



HAL
open science

The Genome Sequence of the Cyanobacterium *Oscillatoria* sp. PCC 6506 Reveals Several Gene Clusters Responsible for the Biosynthesis of Toxins and Secondary Metabolites

Annick Méjean, Rabia Mazmouz, Stéphane Mann, Alexandra Calteau,
Claudine Médigue, Olivier Ploux

► To cite this version:

Annick Méjean, Rabia Mazmouz, Stéphane Mann, Alexandra Calteau, Claudine Médigue, et al.. The Genome Sequence of the Cyanobacterium *Oscillatoria* sp. PCC 6506 Reveals Several Gene Clusters Responsible for the Biosynthesis of Toxins and Secondary Metabolites. *Journal of Bacteriology*, 2010, 192 (19), pp.5264-5265. 10.1128/jb.00704-10 . hal-04580588

HAL Id: hal-04580588

<https://hal.science/hal-04580588v1>

Submitted on 20 May 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

GENOME ANNOUNCEMENTS

The Genome Sequence of the Cyanobacterium *Oscillatoria* sp. PCC 6506 Reveals Several Gene Clusters Responsible for the Biosynthesis of Toxins and Secondary Metabolites[∇]

Annick Méjean,^{1,2*} Rabia Mazmouz,^{1,2} Stéphane Mann,¹ Alexandra Calteau,³
 Claudine Médigue,³ and Olivier Ploux¹

Laboratoire Charles Friedel, UMR CNRS 7223, ENSCP Chimie ParisTech, 11 Rue Pierre et Marie Curie, 75231 Paris Cedex 05, France¹; Université Paris Diderot-Paris 7, 75013 Paris, France²; and Laboratoire d'Analyses Bioinformatiques pour la Génomique et le Métabolisme, CEA, Institut de Génomique, Génoscope & CNRS-UMR8030, CP 5722, 2 Rue Gaston Crémieux, CP 5706, 91057 Evry Cedex, France³

Received 18 June 2010/Accepted 16 July 2010

We report a draft sequence of the genome of *Oscillatoria* sp. PCC 6506, a cyanobacterium that produces anatoxin-a and homoanatoxin-a, two neurotoxins, and cylindrospermopsin, a cytotoxin. Beside the clusters of genes responsible for the biosynthesis of these toxins, we have found other clusters of genes likely involved in the biosynthesis of not-yet-identified secondary metabolites.

The presence in the environment of cyanobacteria producing toxins represents a risk for human and animal health (5). It is thus important to develop methodologies to detect these toxic microorganisms in water reservoirs, and so far, PCR-based amplification of genes responsible for the biosynthesis of these toxins is the best method (1). We have been interested in the study of cyanobacteria producing the neurotoxins anatoxin-a and homoanatoxin-a (2, 17, 18). Our goals were first to identify the genes responsible for the biosynthesis of these toxins and to deepen our knowledge of this interesting group of bacteria. For that, we chose *Oscillatoria* sp. PCC 6506 (4, 6, 14), a filamentous benthic cyanobacterium, as our model microorganism and initiated the sequencing of its genome.

Whole-genome shotgun sequencing of *Oscillatoria* sp. PCC 6506 was performed using the 454 technology (GATC, Konstanz, Germany), giving 677,304 reads, with a total number of 164 megabases, representing an estimated coverage of 24. Assembly yielded 419 contigs consisting of 6,729,249 bases with a G+C content of 43.40%. Automatic annotation of this genome using the MaGe pipeline system (16) predicted 6,007 coding sequences (CDS), 61 fragments of CDS, and 84 genes coding for RNA (4 rRNA genes, 70 tRNA genes, and 10 small non-coding RNAs [ncRNAs]).

Oscillatoria sp. PCC 6506 is an aerobic photosynthetic and diazotrophic cyanobacterium that shows transient and dispersed gas vesicles (4, 6). We found 37 genes coding for proteins involved in photosynthesis and the *nif* gene cluster, responsible for nitrogen fixation. However, we could not identify any gene coding for a hydrogenase (15), as for *Synechococcus*

sp. BG043511 (8). Four genes were annotated as gas vesicle protein (*gvp*) genes (13).

Oscillatoria sp. PCC 6506 produces anatoxin-a and homoanatoxin-a, and we recently identified the *ana* cluster of genes, responsible for the biosynthesis of these alkaloids (3, 10, 11). We also identified the cluster of genes (*cyr*) responsible for the biosynthesis of cylindrospermopsin (9, 12). Cyanobacteria are known to produce a wide range of secondary metabolites (7), and 3.7% of the total annotated CDS in this genome were dedicated to secondary metabolism. We identified, beside the *ana* and *cyr* clusters, four other clusters of genes containing polyketide synthase and nonribosomal peptide synthase coding genes, likely involved in the biosynthesis of secondary metabolites.

We found 51 transposase genes in the *Oscillatoria* sp. PCC 6506 genome, some close to the biosynthetic gene clusters identified, suggesting horizontal gene transfer events.

In conclusion, we present here the sequence of the first genome of an *Oscillatoria* cyanobacterium strain, a very common genus found in the environment, and the first genome of a neurotoxin-producing cyanobacterium.

Nucleotide sequence accession numbers. This genome has been deposited in the DDBJ/EMBL/GenBank databases (accession no. CACA01000001 to CACA01000377). This first version contains 377 contigs over 419, because we removed the 42 contigs for which the size was less than 500 bp. MaGe annotation data will be made available to the public at the MaGe CyanoScope website (https://www.genoscope.cns.fr/agc/microscope/about/collabprojects.php?P_id=68) at the same time as the DDBJ/EMBL/GenBank release.

* Corresponding author. Mailing address: Laboratoire Charles Friedel, UMR CNRS 7223, ENSCP Chimie ParisTech, 11 Rue Pierre et Marie Curie, 75231 Paris Cedex 05, France. Phone and fax: 33 1 44 27 67 01. E-mail: annick-mejean@enscp.fr.

[∇] Published ahead of print on 30 July 2010.

This work was supported by the Institut Pasteur, the Ecole Nationale Supérieure de Chimie de Paris, the Centre National de la Recherche Scientifique (URA 2172 and UMR7223), the INSERM grant Multiorganismes from Aventis Pharma (Groupe Sanofi-Aventis) and

Bayer Pharma, and by the Agence Française de Sécurité Sanitaire de l'Environnement et du Travail, grant Environnement et Santé.

We thank R. Rippka for providing the axenic strain *Oscillatoria* sp. PCC 6506 and for valuable advice concerning the cultures of cyanobacteria. N. Tandeau de Marsac, I. Iteman, and S. Cadel-Six are all thanked for their constant support and for valuable scientific discussions during the course of this work. We thank Z. Rouy for helping us during the submission of the genome.

REFERENCES

1. Burns, B. P., M. L. Saker, M. C. Moffitt, and B. A. Neilan. 2004. Molecular detection of genes responsible for cyanobacterial toxin production in the genera *Microcystis*, *Nodularia*, and *Cylindrospermopsis*. *Methods Mol. Biol.* **268**:213–222.
2. Cadel-Six, S., C. Peyraud-Thomas, L. Brient, N. Tandeau de Marsac, R. Rippka, and A. Méjean. 2007. Different genotypes of anatoxin-producing cyanobacteria coexist in the Tarn River, France. *Appl. Environ. Microbiol.* **73**:7605–7614.
3. Cadel-Six, S., I. Iteman, C. Peyraud-Thomas, S. Mann, O. Ploux, and A. Méjean. 2009. Identification of a polyketide synthase coding sequence specific for anatoxin-a-producing *Oscillatoria* cyanobacteria. *Appl. Environ. Microbiol.* **75**:4909–4912.
4. Castenholz, R. W., R. Rippka, M. Herdman, and A. Wilmoth. 2001. Subsection III, order Oscillatoriales (Elenkin 1934), p. 539–562. *In* D. R. Boone, R. W. Castenholz, and G. M. Garrity (ed.), *Bergey's manual of systematic bacteriology*, 2nd ed., vol. 1. The Archaea and the deeply branching and phototrophic bacteria. Springer Verlag, New York, NY.
5. Chorus, I., and J. Bartram (ed.). 1999. Toxic cyanobacteria in water: a guide to their public health consequences, monitoring and management. Spon Press, London, United Kingdom.
6. Herdman, M., I. Iteman, and R. Rippka. 2005. Catalogue of cyanobacterial strains, 2nd ed. Institut Pasteur, Paris, France.
7. Kalaitzis, J. A., F. M. Lauro, and B. A. Neilan. 2009. Mining cyanobacterial genomes for genes encoding complex biosynthetic pathways. *Nat. Prod. Rep.* **26**:1447–1465.
8. Ludwig, M., R. Schulz-Friedrich, and J. Appel. 2006. Occurrence of hydrogenases in cyanobacteria and anoxygenic photosynthetic bacteria: implications for the phylogenetic origin of cyanobacterial and algal hydrogenases. *J. Mol. Evol.* **63**:758–768.
9. Mazmouz, R., F. Chapuis-Hugon, S. Mann, V. Pichon, A. Méjean, and O. Ploux. 2010. Biosynthesis of cylindrospermopsin and 7-epicyclindrospermopsin in *Oscillatoria* PCC 6506; identification of the gene cluster and toxin analysis. *Appl. Environ. Microbiol.* **76**:4943–4949.
10. Méjean, A., S. Mann, G. Vassiliadis, B. Lombard, D. Loew, and O. Ploux. 2010. In vitro reconstitution of the first steps of anatoxin-a biosynthesis in *Oscillatoria* PCC 6506: from free L-proline to acyl carrier protein bound dehydroproline. *Biochemistry* **49**:103–113.
11. Méjean, A., S. Mann, T. Maldiney, G. Vassiliadis, O. Lequin, and O. Ploux. 2009. Evidence that biosynthesis of the neurotoxic alkaloids anatoxin-a and homoanatoxin-a in the cyanobacterium *Oscillatoria* PCC 6506 occurs on a modular polyketide synthase initiated by L-proline. *J. Am. Chem. Soc.* **131**:7512–7513.
12. Mihali, T. K., R. Kellmann, J. Muenchhoff, K. D. Barrow, and B. A. Neilan. 2008. Characterization of the gene cluster responsible for cylindrospermopsin biosynthesis. *Appl. Environ. Microbiol.* **74**:716–722.
13. Mlouka, A., K. Comte, A. M. Castets, C. Bouchier, and N. Tandeau de Marsac. 2004. The gas vesicle gene cluster from *Microcystis aeruginosa* and DNA rearrangements that lead to loss of cell buoyancy. *J. Bacteriol.* **186**:2355–2365.
14. Rippka, R. 1988. Isolation and purification of cyanobacteria. *Methods Enzymol.* **167**:3–27.
15. Tamagnini, P., E. Leitão, P. Oliveira, D. Ferreira, F. Pinto, D. J. Harris, T. Heidorn, and P. Lindblad. 2007. Cyanobacterial hydrogenases: diversity, regulation and applications. *FEMS Microbiol. Rev.* **31**:692–720.
16. Vallenet, D., L. Labarre, Z. Rouy, V. Barbe, S. Bocs, S. Cruveiller, A. Lajus, G. Pascal, C. Scarpelli, and C. Médigue. 2006. MaGe: a microbial genome annotation system supported by synteny results. *Nucleic Acids Res.* **34**:53–65.
17. van Apeldoorn, M. E., H. P. van Egmond, G. J. Speijers, and G. J. Bakker. 2007. Toxins of cyanobacteria. *Mol. Nutr. Food Res.* **51**:7–60.
18. Wonnacott, S., and T. Gallagher. 2006. The chemistry and pharmacology of anatoxin-a and related homotropans with respect to nicotinic acetylcholine receptors. *Mar. Drugs* **4**:228–254.