Transforming Waste into New Antibiotics, TWIN-A

Background

Antimicrobial resistance constitutes a major global threat for public health and the associated costs are both economical and societal. Infections caused by resistant and antibiotic-tolerant bacteria, such as those mediated by the opportunistic biofilm forming *Pseudomonas aeruginosa*, are alarmingly rising and increasingly dependent on the use of last-resort drugs, such as colistin. Moreover, the multidrug-resistant, biofilm-forming *Staphylococcus aureus*, the causative species of hospital-associated infections, is of especially serious concern. Despite the recognized and urgent need for new antimicrobial compounds for clinical use, only two new classes of antibiotics have been brought to market in the last 30 years.

Following the same logic as in our previous work on natural compounds, we believe that potent antimicrobial compounds have evolved in bacteria of waste/wastewater treatment processes, similar to antibiotics that are the most effective against single-cell bacteria and enzymes decomposing biofilm structure. Despite their marked microbial diversity, these sources have not been explored for their antimicrobial potency before. Many important bacteria in these processes produce antibiotics and matrix-degrading compounds. However, access to these microbes has been limited by the fact that 99% of environmental bacteria are not cultivable under laboratory conditions.

The “uncultivable” microbial majority is regarded as our planet’s largest unexplored pool of biological and chemical novelty. The recent breakthrough discovery of teixobactin, a very potent antibiotic isolated from previously unculturable soil bacteria, has inspired new research on the relevance of resurrecting the exploration of environmental sources for the discovery of new antibiotics. The key issue in facilitating the culture of soil bacteria was the fact that the culturing was made *in situ* with help of a microwell array. We propose to take similar approach by developing clever microsystems, namely biofilm sensors that can be

used for monitoring the antimicrobial activity *in situ* and microfluidic arrays for isolation of bacterial cells.

Objectives

We investigate low-value waste/wastewater treatment processes as unprecedented sources of antibiotics against biofilm-forming *Staphylococcus aureus* and *Pseudomonas aeruginosa* as well as their drug-resistant strains, by using advanced anti-biofilm and microsystems technologies.

Research methods

Molecular methods are used to find suitable sites for biofilm sensors, to identify the enzyme-producing and biofilm-degrading bacteria as well as to evaluate risk associated with antibiotic resistance in the waste/wastewater treatment processes.

Chemical synthesis is used to create a library of new anti-biofilm compounds mimicking those produced by the identified bacteria but with improved potency.

Selected lead compounds are critically assessed via functional characterization for their anti-biofilm and matrix-degrading effects.

Flexible cellulose-based printed platforms as substrates for biofilm sensors to facilitate screening of biofilm or matrix-degrading compounds at active waste process sites.

New microsystems are designed for “domestication” of the previously unculturable antibiotics-producing bacteria from waste process sites.

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