

■ Market segment dynamics

Nanotechnologies are the creation and use of equipment, instruments or systems based on dimension structures to the order of 1 to several hundred nanometers (billionth meter). Nanobiotechnologies thus involve bridging the gap between biotechnologies and these nanotechnologies for applications in the health field. Therefore, these are essentially multidisciplinary technologies.

To size the market is a delicate exercise, as it is very difficult to obtain figures and especially consistent figures, since the discipline is new and involves many different players.

In 2004, worldwide R&D investments for all nanotechnologies reached e8 billion. The USA accounts for 3 billion, of which more than half comes from private sources. Europe is first for public financing but is far behind the USA and Japan in terms of private financing.

According to a DIGITIP study, turnover for nanotechnologies in 2010 will reach between 700 and e1 000 billion, of which 18% is attributed to the life sciences industry. Products from nanotechnologies will account for 16% of all health-related products.

Three fields are involved in nanobiotechnologies: in vivo and in vitro diagnostics, research for new drugs or new formulations and regenerative medicine.

- Diagnostics

The DNA chip appeared in 1995 and today has become “commonplace”. It is available in specialized chips (for specific diseases, to detect a contaminant in the environment or the presence of GMO's in the food industry). Chips that integrate cells are being developed (cell on chips).

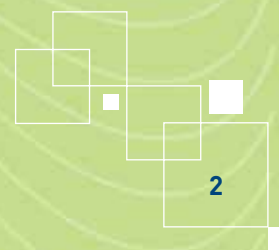
- The lab-on-chip or total analysis micro system. Miniaturisation forces the fluid management system, the chip and the coupling with the analysis system to be integrated into a single device. The integration of these different components is of interest to the Microsystems industry that has R&D teams dedicated to nanobiotechnologies (STMicroelectronics, Hitachi, Motorola and Intel).

The field of imaging benefits a great deal from nanometric approaches. Being able to graft fluorescent molecules in a targeted manner allows for much finer detection.

- Therapy

Molecular modelling: one of the derivatives of progress in these technologies is the ability to display molecular structures and to model the molecules created to meet the specifications of the pharmaceutical industry. Therapeutic molecules which are closest to their target are a major issue. Nanometric methods are important for drug vectorization. The first molecules used were liposomes, largely known to the public due to their use in cosmetics. Other molecular assemblies lead to nanostructures that are functionalized by grafting active molecules (therapeutic or diagnostic). Finally, carbon nanotubes, which are of great interest to nanotechnology scientists, also interest biologists for creating “intelligent” vectors with active components.

French biotechnology companies are particularly efficient in drug vectorization: Nanobiotix and its NanoBioDrugs that target tumour cells; Diatos and its technology that allows penetration of cell cytoplasmic and nuclear membranes; BioAlliance and its technology for the encapsulation of active molecules in nanostructures that enabled it to enter the stock market and Art-in-Cell, a young start-up company that produces original nano-objects from molecular assemblies.



- Regenerative medicine and medical devices (implants, monitoring devices and prosthesis). The miniaturisation of medical devices, thanks to micro and nanometric technologies, help the development of new treatments by being less invasive, thus better tolerated and more efficient. The field of brain degenerative diseases is one of the first applications, but all the therapeutic fields are concerned (cardiovascular, eye and hearing diseases). Nanotechnologies also allow for the development of subcutaneous implants as well as in situ diagnostics and/or continuous drug delivery, allowing for greater freedom of movement for patients who are confined to bed rest.

■ France's attractiveness

The main players are the USA and Japan, followed by Europe. Within Europe, the UK and Germany are ahead of France with regards to money allocated to research. However, France is well represented within European research programs. The CEA Grenoble was chosen to manage the first European nanobiotechnology network "Nano2Life" that heralds the European Institute of Nanobiotechnology.

Designating clusters enables a clearer perspective of the nanobiotechnologies industry in France: the three main clusters are located in Grenoble, Toulouse and Paris.

The LNE, the Laboratoire National de Métrologie et d'Essai (Public agency for certification and accreditation) is one of the best worldwide.

The expected market explosion in the nanobiotechnologies sector can be slowed down by ethical issues. The impact of nanoparticles on health and the environment must be studied and possibly "regulated" to guarantee respect for human well-being and dignity and also to avoid a negative reaction on the part of the general public similar to that encountered by GMO's. In this respect, France uses an approach that involves proper concern for the ethical aspects of the field, on the part of all the players, which promotes a better acceptance by the consumer: ad hoc commissions have been set up. Citizen debates are organized to answer questions.

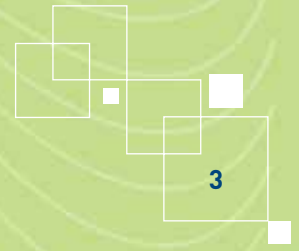
■ International 5players in France

- Nanobiotix, a biotechnology company based in Paris.

NANOBIOTIX is developing a new concept in the fight against cancer that is especially innovative, "NanoBiodrugs", which are nanoparticles of a few nanometers diameter, composed of a remotely activated heart covered with biological agents, enabling the highly specific targeting of tumour cells and their selective destruction, thus leaving the healthy tissues intact.

Nanobiotix, based in Paris, has in its portfolio four families of nanoparticles, each concerning one type of physical agent. They are developed under the name of "Nanobiodrugs" following the exclusive license acquired from the SUNY University or their own patents.

NANOBIOTIX has also opened an office for scientific and clinical research in the Bioparc Lyon nursery, and has established a high-level scientific collaboration with the INSERM U133 team of



Lyon. Greatly supported by the CANCEROPOLE LYON AUVERGNE RHONE-ALPES, this collaboration will grow rapidly due to the participation of other regional cancer specialists and the clinical infrastructure of HOSPICES CIVILS DE LYON. (source Lyon Bioadvisor + Nanobiotix).

- Partnership between CEA LETI and Yamatake

The collaboration between the Japanese company, Yamatake, and CEA-Léti consists in validating and producing a new generation of DNA chips automatically. It aims to validate the basic functions of an in situ oligonucleotides synthesis system in micro wells of 300 μm diameter to produce these DNA chips. The team also optimized the synthesis process. The collaboration has been successful because Yamatake is currently marketing these chips in Japan.

The CEA owns patents for the DNA biochip technology. Yamatake has the expertise in MEMS (micro electronic mechanical system) and has ad hoc equipment for production.