Spring 1999

Discovery

The Newsletter of the Institute of Human Virology

FROM LABORATORY TO CLINIC

ROBERT C. GALLO, M.D.
Director of the Institute

Message From the Director

The IHV, Viruses, and Cancer

There is an increasing connection made in basic research between viruses and cancer. IHV faculty are at the forefront of this research today as this issue of *Discovery* describes. From AIDS-associated cancer to cervical cancer, the Institute's streamlined approach allows our researchers to expedite research from the laboratory to the patient.

In collaboration with the University of Maryland Medical System's Greenebaum Cancer Center, the Institute has created a Viral Carcinogenesis Program to this effect. We are trying to understand the mechanisms by which viruses cause tumors and ultimately improve treatment in virus-associated malignancies.

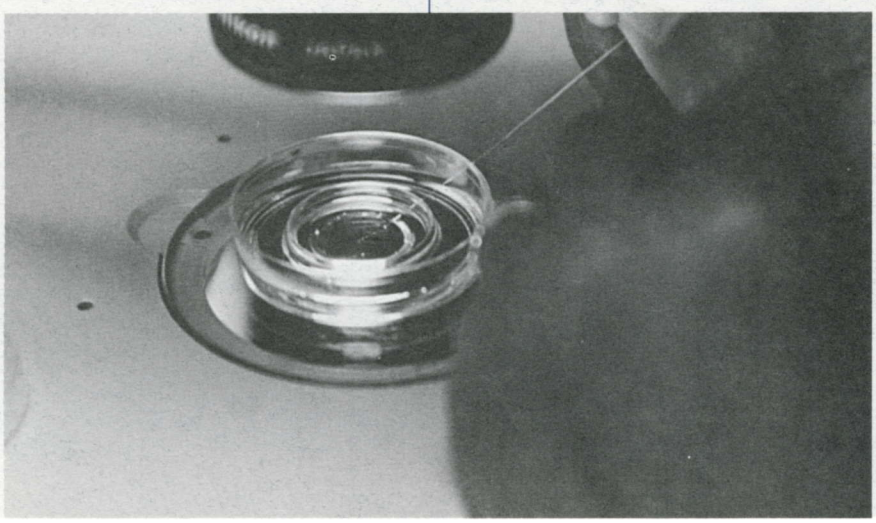
More specifically, the goal is to conduct and analyze innovative clinical trials of antiviral strategies designed from findings generated in the laboratory for the treatment of several cancers whose pathogenesis may be associated with viral factors. In keeping with our mission, the object is to then take observations generated by clinical trials back to the lab for continuing dissection of pathogenic mechanisms and drug development.

The following pages describe some of our specific research areas within the Viral Carcinogenesis Program:

• It has been established that human herpes virus 8 is necessary for Kaposi's sarcoma, a skin-cancer associated with HIV. But the contribution of HHV8 to the pathogenesis of KS is not yet understood. Researchers in the Basic Science Division are approaching this challenge from a few different directions.

• Rates of adult T-cell leukemia (ATL), a blood and lymph gland cancer, are rising in the Caribbean and proof that it stems from a retrovirus (HTLV-1) positions Institute researchers perfectly to search for a cure because of our early history in the field. The blood test I and my co-workers designed at the Laboratory of Tumor and Cell Biology at the National Cancer Institute is the same test used to suppress HTLV-1 infection in the United States. Epidemiologist Farley Cleghorn is working against the clock to implement use of the test in the Caribbean.

• David Oldach of the IHV and the University of Maryland School of Medicine is conducting research on hepatitis C virus—a virus that can lead to liver disease. Currently scientists are unable to grow HCV *in vitro*, which is a major hurdle in this research arena. Oldach is working to understand why the cells die in order to hopefully counter the phenomenon and thus give the field the development that it needs. ▼



inside:

What Causes Kaposi's Sarcoma?

Researchers Have the Suspects Lined Up and Are Interrogating With Force

If any disorder has people scratching their heads most at the IHV, it's Kaposi's sarcoma (KS), a disease that afflicts ten percent of HIV-1-infected individuals and whose hallmark is purplish-red skin patches. These lesions stem from overproduction of faulty blood vessels.

"Kaposi's is a fascinating tumor that has many mysteries to it," said Robert Gallo, Director of the IHV. As he points out, KS wears many hats—it sometimes has all the features of an invasive cancer, but more often resembles a milder growth disorder. And unlike most tumors in which one cell type predominates, KS tumors are comprised of a combination of cell types—predominantly the cells that line blood vessels and various white blood cells.

KS often only surfaces in people with suppressed immune systems, yet for some perplexing reason, it also crops up in elderly Jewish men of Slavic origin, in elderly Greek or Italian men, and in children and adults of both sexes in African countries that hover around the equator. "What makes this so fascinating," said Gallo, "is what do all these groups have in common?"

A common feature among KS risk groups could point to a common cause. But the only thing shared by this motley crew of KS patients is a recently discovered herpes virus called HHV8 that is perplexing in its own right. Although HHV8 is thought to afflict as many ten percent of all people worldwide, a much smaller percentage actually develops KS, so clearly HHV8 alone is not enough to cause KS. In addition, in KS cells kept in culture the virus mysteriously disappears, even though the cells continue to resemble a KS tumor. And HIV-1-infected individuals are as much as 50,000 times more likely to develop KS than those not infected with HIV—a dramatic jump in susceptibility. "Why does HIV make KS enormously take off?" asks Gallo. "If it's because of immune deficiency, why not other tumors—why this particular one?"

To help solve that and other mysteries surrounding KS, a number of IHV investigators are researching the disorder, including Sandra Colombini, who is studying how various white blood cells and their growth factors may foster KS, and Felipe Samaniego and Marvin Reitz, who are exploring the genes and proteins of HHV8 and HIV that may play a role in causing the disorder. The findings of these researchers suggest KS could stem from a virally induced persistent inflammation of the blood vessels that leads to their excessive and abnormal growth, and eventually to the development of a malignant tumor.

The fundamental findings IHV researchers are generating on KS are likely to have a ripple effect in the cancer field at large, especially considering KS is a disorder characterized by excessive proliferation of blood vessels—something that all solid tumors need to grow and prosper. If researchers uncover what causes that excessive growth of blood vessels and what compounds stop it, those same compounds might be used to treat breast or colon cancer cells, for example. Indeed, compounds discovered by Gallo and the IHV's Joseph Bryant and Yanto Lunardi-Iskandar, while working on a KS animal model, have already been shown to markedly shrink KS lesions in patients and restrict the growth of other kinds of cancers. (See Summer 1998 *Discovery*.)

Sandra Colombini studies the connection between cytokines and KS.

Likely Suspects

The IHV's story of KS research has the flavor of a who-done-it mystery—a number of likely biochemical suspects for causing KS have been pinpointed, but which of these will be definitively shown to play a starring role in causing the disorder remains to be seen.

Colombini, for example, is highly suspicious of compounds known as inflammatory cytokines. These molecules give off homing and "divide and conquer" signals to white blood cells to activate them

(Continued on next page)

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Photography: Ann Grillo, pgs. 2, 3, 4, 5, 6, 8

(continued from previous page)

at a particular site in the body. Inflammatory cytokines can also trigger the sprouting of blood vessels. Colombini discovered inflammatory cytokines are present in high amounts in KS tumors and that they can boost the number of HHV8 viral particles present in white blood cells, which she has shown are the main cells to harbor HHV8. She is currently exploring which cytokines are important in KS and which cells they can act upon.

Clues to what may be triggering such large-scale production of inflammatory cytokines are being provided by Samaniego, who is exploring how a protein produced by HIV-1, called Tat, might team up with HHV8 to foster KS. He has shown that Tat stimulates the production of inflammatory cytokines and boosts the number of copies of HHV8 virus particles in cell cultures. He also has experimental evidence that this protein can flip on the cellular switch in endothelial cells that is frequently used to trigger growth of new blood vessels.

Samaniego also suspects that an HHV8 gene, called K1, is pivotal in causing KS tumors. This gene's protein product mimics the receptor that activates certain white blood cells. Samaniego has a hunch that K1 triggers the proliferation of white blood cells. These cells then give off inflammatory cytokines that boost production of HHV8 and prompt blood vessels to sprout at the KS tumor site. He has shown that when you add K1 to cultures of the cells that line blood vessels, these human endothelial cells proliferate more. He's now assessing what happens when the K1 gene is put into mice.

Meanwhile, Reitz has uncovered about six other genes in HHV8 that are highly suspect because they govern cell growth or death—processes that when set awry trigger KS and other tumors. "One defense we have against a virus is to make the cells infected with the virus die," said Reitz, and as a way of fighting back "a number of HHV8's genes are designed to keep cells from dying."

Another HHV8 gene prompts cells to divide, while several other genes put out proteins that resemble chemokines—messenger molecules generated by the immune system to draw white blood cells to sites of infection or injury. These white blood cells can not only harbor HHV8, but can also generate inflammatory cytokines leading once again to more blood vessel formation. Some of HHV8's chemokines have been shown by others to stimulate blood vessel growth in animals. Reitz has also uncovered an HHV8 gene that resembles an inflammatory cytokine, called Interleukin 6.

"I think these genes are important players in KS," said Reitz, "but thinking they're so and knowing they're so are two different things." To help assess the role these genes might play in KS, Reitz is using genetic engineering techniques to slip the individual genes into mice to see what effects they have in the animals. Results from these experiments are expected over the next year or so.

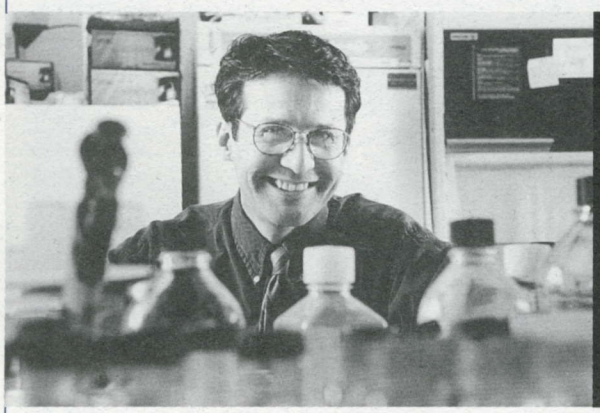
Clearer Picture

When all these findings are pulled together, a clearer picture of what might cause KS—at least in HIV-infected individuals—begins to emerge. This scenario may be possible, for example: John Doe, who is infected with both HIV-1 and HHV8, cuts himself while shaving. This minor injury draws HHV8-infected white blood cells to the site. Once there, the excess of inflammatory cytokines prompted by HIV-1, HHV8, or by the large numbers of white blood cells induced by these viruses, fosters the production of blood vessels. The cytokines also enable HHV8 to flourish and to possibly infect the cells lining these blood vessels. At this point a telltale reddish-purple KS lesion may surface on John Doe's face. Eventually, enough HHV8 genes that stimulate blood vessel formation and govern cell death or division may be activated to trigger a full-blown malignant tumor to develop. Now the KS lesion may become a deadly invasive cancer.

"All these factors are likely to be important," said Samaniego. "It may not be a simple answer—like one gene gets turned on and then you get KS. You need other genes to keep the virus alive and dividing, and to stimulate white blood cells. But you have to start somewhere and we take things one piece at a time and test them."

The findings are just beginning to solve some of the mysteries surrounding KS. But Samaniego notes, "the attraction of the fact that HHV8 causes almost all KS tumors is there's so many aspects to this virus that the next hundred researchers could work on this same virus and come up with different properties, some of which will contribute to the promotion of KS."

In other words, researchers may be scratching their heads about KS for many years to come... ▼



Felipe Samaniego of the IHV and the Greenebaum Cancer Center, who holds an appointment at the University of Maryland School of Medicine, works on his hunch that an HHV8 gene is pivotal in making Kaposi's sarcoma tumors.

Secchiero Works to Pinpoint Viral Cause of Multiple Sclerosis

Researcher Sees Promising Link Between MS and Herpes Virus

In many ways, the crippling nervous system disorder multiple sclerosis (MS) behaves like a disease caused by a virus: there are geographic hotspots where it is particularly prevalent; moves to or from those areas can influence a person's risk of developing MS; and the disorder is strikingly similar to those caused by certain viral infections in animals or humans. For much of this century, consequently, researchers have tried to pinpoint the virus that causes MS. Based on the pattern of MS infection that is seen in people, such a virus would commonly infect children, persist in the body after infection subsides, and target cells of both the nervous and immune system.

"This study keeps alive the possibility that HHV-6 is linked to Multiple Sclerosis and suggests that it's time to move on that." —Paola Secchiero, Division of Basic Science

Although several viruses have met those criteria and been suggested as causes for MS, none have yet to hold up under scrutiny. A new contender that is showing promise, however, is the herpes virus HHV-6, which causes childhood roseola. Paola Secchiero of the IHV's Division of Basic Science and Steven Jacobson of the National Institute of Neurological Disorders and Stroke have shown that people with relapsing-remitting MS are much more likely to have blood IgM antibodies for HHV-6 than normal individuals. The researchers were also able to detect the virus in the serum samples taken from some MS patients, yet unable to find it in normal individuals.

Once an initial infection with HHV-6 subsides, the virus persists in an inactive state in a person's cells. It is intriguing, consequently, that some of the same factors likely to prompt HHV-6 to become active again, such as stress and infection with another agent, are also linked to MS flare-ups. The researchers are currently assessing if the presence of HHV-6 DNA in serum and HHV-6 IgM antibody levels correlate with a worsening of MS symptoms.

Paola Secchiero sees significant similarities between the disorder and the virus.

Although Secchiero and Jacobson's findings support previous findings by others that linked MS to HHV-6, more evidence is needed before HHV-6 moves definitively from the status of innocent bystander to prime suspect in the cause of MS. As Secchiero notes, "This study keeps alive the possibility that HHV-6 is linked to MS and suggests that it's time to move on that." ▼

Retroviral Leukemia Studied in the Caribbean

IHV is Making Headway Against Viral Carcinogenesis from Basic Research to Public Policy

The surprising discovery at the turn of the century that an agent later shown to be a retrovirus caused cancer in chickens launched a search for a viral cause of human cancers. Eventually, animal models linked these agents to mammalian cancers and fundamental molecular research revealed the first oncogenes and the enzyme, reverse transcriptase, needed to translate the RNA of the virus to DNA for which Howard Temin and David Baltimore received the Nobel Prize.

However, there was great skepticism in 1979 when Robert Gallo reported the discovery of a human retrovirus called human T-cell leukemia virus type I (HTLV-I). In fact Gallo's sentinel paper was rejected by the *Journal of Virology* (Gallo has the rejection letter framed in his office) and published in the *Proceedings of the National Academy of Sciences.* His discovery opened the field of human retrovirology and the door for the subsequent discovery of a closely related virus, HTLV-II.

William Blattner, Director of the Division of Epidemiology and Prevention, played a key role in scientific detective work which helped link HTLV-I virus to a form of human leukemia/lymphoma (cancer of the blood/lymph glands) called adult T-cell leukemia (ATL). And nearly twenty years later, HTLV-1 has been definitively shown to cause ATL by several researchers including Blattner and his IHV colleague Farley Cleghorn.

Along with Courtenay Bartholomew of the University of West Indies School of Medicine in Trinidad, Blattner and Cleghorn established that HTLV-1 is particularly prevalent in the Caribbean,

(Continued on page 8)

Developing the Holy Grail:

Investigator Focuses on Overcoming Major Obstacle in Hepatitis C Virus Research

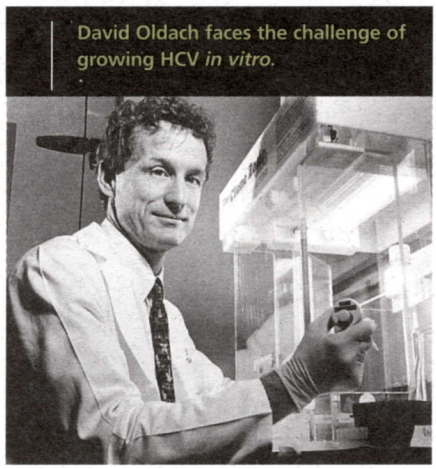
When you ask David Oldach, of the IHV's Clinical Research Division and the University of Maryland School of Medicine what motivates him to spend his time doing painstaking research on hepatitis C virus (HCV), he cites the enormous burden that has been attributed to this virus. "Hepatitis is a dreadful debilitating disease," he said.

Although vaccines and blood screening have substantially lowered the incidence of hepatitis A and B, greater than four million Americans are infected with HCV. HCV infection is chronic in most individuals, among them the majority will suffer little if at all as a result of the disease. However, up to 25 percent may develop cirrhosis, leading in some to end-stage liver disease and/or hematoma. HCV infection is now the leading cause of liver disease resulting in transplantation in this country.

A major stumbling block to making progress in the fight against HCV is that scientists have not been able to induce cultured liver cells to replicate HCV consistently or at high copy numbers. Consequently, insufficient quantities of virus are available for use in research on drug and vaccine development. Oldach and colleagues, however, are exploring a number of novel avenues for countering that problem. "We're trying to make tools and the one tool that's absolutely needed is a method for growing HCV *in vitro*. The real home run will be making a system where the virus can grow robustly."

Oldach and colleagues are pursuing a multi-pronged attack to develop such a system, which he calls the Holy Grail of HCV research. In collaboration with a Baltimore biotech firm, they will use human cells from livers that were rejected for transplants to assess what compounds boost their ability to be infected and produce large quantities of HCV.

But these cells only last two weeks before they die unless they are tinkered with in the lab so they can be grown in culture. Once they achieve the ability to maintain themselves indefinitely in culture, however, they lose their ability to be infected with HCV. To get around this catch-22, Oldach is taking biochemical snapshots before and after he changes the cells from being ordinary liver cells to those that can be grown in culture. He hopes to find differences indicating which compounds are needed to restore the susceptibility of cultured liver cells to HCV.



David Oldach faces the challenge of growing HCV *in vitro*.

Because mice are not susceptible to HCV infection, Oldach is also transplanting human liver cells into specialized strains of mice with hampered immune systems that are unable to reject the transplanted cells. Some strains to be examined are genetically programmed to destroy their own liver cells as they mature, thus creating a potentially more available niche for transplanted human cells. Currently humans, chimpanzees, and possibly tree shrews are the only species known to support HCV infection, but each are too expensive to use for drug screening or vaccine research. An HCV mouse model consequently, would be a valuable addition.

Although these research projects have just begun, results so far are encouraging, Oldach says—and he is anxious to get back into the lab to get more. ▼

Clinical Researcher Gently Battles to Reverse Cancerous Cervical Lesions

Although fairy tales and Greek myths claim it can't be done, Priscilla Furth is trying to reverse fate. Not the fate of storybook characters, but rather the fate of a small cadre of cells destined to become cervical cancer.

Detected on a Pap smear, these cells show several telltale signs that they are on the pathway to malignancy. Most of these pre-malignant groups of cells, or lesions, will revert back to being normal. The current way of dealing with them, consequently, is to take a wait-and-see approach, and if a woman has several abnormal Pap smears in a row, then the lesions are snipped out. The major downside to this approach is that removal of such lesions can hamper a woman's fertility and in some cases completely take away her ability to bear children.

"I think we can treat cervical disease better," said Furth of the IHV's Division of Clinical Care and Research. "If we have a woman whose lesions aren't reverting on their own, maybe we could use drugs to give her cells a little nudge so they become normal again."

To help find out what drugs might reverse cervical pre-malignant lesions, Furth is trying to unravel all the steps that cervical cells take to become cancerous. The vast majority of cervical cancers are initially triggered by infections with certain strains of the human papilloma virus (HPV), for which there is no treatment. "If you are infected with these strains, the time between when you first get infected and the time when you first develop cancer is ten years or longer," notes Furth. "During that time, the virus sits in your cervix causing progressive genetic changes in the cells that it has infected."

Furth is using animal models to identify which of those genetic changes are linked to cancer progression, as well as which ones are reversible. Once she has that information in hand, she plans to try out various drugs to uncover those that can act on the key genetic pathways to prod cervical pre-malignant lesions back to normalcy. By determining which genetic changes are reversible, in addition, Furth hopes to come up with a way to distinguish cervical lesions that have to be removed or destroyed from those that can be treated more gently with drugs. Although she has years of hard work ahead of her until she might be able to realize her goals, Furth is up to the challenge. "There should be a way to medically treat cervical disease—it shouldn't be that impossible," she said.

CERVICAL CANCER

IHV Grants

December, 1998—February, 1999

Laboratory Grants

Priscilla Furth (subcontract to the University of Alabama for participation in an NCI-funded contract), $266,833 for two-year project, *Mouse Models for Chemopreventive Screening.*

George Lewis (Biovector Therapeutics), $430,000 for three-year project, *Development of an HIV Vaccine Using Synthetic Gene Transfer.*

David Oldach (Maryland Dept. of the Environment), $52,500 for equipment as matching support of a three-year EPA-funded project, *ECHOHAB Dinoflagellate Molecular Ecology.*

Clinic Grants

David Oldach (NIH/NIAID), $149,000 for a two-year project, *Needlestick HCV Exposure Among Health Care Workers.*

Robert Redfield (Sarawak Medichem Pharmaceuticals/Quintiles), support for a clinical trial, *Phase 1B Dose Range Study (+)- Calanolide A.*

Training/Other Grants

William Blattner (subcontract to Clinical Trials and Surveys Corporation for participation in an NIAID-funded contract), $950,196 for a five-year project, *Women and Infants Transmission Study Statistical and Clinical Coordinating Center.*

Kathy Flynn, Chief Financial Officer, provides overall financial management and fiscal oversight for the Institute of Human Virology.

Rose Danella (World AIDS Foundation), $70,000 for a one-year project, *HIV/AIDS Risk-Reduction Intervention for Pre-Adolescent and Adolescent Girls in the Bahamas.*

John Lambert (World AIDS Foundation), $80,000 for a two-year project, *Prevention of HIV Perinatal Transmission in Rio and Sao Paulo, Brazil.*

• NCI—National Cancer Institute • NIAID—National Institute of Allergy and Infectious Diseases • NIH—National Institutes of Health

Journal of Human Virology Update

The Literature Selection Committee of the National Library of Medicine recently selected the Journal of Human Virology (JHV) to be indexed and included in the MEDLARS system. The Committee's decision to include the JHV in Index Medicus and MEDLINE attests to its recognition of the high quality of the peer-reviewed manuscripts published in the Journal and their important contribution to scientific literature.

Indexing will begin with Volume 1, Number 1, so all past contributors will have their articles accessible through Index Medicus and MEDLINE and available online in the United States and throughout the world at <http://igm.nlm.nih.gov/>. Citations from articles indexed, the indexing terms, and the English abstract printed in the Journal will be included in the databases and will appear "live" in the next several months.

The editors are most appreciative of the confidence and support shown by so many in the Journal and their willingness to send articles to a non-indexed journal. Now that the Journal is indexed, there is every expectation that these authors will consider publishing another article in the Journal and that others will be encouraged to submit manuscripts for the first time.

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IHV News Briefs

Philanthropic Update

With one quarter remaining in FY 99, indications are that the IHV's philanthropic program will exceed its goals for the year. Having launched its philanthropic program in the summer of 1998, the IHV stands to bring in well over a half million dollars—not bad for an institution that is less than three years old.

IHV Commercialization Moves Forward

The IHV has executed a sponsored research agreement for vaccine testing with BioVector, a French company, and discussions are under way with another European vaccine company to combine a technology developed at the IHV with a technology they now possess. This will include a significant amount of sponsored research at the IHV. Discussions are also moving forward to establish a corporate relationship with a company wishing to develop a test to detect prions.

On a similar note, at the January 21 meeting of the IHV's Board of Advisors, members discussed options regarding commercialization of IHV technology. Board Member Lt. Governor Kathleen Kennedy-Townsend, who plays an expanded role in Maryland economic development, reiterated the value of the IHV's interest in local economics and indicated personal interest in the subject.

Also at the meeting, IHV staff announced development of a proposal to launch and spearhead a minority clinical trials network to begin locally and eventually move nationally.

The next Board meeting will be held April 29, 1999.

Published

Recent IHV Journal Articles

Induction of programmed cell death in Kaposi's sarcoma cells by preparations of human chorionic gonadotropin.
J Natl Cancer Inst 1999 Jan 20;91(2):135-43
Samaniego F, Bryant JL, Liu N, Karp JE, Sabichi AL, Thierry A, Lunardi-Iskandar Y, Gallo RC

Extracellular HIV-1 Tat Protein Up-Regulates the Expression of Surface CXC-Chemokine Receptor 4 in Resting CD4+ T Cells.
J Immunol 1999 Feb 15;162(4):2427-2431
Secchiero P, Zella D, Capitani S, Gallo RC, Zauli G

"Real-Time" polymerase chain reaction.
Gastroenterology 1999 Mar;116(3):763-4
Oldach D

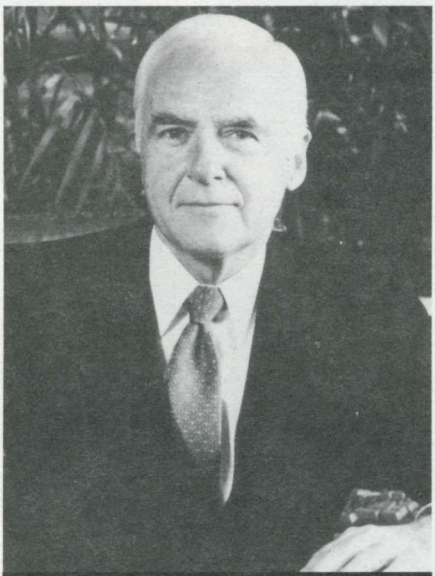
Discovery Facts

from the CDC HIV/STD/TB Prevention News Update

- 3.9 million Americans have chronic liver disease.
- Experts estimate that as many as 24 million Americans are infected with HPV.
- Kaposi's sarcoma is the leading cause of cancer among men and the second leading cause of cancer among women in Uganda, Zambia, and Zimbabwe.

b Gray

Hits the Pavement to



Gray is a Board of Advisors member and an enthusiastic fundraiser for the IHV.

helped others make their mark in history, Gray tries to be there to nudge that potential along. "Sometimes people can get into positions where individually they can make a great difference," he said, "but sometimes they can make a difference simply by helping others make that difference." ▼

Call for Abstracts

1999 International Meeting of the Institute of Human Virology

A Symposium on HIV/AIDS & Cancer Biology

August 28-September 2
Renaissance Harborplace Hotel
Baltimore, Maryland

Abstract Deadline: May 28, 1999

We encourage investigators in the fields of HIV/AIDS or cancer biology to submit abstracts for consideration for presentation. Submission materials are available from our website: www.ihv.org

Early Registration Deadline: June 15, 1999

For complete program information or to obtain registration materials
Phone: 410.706.8614
Fax: 410.706.1952
Email: serody@umbi.umd.edu
Website: www.ihv.org

IHV *in the* NEWS

Time Magazine, March 31, 1998: "Fighting AIDS/Who Discovered the AIDS Virus?" sidebars to Time 100's Scientists and Thinkers special issue.

Baltimore Sun, March 4, 1999: "UM Virology Institute Patents Vaccine System," bactofection opens new field of vaccine delivery.

Baltimore Sun, February 25, 1999: "Pfisteria Found in 5 Rivers," IHV researcher says no signs of serious illness found in 1998.

The Scientist, January 18, 1999: "Cancer and AIDS: A Symbiotic Relationship."

Baltimore Business Journal, December 11, 1998: "Colleges See Profits in Researchers' Ideas," discusses university research and start-up companies.

From the Paul Ehrlich Prize Ceremony, March 14, 1999, excerpts from laudatio by Reinhard Kurth, President, Paul-Ehrlich Institut:

"In viewing the individual and his research, there are evident parallels between Paul Ehrlich and Robert Gallo. Both can be characterized as indefatigable scientists of high renown in their quest for new knowledge and truth, and in their desire to improve the health of human kind...the seminal truths revealed in Professor Gallo's work have already opened successive cascades of new discoveries and practical progress in medicine."

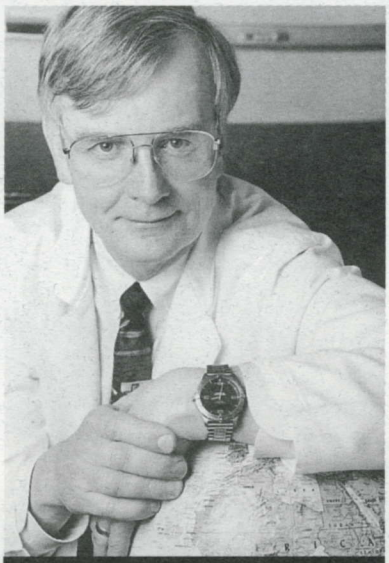
For copies, please contact Jennifer Schorr

THE INSTITUTE OF HUMAN VIROLOGY (IHV) at the University of Maryland was established to create and develop a world-class center of excellence focusing on chronic viral diseases and virally linked cancers. The IHV is dedicated to discovery, research, treatment, and prevention of these diseases and cancers. Its unique structure seeks to connect cohesive, multidisciplinary research and clinical programs so that new treatments are streamlined from discovery to patient. The IHV serves patients locally and the scientific community globally.

Retroviral Leukemia, Cont.

and documented that it causes about half of all cases of non-Hodgkin lymphoma there. The team also helped establish the role of HTLV-I as the cause of a nervous system disorder similar to multiple sclerosis, called Tropical Spastic Paraparesis. Their studies demonstrated that HTLV-I is transmitted through breast milk, blood products, and sexual contact, providing the basis for recommendations from the United States Public Health Service for preventing HTLV-I infection and counseling those infected. Among the Public Health Service's recommendations was the requirement for blood bank screening for HTLV-I employing the HIV blood test developed in Gallo's laboratory.

While HTLV-I is screened in the U.S. blood supply, many countries in the developing world cannot afford such testing.



Blattner is using ATL as a model for unlocking cancer's secrets.

"Eliminating HTLV-1 in the blood supply would be very important to the countries in the Caribbean," said Cleghorn, who is currently working with several Caribbean nations to institute measures that lower the risk of transmitting HTLV-1.

Blattner and Cleghorn are now trying to define the role of HTLV-1 in disease by measuring levels of virus using techniques developed by collaborators at the National Cancer Institute. The research indicates that level of virus may be correlated with disease occurrence. Ultimately, antiviral treatment that lowers viral level may facilitate treatments for this largely fatal disease.

Worldwide, approximately twenty percent of cancers are caused by viruses. "Although ATL is a relatively rare cancer, research on HTLV-1 provides a model for understanding the mechanisms of viral carcinogenesis," says Blattner. "Such insights are vital to unlocking cancer's secrets. And the Institute's expanding viral oncology research program, a partnership with the University of Maryland's Greenebaum Cancer Center, integrates a multidisciplinary approach of basic and epidemiologic research." ▼

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