



Multimeric

Multimeric Biotherapeutics, Inc.

Multimeric Biotherapeutics Technology Used in New Vaccine Research

SAN DIEGO, January 27, 2014 – Multimeric Biotherapeutics, Inc., a biopharmaceutical company developing its patented forms of TNF SuperFamily ligands for the treatment of cancer and infectious diseases, today announced the application of its technology in research leading to new, more powerful vaccines called the MagaVax™ platform. MagaVax™ stands for Multimer Antigen Adjuvant Vaccine.

The new research findings are published in the current issue of *Journal of Virology*. They demonstrate that a vaccine targeted to a unique receptor in the immune system can lead to unprecedented T cell responses to HIV. The receptor involved is called “CD40” and the vaccine uses a special form its natural binding protein, CD40 ligand (CD40L), to bring the HIV protein to key immune cells called dendritic cells (DCs). Dendritic cells were first recognized by the late Ralph Steinman, who was awarded the Nobel Prize in 2011 for this discovery. Dr. Steinman showed that dendritic cells are the “gatekeepers” of the immune system and work by collecting and processing foreign proteins (“antigens”) in order to alert the rest of the immune system. An essential step in this process is that the dendritic cells must become activated through the CD40 receptor. The new finding comes from the laboratory of Geoffrey W. Stone, Ph.D., Assistant Professor of Microbiology and Immunology at the University of Miami Miller School of Medicine. Dr. Stone and his collaborators have found that directly coupling the foreign protein antigen to special form of CD40 ligand leads to extraordinarily strong CD8+ T cell responses in studies in mice. In the case of an HIV protein, the vaccinated mice were able to completely fend off infection by more than 10 million model viruses containing the HIV protein antigen. This type of extreme immune protection is called “sterilizing immunity” and is rarely seen in vaccine studies.

“The key to the vaccine’s effectiveness is that it contains a new form of CD40 ligand connected to the foreign protein antigen,” explained Dr. Stone. “This means that the dendritic cell both receives the antigen and is activated by its CD40 receptor at the same time,” Dr. Stone said.

The new form of CD40 ligand used in the studies is a modification of the UltraCD40L™ being developed by Multimeric Biotherapeutics, Inc.

The study, “Vaccination with a Fusion Protein That Introduces HIV-1 Gag Antigen into a Multimer CD40L Construct Results in Enhanced CD8+ T Cell Responses and Protection from Viral Challenge by Vaccinia-Gag,” appears in the February 2014 issue of *Journal of Virology*. The findings suggest a potential breakthrough in creating a vaccine to fight HIV.

Funded primarily by a grant to the University of Miami from the National Institutes of Health (NIH) with additional support from the Stanley J. Glaser Foundation, the study was conducted at the University of Miami and its federally funded Center for AIDS research (CFAR). Co-authors on the report by Dr. Stone are Dr. Sachin Gupta, James M. Termini, Francesca N. Raffa, and Cindi-Ann Williams who are all members of Dr. Stone’s research group at the University of Miami. An additional co-author is Dr. Richard S. Kornbluth who is the President and Chief Scientific Officer of Multimeric Biotherapeutics, Inc., La Jolla, CA. Dr. Kornbluth has previously worked with Dr. Stone on ways to use Multimeric’s many-trimer CD40 ligand technology to enhance vaccines.

The key result of the new vaccine is a very strong response by CD8+ “killer” T cells. Large numbers of these CD8+ T cells can protect against HIV, influenza, malaria, and cancer. However, no current vaccines generate enough CD8+ T cells to be effective. Consequently, the new, more effective vaccine design promises to have important applications for the prevention and treatment of diseases that affect millions of people.

"Vaccine-induced protection against HIV has been very difficult to achieve. In part, this is because it has been difficult to make a vaccine that gives large numbers of strongly protective CD8+ T cells," said Dr. Stone. "This new vaccine design takes us to a new level in stimulating the immune system to make these very important cells. The next steps are to test this vaccine in monkeys and then in humans."

About UHealth - University of Miami Health System

Powered by the University of Miami Miller School of Medicine's ground-breaking research, clinical trials, and medical education, UHealth provides life-saving care. The comprehensive network includes Bascom Palmer Eye Institute, Sylvester Comprehensive Cancer Center, the Center for Aids Research (CFAR), University of Miami Hospital and more than 30 outpatient facilities in five counties.

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About Multimeric

Multimeric Biotherapeutics, Inc. ("Multimeric") was formed around technology invented by Dr. Richard Kornbluth when he was at the University of California San Diego. This provides for many-trimer forms of the TNF SuperFamily (TNFSF) ligands called MegaLigands™ and UltraLigands™. Current products under development are MegaCD40L™ as a vaccine adjuvant and cancer immunotherapy agent, MegaOX40™ for cancer immunotherapy, and Ultra4-1BBL™ for growing anti-tumor T cells in vitro. The company has received funding from its founders, angel investors, and NIH grants. It operates out of fully equipped laboratory space in the San Diego Science Center. For more information, please visit the company website at www.multimericbio.com

Online reference: <http://jvi.asm.org/content/88/3/1492.abstract>