

ESTABLISHMENT OF A CHRONIC ORTHOPAEDIC INFECTION MODEL WITH MATURE BIOFILM FORMATION USING AN *IN VITRO-IN VIVO* HYBRID APPROACH

Raphaëlle Youf, Jana Krieger, Adèle Huc, Luc Brasz, Ruth Schewior, Gopala Mannala, Volker Alt, Martijn Riool

Department of Trauma Surgery, University Hospital Regensburg, Franz-Josef-Strauß-Allee 11, 93053 Regensburg, Germany

From acute to chronic orthopaedic infections

- Biomaterial-associated infections (BAI) is one of the most common complications in trauma patients.
- Despite the use of conventional local and systemic antibiotic therapies after surgery, persistent/chronic infections caused by *Staphylococcus aureus* could lead to therapeutic failures.
- Rifampicin, one of the only antibiotics recommended against biofilm-related infections, is efficient to treat early diagnosed infections. However, against late-onset infections involving persistent biofilms, its efficacy is drastically decreased, reducing therefore the choice of treatment options
- Various rifampicin resistance mechanisms and the dysregulation of the host immune system could be involved.
- The development of *in vivo* chronic BAI models to optimize antibiofilm treatments is a major challenge.
- Previously, our team established an early-stage biofilm implant infection model in *Galleria mellonella* larvae.
- We aim to develop *in vitro* and *in vivo* assays to evaluate the impact of biofilm maturation on the treatment efficiency of rifampicin against *S. aureus*.

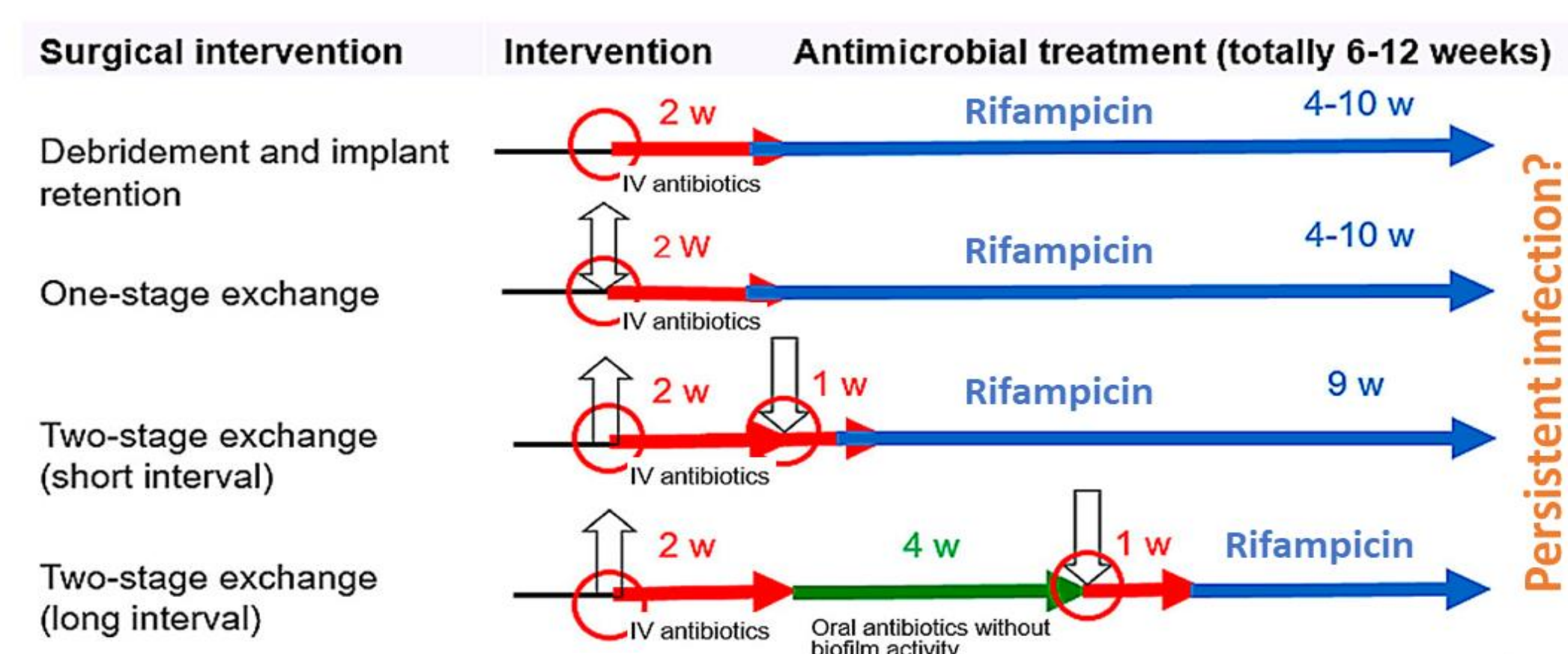
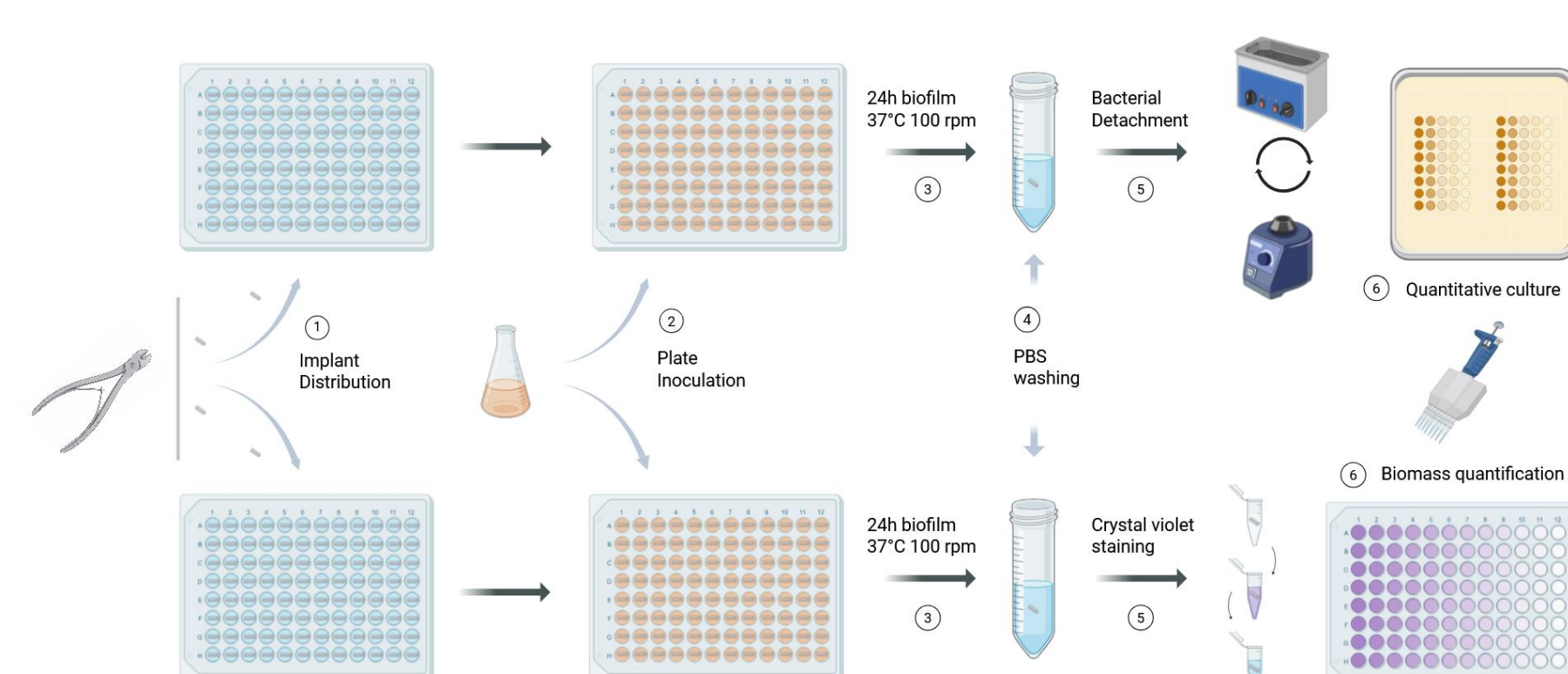


Figure 1. Treatment algorithm for implant-associated infections. Adapted from Conen, A., et al. 2020. *Swiss medical weekly*, 150, w20208.

Characterization of biofilm producers



Parameters:

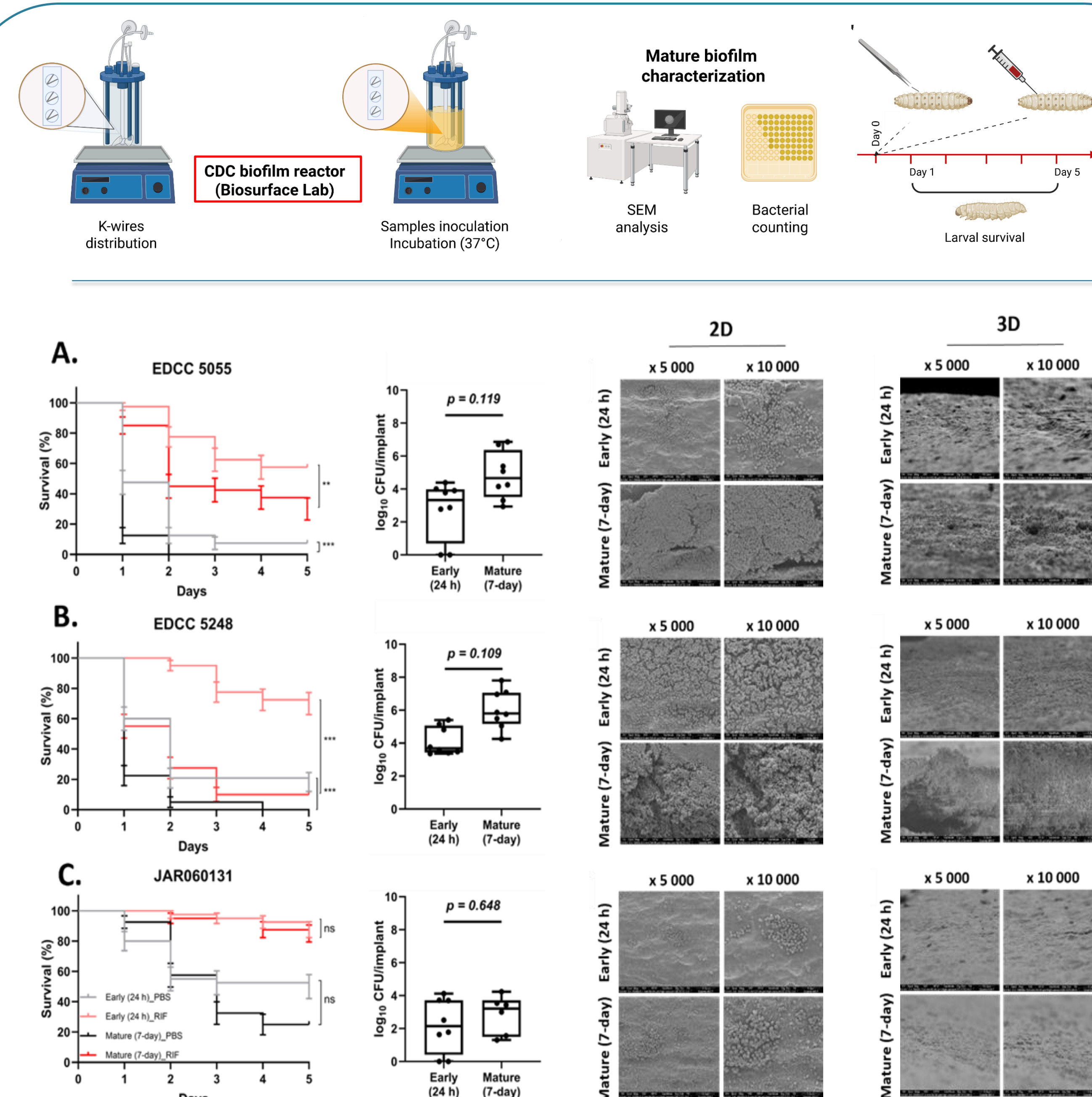
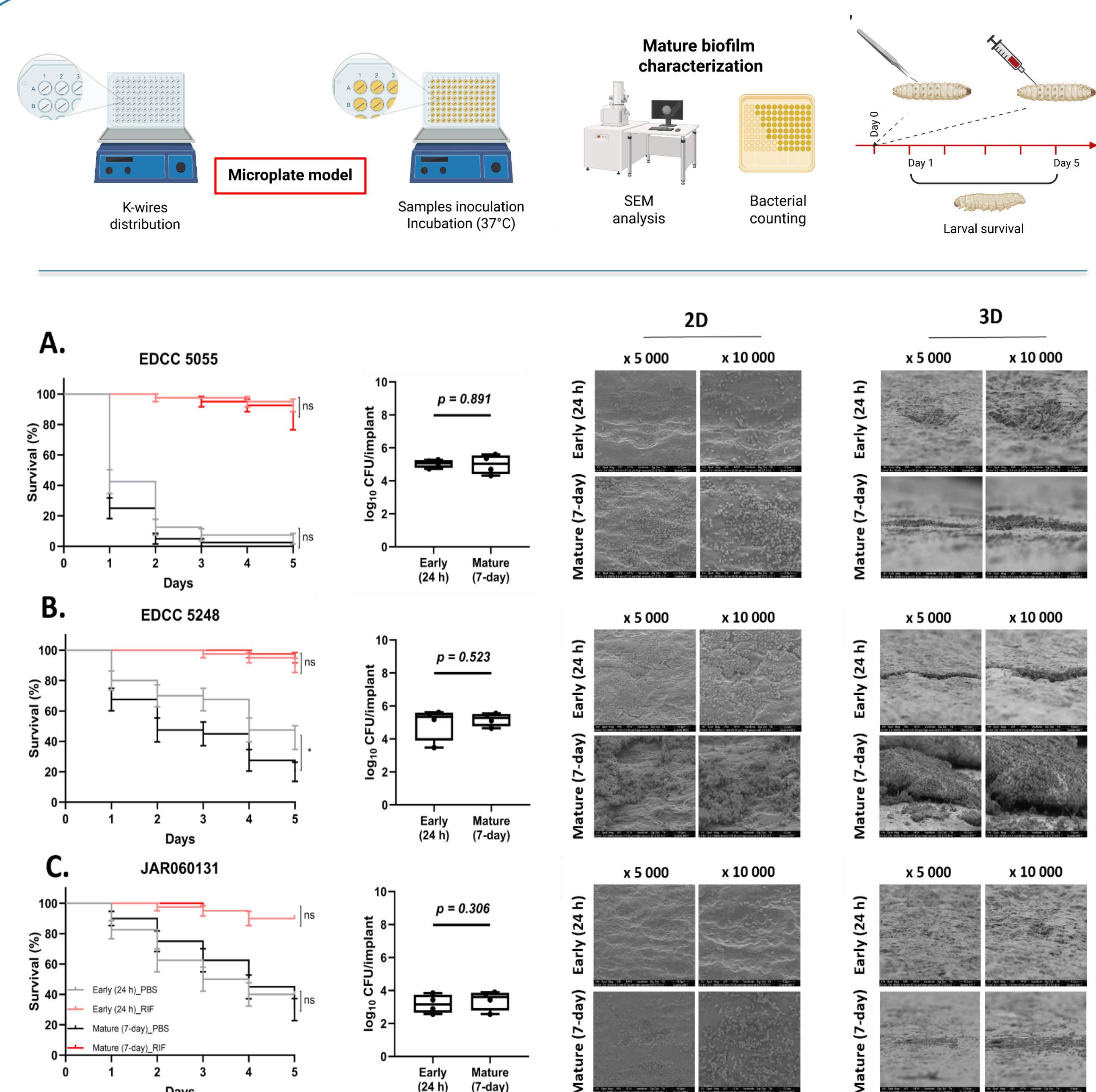
Weak biofilm:
 $x < 2 \times \text{ODc}$
viable burden of $< 3.00 \log_{10} \text{CFU/K-wire}$

Moderate biofilm:
 $2 \times \text{ODc} \leq x < 4 \times \text{ODc}$
viable burden of $> 3.00 \log_{10} \text{CFU/K-wire}$

Strong biofilm:
 $x \geq 4 \times \text{ODc}$
viable burden of $> 3.00 \log_{10} \text{CFU/K-wire}$

<i>S. aureus</i> strain	Clinical source	Log ₁₀ CFU/K-wire	CV/K-wire	Biofilm forming capacity	Selected
EDCC 5464	Human, FRI	3.51 ± 0.71	1.59 ± 1.02	strong	no
EDCC 5055	Human, wound, groin	4.17 ± 0.56	1.24 ± 0.66	strong	yes
EDCC 5495	N/A	3.25 ± 0.34	1.11 ± 1.05	strong	no
EDCC 5249	N/A	3.88 ± 0.25	0.52 ± 0.24	moderate	no
EDCC 5471	N/A	4.20 ± 0.93	0.49 ± 0.16	moderate	no
EDCC 5248	Human, oral cavity	4.26 ± 0.47	0.34 ± 0.16	moderate	yes
EDCC 5456	Human, PJI	2.35 ± 0.72	0.25 ± 0.04	weak	no
EDCC 5003	N/A	2.73 ± 0.90	0.25 ± 0.03	weak	no
JAR060131	Human, PJI	1.88 ± 0.55	0.20 ± 0.08	weak	yes

Development of an *in vitro-in vivo* models



Toward optimizing treatment strategies for chronic infections

Conclusions

- High variability in between strains to initiate the maturation on orthopaedic metallic implants.
- Biofilm maturation under dynamic growth conditions promoted dense and multilayered communities.
- Rifampicin treatment-failure due to biofilm maturation was observed when using the CDC biofilm reactor.

Perspectives

Combinatorial treatment based on rifampicin are investigated in the lab by using this experimental set-up to improve rifampicin treatment in case of infections involving highly matured biofilms

Raphaëlle Youf, PhD.

Lab. Experimental Trauma Surgery,
Department of Trauma Surgery,
University Hospital Regensburg,
Franz-Josef-Strauss-Allee 11,
93 051 Regensburg, Germany



raphaelle.youf@ukr.de

