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Chilean president's first cousin shares prestigious HU young researcher award

Judy Siegel-Itzkovich, THE JERUSALEM POST Jun. 6, 2007

A Hebrew University doctoral student who is the first cousin of the president of Chile has won a prestigious research prize for developing a "knockout technique" in special "antibody nose drops" against allergies that he tested successfully on lab mice.

The Hebrew University of Jerusalem School of Pharmacy has come up with a new approach that offers hope for getting rid of them.

Chilean-born Ido Bachelet, a first cousin of Chilean president Michelle Bachelet, who is doing research at the HU School of Pharmacy, is the winner of the Barenholz Prize, named for the donor of the prize money and noted researcher, Prof. Yehezkel Barenholz of the Hebrew University-Hadassah Medical School.

The Barenholz Prize will be awarded at this week's 70th HU Board of Governors meeting in Jerusalem to two young people for "creativity and originality in applied research."

Bachelet, who is working under the supervision of Prof. Francesca Levi-Schaffer, is one; the other is doctoral student Danny Goldstein, also at the School of Pharmacy, who has designed a novel method of drug delivery to inhibit the growth of prostate cancer cells.

Bachelet's research has focused on mechanisms that regulate the function of mast cells - the "villains" in triggering allergic reactions. When exposed to allergens, mast cells react violently and release a huge array of pro-inflammatory substances, of which histamine is a well-known example. These substances lead to acute symptoms ranging from stuffy nose, rash and airway constriction, to the lethal shock known from food or venom allergies. Later on, they attract inflammatory cells that will maintain the response, which often persists as a chronic disease.

Although allergies are usually not perceived as lethal, they often can be. In 2005, over 250,000 people around the world died from asthma. The World Health Organization estimates that this rate will increase by 20 percent within the next decade if urgent action is not taken. Asthma is the most common chronic disease among children.

Bachelet has identified a receptor protein on mast cells, termed CD300a. This receptor has a prominent negative effect on mast cell activity, virtually shutting down the cell from unleashing allergic responses. Unfortunately, CD300a is widely found throughout the immune system, and simply targeting it could result in undesired, overall immune suppression with serious consequences, as can happen with steroids.

To overcome this problem, Bachelet and his research colleague Ariel Munitz have designed a small, synthetic, antibody fragment that has the unusual ability of recognizing two targets simultaneously - the receptor CD300a and a mast cell-specific marker. Thus, the antibody targets CD300a only on the surface of mast cells, avoiding suppression of other immune cells. This

antibody potently eliminated four different types of allergic diseases in mice. Moreover, when mice suffering from severe chronic asthma received the antibody in nose drops, they completely reverted to normal, healthy mice in less than two months.

This pioneering project, termed RECEPTRA, presents a novel therapeutic strategy for acute and chronic allergic diseases and is currently being licensed through Yissum, HU's technology transfer company, to pharmaceutical companies for further development and eventual clinical trials. Based on its enormous potential, Bachelet and his team predict that with further development, their technology will become the first line of allergy therapy in the near future.

Goldstein focused his work on prostate cancer, which is the second leading cause of cancer-related death in men. Present treatments for metastatic prostate cancer, in which deadly cells spread to other parts of the body, include hormonal therapy, chemotherapy and radiotherapy, which frequently have serious side effects.

The well-known chemotherapy drug paclitaxel exhibits a wide spectrum of anti-tumor activity. However, its therapeutic application in cancer therapy is limited, in part, due to its low water solubility, making it difficult to effectively deliver the drug to the points needed. It is also known to induce hypersensitivity reactions. Therefore, novel methods are needed that would allow for delivery of effective concentrations of paclitaxel over extended time intervals while minimizing toxicity.

Targeting drugs to prostate cancer metastases is one of the most challenging goals in treating such patients. Drug carriers such as nanoemulsions, liposomes (fatty droplets) and nanoparticles have shown great potential as delivery systems for an increasing number of active molecules. But even though they are capable of enhanced accumulation in the target tissue, these carriers cannot achieve their missions unless specific binding agents are attached to them which will ensure that they succeed in attaching to the targeted tissues.

It has been shown that the HER2 receptor is over-expressed in prostate cancer cells. It was also known that trastuzumab (an antibody) binds specifically to HER2. But there had been no clinical data indicating that this antibody would provide any relief for prostate cancer patients. Goldstein, a student of Prof. Simon Benita, was able to show that attaching trastuzumab molecules to the surface of oil droplets in nanoemulsions made possible the targeting of such droplets to cells over-expressing the HER2 receptor.

He coupled trastuzumab with emulsions containing the toxic agent paclitaxel-palmitate and evaluated the efficiency of these emulsions in laboratory tests on cancerous prostate cells and on mice with induced prostate cancer. He found that this emulsion compound did not cause a hypersensitive reaction upon injection and even yielded better results than known drug treatments while inhibiting tumor growth substantially.

Goldstein cautions, however, that this inhibiting activity of tumor metastases growth was not absolute and that while the results were encouraging, there was a need for further research to combat metastatic prostate cancer.

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