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Cancer immunotherapy shows itself to be a path that is both efficacious and non-toxic.

Cancer immunotherapy is aimed at strengthening the patient's defenses. The duration of that stimulation is one of the issues raised by this type of treatment. And one has to avoid an over-reaction that would lead to auto-immune diseases.

The strategy of immunotherapy is to recreate a defense where one no longer exists. Immunotherapy offers three angles of attack: targeting the cancer cell; combating the immunosuppression induced by the tumor; and preventing vascularization. The first approach is aimed at stimulating T lymphocytes by injecting a product loaded with a tumor-specific antigen directly into the patient. The second is an autologous cell therapy using cells that are modified to present tumor antigens. Lastly, the third approach is a gene therapy that is based on the injection of viral vectors that code for tumor antigens. The strategies which affect immunity do not necessarily have an effect on the T cells and macrophages; they may, for example, target NK (natural killer) cells. In that case, one uses other immune-system molecules as the agent. NK cells are regulated by activator and inhibitor signals and can directly kill a large number of tumor cell lines.

For many researchers, however, non-vectorized antigens do not induce strong enough immune responses. There is no shortage of ideas in this area. One can use bacterial toxins to deliver the antigens into cells presenting antigens. In tandem with the dendritic strategy, another strategy involves the use of exosomes, which are vesicles secreted by dendritic cells. Moreover, why not extract them from patients and load them with antigens, as one does for dendritic cells themselves?

Another therapeutic vaccine method takes the form of a gene therapy involving the injection of viral vectors coding for tumor antigens. ■ HÉLÈNE GUYOT

AN INTERVIEW WITH FRANÇOIS IRIS

Co-founder of Bio-Modeling systems

Bio-Modeling Systems (Paris) uses in silico negative selection process for hypothesis driven drug discovery.

« Most approaches to improving prediction have focused on positive selection. Parisian firm Bio-Modeling's concept is totally different: we find a link between a gene and a disease and then try to prove it wrong. We have developed a set of validated, computer-driven solutions to these problems (CADI) and, to date, ten predictive models of complex human pathologies or biological processes have been produced. Four have been tested, by independent a posteriori experimentation, and validated (Ras-dependent breast cancer, model and therapeutic approaches validated in vitro; therapeutic resistance to Tamoxifen, model validated in vitro; Müllerian regression, model validated in vivo; and Creutzfeld-Jakob disease, model validated in vivo [rodents and primates].) Two have been published (NAR & J.Mol.Endocrinol.) and the other two are being made ready for publication.

The predictive biological models thus produced remain highly theoretical and it is absolutely necessary that they be experimentally verified. However, these predictive models present experimental scientists with the enormous advantage of knowing precisely what should be investigated, where, when, how, and why. »■ HELENE GUYOT

COMPANY NEWS

Immutep – Lag-3 is an immune system mediator

The concept applied by Immutep, a company based in the Paris region that was set up in 2001 to exploit the work carried out by Frédéric Triebel at the Institut Gustave Roussy, is based on the soluble protein Lag-3 (for lymphocyte activation gene-3).

It is an immunomodulating protein expressed on the surface of activated T cells. Two venture capital firms, Innoven and H21, have invested in Immutep, which is run by John B. Hawken, a biotech management specialist. The company's lead compound is IMP 321 (ImmuFact), a powerful T cell immunostimulation factor derived from the soluble form of the Lag-3 protein. The latter binds with great affinity to the MHC molecules expressed by dendritic cells. In effect, the operation results in the maturation of dendritic cells and enables them to migrate to the lymph nodes, improving the cross-presentation of the antigens to the T cells.

Another Immutep technology, ImmuCcine, is designed to produce immunostimulatory therapeutic vaccines. Through the covalent liaison of an antigen to IMP321 via a fusion protein, one can bring about the vectorization of the antigen to the dendritic cell and at the same time trigger an immunostimulatory effect. Immutep's third technology is ImmuTune, which entails using specific Lag-3 antibodies to achieve control over the immune response.

In a recent publication, Lag-3 was shown to be an indicator of survival in breast cancers that express estrogen or progesterone captors. Immutep is nox rising its second round of funding for 13 million euros, but CEO John Hawken is not giving any details about the operation at this time. ■ HG

NEWS

U3 Pharma (Martinsried, Germany) raised EUR 27 million in a series C round led by Life Sciences Partners. U3 Pharma has two lead antibodies in preclinical development for cancer: U3-1287, which targets a receptor tyrosine kinase, and U3-1565, which targets a receptor tyrosine kinase ligand. Both humanized antibodies are partnered with Amgen and are expected to enter the clinic in 2007.

Curalogic (Copenhagen, Denmark) updated its IPO plans and now expects to raise DKK 187.5 million ($32.1 million) through the sale of 2.5 million shares at DKK 75. Last week, the company proposed to raise about DKK 200 million ($34.7 million) in the offering, for which Danske Bank is coordinator Curalogic expects the shares to begin trading on the Copenhagen Stock Exchange on June 2. The company's oral immunotherapy targeting ragweed allergy has completed Phase II trials and is expected to enter Phase III testing in April 2007.

Novartis Institute for Tropical Diseases (NITD) will begin a public-private partnership to discover next-generation malaria drugs. The Wellcome Trust, the Singapore Economic Development Board and Medicines for Malaria Venture, have granted about $20 million in funding. NITD, which is based in Singapore, will manage the program and conduct joint research with several institutions, including the Genomics Institute of the Novartis Research Foundation and the Swiss Tropical Institute.

Scientists in Sweden are adapting a cancer vaccine for use in humans following animal tests that successfully stopped tumor growth. The vaccine works by mimicking the effects of angiostatin, a piece of a protein that suppresses tumor growth by cutting off blood supply. The immune antibodies produced in the body as a result last longer in the bloodstream than angiostatin.

Switzerland : an attractive business location

With 138 biotech companies, 50 % of which are developing human therapeutics, and 91 suppliers to the biotech industry, Switzerland can boast the greatest density of biotech companies in the world in relation to its population. In 2005 the Swiss biotech industry generated revenues of 3.8 billion euros and employed 14,000 people. While this little country of less than 8 million inhabitants does not have tax provisions targeted specifically at young innovative businesses, as France does, it nevertheless has an advantageous tax regime for all entrepreneurs.

Switzerland has a federal tax system and the 26 cantons have complete authority over direct taxation. The Swiss tax authorities generally display considerable flexibility and are open to compromises. The maximum tax rate in 2005 was 21 %, one of the lowest in Europe. Companies can benefit from partial or total federal tax reliefs for a maximum period of 10 years, and in some cantons tax exemptions can reach 100 %. The canton of Fribourg offers among the most favorable tax conditions anywhere in Switzerland. « Our canton encourages the development of biotechnology companies, explains Christoph Aebischer, of the Economic Promotion Office of the canton of Fribourg. We utilize both fiscal and financial means to support this sector. »

In addition, Swiss biotech companies have easier access to venture capital. A federal law on venture capital companies (VCCs) was passed in 1999 to facilitate the emergence of young innovative companies of one to 10 employees. Tax concessions are awarded to VCCs if 50 % of their own funds are invested in « new enterprises undertaking innovative projects ».

Biotech companies thus raised 189 million euros in 2005, putting Switzerland in third place in Europe. A large proportion of those funds was provided by the Swiss Private Equity and Corporate Finance Association (SECA), which supports biotech companies from the early phases of their creation through to their listing on the stock market. ■ STÉPHANIE COHEN.

ECONOMY

Living with equity gaps

Getting funding for biotech depends on the venture capital cycle you are in, Stephen Harmston, global research analyst at Dow Jones, told Europe Unlimited's Finance and Biotech meeting for the life sciences. High levels of early-stage investment in 1999/2000 had resulted in less follow-up funding rounds over the past few years. Harmston suggests that the private equity (PE) market for biotech is characterized by a 10-year cycle. Since 2000 the number of active investors worldwide fell by 49 % in the US (1,417 in 2005) and 52 % in Europe (613 in 2005), out of which 148 in Europe (475 in the US) closed four or more deals a year. Seed financing apart, the equity gap is mostly felt at the later stages. Whereas a start-up faces a financing gap in the range of €250,000 to €2 million today, more mature ones need up to 10 million euros. Across the sector as a whole, those that are short of funds add up. In Europe, 944 vc-backed firms last obtained fresh funding in 2000 and 2001, receiving a cumulative injection of 11bn euros. Management should start to worry about external shareholder value early on, says Harmston, pointing out that the later-stage equity gap arises « when more mature companies have a growth too moderate for venture firms, but are too small for expansion capital ». The shortage of investment funding is something the industry had to live with in a more creative way, he concluded. ■ WOLF KRONER, BIOWORLD EUROPE .

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