

Application of bacteria as microbial factories for natural products

Bacteria may be described as tiny chemical factories that take up simple molecules like sugars or alcohols as nutrients and utilize them to build all components that are necessary for basic cell metabolism, thus so called primary metabolites, via their intrinsic enzyme machinery. In addition, they are able to synthesize a diverse spectrum of often species-specific secondary metabolites. These are more complex molecules which fulfil distinct functions beyond the primary metabolism. Because of these specific functions, e.g. repellence of competing organisms, they are often of great value for human use, e.g. as antibiotics. Such compounds are often also simply called natural products, to distinguish them from substances with similar properties but originating in organic chemistry. Since the recovery of such valuable natural products from natural producers is typically limited, there is an increasing demand to exploit the cell machinery of bacteria and direct it towards desired natural products by molecular engineering, thus generating small designer cell factories.

A particularly suited organism is the soil bacterium *Pseudomonas putida*, because it is especially robust, non-pathogenic and supplies many different biochemical building blocks. In this publication, we sum up fascinating studies published by leading experts in this field which report the biosynthesis of various classes of natural products with *P. putida* cell factories (Fig. 1), like pigments, antibiotics, surfactants, flavours, biodegradable polymers or fine chemicals.

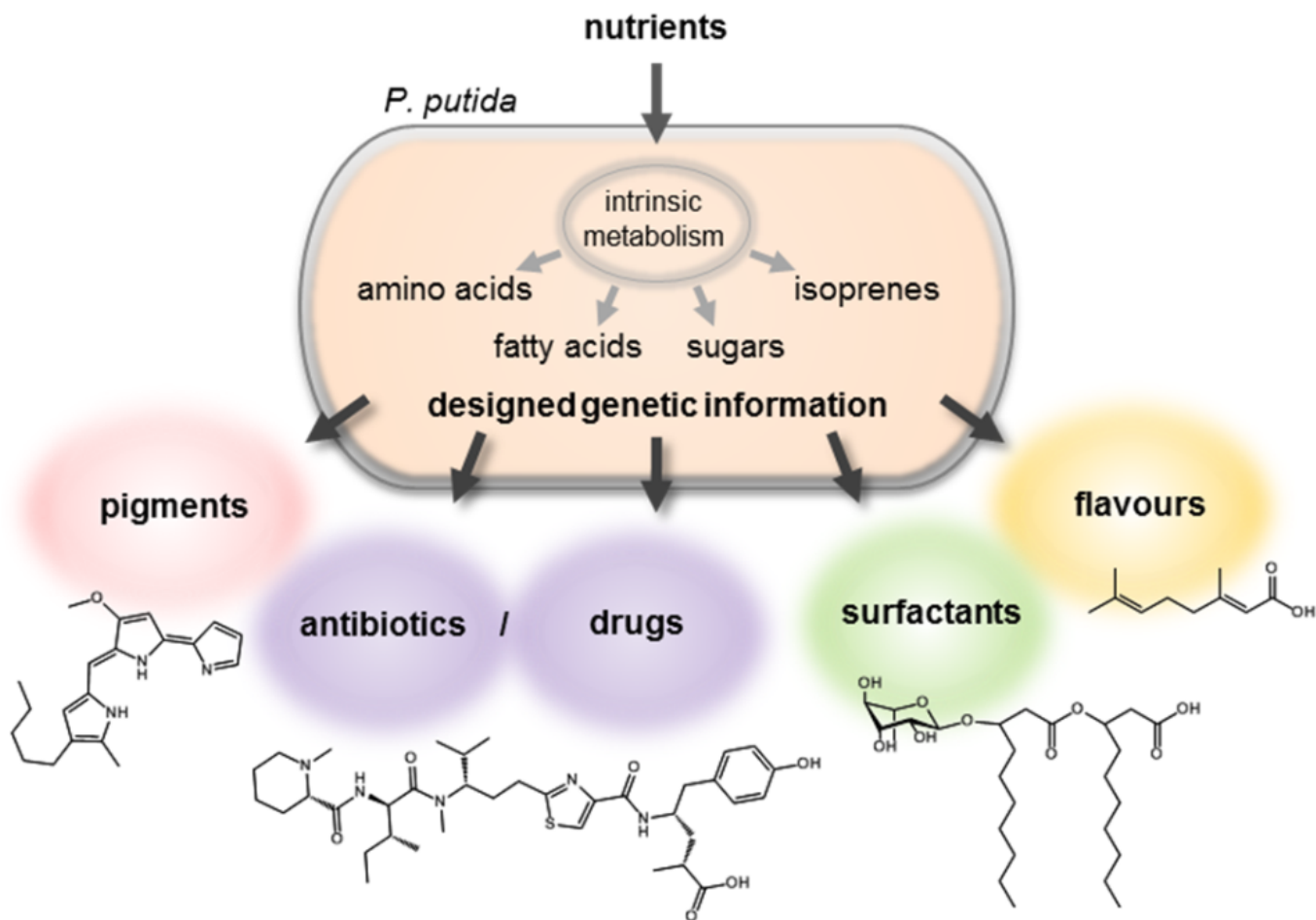


Fig. 1 Utilization of *Pseudomonas putida* as cell factory for the production of different natural products.

Different specific molecular tools were developed to enable stable transformation of *P. putida* into such designer cell factories. This is basically achieved by specific transfer and activation of a natural producer's DNA, which contains the genetic blue print for the biosynthesis of secondary metabolites, in *P. putida*. Many of the studies furthermore report on engineering efforts for intricate fine-tuning of cell metabolism to establish especially efficient production performance. One example is the biosynthesis of the antimicrobial and antitumor pigment prodigiosin with *P. putida*. Here, a complex assembly line containing 14 different enzymes was functionally implemented in *P. putida* and transformed it into an efficient red-coloured prodigiosin production factory.

Current exciting new approaches to rethink and redesign basic functions of the cell shall further optimize the bacterium for improved performance in the execution of biosynthetic pathways in the

future.

A variety of applications arise for such engineered bacterial cell factories (Fig. 2).

First, they enable the elucidation and investigation of new bacterial or plant secondary metabolite pathways, as well as the high-level production of the respective compounds allowing their characterization and application. Such metabolites, and also cell derived delivery structures may find applications in human or animal health. Moreover, engineered *P. putida* may be applied in the remediation of toxin contaminated soils to adsorb and destroy the toxic substances. Further potential applications exist in the field of sustainable plant cultivation, since several metabolites are known to improve plant health and growth. This can be effectuated via different mechanisms. Certain metabolites can, for instance, directly trigger enhanced plant growth as signal molecules; others can indirectly support plant growth by inhibition of plant pathogens or by shaping a beneficial microbiome around the plant.

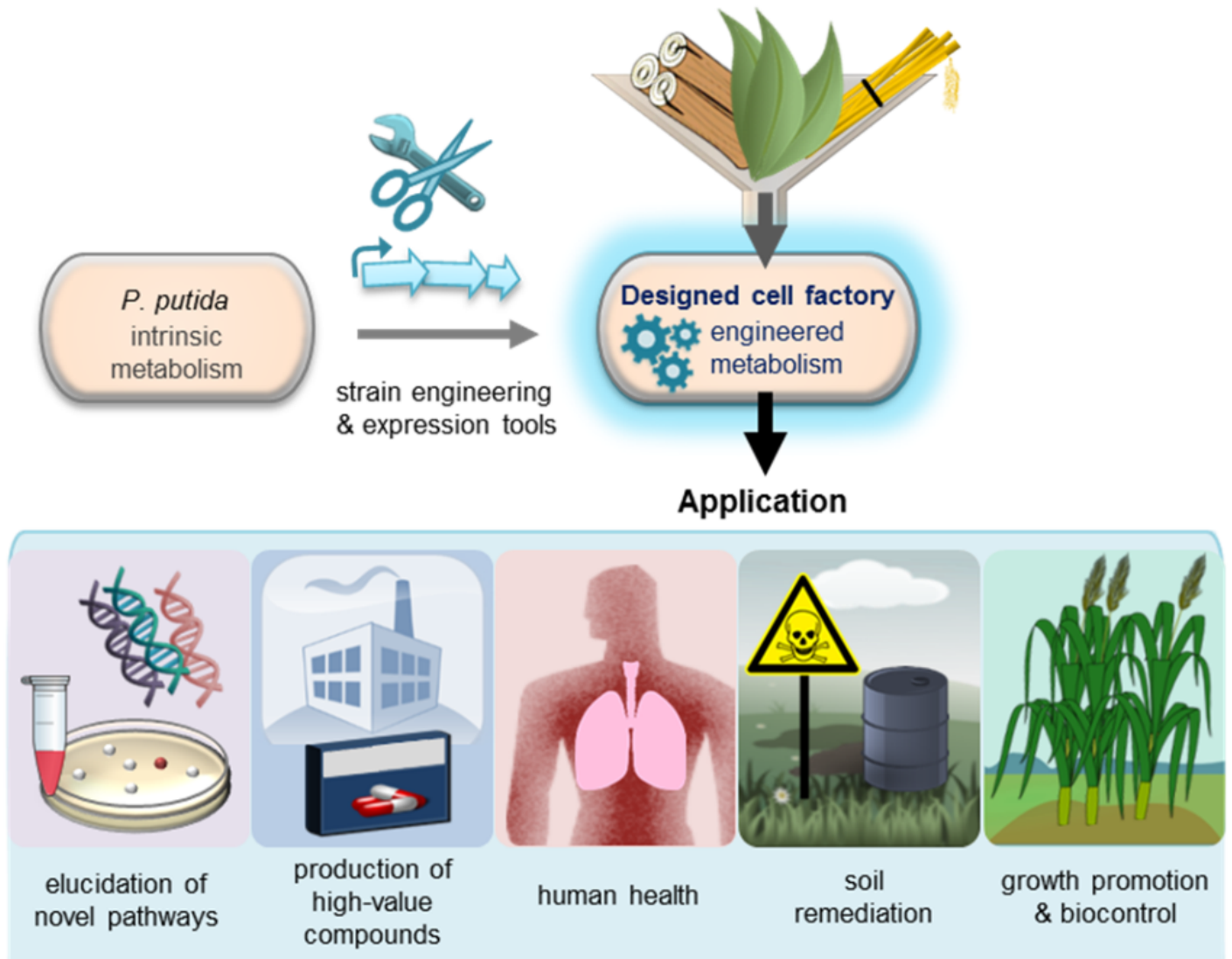


Fig. 2 Perspectives in *Pseudomonas putida* research and application.

The reviewed studies demonstrate the potential of microbial cell factories in general and *P. putida* in particular in highly diverse fields of application and may inspire further exciting developments towards the establishment of *P. putida* based microbial cell factories as a platform for production of various natural products in the future.

Publication

[Pseudomonas putida-a versatile host for the production of natural products.](#)

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