New advanced blood infection model

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Project supported in 2018 by:

Danmarks 3R-Center
RRR

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Region Syddanmark

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Svendborg Sygehus

Bloodstream infections

- Intravenous catheters – a common primary cause
- 10-15% of cases lead to complications (endocarditis etc.)
- Staphylococci are main causative pathogens.

Current models of vascular infections with *S. aureus*

In vitro models

Advantages

- Inexpensive
- Continuous visualization

Disadvantages

- Often static
- Often artificial media
- Short experiments (cells)

In vivo models

Advantages

- Use relevant flow
- More human-like
- Longer experiments

Disadvantages

- *S. aureus*' virulence factors often human specific
- Terminal procedures
- Painful for animals

Example of a mouse model of vascular infections with *S. aureus*

Open access video can be found at: https://www.jove.com/video/52862/

Claes J, Liesenborghs L, Lox M, Verhamme P, Vanassche T, Peetermans M (2015). In vivo model to study bacterial adhesion to vessel wall under flow conditions. Journal of Visualized Experiments (JoVE). e52862.

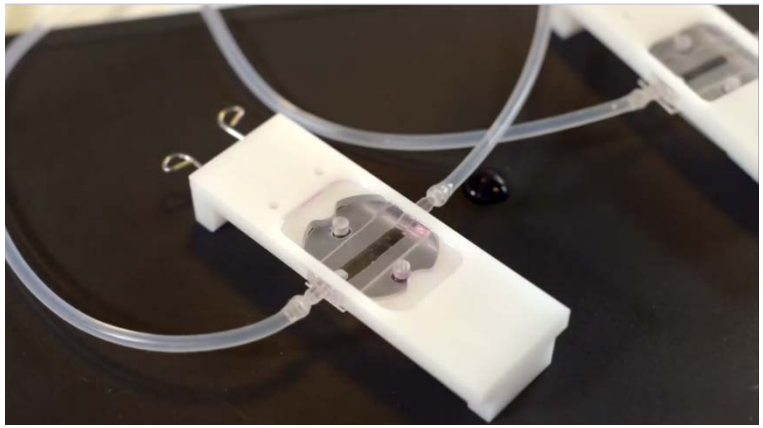
In the current project: Laboratory model systems were used to mimic the *in vivo* infection:

- *Staphylococcus aureus* biofilms on biomaterial in flow of human plasma

- *In vitro* infection of endothelium cell layer under flow

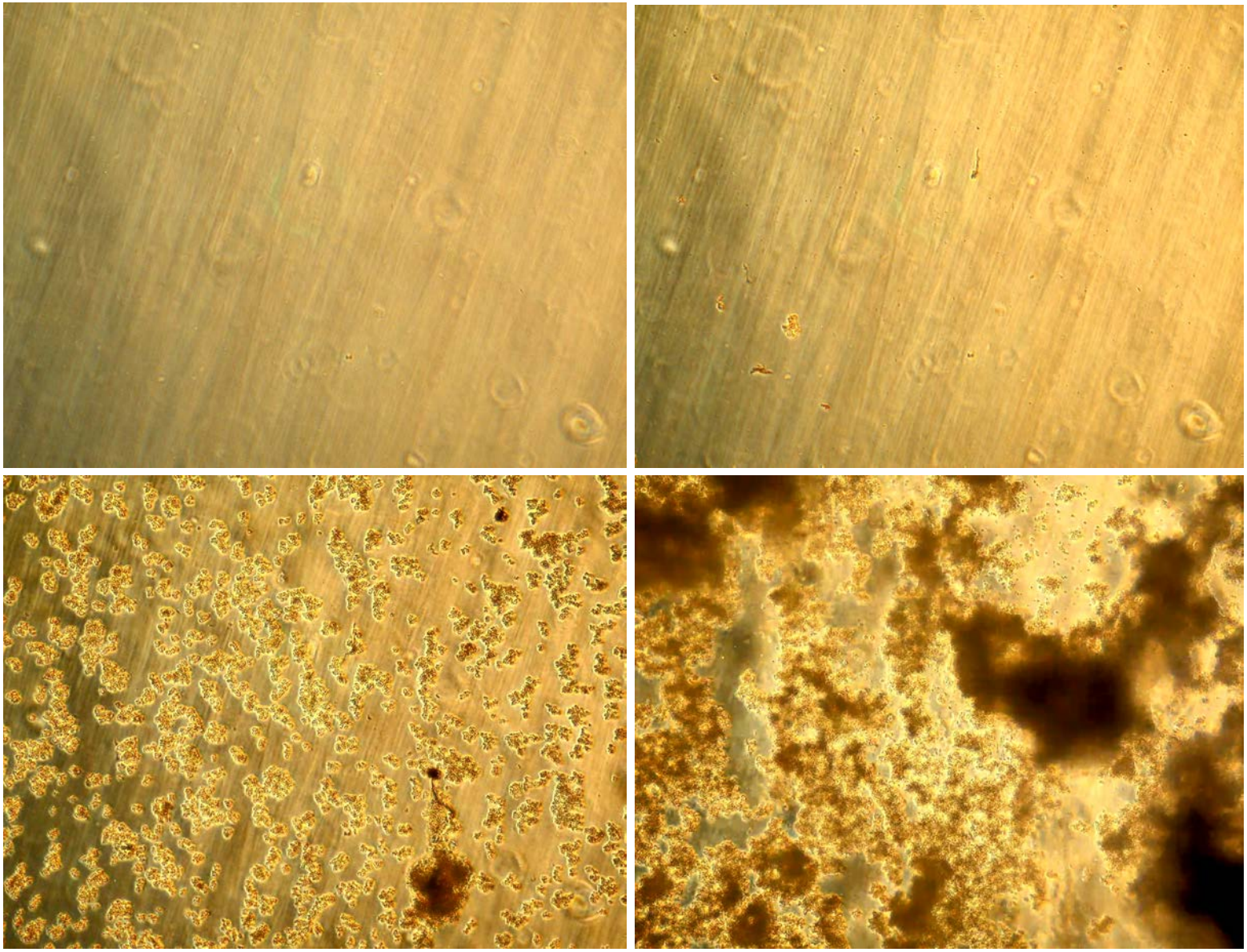
- Enables:

1) in vivo-like medium 2) continuous visualization
3) long-term experiments.



(Further info: http://videnskab.dk/miljo-naturvidenskab/bakterier-i-klumper-giver-livsfarlige-infektioner)

S. aureus biofilm formation and dispersal on catheter material (images from movie)

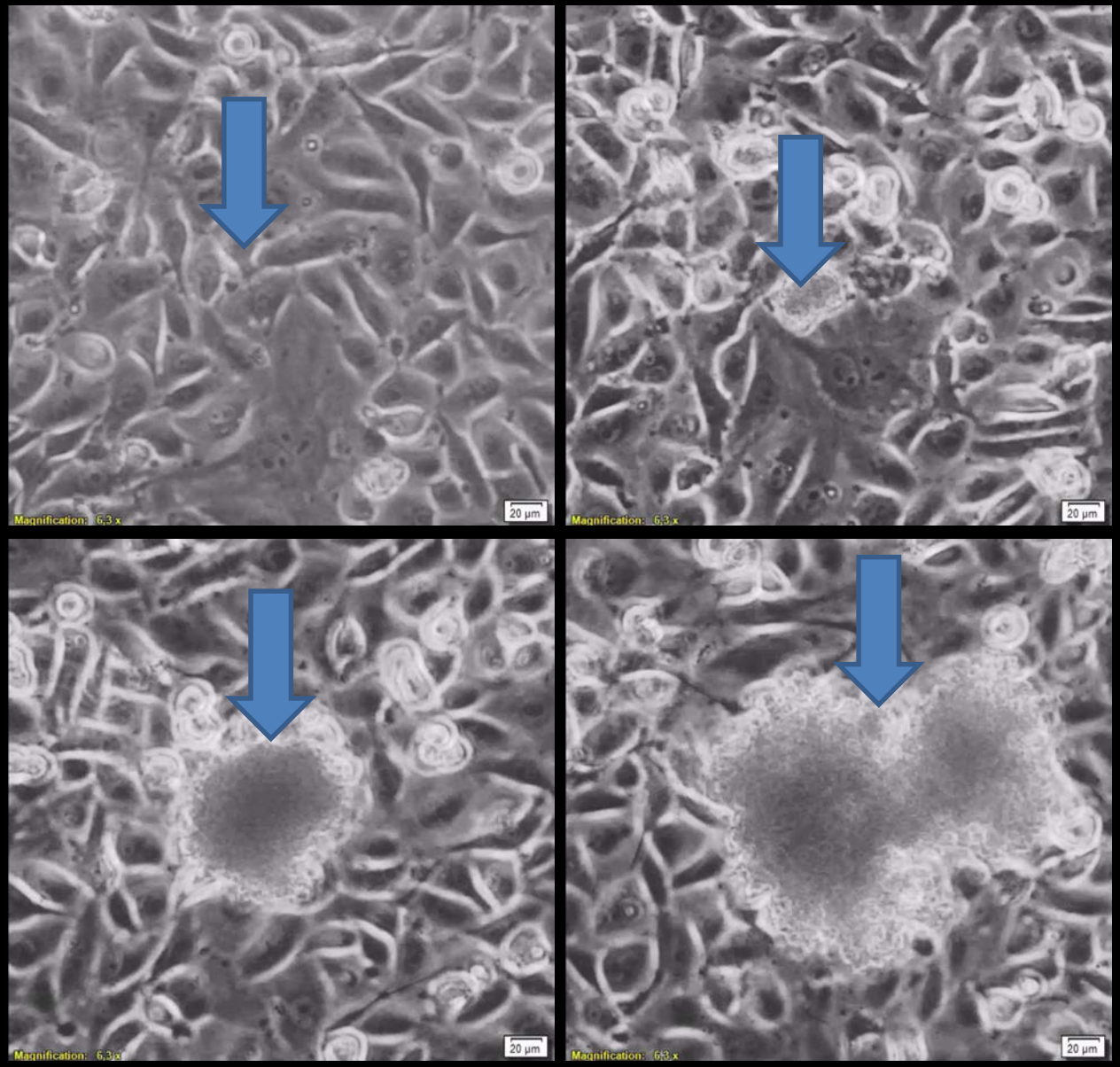


Bloodstream model at low shear

Figure can be found at (Figure 4):
https://onlinelibrary.wiley.com/doi/10.1111/cmi.12785

Grønnemose et al. (2017). A novel in vitro model for haematogenous spreading of *S. aureus* device biofilms demonstrating clumping dispersal as an advantageous dissemination mechanism. Cellular Microbiology. 19:e12785.

Images of bloodstream model at high shear
showing growing *S. aureus* colony (blue arrows)



Conclusion:

Model enables more information from *in vitro* studies prior to animal/clinical trials

Thus can be used to:

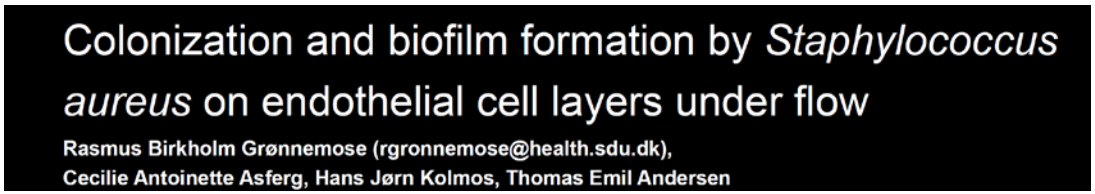
1) improve treatment regimens

2) improve devices placed in the bloodstream:
   - IV catheters
   - Vascular grafts

   - Better *in vitro* tests leads to a reduction in animals used in pre-clinical animal trials

Outcome of the project:

- *Two manuscripts in preparation*
- *Poster at Biofilms8, Aarhus, May 2018*



Thanks to:

Dept. Of Clinical Microbiology, OUH
Senior scientist Thomas Emil Andersen
Prof. Hans Jørn Kolmos

Dept. of Vascular Surgery, OUH
Prof. Jes S. Lindholt

Thrombosis Research Group,
Hospital of Southwest Jutland
Assoc. prof. Yaseelan Palarasah

Thanks to the Danish 3R-Center for financial support!

Danmarks 3R-Center
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