

ESKAPEES

versus

Cyclic AMPs and 2-AIs: How to win the battle on surfaces

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Department of Biochemistry
Stellenbosch University



Triple A COAT



Stellenbosch

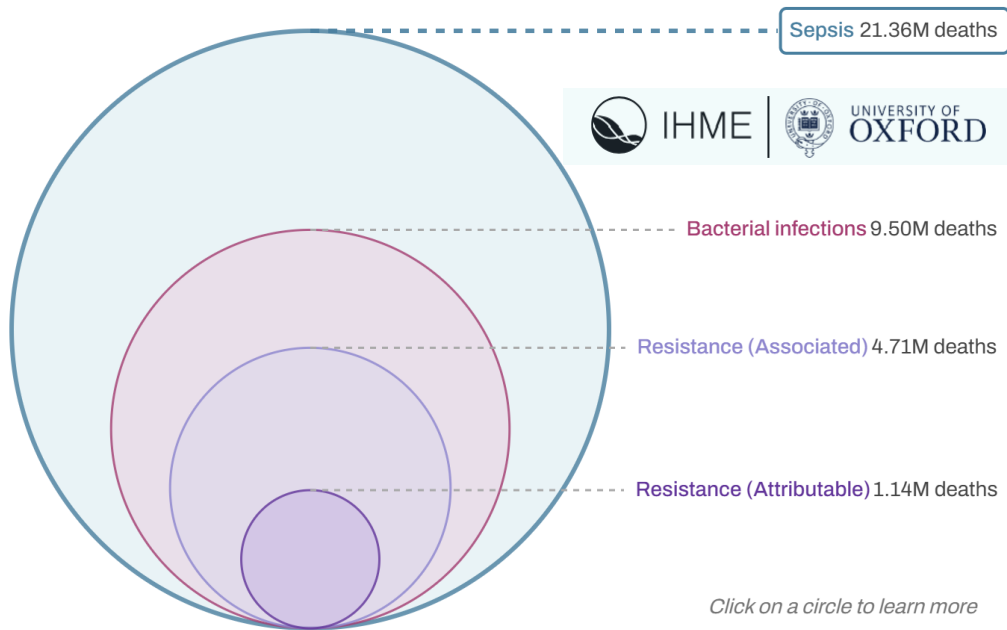
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EU Horizon

What/Who are the **ESKAPEES** in the surface battle ?

Composition of global infection-related deaths 2021



E — *Enterococcus faecium*

S — *Staphylococcus aureus*

K — *Klebsiella pneumoniae*

A — *Acinetobacter baumannii*

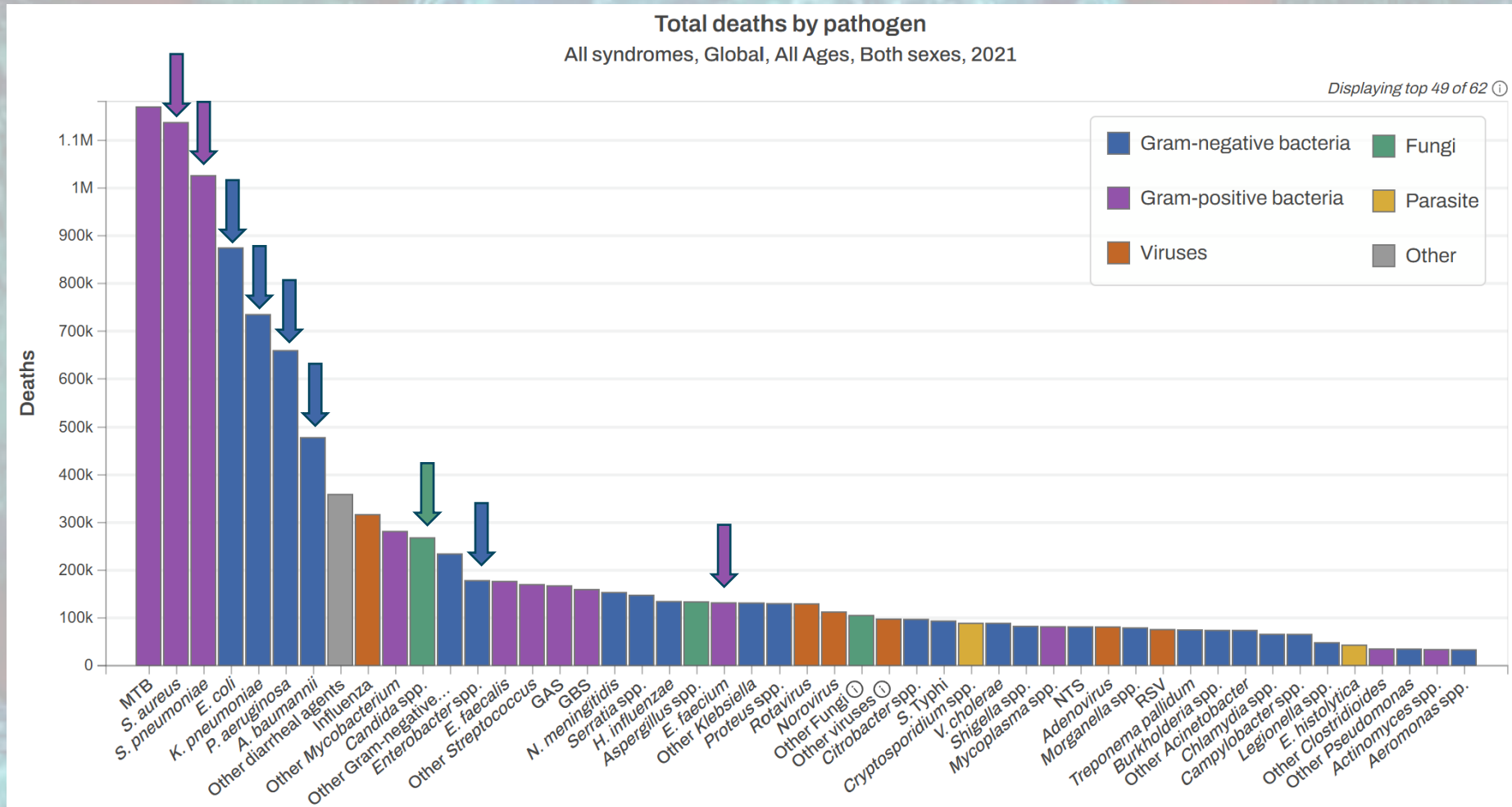
P — *Pseudomonas aeruginosa*

E — *Enterobacter* species

E — *Escherichia coli*

S — *Streptococcus pneumonia*

Six of the **ESKAPEES** are the top killers of humans globally



IHME

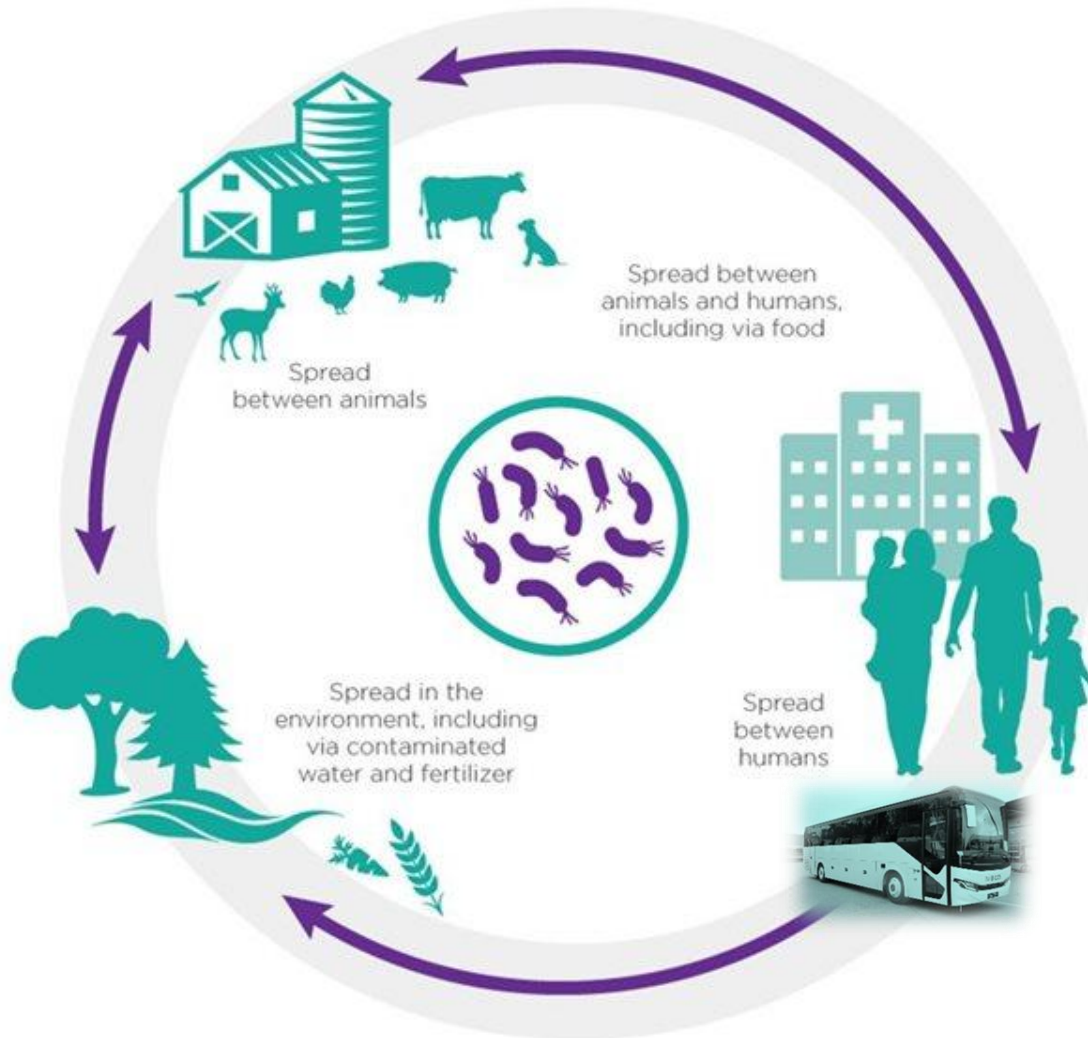


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<https://vizhub.healthdata.org/microbe/>

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Why take the battle in the AMR war to surfaces and not directly into the clinic?



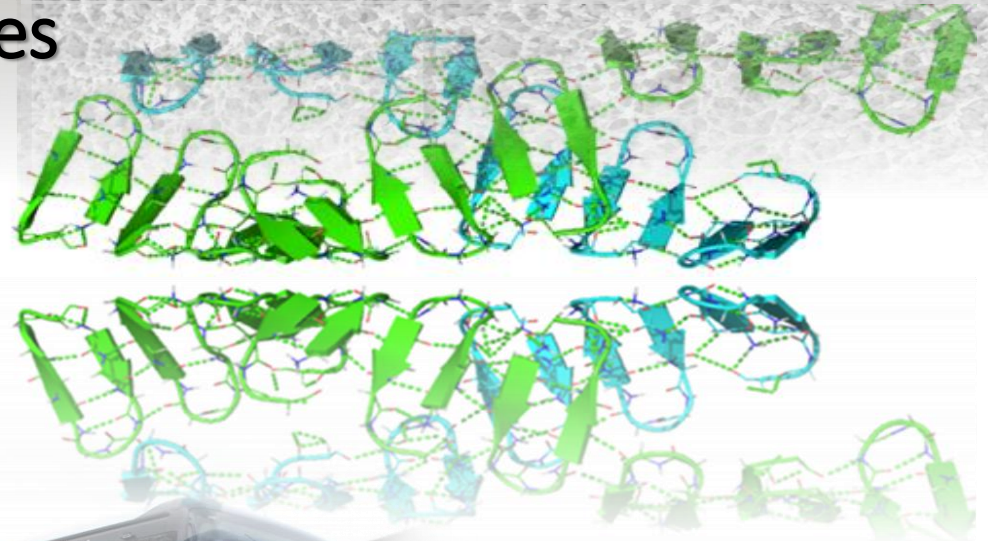
Antimicrobial resistance spread via surfaces is the “engine” of the cycle

Source: Public Health Agency of Canada

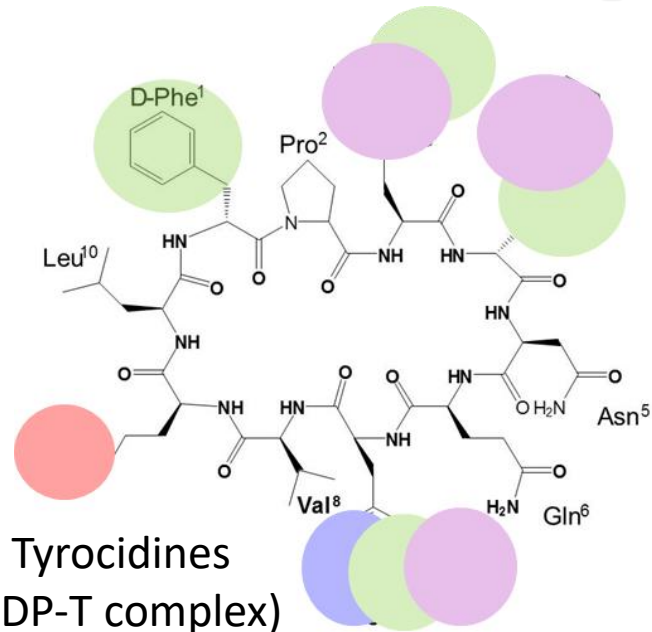
<https://asm.org/articles/2024/october/antimicrobial-resistance-pandemic-breaking-silence>

Sterilising weapons from NATURE and the LAB

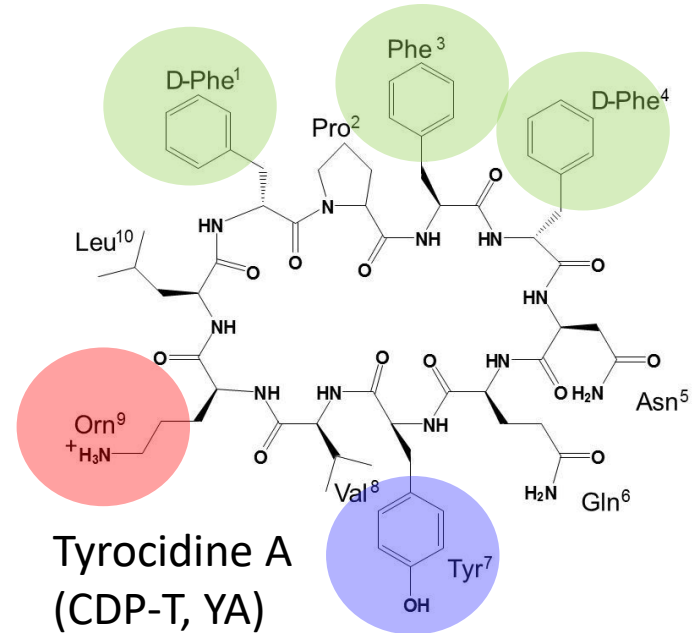
Natural cyclic antimicrobial peptides and 2-amino imidazoles for creating antimicrobial materials, sterile films and surfaces



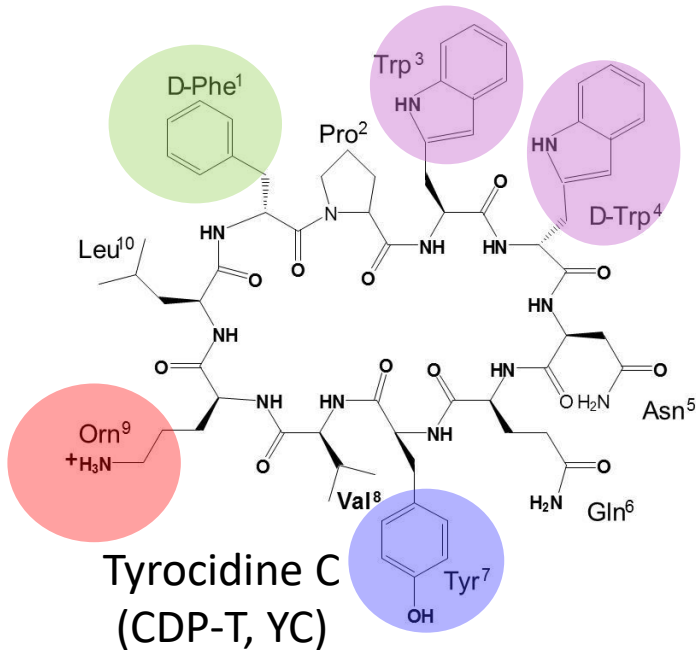
Our natural weapons: Cyclic decapeptides



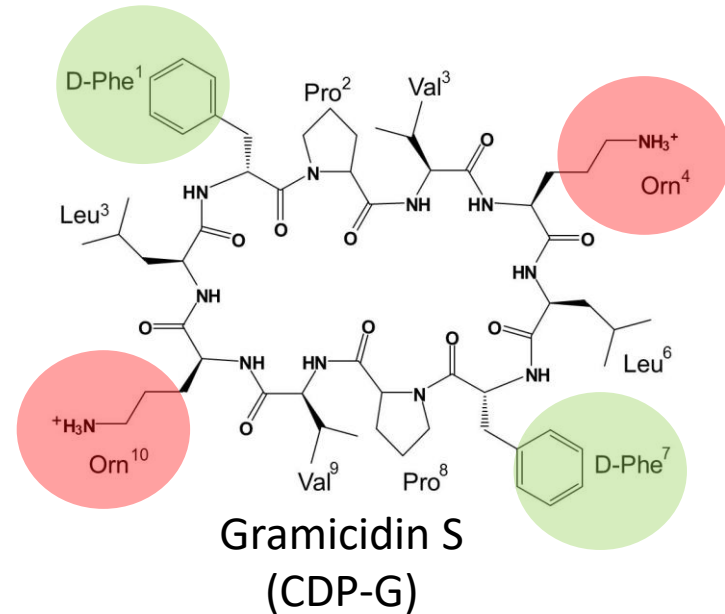
Tyrocidines
(CDP-T complex)



Tyrocidine A
(CDP-T, YA)

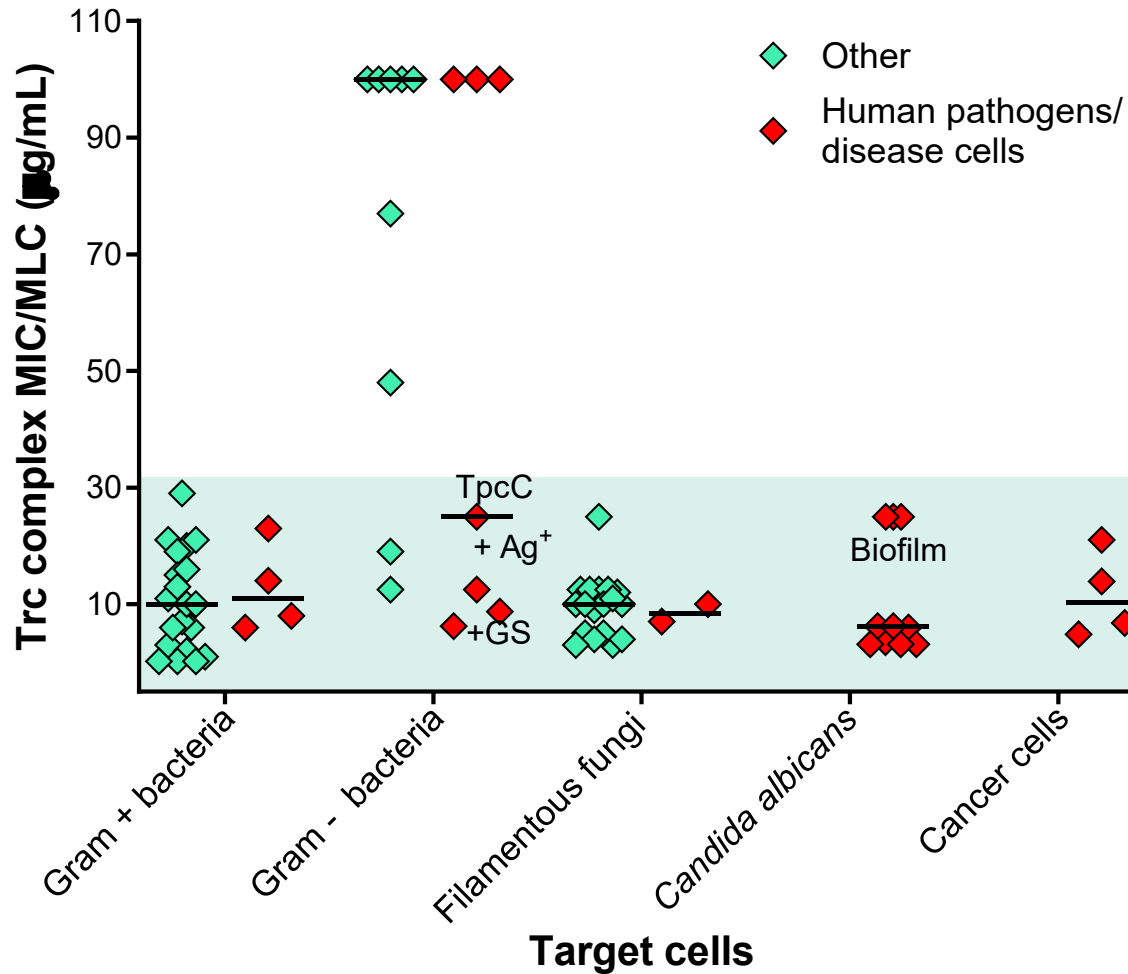


Tyrocidine C
(CDP-T, YC)



Gramicidin S
(CDP-G)

Why use cyclic AMPs ?

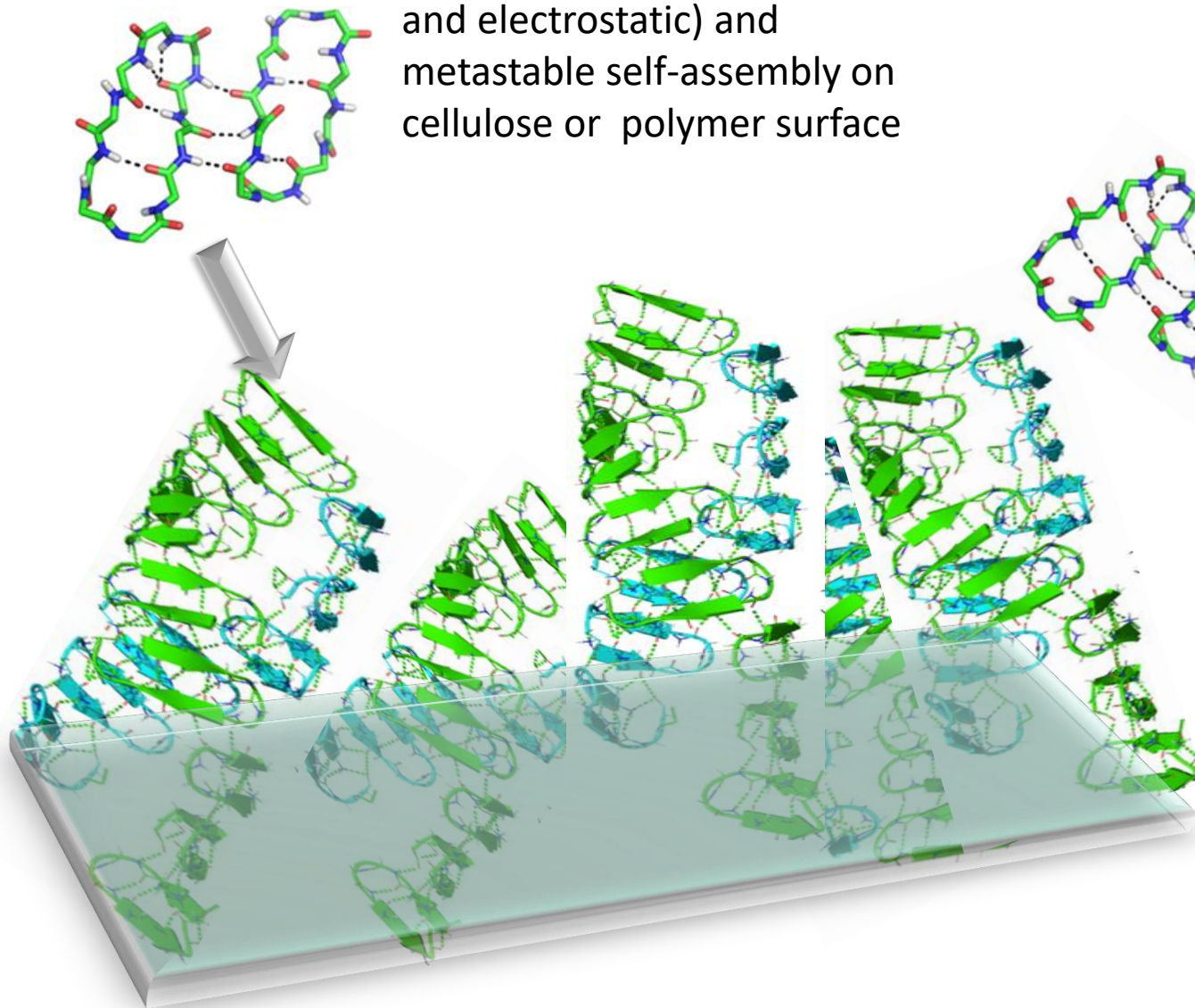


- About 80 years of use as topical antibiotics, without documented resistance or skin toxicity
- Multiple targets, rapid multiple modes of action
- Broad spectrum activity, including antiviral activity against human CoV
- Naturally synergistic mixtures
- High stability, but biodegradable
 - Wet and dry temperature stable up to 120°C
 - pH stable, UV stable
- Economical production
 - 1-3 g/L of culture

Data from BIOPEP Peptide group
Stellenbosch University

CDP material and surface treatment

CDP adsorption (hydrophobic and electrostatic) and metastable self-assembly on cellulose or polymer surface



Release of amphipathic CDP dimers/oligomers when bacteria/fungi binds

Lysis of bacterium/
fungal cell

The material treatment battle

Do the CDPs maintain activity in/on materials ?



antibiotics

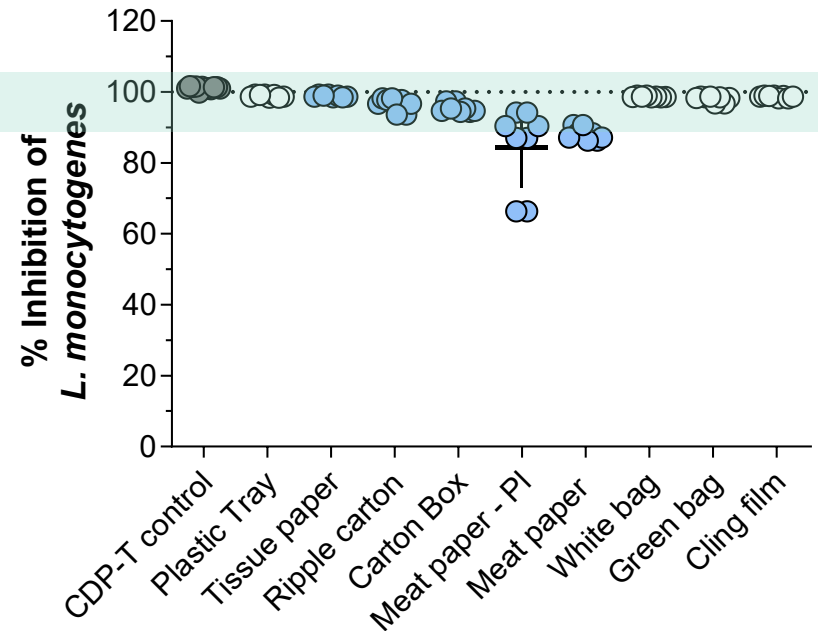
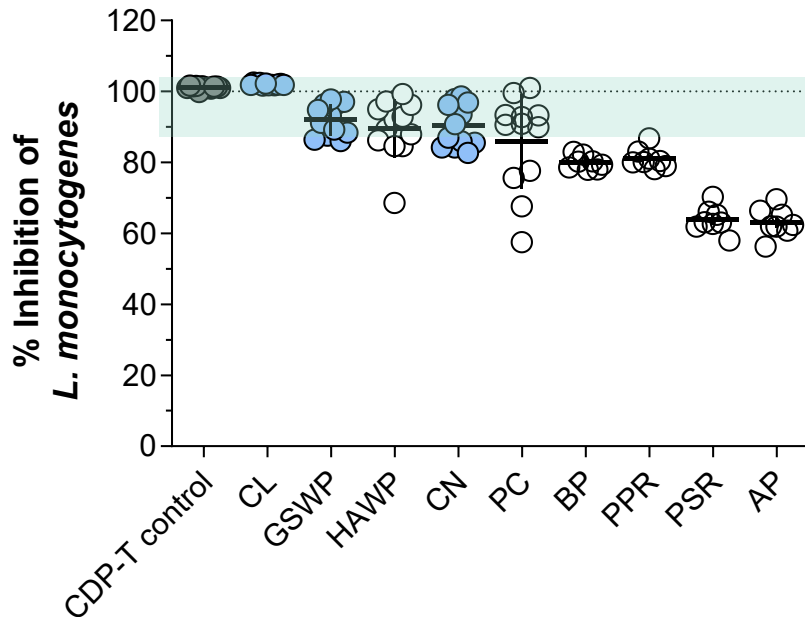
Antibiotics 2022, 11, 174. <https://doi.org/10.3390/antibiotics11020174>

Article

Creating Robust Antimicrobial Materials with Sticky Tyrocidines

Wilma van Rensburg * and Marina Rautenbach *

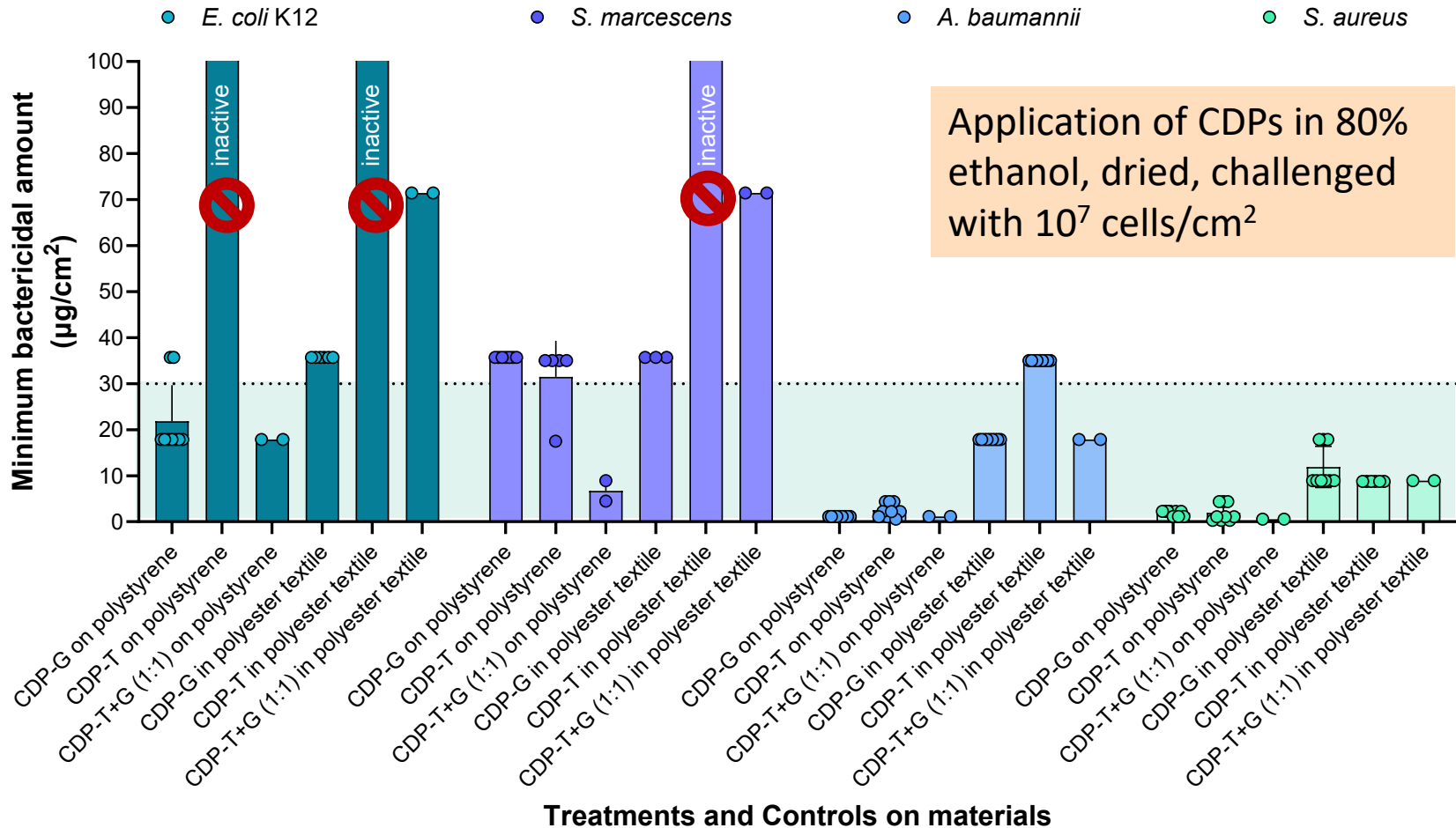
Dip application with CDP-T in water, dried, challenged with 10^7 cells/cm²



Cellulose (CL), mixed cellulose filters GSWP (0.22 μ m) and HAWP (0.45 μ m); cellulose nitrate (CN – 0.45 μ m), polycarbonate (PC – 0.4 μ m), black polystyrene plate (BP), polypropylene round bottom plate (PPR), polystyrene round bottom plate (PSR) and polystyrene plate (AP)

The ongoing material treatment battle

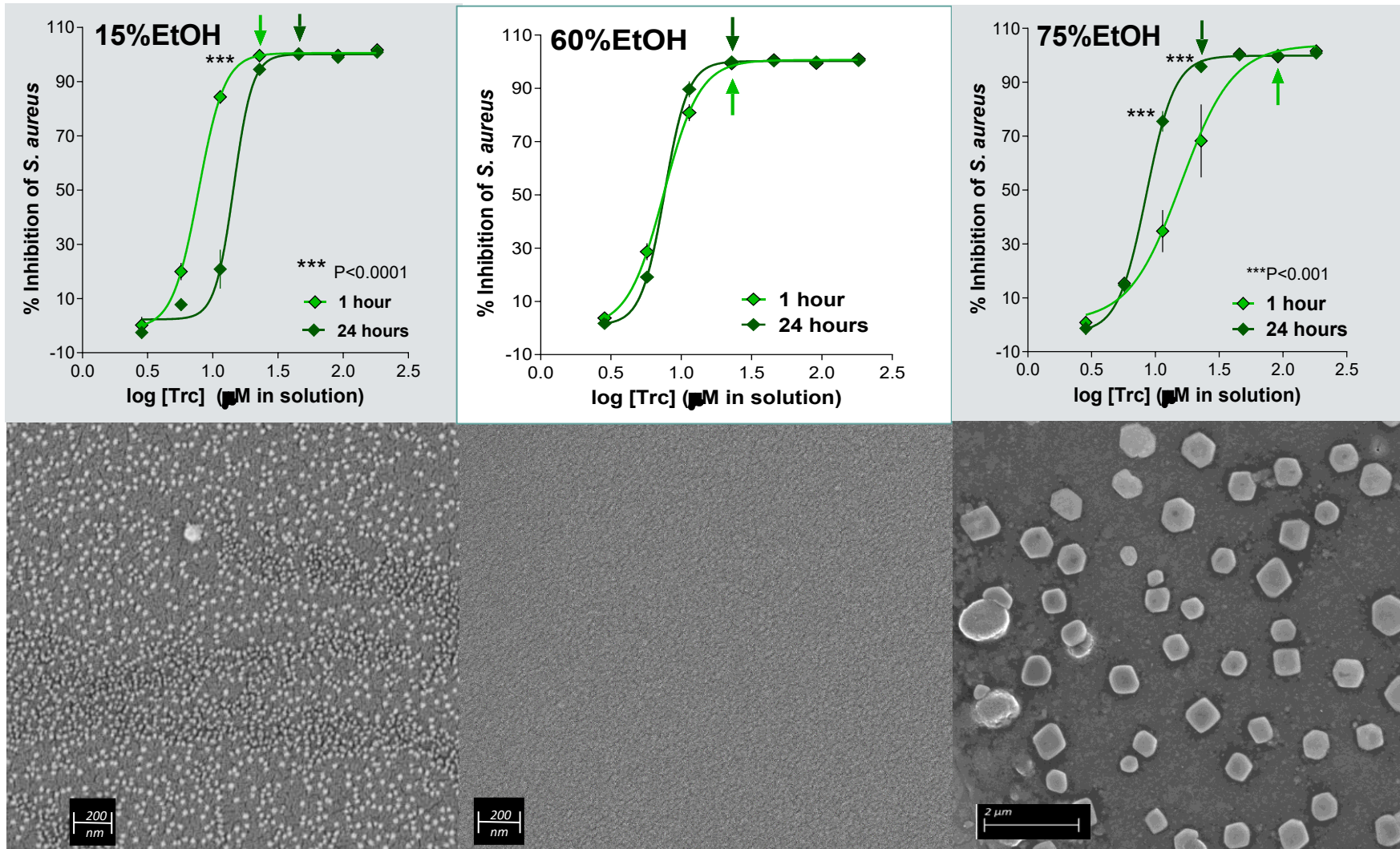
CDPs are active on hard plastics and textiles – **sometimes...**



Data from Dr Alana de la Harpe, BIOPEP, Stellenbosch University

How to win the surface depositing battle ?

Rather go with CDP films than CDP nanoparticles or crystals

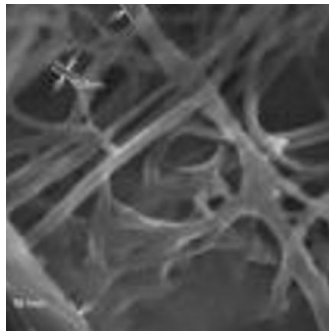
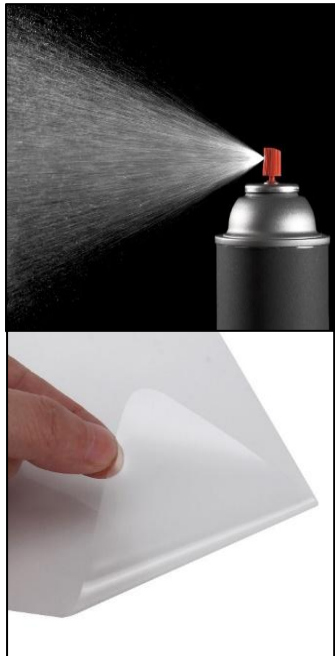


Making sterile films for surfaces

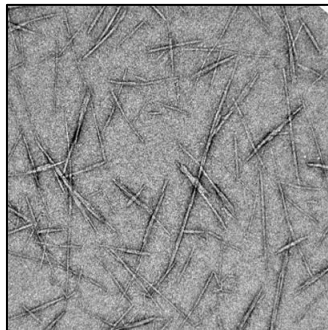


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Nanocelluloses for functionalisation by CDPs in spray films and in sheet films



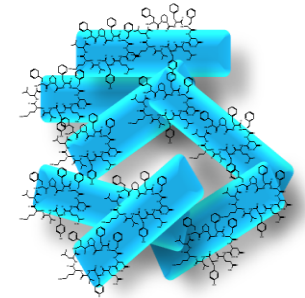
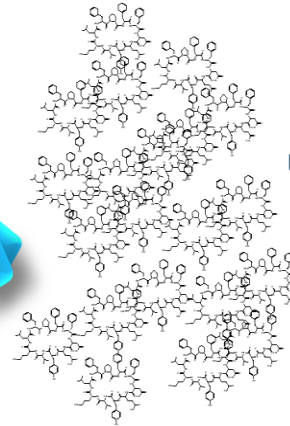
CNF
Valida, SAPPI



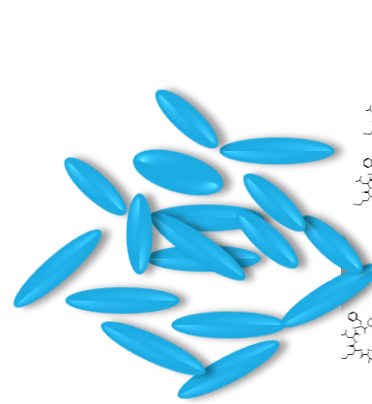
CNC
Melodea



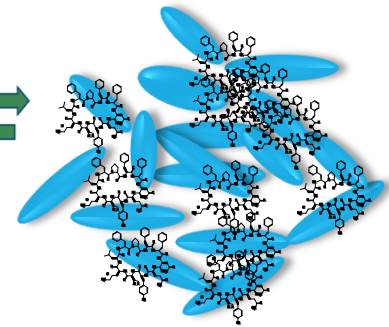
CNF



CDP-CNF



CNC

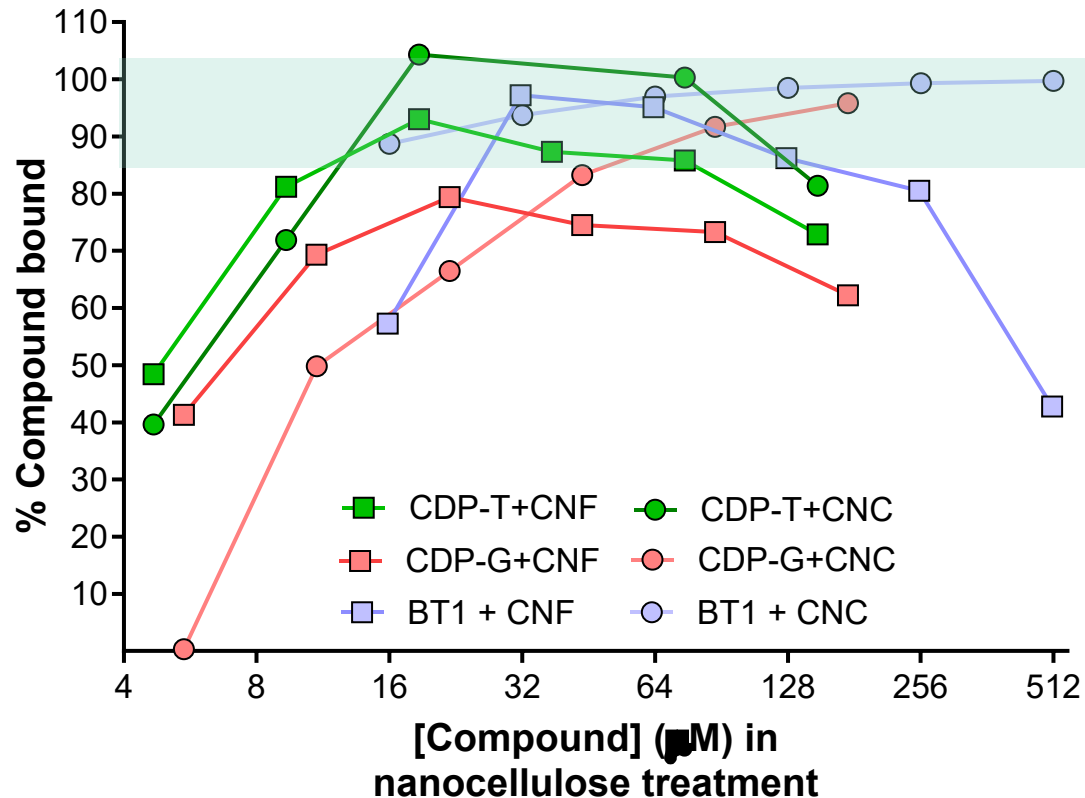


CDP-CNC

CDP-T dimers
CDP-G monomers

Making sterile films with nanocelluloses

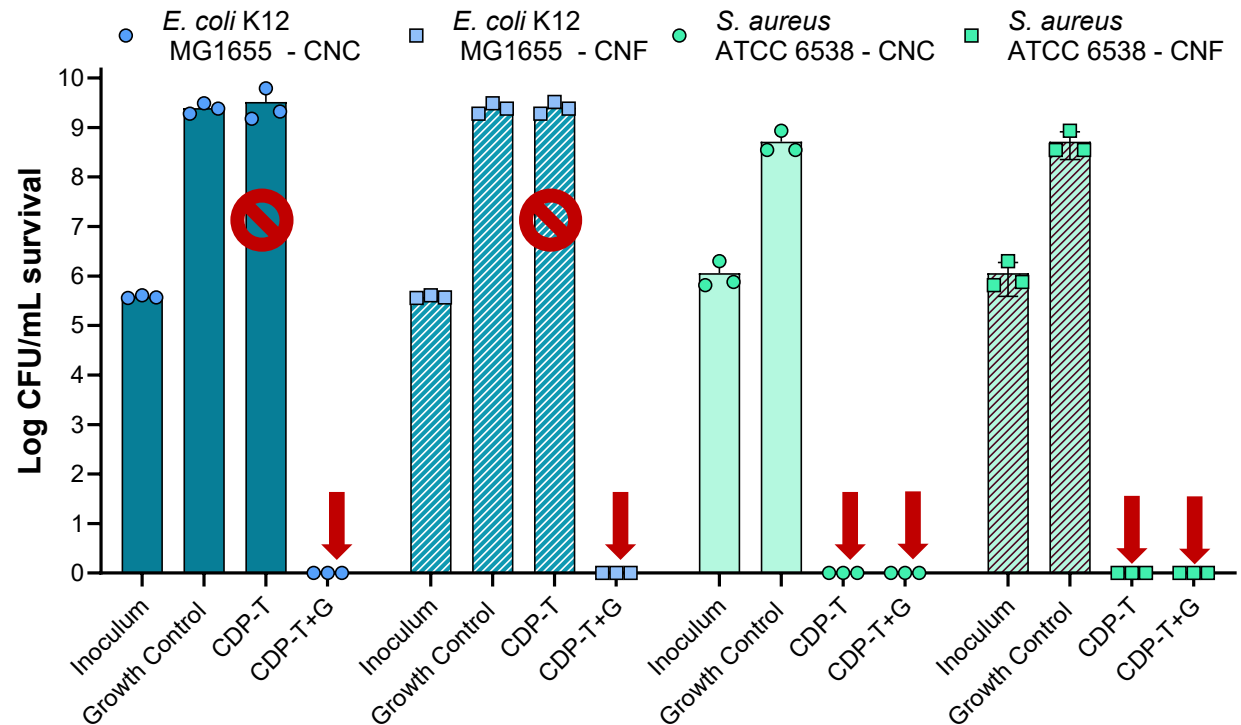
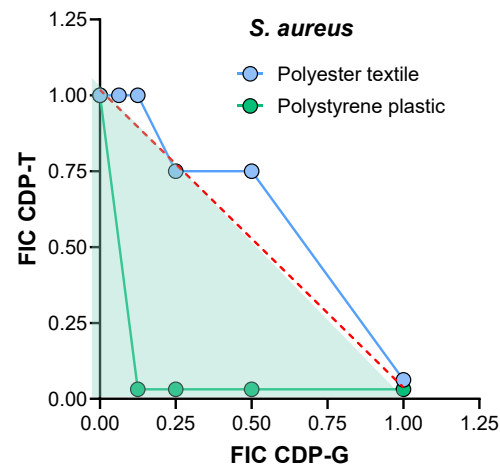
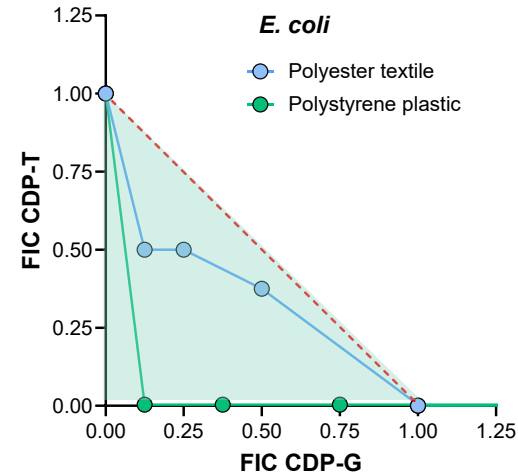
Check if the CDPs are binding to the nanocellulose carrier



Data from Triple-A-Coat project, EU Horizon
Simon Berge, BIOPEP, Stellenbosch University

Wining the sterile nanocellulose battle

Do not fight alone and choose alliance for CDP-T carefully



Treatments and Controls on 1% CNC and CNF

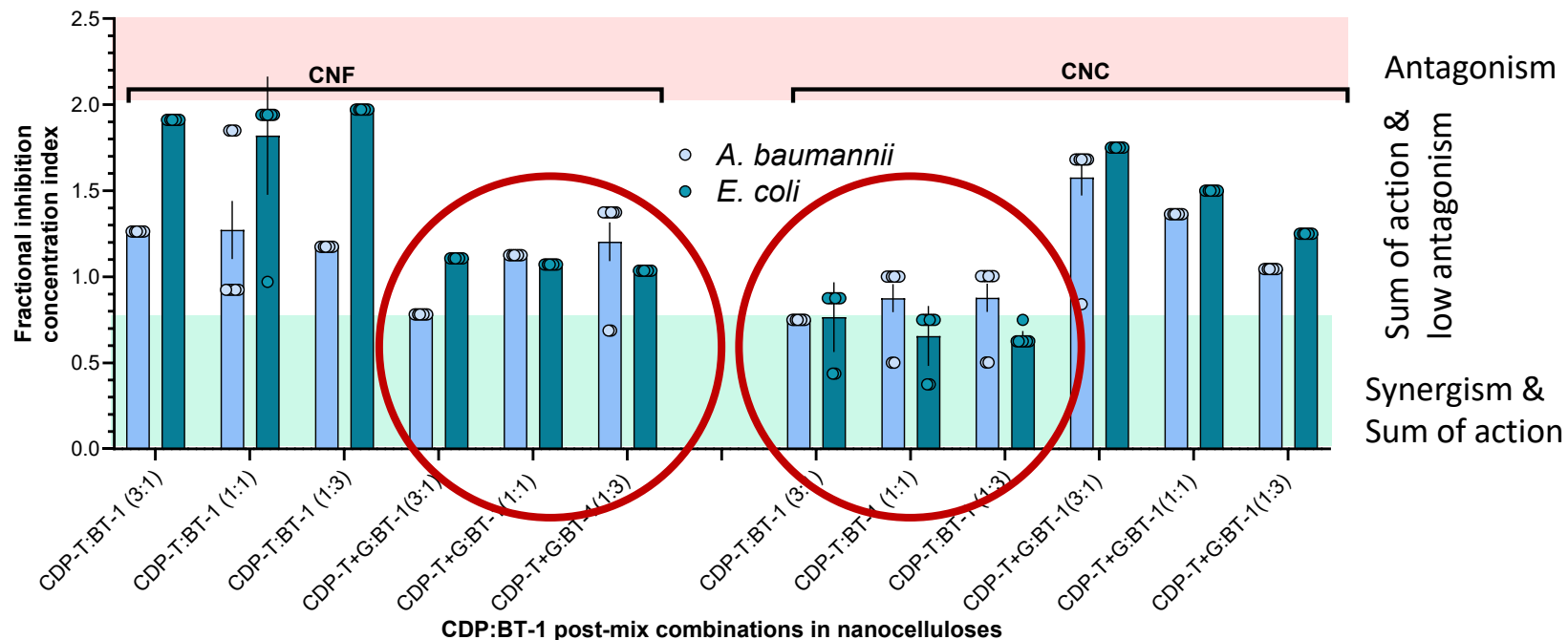
Data from EU Horizon Triple-A-Coat project
Dina El Jaramany, MICA, KU Leuven

How to win the sterile film battle ?

Do not fight alone and choose alliance for CDPs carefully



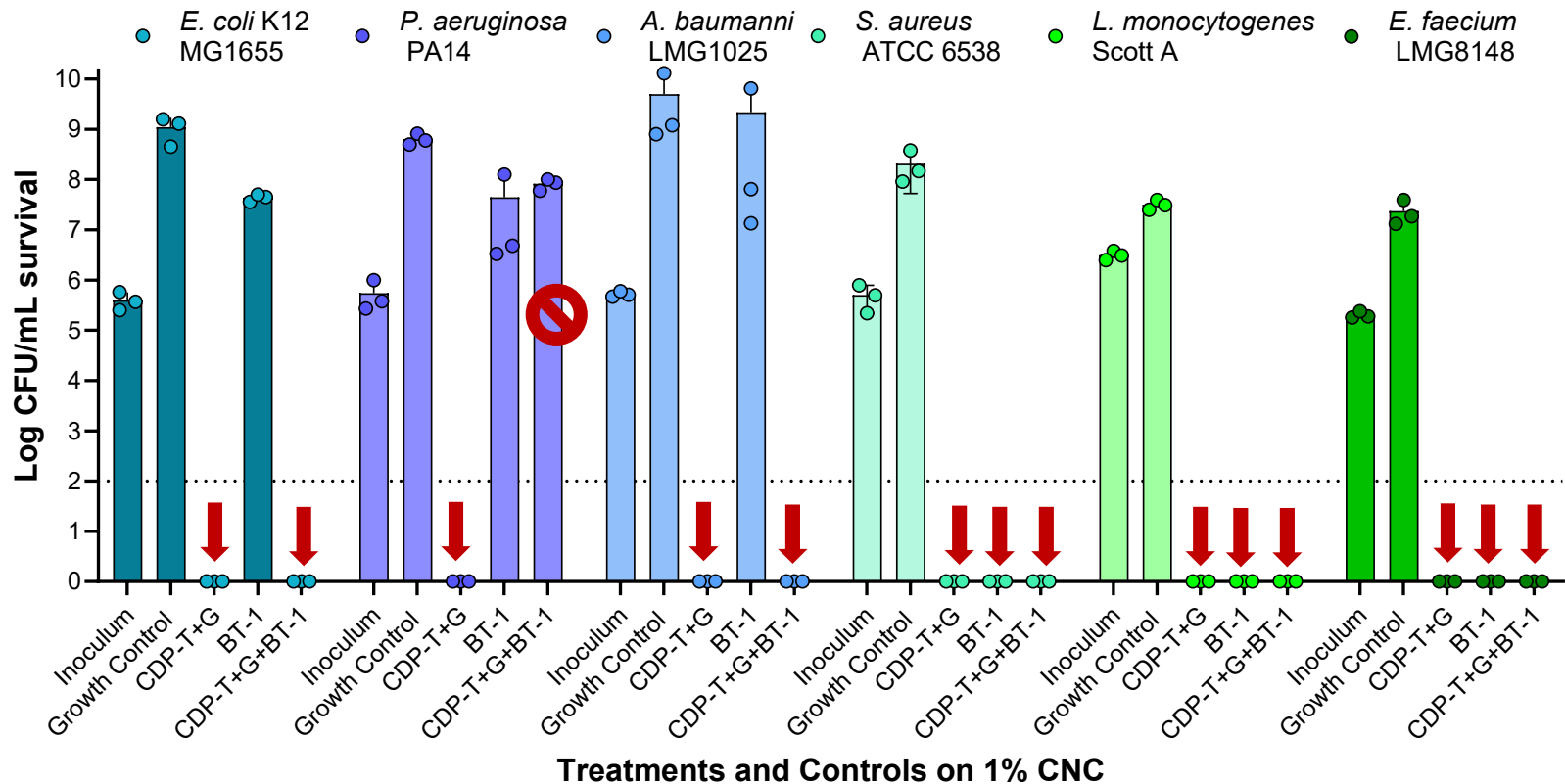
- 2-AIs have good broad spectrum antibiofilm/antimicrobial activity, but is **not antiviral**
- Resistance potential is limited because of multi target MOA
- Could have **some toxicity**



Data from Triple-A-Coat project
Simon Berge, BIOPEP, Stellenbosch University

Wining the sterile nanocellulose battle

Gram-negatives are fighting back and could **ESKAPE**, but can be eliminated synergistic CDP-combinations

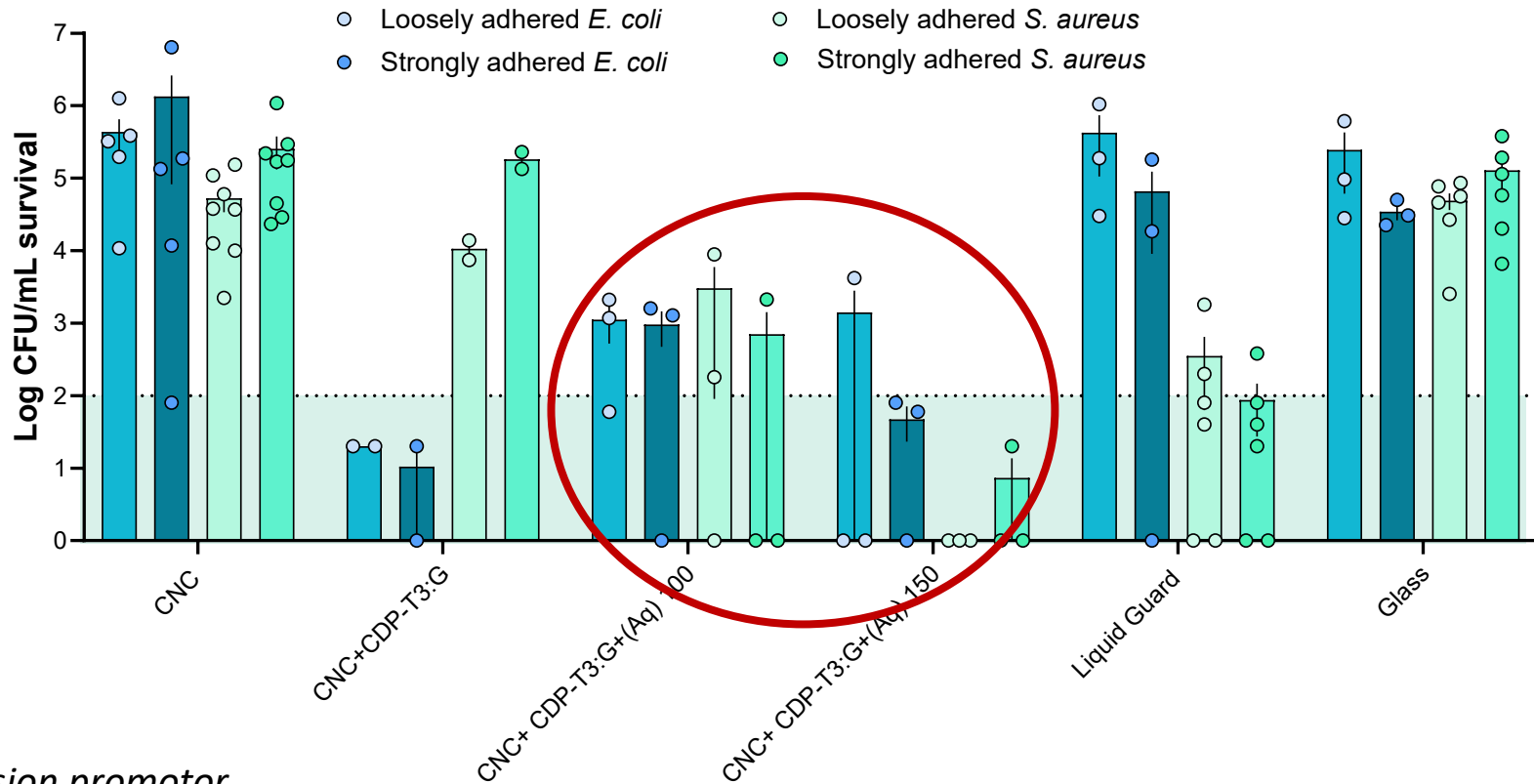


Data from EU Horizon Triple-A-Coat project
Dina El Jaramany, MICA, KU Leuven

Are we winning the lasting sterile film battle ?

Films with CDPs are active on glass – **sometimes...**

1.5% CNC-CDP coated glass challenged for 2 hours with 10^7 CFU/mL



Adhesion promotor
Aq – AqiBond™

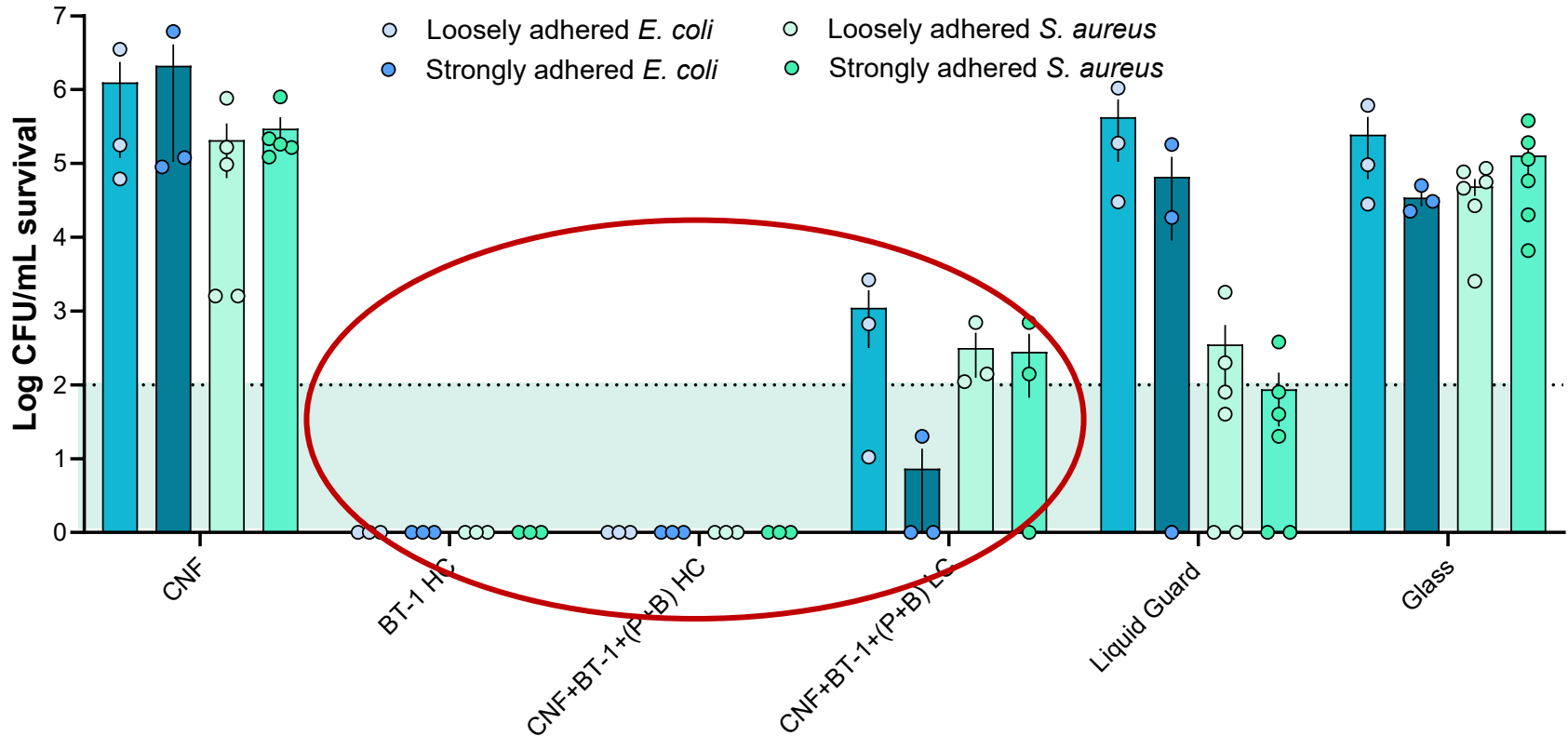
Treatments and controls on CNC coated glass

Data from EU Horizon Triple-A-Coat project
Dina El Jaramany, MICA, KU Leuven

Are we winning the lasting sterile film battle ?

Films with BT-1 are active on glass – **mostly ...**

1.5% CNF coated glass challenged for 2 hours with 10^7 CFU/mL



Adhesion promotor

P – PDA

B – Boric acid

Treatments and controls on CNF coated glass

HC = high concentration

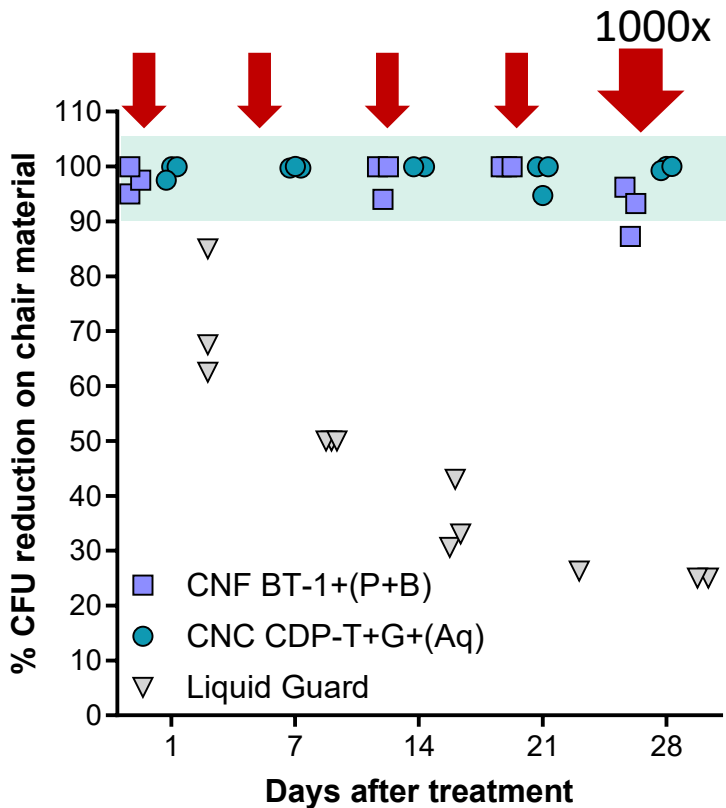
LC = low concentration

Data from EU Horizon Triple-A-Coat project

Dina El Jaramany, MICA, KU Leuven

A victory in the real lasting sterile film battle

CNC-CDP films and CNF-BT-films are keeping the bus chairs cleaner and safer





Funders:

BIOPEP Peptide Fund
EU Horizon
NRF (bursaries)



*Post-graduate students
and post-docs
in the BIOPEP group*



Collaborators:



Triple A COAT
CONSORTIUM



Theo
Willemse

Simon
Berge

Alana de
La Harpe

Dina El
Jaramany
MICA, KUL

KU LEUVEN

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