Therapy and Active Substances | Medicine and Pharmaceuticals | Technology Offer

New CF treatment: Inhibitors of bacterial quinolone biosynthesis in *P. aeruginosa* and *B. cepacia*

Field of application

Pseudomonas aeruginosa is a worldwide spread bacterium and is known to cause severe diseases, especially in chronically ill or immune-compromised patients. An infection thus hits cystic fibrosis (CF) patients particularly hard, since an additional chronic infection of the respiratory system results in a drastic drop in lung function. It has also been confirmed that the pathogen leads to a long-term change of the microbiome in the lung.
Depending on the bacterial population density, an attack is coordinated via messenger substances (quinolones); the targeted disruption of this signaling process can efficiently contain an attack. Given the fact that antibiotics are less and less effective in the long term, one promising approach is to use efficient inhibitors in the fight against pathogenic bacteria, especially when it comes to chronic diseases.

State of the art

Various inhibitors of signaling pathways (i.e. quinolone biosynthesis) are already known, but their efficacy has so far not been sufficiently demonstrated in living cells, or the necessary concentrations have been too high. Up to now, the inhibition of this signaling pathway has therefore been irrelevant in terms of pharmacological effects. This is now set to change.

Innovation

The compound described here effectively inhibits the production of 2-alkyl quinolones (via PqsD or HmqD), i.e. the signal-based coordination of attacks among the pathogenic bacteria and the associated toxin production, thus curbing the spread of pathogens. At the same time immunosuppression is stopped.
An infection with such a pathogen is associated with significantly impaired lung function, particularly in CF patients. By inhibiting the bacterial signaling pathways, the spread can be effectively controlled without causing side effects or resistance.
This new and highly potent compound could be used in place of or together with antibiotics and thus be of great benefit in the longer term, especially (but not exclusively) for CF patients.

Patent portfolio

An EP patent application is pending.

Your benefits at a glance

- ✓ Complete inhibition of quinolone biosynthesis
- ✓ Selective binding and high activity at low concentrations
- ✓ Efficacy confirmed *in situ* in cell cultures of pathogenic *P. aeruginosa* and *Burkholderia*
- ✓ Avoidance of new resistances and increase of antibiotic effect through a combination of active ingredients

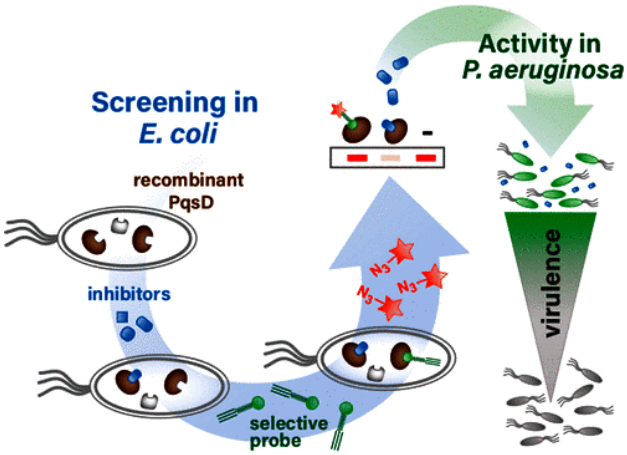

Figure: Diagram of the activity-based test strategy for identifying suitable PqsD inhibitors: Virulence factors are inhibited by preventing the production of quinolone quorum sensing signals [image: University of Konstanz].

Technology transfer

TLB GmbH manages inventions until they are marketable and offers companies opportunities for license and collaboration agreements.

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