



PhD project title

Optimization of super-resolution microscopy for the determination of optimal therapeutic treatment conditions for viral and bacterial co-infections

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Abstract

Influenza constitutes a major health problem, occurring as seasonal epidemic and sporadic pandemic outbreaks. A common complication of influenza is a secondary bacterial infection, e.g. *Staphylococcus aureus*, which often leads to a severe or fatal outcome. A major problem in severe co-infections concerns a limited arsenal of anti-effectives against influenza virus (IV) and/or *S. aureus*. When IV is detected, the anti-viral medication oseltamivir is recommended. However, an antibiotic treatment to prevent bacterial co-infection is not explicitly advised, due to continuously increasing rates of antibiotic resistances. Thus, the development of individualized test systems for existing anti-infective strategies and new combinatory therapies are urgently required. In this context, it needs to be explored whether more sensitive analysis techniques such as super-resolution optical microscopy approaches are able to detect tiny changes in protein organization induced by therapeutic treatments that are otherwise missed by conventional microscopy or biochemical analyses. Therefore, the previously developed human alveolus-on-chip model will be applied for investigation of the immune response during lung (co-)infections and upon different anti-viral and antibiotic treatment conditions. More particularly, treatment efficacies for different substances and combinatory treatments (e.g. oseltamivir/macrolide combination) will be investigated in an infection-dose-dependent manner. Additionally, detection limits for pathogens and tissue damage will be analyzed in an infection-dose- and spatiotemporal-dependent manner in order to evaluate the usability of different microscope techniques.

Relevance for the theme “Microbial Communication”

Secondary bacterial infections are a common complication of influenza, which often lead to a severe or fatal outcome of IV infections. The hallmark of severe pneumonia is a deleterious excessive inflammation of the lungs, which promotes pulmonary collateral damages, limited respiratory capacity, and possibly death of the patient. The mechanisms leading to enhanced susceptibility for secondary bacterial infections during influenza are not well understood but may depend on complex host-pathogen interactions which arise from (i) the replication of the pathogen(s) and/or (ii) the host immune response. Both IV replication and host cytokine responses are controlled by pathogen-induced signaling mechanisms and, additionally, bacteria interfere with host cell mechanisms for their own benefits.

Most likely, IV and bacteria, amongst which *S. aureus* is of major importance, synergize to increase the immunopathology of patients.