BioCubaFarma
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BioCubaFarma: accelerating the development of cancer immunotherapies

The Center of Molecular Immunology, a core institute of the Cuban organization of Biotechnology and Pharmaceutical Industries, BioCubaFarma, specializes in the development and manufacture of monoclonal antibodies, immunomodulators and molecular vaccines for cancer immunotherapy.

The Center of Molecular Immunology (CIM) is 1 of 34 companies and institutions in a network of resources and capabilities that constitutes the backbone of BioCubaFarma, the Cuban organization of Biotechnology and Pharmaceutical Industries. BioCubaFarma is a holding company that manages and coordinates national efforts in the biopharma sector to produce medicines and medical equipment that provide high-quality life science services with great economic and social impact. The biotechnology and pharmaceutical industry is one of Cuba's strategic industries, supplying goods, technologies and services that comply with the high-international-quality standards in the sector.

The CIM specializes in the development and manufacture of products for the diagnosis and treatment of cancer and of other diseases related to the immune system, such as atherosclerosis and other autoimmune conditions.

Building on Cuba's homegrown scientific and technical expertise and the government's substantial support for and investment in biotechnological and pharmaceutical research and development, the CIM has amassed a large portfolio of patented inventions, with 750 patents registered outside Cuba. These assets, together with a deep pipeline of products in development, have enabled the CIM to establish more than 40 partnerships worldwide—ranging from research collaboration agreements to licensing and codevelopment agreements—and three joint venture companies in China, Singapore and Thailand. The CIM is also seeking potential partners with an interest in investing in Cuban immuno-oncology assets through venture funding or similar mechanisms.

Nanoparticles against cancer

One of the hallmarks of cancer is its ability to generate tumor-derived factors that compromise the normal function of the immune system. Myeloid cell production or myelopoiesis, in particular, can be affected by such factors, resulting in defective myeloid populations. A combination of defective myeloid cells, also known as myeloid-derived suppressor cells (MDSCs), and reduced levels of M1 macrophages and dendritic cells, dramatically reduces the effectiveness of the immune response to tumors.

Modulation of the myeloid compartment in cancer and, more specifically, suppression of MDSCs are currently achieved by one of three strategies: suppression of MDSC activity, MDSC elimination or induction of MDSC differentiation.

Fig. 1 | BioCubaFarma's Center of Molecular Immunology. The Center of Molecular Immunology (CIM)—1 of 34 companies and institutes that constitute BioCubaFarma—develops and manufactures monoclonal antibodies, immunomodulators and molecular vaccines for cancer immunotherapy.

Pioneering work at the CIM (**Fig. 1**) has shown that very small size proteoliposomes (VSSP) could be used as immunomodulators to counter tumor-induced immunosuppression and stimulate a potent immune response against tumor antigens. VSSPs reverse tumor-induced aberrant myelopoiesis by reducing the immunosuppressive activity of MDSCs, promoting the differentiation of MDSCs into DCs, and reducing the levels of M2 macrophages in the tumor microenvironment.

VSSP-iMod brings these three activities together, making it a 'first-in-class' product for MDSC modulation.

VSSP-iMods are nanoparticles, 15–20 nm in diameter, that consist of *N*-acetyl GM3 gangliosides in complex with *Neisseria meningitidis*–derived outer membrane vesicles. VSSP-iMod is formulated for subcutaneous administration.

A physician-led clinical trial in patients with metastatic renal carcinoma (MRC) has shown a decrease in circulating MDSCs and a positive effect on survival. A phase 1/2 clinical trial in MRC is scheduled to start in the second half of 2018.

The CIM is also recruiting patients for a window-of-opportunity clinical trial in patients with breast carcinoma.

VSSP-iMod is produced using a good manufacturing practice (GMP) process at a semi-industrial scale. The current version of VSSP-iMod contains the natural ganglioside, but ongoing efforts to substitute the molecule with a synthetic version are underway. Implementation of a new formulation is planned for the last quarter of 2018.

Partnering with the CIM

The CIM has an open and very flexible approach to collaboration with external partners through mechanisms that range from research collaboration agreements to licensing and codevelopment agreements. In addition, the CIM is seeking potential partners interested in investing in the center's immuno-oncology assets through venture funding or similar mechanisms.

In the case of VSSP-iMod, the CIM is seeking corporate partnerships for codevelopment, registration and marketing of the product in selected territories. Establishment of a joint venture in the special development zone of Mariel, Havana and Cuba would be of particular interest to the CIM.

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