Activity of combinations of an enzymatic cocktail (CDD) with antibiotics against biofilms of clinical isolates of ESKAPE pathogens

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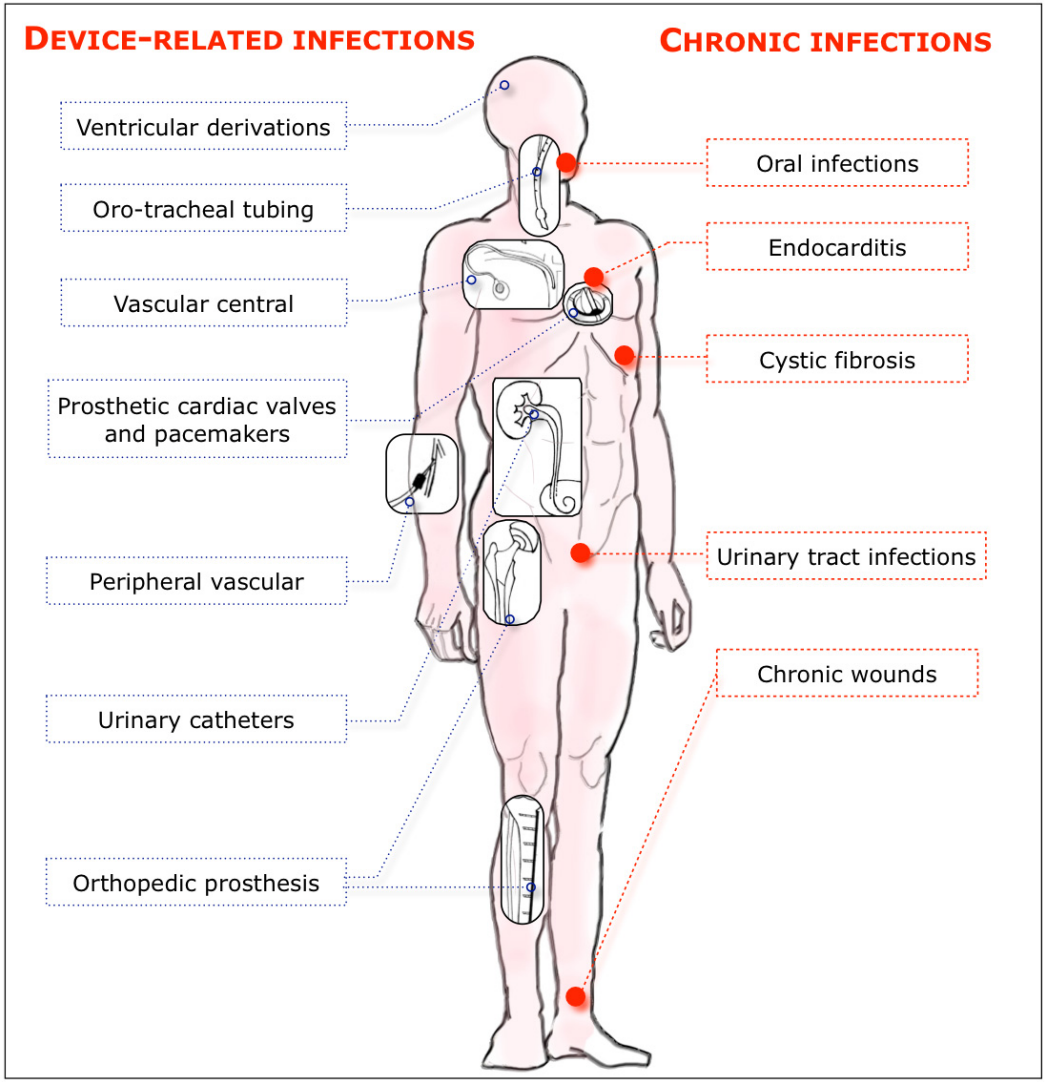
There is no Escape from the ESKAPE Pathogens

"ESKAPE" Pathogens

- *Enterococcus faecium*
- *Staphylococcus aureus*
- *Klebsiella pneumoniae*
- *Acinetobacter baumannii*
- *Pseudomonas aeruginosa*
- *Enterobacter* species



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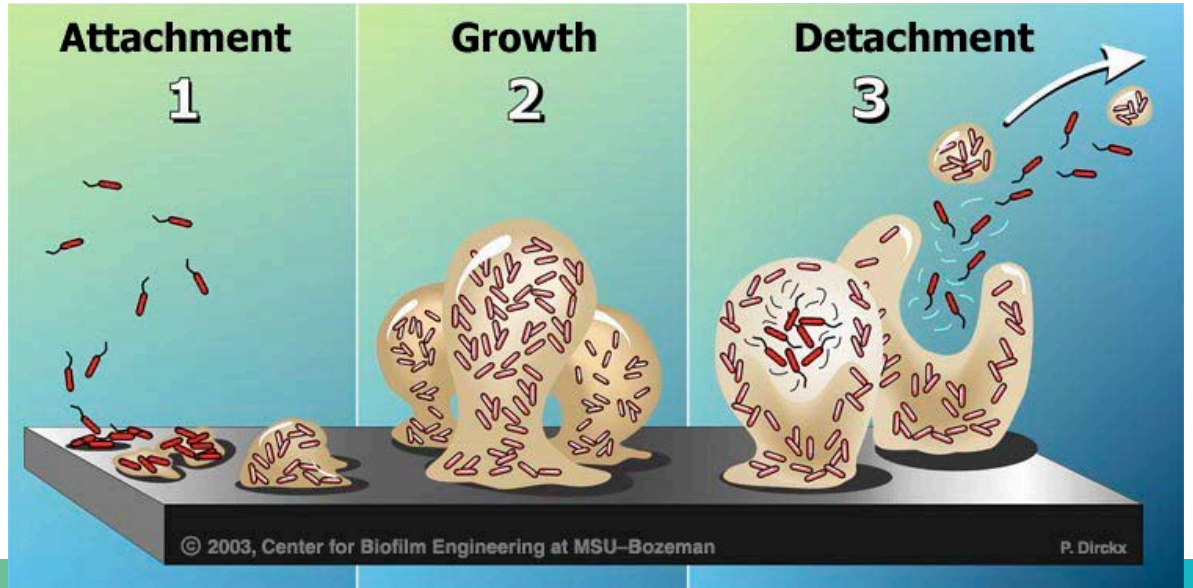
Biofilms facts

- 99% of bacteria grow as aggregated, sessile communities (biofilm)
- Bacteria within biofilm are highly protected and highly resistant to antibacterial treatments (up to 1000 times more resistant to antibiotics than planktonic bacteria)

- Bacteria within biofilm are genetically different than bacteria in the planktonic state
- NIH estimates more than 80% of infections in humans are caused by microbial biofilm.



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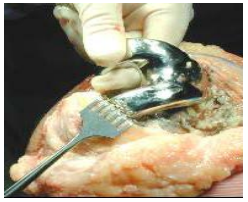
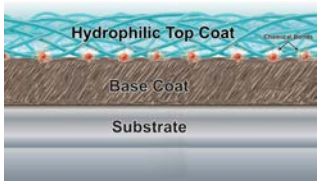
Current therapy and prophylaxis of Biofilm Infections

Physical and surgical methods: in cases of infected medical devices, removal of the device is often necessary to treat the infection.



Antimicrobial therapy: poor access
β-lactams, fluoroquinolones, aminoglycoside,

Preventing microbial attachment



Goal of the study

Develop a new enzymatic combination to specifically restore activity of antibiotics and eradicate ESKAPE biofilm.

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Methods

In vitro **static biofilm model**

Ex vivo **biofilm model: Human urinary catheter**

Assessment of enzymatic activity against Biofilm matrix

Crystal violet assay

Assessment of enzymes-antibiotics activity against bacterial viability

Resazurin assay

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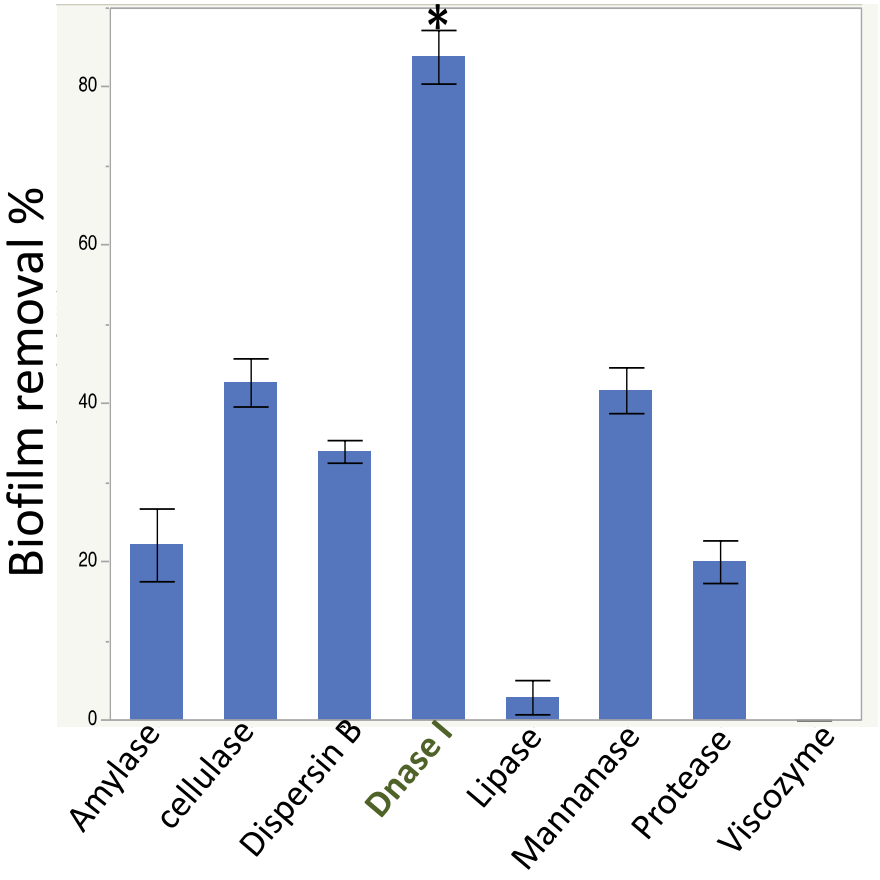
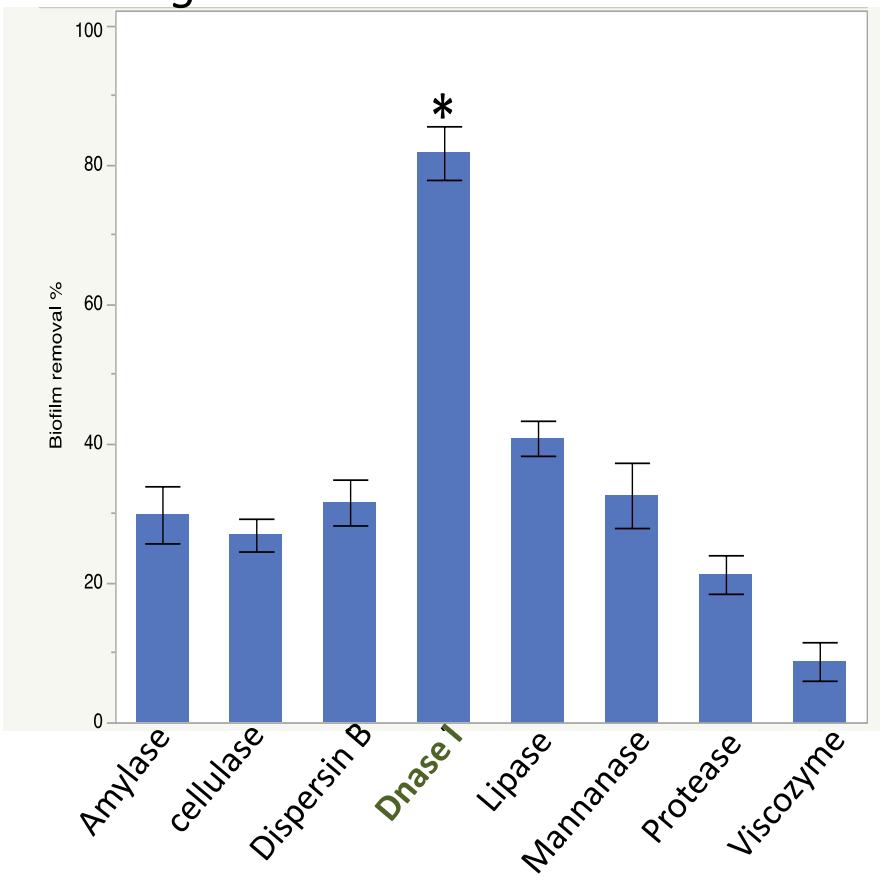
Design of a broad spectrum enzymatic cocktail

E.coli



P.aeruginosa



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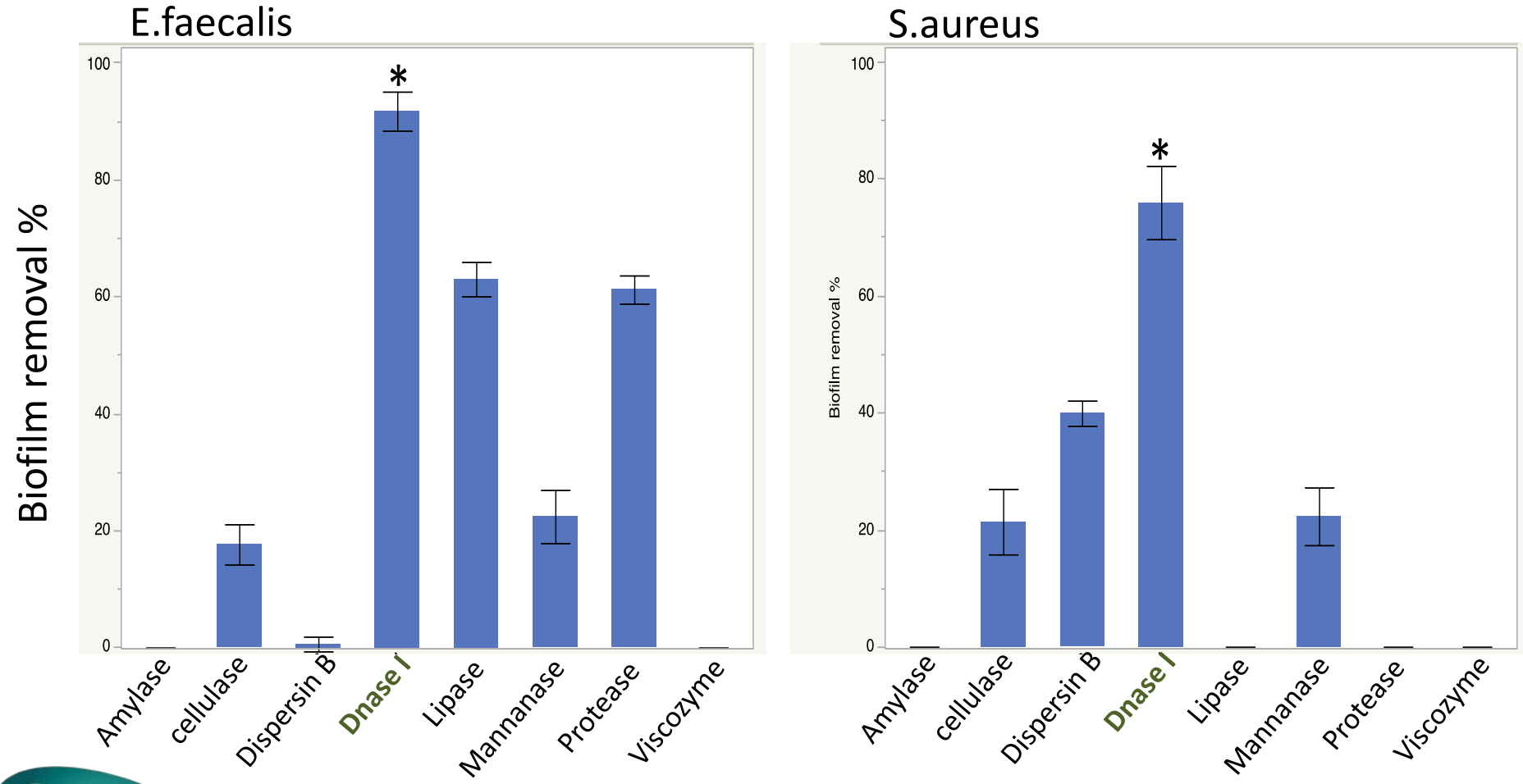
Design of a broad spectrum enzymatic cocktail



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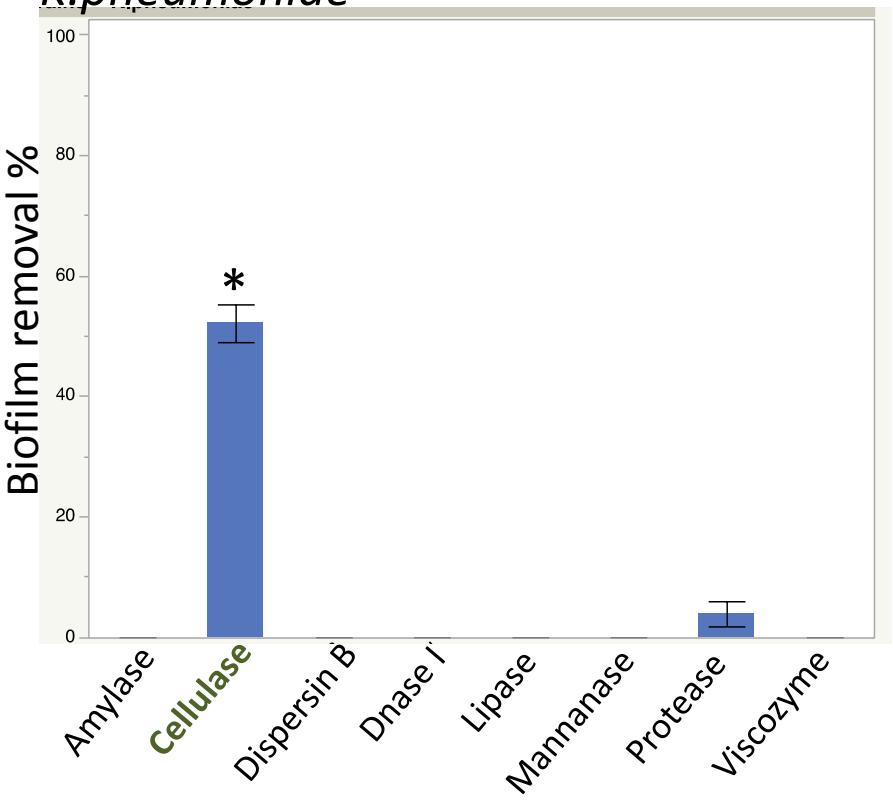
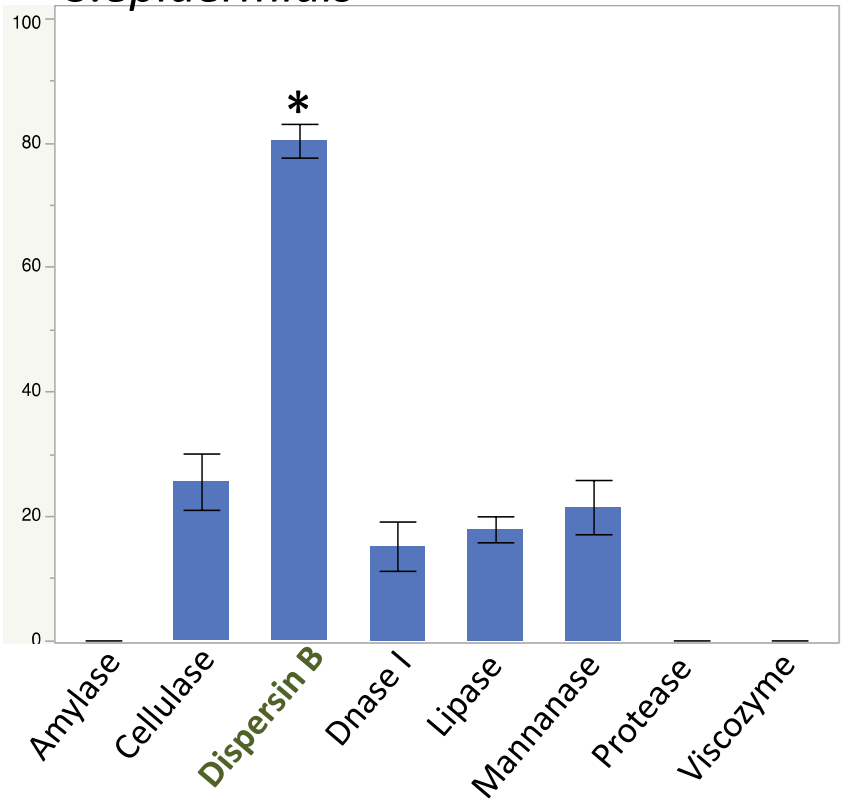
Design of a broad spectrum enzymatic cocktail

K.pneumoniae



S.epidermidis



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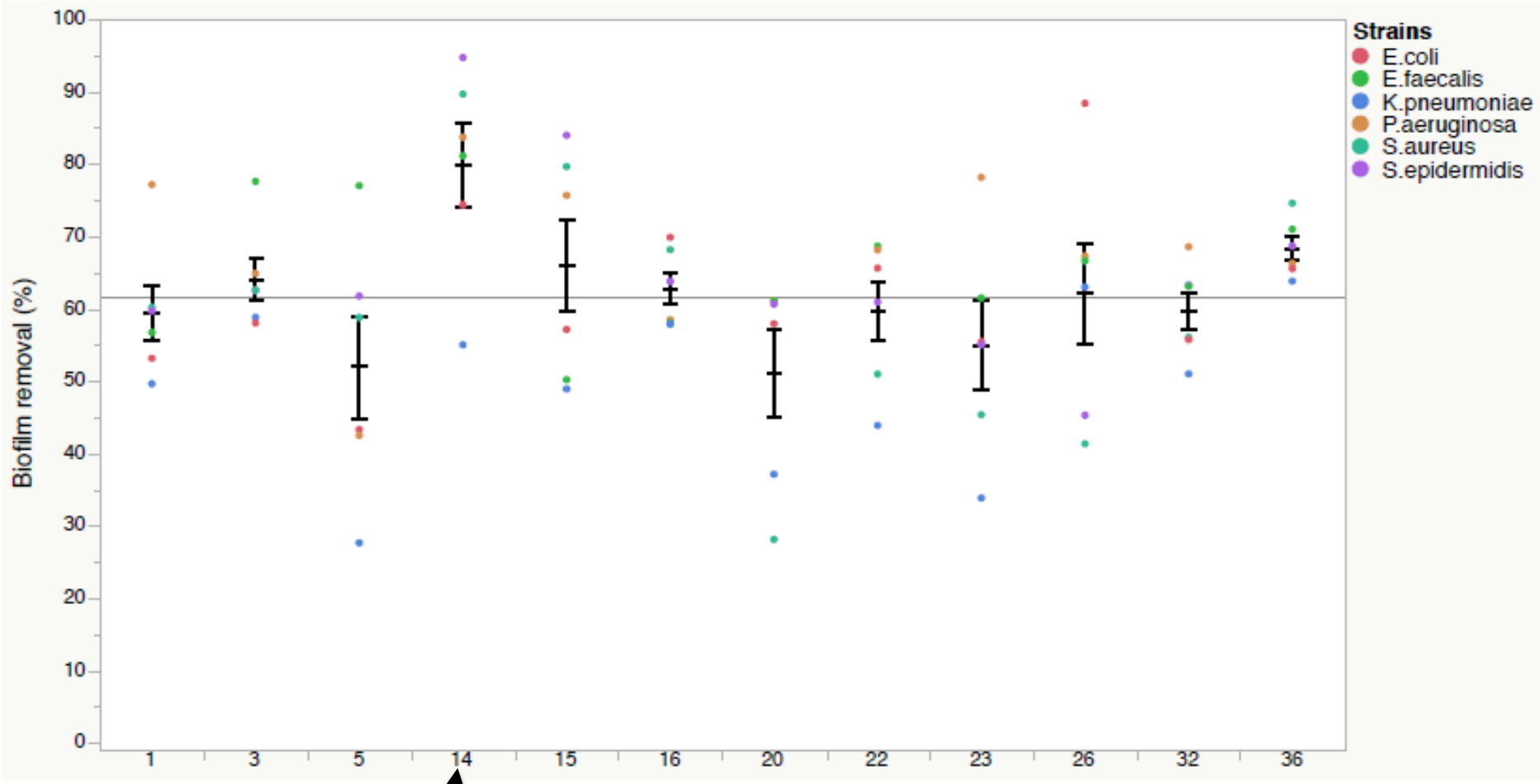
Percentage of biofilm removal after exposure to combinations used for enzymatic cocktail design



Enzymatic cocktail CDD

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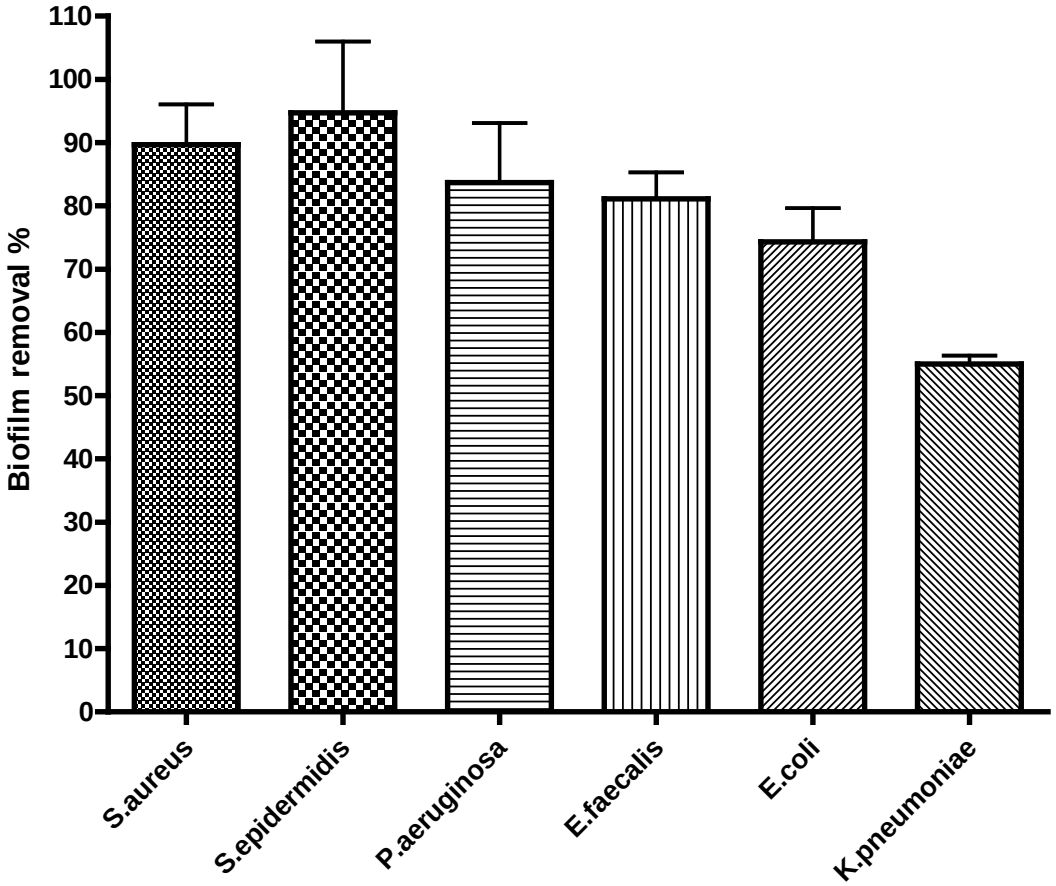
Percentage of biofilm removal after exposure to enzymatic cocktail CDD in *In vitro* biofilm models

***In vitro* static biofilm model**



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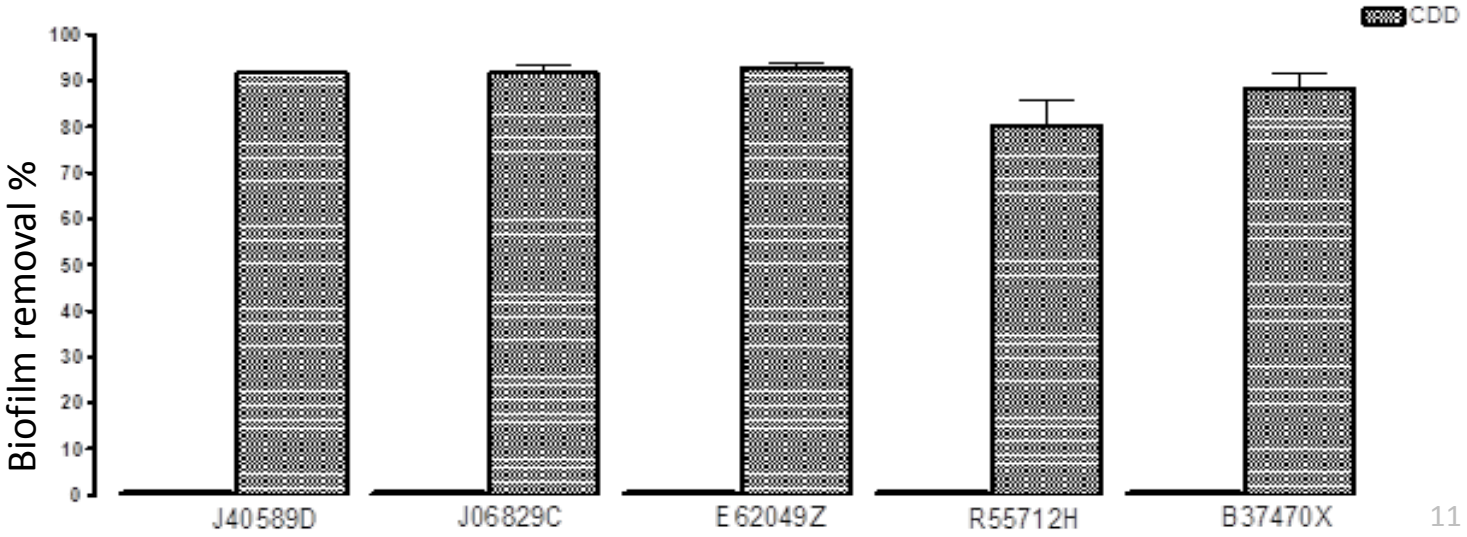
Percentage of biofilm removal after exposure to enzymatic cocktail CDD in *Ex vivo* biofilm models

Ex vivo biofilm model: Human urinary catheter

Crystal violet assay



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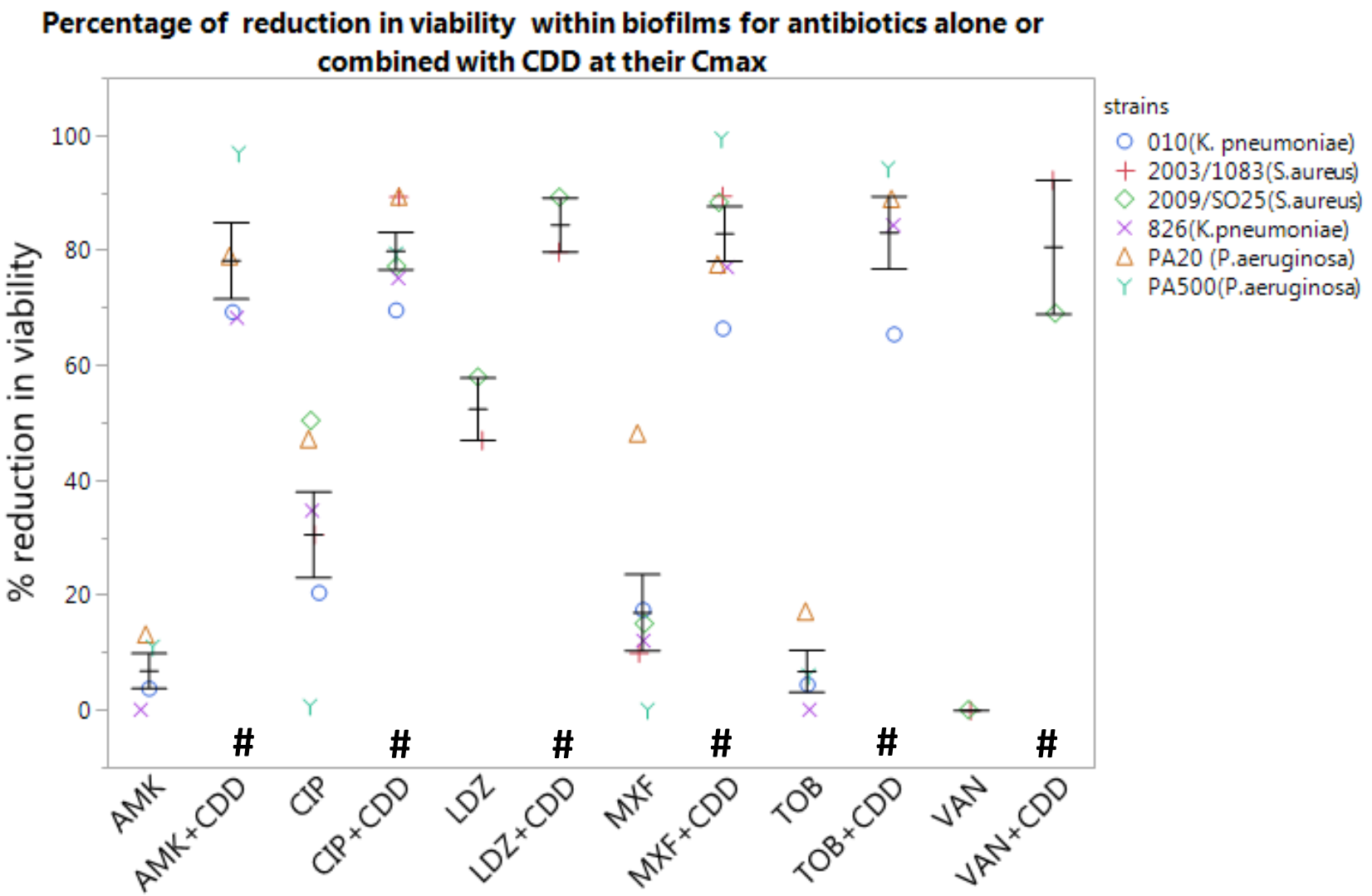

 # highlights combinations for which the mean reduction was higher than that observed for drugs alone (Statistical analysis: one-way ANOVA with Tukey's post-hoc test)

reduction in viability compared to untreated control

Take home messages

CDD showed highest biofilm removal against ESKAPE biofilms of *S.aureus (*89%*), S.epidermidis (*94%*), P.aeruginosa (*83%*), E.faecalis (*81%*), E.coli (*74%*) and K.pneumoniae* (55%)

At human Cmax TOB, AMK, MXF, CIP, VAN, LDZ were weakly active against bacteria growing in biofilms

Combining CDD with 6 antibiotics belonging to 4 classes proves highly synergistic against biofilms of 6 clinical isolates.

This opens perspectives for testing these enzymes as adjuvant for the treatment of biofilm infections.

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Thank you for your attention!

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