Light4Lungs: Addressing antimicrobial resistance for treating chronic lung infections through a novel inhalable photodynamic therapy.

Light4Lungs: Addressing Antimicrobial Resistance in Chronic Lung Infections

The goal of Light4Lungs is to **address the problem of antimicrobial resistance (AMR) in the treatment of chronic lung infections,** the leading cause of morbidity and mortality in patients with diseases such as cystic fibrosis and hospital-acquired lung infections.

Chronic bacterial infections in the lungs are particularly exemplified by the case of P. aeruginosa-induced progressive respiratory failure, which stands as the primary cause of morbidity and mortality in individuals with cystic fibrosis. Additionally, various pathogens, including MRSA, significantly contribute to chronic and acute lung infections, whether acquired in hospital settings or otherwise. The only available treatment for these infections is the use antibiotics.

However, current antibiotics are often insufficiently effective because of AMR.

Antimicrobial resistance: A global threat

Antimicrobials – including antibiotics, antivirals, antifungals, and antiparasitics – are medicines used to prevent and treat infectious diseases. AMR occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobial medicines.

As a result of drug resistance, infections become difficult or impossible to treat, increasing the risk of disease spread, severe illness, disability and death (Figure 1).

This issue affects all countries regardless of income level, disproportionately impacting vulnerable populations and those in low-resource settings (Figure 2).

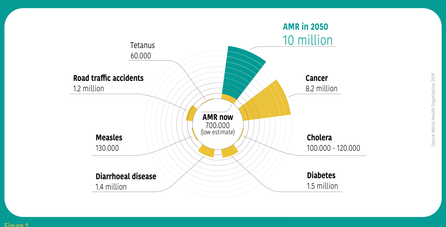


Figure 1
Estimation of the number of deaths caused by AMR in 2025

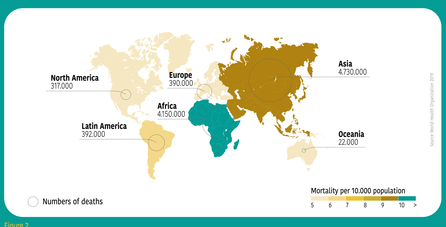


Figure 2
Number of deaths due to AMR according to WHO in 2019.

The vision of Light4Lungs

The expectations for new antibiotics are not very good, and it is likely that they will induce resistance as well. Moreover, a large number of chronic bacterial infections involve bacterial biofilms, which are inherently recalcitrant to antibiotics. Thus, alternative anti-infective approaches that are effective against bacterial biofilms and do not cause resistance themselves are urgently needed.

The Light4Lungs vision is to make advancements towards the development of a novel therapeutic scheme based on inhalable light-emitting aerosol particles containing long-decay phosphorescent compounds.

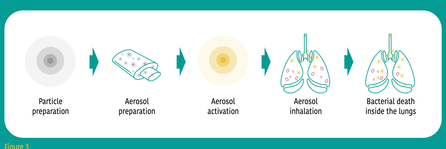


Figure 3
The concept behind Light4Lungs.

The concept behind Light4Lungs is depicted in Figure 3. In a first step, the vision was to develop novel light-emitting. Then an aerosol form would be developed, whereby the particles' emission could be activated prior to irradiation. Next, the active lightemitting particles would be delivered to the lungs where they would trigger the photodynamic effect on the pathogenic bacteria, killing them.

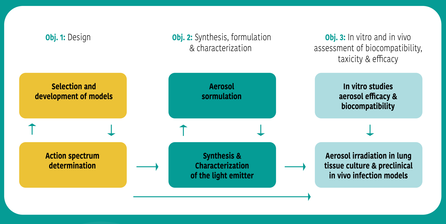
The concept of the project involved several high-risk challenges from the beginning:

- While light-emitting materials with persistent luminescence have been reported, their biocompatibility and light emitting performance are not fit for therapeutic purposes. The use of breathable therapeutic light sources, did not exist at a prototype level. Thus, realization of a breathable source that can deliver a sufficiently high light dose to provide effective phototherapy in the lungs has been a high-risk challenge of the project.
- The second high-risk challenge was the antimicrobial efficacy of the new aerosol light-source. The challenge was to supersed the state-of-the-art in aerosol drug delivery science by developing new aerosol formulations and inhalers capable of delivering a sufficient number of light-emitting particles to the infected regions of the lungs.

The implementation of Light4Lungs

The Consortium implementing the Light4Lungs Project has 8 partners from 4 countries and is highly interdisciplinary and synergetic. It combines several different scientific areas from photonics to medicine, including materials chemistry, physical chemistry, photo-physics, pharmaceutics, photobiology and microbiology.

The Light4Lungs work plan was designed following the development sequence of the therapies envisioned, in three successive steps as shown in Figure 4. (1) definition of the treatment component properties; (2) development of the lightemitting particles and their aerosol formulation and (3) assessment of antimicrobial efficiency.



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