

Gates Grant for \$8.4 Million Goes to School of Medicine AIDS Researchers

LED BY A LONGTIME AIDS researcher at the School of Medicine, an interdisciplinary team of scientists has received a multimillion-dollar grant from the Bill & Melinda Gates Foundation to develop novel AIDS vaccines. The team, led by Susan B. Zolla-Pazner, Ph.D., Professor of Pathology, is one of the recipients of the Gates Foundation's Collaboration for AIDS Vaccine Discovery grants. The goal of these grants, which were announced in July, is to accelerate the development of an AIDS vaccine.

Dr. Zolla-Pazner's team, which received a three-year grant for \$8.4 million, involves collaborating researchers in immunology, virology, crystallography, and structural and computational biology. They will use sophisticated techniques to find out whether a section of the outer coat of the human immunodeficiency virus (HIV) can be used as a target for powerful neutralizing antibodies that defeat common strains of the virus.

Despite the enormous variability of HIV—one of the biggest stumbling blocks

to developing effective vaccines—Dr. Zolla-Pazner's research suggests that this section of the virus appears to be “structurally conserved” across HIV strains. A more thorough under-



THE ALPHA ROYAL MEDICAL CENTER IN BAMENDA, CAMEROON, IS ONE OF THE SITES OF THE NYU AIDS VACCINE DISCOVERY PROJECT. SHOWN WITH ITS STAFF ARE DR. SUSAN ZOLLA-PAZNER (THIRD FROM LEFT), WHO HEADS THE PROJECT, AND DR. PHILLIPE NYAMBI (FAR LEFT) OF THE SCHOOL OF MEDICINE. THE NYU RESEARCHERS HAVE WORKED IN MANY REGIONS OF CAMEROON.

standing of this conservation may lead to vaccines that can elicit neutralizing antibodies against most strains of HIV.

For the Gates project, Dr. Zolla-Pazner has recruited colleagues who are affiliated with eight institutions, four in the United States, and two each in India and Cameroon in West Africa, where she has established many long-term collaborations.

“This is a proof-of-principle project,” says Dr. Zolla-Pazner. “If it succeeds, it could be extended to the study of other parts of the HIV virus as well as to other disease-causing organisms.”

Since the early 1980s, Dr. Zolla-Pazner's laboratory at the Manhattan Veterans Affairs Medical Center, an affiliate of NYU Medical Center, has focused on pieces of the outer coat of the HIV virus, and on the antibodies elicited by these pieces, as the basis for AIDS vaccines.

Over the years, she and other scientists have found some six regions of the outer coat of the virus, which is studded with a protein called

gp120 in clouds of sugar. These regions induce antibodies that block the ability of the virus to infect cells. However, almost all of them have proved to be problematic. One region that remained promising was the so-called V3 loop of the gp120 protein, according to Dr. Zolla-Pazner. This region is used by the virus to gain a foothold on immune system

cells targeted by HIV. During the process of infection, the V3 loop remains at least partially exposed to the immune system and produces strong antibodies that don't react with any of the body's own proteins.

Dr. Zolla-Pazner's laboratory has already isolated powerful neutralizing antibodies from the blood of individuals infected with subtype B of HIV, which is found mainly in AIDS patients in the United States and Europe. As part of the Gates antibody project, her colleagues will collect blood from HIV infected individuals in Cameroon and India in order to cull additional antibodies from people infected with subtypes A and C, which predominate in Cameroon and India. Subtypes A, B, and C account for about 86 percent of all HIV strains.

The researchers plan to select the most powerful antibodies found in individuals infected with different strains of HIV. Then they will identify the sections of the V3 loop targeted by the antibodies and incorporate these structures into genetically engineered vaccines that will be tested in rabbits. The hope is that their work will provide a platform for the development of AIDS vaccines in humans.

Dr. Zolla-Pazner's colleagues include Phillippe N. Nyambi, Ph.D., Miroslaw K. Gorny, M.D., Ph.D., Catarina E. Hioe, Ph.D., Xiangpeng Kong, Ph.D., Timothy J. Cardozo, M.D., Ph.D., and Suman Laal, Ph.D., at the School of Medicine. ●

—Marjorie Shaffer