From microbial ecology to marine biotechnology

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The Kieler Wirkstoff-Zentrum KiWiZ (Centre for Marine Natural Products) at IFM-GEOMAR is investigating opportunities to use substances from microbial communties for medical and other applications. The new field of Marine Biotechnology is an emering area in Marine Sciences.

In recent years, communities of microorganisms associated with various marine macroorganisms have received much attention. In particular, microbial communities associated with sponges, macroalgae or bryozoa were intensively studied both by genetic analysis with the 16S rRNA gene as marker molecule and by pure cultures investigations. The microbial potential to produce biologically active secondary metabolites was determined with emphasis on metabolite-driven interactions between different organisms in these communities.

Bacterial communities of the alga *Laminaria saccharina,* which were one of the major study objects, not only are highly diverse but also harbour specific bacteria. One example is the new bacterium *Kiloniella laminariae* which is the first known representative of a completely new phylogenetic line, a new order of the Alphaproteobacteria (Wiese et al., 2009a). Specifically different bacterial communities are found on the surface of the rhizoid, cauloid, phylloid, and thallus tip of *Laminaria saccharina* (Staufenberger *et al*., 2008). This finding and the specific association of bacteria with algae in general (Lachnit et al., 2009) strongly indicates interactions between the algae and the bacteria shaping the community structure in a specific manner. Small molecules with biological activities are considered to play an important role in these interactions. An interesting example is a *Pseudomonas* strain isolated from the thallus of *Laminaria saccharina* (Wiese et al., 2009b) which produces four different biologically active substances: 2,4-diacetyl phloroglucinol and pyoluteorin are inhibiting other bacteria, phloroacetophenone and rhizoxin S1 inhibit fungi. The production of these substances is in favour of the producer by inhibition of competing microorganisms but also in favour of *Laminaria saccharina* by protecting the alga from overgrowing microorganisms and from pathogens.

Another research focus is dealing with sponge-associated microorganisms and possible interactions between these microorganisms and the sponge. To a great part, bacteria associated with the sponge *Halichondria panicea* are able to produce antibiotically active substances and the analysis of actinobacterial isolates from this sponge demonstrated their ability to produce a great number of known bioactive substances but also revealed many so far not identified possibly new compounds. Quite interestingly there are multiple interactions between these bacteria based on their excreted secondary metabolites, though these interactions are poorly understood. Interestingly, low concentrations of the antibiotic bacitracin, which is produced by a *Bacillus* species, stimulated the production of new biological active substances in a *Streptomyces* strain isolated from the sponge (Mitova et al., 2008). These substances, different streptophenazines, in turn inhibited the growth of various *Bacillus* strains. Representatives of both genera, *Streptomyces* and *Bacillus*, co-occur in the bacterial communities of *Halichondria panicea* and therefore the findings in the laboratory may very well be of relevance in the environment. These few examples demonstrate the importance of interspecies interactions in the microbial communities associated with sponges and

Figure 1 (left): Examples of different marine organism such as sponges, algae, bacteria and fungi.

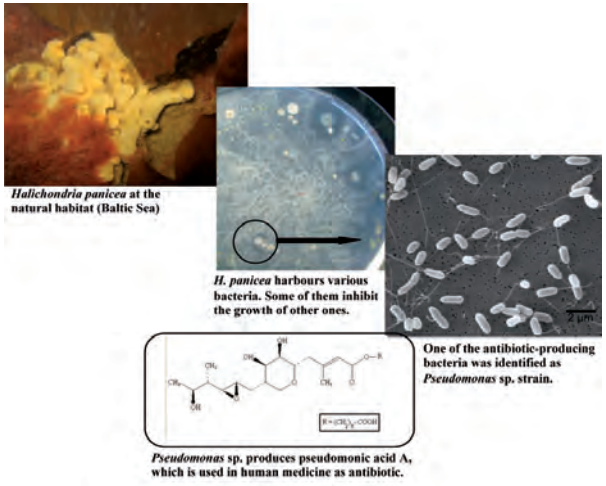

Figure 2: From the habitat to the biologically active compound.

other marine macroorganisms.

Despite of their presumed ecological relevance, biologically active substances from marine microorganisms represent a great potential for biotechnological application. Therefore, in the Research Unit Marine Microbiology and the Kieler Wirkstoff-Zentrum (KiWiZ) classical and molecular approaches are combined not only to evaluate the ecological significance of secondary metabolites produced by marine bacteria and fungi but also to establish their biotechnological potential. This is a promising approach because marine microorganisms have only recently been attained significant interest in this respect, many of these represent specific marine forms of life and a particularly high percentage of microorganisms associated with various marine macroorganisms is able to produce biological active substances. One of the most promising applications of such secondary metabolites from marine microorganisms is their use as drugs in the treatment of human diseases. Because there is a strong need for the detection of new drugs, e.g. for the treatment of infectious, cancer, inflammation or metabolic diseases such as diabetes, research on natural products as performed at the KiWiZ is highly demanded. In particular a project on the establishment of a substance library of marine natural products is of great significance, because it is supposed to meet the urgent demand for new chemical structures for drug development. The KiWiZ is well established for this research: it uses a great collection of biologically active strains of marine bacteria and marine fungi derived from different marine habitats, has profound technical equipment for microbiological and chemical analyses, uses a number of established bioassays for activity measurements, and has an engaged interdisciplinary team for laboratory work and networking with local, national and international partners. Interesting substances are promoted for applications in cosmetics, plant protection and pharmacy and the application of most promising candidates is protected by patents. Patent protection was achieved for cyclodepsipeptides produced by a sponge-associated fungus *Scopulariopsis brevicaulis* (Imhoff et al., 2008, 2009). Recently, also antitumoral drug candidates, new benzanthrins from a sponge-associated *Streptomyces* strain, were patented (Schneemann et al., 2010).

We are therefore convinced, that small biological active molecules from marine microorganisms provide great perspectives both for in depth ecological studies and for biotechnological applications.

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