MaCuMBA project news

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MaCumBA is a four-year research project that aims to uncover the untold diversity of marine microbes using cultivation-dependent strategies. This joint venture of 23 partner institutions from 11 EU countries is led by the Royal Netherlands Institute for Sea Research (NIOZ), and has a budget of more than €12 million, of which €9 million is funded by the EC Seventh Framework Programme.

Prof Fergal O'Gara is the leader of MaCuMBA Work Package 5 (WP5), *Cell to cell communication in community cultures, isolation and cultivation.* He is the director of the BIOMERIT Research Centre (BRC) at University College Cork (UCC), Ireland.

Prof Fergal O'Gara

What is cell- cell communication and how might it be used to improve the isolation of uncultured microorganisms and the cultivation efficiency of cultivated microorganisms?

Cell-cell communication is the broad term used to describe how small molecules, or chemical messages, produced and perceived by bacteria effectively control behaviour both within and between species. Initially our understanding of cell-cell communication was centred on a process called Quorum Sensing. This term reflected the fact that a threshold or quorum of signal was required before activation of the receptors by which bacteria sense and respond to change in their environments.

More recently, the discovery that these small molecules can control interspecies interactions has broadened our understanding of cell-cell communication. As with all forms of communication, the outcome can be of either a positive or negative nature. In some cases, the secretion of signal molecules can promote the growth of co-habiting bacteria. Conversely, these signals can also be detrimental to the growth and survival of competing species. We have recently identified several signal compounds that modulate the growth of marine organisms and we will continue to characterise new molecules through the course of MaCuMBA.

One of the major limitations affecting the culturability of microorganisms is the complexity of their growth requirements. Therefore, the identification and characterisation of growth promoting signals can be used to supplement cultivation media and enhance the diversity of culturable organisms isolated from the marine environment. By the same token, interference with growth limiting signal molecules would facilitate the growth of species that would otherwise not be possible.

This WP has a focus on microorganisms from marine sponges, what makes these organisms particularly interesting for this research?

Marine microbial communities, which are extraordinarily diverse, can account for up to 40% of the biomasss of marine sponges. Therefore, it comes as no surprise that marine sponges host active microbial communities that are engaged in the production of a diverse repertoire of cell-cell signal molecules, secondary metabolites and enzymatic activities. However, our capacity to exploit these activities is greatly limited by our inability to cultivate the producing organisms. One of the key developments that will emerge from MaCuMBA will be our capacity to harvest the extent of the novel activities in these marine sponges.

The BIOMERIT Research Centre (BRC) works closely with the Environmental Research Institute (ERI) at UCC, which is a partner in the PharmaSea project, this issue's Petri Dish Profile; will there be any collaboration between the BRC and the ERI on the work being done as part of MaCuMBA and PharmaSea?

There is a hugely beneficial synergy between the BRC and ERI independent research programmes, which adds greatly to the capacity of both centres to deliver on and exploit the outcomes of the MaCuMBA and PharmaSea EU collaborative projects. Collaboration between the BRC and ERI is ongoing, particularly in the area of metagenomic mining and bioactive screening. Many of the technologies and molecular tools that are being developed by both centres have uses that span both projects and the expertise is readily shared.

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The MaCuMBA logo includes an asterisk which represents both a microorganism and a reference to the full project title, which is Marine Microorganisms: Cultivation Methods for Improving their Biotechnological Applications

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Will the results of any other MaCuMBA WPs directly feed into the work of WP5?

One of the strengths of the MaCuMBA programme is the integration of expertise and technological capabilities that exist in the consortium. New isolates and metagenomic libraries (WP7) will provide a vast resource for the identification of novel signal molecules and pathways, with further scope provided by the sequencing of genomic and metagenomic libraries (WP6). The BRC has already developed and had success with the screening technologies required to mine the marine samples for signal molecules. The provision of new samples and data from other WPs will greatly enhance the outputs from WP5. Equally, the outputs from WP5 will feed into several other WPs, e.g. WP6 where the genomes of marine organisms producing signal molecules will be examined.

What impact might the work carried out by WP5 have beyond the scope of the MaCuMBA project?

A key factor underpinning WP5 is the current dearth of knowledge surrounding cell-cell communication in the marine environment. An exciting development that will arise from WP5 will be the identification and characterisation of new pathways and new signal molecules in species for which cell-cell communication has not previously been shown. These new systems will provide novel theories with which to understand cell-cell communication in a range of niches, including within the polymicrobial communities that exist during infection.

What are the next milestones your WP aims to achieve?

Early successes in the MaCuMBA project have been the identification of new cell-cell communication molecules produced by organisms isolated from marine sponges. These signals have the potential to greatly influence the isolation of uncultured microorganisms and the next milestones in the project will seek to evaluate this potential. The next milestones associated with WP5 will be the profiling and characterisation of cell-cell signalling systems in the marine environment. Obviously this will then be linked to the development of improved culturing methods for marine organisms through supplementation with or antagonism of signal molecules. Finally, the expression of silent biosynthetic gene clusters in response to these signal molecules will provide a previously untapped source of bioactive compounds, both industrial enzymes and pharmaceuticals.

Second MaCuMBA Project Meeting

MaCuMBA will hold its second project partner meeting at the Station Biologique de Roscoff, France, on 23-27 September 2013. The meeting will provide the project's partners with the opportunity to assess the progress that has been made by MaCuMBA so far. This meeting will include plenary meetings and lectures on topics relating to the work package themes from participants working in or closely with MaCuMBA. There will also be two days of workshops and lab visits, during which partners will be able to work in the lab together and share isolation techniques and knowledge.

Watch this space for a report from this meeting in the next issue of MaCuMBA Project News.

Publications

MaCuMBA Project News is only one of the channels through which the work done as part of MaCuMBA is communicated! We thank all MaCuMBA partners who have already made efforts to disseminate MaCuMBA and its results through communication and engagement with other scientists and actors beyond the research community. This section includes details of some of the growing number of scientific publications acknowledging MaCuMBA:

- **Metagenomics uncovers a new group of low GC and ultra-small marine Actinobacteria**
  Ghai, R., Megumi Mizuno, C., Picazo, A., Camacho, A. and Rodriguez-Valera, F. 2013. Scientific Reports, 3 (2471). Available from: DOI:10.1038/srep02471
  Shortened URL: http://bit.ly/14ga1MW
- **Draft Genome of *Spiribacter salinus* M19-40, an Abundant Gammaproteobacterium in Aquatic Hypersaline Environments**
  Leon, M.J., Ghai, R., Fernandez, A.B., Sanchez-Porro, C., Rodriguez-Valera, F. and Ventosa, A. 2013. Genome Announcements, January-February (1). Available from: DOI: 10.1128/genomeA.00179-12
  Shortened URL: http://bit.ly/17PvL35
- **Complete Genome Sequence of the Copiotrophic Marine Bacterium *Alteromonas macleodii* Strain ATCC 27126^T**
  Gonzaga A., López-Pérez M., Martin-Cuadrado A.B., Ghai R. and Rodriguez-Valera F. 2012. Journal of Bacteriology, 194(24). Available from: DOI: 10.1128/JB.01565-12
  Shortened URL: http://bit.ly/1fYGdpG
- **Insights into the Physiology and Ecology of the Brackish-Water-Adapted Cyanobacterium *Nodularia spumigena* CCY9414 Based on a Genome-Transcriptome Analysis**
  Voß B, Bolhuis H, Fewer DP, Kopf M, Möke F, et al. 2013. PLoS ONE, 8(3). Available from: DOI: 10.1371/journal.pone.0060224
  Shortened URL: http://bit.ly/15Vvkzl
- **Multiple microalgal partners in symbiosis with the acantharian *Acanthochiasma sp.* (Radiolaria)**
  Decelle, J., Siano, R., Probert, I., Poirier, C. and Not, F. 2012. Symbiosis, December, 58 (1-3), pp. 233-244. Available from: DOI: 10.1007/s13199-012-0195-x
  Shortened URL: http://bit.ly/1egoIWx
- **Polyclonality of Concurrent Natural Populations of *Alteromonas macleodii***
  Gonzaga, A., Martin-Cuadrado, AB., López-Pérez, M., Megumi Mizuno, C., García-Heredia, I., Kimes, N.E., Lopez-García, P., Moreira, D., Ussery, D., Zaballos, M., Ghai, R. And Rodriguez-Valera, F. 2012. Genome Biol Evol, 4 (12). Available from: DOI: 10.1093/gbe/evs112
  Shortened URL: http://1.usa.gov/1apC5i0
- **Summer community structure of aerobic anoxygenic phototrophic bacteria in the western Arctic Ocean**
  Boeuf, D., Cottrell, M.T., Kirchman, D.L., Lebaron P. and Jeanthon, C. 2013. FEMS Microbiology Ecology, 85 (3), pp. 17–432. Available from: DOI: 10.1111/1574-6941.12130
  Shortened URL: http://bit.ly/15j4RQE
- ***Prochlorococcus* and *Synechococcus* have Evolved Different Adaptive Mechanisms to Cope with Light and UV Stress**
  Mella-Flores, D., Six, C., Ratin, M., Partensky, F., Boutte, C., Le Corguillé, G., Marie, D., Blot, N., Gourvil, P., Kolowrat, C. and Garczarek, L. 2012. Front Microbiol, 3(285). Available from: DOI: 10.3389/fmicb.2012.00285
  Shortened URL:http://bit.ly/15QHtN1

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Under the Microscope: Marine Microorganisms in the news

Super Sunscreen from Fjord Bacteria
A microorganism living in Trondheim Fjord will provide you with better protection against skin cancer and malignant melanomas.
Shortened URL: http://bit.ly/196MlyD

A Slimy Marine Organism Fit for Biofuel and Salmon Feed
It sounds too good to be true: a common marine species that consumes microorganisms and can be converted into much-needed feed for salmon or a combustible biofuel for filling petrol tanks.
Shortened URL: http://bit.ly/17aaK1G

Newly Discovered Marine Viruses Offer Glimpse into Untapped Biodiversity
Studying bacteria from the Baltic Sea, University of Arizona researchers have discovered an entire array of previously unknown viruses that barely resemble any of the known bacteria-infecting viruses.
Shortened URL: http://bit.ly/1bnxf8w

First Global Atlas of Marine Plankton Reveals Remarkable Underwater World
To begin to identify where, when, and how much oceanic plankton can be found around the globe, a group of international researchers have compiled the first ever global atlas cataloguing marine plankton ranging in size from bacteria to jellyfish.
Shortened URL: http://bit.ly/14o9euq

Metagenomics: Hunting for New Genes by Sequencing Seas Samples
Mass DNA sequencing has led to a better knowledge of marine micro-organisms in their environment and helps to discover new genes of interest. However, it is only part of the answer for biotech applications.
Shortened URL: http://bit.ly/12nPO6j

Compound Discovered at Sea Shows Potency against Anthrax
A new chemical compound from an ocean microbe could one day set the stage for new treatments for anthrax and bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA).
Shortened URL: http://bit.ly/12I1LV4

Scientists Discover Thriving Colonies of Microbes in Ocean 'Plastisphere'
Scientists have discovered a diverse multitude of microbes colonising and thriving on flecks of plastic that have polluted the oceans—a vast new human-made flotilla of microbial communities that they have dubbed the "plastisphere".
Shortened URL: http://bit.ly/14d5IAo

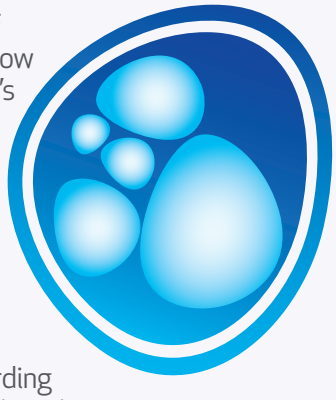
'Immortal' Irish marine animal provides hope for research into ageing
Hydractinia echinata has the power to regenerate any lost body part, can clone itself and does not age biologically.
Shortened URL: http://bit.ly/17R2SIh

Culture Club: MaCuMBA Researcher Profiles

Just like the marine microorganisms it studies, the MaCuMBA project relies on a community structure to thrive. Here we meet some of the scientists from all over Europe working together to achieve the project's aims.

Mariane Schmidt
Postdoctoral Researcher
Technical University of Denmark

Mariane holds a PhD in microbiology and biotechnology from the University of Copenhagen, Denmark. She has worked for several years in research in the field of extremophilic aquatic bacteria with industrial potential. She has mainly focused on the discovery of novel hydrolytic enzymes, using both classical growth dependent assays and high-throughput methods. For the past three years Mariane has had a postdoctoral fellowship as a molecular biologist working on mutagenesis and expression of virulence factors in *E. coli*, but now – being employed in Lone Gram's research group at Technical University of Denmark (DTU) Systemsbiology – she is returning to aquatic microbiology. As part of the MaCuMBA project she will investigate and develop isolation, culturing, and screening techniques regarding optimisation of production of bioactive compounds in marine bacteria.



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Petri Dish Profiles: PharmaSea

In our series of Petri Dish Profiles, MaCuMBA Project News features other European-funded projects related to the study of marine microorganisms. In this issue, we talk to Prof Marcel Jaspars, Director of the Marine Biodiscovery Centre of the University of Aberdeen, Scotland, about the PharmaSea Project.

Prof Marcel Jaspars

What are the overall objectives of the PharmaSea project?

The PharmaSea project focuses on biodiscovery research and the development and commercialisation of new bioactive compounds from marine organisms, including deep-sea sponges and bacteria, to evaluate their potential as novel drug leads or ingredients for nutrition or cosmetic applications. By choosing deep and cold marine environments we hope to uncover novel diversity not seen before. Deep ocean trenches are islands of diversity in which evolution may have progressed differently. The final goal is to deliver one or two drug candidates with some preclinical evaluation carried out on them. In addition we hope to have a number of unique compounds with associated potent and selective bioactivity which we can take forward via other mechanisms. We have decided on a very steep discovery funnel so that at each step only the most promising compounds are taken forward.

PharmaSea will collect microorganisms from some of the hottest, deepest and coldest places on the planet, what are the challenges to be faced in collecting samples from such extreme environments?

Only a handful of samples have ever been taken from deep trenches and investigated, so the project is breaking new ground. We will employ strategies commonly used in the salvage industry to carry out the sampling. Using fishing vessels, researchers will drop a sampler on a reel of cables to the trench bed to collect sediment. Scientists will then attempt to grow unique bacteria and fungi from the sediment using selective isolation protocols and paying special attention to the nutrient environment where the sediments were collected, which can be extracted to isolate novel drug-like molecules for pharmacological testing.

Collecting samples from environments such as deep sea trenches can be an expensive process, will you be collaborating with other projects or organisations to carry out cruises and collection expeditions?

We will develop our own deep sea sampling equipment, which will be tested in the Atacama Trench off the cost of Chile in late 2013/early 2014. In addition to this we will collaborate with other projects, such as MaCuMBA, to obtain novel microbial strains, and also with other teams mounting cruises to sample deep trenches. In addition we will apply for cruise time or places on planned cruises to obtain marine sediments for our work.

What new products might be developed using the results of PharmaSea?

The PharmaSea project focuses on discovering new marine bacteria that can produce novel antibiotics. There hasn't been a completely new antibiotic registered since 2003, so there is a real lack of good antibiotics in development at the moment. We might also find novel ingredients for nutrition or cosmetic applications.

Will the development and commercialisation of these products be carried out as part of the PharmaSea project?

We anticipate that we will have one or two compounds that we can take into small animal trials at the end of the project. This may then be developed by the PharmaSea industry partners, or we may partner with pharmaceutical companies if warranted. There may also be other Intellectual Property arising from the project that we will not be in a position to commercialise, so we will try to licence this to the relevant industry sector.

Designed and developed by AquaTT

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