

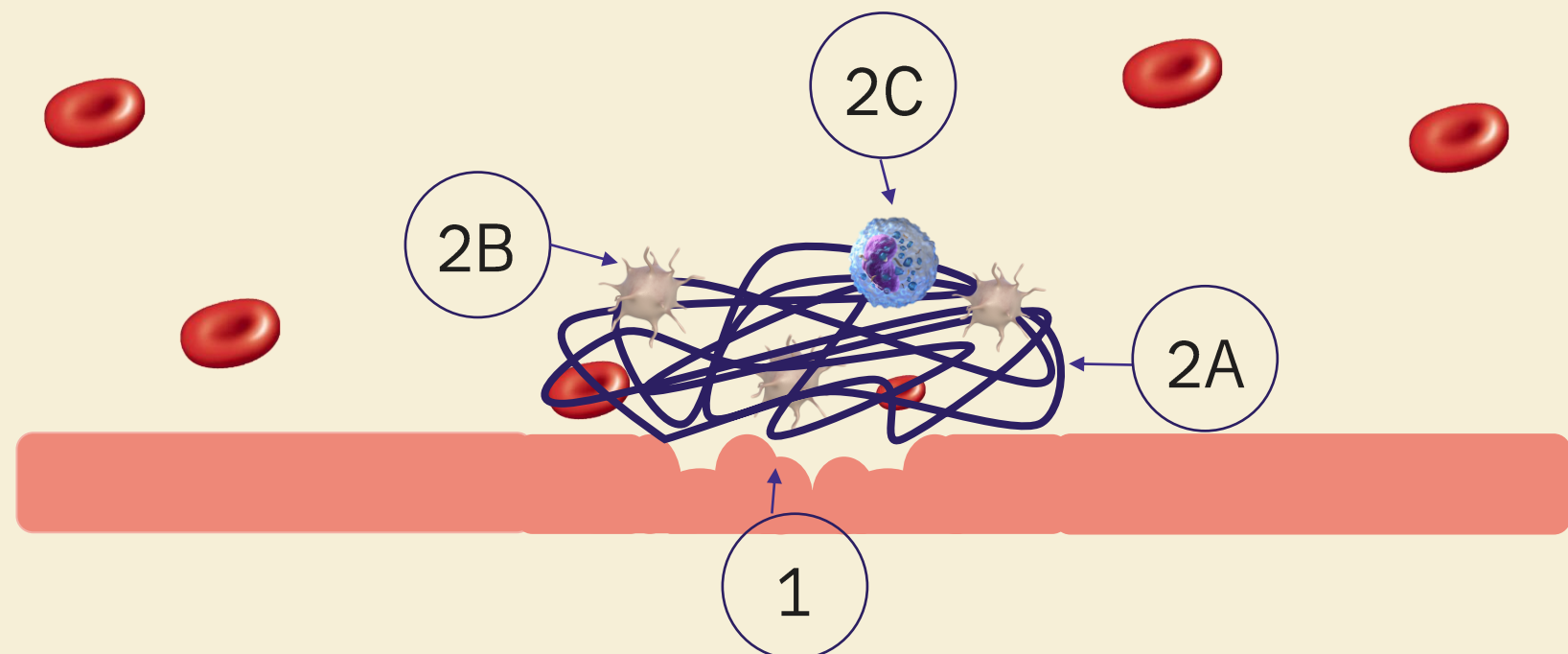
Dynamic of antibiotic tolerance correlates to biofilm formation in an infective endocarditis (IE) simulation model

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Background

Infective Endocarditis (IE):

- Infection of inner surface of the heart, often involving native or prosthetic valves¹
- Most common microbial etiologies: *Staphylococcus aureus*, *Streptococcus spp.*, *Enterococcus faecalis*
- Pathophysiology²:
Minor endothelial defect (1) → healing response: sterile vegetation (2) of fibrin (A), thrombocytes (B) & immune cells (C) → can be colonized during temporary bacteremia → growth of infected vegetation, biofilm formation and increased inflammation



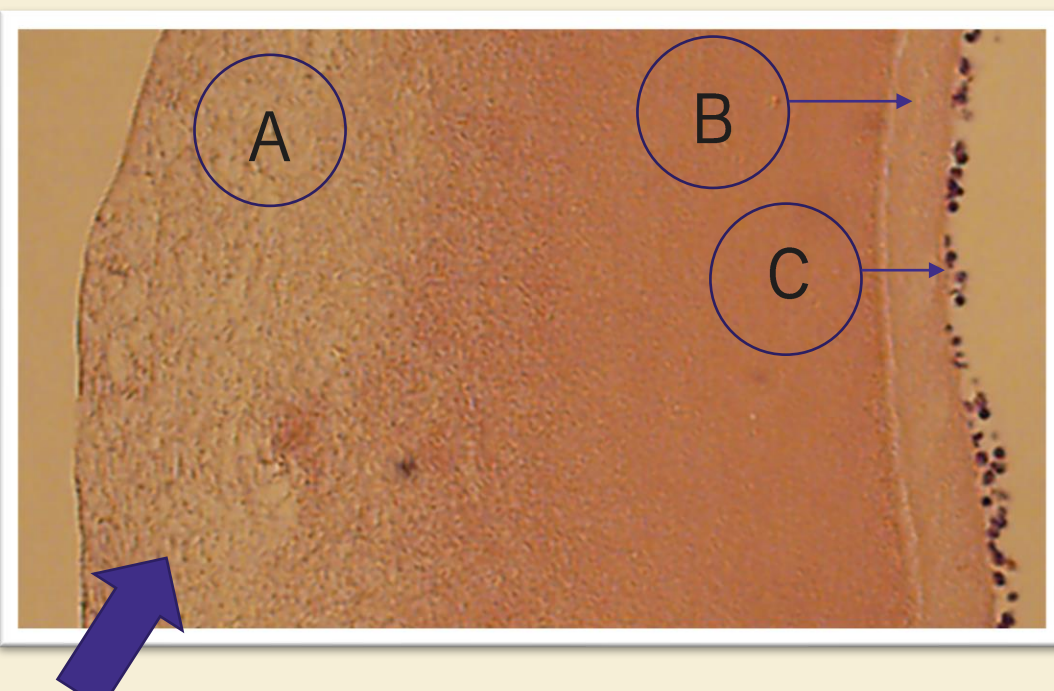
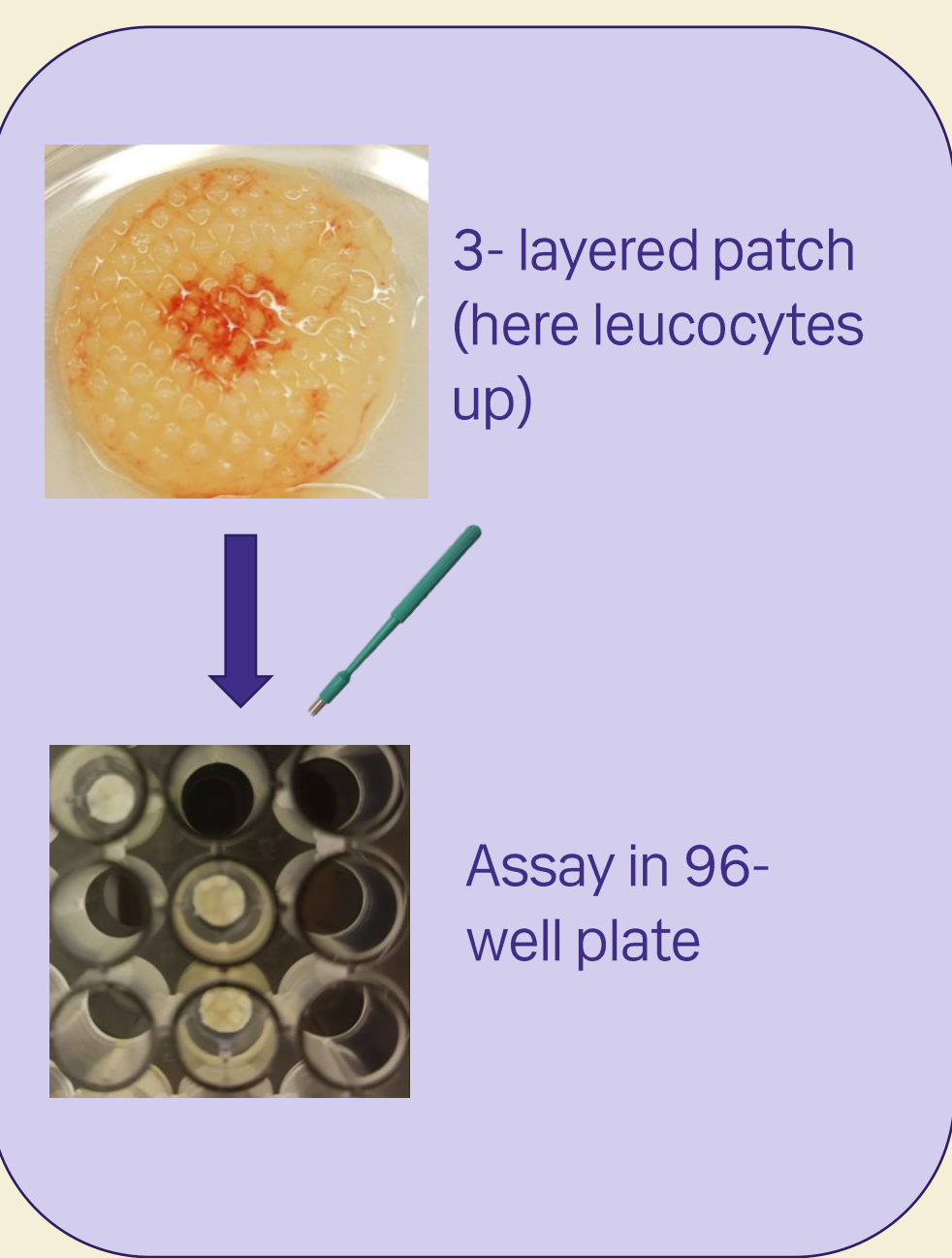
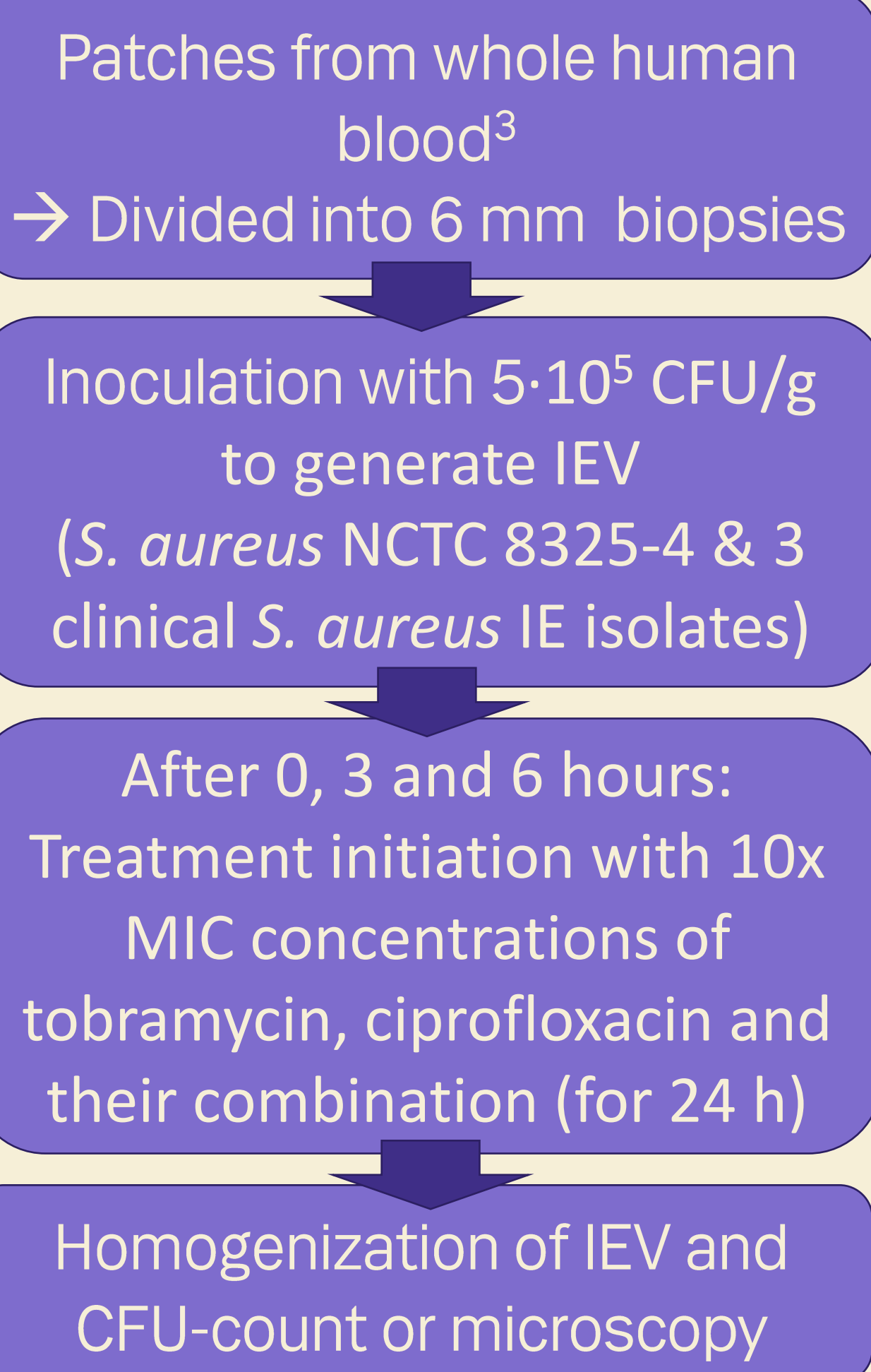
- High mortality
→ Models needed to predict new effective treatment

Aim

Investigate the dynamic between appearance of bacterial aggregates and development of antibiotic tolerance

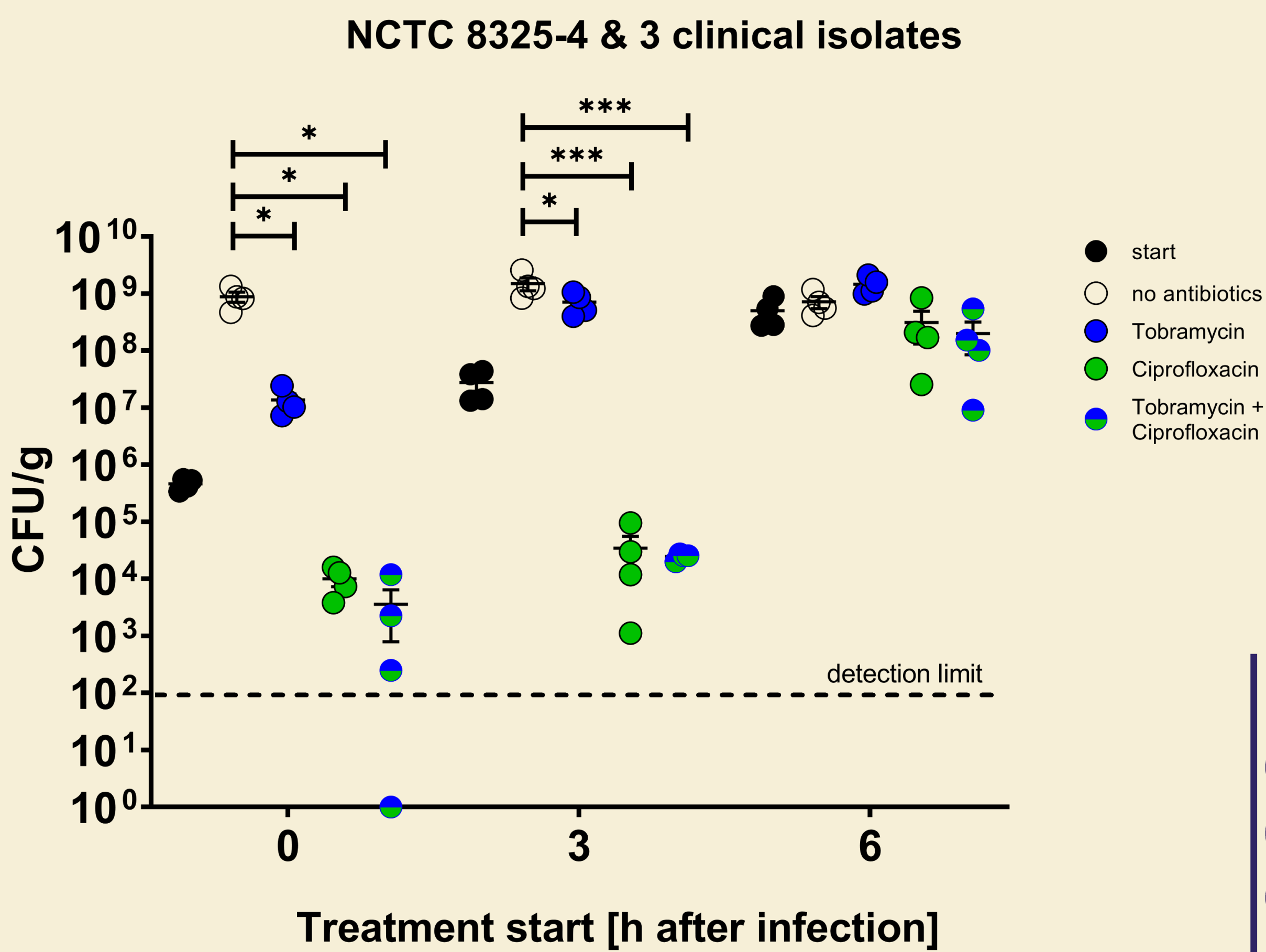
Method

Simulated IE Vegetations (IEVs)

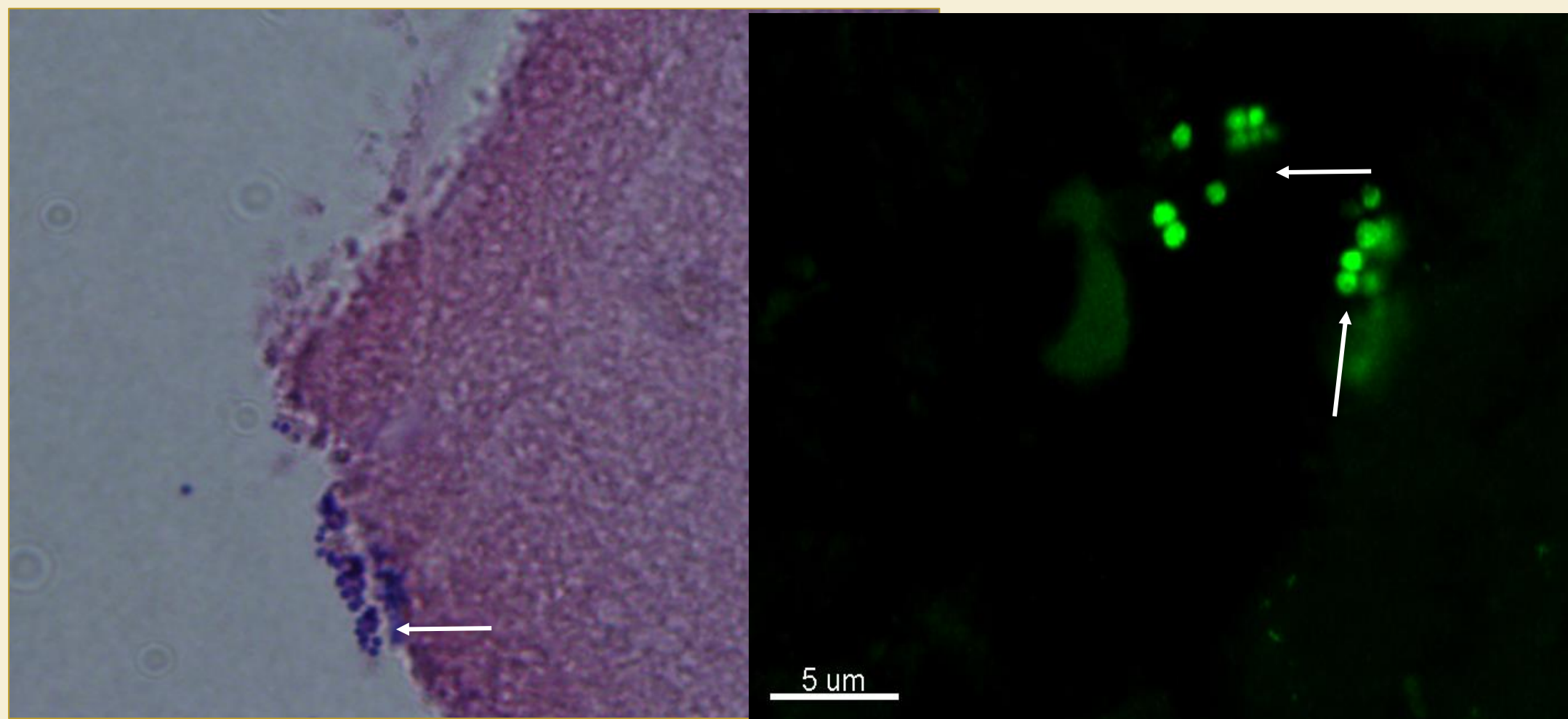


Same components as sterile healing vegetation in IE:
3-layered IEVs: Fibrin (A), thrombocytes (B) and leucocytes (C)

Results



- Treatment becomes inefficient on mature biofilms, coinciding with appearance of bacterial aggregates
- One data point represents data for one *S. aureus* strain (2-3 blood donors each)



- Visible biofilm aggregates on fibrin layer after 6 hours
- No visible biofilm aggregates after 0 and 3 hours

Time course of Biofilm development correlates with development of antibiotic tolerance

- Biofilms appear mature at 6h after inoculation
- Tolerant towards 10x MIC concentrations of tobramycin, ciprofloxacin and their combination
- Microscopically visible aggregate formation

Relevance

- Model to rapidly screen new/optimal treatment strategies for IE (e.g. antibiotic combinations or non-antibiotic, anti-biofilm strategies)

Discussion

References:

- ¹Holland et al., 2017, Nat Rev Dis Prim
- ²Werdan et al., 2014, Nat Rev Cardiol.
- ³Schwartz et al., 2021, APMIS

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