

New method to activate Streptomyces secondary metabolism cryptic pathways

PROJECT DETAILS

Funding Programme: Horizon 2020
Sub-Programme: Excellent Science
Funding Scheme: ERC Proof of Concept

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Total Project Budget: € 150.000'00

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UniOvi Budget: € 150.000'00

CORDIS link: <https://cordis.europa.eu/project/id/835857>

PROJECT DESCRIPTION

The aim of the StrepCrypPath is to test the industrial potential of a new approach to enhance Streptomyces secondary metabolism, discovered in our ERC-StG Strp-differentiation (280304) project. We discovered a pleiotropic regulator of differentiation and secondary metabolism in the *S. coelicolor* model strain. The *S. coelicolor* strain lacking this regulator is the first Streptomyces reported to produce secondary metabolites during its whole developmental cycle, including germination, the exponential growth phase and the stationary stage. *S. coelicolor* encodes 30 secondary metabolites, but only two are produced in high amounts under the culture conditions used in our lab. The expression of 15 secondary metabolite clusters (50% of the total), including 6 predicted to participate in secondary metabolite biosynthesis never observed in the lab (cryptic pathways), is activated/enhanced, in our mutant.

The gene encoding this new regulator is highly conserved in Streptomyces. We will explore if the inactivation of the orthologues of this regulatory gene in industrial streptomycetes causes the same phenotype observed in *S. coelicolor*: secondary metabolism and cryptic pathway activation. We will create integrative conjugative plasmids harbouring antisense mRNAs to inactivate this gene. We do not expect that this method will enhance and/or activate all secondary metabolite clusters. However, if as it happens in *S. coelicolor*, we can activate/enhance 50% of the secondary metabolite pathways, including several cryptic pathways, in any streptomycete, we can revolutionise the screening for new secondary metabolites from streptomycetes.

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