# Synthetic biology strategies to unlock marine natural products


## Summary:

Natural products (NPs; chemical compounds produced by living organisms) are key drivers of scientific innovation and biotechnological development. Their impact is undeniable: for instance, one-third of all FDA-approved small molecule drugs (1981-2019) are either NPs or NPs derivatives. Their contribution and impact over the years highlights the need to keep exploring and identifying novel NPs as they remain a rich source of unique chemical diversity and innovation.

With advances in genome mining, synthetic biology, and metabolomics, the search for new NPs is no longer limited to traditional isolation. At CIIMAR, we are developing an integrated workflow for genome mining and heterologous expression of NPs biosynthetic gene clusters (BGCs) from our unique collection of marine actinobacteria.

Heterologous expression is a technology that still presents challenges that need to be addressed. Our recent work has focused on identifying BGC through genome mining and developing a first-generation expression platform using synthetic biology concepts. The next step, and the goal of this project, is to upgrade and optimize our expression platform by developing synthetic biology-based molecular tools to improve the orthogonality and modularity of the existing platform, allowing for more efficient and specific production of NPs.

This proposal offers an exciting opportunity to work at the intersection of synthetic biology, marine biotechnology and natural product discovery. The project will allow to gain hands-on experience in advanced molecular biology techniques and contribute to a project with real potential impact on drug discovery and sustainable biotechnological applications.


## Main Metodologies

The project will employ a multidisciplinary approach based on the synthetic biology Design-Build-Test-Learn (DBTL) framework to develop novel molecular tools for implementation in our expression platform. First, computational tools will be used to design orthogonal regulatory and structural building blocks which will be assembled into functional modules. These modules will be built and implemented using advanced molecular cloning and CRISPR-based editing tools. The test phase will involve evaluating the performance of the newly developed systems under defined conditions, using both proof-of-concept constructs and selected biosynthetic gene clusters (BGCs). Finally, experimental data will be analyzed and integrated, enabling iterative optimization of the platform.

## References


**(1)** Albuquerque et al. (2021). Complete genome sequence of two deep-sea Streptomyces isolates from Madeira archipelago and evaluation of their biosynthetic potential. Marine Drugs, 19: 621 – DOI: 10.3390/md19110621

**(2)** Marques et al. (2020). Engineering Corynebacterium glutamicum with a comprehensive genomic library and phage-based vectors. Metabolic Engineering, 62: 221-234. DOI: 10.1016/j.ymben.2020.08.007


## Main Supervisor


Marta Vaz Mendes / Microbial Biodegradation and Bioprospecting


## Place of Work

CIIMAR headquarters - Interdisciplinary Centre of Marine and Environmental Research, Terminal de Cruzeiros do Porto de Leixões

## Will the Proposal research idea be funded by a specific project?

No

## Contact


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