

# Biosynthesis of anatoxin-a, a neurotoxin of cyanobacteria: a study combining genomic, biosynthetic and molecular approaches

*Annick Méjean<sup>1</sup>, Sabrina Cadel<sup>1</sup>, Caroline Peyraud-Thomas<sup>2</sup>, Stéphane Mann<sup>1</sup> & Olivier Ploux<sup>1</sup>*

<sup>1</sup> *Laboratoire de Biochimie des micro-organismes: enzymologie, métabolisme et antibiotiques, UMR7573, ENSCP, 11, rue Pierre et Marie Curie, 75231 Paris Cedex 05 - France*

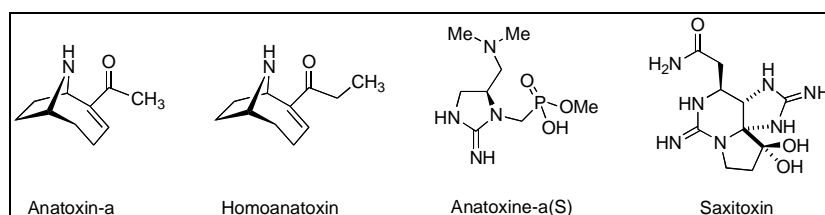
<sup>2</sup> *Unité des Cyanobactéries, Institut Pasteur, 75724 Paris Cedex 15 - France*

Cyanobacteria are gram-negative photosynthetic micro-organisms of an extraordinary morphological and genetic diversity (over 150 genus and 2000 species identified by the botanical code). Cyanobacteria colonise aquatic (fresh water, brackish water, or seawater) and terrestrial niches worldwide, and have been described in virtually every possible environment. A large number of cyanobacteria produce secondary metabolites that are toxic to animals and humans and four major toxin families have been described: hepatotoxins (microcystin, nodularin), neurotoxins (anatoxin-a and its homolog homoanatoxin, anatoxin-a (S) and saxitoxine), cytotoxins (cylindrospermopsin) and dermatotoxins (lyngbyatoxin).

In particular, anatoxin-a or homoanatoxin may provoke the death of animals in a few minutes and there is no antidote for these molecules. Indeed, repeated animal poisonings leading to death after ingestion of contaminated water, have been reported in several locations in the world and attributed to the presence of neurotoxic cyanobacteria in the water that the animals drank. Moreover, anatoxin-a producing cyanobacteria have been isolated from animal poisoning sites<sup>1</sup>.

Although a fair amount of work has been done on the chemistry<sup>2</sup>, the pharmacology<sup>3</sup>, and the analytical detection of anatoxin-a and homoanatoxin, the biosynthesis of anatoxin-a and the genes implicated remain elusive and detection of neurotoxic cyanobacteria in water samples is not possible since we cannot distinguish toxic from non toxic cyanobacteria.

Using chemical, biochemical and genomic approaches we propose an original biosynthetic pathway for anatoxin-a involving PolyKetide Synthases and the development of a simple PCR-based methodology for the monitoring of anatoxin-a producing cyanobacteria in the environment.



<sup>1</sup>Cadel-Six, S., Peyraud-Thomas, C., Brient, L., Tandeau de Marsac, N., Rippka, R., Méjean, A. (2007) *Appl. Environ. Microbiol.* **73**, 7605-7614

<sup>2</sup> Parsons, P. J., Camp, N. P., Edwards, N., Sumoreeah, R.L. (2000) *Tetrahedron*, **56**, 309-315

<sup>3</sup> Thomas, P., Brough, P. A., Gallagher, T., Wonnacott, S. (1994) *Drug Dev. Res.*, **31**, 147-156