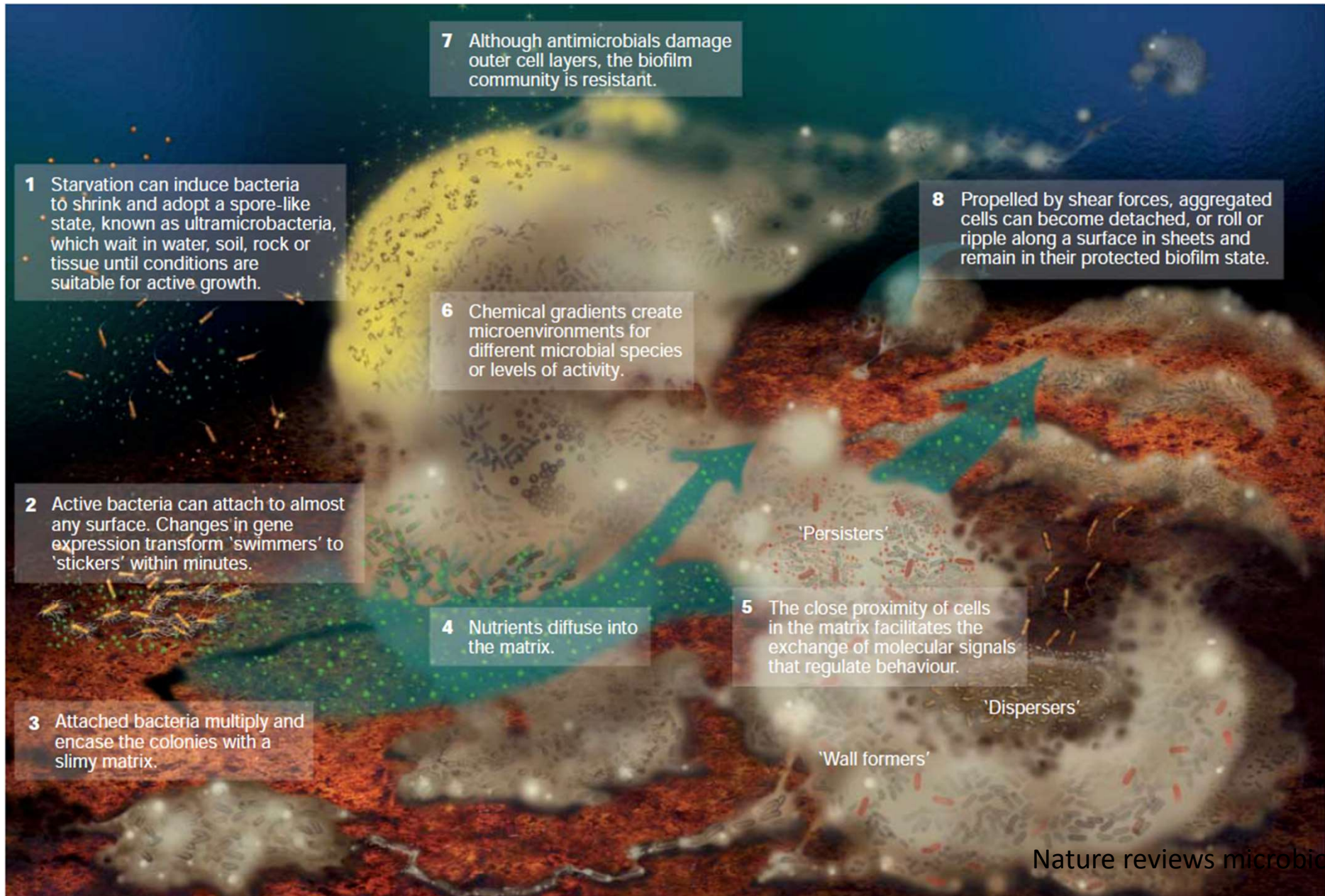
**8 h**

La surface du matériel est recouverte par une couche épaisse de "slime"



**24 h**

Des bactéries émergent du biofilm, libres et prêtes à se fixer ailleurs



## Biofilm rôle

- Apporte un environnement stable pour la pousse bactérienne
- Favorise les échanges entre bactéries
- Stabilise la colonie bactérienne à la surface du substrat

1 min

3 h

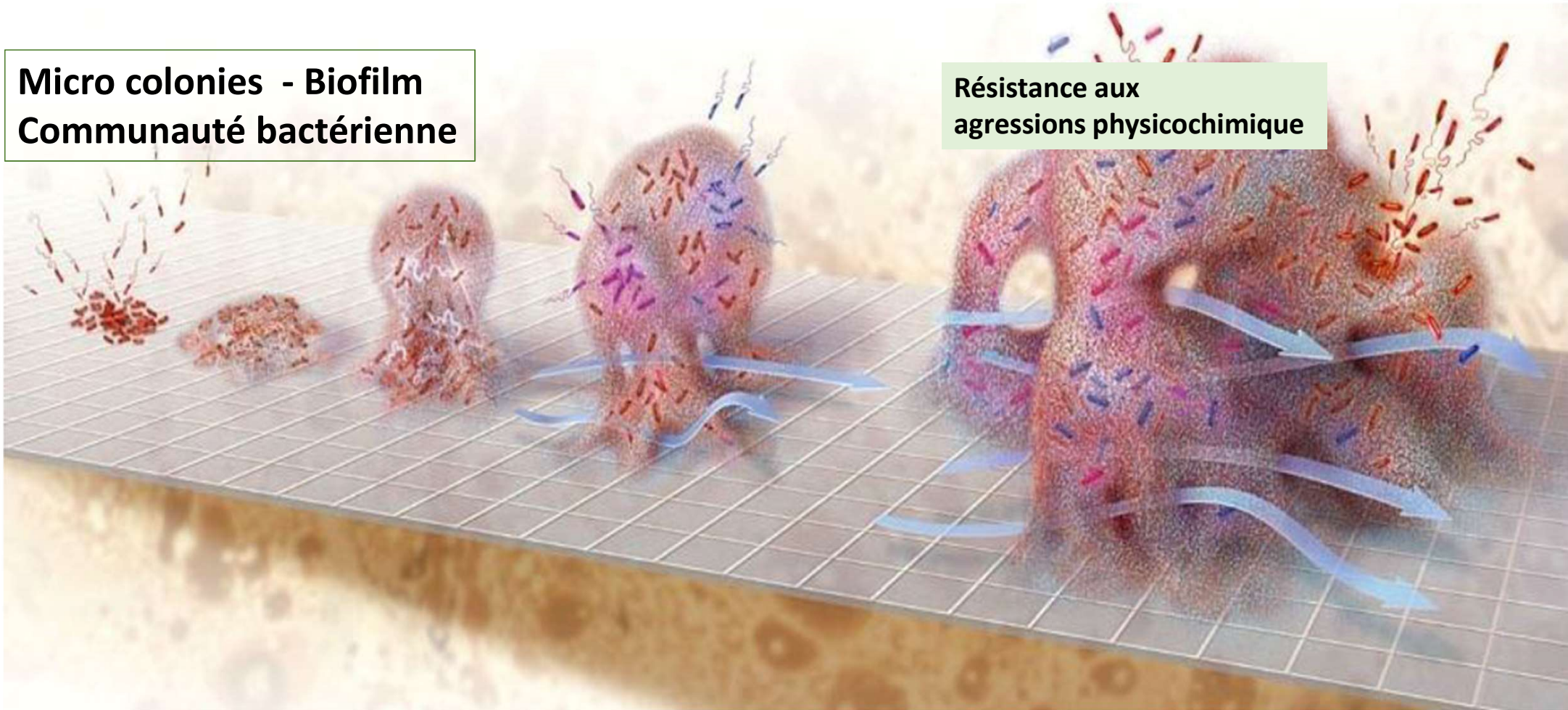
12 h

1 day



3 days

**Micro colonies - Biofilm**  
**Communauté bactérienne**



**Résistance aux**  
**agressions physicochimique**

D'après Keith Kasnot, Scientific American 2001

## Biofilm rôle

- Apporte un environnement stable pour la pousse bactérienne
- Favorise les échanges entre bactéries
- Stabilise la colonie bactérienne à la surface du substrat
- Protège d'une grande variété d'agressions possibles:
  - Exposition aux UV
  - toxicité du métal
  - exposition acide
  - Déshydratation
  - substances toxiques



1 min

3 h

12 h

1 day

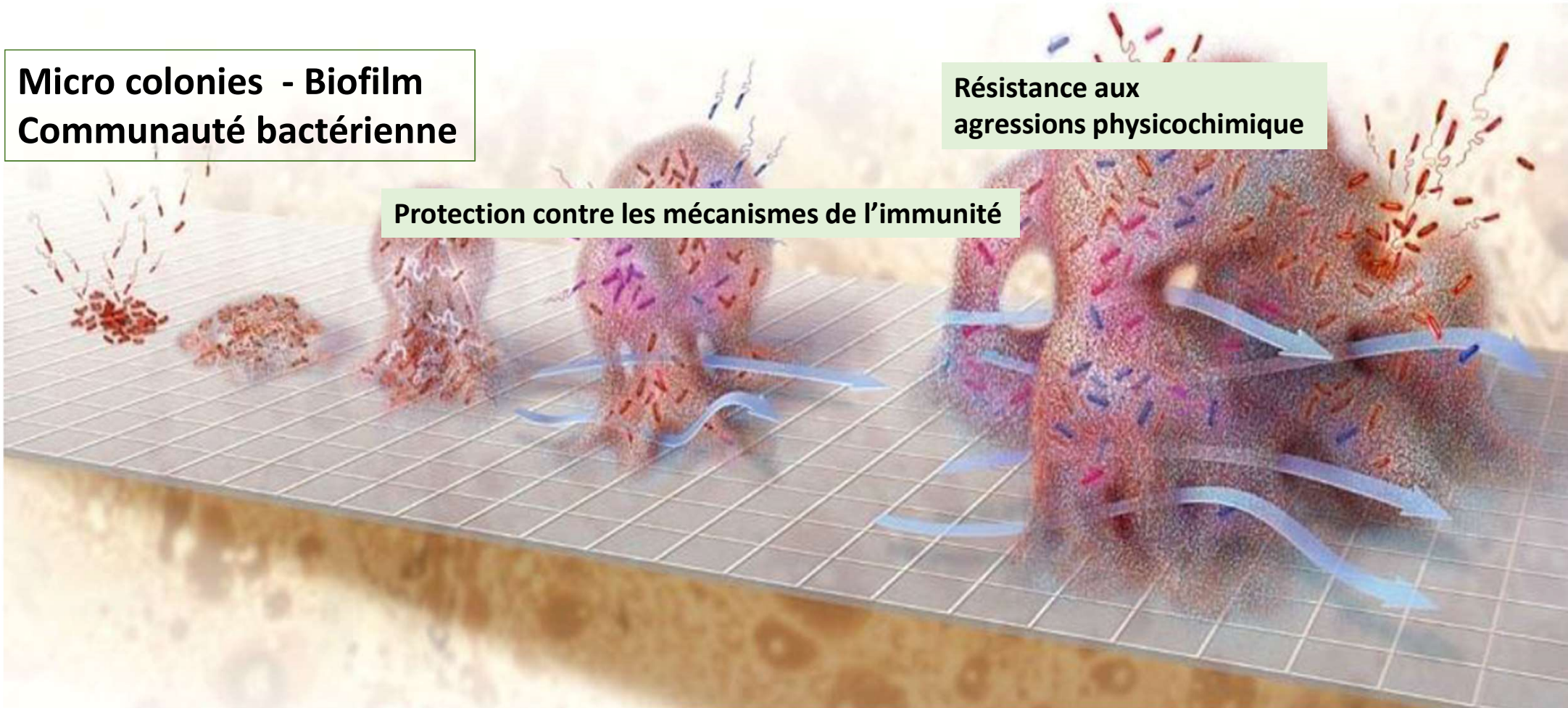


3 days

**Micro colonies - Biofilm**  
**Communauté bactérienne**

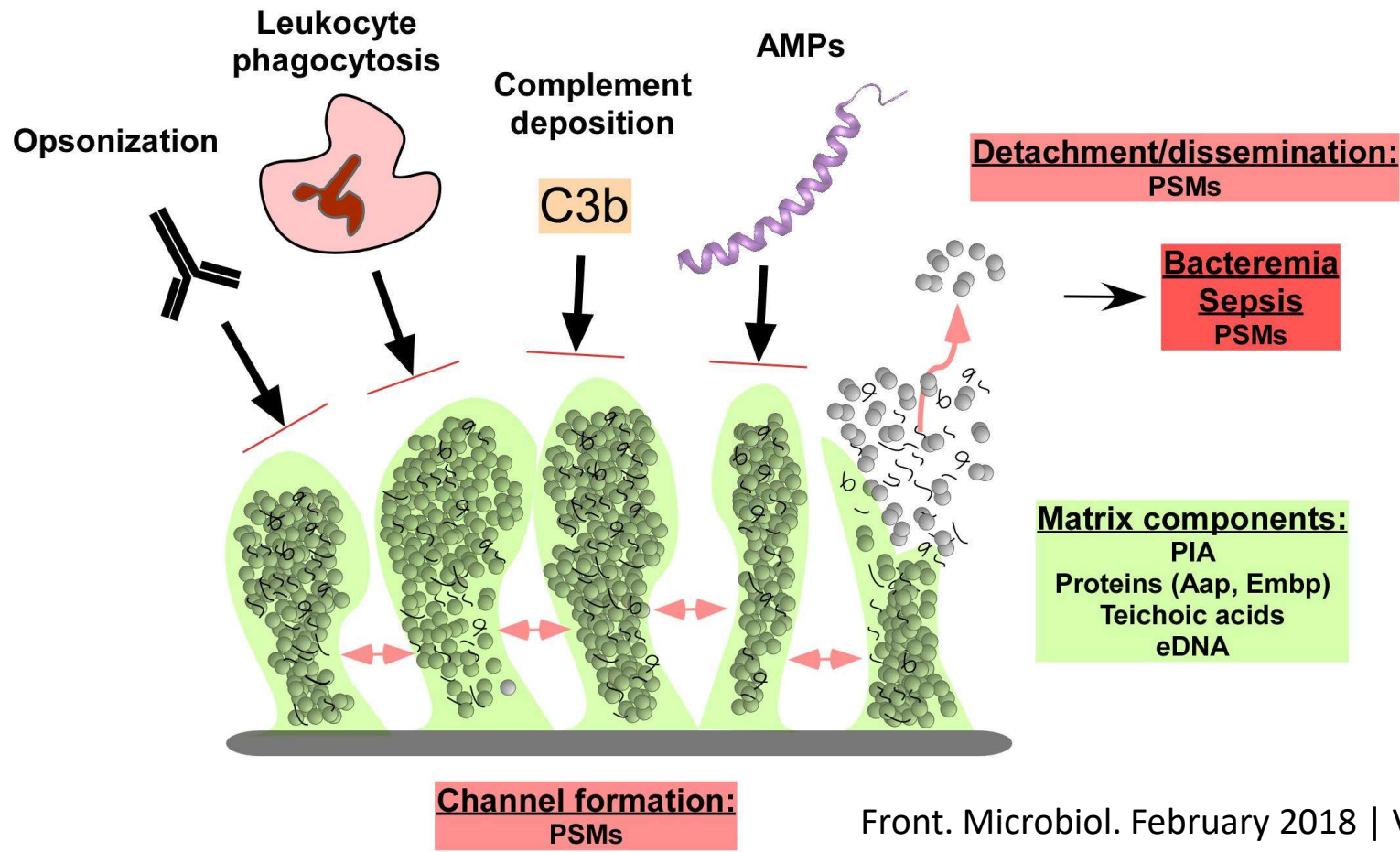
Protection contre les mécanismes de l'immunité

Résistance aux  
agressions physicochimique



D'après Keith Kasnot, Scientific American 2001

## BIOFILM INHIBITS:



1 min

3 h

12 h

1 day



3 days

**Micro colonies - Biofilm**  
**Communauté bactérienne**

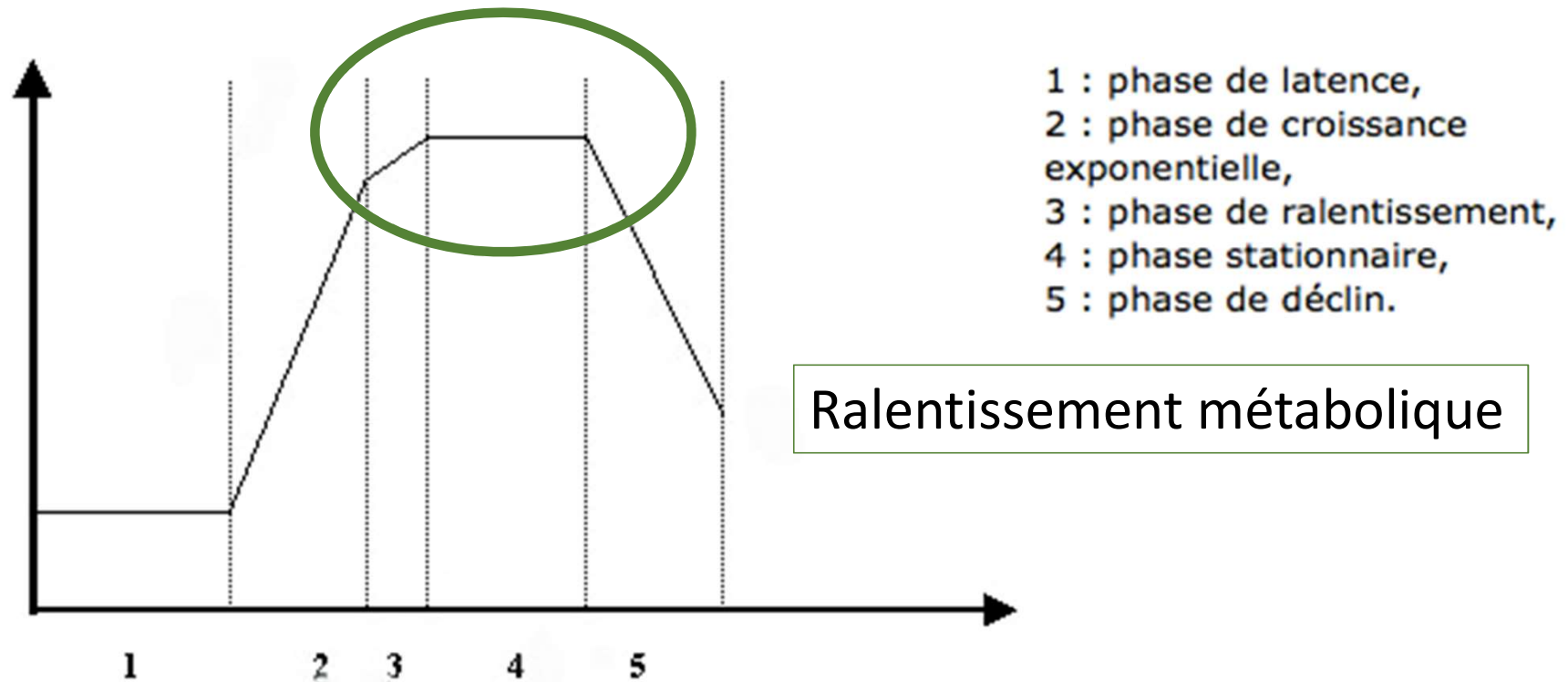
Protection contre les mécanismes de l'immunité

Résistance aux  
agressions physicochimique

Modifications du  
comportement bactérien

D'après Keith Kasnot, Scientific American 2001

## Biofilm modification du comportement bactérien. Phase stationnaire de croissance



Ralentissement métabolique

## Biofilm modification du comportement bactérien. Phase stationnaire de croissance

**Table 2.** Minimum bactericidal concentration (MBC) of *Staphylococcus epidermidis* B3972.

Antibiotic	Phases of bacterial growth ( $\mu\text{g/ml}$ )		Fold increase
	Logarithmic	Stationary	
Vancomycin	4	50	12.5
Daptomycin	2	12.5	6
Teicoplanin	4	12.5	3
Ciprofloxacin	0.5	100	200
Rifampin	0.06	0.15	2.5
Netilmicin	8	400	50

A. F. Widmer, The Journal of Infectious Diseases 1990;162:96-102

# Killing of Nongrowing and Adherent *Escherichia coli* Determines Drug Efficacy in Device-Related Infections

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 1991, p. 741-746

ANDREAS F. WIDMER,<sup>1†</sup> ADRIAN WIESTNER,<sup>1</sup> RENO FREI,<sup>2</sup> AND WERNER ZIMMERLI<sup>1\*</sup>

TABLE 4. MBC for *E. coli* ATCC 25922 in the logarithmic and stationary phases of growth

Drug	MBC ( $\mu\text{g/ml}$ ) in:	
	Log phase	Stationary phase <sup>a</sup>
Co-trimoxazole (TMP/SMX) <sup>b</sup>	0.06/1.2	80/1,600
Aztreonam	0.125	100
Fleroxacin	0.07	4
Ciprofloxacin	0.02	0.02

<sup>a</sup> The MBC was determined with bacteria in the stationary phase of growth (see text).

<sup>b</sup> Trimethoprim-sulfamethoxazole (TMP/SMX) was tested in vitro with a mixture of 1:20.

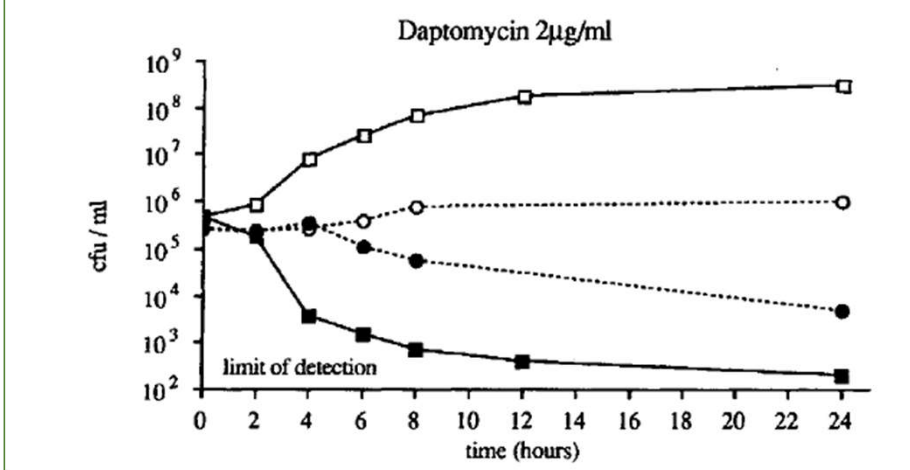
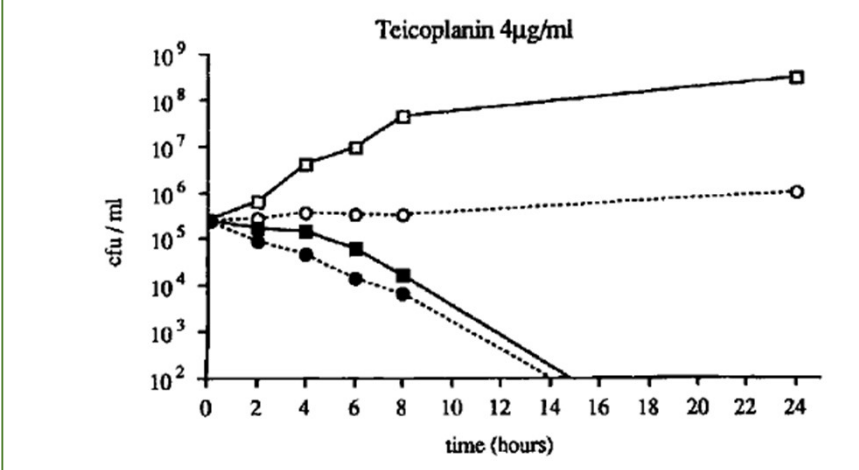
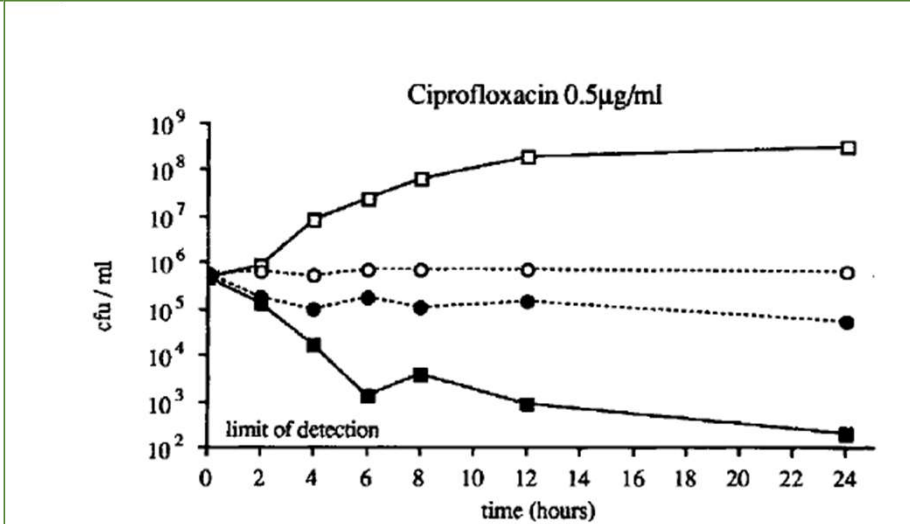
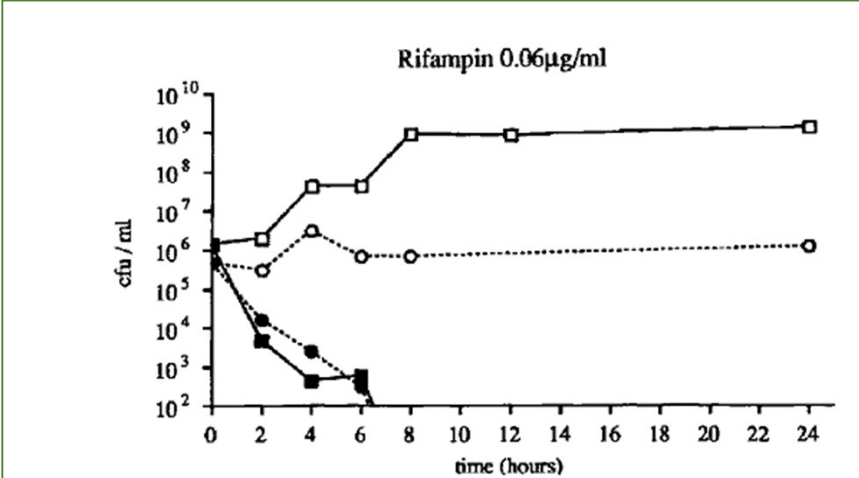
*Staphylococcus epidermidis* B3972 Producteur de Slime.

Croissance  
Logarith-  
mique

■ ATB  
□ Contrôle

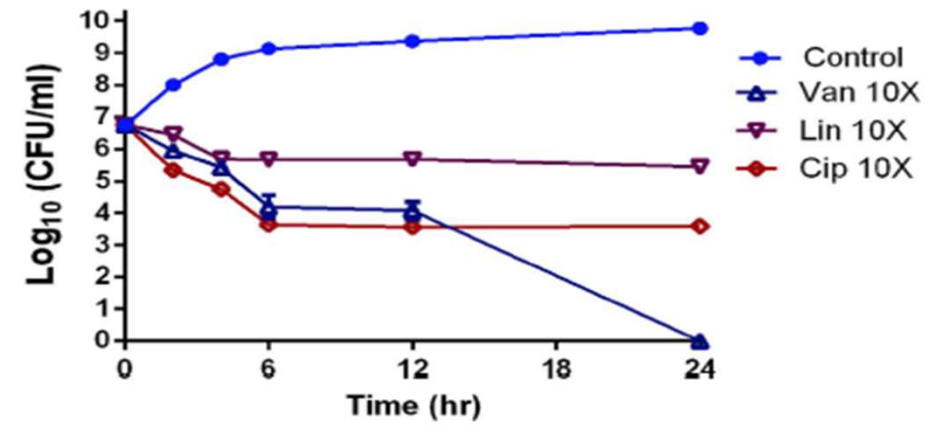
Croissance  
stationnaire

● ATB  
○ Contrôle

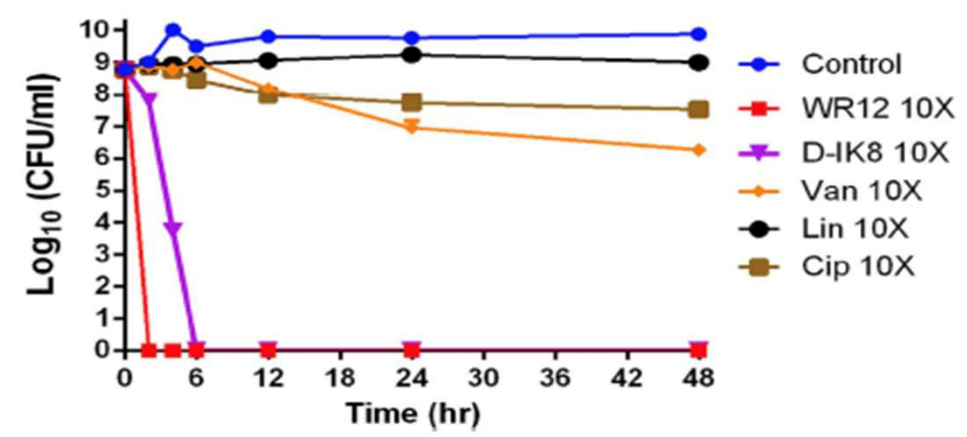


# Biofilm modification du comportement bactérien. Phase stationnaire de croissance

b- Logarithmic phase of MRSA USA300



d- Stationary phase of MRSA USA300



Nature /scientific report  
2016 DOI: 10.1038/srep29707

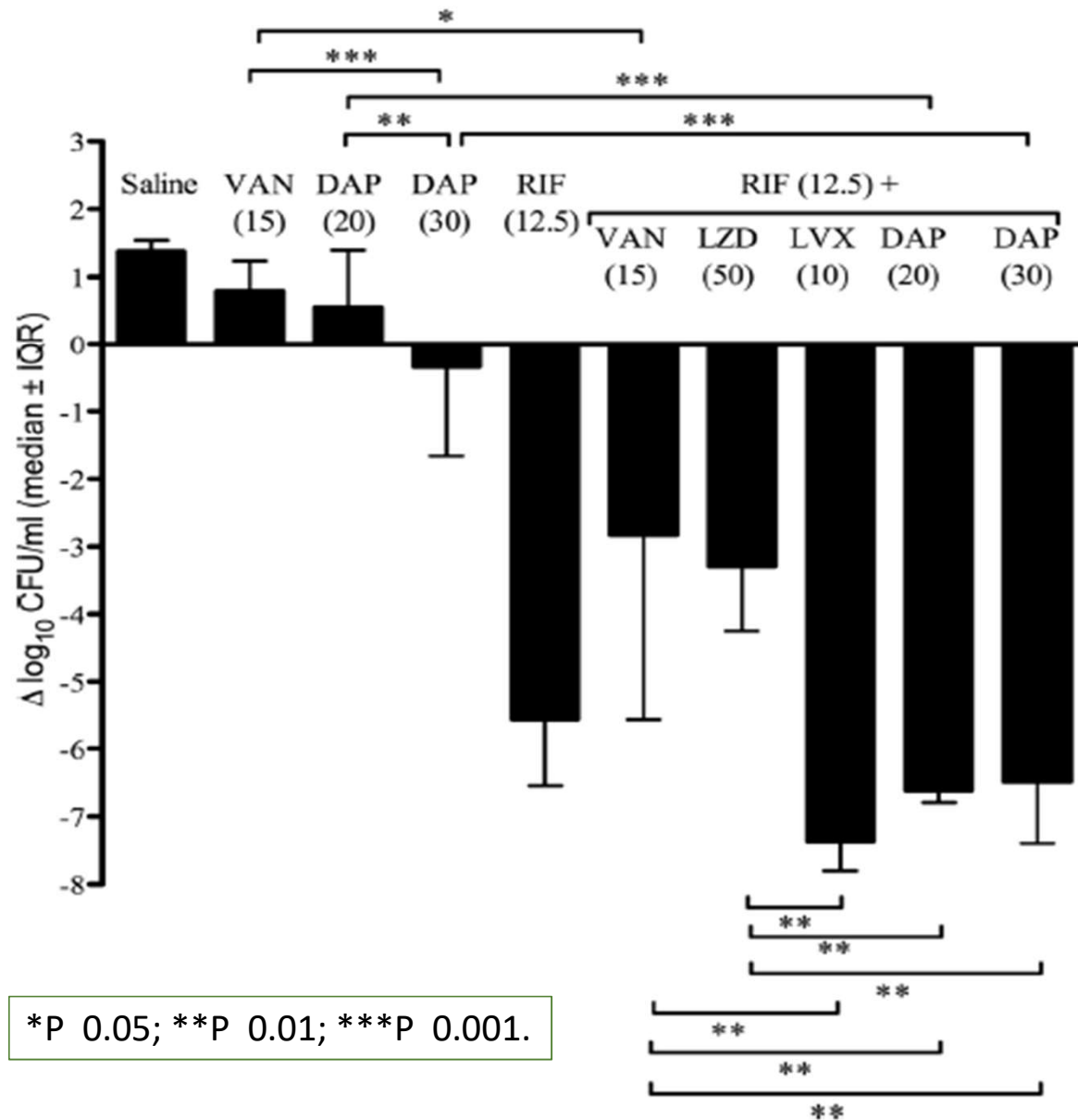


## Infection de matériel étranger Efficacité des antibiotiques. Modèles animaux

Micro-organismes	antibiotiques	CMB (phase log)	% guérison	Auteur
<i>S. epidermidis</i>	vancomycine	4	17	Widmer, JID 1990
	ciprofloxacine	0.5	0	
	rifampicine	0.06	100	
<i>S. aureus</i>	vancomycine	2.5	0	Frei, ICAAC 1990
	ciprofloxacine	0.62	17	
	rifampicine	0.12	50	
<i>E. coli</i>	cotrimoxazole	0.06	0	Widmer, AAC 1991
	ciprofloxacine	0.02	92	

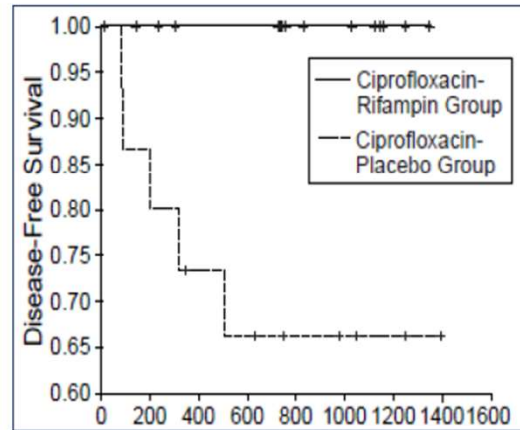
# Efficacy of Daptomycin in Implant-Associated Infection Due to Methicillin-Resistant Staphylococcus aureus : Importance of Combination with Rifampicin

Antimicrob. Agents Chemother, July 2009, p. 2719–2724

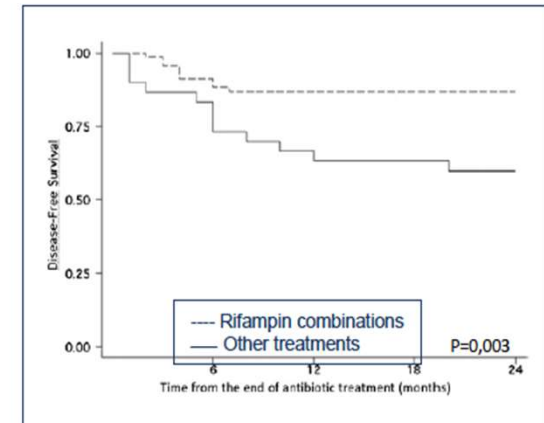


**Infections de Prothèses  
articulaires à *S. aureus*.  
Efficacité selon les ATB**

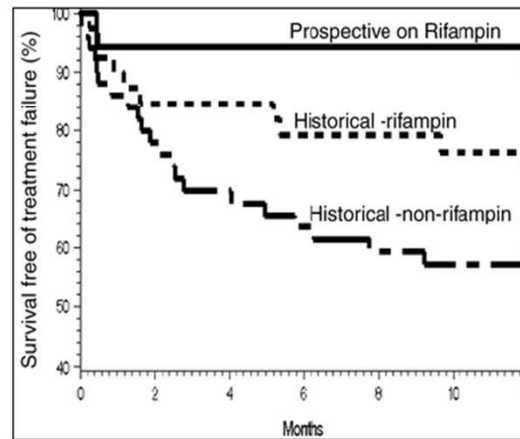
# Combinaisons de Rifampicine dans les IPOA à staphylocoques (*S. aureus* et SCN)



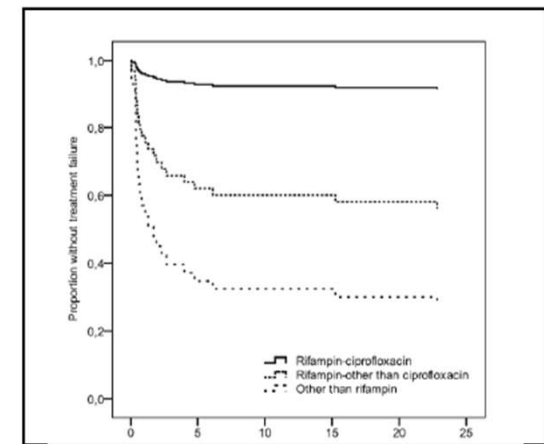
Zimmerli W *et al.* JAMA 1998



Senneville E *et al.* Clin Infect Dis 2011

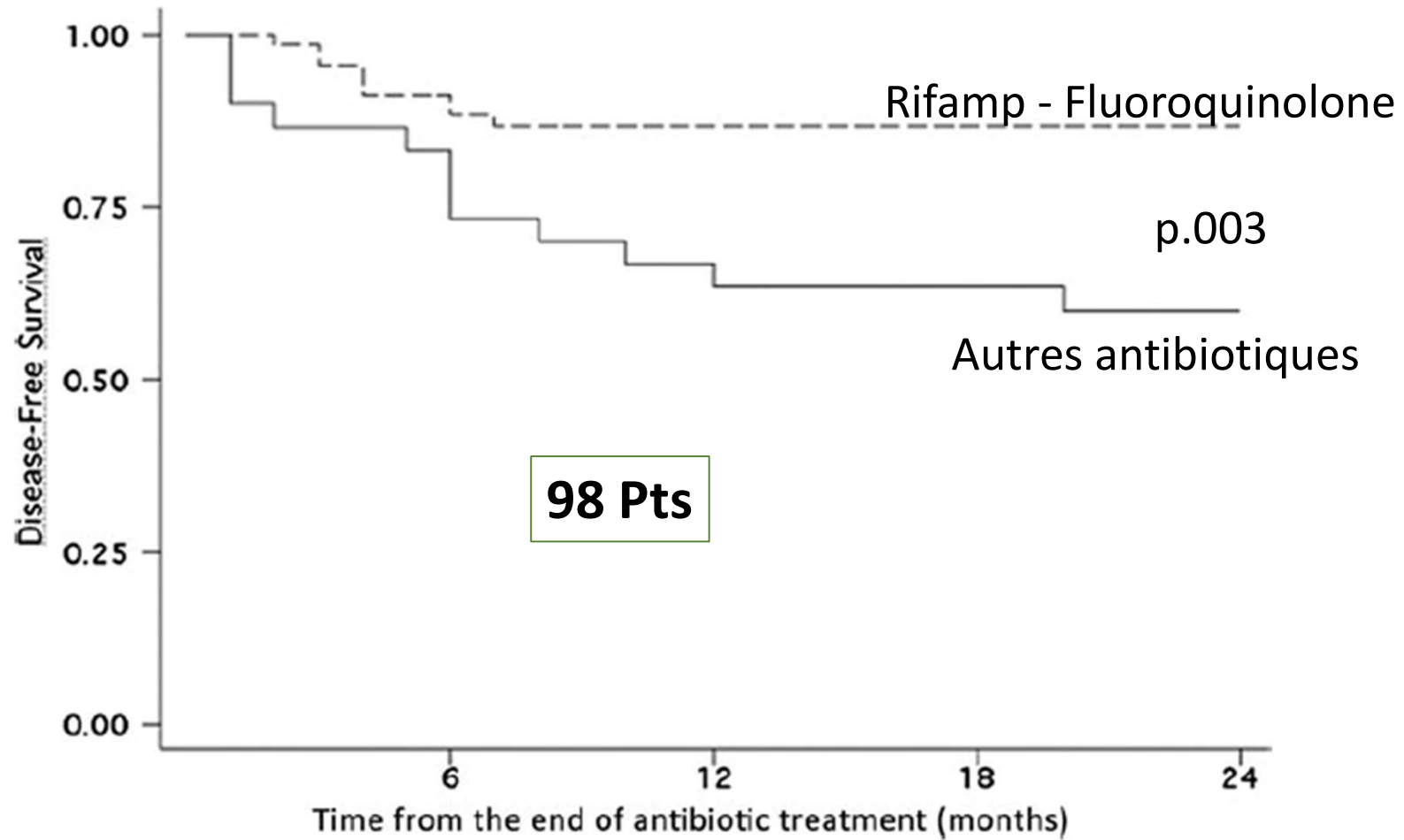


El Helou OC *et al.* Eur J Clin Microbiol Infect Dis. 2010

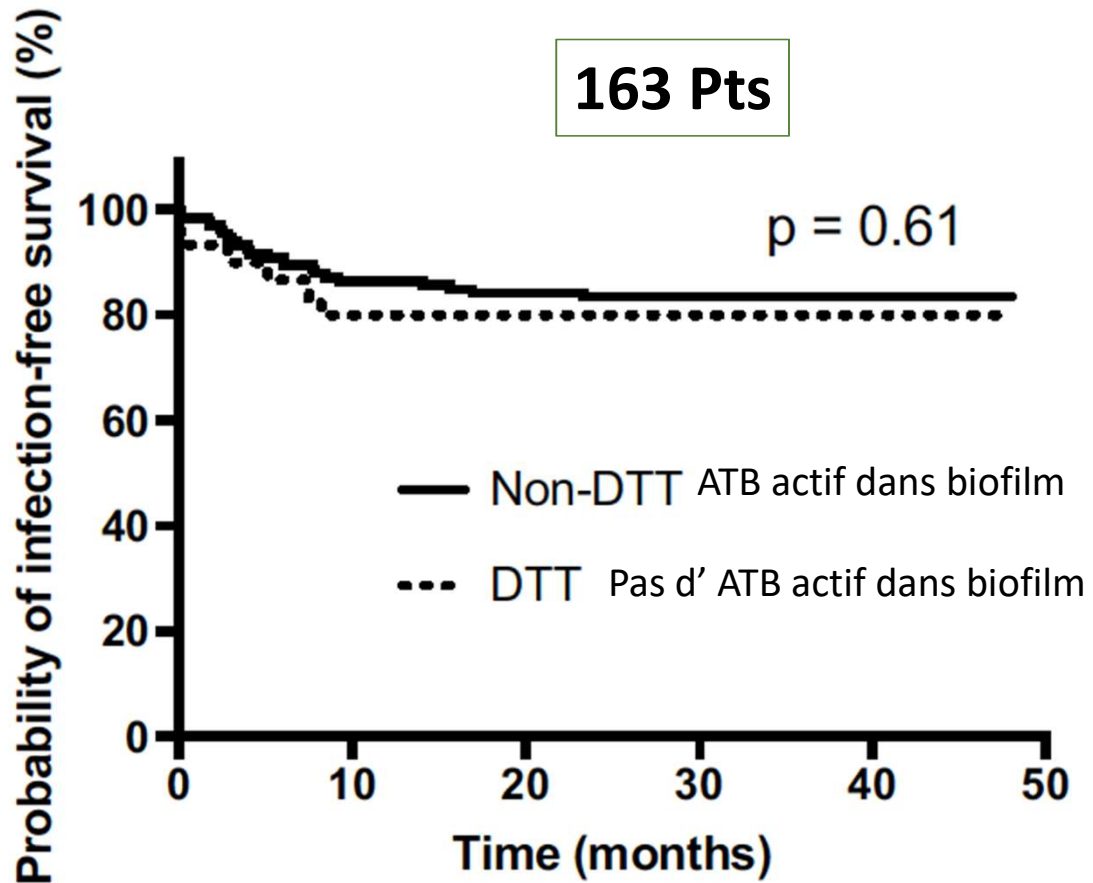


Puhto AP *et al.* Int Orthop 2015

## Infections de Prothèses articulaires à *S. aureus*. Efficacité selon les ATB



## Infections de Prothèses articulaires. Efficacité selon les ATB



## Infections de Prothèses articulaires. Efficacité selon les ATB

**Table 2** Treatment and outcome characteristics of all patients

Variable	All patients ( <i>n</i> = 163)	Pas d' ATB actif dans biofilm	ATB actif dans biofilm	<i>p</i> value
		DTT PJI group ( <i>n</i> = 30)	Non-DTT PJI group ( <i>n</i> = 133)	
<b>Treatment</b>				
Time until reimplantation (days)	63.9 ± 34.5	89.4 ± 50.5	58.1 ± 26.9	<0.001
CRP prior to reimplantation (mg/l)	11.9 ± 13.1	10 ± 11.8	12.3 ± 13.4	0.164
Total duration of antimicrobial therapy (days)	123.3 ± 57.7	150.8 ± 74.7	117.4 ± 51.7	0.003
Duration of i.v. antimicrobial therapy (days) <sup>a</sup>	32.8 ± 20.2	50.4 ± 31	29 ± 14.7	<0.001
Duration of oral antimicrobial therapy (days) <sup>a</sup>	84.1 ± 32.2	90.1 ± 47.3	82.8 ± 28.2	0.553
No. of revisions during interval	1.7 ± 1.3	2 ± 1.6	1.5 ± 1	0.324
Duration of hospital stay (days)	31.2 ± 15.9	44.5 ± 26.5	28.2 ± 10.4	<0.001

## Les bactéries productrices de slime

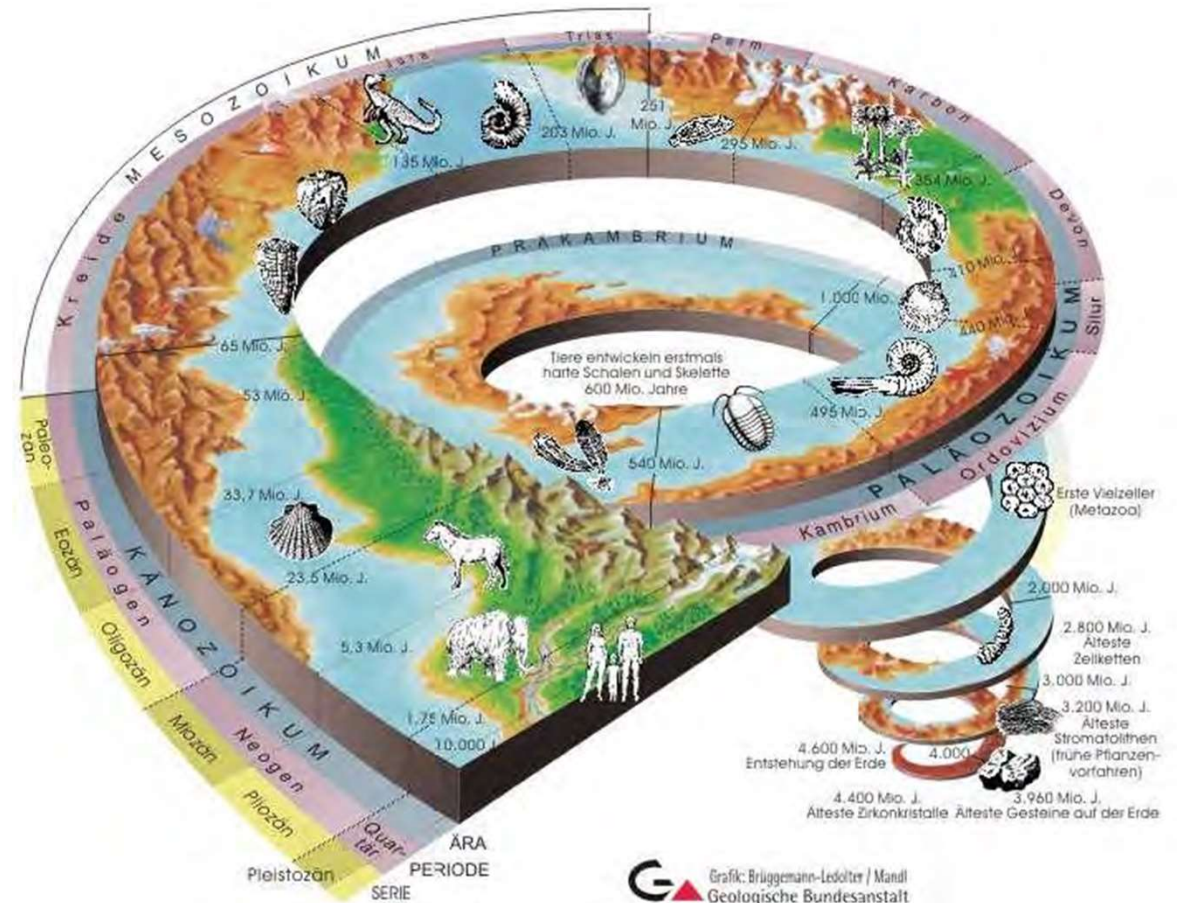
---

- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Streptococcus sp* (non groupables)
- *Enterococcus sp*
- *Pseudomonas aeruginosa*
- *E coli, Enterobacter sp, Proteus sp*
- Anaérobies : *bacteroides sp*,  
corynebactéries

1/ Adh rence et  
organisations bact riennes

2/ Variants microcolonies

3/ Persistance intra cellulaire





# Small Colony Variants

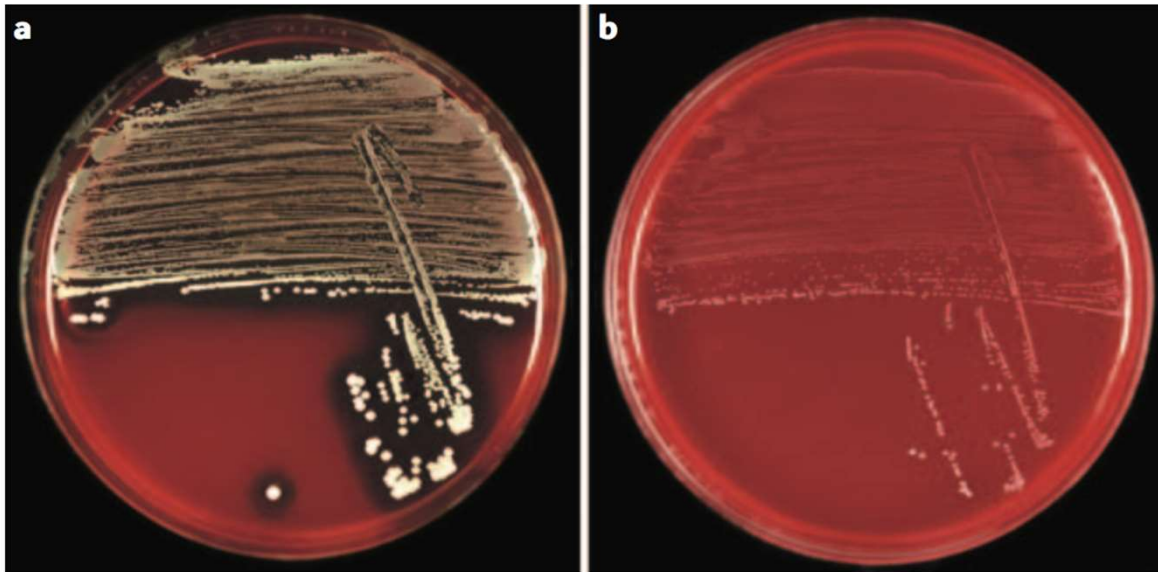


Figure 1 | **Small colony variants.** Columbia blood-agar plates that show the normal (a) and the small colony variant (b) phenotype of *Staphylococcus aureus* are shown.

# Small Colony Variants

## Phénomène d'adaptation auxotrophique

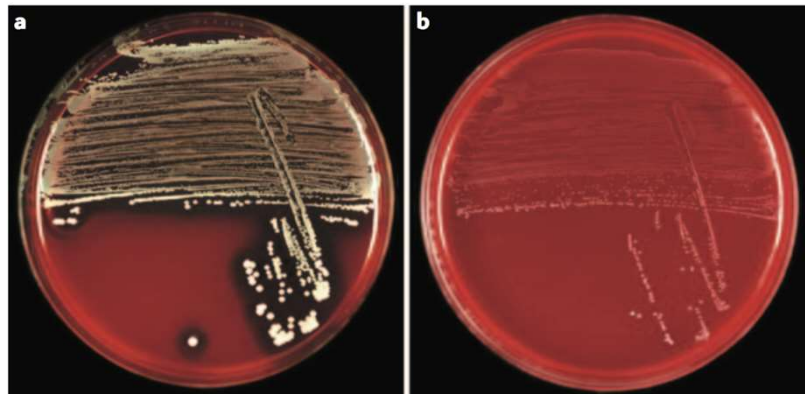


Figure 1 | **Small colony variants.** Columbia blood-agar plates that show the normal (a) and the small colony variant (b) phenotype of *Staphylococcus aureus* are shown.

- **Déficit en transport d'électron**  
Altération de synthèse de médianone & hémine
- **Déficit en biosynthèse de thymidine**

# Small Colony Variants

Modifications phénotypiques

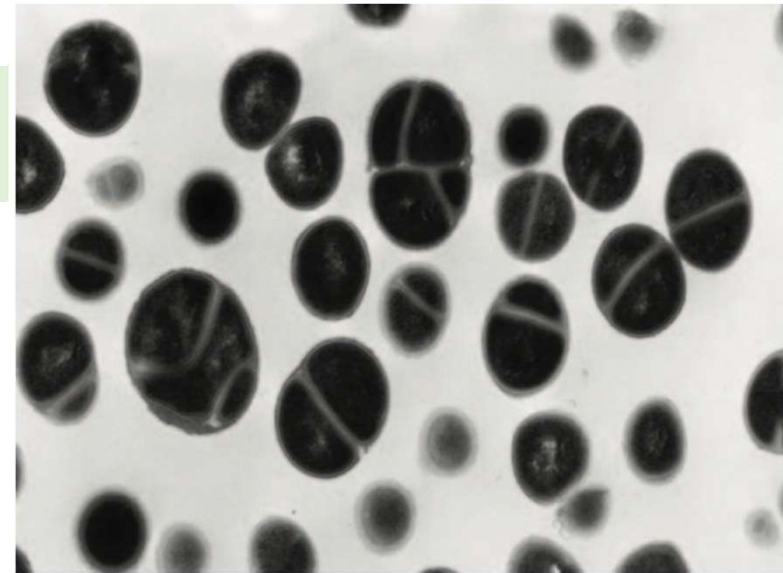


Figure 5 | Altered cellular morphology of haemin-auxotrophic small colony

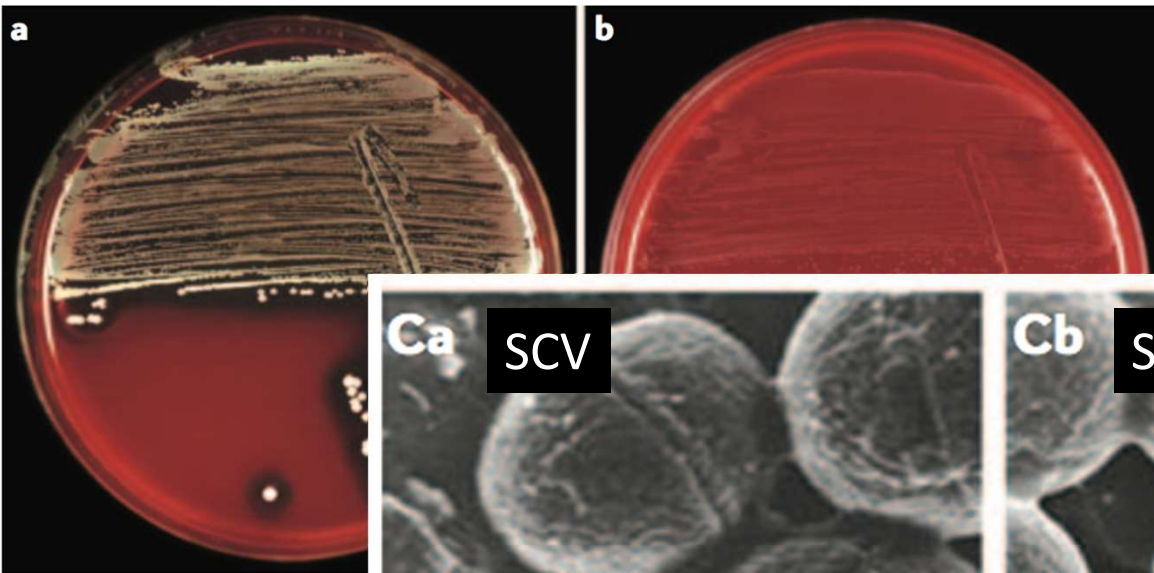
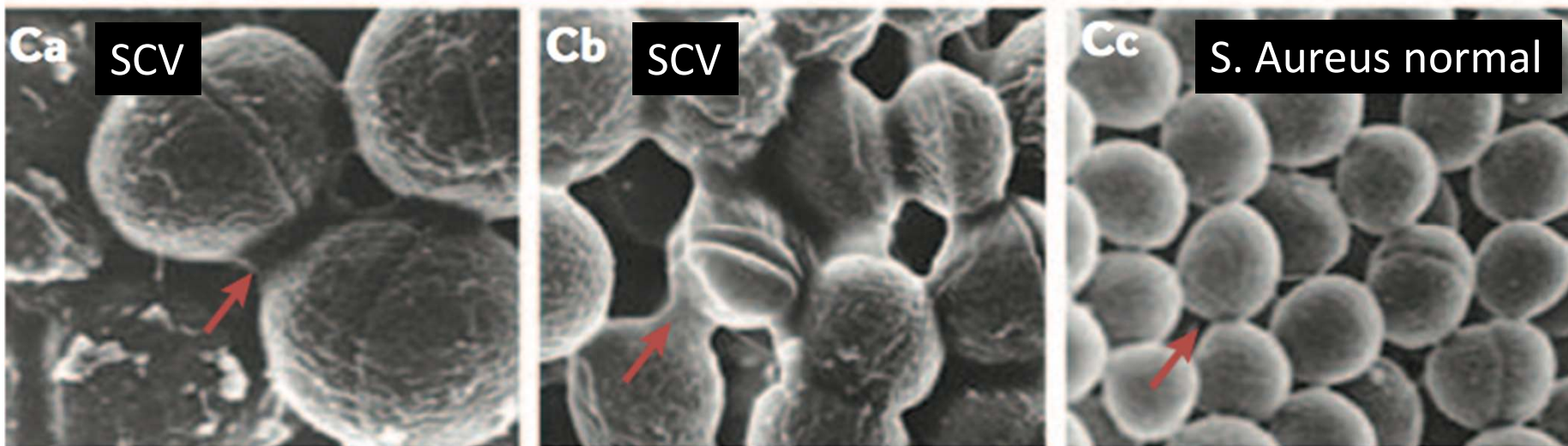


Figure 1 | **Small colony var** and the small colony variant



Nat Rev Microbiol 2006(4)295

# Small Colony Variants

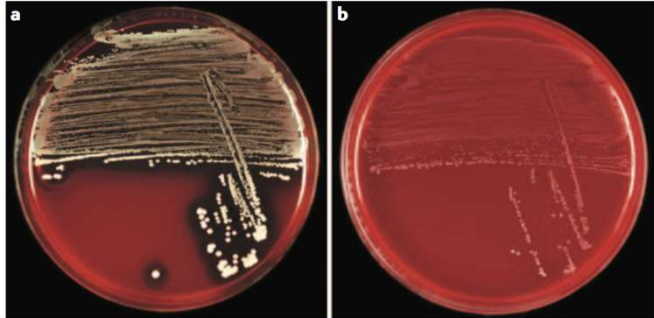


Figure 1 | **Small colony variants.** Columbia blood-agar plates that show the normal (a) and the small colony variant (b) phenotype of *Staphylococcus aureus* are shown.

Petites colonies

Pousse lente

↘ Activité oxydatives / métaboliques

↗ Capacités d'adhérence

↘ Production de certains facteurs de virulence

# Small Colony Variants

Petites colonies

Pousse lente

↘ Activité oxydatives / métaboliques

↗ Capacités d'adhérence

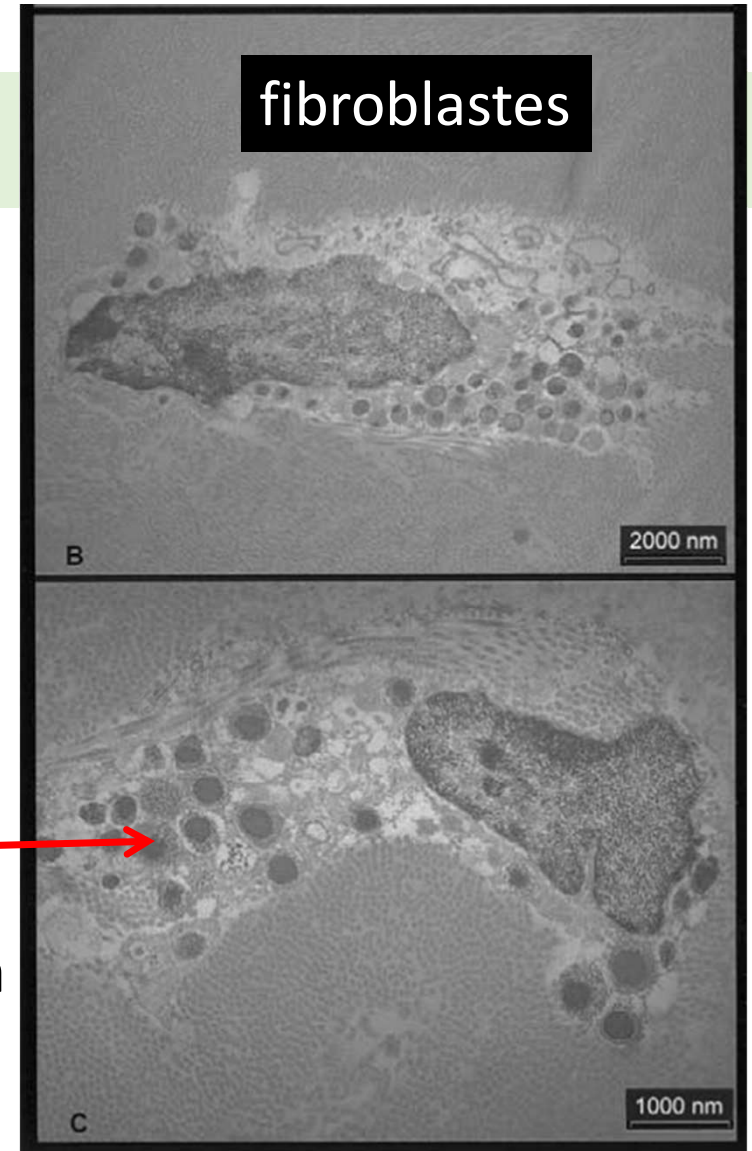
↘ Production de certains facteur  
de virulence

Uprégulation des gènes de persistance

Facilitation de la persistance intracellulaire

Uprégulation des gène de formation du biofilm

**SCV** →



# Small Colony Variants

- Petites colonies
- Pousse lente
- Activité oxydatives / métaboliques
- Capacités d'adhérence
- Production de certains facteur de virulence
- Uprégulation des gènes de persistance
- Uprégulation des gène de formation du biofilm

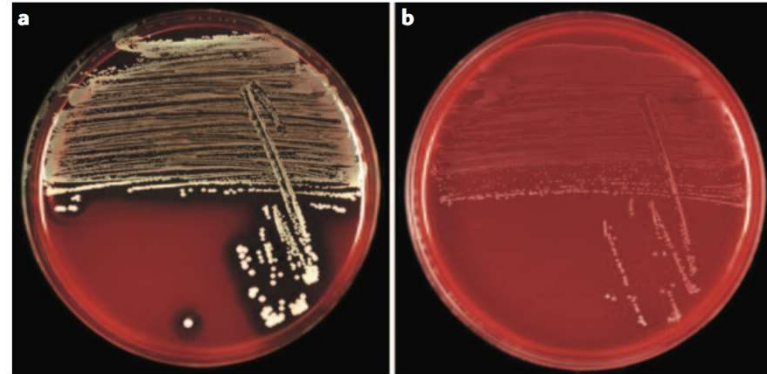


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## Small colony variants (SCVs) of *Staphylococcus aureus* – A bacterial survival strategy

Barbara C. Kahl \*



# Small Colony Variants

## Persistent and Relapsing Infections Associated with Small-Colony Variants of *Staphylococcus aureus*

Richard A. Proctor, Petra van Langevelde,  
Mar Kristjansson, Joel N. Maslow, and Robert D. Arbeit

*From the Departments of Medicine and Medical Microbiology and Immunology, University of Wisconsin-Madison Medical School, Madison, Wisconsin; and the Department of Medicine, Veterans Affairs Medical Center, and the Departments of Medicine and Microbiology, Boston University School of Medicine, Boston, Massachusetts*

**Table 1.** Clinical characteristics of patients with persistent and relapsing infection associated with *S. aureus* SCVs.

Case no.	Type(s) of infection (site)	Interval between episodes of infection	Duration of clinically persistent infection despite treatment	Change in treatment regimen closely associated with clinical response
1	Osteomyelitis (femur)	54 y	6 d	Substitution of clindamycin (iv) for vancomycin
2	Osteomyelitis (femur)	29 y	>4 w	...*
3	Sinusitis (maxillary sinus)	4 mo	>3 w	...*
4	Osteomyelitis, septic arthritis (hip prosthesis)	6 mo	8 w	Surgery (removal of prosthesis)
5	Muscle abscesses, septic arthritis (thighs, hips)	4 y <sup>†</sup>	12 w	Addition of vitamin K and TMP-SMZ to vancomycin, rifampin

\* There was a very delayed response to continued conventional treatment with parenteral  $\beta$ -lactam antibiotics (see text for details).

<sup>†</sup> Isolate from initial episode of infection was not identified as *S. aureus* but was phenotypically consistent with SCVs (see text for details). CID 1995;20 (January)

## Small Colony Variants relation avec les antibiotiques

Résistance par mécanisme spécifique décrite pour  
fluoroquinolones, aminosides, Co trimoxazole

Induction de formation de SCV par exposition à  
Co-trimoxazole, fluoroquinolone



## Clinical Characteristics and Outcomes of Prosthetic Joint Infection Caused by Small Colony Variant Staphylococci

TABLE 3 Antimicrobial susceptibility and auxotrophy testing results for isolates recovered from subjects with SCVs

Susceptibility or auxotrophy result	No. (%) for SCV status:	
	Yes ( <i>n</i> = 42)	No ( <i>n</i> = 34)
<b>Antimicrobial susceptibility testing</b>		
Oxacillin susceptible <sup>a</sup>	20 (47.6)	21 (61.8)
Gentamicin susceptible	36 (85.7)	30 (88.2)
Rifampin susceptible	37 (88.1)	33 (97.1)
Minocycline susceptible	42 (100)	33 (97.1)
Vancomycin susceptible	42 (100)	34 (100)
Trimethoprim-sulfamethoxazole susceptible <sup>b</sup>	34 (85.0)	31 (91.2)

# Small Colony Variants Sensibilité Antibiotiques

AAC  
2018 62 Issue 4

## 10 souches S.aureus Paires de SCV & souche parent

MIC data ( $\mu\text{g/ml}$ )<sup>a</sup>

Antimicrobial agent	NP			SCV		
	MIC <sub>50</sub>	MIC <sub>90</sub>	Range	MIC <sub>50</sub>	MIC <sub>90</sub>	Range
$\beta$ -Lactams						
Benzylpenicillin	0.094	2	0.023–24	0.125	1.5	0.016–4
Ampicillin	0.25	3	0.094–12	0.25	1.5 (2)	0.023–4 (0.023–6)
Ampicillin-sulbactam	0.19 (0.25)	1	0.094–1.5	0.19	0.75	0.016–0.75 (0.016–1)
Piperacillin	1.5	4	0.75–24 (0.75–32)	1.5	3	0.25–4 (0.25–12)
Piperacillin-tazobactam	1	2	0.75–3	0.5	1	0.064–2
Oxacillin	0.38	0.75	0.19–1	0.125	0.5	0.023–0.5
Cefoxitin	2	3	1–3	1	3	0.25–4
Cephalothin	0.38	0.5	0.19–0.75	0.125	0.38	0.016–0.5
Cefuroxime	0.75	0.75	0.38–1.5	0.25	0.75	0.064–0.75
Ceftriaxone	3	4	2–6	2	4	0.38–4
Cefepime	3	3	1.5–3 (1.5–4)	1.5	3	0.38–3
Imipenem	0.064	0.094	0.047–0.094	0.023	0.064	0.012–0.064

cc

# Small Colony Variants Sensibilité Antibiotiques

AAC  
2018 62 Issue 4

## 10 souches S.aureuscPaires de SCVc& souche parent

MIC data ( $\mu\text{g/ml}$ )<sup>a</sup>

Antimicrobial agent	NP			SCV		
	MIC <sub>50</sub>	MIC <sub>90</sub>	Range	MIC <sub>50</sub>	MIC <sub>90</sub>	Range
Non- $\beta$ -lactams						
Vancomycin	1	1.5	0.75–1.5	1	1.5	0.75–2
Daptomycin	0.19	0.25	0.094–0.38	0.094 (0.19)	0.38	0.094–0.5
Moxifloxacin	0.064	0.064	0.032–0.064	0.047	0.19	0.023–0.19
Clarithromycin	0.38	0.75	0.094–256	0.19	1.5	0.023–256
Clindamycin	0.094	0.125	0.064–0.125	0.064	0.19	0.016–0.38
Linezolid	0.5 (0.75)	1 (1.5)	0.25–1 (0.25–1.5)	0.38	1.5	0.094–1.5
Rifampin	0.012	0.016	0.006–0.016	0.008	0.012	0.003–0.016
Fosfomicin	4	12	1.5–16	4	12	0.064–16
Quinupristin-dalfopristin	0.5	0.5 (0.75)	0.25–0.75	0.38	0.5	0.047–0.75
Tigecycline	0.38	0.5	0.19–0.75	0.38	0.5 (0.75)	0.094–0.75
Trimethoprim-sulfamethoxazole	0.032	0.047	0.023–0.19	0.032	0.094	0.003–0.125
Gentamicin	0.38	24	0.125–256	0.125 (0.25)	4	0.064–256
Mupirocin	0.094	0.19 (0.38)	0.094–0.19 (0.094–0.38)	0.094	0.19	0.064–0.19

# Clinical Characteristics and Outcomes of Prosthetic Joint Infection Caused by Small Colony Variant Staphylococci

Aaron J. Tande,<sup>a,b</sup> Douglas R. Osmon,<sup>a</sup> Kerryl E. Greenwood-Quaintance,<sup>b</sup> Tad M. Mabry,<sup>c</sup> Arlen D. Hanssen,<sup>c</sup> Robin Patel<sup>a,b,d</sup>

Tande et al Mbio 2014

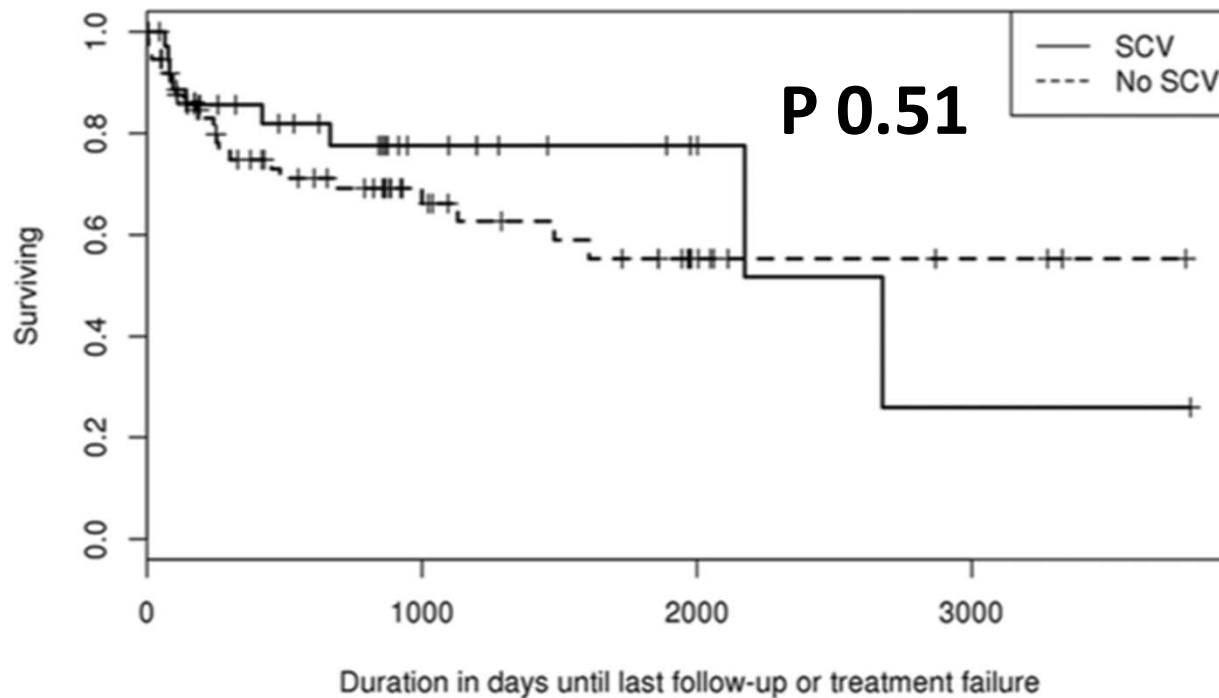
TABLE 1 Medical and orthopedic surgical history and PJI presentation<sup>c</sup>

Characteristic <sup>d</sup>	SCV <sup>b</sup>		P value
	Yes (n = 38)	No (n = 75)	
<b>Demographic factors</b>			
Age in yr, median (range)	64 (25–85)	63 (36–84)	0.49
Female sex	16 (42.1)	31 (41.3)	1
Diabetes mellitus	10 (26.3)	20 (26.7)	0.97
Rheumatoid arthritis by ACR criteria	1 (2.6)	5 (6.7)	0.66
Rheumatoid or inflammatory arthritis	3 (7.9)	11 (14.7)	0.38
CKD	2 (5.3)	6 (8.0)	0.72
<b>Orthopedic history</b>			
Joint age in days, median (range)	1,295 (216–13,712)	646 (23–11,883)	0.007
Prior arthroplasty revision	32 (84.2)	52 (70.3)	0.17
Time since last surgery in days, median (range)	743 (31–10,030)	306 (20–8,686)	<0.0001
Cemented arthroplasty	33 (86.8)	60 (80.0)	0.44
Duration of PJI symptoms in days, median (range)	491 (14–2,306)	165 (2–1,656)	0.0003
Prior surgery for this PJI	23 (60.5)	28 (37.3)	0.03
Receiving 120 or more days of antibiotics in prior 6 mo	16 (42.1)	17 (22.7)	0.048
Serum WBC in 10 <sup>6</sup> cells/liter, median (range)	7.3 (4.5–11.7)	7.5 (5–25.5)	0.15
Serum ESR in mm/h, median (range)	46 (5–111)	43 (3–123)	0.54
Serum CRP in mg/liter, median (range)	23 (5–222)	44 (3–269)	0.2
Preoperative SF aspirate SF WBC in cells/ $\mu$ l, median (range)	26 (68.4)	51 (68.0)	0.13
SF neutrophil %, median (range)	28,574 (8,175–155,000)	44,275 (629–1,071,472)	0.13
	88 (79–98)	91 (51–100)	

Tande et al Mbio 2014

# Clinical Characteristics and Outcomes of Prosthetic Joint Infection Caused by Small Colony Variant Staphylococci

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Remplacement prothétique en 2 temps 100 % des patients

Tande et al Mbio 2014

Small Colony Variants : bactéries pour lesquelles des phénotypes SCV ont été décrits

*Staphylococcus aureus*

*Staphylococcus coagulase négative*

*Pseudomonas aeruginosa*

*E. coli,*

*N. Gonorrhoeae*

*S. Typhimurium Shigella*

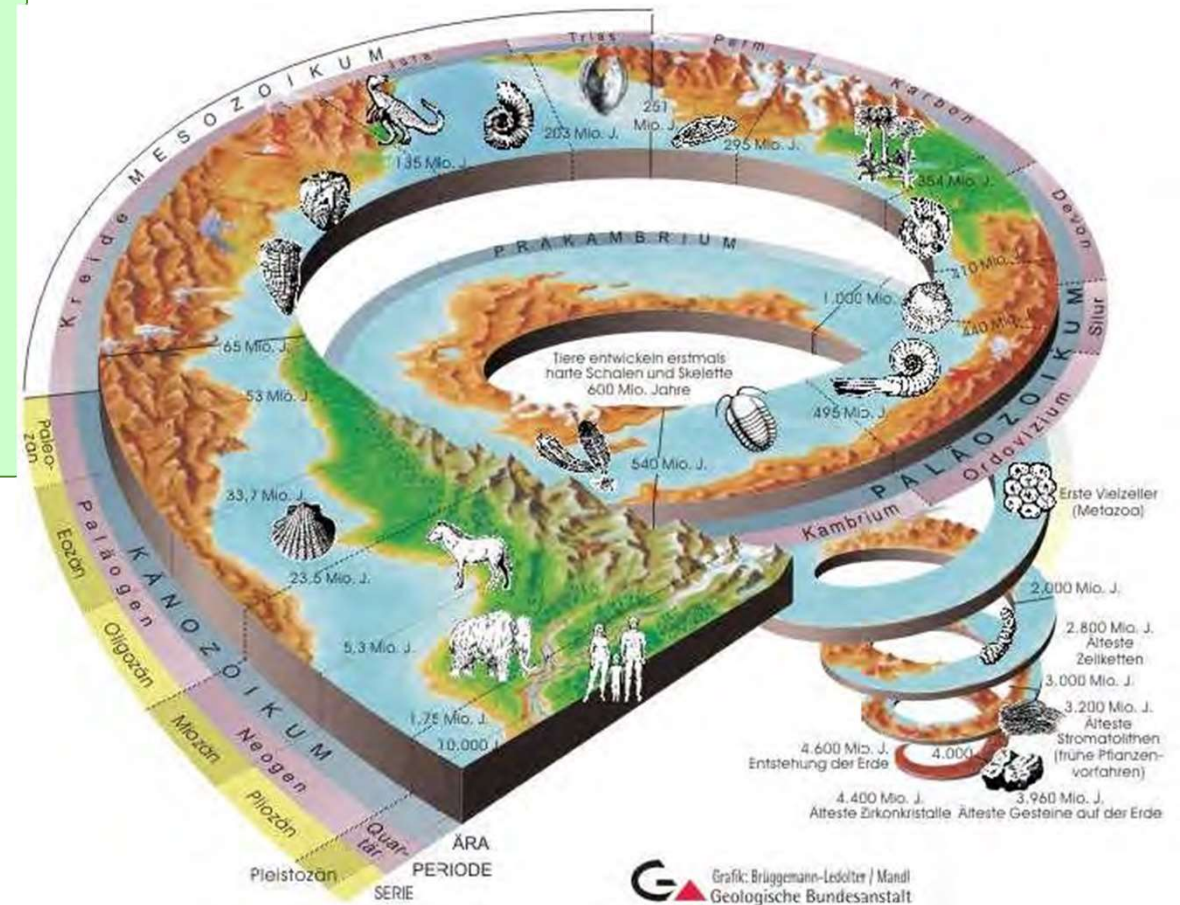
*Proteus sp., Klebsiella pneumoniae, Providencia stuartii,*

*Enterobacter cloacae, S. marcescens, Citrobacter freundii*

1/ Adh rence et  
organisations bact riennes

2/ Variants microcolonies

3/ Persistance intra cellulaire



Microcolonies forming biofilm identified :

- 3.3–3.4 billion years South African Kornberg formation
- 3.2-billion years deep-sea hydrothermal rocks of the Pilbara Craton, Australia



Internalisation dans les cellules non phagocytaires

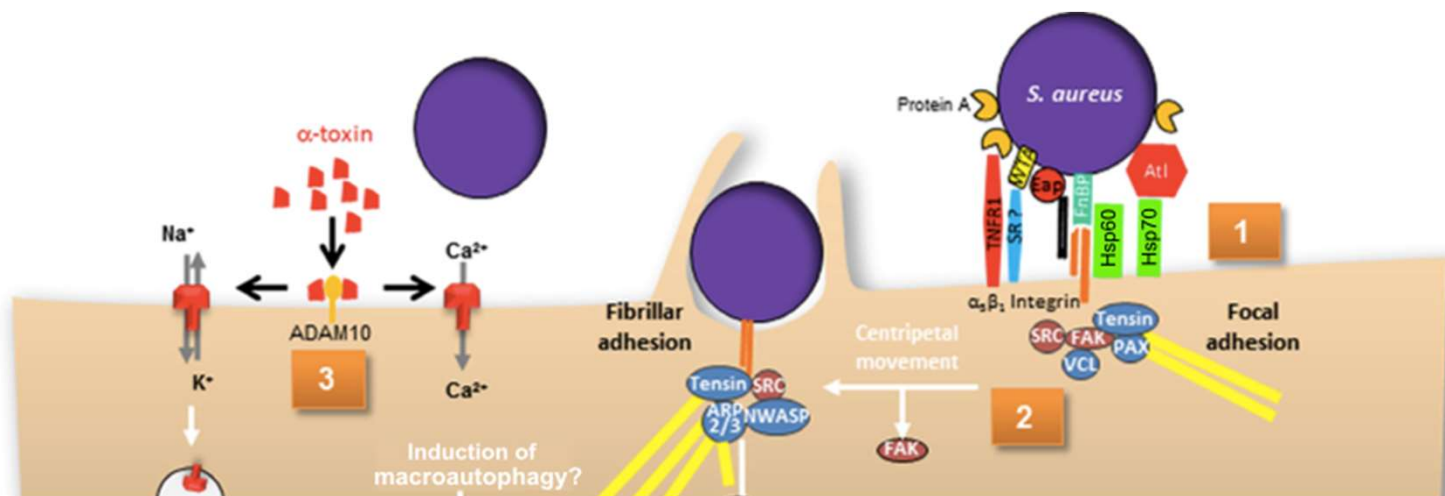


Persistence intracellulaire



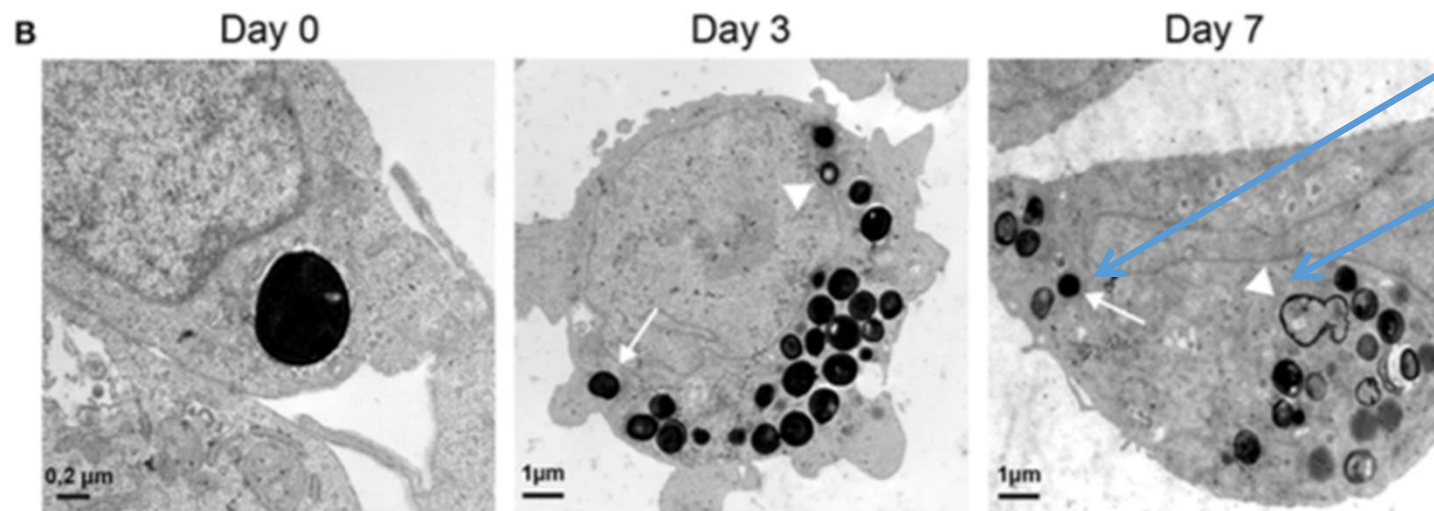
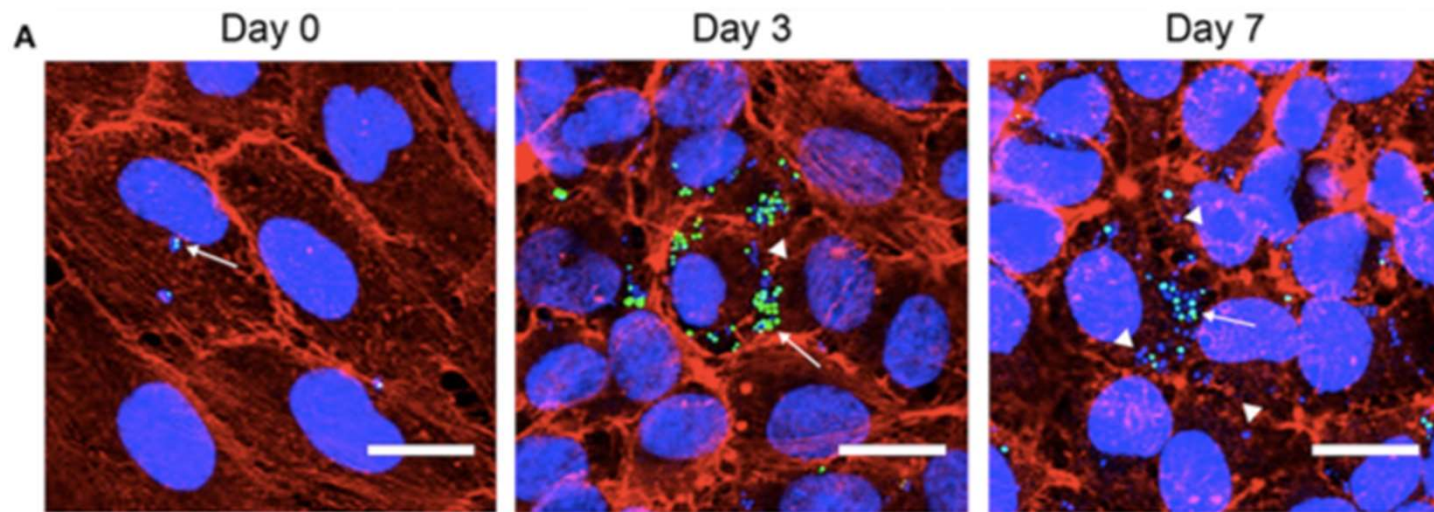
Échappement du compartiment intra cellulaire

# Internalisation dans les cellules non phagocytaires



Fibroblastes  
Cellules endothéliales  
Ostéoblastes  
kératinocytes

# Persistence intracellulaire

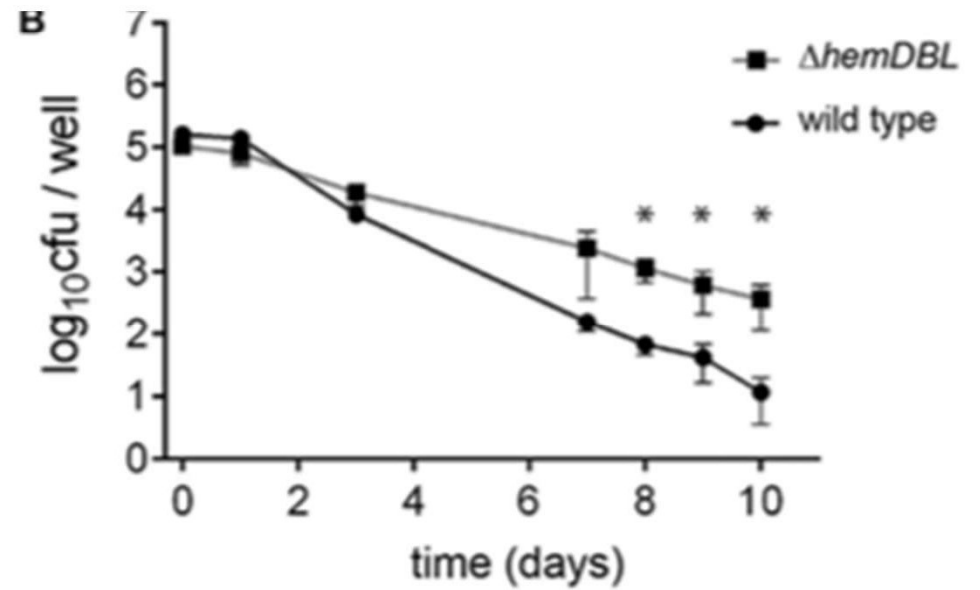
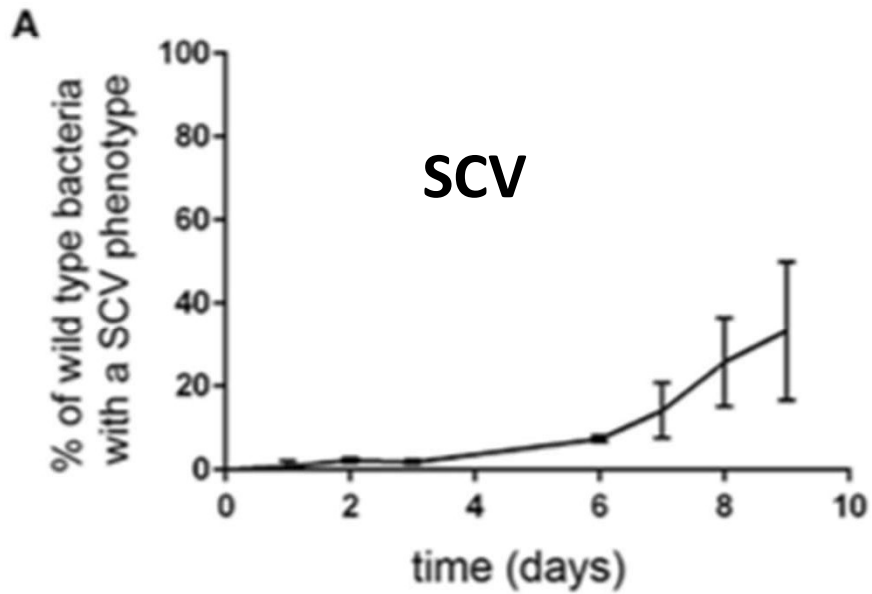
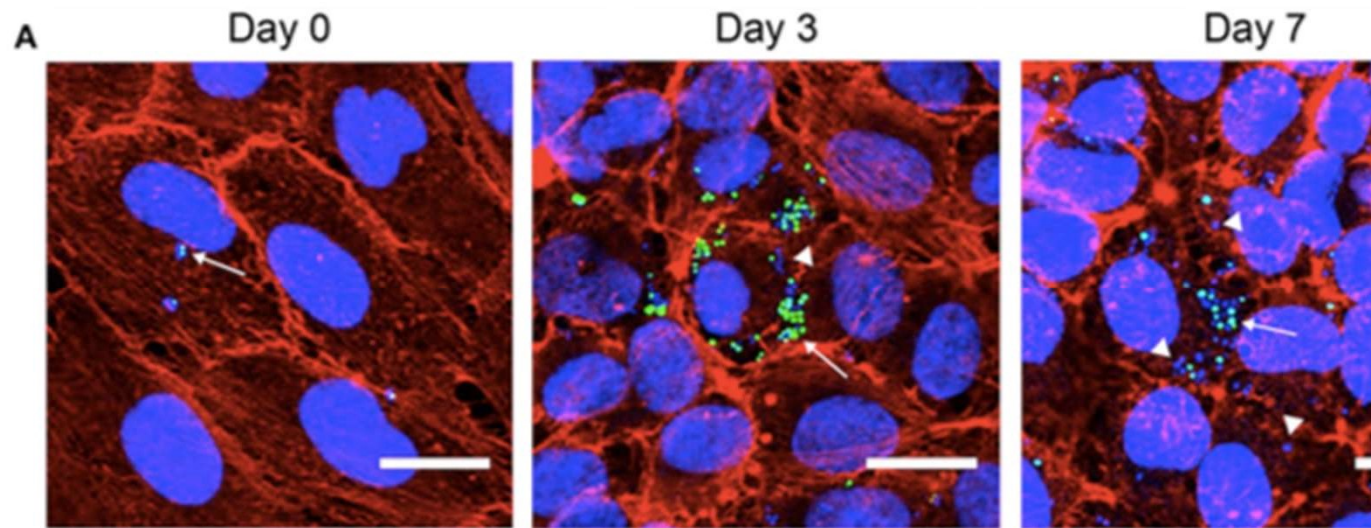


**C vivantes**

**C mortes**

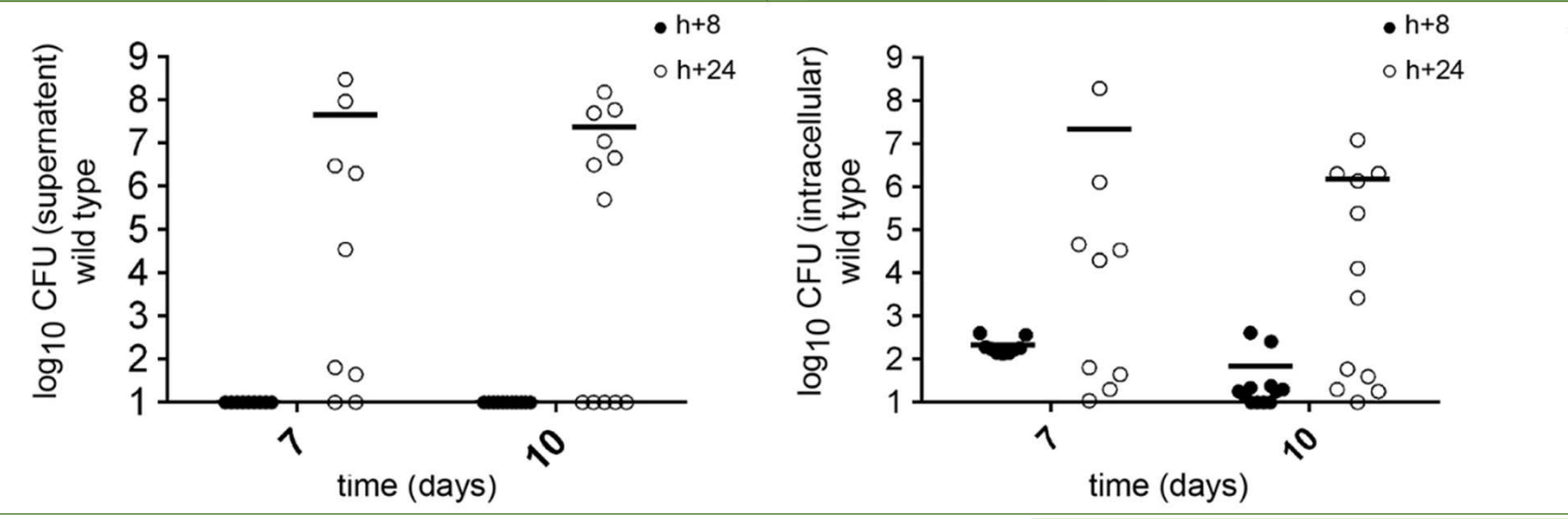
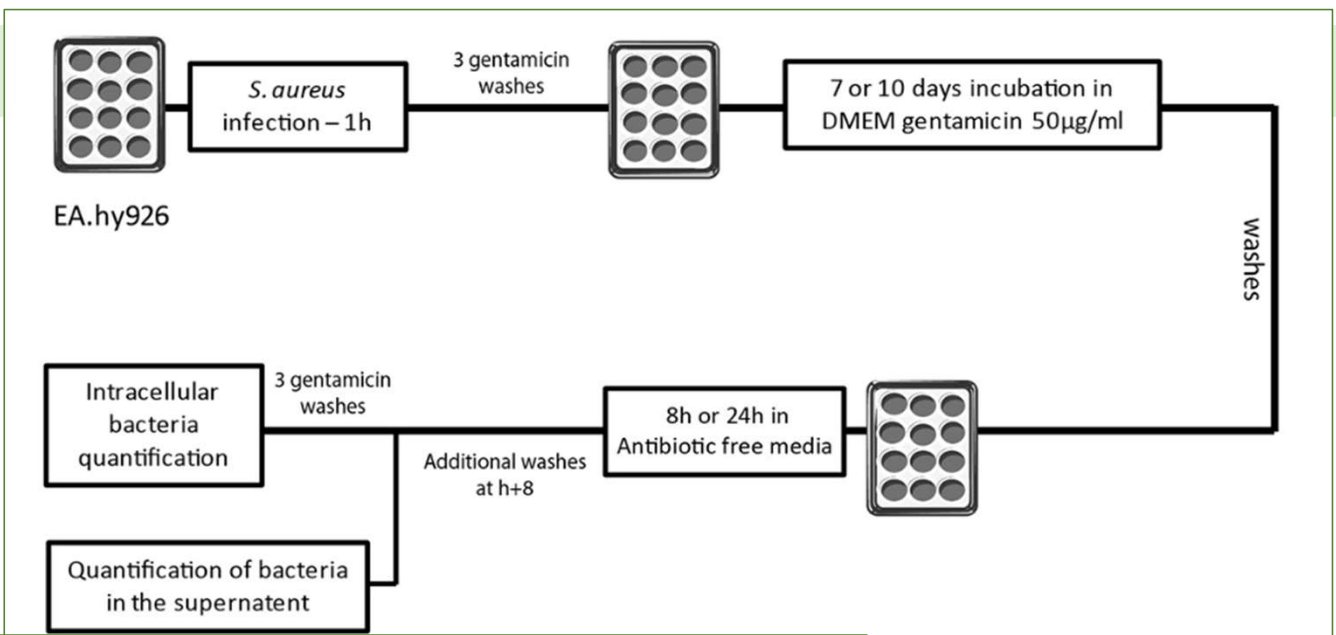
Frontiers in Microbiology  
July 2017  
Volume 8 | Article 1354

# Persistence intracellulaire



# Persistence intracellulaire

## Échappement du compartiment intra cellulaire

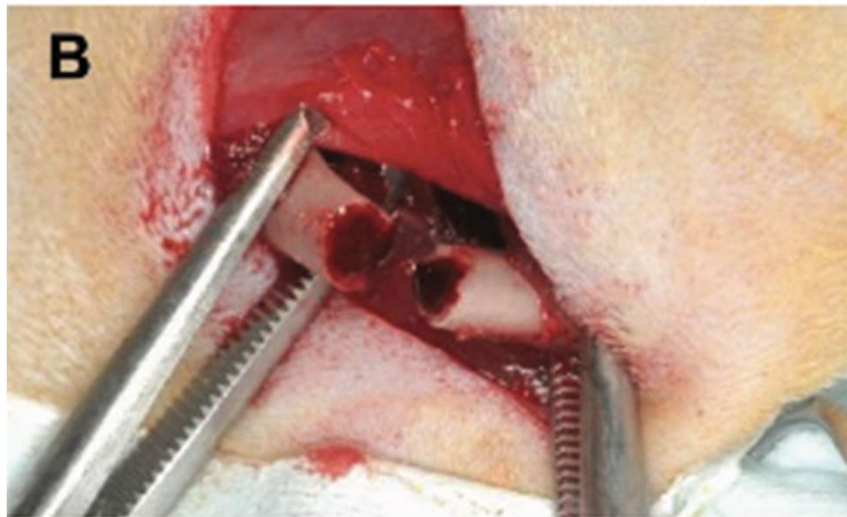


## INTRA-CELLULAR *STAPHYLOCOCCUS AUREUS* ALONE CAUSES INFECTION *IN VIVO*

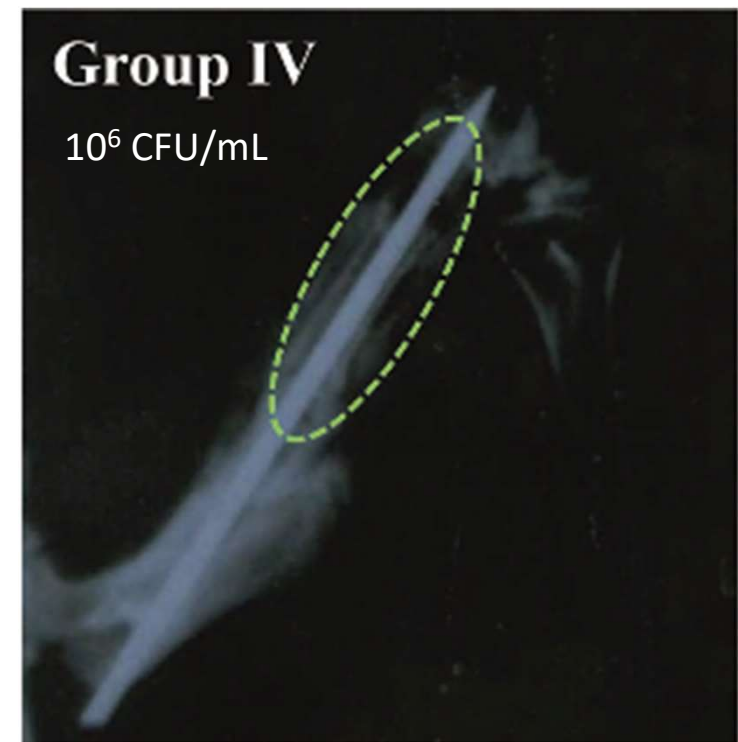
Therwa Hamza<sup>1,2</sup>, Matthew Dietz<sup>1</sup>, Danh Pham<sup>1</sup>, Nina Clovis<sup>1</sup>, Suzanne Danley<sup>1</sup> and Bingyun Li<sup>1,2,3,4,\*</sup>

Rat bone

Inoculation  $10^6$  osteoblasts infected with  $10^6$  CFU intra-cellular *S. aureus*

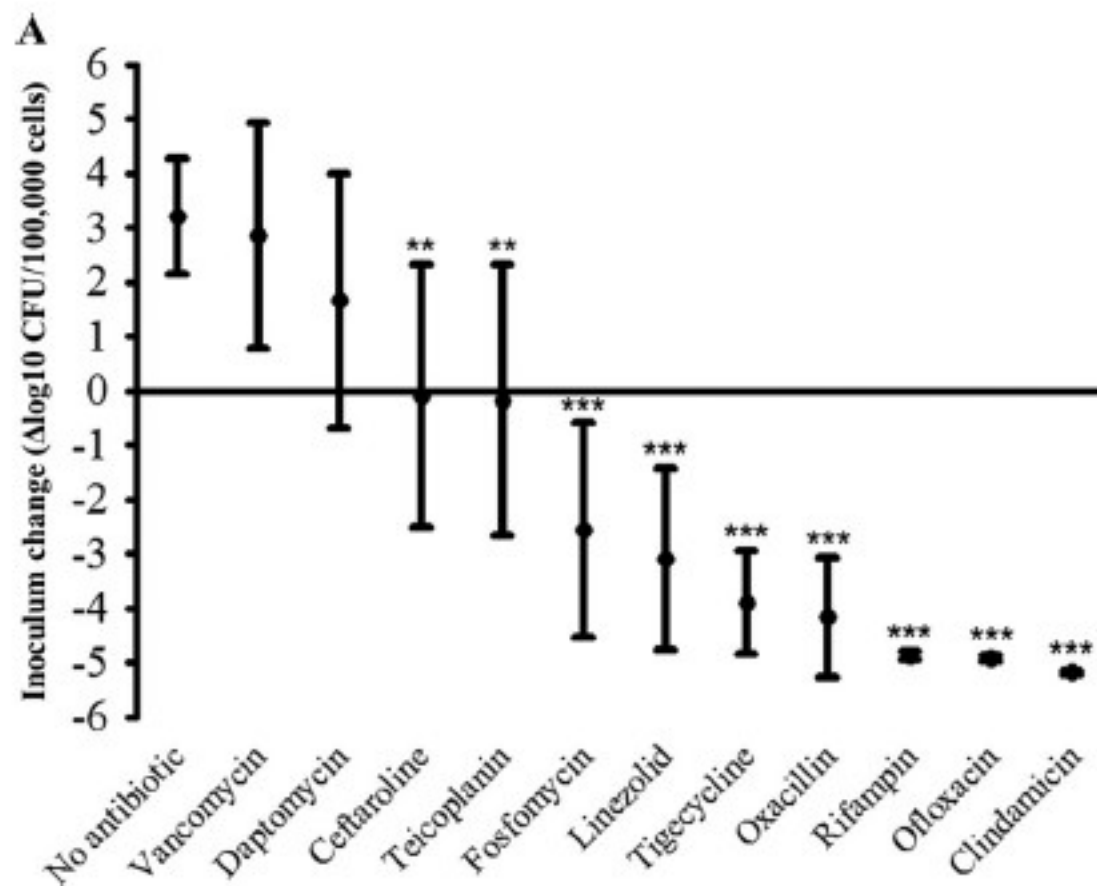


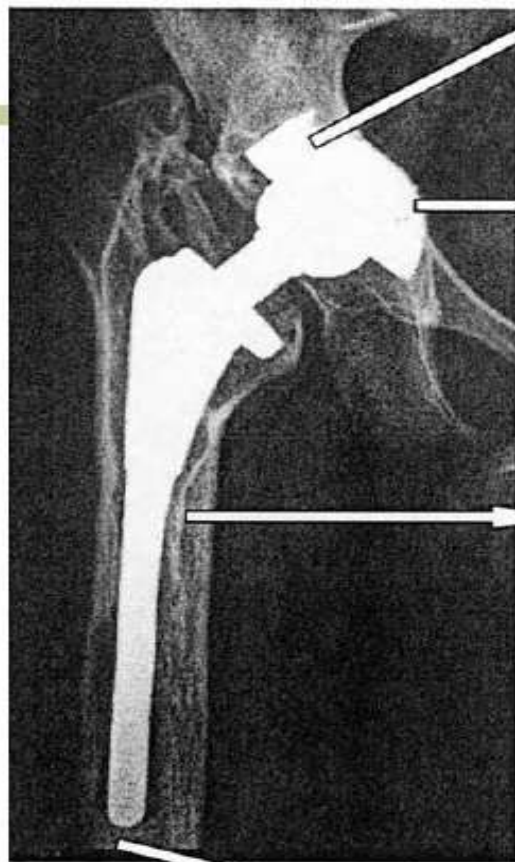
Day 21



## Antimicrobial Activity against Intraosteoblastic *Staphylococcus aureus*

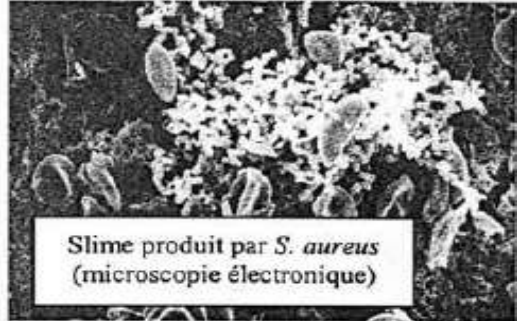
Inoculum intra  
ostéoblastique





**Les altérations du métabolisme bactérien au voisinage des matériaux infectés responsable d'un phénomène de tolérance aux antibiotiques, même bactéricides (small colony variant)**

**Le slime** (substance polysaccharidique extracellulaire) et le **biofilm** bactérien semblant responsable de :  
 - une adhésion bactérienne plus forte,  
 - une virulence particulière et  
 - une moindre sensibilité aux antibiotiques



Slime produit par *S. aureus* (microscopie électronique)

**Les altérations du système macrophagique** par des éléments prothétique: métal, polyéthylène... ou des éléments périprothétiques (ciment)



Particules de polyéthylène sur une néocapsule articulaire (microscopie électronique)



Bouchon de fût fémoral

**Les réservoirs de germes inaccessibles aux antibiotiques** (ciment, granulome...)

Revue générale  
 Infections de prothèse articulaire  
 Prosthetic joint infections  
 L. Bernard \*



1/ Adh rence et  
organisations bact riennes

2/ Variants microcolonies

3/ Persistance intra cellulaire

Merci de votre attention

