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Editorial

Demanding Novel Tools for Engineering Streptomycetes

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Streptomyces are chosen among many other microorganisms for producing clinically useful naturally originating pharmaceuticals. Presence of plentiful cryptic novel secondary metabolite biosynthetic gene clusters has been revealed after the successful completion of genome mining of several Streptomycetes [1]. These gene clusters have potential to synthesize a large diversity of compounds that have never been detected previously, including aminoglycosides, anthracyclines, bacteriocins, beta-lactams, nonribosomal peptides, polyketides, terpenoids, shikimate-derived metabolites, macrolides, and other natural products [2]. Despite the dominance of Streptomycetes and existence of numerous engineering approaches for improving them as an intelligent chemical-factory [3], they still lack well established, efficient, easy handling and precise genome engineering tools for strain improvement.

Synthetic biology is in a critical phase of development in context to Streptomycetes, where it can move from proof-of-principle studies to real-world applications [4]. It is considered as the major future trend for biotechnology. However, the complex life history of Streptomycetes has limited its exploitation. The ease and rapidly decreasing costs of genome sequencing have made genome mining the most promising source of drug discovery. Synthetic biology offers a new perspective to exploit this potential of Streptomycetes further by generating engineered strains hardly found in the nature [5-6]. Synthetic biology holds the promise of engineering biological systems to exhibit beneficial characteristics, while eliminating unwanted traits. It brings together engineering and biology to design novel biological devices from natural parts such as genes, promoters, operators, terminators, vectors and so on [4]. The aim of synthetic biology is to control cellular behavior by applying engineering tools and use characterized parts to achieve desired functions opening completely new possibilities in drug discovery. This kind of predictive model facilitates a better understanding and manipulation of gene clusters to examine the function of individual biosynthetic genes, and the engineered production of metabolites. This facilitates the manipulation of such biosynthetic pathways by molecular genetic techniques.

The newly increased ability to sequence and synthesize entire genomes enables a new engineering-style approach to manipulating biological systems [7]. Now, much of the potential of synthetic biology is realized only at the level of proof-of-principle studies and general plans. But some areas of microbiology are already geared up for applied synthetic biology. The field of secondary metabolism, especially the discovery and production of bioactive compounds, including antibiotics is particularly well positioned for such a strategy. Biosynthetic pathways for secondary metabolites are modular at multiple levels, and therefore are a natural target for re-engineering and the synthetic creation of additional chemical diversity [8-13]. Therefore, designing efficient protein expression platforms [14] and cloning approaches for multiple genes [15-16], designing and construction of genetic networks of metabolite producing biosynthetic gene clusters [17], activation of cryptic secondary metabolites pathways, generation of clean host for secondary metabolites production, generation of Streptomycetes hosts for heterologous production of secondary metabolites are few areas that need to be concentrated for achieving the recent demand of developing efficient cell-factories.

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