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Marine biotechnologies and synthetic biology, new issues for a fair and equitable profit-sharing commercial use

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ABSTRACT

The sea will be a source of economic development in the next years. Today the research works in marine biotechnologies supply new products and processes. The introduction in the laboratories of a new technology, synthesis biology, is going to increase the possibilities of creation of new products.
Exploitation of product stemming from marine biodiversity has to be made with regard to various rights among which industrial property law, maritime law and the Convention on BioDiversity.
All participants involved in the promotion of research in marine biotechnology must address the fair and equitable sharing of any commercial exploitation. Carrying out work involving synthetic biology has increased the number of unanswered questions about how operators should manage in order to avoid any threat of being sued for infringements of IP rights or for alleged bio-piracy. This paper, by no means exhaustive in the field, analyzes some of the issues raised on the modification to the landscape in marine biotechnology by the advent of synthetic biology. Such issues indicate how important the collaboration between researchers, industrialists, lawyers is for allowing proper use of marine biotech.

1 . Introduction

At the end of 2013, France launched the global "Innovation 2030" challenge (http://www.innovation2030.org/en/). The purpose was to bring to the foreground new talents and to support them in their growth. 100 projects of innovative businesses were selected. Topics covered include the input of marine research as a source of new products and processes, and of the use of synthetic biology in the sea. The introduction of synthetic biology as a new tool for R&D raises new issues in the complex field of industrial use of biodiversity.

The combination of marine research and synthetic biology is promising. Oceans are spaces that have been insufficiently exploited yet. They contain a very large biodiversity which could provide new products and industrial processes. Considering the development of synthetic biology, in particular within the framework of programs aiming at industrial applications, there is little doubt that marine biotechnology will fully benefit from this emerging technology which can be broadly described as "the design and construction of novel artificial biological pathways, organisms or devices, or the redesign of existing natural biological systems."

Despite the fact that the future of synthetic biology in the field of research in marine biotechnology looks bright from a technical point of view, it will however raise new questions in the complex domain of the industrial use of biodiversity.

This article aims at addressing a number of issues that will be inevitably raised to the various stakeholders of the innovation process.

2 . Economic challenges

The use of any form of biodiversity is part of what is called "bioeconomy" (Arundel and Sawaya, 2009). The biodiversity originating from various marine environments is already the source of many products with strong economic value. The global market of marine biotechnology was estimated at 2.8 billion dollars in 2010 with annual increase of 4 to 5% (OECD, 2013). There are numerous marine living beings of industrial interest such as plants (e.g. green, red or brown algae), animal or micro-organisms (bacteria, fungi). Sponges and corals developed defense systems based on the production of chemical substances. These metabolites can become new drugs. Enzymes of species living near hyperthermal sources were identified, which have been found to have industrial applications and have been proven to be extremely useful in the field of molecular biology.

Biodiversity resulting from various marine environments is thus already at the origin of many products with strong economic value. Examples include omega 3 fatty acids like EPA or DHA from fish oil, anti-viral drugs like Acyclovir (Zovirax®), an anti-viral chemical obtained from nucleosides isolated from a Caribbean marine sponge and used for the treatment of herpes infections, Trabectedin (Yondelis®), the

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marine-based drug developed by PharmaMar in partnership with Johnson & Johnson Pharmaceutical R&D. Trabectedin was discovered in the Caribbean sea squirt *Ecteinascidia turbinata*. It was the first drug of marine origin developed for fighting cancer.

The Deep VentR DNA Polymerase, an enzyme developed for laboratory use, is a high-fidelity thermophilic DNA polymerase isolated from *Pyrococcus* species GB-D, a micro-organism living in submarine thermal vents at 2010 meter depth and able to grow at temperatures as high as 104 °C. The green fluorescent protein (GFP), a protein widely used in cell and molecular biology, was first isolated from the jellyfish *Aequorea victoria*.

The cosmetics industry makes use of exopolysaccharides (EPS) as personal care bioactive ingredients. Marine ecosystems are rich in EPS-producing bacteria that can be isolated from water column, sediments, animals, etc. Examples of commercialized products include Abyssine® from Lucas Meyer which is an exopolysaccharide from an extremophile bacterium living in deep sea hydrothermal vents and the Resilience® skin care products (Estee Lauder) that are based on pseudopterosins, a series of diterpenoid isolated from sea whip *Pseudopterogonia elizebethae* as an anti-inflammatory compound.

Microalgae are also a source of products in the skin care market, like XCELL-30® from Greensea, that was developed from microalgae which are endemic to Madagascar, or Alguronic acid which is a trade name created by Solazyme for an undetermined mix of polysaccharides produced from microalgae. In 2011 Alguronic acid was introduced in the market as an active ingredient in a commercial product called Algenist anti-aging skincare formulas (Martins, 2014).

Algae are also expected to become a new source of biofuels, which could be an alternative to fossil fuels. Many companies like Solazyme have activities in the US and Europe. Sapphire Energy already began commercial sales of algal biofuel.

In the future, new applications in the fields of energy, environment, cosmetic, health, food, materials are anticipated, as marine environments are a largely under-utilized reservoir of genetic diversity (Ritchie et al., 2013).

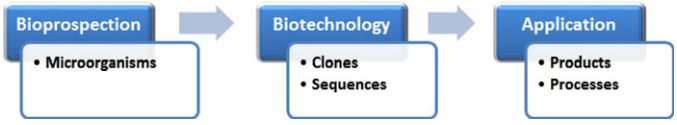
Biodiversity in the oceans is significantly broader than that of the terrestrial environments. However, it is still largely unknown. Compared to terrestrial biodiversity, it used to be more difficult to access to, but the new tools of biotechnology will make it easier to use this amazing potential and virtually untapped source of innovation (OECD, 2013). DNA sequencing and synthesis, biological modeling and the use of high-throughput robots, genomic, proteomic methods and synthetic biology have been introduced in laboratories and their use is increasing exponentially.

More than in other fields of scientific research, marine biotechnology requires partnerships between governmental institutes and private businesses. Many governments, including the French government, have invested in marine biotechnology research, and the private sector is also attracted by the opportunities provided by the sea.

However, there is a long way to go from prospection for genetic biodiversity to a marketed product. This way is often long and expensive. At each stage of the route, different stakeholders may have complementary interests and other opposite interests.

3 . From the "traditional" research work on biodiversity to the commercial product

Since the earliest days of biotechnology, the development of a biotech product requires multidisciplinary skills (microbiology, chemistry, knowledge in fermentation, process technologies, etc.). This has a strong impact on the timeframe of such research and development but also on the scope of freedom to operate studies that should be implemented in order to avoid risks of infringing property industrial rights held by third parties. Bio-prospection generally results in the isolation of a living organism, which is the starting point of the whole process. It is a material element (micro-organism, etc.) found in nature. From this raw material the researcher will extract information which will be the true starting point of the development. This information, which can appear under various forms such as for example genetic sequences, clones or secondary metabolites, is transformed into value by the creation of a new product, or by the implementation of a new process.



Bio-prospectors are at the earlier stage of the value chain and manufacturers are at the end. Both R&D teams from governmental institutes and from industrial companies may work independently or team up into a consortium.

In all cases both have to ask themselves the good questions concerning the industrial property rights but also their compliance with other sources of rights that influence the exploitation of marine biodiversity such as the Convention on BioDiversity (Bloch, 2012). This analysis is necessary for fully securing a safe exploitation of the research results.

To take into account possible conflicts in the exploitation of the research results, partners establish consortium agreements which describe the research aim and work plan, and the agreement of the partners concerning in particular the management of the inventions arising from this research. Many provisions do not raise any problem, however, those concerning publication of results, exploitation and the related financial commitments are generally controversial between the partners (Tichet et al., 2010). Academic groups generally wish to publish the results of their work, while the industrial partners look for patent filling. However, a publication before patent filing would destroy the novelty of the invention.

Nowadays, there are contractual models that are satisfactory to all partners within the "classical" framework of research. But access to biodiversity and the questions of the fair and equitable sharing of benefits arising from these genetic resources remain under discussion because the politic entity that rules the territory where bio-prospection took place is only very rarely considered in such consortium agreements. The Convention on BioDiversity is often ignored both by private and governmental stakeholders, either because they have simply never heard about it, or because they don't know how to comply.

4 . The rights about which it is necessary to worry for a safe industrial and commercial use of marine biodiversity

It is important to analyze the results of research stemming from programs of marine biotechnology with regard to several sources of law such as the industrial property laws and conventions, the maritime law, and the Convention on Biological Diversity (CBD) (Tardieu Guigues et al., 2013).

Within the industrial property several branches coexist. During the implementation of research programs in marine biodiversity, patent law has to be considered in priority. Results of the research can be protected by filing one or more patent applications. A patent covers an invention which could arise from work made using the marine resource. It will become a property right for its owner. However certain conditions will be necessary to have the patent granted.

According to its legal definition, an invention is a solution to a specific technological problem. Discoveries, scientific theories and mathematical methods shall not be regarded as an invention.

The invention can relate to a product, a process, a device, a new use of a product or a process. However, all the substantive patent laws