



# Boletín Médico del Hospital Infantil de México

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## EDITORIAL

### Perspectives in cancer: molecular findings, computational-designed drugs, and patient care



### Perspectivas en cáncer: los hallazgos moleculares, el diseño de fármacos por métodos computacionales y el cuidado de los pacientes

Cancer is the leading cause of death in developed countries and the second leading cause of death in developing countries. Despite the advances in research and treatment, more than seven million people in the world die from cancer each year. About 12.7 million new cases of cancer and 7.6 million deaths were estimated worldwide in 2008, with 56% of cases known and 64% of these deaths in developing countries.

In Mexico, cancer is the third leading cause of mortality affecting both men and women. In 2010, cancer was responsible for the death of seventy thousand people, representing 11.9% of total recorded deaths. The frequency of cancer in children under 14 years of age increases progressively, and it is estimated that within a decade deaths related to cancer will be an alarming situation. Within the various childhood cancers, those of leukemia, lymphoma, and central nervous system tumors represent the most frequently diagnosed cancer types. In only 20 years (from 1981 to 2000), the frequency of leukemia in Mexican children was doubled. For more than six decades, the Hospital Infantil de México Federico Gómez (HIMFG) has been a leader in the treatment of childhood cancer in Mexico. Of all children treated at the HIMFG, 20% have some form of cancer. The oncology department receives an average of 150 new patients a year. In the case of patients with acute lymphoblastic leukemia, 80-85% of cases result in full remission after five years. However, 15-20% of patients develop resistance to chemotherapy (the treatment of choice for this disease) and die mainly due to the toxic effect of these drugs. For all the above, the urgency to generate more knowledge about the pathophysiology of cancer, which is a prevalent disease in both adults and children, is reflected. This knowledge will allow patients to be diagnosed earlier and propose new and improved therapeutic options. In this issue of the *Boletín Médico del Hospital Infantil de México*, entitled "Perspectives in cancer: molecular findings, computational-designed drugs, and patient care," a group

of researchers present different perspectives. Review and research articles range from the importance of interactions between macromolecules in the regulation of cancer to the relevance of the measure of the quality of life and medical interventions in children with cancer.

The evasion of apoptosis, which is one of the defining characteristics of cancer, is discussed by Victoria-Acosta et al., regarding one of its main mechanisms: the overexpression of apoptosis inhibitory proteins (IAPs), which inhibit active caspases.<sup>1</sup> XIAP is the most studied member of the IAPs with significant implications in carcinogenesis. Likewise, XAF1 is an antagonist reactivating apoptosis XIAP through repression of caspases. However, XAF1 is commonly silenced in cancer; thus, it has been postulated as a tumor suppressor gene. This article shows a detailed description of transcriptional mechanisms of this tumor suppressor gene and the biological role of epigenetics configuration in their transcriptional silencing.

The topic of anticancer drug-design requiring the application of advanced molecular biology technics to generate targeted immunotherapies, such as the use of antibody-mediated transferrin receptor-targeting (TFR1) present in cancer cells, is elegantly presented by Luria-Pérez et al.<sup>2</sup> The authors mention different studies that suggest that therapies targeting TFR1 directly or through delivery conduits remain an attractive alternative for the treatment of cancers that overexpress the receptor. On the other hand, evidence of cells involved significantly in this complex process such as mesenchymal stem cells (MSC), are capable of regulating the immune system and favor the development of various cancers. M. Castro-Manreza provides a detailed description of some of the most important mechanisms used by MSC to regulate the immune response.<sup>3</sup> MSC present immunosuppressive properties which play a major role in cancer development; cytokines, chemokines, and factors secreted by cancer or other cells from tumor stroma are capable of modulating the functions of MSC.

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Hernández-Luna et al. showed that the transfection of prostate cancer cells (PC3) with a plasmid encoding a recombinant protein of an antagonist peptide from the BH3 region of the Bax protein fused to the GFP reporter protein (BaxGFP) can induce apoptosis of these tumor cells. Furthermore, the selective transport of this plasmid to the tumor cell with *Salmonella enterica* (serovar Typhimurium strain SL3261), a live-attenuated bacterial vector, can induce sensitization of the tumor cell to the action of drugs, such as cisplatin.<sup>4</sup>

Regarding clinical insights, Eguía-Aguilar et al. present a case report on the origin and prognostic implications of molecular findings in alveolar rhabdomyosarcoma. The patients with alveolar rhabdomyosarcoma often have metastasis at diagnosis and have a short median survival. In addition to this, the presence of proteins of the fusion gene PAX3/7-FOXO1 is associated with an unfavorable prognosis.<sup>5</sup>

A study of public microarray datasets for evaluating the TRPM2 channel as a biomarker in breast cancer is presented by Sumoza-Toledo et al. The results revealed that TRPM2 mRNA is overexpressed *in situ* and invasive breast carcinoma in comparison to normal breast tissue. TRPM2 is a promising biomarker for aggressiveness of breast cancer and a potential target for the development of new therapies.<sup>6</sup>

This issue also addresses a fascinating and novel topic named AllergoOncology: the immune response mechanisms developed during the allergic response display either pro-tumor or anti-tumor effects. Tirado-Rodríguez presents a review that deals with the major soluble mediators and cells present in allergic diseases that may play a fundamental role in the development or inhibition of cancer.<sup>7</sup>

In the last decade, diet has taken great relevance due to the drastic and global nutritional change. Especially in our country, as Mexico holds the highest rate of children obesity and the second highest rate of adult obesity. Extensive studies have addressed the therapeutic effects of omega-3 polyunsaturated fatty acids ( $\omega$ -3 PUFAs), and the opposite effect of omega-6 ( $\omega$ -6) PUFAs against different human diseases, including cancer. Hankinson and colleagues, from the University of California Los Angeles (UCLA), present an epidemiological and experimental study about the development of some important types of cancer (colon and colorectal carcinoma, breast cancer, prostate cancer, lung cancer, and neuroblastoma) in the relation to the ingestion to  $\omega$ -3 and  $\omega$ -6 (PUFAs).<sup>8</sup>

Regarding patient care and quality of life, M. Zapata-Tarrés presents a systematic review of instruments to measure the quality of life in patients undergoing oncological treatment. On the other hand, Barajas and Garduño

describe available scientific evidence about the efficacy and security of medical interventions used for handling and prevention of treatment-induced symptoms in children with cancer.<sup>9,10</sup>

This special issue will give readers an updated overview after they have covered some important molecular and cellular mechanisms to the pathophysiology of cancer.

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