IFM-GEOMAR

Leibniz-Institut für Meereswissenschaften
an der Universität Kiel

IFM-GEOMAR Report 2002-2004

From the Seafloor to the Atmosphere

- Marine Sciences at IFM-GEOMAR Kiel -

June 2005

Preface

For the first time, the Leibniz Institute of Marine Sciences (IFM-GEOMAR) presents a joint report of its research activities and developments in the years 2002-2004. In January 2004 the institute was founded through a merger of the former Institute for Marine Research (IfM) and the GEOMAR Research Center for Marine Geosciences. This report addresses friends and partners in science, politics and private enterprises. It gives an insight into the scientific achievements of IFM-GEOMAR and its predecessor institutes during the last three years.

3.10 New Natural Products from Marine Microorganisms

Bacteria and other microorganisms often are living in close association with higher organisms. Associations of bacteria with sponges are among the most interesting but also the most complex objects to study the interactions between microorganisms and their host partner. In fact, the association of microorganisms with sponges is one example of numerous cases where these associations have been described. These associations gained much interest during recent years, because the production of biological active substances was reported. Though convincing evidence does exist only in a few cases, it was tempting to assume that microorganisms associated with these animals produce the active substances. They may contribute to the integrity of their hosts and their defence by the excretion of antibiotic and other biologically active substances. In particular sessile marine organisms like sponges are considered to depend on chemical defence mechanisms against predatory animals, but also against attacks of pathogenic microorganisms.

In the studies on the interaction between marine sponges and microorganisms, the Marine Microbiology group focused on selected sponge species which were analysed by microscopy, genetic studies on the associated bacteria and culture studies, which aimed at the isolation of antibiotically active bacteria. The microscopic studies revealed large differences in the association of bacteria with different sponges. Suberites domuncula e.g. showed only a small number of bacteria on its interior surfaces (Fig. 1), while the sponges Halichondria panicea (Fig. 2) and Ircinia fasciculata revealed abundant and highly diverse bacterial assemblages. This could be seen in the electron microscope but also was reflected in the high diversity of bacteria isolated from these sponges. Sponge-species specific association of bacteria was demonstrated by comparison of the bacterial community associated to different specimen of the Mediterranean sponge Chondrilla nucula from locations in the Adriatic Sea and in the Ligurian Sea. The bacterial communities of the studied sponges to a large extent contained bacteria that were genetically related to clusters found as characteristic members of sponge associated communities. Almost identical clone sequences were found in specimen from the different locations. Interestingly the sponge Thetya aurantium showed two clearly distinct morphological communities associated with exterior and interior cells, which could be shown by microscopic studies and was affirmed in denaturing gradient gel electrophoresis and 16S rDNA cloning experiments (Fig. 3). These findings support the assumption that at least part of the bacteria found in sponges are specifically associated with the animals and may have adapted during evolutionary processes to the sponge environment (in contrast to bacteria ingested as food particles).

Current studies concentrate on the role of bacteria and fungi producing antibiotic substances in association with sponges. Penicillin was the first antibiotic substance used in medical treatments. It was found by Fleming in 1928 and some years later forced into application by others. Meanwhile a whole array of different antibiotically active compounds is known. However, the strong increase of resistant bacteria causes severe problems in medical treatment and reinforces new investigations to search for compounds that are active even against multi-resistant pathogens.

Sponges are considered as one of the most important sources of natural substances with antibiotic, antitumoral or antiviral activities. This makes sponges a potentially important source of new products for medical treatment.

Figure 1: Suberites domuncula: (A)+(B) electron microscopic exposure of the sponge tissue with only very low numbers of bacterial cells.

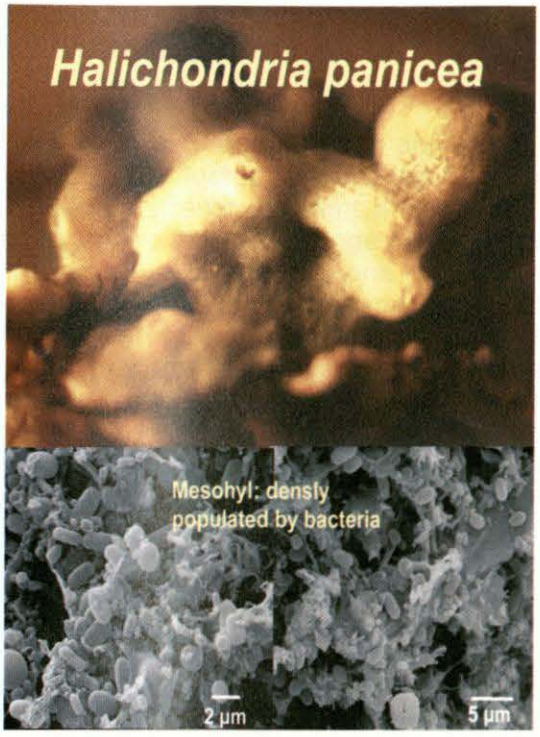

Figure 2: The breadcrumb sponge Halichondria panicea with electron microscopic pictures of its interior showing abundant bacteria.

However, in most cases it has not been demonstrated whether the sponge cells or their microbial associates produce the active substances. In fact, more and more cases become known in which it could be demonstrated that rather the associated bacteria and not the animal host produce the biological active compounds. These circumstances were an important motivation to concentrate on microorganisms associated with sponges (and other marine invertebrates) in the search for new natural substances.

At IFM-GEOMAR we have isolated and tested large numbers of bacteria and fungi for important biological activities, including antibiotic action against other microorganisms. Associated project partners have tested against multiresistant bacteria and for antitumoral and antiviral activities. Several hundred biologically active marine bacteria and fungi are currently treated in detailed biological and chemical analyses. New biologically active chemical compounds have been identified by our chemical partners. Several compounds were patented and one of these, Sorbicillacton A, is in an advanced stage of the development for medical treatment. Sorbicillacton A is produced by a fungus isolated from a marine sponge and was promoted within the "Centre of Excellence BIOTECmarin". BIOTECmarin is a national research project focusing on molecular biotechnology and bioactive compounds in marine sponges and sponge-associated microorganisms. The chemical structure was elucidated by chemists at the University of Würzburg. The biosynthetic pathway was established in joint experiments of the Marine Microbiology at IFM-GEOMAR and the chemistry group, and the important biological activities against viruses and cancer cells were established by partners at the University of Mainz.

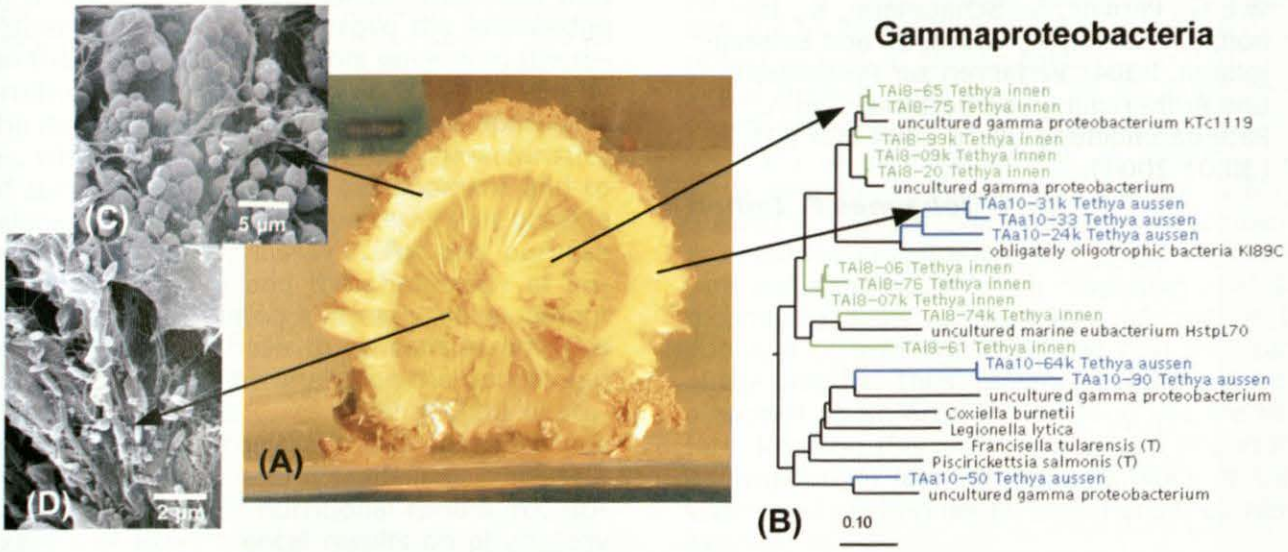

Figure 3: (A) Cross section of the marine sponge Tethya aurantium (Sea-orange), (B) The phylogenetic tree of gammaproteobacteria demonstrates specific association of different bacteria with the interior (shown in green) and the exterior (shown in blue) cell tissue of the sponge, (C) + (D) electron microscopic exposures (REM) of interior (D) and exterior (C) parts of the sponge.

Research on natural substances is a multidisciplinary task and the activities of Marine Microbiology at IFM-GEOMAR are part of an integrated network of research groups and small companies on a local and national scale. In addition, international collaborations with institutions in China and Indonesia extend these activities. Projects are funded as part of the national "Centre of Excellence BIOTECmarin" and by federal and local ministries that specifically support cooperation with companies.

IFM-GEOMAR Contributions

Imhoff, J.F., and Stöhr, R., 2003: Sponge-associated bacteria: General overview and special aspects of the diversity of bacteria associated with Halichondria panicea. In: *Marine Molecular Biotechnology, Vol. 1 Sponges (Porifera)*, W.E.G. Müller (Ed.). Springer New York, 35-57.

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Bringmann, G., Lang, G., Gulder, T.A.M., Tsurata, H., Mühlbacher, J., Maksimenka, K., Steffens, S., Schaumann, K., Stöhr, R., Wiese, J., Imhoff, J.F., Perovic-Ottstadt, S., Boreiko, O., and Müller, W.E.G., 2005: The first sorbicillinoid alkaloids, sorbicillacton A and B, from a sponge-derived Penicillium chrysogenum. *Org. Chem.*, submitted.

Bringmann, G. Lang, G., Gulder, T., Müller, W.E.G., Perovic, S., Schaumann, K., Imhoff, J.F., Stöhr, R., Wiese, J., and Schmaljohann, 2004: Verfahren zur Produktion und Aufreinigung von Sorbicillacton A. Patentanmeldung DE 10 2004 004 901.7 (30.01.2004).

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