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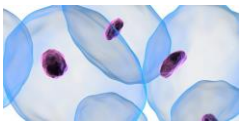

Using novel genetic engineering technologies in antibiotic discovery

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Type of thesis: Experimental

Required competences: Basic microbiology (cell culture, transformation) and molecular biology (PCR design, cloning)

Acquired competences: Advanced molecular biology techniques (TAR, CRISPR/cas, RAGE) , biochemistry and analytic techniques

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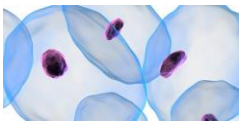
Description

The overuse of antibiotics has led to the apparition of bacteria resistant to our whole arsenal of antimicrobial agents. The World Health Organization (WHO) urges the development of new antibacterial products against 12 families of bacterial pathogens that pose the greatest threat to human health [1]. Soil bacteria are a vast source of natural products with biological functions, including unknown antimicrobials. However, the production of these compounds in its natural hosts is often hindered by the biological characteristics of these bacteria (slow growth in laboratory conditions, lack of genetic manipulation tools, low yields, etc...).

We aim at developing a workflow for the heterologous production and derivation of complex natural compounds, such as Non-Ribosomal Peptides (NRPs) and Polyketides (PKs), in *Pseudomonas putida*. This is a versatile microorganism emerging for the production of natural products [2,3]. Given the size and complexity of the gene clusters involved in the production of NRPs and PKs, which difficulties their manipulation by traditional techniques, the workflow will include steps of assembly and mutagenesis in yeast [4]. To obtain multiple derivates, we will establish an automated high-throughput mutagenesis platform using CRISPR/Cas9 [5].



References

[1] World Health Organisation.(2017). *Global priority list of antibiotic-resistant bacteria to guide reseach, discovery, and development of new antibiotics*.

[2] Domröse A. *et al*. (2015). Front Microbiol. 2015 Sep 15;6:972.

[3] Wenzel SC. *et al.* (2005). Chem Biol. 2005 Mar;12(3):349-56.

[4] Noskov VN. et al. (2003). BMC Genomics. 2003 Apr 29;4(1):16.

[5] Smanski MJ. *et al.* (2014). Nat Biotechnol. *2014 Dec;32(12):1241-9*