CSIC Doctoral Network in Synthetic Biology: Engineering Biomolecular and Cellular Systems

CALL #1 - Doctoral Project Proposals

REFERENCE: IBMCP#1-P1

TITLE: Gene Mining and Synthetic Gene Circuits for Plant Biopharming

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SYNBIO-CSIC Axes [1]

Top-down Synthetic Biology
- Reprograming plants with synthetic circuits for an enriched composition
- Engineering plant-based biofactories for the production of added-value compounds

PROJECT DESCRIPTION

Many economically important metabolites, from pharmaceutical drugs to food additives, are only present in minute amounts in wild or semi-wild plant species. Following gene for the identification of missing steps in the corresponding biosynthetic pathways and integration of the identified genes into synthetic gene circuits, entire metabolic pathways can be reconstructed in more tractable hosts. In this project we will focus, among others, on the apocarotenoid azafrin, a healthy food colorant extracted from the roots of wild hemiparasitic plants whose commercial production remains challenging due to the scarcity of natural sources and the limited understanding of its biosynthetic pathway.

The **objectives** of this thesis are: i) identifying the genes involved in the biosynthesis of azafrin from carotenoids (which are metabolites found in all plants), ii) designing tunable gene circuits for the controlled production of azafrin in microbial and plant hosts, and iii) optimize the production of azafrin in plants for efficient biopharming. To accomplish these objectives, we will combine metabolic modeling and omics-based approaches for gene mining, combinatorial use of synthetic promoters and regulatory elements for the construction of gene circuits, and automated biocircuit design tools to engineer highly efficient and tunable biomanufacturing of azafrin in plant biofactories.

Besides achieving a deeper understanding of plant metabolic pathways and azafrin biosynthesis in particular, the **expected outcomes** of the proposed project include valuable insights for the sustainable production of this metabolite. Production of azafrin in plant biofactories might revolutionize the food coloring market by becoming a natural alternative to synthetic food colorants and it might also have an impact in drug

[1] SYNBIO-CSIC TOPICS
Bottom-up synthetic cell engineering: reconstituting life-like molecular systems and functional modules, and integrating them within artificial and natural cells
Top-down synthetic biology: from protein engineering to the reprogramming of cell circuitry and essential processes to achieve novel functions, from cell therapeutics to cell factories.
Computational synthetic biology: applying robotics, AI, and machine learning tools.

development. By addressing the demand for clean-label ingredients and environmentally friendly production methods, this research aligns with global efforts towards sustainable food systems and public health.

Secondments: They will be conducted at key collaborating laboratories of associated partners, determined in coordination with the selected candidate, to enhance project outcomes and training quality. It is expected that part of the bioproduction of azafrin will be carried out during secondments in biotech companies such as MadeInPlant (https://madeinplant.com/), which has proprietary variants of the plant *Nicotiana benthamiana* optimized as a biopharming chassis, or/and Naplatec (https://naplatec.com/), a company devoted to the production of apocarotenoids in tomato.

Preferred profile of the candidates: Candidates should hold a Master's degree in biotechnology, synthetic biology, or molecular biology (or a related subject area), have technical skills in molecular biology and bioinformatics, and basic knowledge of metabolic engineering and synthetic biology.