

**TITLE:** EVALUATION OF THE BIOSYNTHETIC POTENTIAL OF CYANOBACTERIA *PHORMIDIUM* SP. LEGE 05292 BY MEANS OF GENOMIC MINING

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## **ABSTRACT**

The genomic revolution has shown that the biosynthetic potential of microorganisms remains largely unexplored, since many microorganisms have more biosynthetic gene cluster than the number of natural products isolated from them. The identification of these clusters in genomic sequences emerges as a solution to the frequent rediscovery of compounds through traditional chemical approaches. Cyanobacteria, especially filaments, holds great potential in the production of secondary metabolites with complex chemical characteristics and rearrangements of rare atoms, being the source of several substances of biotechnological interest. The *Phormidium* sp. LEGE 05292 was described by the allelopathic properties of its exudate inhibiting the growth of *Chlorella vulgaris* and consequent identification of four variants of portoamides (A-D), cyclic peptides containing amino acids unusually modified. Portoamides A and B synergistically showed high cytotoxic potential in H460 lung cancer cell lines. In order to identify the genes involved in the biosynthesis of portoamides and to verify the potential of this isolate, the non-axency culture of *Phormidium* sp. LEGE 05292 which involved the use of metagenomic analysis tools. The assembly was carried out in two stages, the first one using several metagenomic assemblers and the second one *de novo* genomic assembly using the results of the first to improve the final assembly. The genomic data of each association microorganism were recovered using the automatic binning method. Genetic groupings were evaluated with the antiSMASH program, allowing the prediction of 17 clusters probably involved in the biosynthesis of natural products, including one involved in the production of aminoglycoside-aminocyclitol antibiotics, 5 of bacteriocins, one in the production of polyketide synthase (PKS) , 7 in non-ribosomal peptides (NRPS), including 2 PKS/NRPS hybrids, these being the probable genes involved in the production of portoamides. The results show that this cyanobacterium is very prolific in the production of secondary metabolites and arouses interest for the future isolation of these compounds based on the prediction of their structures by heterologous expression techniques in vitro.

**Keywords:** Cyanobacteria; Natural Products; Portoamides

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