In 1992, the Community Research Initiative on AIDS (CRIA) and the Gay Men’s Health Crisis (GMHC) teamed up to inform our communities about a promising new area of scientific research: vaccines and immune therapies. More than 800 people with AIDS and their caregivers gathered to hear five of the world’s leading HIV vaccine researchers talk about their work. Because there was so much community interest, CRIA and GMHC decided to make this forum an annual event.

In 1993, the 2nd Annual Forum on Vaccine and Immune Therapies drew more than twenty leading scientists from around the world. More than 1500 attendees learned about the latest immune system research, animal models for HIV vaccine and immune therapy, and clinical studies of vaccine products.

“All of us involved, and especially you the community, must understand that this is high-risk research,” said NIH Director Dr. Bernadine Healy in her opening speech. “But we all know this and are willing— together—to go forward. We are ready because people are dying. Part of my reason for being here is to let you know how committed NIH is — and how committed I am personally as a physician — to this effort.”

CRIA’s Program Coordinator Gary Bonasorte joined Dr. Healy in her call for cooperation: “For the first time in the history of the epidemic, we can come together, united, to search for effective treatments, and eventually, a cure for AIDS. Tonight, tomorrow, we are working together. Let’s try to continue in this spirit of harmony until we have ended the AIDS epidemic.”

Next year’s Vaccine and Immune Therapy Forum is tentatively scheduled for February 24th & 25th, 1994. Call (212) 924-3934 for more details.

Introduction to Immune Therapies by Joseph A. Sonnabend, MBBCh, MRCP

Traditionally, we think of vaccines as preventing disease. Although ancient Chinese and Arabic writings discuss the deliberate transmission of mild strains of smallpox, Dr. Edward Jenner is generally credited with introducing vaccination in the West. In 1796, Dr. Jenner observed that patients who had been ill with the relatively benign cowpox did not develop the more virulent smallpox. He then began transmitting cowpox intentionally as a preventative therapy, creating a new science of disease prevention.

Vaccination is technically the deliberate creation of an immune response, and some scientists have proposed that this could also prove to be useful in enhancing immunity in individuals who are already infected with a pathogen. However, there is no precedent for the use of a vaccine as a means of treatment rather than prevention. The use of rabies vaccination in already-infected people has mistakenly been offered as an example of the success of post-exposure vaccination. The incubation period of rabies is so long that a vaccine can induce an immune response before the virus reaches the central nervous system. HIV is not comparable to rabies.

Two uses of HIV vaccination are being explored: prevention of infection, and treatment of those already infected. There are many obstacles to the development of both preventative and therapeutic vaccines for HIV, particularly for the latter as no precedent exists. One of the most important obstacles to the development of both types of vaccines is our lack of understanding of correlates of immunity. In other words, we don’t know what a vaccine would have to do in order to be effective. This problem is
If you were or are HIV+, asymptomatic, with 2-500 CD4+ cells, would you enter a therapeutic HIV vaccine study and why?

"Probably not, because I'm satisfied with the present therapies I'm on. If I were looking to change my regimen, the vaccines would be the first thing I'd consider."

Peter Staley, Member, Treatment Action Group (TAG)

IMMUNE THERAPIES contd. from p. 1

discussed at greater length by Gregg Gonsalves on page 7. Additional obstacles to the development of immune-based treatment for HIV disease include the relative newness of modern immunology, and the fact that so many aspects of the immune system are dysfunctional in people with AIDS, obstacles compounded by our imperfect understanding of the mechanisms underlying the development of these functional abnormalities. Stimulating or inhibiting activity in one area of the immune system may have unexpected and unceivable results in other areas.

Currently, there are about twenty-two candidate vaccines that are being studied in both seropositive and seronegative people. Most of these products are based on proteins found on the surface of HIV. The artificial proteins are usually given with an adjuvant, a substance that enhances the immune response. There are also studies of vaccines based on proteins from the inner core of HIV, as well as products using whole killed virus, HIV proteins attached to other "carrier" proteins, and combinations of HIV proteins. There are another twenty-five vaccine products in early, pre-clinical test tube and animal studies.

Many scientists today are expressing guarded optimism about this research. Others are skeptical about the possibility of developing a therapeutic vaccine, and some are even of the opinion that a preventative vaccine is not feasible. However there should be some optimism that newer studies on the immunological disorders of AIDS will result in a greater understanding of their nature and therefore the ability to target interventions in a rational manner.

MONKEY BUSINESS

Testing protective and therapeutic vaccines is very difficult, in part due to the lack of appropriate animal models. While almost every species has an immunodeficiency virus, similar to HIV, it is generally unclear how the clinical diseases the viruses cause are related to AIDS. For instance Simian Immunodeficiency Virus (SIV) infects most monkeys, however it causes AIDS only in chimpanzees and in rhesus monkeys.

Dr. Ronald Desrosiers presented results at the CRIA/GMHC Vaccine Forum of studies using live SIV from which the nef gene, which manufactures a protein that regulates viral reproduction, has been deleted. Dr. Desrosiers found that these viruses reproduced poorly in rhesus monkeys and appeared not to cause disease in this normally susceptible host.

So far the monkeys have remained disease-free for three years. Rhesus monkeys vaccinated with live nef-deleted SIV were completely protected from injection of live, pathogenic SIV. Deletion of nef or of multiple genes from HIV may provide the means for creating a safe, effective, live, attenuated (weakened) virus vaccine to protect against AIDS. Despite their efficacy in preventing SIV infection, early attempts to use these live attenuated vaccines to treat infected monkeys were unsuccessful.

"Personally, I find it hard to see how nef-deleted virus could reverse the course of HIV disease," Desrosiers said.

Currently, Dr. Desrosiers is working with a new version of the vaccine, with deletions of the nef, vpr and LTR genes. Similar vaccines for humans could be created by deleting analogous segments of HIV. However, the relevance of these studies to the human disease is unknown. Dr. Desrosiers suggested that there was a risk that the live attenuated viruses could cause delayed disease, in which the asymptomatic period would be significantly extended, but ultimately the subject would become ill. This may make study of the product as a prophylactic vaccine difficult.

Dr. Margaret Johnston, director of Basic Research at the NIAID, asked the audience how many HIV-negative people among them would be willing to enroll in a prophylactic vaccine study using a live attenuated virus. Only five people raised their hands.

"Well," said Dr. Johnston, "We don't need many more people than that for an initial safety trial."
NATURAL IMMUNITY

Adapted from The Immune System - How It Works, a publication of the US National Institutes of Health

THE IMMUNE SYSTEM

The basis of the immune system is the body’s remarkable ability to distinguish between self and other. The body’s immune defenses recognize cells that carry distinctive “self” marker molecules. But when immune cells encounter molecules or organisms carrying markers that say “other,” they mount an immune response. Anything that can trigger this immune response is called an antigen.

Some immune cells attack many kinds of antigens, while others are highly specific. To work effectively, several different types of immune cells usually cooperate. Sometimes immune cells communicate by direct physical contact, sometimes by releasing chemical messengers called cytokines.

When an antigen appears, a few cells specific to that antigen multiply into a full-scale army. After their job is done, most fade away. In order to have all the cells needed to recognize millions of possible enemies, the immune system stores just a few of each kind.

Lymphocytes are one of the main types of immune cells. B cells and T cells are the main types of lymphocytes.

Humoral Immunity

B cells work chiefly by secreting substances called antibodies into the body’s fluids. Antibodies attack antigens circulating in the bloodstream, however, they are powerless to penetrate cells. The job of attacking cells that have been infected by viruses or distorted by cancer is left to T lymphocytes or other immune cells.

Each B cell is programmed to make one specific antibody. For example, one B cell will make an antibody that blocks a virus that causes the common cold, while another produces an antibody that attacks a bacterium that causes pneumonia.

When a B cell encounters its triggering antigen, it gives rise to many large cells known as plasma cells. Every plasma cell is essentially a factory for producing antibody. Each of the plasma cells descends from a given B cell manufactures millions of identical antibodies and pours them into the bloodstream.

An antibody matches an antigen much as a key matches a lock. Some match exactly; others fit more like a skeleton key. But generally, whenever antibody and antigen interlock, the antibody marks the antigen for destruction.

Cellular Immunity

T cells contribute to the immune defenses in two major ways. Some direct and regulate the immune responses. Others are killer cells that attack cells that are infected or cancerous.

Regulator T lymphocytes work primarily by secreting potent chemical messengers known as cytokines. Binding to target cells, cytokines mobilize many other cells and substances. They encourage or discourage the growth of cells, trigger cell activity, direct cell traffic, destroy target cells, arouse phagocytes, and other functions.

Natural killer cells (NK cells) are another kind of lethal white cell, or lymphocyte. Like killer T cells, NK cells are armed with granules filled with potent chemicals. But killer T cells only attack their specific matching targets; natural killer cells attack any foe. Both kinds of killer cells slay on contact. The deadly assassin binds to its target and delivers a lethal burst of chemicals.

Phagocytes are large white cells that can swallow and digest, microbes and other foreign particles. Monocytes are phagocytes that circulate in the blood. When monocytes migrate into tissues, they develop into macrophages, or “big eaters.” Specialized types of macrophages can be found in many organs, including the lungs, the kidneys, the brain and the liver. Macrophages play many roles. As scavengers, they rid the body of worn out cells and other debris. They display bits of foreign antigen in a way that draws the attention of matching lymphocytes. And they churn out an amazing variety of powerful cytokines which are vital to the immune responses.

Granulocytes are another kind of immune cell. Granulocytes are white blood cells that contain granules filled with potent chemicals, which allow the granulocytes to destroy microorganisms. Types of granulocytes include neutrophils, eosinophils, basophils, and mast cells.
Immuno AG
rgp160

Immuno AG’s rgp160 is an experimental AIDS vaccine therapy that mimics a protein on the envelope of the Human Immunodeficiency Virus (HIV). The product is produced by recombinant DNA technology, or genetic engineering. Immuno’s rgp160 is different from other gp160-based AIDS vaccines currently in development because it is grown in mammalian cells, and because the shape of the protein closely resembles the shape of the gp160 protein on native HIV.

Pre-clinical studies of this vaccine in HIV-infected chimpanzees demonstrated sustained cell-mediated immune response to the protein. In addition, studies in uninfected chimpanzees have shown some protection from HIV challenge.

Early clinical studies of Immuno rgp160, involving HIV-negative volunteers, showed that the vaccine produced cell-mediated immune response in 100% of participants, and antibody response in 95% of participants.

U.S. Phase I clinical studies of this vaccine in HIV-positive volunteers have begun at three sites. A total of 55 volunteers with CD4+ counts greater than 600 has been enrolled in this double-blind, placebo-controlled study. Additionally, two European studies, involving a total of almost 200 patients with CD4+ counts greater than 200, are now enrolling.

Immuno rgp160 is the first candidate AIDS vaccine to emerge from the Immuno AIDS Research Program. "Immuno has made a significant, long-term commitment to AIDS research, said Dr. Martha Eibl, director of the Immuno’s AIDS research effort. "We are exploring other AIDS vaccine approaches, including whole virus vaccines, oral vaccines and immune response modifiers."

Currently, the company has more than six other products in various stages of preclinical development.

Genentech MN rgp120/HIV-1 IIIB rgp120/HIV-1

Genentech is testing two experimental AIDS vaccines using genetically engineered forms of HIV envelope glycoprotein gp120 derived from HIV-1 strains MN and HIV-1 IIIB, and grown in Chinese hamster ovary cells. The MN strain is similar to approximately 60% of North American isolates, whereas the IIIB strain is similar to only 5% of U.S. isolates.

The two vaccines were compared in preclinical studies to assess ability to prevent gp120 from attaching to synthetic CD4+ molecules, to generate anti-gp120 antibodies, and to neutralize various clinical isolates of HIV-1. The MN vaccine reacted to five diverse isolates, while the IIIB vaccine reacted only to the IIIB strain of HIV-1.

A placebo-controlled trial of the IIIB rgp120 vaccine in 42 patients with less than 500 CD4+ cells/mm³ showed 100% of recipients developed new antibody response and proliferative cellular response. The degree of cellular response appeared to be dose-dependent. No effect of CD4+ binding antibody, neutralization of HIV or change in cellular response to HIV envelope was observed. Another ongoing study compares the two vaccines in 122 patients with more than 500 CD4+ cells/mm³.

Immune Response Corporation
HIV-Immunogen "The Salk Vaccine"

Immune Response Corp.’s HIV-Immunogen is an experimental AIDS vaccine therapy that uses whole inactivated virus. Scientists hope that using whole virus instead of viral protein subunits will stimulate immune responses that are capable of suppressing more diverse strains of HIV. Early clinical studies of HIV-Immunogen suggest that the drug is safe and well-tolerated.

22 patients with AIDS-Related Complex (ARC) have been followed for approximately four years and no side effects have been noted. In another trial involving 54 HIV+ asymptomatic patients with more than 600 CD4+ cells/mm³, treated patients had reduced viral burden in peripheral blood as compared with the control group. Increased anti-HIV antibodies and Delayed Type Hypersensitivity (DTH) response has also been noted.

Richard Trauger, Ph.D., head of Immunology for Immune Response Corp., said, "We want to capitalize on the patient’s innate immunity. We would like to induce that cell-mediated response that may have waned or disappeared. We would like to enhance the antibody response as well. We want to enhance the immune system to control the spread of virus on its own."

Why did you decide to enter a therapeutic vaccine study?

I heard about therapeutic vaccines when there was no treatment option for people with high T-cells, and participating in a study seemed like a low-risk thing to do that might help. So I decided to enter a study of a therapeutic vaccine. This is a thing that might help a person’s immune system fight off the virus without taking toxic drugs.

Bill Snow, Member ACT UP/Golden Gate
If you were or are HIV+, asymptomatic, with 2-500 CD4+ cells, would you enter a therapeutic HIV vaccine study and why?

Not right now — if and when we have some surrogate or clinical evidence of their efficacy, I might reconsider.

Gregg Gonsalves, Member, Treatment Action Group (TAG)

Yes. If a potential treatment appears relatively non-toxic in the short term, it doesn’t cost me a lot of money, and I don’t have to stop the other drugs I’m on, then I’m willing to try it. I doubt these vaccines will be a “magic bullet” — just as I doubt any drug currently under development will be — but I hope that each drug has a small effect and that added together they’ll be some larger benefit.

Stephen Gendlin

I would not enter a therapeutic vaccine study. Actually, it depends on the study. I wouldn’t consider a study that tested the efficacy of a single product, but I might consider a study that evaluated the feasibility of this entire approach.

Joseph A. Sonnabend, MD, Medical Director
Community Research Initiative on AIDS

MICROGENESYS VAXSYN (rGP160)

MicroGeneSys’s VaxSyn is a synthetic version of the envelope protein gp160 produced in insect cells and administered with an alum adjuvant. The VaxSyn product is the most extensively studied of all of the HIV vaccine products. In the test tube, lymphocytes from patients inoculated intramuscularly with 40 or 80µg of VaxSyn developed cytolytic T lymphocyte responses (CTL).

Another study found that, in vitro, lymphocytes that had been primed with VaxSyn killed HIV-infected cells, recognized gp160 from several viral strains, and did not kill uninfected CD4+ cells with gp120 bound to their surface.

In a clinical study of 30 HIV+ patients, 19 of 30 treated patients demonstrated improvements in gp160-specific humoral and cellular immune responses. Positive response was correlated with greater number of injections and higher baseline CD4+ values. Long-term follow-up showed positive response in 28 of 30 patients.

Another study found that patients given escalating doses of VaxSyn over twelve months resulted in enhanced cell-killing activity against targets with gp160 on their surface and increased levels of antibodies to gp160.

A combination of VaxSyn and a p24 antigen-based vaccine produced an immune response in 16 HIV+ people with CD4+ cell counts of 2-500, whereas 14 patients with less than 200 CD4+ cells had no significant immune response. A similar study in patients with less than 400 CD4+ cells found enhanced HIV specific T & B cell responses in patients treated with VaxSyn. The addition of AZT produced no extra response.

Finally, 26 patients randomly assigned to receive VaxSyn or hepatitis B vaccine showed increased HIV-specific cellular immune response to VaxSyn but not to hepatitis B vaccine.

THE BIOCINE COMPANY (CHIRON & CIBA-GEIGY) ENV 2-3

Biocine’s ENV 2-3 is a synthetic version of the HIV-1 envelope protein gp120 produced using genetically engineered yeast. The vaccine is given with an adjuvant called MFP-59, and studies are evaluating addition of an immune modulator called MTP-PE. Early clinical studies are still ongoing. An NIH study is comparing ENV 2-3 and adjuvant with and without MTP-PE.

Another ongoing NIH study is comparing ENV 2-3 with four other vaccine products, including two versions of MicroGeneSys’s gp160 and Genentech’s two gp120 vaccines. Preliminary results indicate that this vaccine is safe, and some safety and efficacy data are expected this year.

TELL US WHAT’S ON YOUR MIND

CRIA is currently in negotiation with several vaccine companies to conduct studies in the New York area. If you would like to receive information on upcoming CRIA studies, fill out your name and address below, and send it to:

Community Research Initiative on AIDS
275 Seventh Avenue
20th Floor
New York, NY 10001

Please also take the time to participate in our opinion survey. We’d like to know how you would answer the following question:

If you are or were HIV+, asymptomatic with 2-500 CD4+ cells, would you consider entering a therapeutic vaccine study, and why?

________________________________________________________________________
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Yes! Please add my name to the CRIA mailing list, and send me information about your upcoming studies!

Name________________________
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City, State, Zip:_________________
Other Vaccines in Clinical Trials:

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POLITICAL SCIENCE

In October, 1992, after intense lobbying by former Senator Russell Long, Congress appropriated $20 million to the Department of Defense for clinical trials of the MicroGeneSys gp160 candidate vaccine. The vaccine is a copy of a protein found on the surface of HIV. Early studies of gp160 in small groups of relatively healthy HIV+ patients suggest that the product is safe in the short-term, and that it may stabilize T4 decline for a period of time.

However, the legislation provided for alternative uses of funds if the Secretary of Defense, the Commissioner of Food and Drugs, and the Director of the National Institutes of Health (NIH) all agreed that the proposed single-agent study should not go forward. Usually, scientific proposals are carefully scrutinized by scientists during funding applications.

The appropriation legislation, however, called for scientific review after funding appropriation.

This appropriation generated much heated criticism on all sides. Some activists, complaining that NIH vaccine research had progressed too slowly, and praised Congress’s effort to speed studies. However, many scientists and some activists believed that, by appropriating funds outside of the traditional scientific review process, Congress had overestimated its ability to evaluate the promise of new therapies.

In response to the appropriation, NIH Director Bernardine Healy, MD, convened a panel of experts to establish the NIH position on these studies. Dr. Healy’s panel made four major recommendations: 1) That a trial of MicroGeneSys’s gp160 vaccine alone would not be adequate; 2) that, due to the unique nature of the HIV epidemic, the funds should be used to test the therapeutic efficacy of AIDS vaccines; 3) that several different products should be tested; and 4) that vaccine trials should include a broad base of HIV+ people, not limited to military personnel.

The NIH design team also presented a program to the subcommittee calling for a focus on individuals with HIV infection whose CD4+ counts are between 200 and 500 cells/mm3.

Recently, the Department of Defense announced that it would conduct a single-product study in spite of the NIH recommendations. A coalition of scientists, advocates, and representatives of NIH and the Clinton Administration, coordinated by CRIA’s Gary Bonasorte, continues to lobby for a study design that would compare the Immuno AQ product, the MicroGeneSys product, the Salk Vaccine, the Genentech product and a placebo. With so much money at stake, the only sure bet is that controversy will continue to surround this appropriation.
Correlates of Immunity in HIV Infection: What Protects Against Infection and Progression of Disease

by Gregg Gonsalves

What is the specific nature of the immune response you would hope to elicit in designing an effective prophylactic vaccine against HIV or a useful immune-based therapy for those already infected with the virus? Would you hope to evoke a strong neutralizing antibody response, a strong cytotoxic T-lymphocyte (CTL) response, a combination of the two, or none of the above? Against which part of the virus would you hope this immune response would be directed: the outer sugary envelope of the virus, its RNA-bearing core, or yet some other viral component? What will protect against infection or progression of disease? Finding out what constitutes a successful immune response against HIV is one of the holy grails of AIDS research. At the Second Annual CRIA/GMHC Community Forum on HIV Vaccine and Immune Therapies, researchers from around the country presented results of studies designed to provide the beginning of answers to these critical questions.

Dr. Bonnie Matheson, of the Division of AIDS, NIAID introduced the topic by surveying the current state of knowledge derived from animal and human cohort studies and charted directions for future research. The next two speakers presented their work on a unique population of people with HIV infection. These individuals, who have been called "long-term survivors,” have been infected with the virus for many years and have near normal and stable CD4+ cell counts. Long-term survivors have managed to hold back HIV’s assault on the immune system and may hold important clues about the nature of a successful immune response to the virus. Dr. Bruce Walker of Harvard Medical School has been examining a group of men from the San Francisco City Cohort Study who have been HIV+ for more than ten years with CD4+ cell counts above 500/mL, focusing on the level of their CTL responses to HIV and the identification of specific viral epitopes recognized by the CTLs of these individuals. Dr. Linda Baum of the Chicago Medical School has been studying Antibody-Dependent Cellular Cytotoxicity (ADCC) activity in a group of men from the Multicenter AIDS Cohort Study (MACS) who have had stable or rising CD4+ cell counts and who were HIV+ when they joined the MACS in 1984. While pointing out that further investigation is needed, Dr. Baum suggested that these men have stronger ADCC responses to gp120 as compared to controls.

The fourth speaker, Dr. Richard Koup of the Aaron Diamond AIDS Research Center at NYU, presented his work on the immune response in primary HIV infection. In acute infection with HIV, there are high titers of HIV in the blood. However, within a few weeks, the level of viremia drops considerably.

Dr. Koup has been trying to figure out the particular immune mechanism which is responsible for bringing viral replication under control during this initial phase of the disease. In studies of several individuals, Dr. Koup has correlated the decrease in viral load with CTL activity against the virus. Neutralizing antibodies appeared later, only after the viral titers have dropped.

The last speaker, Dr. Larry Arthur of the Frederick Cancer Research and Development Facility, associated with the National Cancer Institute, offered a report of a novel discovery. Dr. Arthur has discovered that cellular proteins are bound to the surface of HIV. In particular, Dr. Arthur has noted the presence of major histocompatibility (MHC) antigens embedded in the viral envelope. Dr. Arthur's findings may have important implications for the pathogenesis of the disease. Antibodies to MHC antigens have been able to neutralize HIV in vitro and have been detected in the sera of some individuals infected with the virus and may play a protective role in vivo. In addition, MHC antigens are key players in the immune system and their presence on the surface of the virus may disrupt the delicate mechanism of cell signalling between lymphocytes and antigen-presenting cells.

The CRIA/GMHC Forum was one of the rare occasions when basic HIV research has been presented before the community. Knowing what kind of immune response might be beneficial in protecting against HIV infection or disease progression is valuable information for those considering entering a clinical trial of an HIV immunogen.
GLOSSARY

**Adjuvant**: Any substance which enhances the immune-stimulating properties of an antigen or the pharmacologic effect of a drug.

**Antibodies**: Molecules in the blood or secretory fluids that tag, destroy, or neutralize bacteria, viruses or other harmful toxins. They are members of a class of proteins known as immunoglobulins, which are produced and secreted by B-lymphocytes in response to stimulation by antigens.

**Antigen**: A substance which, when introduced into the body, is capable of inducing the production of a specific antibody.

**Attenuated Virus**: A weakened virus whose ability to infect or produce disease is potentially reduced.

**B-Cells**: A type of white blood cell (lymphocyte) that comes from the bone marrow. It is one of the two lymphocytes that play a major role in the body's immune response. B-cells work as precursors of plasma cells, which secrete antibodies into the body's fluids.

**Basophil**: A type of granulocyte.

**Cellular Immunity**: One of two fundamental but overlapping branches of the immune system (Humoral Immunity is the other). The cell-mediated immune response relies on cells that bind to, digest and break down invaders.

**Cytokines**: Molecules released by immune cells that regulate the immune response.

**Delayed-Type Hypersensitivity (DTH)**: A cell-mediated immune response measured through the formation of an induration on the skin.

**Eosinophil**: A type of granulocyte.

**Granulocyte**: A white blood cell containing granules, small masses of chemicals that can degrade organisms.

**Humoral Immunity**: One of two fundamental but overlapping branches of the immune system (cell-mediated is the other). The term “humor” refers to body fluids, primarily serum and lymph. Molecules of the humoral immune system are proteins collectively called immunoglobulins, a single such molecule is called an antibody.

**Immunoglobulin**: See antibodies.

**Lymphocytes**: One of two kinds of small white blood cells (leukocytes) responsible for much of the immune response. Lymphocytes normally include 25% of the total white blood cell count but increase in number in response to infection. They occur in two forms: B cells and T cells.

**Macrophage**: Any large cell that can surround and digest foreign substances in the body, such as protozoa or bacteria. Macrophages are found in the liver, spleen, and in the loose connective tissue.

** Mast Cell**: A type of granulocyte.

**Monocyte**: A relatively large cell found in the circulating blood, the lymph nodes, spleen, bone marrow and loose connective tissue. Monocytes are precursor cells for Macrophages.

**Natural Killer (NK) Cells**: A type of lymphocyte that seeks out and destroy invaders.

**Neutrophil**: A type of granulocyte.

**Pathogen**: Any virus, microorganism or substance causing disease.

**Phagocyte**: A cell capable of ingesting bacteria, foreign particles and other cells.

**Plasma Cell**: A type of cell that is derived from B cells and is responsible for production of antibodies.

**T-Cells**: One of two types of white blood cells that are primarily responsible for immune response. T-cells are mainly responsible for cell-mediated immunity.

**Vaccine**: Any preparation intended to invoke an immune response.

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YES! I want to help CRA test promising experimental drugs for AIDS/HIV infection. Enclosed is my contribution of:

- $ 25
- $100
- $500
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