



# project news

www.macumbaproject.eu

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Welcome to the sixth newsletter of the MaCuMBA project. In this issue: Interview with WP7 leader Professor Lone Gram P.1-2 Culture Club: Meet Marion Navarri and Alberto Vallejo Ayuso P.2 Partner Updates: MicroDishBV and Ribocon P.3-4 Training Update: Universidad Miguel Hernández Metagenomics Course P.5-6 Petri Dish Profile: BAMMO P.5-7 Under the Microscope: Marine Microorganisms in the news P.8



**Prof Lone Gram is the leader of MaCuMBA Work Package 7 (WP7), Screening for industrial targets from cultured marine bacteria. She is a professor at the Department of Systems Biology, Technical University of Denmark.**

Prof Lone Gram

## What is the aim of your work package and how will it contribute to the overall objectives of the MaCuMBA project?

The aim of WP7 is to evaluate the potential biotechnological use of the marine microorganisms that are isolated and/or cultured in MaCuMBA. WP7 thus addresses a key objective of MaCuMBA, the full title of the project being: Marine Microorganisms: Cultivation Methods for Improving their Biotechnological Applications.

## Where will the microorganisms to be examined in this work package come from?

The microorganisms examined in WP7 come from all parts of MaCuMBA. Several partners are working on bringing new, hitherto uncultured microorganisms into cultivation, and these (or sub-sets of these) will be tested

in the WP7 assays. A key parameter here is so-called de-replication, which is the process of testing samples of mixtures which are active in a screening process, so as to recognise and eliminate from consideration those active substances already studied. Since it is not possible to test thousands of strains, partners must de-replicate by, for example, selecting different species or microorganisms with different functional characteristics. We will also test microorganisms that the MaCuMBA partners had cultivated before the start of the project. Several of these have already been screened for biotechnological potential such as antibiotic activity, hydrolytic enzymes or anti-cancer agents. However, we have discovered that the compounds found through classical cultivation and bio-assay-guided fractionation (a method used to isolate a pure chemical agent from its natural origin) are only a fraction of the compounds that the genomes reveal could be produced. We therefore hypothesise that these so-called silent gene clusters, which encode compounds that are likely to be bioactive, can be obtained by cultivating the microorganisms under conditions that mimic the marine environment. Hence we use low nutrient conditions, addition of marine polymers, co-cultivation with other bacteria and, as described in WP5, the use of cell-cell signals.

## What are the main characteristics/bioactivities you will be looking for in the microorganisms?

The 13 partners of WP7 collectively cover quite an impressive range of bioactivities. Several partners can test for antibacterial activity. Here we search for both classical antibiotic activity and for so-called anti-virulence activity, since we test microorganisms and extracts for the ability to interfere with quorum sensing (a system of stimulus and response correlated to population density) in pathogenic bacteria. Several partners screen for enzyme-activities or for lipid and polymer-production and others for anti-cancer, anti-Alzheimer or anti-UV-activities. In total, the potential uses of these compounds range from ingredients, to industrial processing components, to pharmaceutical drugs.

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### What kinds of new bio-industrial products might be developed as a result of the work done by your WP?

I do not believe that new bio-industrial products as such will be developed. We have chosen to screen for a range of known activities. However, I hope that based on WP7 activities, we can point to particular groups of microorganisms as the most promising with respect to particular activities, and that we can also conclude whether the nature-mimicking cultivation concept will indeed unlock hitherto silent activities.

### What are the next milestones WP7 aims to achieve?

WP7 has several deliverables in the second year of **MaCuMBA**. Partners working on cyanobacteria will have chemically profiled these by month 24 and partners working on antibacterial activities will, by month 30, have tested a collection of bacteria for antifouling properties. Our first milestone is at month 36 where we have promised to screen deep-sea fungi for their antimicrobial activities.

### Why do you think projects such as MaCuMBA are important?

I think projects such as **MaCuMBA** are very important because they cover a continuum from very basic science to very applied science. We have so-far only been able to bring approximately 1% of marine microorganisms into culture and, despite the enormous potential of sequencing methods, I believe that a real understanding of an organism, its physiology and its role in the biochemical cycle requires that we can cultivate and study it. Therefore the **MaCuMBA** effort

to cultivate hitherto uncultured marine microorganisms is key to a better understanding of nature. We also know that microorganisms are a tremendous source of useful compounds – and also that mankind has an immense need for such compounds, e.g. as disease control agents. Using this as a driver to bring more microorganisms into culture, and to re-culture the ones we already have, brings a tremendous societal importance to the project. The biotechnological aspect clearly evokes interest in **MaCuMBA** on a much broader scale than the pure ecology.



Prof Gram's Research Group

## Culture Club: Meet the scientists making MaCuMBA possible



### Marion Navarri, PhD student, European University of Brittany, France

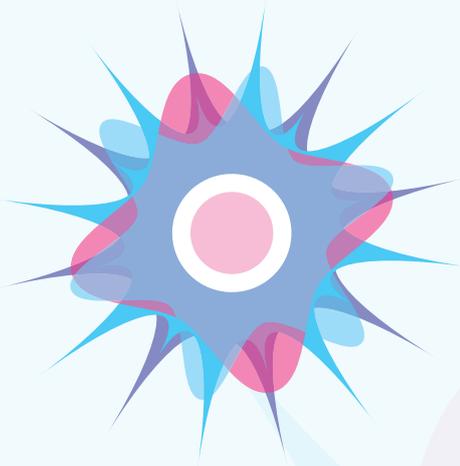
Marion is a PhD student at the Laboratoire Universitaire de Biodiversité et d'Ecologie Microbienne (LUBEM) at the European University of Brittany (Partner 3). Her PhD director is Pr. Georges Barbier, and her supervisors are Dr. Gaëtan Burgaud and Yannick Fleury. Within the **MaCuMBA** project, Marion is involved in WP7 dealing with the biotechnological potential of deep-sea fungal strains. Objectives of the PhD are to screen the fungal strains isolated during WP2 for their biotechnological applications (antimicrobial activities), to isolate bioactive molecules and to elucidate their structure.



### Alberto Vallejo Ayuso, Project Assistant, AquaTT

Alberto holds a degree in biology from the Universidad Autonoma de Madrid, Spain. He joined AquaTT in 2011. As a project assistant, he provides support to AquaTT's project officers by helping with project management, dissemination and knowledge transfer tasks as part of a number of EC-funded projects. He also manages PiscesTT Jobs, AquaTT's free recruitment portal.

As part of the **MaCuMBA** project, Alberto is involved in WP1 (Project Management) and WP9 (Dissemination, Knowledge management and linkages), collaborating in the organisation of project meetings and carrying out the dissemination and knowledge transfer of the outputs of the project.



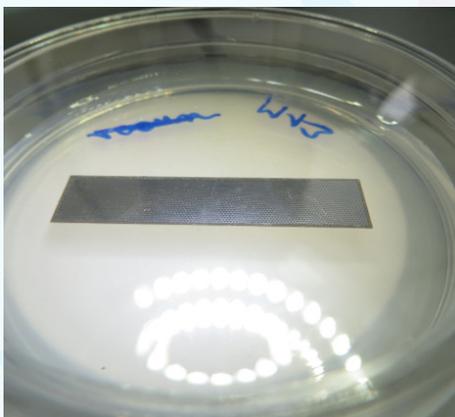
## Partner Update: MicroDish BV

**MaCuMBA Project Partner MicroDish BV** is a biotechnology company located in Utrecht, the Netherlands. MicroDish has developed the MicroDish Culture chip (MDCC), which is a disposable device used for the culture of microorganisms consisting of a massive number of miniaturised Petri dishes on a single chip.

MicroDish has adapted the MDCC so that it can be deployed in the natural environment for co-culture and enrichment. This is intended to allow incubation of the MDCC in new situations and to extend the range of applications of the culture chips, including the move towards higher throughput. As part of the **MaCuMBA** project, the MDCC and in situ culture chambers are being used to culture marine microorganisms from various sampling sites using seawater from the same site whilst in contact with the natural environment.

Representatives from MicroDish were involved in the sampling activity at the recent **MaCuMBA** General Assembly in Roscoff, France.

MicroDish Chief Scientific Officer, Dr Colin Ingham, said: "The work in Roscoff was of great value for MicroDish as it provided excellent access to the marine environment and great facilities, including an aquarium, which allowed us to make isolations of novel microorganisms. Particularly helpful were the divers and staff from the Station Biologique Roscoff, who placed the cultivation chambers in the sea to allow the cultivation of microorganisms in their natural habitat, and who also later recovered the chambers along with the entrapped microorganisms. Our visit to Roscoff was more than a good academic networking opportunity, it also allowed considerable scientific progress. That there is more practical work planned for the next **MaCuMBA** General Assembly in Spain is very welcome!"



Close up of an MDCC just after inoculation with an environmental sample



An MDCC placed under a dissection microscope for examination of microcolonies



Microdish CSO Dr. Colin Ingham with DSMZ Postdoc Dr. Cendrella Lepleux taking a well-deserved lunch break during the research activity funded by ASSEMBLE



Microdish scientist Dr. Zalan Szabo after taking a sample during low tide at the Biological Station in Roscoff

## Partner Update: Ribocon



MaCuMBA consortium partner **Ribocon** is a professional bioinformatics services and solutions provider for microbiology, serving academia and industry worldwide. Here, **Dr Michael Richter**, bioinformatics project manager at **Ribocon**, tells us about the **JSpecies** web service which will be used as part of **MaCuMBA WP6, Sequencing, genomic and metagenomic libraries and (meta)genome analyses**.



Dr Michael Richter

### What does the JSpecies software do?

Broadly speaking, the JSpecies software mimics, via computer simulation, a laboratory technique named DNA-DNA hybridisation (DDH), which measures the degree of genetic similarity between pools of DNA sequences. DDH has been the gold standard for genomically defining

species for nearly 50 years now, despite the complexity of its experimental design and the time-consuming nature of the processes involved. Now, in the era of genomics, scientists have access to thousands of publicly available genomes and cost-saving genome sequencing of their own isolates. This is facilitated by more user friendly and exact approaches such as those enabled by the JSpecies software. The corresponding JSpecies web service (JSpeciesWS) represents the latest development of the underlying infrastructure in terms of usability, flexibility, and efficiency.

### How was this software developed?

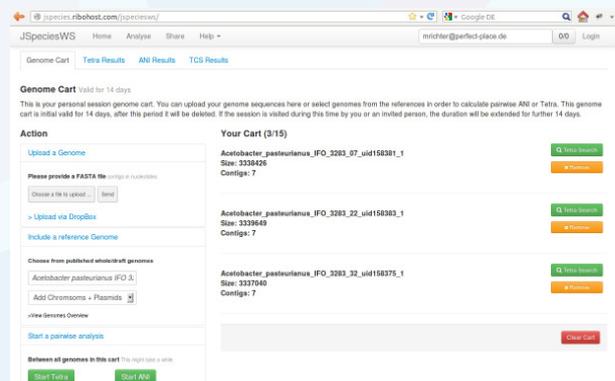
JSpecies has originally been developed together with Ramon Rosselló-Móra, from the Spanish research institute IMEDEA, in 2009 as stand-alone software and was published in the Proceedings of the National Academy of Sciences of the United States of America (PNAS) (<http://www.pnas.org/content/106/45/19126>). The JSpeciesWS is an online implementation of the core software for easy user-access and extended functionality. This includes options to share results among users, a centralised online reference database of all published whole and draft genomes (~10.000), and the TETRA Correlation Search (TCS) which allows users to search for similar organisms within the reference database in seconds, based on their complete genome sequences.

### How will the JSpeciesWS be applied as part of the MaCuMBA project?

Within the **MaCuMBA** project, thousands of new microbial isolates will be produced, classified and further characterised. Many of them will be selected for genome sequencing and detailed description, always starting with the central question of microbial systematics (classification). This process will be supported by the easy-to-use JSpeciesWS which will help to taxonomically describe novel species using state-of-the-art data.

### When will the software be made readily available?

The service is already available online at: <http://jspecies.ribohost.com/jspeciesws/>. Two supporting publications are planned for 2014, a technical note describing the service and a use-case based on the comparison of a larger set of genomes for their taxonomic classification, in cooperation with the **MaCuMBA** partner, the University of Amsterdam (Prof Gerard Muyzer).



A screenshot of the JSpeciesWS

### What impact do you hope the JSpeciesWS will have?

The comparative efforts undertaken to evaluate average nucleotide identity (ANI) as a mirror for DDH led us to ascertain that ANI, with the support of TETRA values, is the parameter that can immediately substitute for DDH. Especially, for closely related organisms (e.g. > 97% identity over 16S rRNA) this kind of analysis will be very important in order to circumscribe a novel species. The overall growing databases for genome sequences will further attract this kind of analysis by providing a comprehensive search space.

## Universidad Miguel Hernández Metagenomics Course

The Evolutionary Genomics Group (EGG) of Universidad Miguel Hernández (UMH) held a metagenomics course in Alicante, Spain, from 9-13 December 2013. The course aimed to provide an overview of both practical and theoretical aspects of postgenomic microbiology in microbial ecology. The programme consisted of lectures and practical work regarding data analysis, biomass collection and nucleic acid extraction from marine samples. The presentations made during the course are now available to download from [www.egg.umh.es/course.html](http://www.egg.umh.es/course.html). Here, **MaCuMBA** researchers who attended the course give their feedback.



**Name:** Mariane Schmidt  
**Position:** Postdoctoral Researcher  
**Institute:** Technical University of Denmark

**Please provide a short description of your current role in the MaCuMBA project**

I am a postdoctoral researcher working in Prof Lone Gram's lab, and my role in **MaCuMBA** is – in collaboration with other partners –



to create cultivation systems that mimic the natural environment of marine bacteria in order to promote growth and production of secondary metabolites such as antimicrobial compounds and hydrolytic enzymes. I focus on several different cultivations systems, the most prominent right now being the utilisation of defined natural substrates such as carrageenans, agar and other polymers found in the marine environment. However, I also attempt to culture marine bacteria on media composed of more undefined substrates like algal exudates.

**What were your reasons for applying for this course?**

My reasons for applying for the course was that I wanted to learn how to handle metagenomic data, since my primary approach on evaluating culturability of my selected media will be through metagenomic sequencing.

**What was your overall impression of the course?**

The course had some very interesting lectures on what you can use metagenomics for.

**What part of the course did you enjoy the most?**

I really enjoyed the lectures. It was great to get an impression of what people are doing with metagenomics

**What part of the course do you think will be most useful for your work as part of MaCuMBA and why?**

The most useful thing I got from the course was an idea of exactly how complicated it is to deal with metagenomic data. But from talking to the people at UMH, who are very helpful, I got the impression that they will be available for support and discussions when needed, which is really great!



**Name:** Daniela Clara Cardoso  
**Position:** PhD student  
**Institute:** Royal Netherlands Institute for Sea Research (NIOZ), the Netherlands

**Please provide a short description of your current role in the MaCuMBA project**

I am working with Prof Lucas Stal at NIOZ, currently studying the genetic diversity in the microbial mats

in Schiermonnikoog, comparing the different seasons of the year versus active microorganisms.

**What were your reasons for applying for this course?**

My group is taking its first steps in genomics and since I am going to need to do an analysis of my research results I decided to attend this course.

**What was your overall impression of the course?**

The course was really well organised and we were taught a lot.

**What part of the course did you enjoy the most?**

The part I most enjoyed were the practical classes where we were taught step by step from the beginning, which was perfect for someone that was just starting to learn.

**What part of the course do you think will be most useful for your work as part of MaCuMBA and why?**

I think the practical classes will be most useful for my work as part of **MaCuMBA**, since the knowledge I gained there will allow me to analyse my results properly. I think the theoretical part will also help me have a better overview on genomics.

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**Name:** Catarina Cúcio  
**Position:** PhD student  
**Institute:** University of Amsterdam (UvA), the Netherlands

**Please provide a short description of your current role in the MaCuMBA project**

My PhD research is focused on the interactions between bacteria and seagrasses, a group of ecologically relevant marine flowering plants. I started my participation in the **MaCuMBA** project with the cultivation of bacteria from the regions of sediment in the vicinity of the roots of these plants, and also isolated DNA from the same environment for metagenomics.

**What were your reasons for applying for this course?**

The analysis of metagenomic data is no simple task, therefore this course was very important to prepare me for the upcoming work I will be doing as part of my PhD.

**What was your overall impression of the course?**

The morning lectures were very interesting due to the diversity of the “hot topics” presented. The lecturers were very open to answering questions and clear in their introductions and explanations, and the tutorials were also very helpful.

**What part of the course did you enjoy the most?**

Even though I very much enjoyed the lectures, the practical component was the best part of the course in my opinion. When we return to our own research, it all comes back to the question of “how to?”, and the practical component was great in helping to answer this question.

**What part of the course do you think will be most useful for your work as part of MaCuMBA and why?**

I think that the practical component will be most useful for my work as part of **MaCuMBA**. Thanks to the help of Prof Francisco Rodríguez-Valera and his team, who I want to congratulate for the quality of this course, the UvA will have a metagenomic analysis of the seagrass microbiome by the end of the year!



**Name:** Henk Bolhuis  
**Position:** Senior Scientist  
**Institute:** Royal Netherlands Institute for Sea Research (NIOZ), the Netherlands

**Please provide a short description of your current role in the MaCuMBA project**

I became involved in the **MaCuMBA** project at an early stage when brainstorming with the coordinator, Lucas Stal, about the general outlook of the project and our own contribution. Currently I am the daily supervisor of a PhD student, postdoctoral researcher and technician working on **MaCuMBA**. When possible I like to do lab work dedicated to the isolation of novel species from microbial mats, our model microbial ecosystem.

**What were your reasons for applying for this course?**

I applied for this metagenomics course to gain insight into the available methods in high throughput sequencing and to learn from the personal experience of the lecturers and UvA staff. In addition I wanted to get practical training in basic bioinformatic analysis of these large data-sets.

**What was your overall impression of the course?**

I was impressed by the organisation, lectures, and the practical training that allowed us to work on real data sets so that we could see what happened with the raw data during the different conversions.

**What part of the course did you enjoy the most?**

Although I enjoyed the whole course, I especially liked the practical training and the enthusiasm and patience of the UvA team. Unfortunately I was unable to attend the sampling trip but I heard from my colleagues that this was very informative.

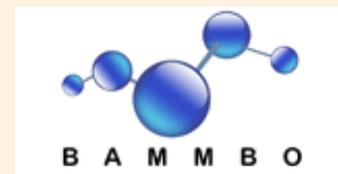
**What part of the course do you think will be most useful for your work as part of MaCuMBA and why?**

For my supervising and participating role in **MaCuMBA**, this course was very valuable for getting insight into benefits and pitfalls of different sequence technologies and available bioinformatic tools. It will allow me to choose the right tools to apply to our research and project deliverables, and to provide better feedback to those I supervise. Finally, this course provided a great opportunity to strengthen my network, meet the lecturers in person and know who to approach if certain questions arise.





# Petri Dish PROFILE:



Dr Patrick Murray



Our series of Petri Dish Profiles of other European-funded projects related to the study of marine microorganisms continues with the **BAMMBO** (Sustainable production of biologically active molecules of marine based origin) project. Dr Patrick Murray, **BAMMBO** Scientific Manager, from Limerick Institute of Technology, Ireland, tells us what it is all about.

## What are the aims of the **BAMMBO** project?

Due to the rich biodiversity of their ecosystems, seas and oceans possess the capacity to produce a variety of molecules with unique features and unmatched biochemical diversity. The **BAMMBO** project has developed sustainable methods to culture marine-based microorganisms such as macro-algae, fungi, bacteria and sponges in an enclosed environment. These organisms produce a wide range of biologically active molecules with potential for immediate market application in industry sectors spanning nutrition, pharmaceuticals, cosmetics and diagnostics. Knowledge, research and innovation are essential elements to maximise the economic, scientific and environmental benefits of the European marine territory. Recognition of the importance of the marine environment is now enshrined in the EU Integrated Maritime Policy and European strategy for marine and maritime research. This promotes a European vision for the oceans and seas as a dynamic economic resource in harmony with the environment and underpinned by excellence in marine science and technological development.

The **BAMMBO** project, valued at €4.2 million, is being co-ordinated by Limerick Institute of Technology (LIT), Ireland, and is a collaborative project involving universities, research centres and industries based in Belgium, Brazil, France, Ireland, Italy, Portugal, Russia and Spain.

## What are the main socio-economic, environmental and sustainability issues with regard to the use of marine organisms for industrial-scale production of high added-value compounds?

Marine biotechnology, which involves marine bioresources either as the source or the target of biotechnology applications, is fast becoming an important component of the global biotechnology sector. Marine biotechnology can make an increasingly important contribution towards meeting societal challenges in

supporting economic recovery and growth in Europe by delivering new knowledge, products and services. The 70,000 km European Union coastline which touches the Mediterranean, Baltic, North and Black seas and the Atlantic and Arctic oceans provides enormous bio-resource potential. The opportunities offered by land-based organisms and their many applications for production of non-food high-value products are recognised. However, in this context the economic and scientific potential of marine organisms has remained relatively under-explored. The **BAMMBO** project has addressed this. The production of these bioactive compounds in **BAMMBO** has been addressed in an environmentally sustainable and conscientious manner.

## What do you think will be the most exciting results of the **BAMMBO** project?

The **BAMMBO** project has established production pathways for marine invertebrate bioactive compounds. In the exploration of marine biomass for high-value bioactive molecules, the project has developed optimised cultivation protocols for target organisms mimicking their specific ecological conditions.



Supercritical Fluid Extraction System Shannon Applied Biotechnology Laboratory Limerick Institute of Technology Ireland

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### How will the results of the project be transferred to relevant stakeholders?

In order to publicise the work being conducted by the consortium and the support being provided by the European Commission, a series of objectives with associated deliverables and milestones have been put in place for the project. The **BAMMBO** dissemination programme is designed to maximise the impact of the **BAMMBO** project and its outcomes for all relevant stakeholders, including the consortium partners, industry, the wider research community, policy makers and society. Dissemination has encompassed a wide variety of media and event formats spanning: publication in scientific journals; patenting; presentations at conferences; hosting workshops specific to the group and the individual participants where applicable; articles in trade magazines and popular press; an overview of the project by Hi-Tech EuroNews; and a dedicated website [www.bammbo.eu](http://www.bammbo.eu) where all information relevant to the project is available to the public. Research outcomes of interest to SMEs are disseminated by means of dedicated annual congresses, seminars and workshops. These have been aimed initially at SMEs associated with the RTD partners followed by relevant SMEs as identified by the **BAMMBO** Project Management Committee and **BAMMBO** Project Advisory Board in addition to networks such as the Enterprise Europe Network. A special meeting has been convened annually to coincide with the Project General Assembly. This meeting will be industrially relevant, with industry representatives (Stakeholders/Collaborators)

attending to hear about technology package offerings arising from the **BAMMBO** project

### Will any of the project partners be involved in commercialisation of the knowledge or technologies resulting from the project?

An Irish company that is a member of the **BAMMBO** consortium, called Algae Health, which is based in Galway, are developing products. You can visit the company website ([www.algaehealth.ie](http://www.algaehealth.ie)) to learn more about them.

### What do you think the legacy of the **BAMMBO** project will be?

The Horizon 2020 vision for European marine biotechnology is the development of an integrated and globally competitive biotechnology sector that would apply advanced tools in a sustainable and ethical manner in order to provide a significant contribution towards addressing key societal challenges in the areas of food and energy security, development of novel drugs and treatments for human and animal health, industrial materials and processes and the sustainable use and management of the seas and oceans. Through **BAMMBO**, marine ecosystems which support a variety of life-forms including microbes (bacteria, cyanobacteria and fungi), micro- and macro-algae and other invertebrates including sponges, corals and molluscs have been investigated and novel sustainable production pathways for high-value added biomolecules have been established.

[www.bammbo.eu](http://www.bammbo.eu)

## Under the Microscope: Marine Microorganisms in the news

### Stirling scientists discover marine algae can help acne sufferers

Research by marine scientists at the University of Stirling's internationally renowned Institute of Aquaculture revealed the cleansing qualities of certain fatty acids including some produced by marine algae. [bit.ly/1aisaP8](http://bit.ly/1aisaP8)

### Changing the conversation — polymers disrupt bacterial communication

A study led by scientists at the University of Nottingham has shown that artificial materials based on simple synthetic polymers can disrupt the way in which bacteria communicate with each other. [bit.ly/1kD4xij](http://bit.ly/1kD4xij)

### Unlocking the secrets of marine carbon cycling

Microscopic marine phytoplankton play a critical role in regulating today's carbon cycles, yet not enough is known about the process. [bit.ly/1fRi8m5](http://bit.ly/1fRi8m5)

### Methane-Munching Microorganisms Meddle With Metals

A pair of cooperating microbes on the ocean floor "eats" methane in a unique way, and a new study provides insights into their surprising nutritional requirements. [bit.ly/1n700qz](http://bit.ly/1n700qz)

### New Species of Marine Algae Identified

The species that historically was quoted as the most abundant of coral algae that forms rodoliths at the Gulf of California in Mexico, is in reality a compound of five different species. [bit.ly/Lq1fq7](http://bit.ly/Lq1fq7)

