Immune response in patients with advanced solid tumors after long-term immunization with a VEGF therapeutic vaccine

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HeberSaVax is a novel therapeutic cancer vaccine designed to produce an immune response against VEGF, with the development of antibodies that block the interaction of VEGF and its receptors, and reduce the bioavailability of this growth factor, thus inhibiting the pro-angiogenic and immune suppressive effects of this molecule. Also, the vaccine elicits cytotoxic T cells that directly kill tumor and other stroma cells that produce VEGF. The vaccine uses a recombinant modified human VEGF as antigen (CIGB-247) and has been tested mainly with two adjuvants: very small sized particles (VSSP) derived from Neisseria meningitidis OMP, and aluminum phosphate. After preclinical studies, two Phase I clinical trials were done where safety, tolerance, and immunogenicity of HeberSaVax were studied in patients with advanced solid tumors. Surviving individuals were eligible to receive off-trial voluntary re-immunizations until death, intolerance, marked disease progression, or patient's withdrawal of consent. The present work is focus in the immunological follow up of these surviving patients after 1 to 4 years of immunizations, without additional oncological treatments. One of the most outstanding findings in this active immunization follow up study is the long-term safety profile of HeberSaVax vaccination. Herein we show that long-term immunization was safe and most of the patients continue to produce anti-VEGF IgG antibodies that block VEGF/VEGF receptor 2 (KDR) interactions. VEGF/KDR positive blocking activity was stable, and in some cases increased with re-immunization. Cells from chronically immunized patients secreted gamma-IFN after in vitro stimulation; in some patients, this response could be classified as CD8+ specific. Our results indicate that long term immunization should continue to be a relevant as part of the HeberSaVax vaccination strategy, and highlight the importance of continuing the clinical development program of this novel cancer therapeutic vaccine candidate.

Biography
Yanelys Morera Diaz was graduated at the Biology Faculty, Havana University. She has been working since as a staff scientist at the Center for Genetic Engineering and Biotechnology, Havana, Cuba. She has worked in the Cancer Immunotherapy Group at the Biomedical Research Area in the fields of Molecular Biology and Immunology, specifically in the development of a therapeutic vaccine candidate for cancer. Yanelys has published several articles, is author of five National awards of the Sciences Academy of Cuba and is author of three Health National Awards. She received a Master in Sciences degree in Biotechnology (CIGB) in 2010 and got her Ph.D. in Biological Sciences from the University of Havana in 2013. For this work she received the National Outstanding Doctoral Thesis Award. Currently, Yanelys Morera is the head of Cancer Immunotherapy Laboratory and is devoted to the study of the immunological response of cancer patients vaccinated with HeberSaVax.

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