

A detailed microscopic image of cyanobacteria, showing long, thin, green filaments with numerous small, rounded cells. The filaments are arranged in a somewhat chaotic, overlapping pattern, typical of a natural culture. The background is a light, neutral color, making the green structures stand out.

Microbiology, genomics and postgenomics applied to the Pasteur Culture Collection of Cyanobacteria (PCC)

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• May 28, 2015

FOR RESEARCH, FOR HEALTH,
FOR OUR FUTURE



The PCC: a gold mine for research

What is a Cyanobacteria?

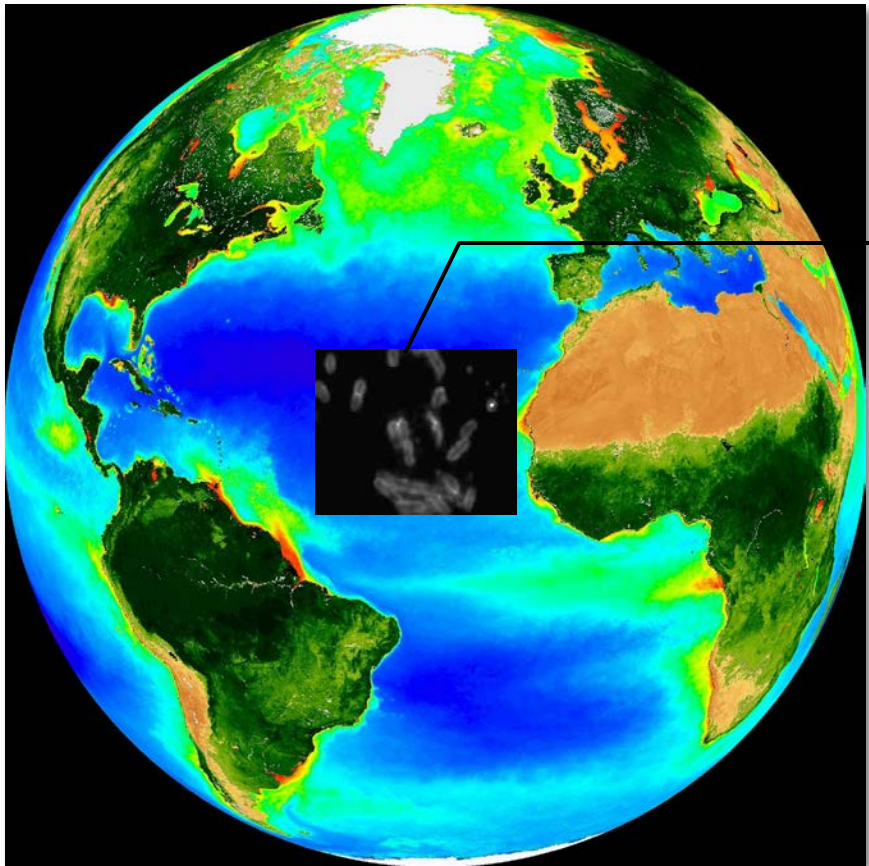
Quick history of the Pasteur Culture collection of Cyanobacteria

What is the PCC?

Working with PCC strains

PCC in the era of omics

Cyanobacteria



- ▶ Change biochemistry and biology on Earth
- ▶ Up to 70% of the total phytoplankton biomass
- ▶ Produce > 30% of the total free O₂
- ▶ > 30% of the total primary production (CO₂ fixation)

Oxygenic photosynthetic prokaryotes

From Berkeley to Paris

- In 1971, Stanier R. and G. moved from Berkeley to the Institut Pasteur in France, with 150 strains of the BCC
- lead a research team on Microbial physiology working on Cyanobacteria
- Implicated in the Bergey's Manual development
- Work on different strains:
 - Pigments, taxonomy, photosynthesis
 - Gas vacuoles in *Anacystis nidulans*
 - Fatty acids



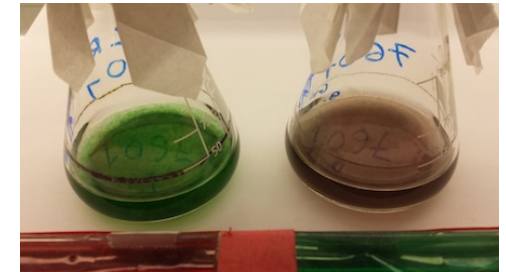
→ Cyanobacteria proposed in Stanier (1974).

Nicole Tandeau de Marsac's time

- In 1988, N. Tandeau de Marsac was named head of the Unit of Cyanobacteria

CCA in *Calothrix* sp. PCC 7601

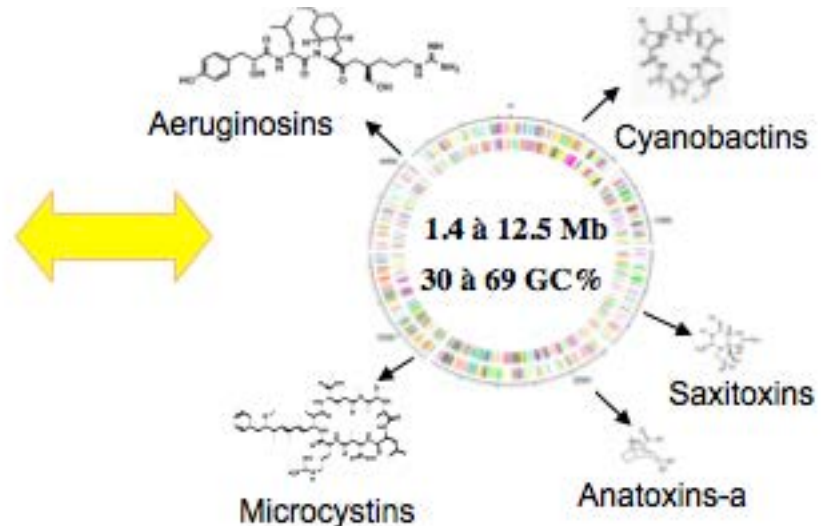
- Working on few models of strains:
 - Phycobilisome, photoregulation,
 - Cellular differentiation of hormogonium,
 - Complementary Chromatic Adaptation,
 - Gas vesicle gene,
 - Phosphorylation of the signal transducer PII,
 - Toxic cyanobacteria *Microcystis* PCC 7806.



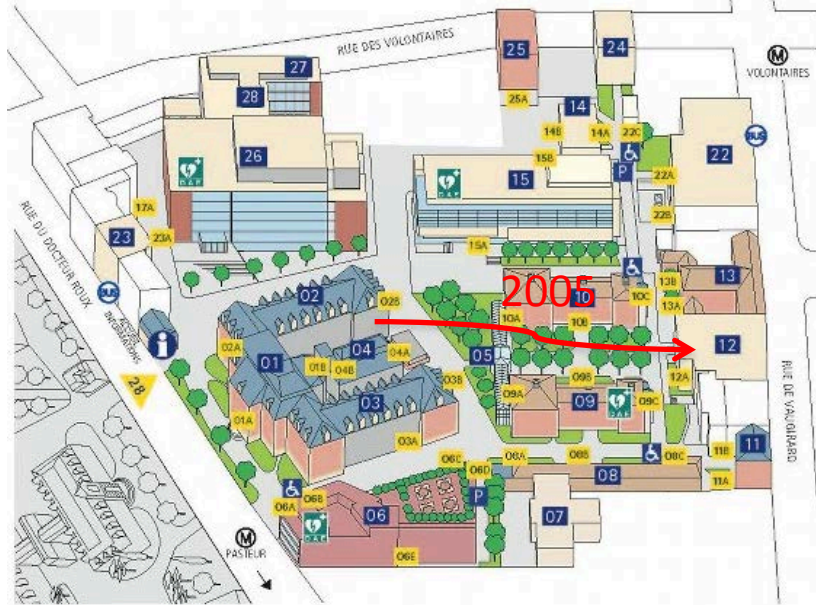
➔ **Light and Cyanobacteria (CCA)**

Collection of Cyanobacteria

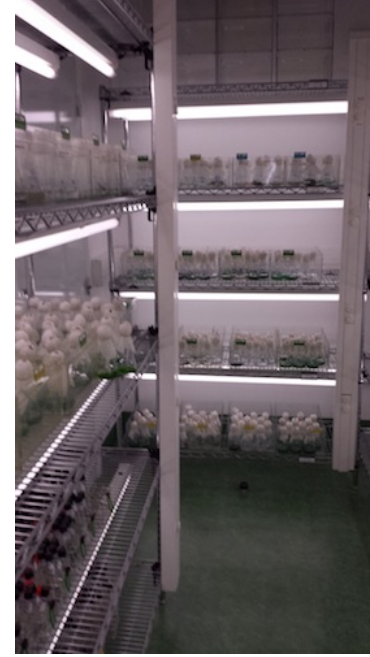
- Since 2009, the Collection of Cyanobacteria maintains the PCC
- Genomics, transcriptomics and metabolomics are applied on the whole collection:
 - to decipher the evolution of the phylum;
 - to study the diversity of the cyanobacterial natural products.



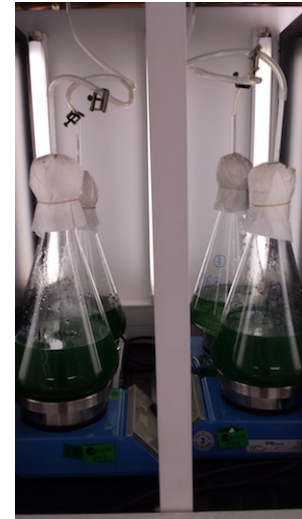
PCC on IP campus



N/D 22° C



Backup 22° C



Biomass 25° C

➔ ~ 750 axenic strains: liquid cultures or slants and cryopreserved.

➔ AT IP, FOR THE LAST 45 YEARS, THE PCC:
A TOOL AT THE SERVICE OF RESEARCH ACTIVITIES



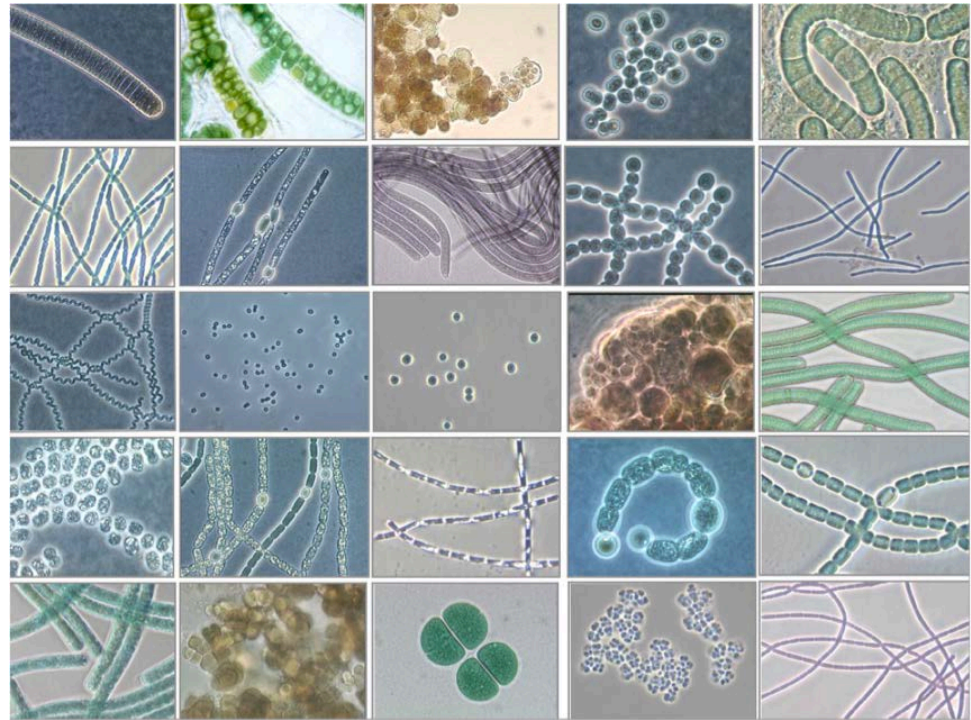
What is the PCC?

One unique microbial resource dedicated to cyanobacteria

Axenic strains (purification, characterisation, 'A know how' for maintain them),

Photo database,

Bibliography database,

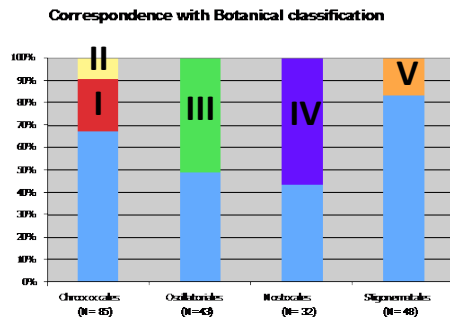
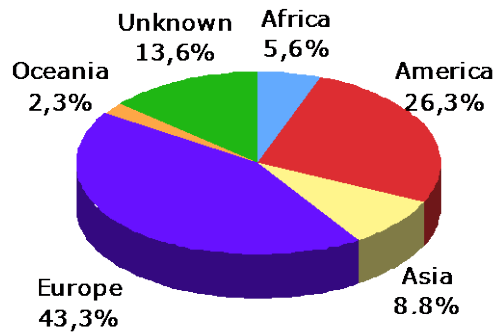


Lot of people for isolation...

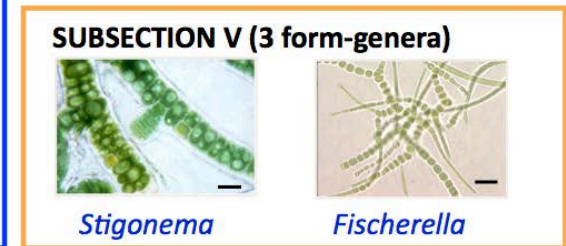
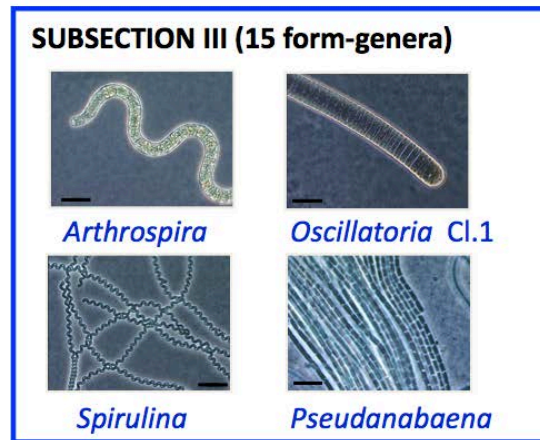
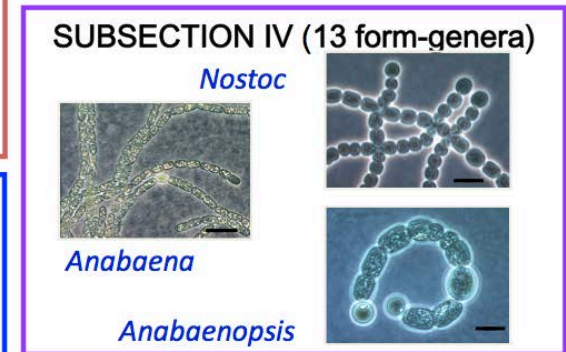
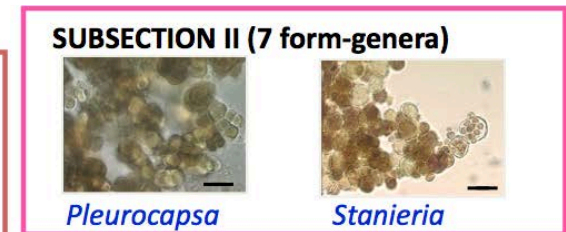
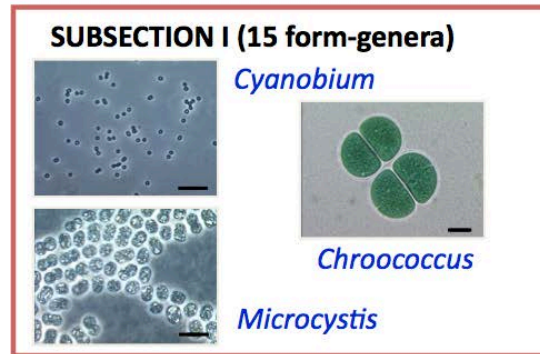
And Rosi Rippka for the identification of all of them

Origins and diversity of PCC strains

Origin of PCC strains



~ 36% described botanical genera



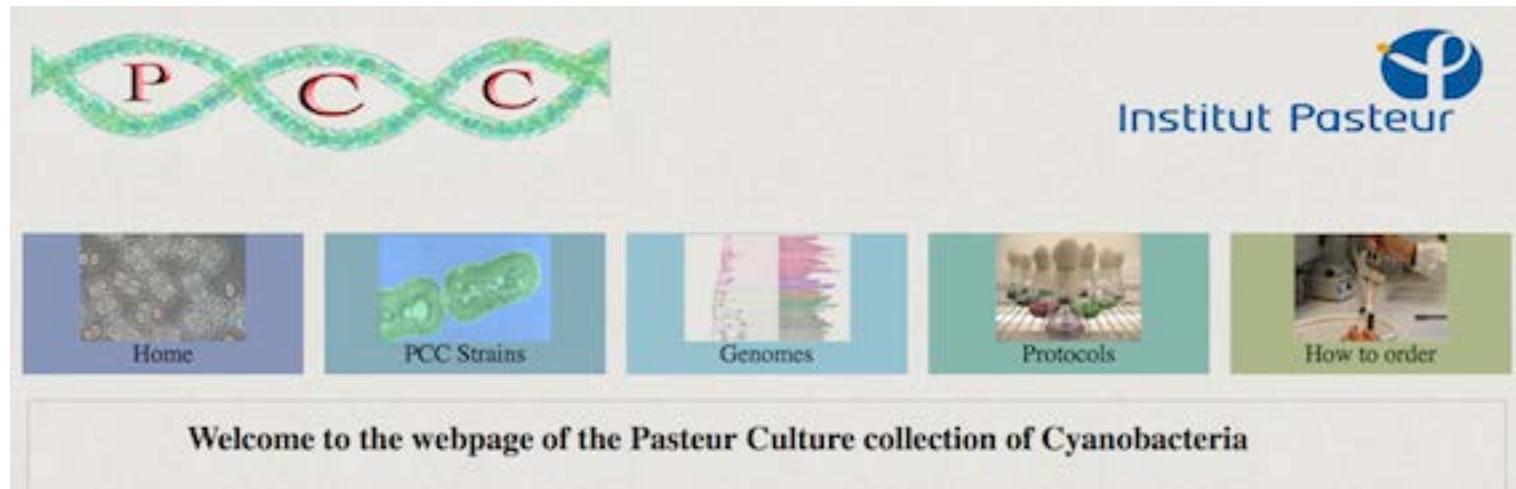
➔ 50 phylogenetic clades

PCC: unique of its kind

Since 2006, it is one of the collection of the Resource Biological Center of Institut Pasteur (CRBIP), certified and under quality control

Reference for the phylum BX of the bacteriological classification (Bergey's Manual, 2001)

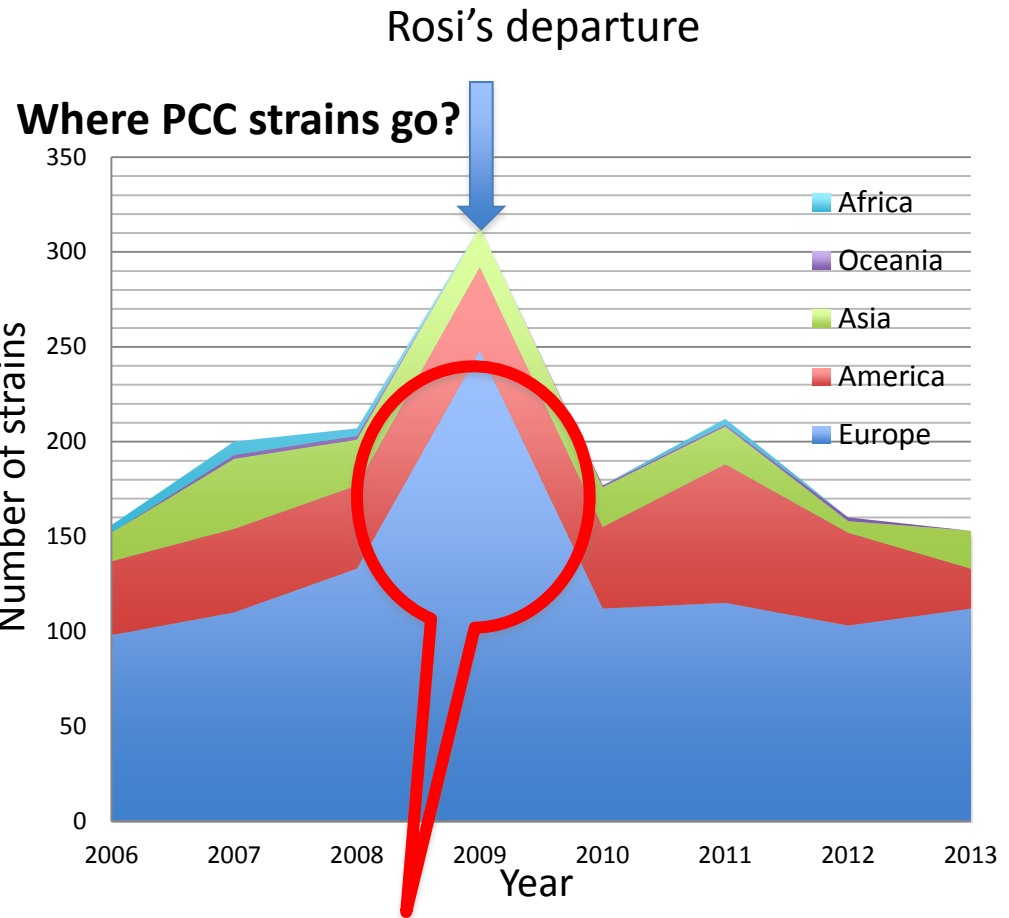
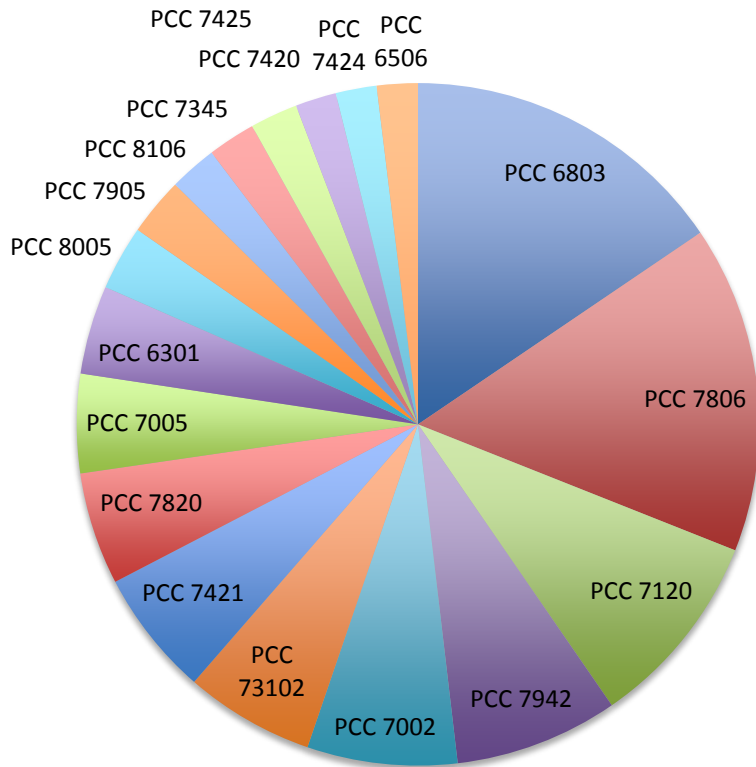
Cyanobacteria.web.pasteur.fr



The screenshot shows the website interface for the Pasteur Culture Collection of Cyanobacteria. At the top left, the letters 'PCC' are displayed in red, each enclosed within a green double-stranded DNA helix. To the right of this is the Institut Pasteur logo, which consists of a blue stylized 'P' inside a circle, with the text 'Institut Pasteur' below it. Below the logo and DNA graphic is a horizontal navigation bar with five buttons: 'Home' (with a micrograph), 'PCC Strains' (with a cyanobacteria cell), 'Genomes' (with a colorful bar chart), 'Protocols' (with laboratory glassware), and 'How to order' (with a person working in a lab). At the bottom of the page, a white banner contains the text: 'Welcome to the webpage of the Pasteur Culture collection of Cyanobacteria'.

PCC stars used all over the world

Top 18 of PCC strains

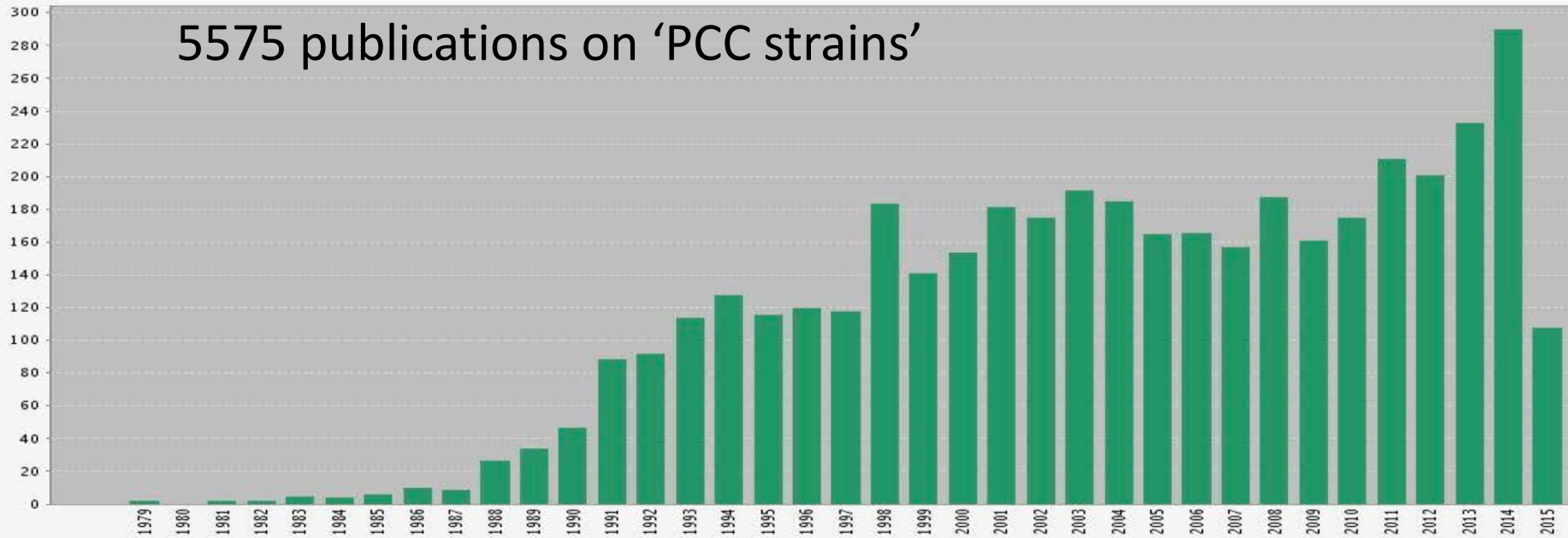


EXCESS OF ORDERS

=> Most corresponds to genome sequenced strains

PCC strains impact Science

5575 publications on 'PCC strains'



Rippka et al., 1979 -->

Photosynthesis
photosystems

Unicel. PCC 6803 -->

Cyanotoxins, NRPS/PKS -->

Heterocystous PCC 7120 -->

Unicel. PCC 7421 -->

Unicel. PCC 6301 -->

Unicel. PCC 7942 -->

Fil. PCC 8005 & PCC 7806 -->

5 PCC Cyanothece -->

70 PCC Strains -->

First section II and V strains



Omics and PCC

Genomics, Transcriptomics, Metabolomics

=> Lot of data: 21,000 cyanobacterial proteins with no detectable similarity to known proteins

=> Scaling-up the study: homologous region through the phylum

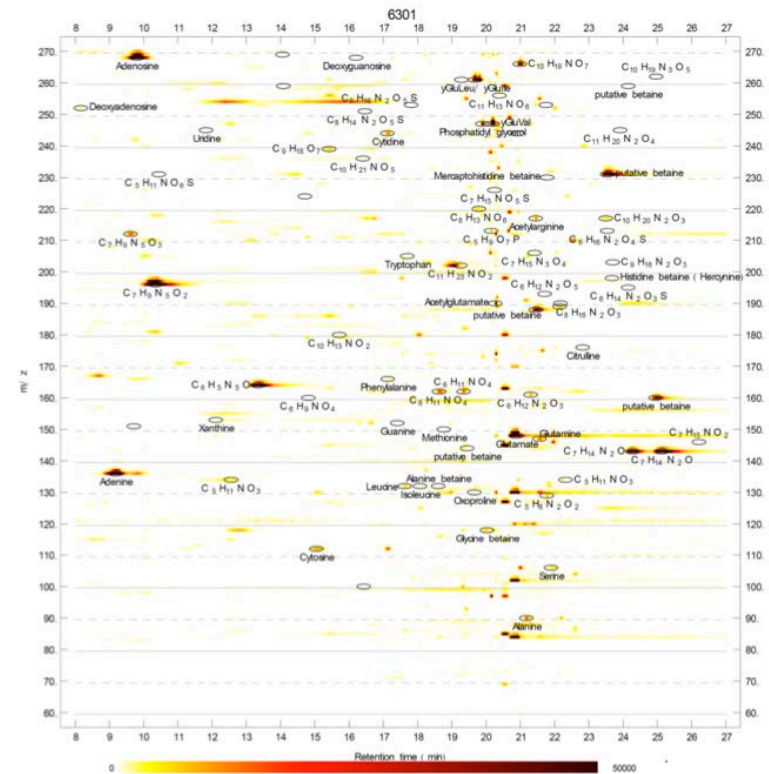
=> Multidisciplinary: to fetch the metabolites, enzymes beyond the sequences

(Shih et al., 2013, PNAS, Calteau et al., 2014, BMC Genomics)

Metabolomics of PCC strains

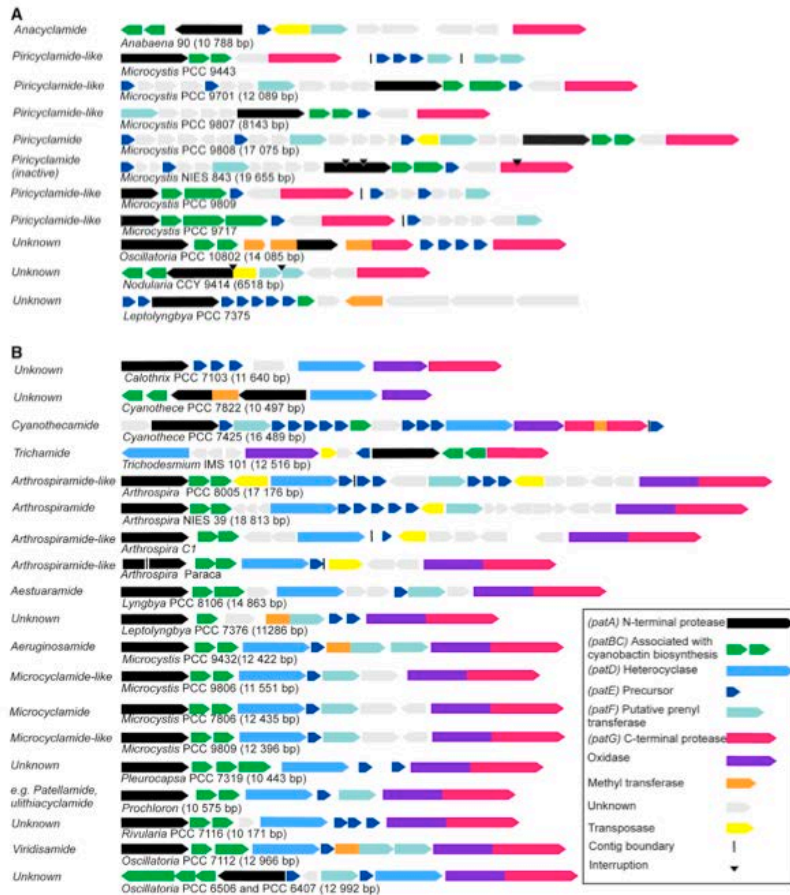
Untargeted metabolomics of PCC 7002 and nine other PCC strains (Baran et al., 2013, *Mar. Drugs*)

- Diverse betaine metabolites
- Unusual glycosides & oligosaccharides
- γ -glutamyl dipeptides...

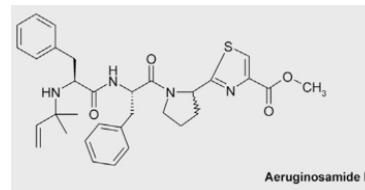


New class of cyanobactins

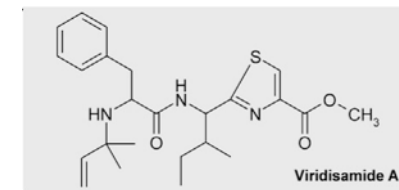
New class of the Cyanobactin family to include highly modified linear peptides (Leikoski et al., 2013, *ChemBiol*)



Microcystis sp. PCC 9432



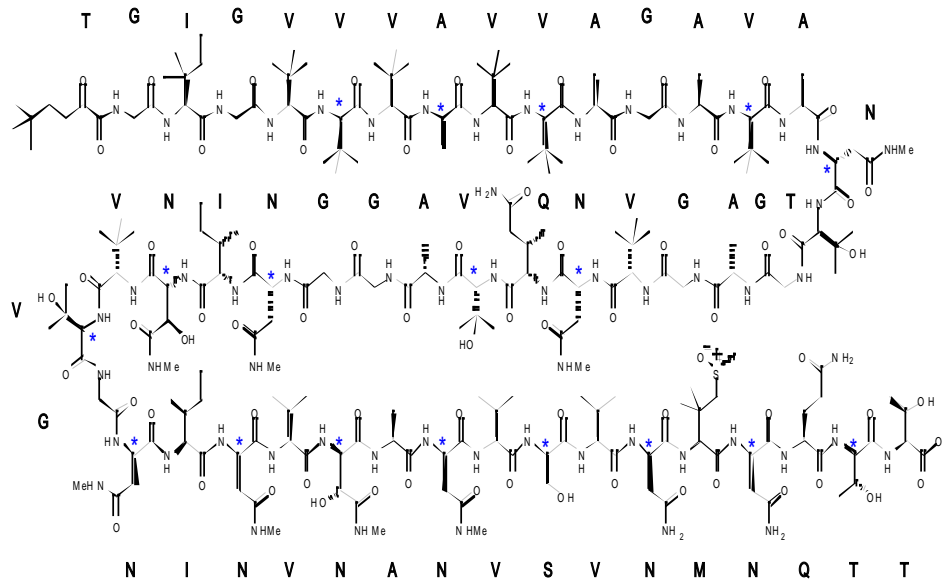
Oscillatoria nigro-viridis PCC 7112



Two short linear cyanobactins with a chain length ranging from three to five amino acids that were N-prenylated and O-methylated on the N and C termini

A new family of bacterial enzyme

rSAM epimerases of three cyanobacteria lead to a new bacterial enzyme family (Morikana et al., 2014, *Angew Chem Int Ed*)



- Polytheonamides A and B from a marine sponge:
- Highly cytotoxic pore-forming;
 - Ribosomal peptide family Proteusin (6 genes);
 - The most extensively modified peptides (48): *PoyD*.

Radical S-adenosyl methionine epimerases of cyanobacteria

GCW**I**AGSRGCGFVTRT

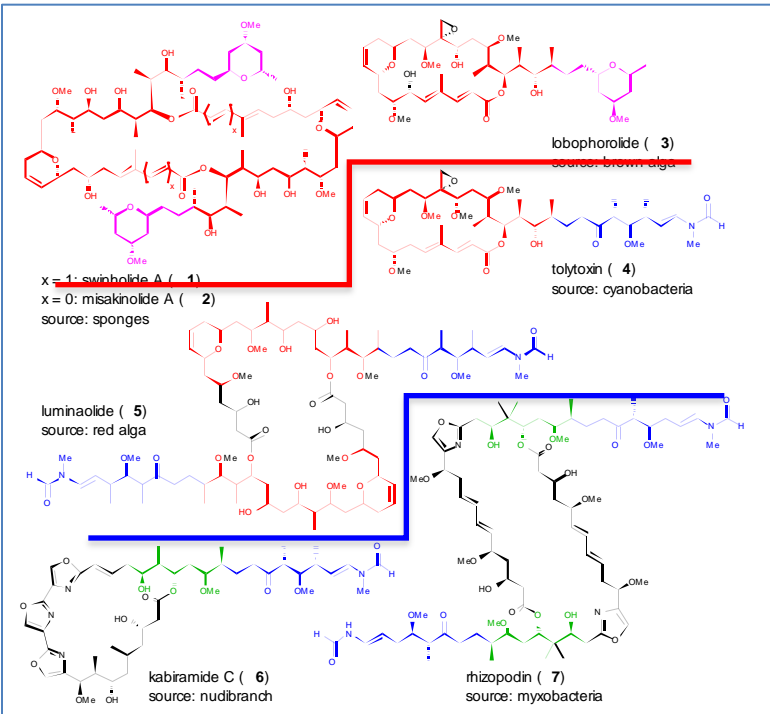
-Epimerase

GCW**D-*allo***-IAGSRGCGF**D-V**TRT

+Epimerase

14 16 18 20

Trans-AT Polyketide Synthase

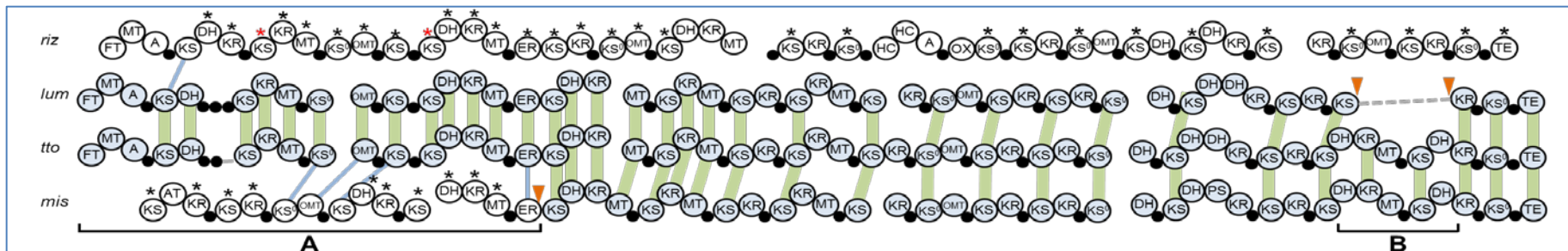


- Diversity of the metabolites, and of the strains harbouring these clusters.

- Actin targeting macrolides – what for?

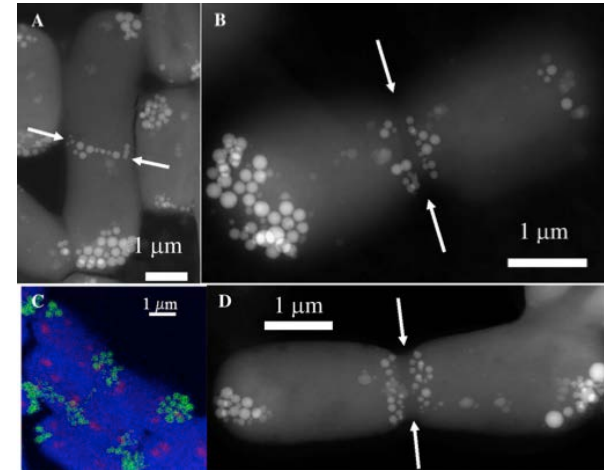
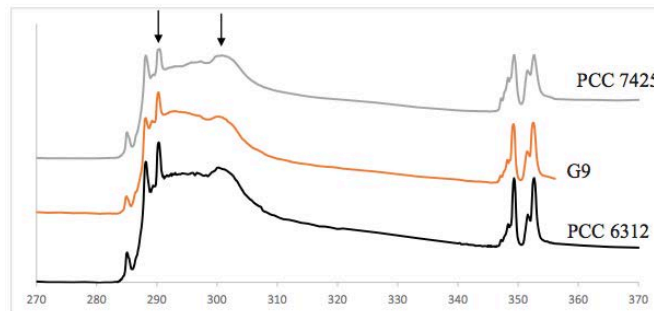
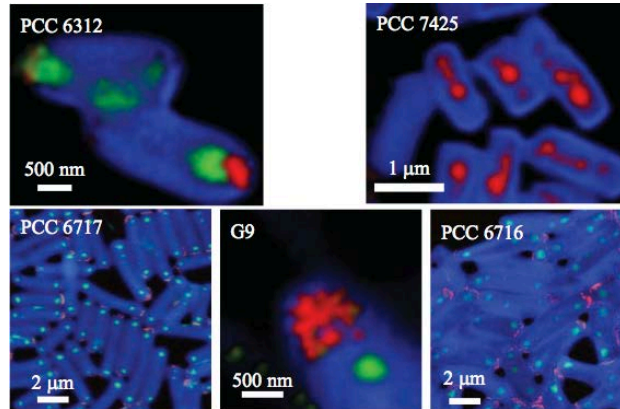
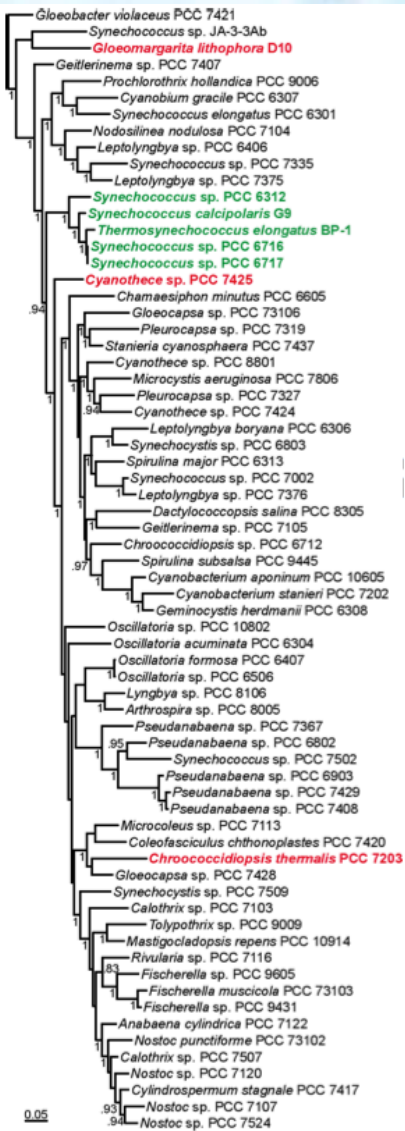
- Can we use these metabolites for human illness?

(Ueoka et al., Nat Chem Biol in press)



Calcification in diverse PCC strains

Intracellular Ca-Carbonate biomineralisation at septum and cell poles or scattered in the cytoplasm (Benzerara et al., 2014 *PNAS*).



Electron microscopy images: Ca in green, P in red and C in blue; Scanning Transmission x-ray microscopy analysis of carbonate inclusions

The background of the slide is a microscopic image of cyanobacteria. It shows numerous green, filamentous structures, some of which are branched. The filaments are composed of individual cells, some of which appear to have a distinct structure, possibly representing heterocysts or specialized cells. The overall appearance is that of a dense, interconnected network of these green filaments.

TAKE HOME MESSAGE

The PCC is a collection of reference for the phylum Cyanobacteria

The diversity of the PCC is more and more represented at the genomic level

As such, the PCC is a tool for research and biotechnology



Thanks

- Past and present collaborators at Pasteur
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- University Paris 7

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