Nanotechnology and Cancer: a Venezuelan experience

Gabriel Escalona Vivas*

"There is plenty of room at the bottom"

Richard Feynman

According to the World Health Organization, cancer was the leading cause of death worldwide, with 8.2 million deaths in 2012.

In the month of June 2013, in the framework of the Scientific Sessions of the Sociedad Anticancerosa de Venezuela, we had the pleasure of listening to Professor Gordon McVie - international authority-founder and editor ecancermedicalscience - in his excellent lecture "Cancer, new strategies for a global solution", who said that we are losing the war on cancer and our main tools are prevention and research.

In a globalized world and with an impressive technological development does not fit into reality demarcate medical advances from technological advances. In this battle against one of the greatest evils of mankind, innovation must be the best friend of medicine, and technology, its main weapon.

Nanotechnology is the study, design, creation or synthesis of materials through the control and manipulation of matter at the molecular scale (NMS), with the aim of creating "devices" with novel chemical, physical and biological properties. Such nano-devices, have typically less than 100 nm dimensions and have the potential to radically change the processes of prevention, detection and treatment of cancer.

The conceptual principles of nanotechnology are attributed to the U.S. physicist and Nobel laureate Richard Feynman, who, in the Congress of the American physical society in 1959, at the California Institute of technology (CalTech), in his lecture titled There is plenty of room at the bottom, he described a process by which we could develop the ability to manipulate atoms and single molecules, using precision tools to build and operate at the same time another set of tools.
of minor proportions, and so on up to the nanoscale. In the words of Feynman: "it is interesting that, in principle, it is possible that a physicist synthesizes any molecule drawn by a chemical". You give the orders and physical synthesizes the molecule. But how? Placing atoms where the chemical has indicated previously and so create the substance. If we develop the ability to see what we are doing and do things at the atomic level, we will help solve many problems arising from chemistry and biology".

For many years the contributions of Feynman were ignored until, in the mid-1980, Erick Drexler published his book *Engines of creation: the coming era of nanotechnology* in which he developed and popularized the concept of nanotechnology, a term used for the first time by the Japanese scientist Norio Taniguchi.

In recent decades, the growth of scientific development in the field of nanotechnology has been impressive. A sample of the strategic importance of the subject has been the investment that the developed countries have made in this area. For the year 2000, President Bill Clinton promoted research in the field through the National Nanotechnology Initiative, with an initial investment of US$ 500 million, followed by a leverage given by President Bush in 2003, authorizing investment by more than 3,630 million dollars over the next four years.

Currently, no commercial activity escapes the use or experimentation in this area. This includes the optimization of products ranging from cleaning products for home and personal use to oil refining, pharmaceutical companies and the creation of improved building materials.

In medicine, we have synthesized a number of nanomaterials with the potential to revolutionize the diagnosis and treatment of a large number of diseases, thanks to its particular properties, such as a large surface area and long half-life time periods in blood compared to other small molecules. Focusing on cancer, the use of nanoscale materials could increase the specificity in the early diagnosis of malignant and premalignant lesions as well as the efficacy of chemotherapeutic agents.

We can define the main areas of study such as those based on target therapies or tumor-targeted, in the transport of drugs and the images for the diagnosis (1). In the first, major research have yielded favourable results with the use of spherical nanoparticles (nanoshell) with dielectric core of gold, bioconjugated to be "molecularly targeted", and the use of Photo-therapy with laser for the destruction of malignant cells with great specificity (2).

With regard to the transport of chemotherapy drugs, the nanoscale platforms more developed are liposomes and structures based on polymers, even with products approved by the Food & Drug Administration (FDA). Doxil ® is the first approved drug, which consists of doxorubicin liposomes for treatment of the Kaposi's sarcoma and ovarian cancer (3), combination that increases the time of the drug in the bloodstream and maximizes their accumulation in tumor.

There are developing, currently in phase III, a large number of combinations for metastatic breast and ovarian cancer (1). Other more complex systems comprised of polymers linked to tumor-
specific and drugs like Docetaxel (BIND-014) have been shown to have greater specificity in experimental tests (4).

In terms of the impact on the techniques and processes used to create images of the human body, (imaging), it stands to reason that, with the metal composition of nanoparticles, diagnostics could be improved through x-ray computed tomography and magnetic resonance imaging studies. In this sense, it has been demonstrated the utility of iron dioxide nanoparticles in the identification of colorectal cancer cells during preclinical studies (5).

Within this great fan of possibilities offered by nanotechnology our multidisciplinary research group, formed by surgeons from the Servicio de Cirugía II of the Hospital Universitario de Caracas, Professors Jimmy Castillo and Manuel Caetano from the laboratory of spectroscopy Laser of the school of chemistry of the Faculty of Science of the Universidad Central de Venezuela with the collaboration of the Sociedad Anticancerosa de Venezuela, we are developing the project *Fluorescent nanosensors for the laparoscopic diagnosis and treatment of colorectal cancer*. To achieve the objectives of the project we have been designing nanoparticles composed of metallic molecules coated and Functionalized with antibodies tumor-specific and fluorophores, in order to identify, during the intraoperative period, tumors, metastatic lymph nodes and the micrometastases of colorectal cancer using laparoscopy equipment. Colorectal cancer is one of the most common worldwide; only in the United States, for the year 2011, there were nearly 147,000 new cases and 50,000 deaths related to this type of cancer (6).

For the year 2010, in Venezuela, cancer deaths occupied the second place of the total deaths, representing 15.3%, among which those of the digestive system ranked first, with 5,804 deaths, positioning colorectal cancer in second place, with 1,132 deaths (7). More than 50% of patients receiving surgical treatment for colorectal carcinoma presented recurrence of disease (8), being the main factors not dependent from the patient and responsible for the recurrence of the disease the inappropriate resection margin and lymphadenectomy.

The use of techniques with agents that allow recreating optical images of the marked tumors, has been gaining a huge interest in the medical community, because of its ability to supply the doctor an image in real time. The unique characteristics of a tumor can be used to mark it using, for example, specific antibodies for antigens expressed on the surface of tumors linked to fluorescent molecules or fluorophores, which are capable of absorbing energy in the form of electromagnetic radiation (light) at a given wavelength and emit electromagnetic radiation at a longer wavelength.

The potential of nanoassembled systems is that nanoparticles are first endowed with molecule that makes them specific to the cancer cell (molecularly targeted) and are then charged with thousands of fluorescent molecules, achieving that absorption of few nanoparticles on the surface of the cancer cell contains a high density of fluorescent molecules. These fluorophores, being illuminated by an appropriate supply, emit enough radiation to be easily detected and achieve a proper oncologic resection guided by fluorescence, which will decrease recurrences, potentially in the long term, and will improve intra-operative staging and, consequently, decrease mortality from this condition.
In the month of July of 2014, and within the framework of the National and International Congress of the Sociedad Venezolana de Cirugía, we will coordinate the Symposium on nanotechnology and medicine, thanks to the collaboration and the joint work of Dr. Jesús Tata.

Innovation projects, even if it is true, are long, slow and complex, are areas of research that puts us to compete scientifically with World Affairs. It is our duty to not sit back and try to add as many human resources trained enough in Venezuela, in the development of these projects, for our patients and for our country.

Dr. Gabriel Escalona Vivas. (gaboes@yahoo.com)

Servicio de Cirugía II, Hospital Universitario de Caracas, Venezuela.

REFERENCES


