LAMS/MACS NEWSLETTER
Harbor - UCLA - LAGLC

December 2008

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A LETTER FROM THE PRINCIPAL INVESTIGATOR

Colleagues

It is amazing to realize that many of you have been loyal to the LAMS/MACS for 25 years and some for almost 30 years. Your devotion and commitment have had a tremendous impact on advancing our understanding, not only of HIV, but of the way in which the human body responds to pathogenic organisms and how viruses behave in the human body. Some of our new studies are also contributing to our understanding of the aging process, metabolic and cardiovascular diseases and normal kidney function. In this newsletter we include a partial list of the discoveries and advances that have been made because of you! We and the world cannot express sufficient gratitude to you all for the commitment and sacrifices you have made.

In this newsletter we update you on some of the new studies we are conducting with your help and we invite you to celebrate 25+ years of scientific achievement and the continuation of the LAMS/MACS for at least another 5 years. It is truly a time to celebrate and reflect on what you have done.

I hope to see most of you at the celebration and to be able to personally express my gratitude and that of the many scientists who are now contributing to the success of the LAMS/MACS. Many of these scientists will be celebrating with us so you will have the opportunity to grill them on the latest!

Roger

25TH ANNIVERSARY CELEBRATION

25th YEAR TRIBUTE TO THE COHORT. WHO'S THE COHORT? YOU ARE! WE ARE GOING TO CELEBRATE LIKE NEVER BEFORE!
Jan Dudley has come back from retirement to help us put on a party. Details to follow. Please save the date:

Sunday, April 26th, 2009

If you are **very likely** to attend would you let us know? We also need to know if you will be accompanied. You can call us at 310-479-6691 or email us at: dmiles@ucla.edu.

A PROMISE ... IT WILL BE FUN!

If you have any pictures of those close to you who have died and would like to have them displayed on a Memory Wall at this event, please submit them to: May Htike, 11600 Wilshire Bl # 26, Los Angeles CA 90025, or email them to dmiles@ucla.edu. You may also bring them in at your next visit.

REQUEST FOR TESTIMONIALS A NOTE FROM JAN

Dear Participants:

We want to celebrate you. We want to come together to wonder at the amazing accomplishments that your dedication and faithfulness to the study has permitted.

We want the party to be a great one and we are on a fund-raising mission to get enough to really do it up right. We want to impress potential donors with your dedication and let them understand why they should contribute to the Tribute to the Cohort.

We don't want your money. It just isn't enough that you have persevered through the last 25 years, coming into the study site to relinquish your precious bodily fluids, *Nooooo*, now we want you to tell us how you feel about it. Why do you keep coming? You love the blood draw, right? You secretly love May? Please tell us your motives and incentives for participating. What impact has the study had on your life? Even a sentence or two will be welcome. Email: dmiles@ucla.edu. Or send in your comments to: LAMS c/o Dennis Miles, 11600 Wilshire Bl, # 26, Los Angeles CA 90025.

I can't wait for the party.

Yours,

Jan Dudley

MACS IN SCIENCE MAGAZINE

The MACS was written up in the JUL 25th, 2008 edition of SCIENCE (VOL 321).

(www.sciencemag.org)

Did you know the annual budget for the four MACS study centers (Chicago, Los Angeles, Baltimore and Pittsburgh) and the MACS data center in Baltimore is $14.4 million? Did you know that the original cohort numbered 5622 men? Did you know that about half of those men were infected when they joined the study? This meant that the researchers had a "built-in" control group in the negative men they had recruited. Did you know that there are more than 150 MACS investigators involved in our project? We follow some 3000 men twice a year. Of those about 1600 are infected and nearly 90% of them take anti-HIV medications. There are over 1 million samples of plasma, serum and cells in our depositories. The researchers have collected more than 100,000 CD4 counts as well as tens of thousands viral loads. The article quotes John Phair, the chair of the MACS executive committee: "The participants give a lot of blood. They're very generous." Understated eloquence, indeed!

POST-EXPOSURE PROPHYLAXIS

One of the most anxiety-provoking situations for participants that we speak with must be the uncertainty about what to do if you think you've been exposed to HIV, and was it risky enough to start a regimen of Post-Exposure Prophylaxis (PEP). Even though guidelines for PEP have been available since 1998, they are not commonly known, even among medical providers. We hope that this article will address most of your questions and concerns about what it is and when to consider it.

First, a quick definition of what PEP is. According to the CDC, it is "the provision of antiretroviral drugs to prevent HIV infection after unanticipated sexual or injection drug-use exposure." The US Department of Health and Human Services recommends that people seek care within 72 hours after exposure to blood, genital secretions or other potentially infectious bodily fluids of a person of unknown HIV status, or when such exposure would represent a substantial risk for transmission if the source (person) was HIV infected. At this point, some of you are wondering, "What if it's been more than 72 hours since the exposure?" The DHHS says that Clinicians might consider administration of PEP if they feel that the diminished potential benefit of PEP still outweighs the risk of adverse affects from the antiretroviral drugs. The potential benefit of PEP does diminish with time after exposure, so again, one must communicate with their medical provider quickly to maximize the effectiveness of PEP.

Second, a PEP regimen lasts for 28 days. The goal is to have the antiretroviral medication (HAART) reduce the risk for acquiring HIV infection. Studies have shown that the sooner PEP is administered, the more likely it is to interrupt transmission. The CDC goes on to say that currently there is no optimal antiretroviral medication or combination that is used for PEP, but that preferred regimens include efavirenz ("Sustiva") and lamivudine ("Epivir") or emtricitabine ("Emtriva") with zidovudine ("Retrovir") or tenofovir and lopinavir/ritonavir (aka "Kaletra") and zidovudine with either lamivudine or emtricitabine. Other regimens are also possible.

If you feel that you have been exposed and you seek PEP, you will likely be asked to provide your clinician additional information to help evaluate your risk, such as: 1) HIV status of the potentially exposed person (you), 2) Timing and frequency of the exposure, 3) HIV status of the source, and 4) Transmission risk from the exposure. In this area, the highest levels of per-act risk for HIV transmission are associated with needle-sharing by injection drug users and unprotected receptive

anal intercourse. Insertive anal intercourse and oral sex represent less (although still substantial) risks.

Baseline HIV testing should be performed on all persons seeking evaluation for potential HIV exposure. And if PEP is initiated, additional testing should be done at 4-6 weeks after exposure, 3 months and 6 months after exposure to determine whether HIV infection has occurred. In addition, testing for other STD's, Hepatitis B and C should be offered.

There are additional factors to consider once you've started PEP. Often, there are side effects associated with the medication. Common side effects include nausea, headaches, fatigue, vomiting and diarrhea. These will vary according to which regimen you are prescribed. Not taking your medications every day (non-adherence) will reduce the effectiveness of the PEP. And even if you do take them as prescribed, it is not 100% guaranteed to prevent HIV infection. One other question I've received concerns cost. PEP is not cheap, a 28 days supply often costs in the range of $600 to $1000. And your health insurance may not cover it. Again, this is a question to discuss with your clinician.

As with anything else here at the LAMS, our staff is happy to discuss this issue with you in greater detail. You can call Max Hechter during the week at 310-825-1073, or during the weekends, if you feel it's an emergency and needs immediate response, you can page him at 1-800-233-7231, pager ID# 90425. You can also email him at hechter@ucla.edu.

The following website was referenced in the preparation of this article:
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5402a1.htm

It also goes into greater detail about PEP than we could fit into the newsletter.

FROM THE JAMISON LAB

Twenty-five years! We can't thank you enough for all you have done. We especially want to thank all those who have participated in the research studies conducted by Dr. Beth Jamieson and her lab. Your participation has made it possible for us to conduct studies that look at the effects of gender and age on HIV/AIDS disease progression.

Although women and men show different responses to HIV infection we're finding that age at the time of infection might be an even more important factor than gender in how well the immune system can respond to the virus and therefore, how fast people lose CD4+ T-cells and progress to AIDS. We just received a five-year grant to investigate how advancing age and HIV-1 infection work together to destroy the CD4+ T-cell compartment. Our research will hopefully allow for a more in depth understanding of the immune system and eventually lead to better drug therapies that not only help suppress the progression to AIDS, but may help all of us respond better to vaccines and infectious diseases during the normal course of aging. We are particularly interested in understanding how age impacts the ability of HAART to restore both T-cell numbers and clinical health so that our studies may lead to a better quality of life for people living long-term with HIV/AIDS. Words cannot express how much we appreciate your commitment and altruism for future generations; without your help and, the help of those that we have lost, none of these advances could have been made.

You may contact Alfonso Coro at:
acoro@mednet.ucla.edu

LONG-TERM HEALTH EFFECTS OF METHAMPHETAMINE USE IN THE MACS

Methamphetamine (MA) use among men who have sex with men (MSM) has become an increasingly important behavioral risk factor associated with co-occurring epidemics of HIV and other biopsychosocial health problems. However, MA research among MSM has generally been limited to cross-sectional or relatively short-term cohort studies. Therefore, our understanding of the factors that predict initiation of MA use, the specific mechanisms of how MA use results in long term health consequences, whether drug use has unique health outcomes among minority MSM, whether MA use results in poorer health outcomes among HIV-positive MSM, or whether resolution of MA use improves health remain poorly defined. These gaps inhibit our ability to respond effectively to the health consequences of MA use among MSM. The goal of the "Long-Term Health Effects of Methamphetamine Use in the MACS" substudy is to help address these gaps. This

prospective substudy involves completing a psychosocial/behavioral survey at two consecutive MACS Visits, 49 and 50. The survey takes about 30-45 minutes to complete and includes a battery of psychosocial measures, early lifetime stressors, ongoing stressors, current sexual behaviors, drug use patterns, and other health risks. Men from all four MACS centers are participating in this substudy.

If you have questions about the study, please contact Dr. Steven Shoptaw at: 310-794-0619, ext 225, or sshoptaw@mednet.ucla.edu.

CURRENT MACS CANCER RESEARCH

Our research interests continue to focus on immune system activation associated with HIV infection, especially as it might contribute to the development of cancers of immune cells. We (Drs. Breen, Martínez-Maza, Detels, and others) are preparing to publish a MACS-wide study of immune system proteins that are associated with activation of B lymphocytes (B cells), which are elevated in the blood of men who develop non-Hodgkin's B cell lymphoma. A new research study is in the planning stages to explore the role of immune system activation and long term HIV infection in another B cell cancer, multiple myeloma. We are also evaluating new technology that expands the number of different immune system molecules that can be detected in a blood sample in a single test.

You may contact Associate Professor Elizabeth Crabb Breen, Ph.D. at: ebreen@mednet.ucla.edu

FROM THE LABORATORY OF DR. OTO MARTINEZ-MAZA

Infection with HIV is known to be associated with an increased risk for the development of several cancers, especially Kaposi's sarcoma (KS) and lymphoma. Our work focuses on developing a better understanding of how HIV infection promotes the development of lymphomas. In other words, we are attempting to better understand the biological changes that are driven by HIV infection, which lead to the development and growth of these cancers.

The MACS provides a matchless opportunity that is rarely available to cancer researchers: the ability to access specimens taken during the several years prior to the clinical diagnosis of cancer. In our current research, we are measuring a variety of biological markers in frozen serum and blood cells collected in pre-lymphoma diagnosis MACS study visits. We have already found that there are marked differences between those MACS participants who went on to develop lymphoma and those who did not. In the future, we will explore additional "biomarkers" for lymphoma, as well as collaborate with clinical colleagues in other studies to determine if these biomarkers can be used clinically as prognostic tools.

If you have any questions, you may contact me at 310-825-2542; or email me at:
omartinez@mednet.ucla.edu

GREETINGS FROM LAGLC

We are sad to say goodbye to Ray Mercado and happy to wish him well in his new career as a teacher in Paris, France.

Eduardo Mercado (no relation to Ray, but what a coincidence!)
LA GLC Study Coordinator

GREETINGS FROM HARBOR-UCLA

MACS/Harbor-UCLA has been on its toes as the MACS Cardiovascular substudy has been well under way throughout the year. This involved many of you coming from the Wilshire, LAGLC and our own Harbor site returning to us after three years. There were a few bumps on the CT road, but hope that most of you had a pleasant experience. We have also been sending results out to your respective sites and, if you haven't received yours, please contact your local MACS coordinator and he/she would be happy to assist you with this matter.

As the CT scans are coming to an end, we have begun the MACS Kidney substudy. The substudy is looking at the effects of HIV and/or HIV medications and its effects on chronic kidney disease. For those MACS guys who see us here at Harbor, please contact Carlos if you would like to know if you are eligible to participate.

You may have heard a new voice while calling our office. It belongs to Lisa Siqueiros! She mostly has

been coordinating the Cardiovascular substudy, but will definitely be more involved with the general MACS study as the follow up phase of the CV substudy becomes less demanding. Our previous coordinator, Carlos Ramos, decided to take a new position at a non-profit organization in Los Angeles assisting in a program for youth. We wish him and Lisa the very best in their new positions.

Carlos Aquino
Harbor-UCLA Study Coordinator

UPDATE ON THE NEUROSPHYCHOLOGICAL STUDY

The neuropsychological (NP) tests taken as part of the MACS visit are designed to evaluate different higher cognitive functions of the brain, such as memory, attention, and motor function. It has been known for a long time that HIV eventually finds its way into the brain, where it can sometimes lead to symptoms such as forgetfulness, decreased attention and coordination, and slower reaction times. HIV infection can also cause a more serious brain disorder called dementia, which involves a loss of function in several areas, such as memory, attention, and problem-solving skills that are severe enough to interfere with everyday functioning. If left untreated, the loss of function associated with HIV dementia can become so severe that the person is not able to drive a car, bathe themselves, or even recognize family members.

Since 1995, when effective HIV medications (HAART therapy) became available, researchers have seen fewer and fewer cases of HIV dementia. The NP tests in the MACS are now important for determining the effects of these HIV medications on the brain and mental functions. For example, researchers have recently found that cognitive declines in HIV-infected persons can be prevented with continued use of HAART therapy. In other words, taking your HIV medications really does help to protect your mental functions! And now that the HIV medications are allowing people to live longer, the NP tests are also useful in determining how HIV infection affects the normal aging process. With increasing age, there are risk factors for cognitive impairment other than HIV, and the NP testing can be helpful to distinguish between age-related causes of cognitive decline versus HIV. [ed. This is one of the many areas in which the contributions of HIV-negative men, as a control group, continue to be important to the research.] Finally, regular NP testing helps researchers identify brain and nerve diseases earlier and more reliably than would be possible through checking a participant's medical records.

Not only are the NP tests important for helping researchers study HIV and brain function, but the tests are also important to the individual participant. In most cases, the NP tests can provide reassurance that there are no signs of mental decline. For participants who have shown cognitive decline in the past, regular NP testing provides a way to monitor further changes in brain function that might signal the need for changes in medical treatments. Researchers have found that the NP tests included in the MACS visit can be used to identify changes in brain functioning as much as 2 years before such changes would be detected by a standard clinical exam. This early detection allows participants to change their medications, or to enroll in experimental clinical treatments specifically targeted at dementia or other brain and nerve diseases.

You may contact Eric Miller for further information at: emiller@ucla.edu

LUNG QUESTIONNAIRE

Smoking-related diseases such as emphysema (also known as chronic obstructive pulmonary disease or COPD) are of particular concern in HIV-positive people. Lung disease resulting from cigarette smoking is associated with worse general health, physical functioning, quality of life, and cognitive functioning in people with HIV. In past studies, people with HIV seemed to develop emphysema more quickly than people without HIV infection and emphysema sometimes occurred even in people who did not smoke. We do not know why this happens and we also do not know the effect of current HIV therapies on the development of emphysema in people with HIV.

Dr. Alison Morris of the University of Pittsburgh and Dr. Eric Kleerup at the University of California, Los Angeles (UCLA) are interested in studying emphysema in HIV+ and HIV- subjects. They are trying to figure out why it occurs and if it can be treated or prevented. Some MACS

participants will have an opportunity to participate in one of several ways. If you have already had a chest CT scan for the MACS cardiovascular study, you could give us permission to look at the lung parts of this scan to determine if you have any emphysema. You could also participate in the full study by coming to UCLA to have lung function testing and a blood draw done. If you have not previously participated in the MACS cardiovascular study, you could come to UCLA to have lung function tests, a blood draw, and a chest CT scan.

This study could help us understand lung disease in people with HIV and how this complication may be treated more effectively and efficiently in the future.

For further information you may contact
Cathy Kessinger at 412-802-8524 or
kessingercj@upmc.edu

NEUROLOGIC COMPLICATIONS OF HIV — WHAT AUTOPSIES HAVE TAUGHT US

The neurologic complications of AIDS and HIV infection are among the most devastating seen in this illness. They can involve the central nervous system (including the brain and spinal cord) as well as the peripheral nerves (producing a disabling neuropathy). About three years after the first cases of AIDS were reported in the *New England Journal of Medicine*, details began to emerge of severe neurologic disability in many AIDS patients, even when they did not have an apparent opportunistic infection. These unfortunate individuals developed personality changes and '*cognitive impairment*', sometimes even dementia, usually a tipoff that there is widespread disease within the brain. It became clear, when brains of affected individuals were examined at autopsy, that there was widespread chronic inflammation in the brain; by the mid 1980s it was proven that HIV could infect the central nervous system to cause this inflammation. The resulting syndrome was described by the term "*AIDS dementia complex*" (ADC).

A few words about the '*autopsy*', a procedure that was pivotal in characterizing structural changes in the brain associated with ADC. Autopsies are performed much less commonly than they were 25 or 30 years ago, largely because there is an erroneous view in the medical community that most abnormalities (described as '*lesions*') can be detected by high resolution imaging modalities such as CT, MRI and PET scanners. Most autopsies these days are done at academic medical centers, relatively few at smaller community hospitals. Many clinical and epidemiologic studies that involve long-term subject follow-up (of which the MACS is a prime example) include an autopsy component. The autopsy is regarded as the "*final examination*" of the patient. In the early days of the MACS, when effective treatments for HIV infection were scarce and often ineffective, many autopsies were performed on study participants. Because of effective treatments for HIV infection in the HAART (highly active anti-retroviral therapy) era, these days we (thankfully!!) perform relatively few autopsies on MACS participants.

Very important data have emerged from autopsy studies of AIDS and HIV infection. In 1987 two important studies emerged from UCLA based upon the study of autopsy tissues. One was an investigation of peripheral nerve specimens sampled at the time of autopsy in AIDS patients, including many MACS participants. Carried out by Dr. Vei Mah in my laboratory, it was among the first to conclusively show that structural abnormalities of peripheral nerve are common in patients with HIV infection. In 1987 we also performed an autopsy on an HIV-infected individual who had an unusual progressive neurologic syndrome. Portions of the brain and cerebrospinal fluid obtained at the time of autopsy were further studied in the laboratory of Dr. Irvin Chen, now Director of the UCLA AIDS Institute. His research group characterized the unique features of the virus strain that had caused this man's severe neurologic disability. This strain of the virus has since been widely used throughout the world to study the neurobiology of HIV infection.

We now recognize that HIV-infected individuals can have a variety of neurologic abnormalities, some caused by opportunistic infections, some by CNS lymphomas, and some by direct HIV infection of the brain and spinal cord. The term ADC is no longer used to describe the syndrome that results from HIV colonization of the brain, having been replaced by "*HIV-associated neurocognitive disorders*", abbreviated as HAND. As well, we now recognize that a distinctive pathology of the spinal cord can result from HIV infection—this is

described as "*vacuolar myelopathy of AIDS*" and can lead to paraplegia (paralysis of the legs).

Is there more to be learned from performing autopsies on individuals who die *with* (though not necessarily *of*) HIV infection? The answer is '*definitely YES*'. We now recognize that HIV-infected people may be uniquely susceptible to aging changes that affect the brain. There is now considerable interest, for example, on whether HIV-infected subjects are at increased risk for developing Alzheimer disease changes in the brain. A small subset of HIV-infected individuals who respond well to therapy, and undergo reconstitution of a failing immune system, are also at risk for IRIS (immune reconstitution inflammatory syndrome), which produces unique inflammatory changes in the brain and other organs.

The goal of all individuals who work on HIV and AIDS is to put themselves out of business! We look forward to a day when HIV infection will be treatable using simple medications without significant side effects. Until then, studies of tissues from subjects with HIV infection have much to teach us.

Harry V. Vinters, M.D. hvinters@mednet.ucla.edu

AUTOPSY PROGRAM UPDATE

Although the LA Men's Study hasn't been advertising this much lately, the Autopsy Program is still enrolling new participants and re-enrolling past participants. A separate consent form outlines the specifics of the program, and this consent form must be periodically updated to stay in effect. The goal of this protocol is to acquire information that can only be obtained through post mortem (after death) collection and examination of tissues. Briefly, participants are asked to provide detailed contact information for next of kin or others who would assist the Study with the timely transport of the participant's remains to UCLA, where the autopsies are performed. Following the autopsy, the participant's remains are transported to Cedar Hill Mortuary in Los Angeles, or another mortuary in the Los Angeles metropolitan area chosen by the participant's next of kin. The Study will pay to have a simple cremation performed at Cedar Hill Mortuary. If another mortuary is chosen, the Study will pay the amount charged by Cedar Hill Mortuary ($725).

If you have any questions about this program, or think that your consent form is out of date, please contact Max Hechter at hechter@ucla.edu or 310-825-1073. He'll be able to respond to questions or concerns you may have about this program.

MACS PUBLICATIONS

Research papers to which you have contributed through your participation in the MACS can be found at: www.statepi.jhsph.edu/macs/macs.html

CHARLIE ROSE

For an enlightening, engrossing and informative panel discussion on AIDS research and its advances, go to:

http://www.charlierose.com/shows/2007/07/24/1/the-cahrlies-rose-science-series-aids.

You can watch the program on-line.

GLOMERULAR FILTRATION RATE (GFR) SUBSTUDY

A kidney function substudy is just beginning. 175 participants from the Los Angeles site will be asked to undergo a test to measure their "glomerular filtration rate", or GFR. This test is a good indicator of kidney function. The main goal of this study is to determine whether HIV infection and treatment for it are risk factors for decline in kidney function. In order to determine if there is a decline, participants will be asked to have the test performed now (a baseline measurement) and then again three years later.

ANAL SWAB SUBSTUDY

Risk factors for anal cancers will be studied in a new substudy being planned.

READY TO COMMIT FOR ANOTHER FIVE YEARS?

It looks certain that our study will be extended through March 2014. Talk about growing old together!

SOME OF THE CONTRIBUTIONS OF THE LAMS/MACS

The information obtained through the men of the MACS has contributed, and will continue to contribute, to our understanding of the processes involved in HIV infection and AIDS, and will lead to strategies to prevent infection of humans by HIV and to strategies/treatments to control the progression and impact of HIV infection.

A partial list of contributions includes:

Identification of the risk factors among men who have sex with men for becoming infected with HIV, providing the basis for behavioral intervention strategies

Documenting the role of recreational drugs on risk behaviors for HIV infection

Documenting changes in the immune system in response to HIV infection

Documenting the natural history of HIV infection, including the average incubation period from date of infection to date of AIDS diagnosis, important information for clinical management and identifying molecular correlates of progression

Documenting the negative impact of concurrent infection with other infectious disease agents on the progression of HIV disease

Demonstrating that onset of cognitive impairment associated with HIV did not usually begin until 6 to 12 months before AIDS diagnosis and is concurrent with onset of rapid immunologic decline

Identification and characterization of key subgroups of men:

- Men resistant to HIV infection (key for developing an innovative "vaccine")
- Long-term non-progressors, men who have successfully coped immunologically with HIV (key for identifying immunologic, virologic and genetic factors associated with coping successfully with HIV)
- Long-term survivors with very low levels of CD4 cells, suggesting the role of non-adaptive (innate, non-specific) immune responses in control of viral replication

Revealing the importance of cell activation in progression of HIV infection (important in developing strategies for long-term survival)

Identifying immunologic and virologic precursors or predictors of HIV malignancies, including lymphoma and Kaposi's sarcoma

Contributed to the discovery of HHV-8 as the causative agent of Kaposi's sarcoma

Identifying that HIV viral load can be used to predict subsequent progression of disease and successful treatment

Demonstrating the public health effectiveness of HAART, its effectiveness outside of a clinical trial

Identifying viral load and CD4 levels at which to initiate treatment

Documenting the effect of HIV infection and anti-retroviral treatment on premature biologic aging and function

Demonstrating that HAART suppression of HIV viral load reduces cognitive (thinking and memory) decline and neurologic impairment

Determining the effectiveness of HAART in preventing AIDS and delaying progression of HIV

Demonstrating the impact of HAART on reducing incidence of lymphoma and increasing survival after diagnosis

Identifying metabolic, cardiovascular and renal complications of HIV infection and treatment

Identification of genetic factors influencing susceptibility to HIV infection (e.g. CCR5), the immune response to HIV infection, response to antiretroviral therapy, and the likelihood of developing complications from HAART

The MACS was cited recently by *Science*, a leading research journal, as one of the three most cost-effective studies of HIV/AIDS.

We cannot overemphasize the key role of the men of the MACS in allowing us to make these scientific advances. Their loyalty and determination is absolutely essential to the success of the MACS!