

B HEPATITIS B

INFORMED

INSIDE

*10th Annual
Princeton Workshop p.3*

*The State of HBV Research
Funding p.5*

*Nucleonics Poised
Against HBV p.7*



*NIH Action Plan for
Liver Disease Research p.8*

Donor List 2004 p.11

Carl's Job p.13



CAUSE FOR A CURE

We are a national non-profit organization dedicated to finding a cure and improving the quality of life for those affected by hepatitis B worldwide.

Hepatitis B Foundation Opens New Research Institute



Concerned about diminishing funds and interest in hepatitis B research, and wanting to take a focused "team-oriented" approach to finding cures for viral hepatitis and liver cancer, the Hepatitis B Foundation (HBF) took a bold step forward. In 2003, the HBF created the *Institute for Hepatitis and Virus Research* (IHVR) - also known as the "Pennsylvania Commonwealth Institute" - which officially opened its doors in August 2004.

As an independent research facility, the IHVR will serve as the research partner of the HBF to fulfill its mission to use discovery science to find therapies and early detection markers for viral hepatitis and liver cancer. Hepatitis B will remain a major focus. Currently, the IHVR encompasses the HBF lab, as well as two other state-of-the-art research labs.

IHVR scientists work as a team, alongside more than 30 Drexel University researchers located at the *Drexel Institute for Biotechnology and Virology Research* (DIBVIR), which is adjacent to the IHVR labs. Since DIBVIR is focused upon virus and liver diseases, this relationship essentially multiplies the IHVR numbers of scientists working on the global problem of hepatitis B and C.

"This is an unusual design for a nonprofit research institute: team oriented, mission focused, and co-localized with a university and biotech facility," explained **Timothy Block, PhD**, president of the HBF, who also serves as the founding director of the IHVR. "We need to think outside of the box in order to stimulate research into novel and effective therapies against hepatitis B."

The innovative programs of the IHVR include a diverse 80,000 compound library and screening program for anti-hepatitis drug discovery, as well as a sophisticated proteomics facility that utilizes two mass spectrometers to examine proteins and other molecules for early detection markers of viral hepatitis and liver cancer from infected individuals. A complementary mission of the IHVR is to nurture biotechnology entrepreneurship in the surrounding region.

"I think hepatitis B is an open book as far as developing new kinds of therapies," said **Andy Cuconati, PhD**, project leader. "Our drug discovery efforts are designed to yield potential drugs with novel underlying mechanisms."

Through powerful partnerships - with the HBF, University of Oxford, Ben Franklin Technology Partners, Drexel Institute, PA Dept. of Health, and others - the IHVR seeks to keep the flame of hepatitis B research alive.

To ensure that the needs of the hepatitis B community are not overlooked, the IHVR is dedicated to the recruitment and training of future researchers, discovering new drugs and therapies, and nurturing biotechnology entrepreneurship.

continued on page 3

**10th Annual
Princeton Workshop
is best ever!**

Read article on page 3



Message from the President

Timothy M. Block, Ph.D.

It Takes a Village

The U.S. National Institutes of Health (NIH) will spend more than \$28 billion in this year. To be sure, this is an enormous amount of money. This amount, however, is divided over tens of thousands of projects, which means each disease gets just a slice of the pie. Indeed, the recently drafted NIH Action Plan for Liver Disease (see page 8) shows that although hepatitis B is still being counted, its slice of the pie is getting smaller.

Having said that, NIH support was integral in the discovery of the hepatitis B vaccine, which is one of the great medical success stories. For people already infected with hepatitis B, however, or facing liver cancer, that past success is of little help. Clearly, more work is needed.

So, how much money should be spent on hepatitis B? That's hard to say since a key breakthrough could come from any one lab. But realistically, good science can't be done alone. It will take a village.

In this issue of *B Informed*, the challenge of maintaining interest in hepatitis B research is a theme. Several of the field's leading scientists express their concern that young people and dollars dedicated to hepatitis B research are becoming scarce (see page 5). Although no one wants to seem mercenary, it would be naive to think that without increased funding, young scientists will choose to pursue this field of study.

With the hepatitis B research community dwindling, the probability of important new discoveries becomes less and less. This is a very worrisome trend that is confirmed by a review of current NIH budget allocations (see page 6).

We have come so far. It would be a shame to drop the ball at this point. The Hepatitis B Foundation and everyone else who cares about this problem must take strong advocacy positions for increasing research dollars. The good news is that we have established a new research institute (see front page), and our current donor list shows that we have many friends who are voting with their wallets! We at the Foundation promise to keep the *Cause for a Cure* alive.



"The Hepatitis B Foundation has been an incredible resource and support for me for the last few years and that is priceless. Knowing that a group of smart people are dedicating their lives to find a cure makes me sleep better at night." *Email 1/18/05*



In The News

Drug Companies Agree to Make Clinical Trial Results Public

Pharmaceutical companies around the world have voluntarily agreed to disclose summary results of completed, industry sponsored clinical trials on free and publicly accessible databases, regardless of outcome, for any medicine approved for marketing in at least one country. For medicines not yet approved or for trials not yet completed, companies agreed that the results should normally be published within one year of approval. Four key international pharmaceutical associations, including the European Federation of Pharmaceutical Industries and Associations, and the Pharmaceutical Research and Manufacturers of America, signed the agreement. *Bmj.com-The General Medical Journal Website 1/15/05.*

Standard Tests Miss Most HBV Infections

Researchers in Canada report that hepatitis B may affect people in the general population at rates higher than previously suspected. Standard hepatitis B tests were performed on 241 dialysis patients, and then a more expensive DNA-based blood test was used. Two patients tested positive for hepatitis B with the standard test, but nine more tested positive on the DNA test. A larger study of about 600 people is now being conducted. *CDC HIV/STD/TB Prevention News Update 1/5/05.*

Caffeine Breath Test Measures Liver Function

Imagine a simple breath test to detect progressive liver disease rather than a risky liver biopsy? An Australian research team has done just that by developing a test that only involves drinking a small quantity of caffeine tagged with a short-lived isotope of carbon, and then blowing into a test tube one hour later. Dr. Gordon Park, a gastroenterologist in Sydney, described the test as "a promising method of assessing the severity of liver disease and monitoring a patient's response to treatment." Caffeine was selected for the test because it is metabolized exclusively through the liver, so the liver function can be measured. "If the liver is not functioning well, metabolism of caffeine is impaired," Parks explained. *Reuters Health 10/11/04.*

Non-Hodgkins Lymphoma Drug May Be Associated with HBV Reactivation

The U.S. Food and Drug Administration (FDA) and the manufacturers of Rituxan therapy for non-Hodgkin's lymphoma have warned health professionals of HBV reactivation along with fulminant hepatitis, hepatic failure, and death in some patients taking this drug. The FDA recommends that patients at high risk of HBV infection be screened before initiation of rituximab therapy. Hepatitis B carriers should be closely monitored for clinical and laboratory signs and symptoms of active HBV infection during rituximab therapy and for several months thereafter. *FDA MedWatch 10/8/04.* [Editor's note: According to HBF medical advisor Dr. Hie-Won Hann, patients with known chronic HBV should be started on antiviral therapy at least two weeks before any immunosuppressive therapy is started in order to prevent HBV reactivation that could lead to liver failure.]

10th Annual Princeton Workshop

HBV Has Us Running in Circles, Covalently Closed Circles, That Is!



10th Annual Princeton Workshop Attendees. (Front L to R): T. London, P. Cote, T. Block, L. Seef, L. Tyrrell, B. Korba; (Middle L to R): D. Standing, S. Xiong, C. Brosgart, S. Wieland, H. Alter, N. Brown, M. Feitelson, K. Laessig, E. Doo, R. Colonno, C. Rogler, C. Pachuk; (Back L to R): W. Mason, S. Locarini, R. Schinazi, A. Mehta, D. Berard, B. Tennant, R. Gish, J. Hoofnagle, M. Bouchard, S. Chandran; (Missing): C. Seeger (Nov. 2004).

The 10th Annual Princeton Workshop, sponsored by the Hepatitis B Foundation (HBF) and held Nov. 4-5, 2004, in Princeton, NJ, took a close look at a small, but troubling topic: hepatitis B viral DNA.

The hepatitis B virus (HBV) chromosome is made of DNA and can exist as a "covalently closed circle" form, abbreviated as "cccDNA." This cccDNA is a different, sturdier form than what is found in the actual virus itself and persists inside liver cells during chronic infection. Even after long term antiviral therapy, cccDNA can be the source of resistance and can lead to "relapses" and "re-establishment"

of infection, even after it is thought that antiviral drugs have worked.

This year's Princeton Workshop was considered to be one of the most stimulating ever, and the international group of 25 leading hepatitis thought leaders and decision makers reached consensus on a key issue: cccDNA has to go.

How to get rid of cccDNA, does interferon reduce cccDNA and how does interferon work, and can drugs be developed that eliminate cccDNA were four of the lead questions the group asked itself this year.

How does a patient's cccDNA level contribute to their responsiveness to therapy? One observation is that regardless of which of the current antiviral therapies are used, there always seems to be only a minority of the treated population that has a sustained response.

In making this point, one must bear in mind that the definition of "responders" varies (such as, Ag conversions, DNA negativity, ALT normalizations, and improvement in histology). However, even allowing for some differences in definition, there seems to be a constant minority of individuals who are predisposed to responding to the various antiviral or immune-mediated therapies currently available. The question then becomes: are these responders the same individuals or are they overlapping groups?

Continued on page 8

Meet the IHVR Scientists Continued from front page

Visit www.ihvr.org



Dr. R. Philips (seated) with J. Krakover in mass-spectrometry lab.

izing in use of mass spectrometry for the study of MHC class I epitopes. Dr. Philip brings more than 20 years of professional scientific experience to the institute.

Mohan Philip, Ph.D., MBA, is Director of Biotechnology and coordinates programs to promote biotechnology entrepreneurship and academic-commercial partnerships. Dr. Philip brings valuable research experience from his successful tenure as an immunologist, pharmaceutical executive, and biotech entrepreneur.

Ramila Philip, Ph.D., Professor, Senior Scientist and Project Leader, Biomarker Discovery, leads the mass spectrometry component and the ELISA development of this project, and serves as scientific manager of the IHVR when the director is unavailable. She is an experienced immunologist special-

Jonathan Krakover, an analytical chemist, assists in the operation of the mass spectrophotometers for the biomarker research program. **Gael Westby** is a research associate who assists in the handling of the compound library and performance of screens for the drug discovery program.

Andy Cuconati, Ph.D., Assistant Professor, Project Leader, Drug Discovery, leads the antiviral drug screening and discovery program at the IHVR. He has 12 years of post-graduate experience in molecular virology and antiviral drug research. Dr. Cuconati joins the project from ViroPharma, where he contributed to a successful effort to discover drugs against potential agents of bioterrorism.



Dr. A. Cuconati (standing) with G. Westby in the drug discovery lab.

HBV Drug Watch

HBV Compounds in Development Winter 2005

FAMILY/DRUG NAME	MECHANISM	COMPANY	WEBSITE	STATUS, USA
INTERFERONS Mimic naturally occurring infection-fighting immune substances produced in the body				
Intron A (Interferon alpha-2b)	Immunomodulator	Schering-Plough, Madison, NJ	www.schering.com	FDA Approved 1991
Pegasys (PegInterferon alfa-2a)	Immunomodulator	Roche, Switzerland	www.roche.com	Phase III / NDA Filed
NUCLEOSIDE ANALOGUES Interfere with the viral DNA polymerase enzyme used for hepatitis B virus reproduction				
Epivir-HBV (Lamivudine)	Inhibits viral DNA polymerase	GlaxoSmithKline, Phila., PA	www.gsk.com	FDA Approved 1998
Hepsera (Adefovir Dipivoxil)	Inhibits viral DNA polymerase	Gilead Sciences, Foster City, CA	www.gilead.com	FDA Approved 2002
Entecavir	Inhibits viral DNA polymerase	Bristol-Myers Squibb, Princeton, NJ	www.bms.com	Phase III / NDA Filed
Emtricitabine (FTC)	Inhibits viral DNA polymerase	Gilead Sciences, Foster City, CA	www.gilead.com	Phase III
Clevudine (L-FMAU)	Inhibits viral DNA polymerase	Bukwang, Seoul, Korea	www.bukwang.co.kr	Phase III, South Korea Phase II, U.S.
Telbivudine (LdT)	Inhibits viral DNA polymerase	Idenix, Cambridge, MA	www.idenix.com	Phase III
NEW Viread (Tenofovir)	Inhibits viral DNA polymerase	Gilead Sciences, Foster City, CA	www.gilead.com	Phase III
Valtorcitabine (monoval LdC)	Inhibits viral DNA polymerase	Idenix, Cambridge, MA	www.idenix.com	Phase II
NEW Amdoxovir (DAPD)	Inhibits viral DNA polymerase	RFS Pharma LLC	under construction	Phase II
ANA 380 (LB80380)	Inhibits viral DNA polymerase	Anadys, San Diego, CA	www.anadyspharma.com	Phase II
Remofovir B (Hepavir B)	Inhibits viral DNA polymerase	Valeant, Costa Mesa, CA	www.valeant.com	Phase II, Europe, USA
Elvucitabine (ACH-126,443)	Inhibits viral DNA polymerase	Achillion New Haven, CT	www.achillion.com	Phase II (Central & Eastern Europe)
RCV (Racivir)	Inhibits viral DNA polymerase	Pharmasset, Tucker, GA	www.pharmasset.com	Phase II, Europe
Pentacept (L-3'-FD4C)	Inhibits viral DNA polymerase	Pharmasset, Tucker, GA	www.pharmasset.com	Preclinical
Robustaflavone (ALS-920)	Inhibits viral DNA polymerase	Advanced Life Sciences, Woodbridge, IL	www.advancedlifesciences.com	Preclinical
NON-NUCLEOSIDE ANTI-VIRALS				
BAM 205	"Small Molecule"	Novelos, Newton, MA	http://novelos.com	Phase II/III China
HepeX-B (XTL-001)	Human monoclonal antibodies	XTL Biopharm, Rehovot, Israel and Cambridge, MA	www.xtlbio.com/	Phase II, Israel & U.S.A. Orphan drug approval in US for liver transplants
UT 231 *Discovered by HBF scientists	Small Molecule	United Therapeutics Silver Spring, MD	www.unither.com	Preclinical HBV (Phase II HCV)
HepBzyme	Nuclease resistant ribozyme	Ribozyme, Boulder, Co	www.rpi.com	Preclinical
Bay 41-4109	Inhibits viral nucleocapsid	Bayer AG, Germany	www.bayer.com	Preclinical
NON-INTERFERON IMMUNE ENHANCERS Boost T-cell infection-fighting immune cells and the body's natural interferon production				
HE2000	Immune Stimulator	Hollis-Eden, San Diego, CA	www.holliseden.com	Phase II, Singapore
Theradigm	Immune Stimulator	Epimmune, San Diego, CA	www.epimmune.com	Phase II
EHT899	Oral Viral Protein	Enzo Biochem, NY, NY	www.enzobio.com	Phase II, Israel
Zadaxin (Thymosin alpha-1)	Immune Stimulator	SciClone, San Mateo, CA	www.sciclone.com	Phase II w/lamivudine Orphan drug approval in US for liver cancer
NEW HBV Core Antigen Vaccine	Immune Stimulator	Microscience, U.K.	www.microscience.com	Phase I
SpecifEx-HepB	Immunological Cell Transfer	CellExSys, Seattle, WA	www.cellexsys.com	Preclinical/Phase I
NEW eRNA Technology	Expressed Interfering RNA	Nucleonics, Horsham, PA	www.nucleonicsinc.com	Preclinical
POST-EXPOSURE AND/OR POST-LIVER TRANSPLANT TREATMENT				
BayHep B	HBV immunoglobulin	Bayer U.S., Pittsburgh, PA	www.bayer.com	FDA Approved 1977
Nabi-HB	HBV immunoglobulin	Nabi, Boca Raton, FL	www.nabi.com	FDA Approved 1999
Anti-hepatitis B	HBV immunoglobulin	Cangene, Ontario, Canada	www.cangene.com	FDA Filing 2001

Sincere thanks to Brent Korba, Ph.D. (Georgetown University Medical Center, Rockville, MD) and Raymond Schinazi, Ph.D. (Emory University Medical School, Atlanta, GA) for their regular review of the HBF Drug Watch Update.

Do Dollars Equal Concern?

The State of HBV Researching Funding

How much money does the U.S. spend on hepatitis B virus (HBV) research? How much should it spend? Both are tough questions to answer, but there is a growing sense in the hepatitis B advocacy community that we may not be getting enough or our fair share.

Since we last visited the question of HBV research funding in our *B Informed* Winter 2000 issue, funding levels for HBV research have remained largely unchanged, while research funding for hepatitis C (HCV) and HIV has increased. Five years later, the gap has widened considerably.

The National Institutes of Health (NIH) budget office places 2005 estimates at \$40 million for HBV research, and \$130 million for HCV. Compare these numbers to the enormous \$2.9 billion for HIV and \$1.6 billion for biodefense agents, and it can be seen how NIH allocations are being prioritized.

"What you're dealing with is flat funding for HBV," said **W. Thomas London, MD**, senior member, Fox Chase Cancer Center, and board member of the Hepatitis B Foundation (HBF). "HBV is perceived to be cured. More people worldwide are infected with it, but it's simply not considered to be an American problem, since most people now get vaccinated for it."

However, HBV remains a serious global health problem with 2 billion people infected and 400 million suffering from chronic HBV infections worldwide. In the U.S., 12 million Americans have been infected and an estimated 1.2 million people are chronically infected.

"[HBV] is something of an epidemic that is flying under the radar, since many people infected with HBV emigrate to the U.S. from other countries," London continued.

"What you're dealing with is flat funding for HBV. [It's] perceived to be cured. More people worldwide are infected with it, but it's simply not considered to be an American problem..." W. Thomas London, MD.

"And so, they are not necessarily diagnosed. Whereas for HCV, many people know someone who is affected, so people in Congress are lobbying for funding because it's very high up on the public radar."

The experts agree that while it's not all about following the money, many scientists gear their research to what is getting funded and to what is on the public radar as important issues in science.

Another problem, posits **Jesse Summers, PhD**, professor of Molecular Genetics, University of New Mexico, is that there are not enough young scientists entering the field. "Of course you have scientists who know of HBV, but the

people who truly know it, many of them are going to be retiring in the next 10 years. I can only think of a couple of people who are in their forties who are primary investigators on it," notes Dr. Summers.

He concludes, "Probably the chief problem is that students are not learning about HBV. They are not being introduced to the field in postdoctoral training in large enough numbers and they are not being encouraged to think of HBV research as a productive career. I think the key is getting the word out that there is still work that needs to be done in this field."

Timothy Block, PhD, HBF president, and professor of Microbiology and Immunology, Drexel University, echoed Summers' concerns. "I'm very worried about the dwindling number of HBV scientists. There are a number of important issues competing for attention in the research arena. But the progress that has been made in HBV research should make the case that this is a problem that can be solved. It's a good investment and an important area where a significant contribution can be made."

"Probably the chief problem is that students are not learning about HBV. I think the key is getting the word out that there is still work that needs to be done in this field." Jesse Summers, PhD.

Unfortunately, there are many emerging diseases and a burgeoning biodefense program that are competing with HBV for both funding and research bandwidth. **William Mason, PhD**, senior member, Fox Chase Cancer Center, notes, "If you look at the NIH database, you see that there is not a whole lot going on in the way of new research funding for HBV - and it seems that, for the new scientists coming up, they are following the funding, which is taking them to other research topics. I think there needs to be more activism at the individual level for HBV. It's really not up there in the face of the people responsible for making the calls on budgeting matters."

Continued on page 6

Fast Fact

Approximately one million people die every year from chronic hepatitis B and its related complications, making it the 10th leading cause of death worldwide.

"I think there needs to be more activism at the individual level for HBV. It's really not up there in the face of the people responsible for making the calls on budgeting matters."
 William Mason, PhD.

While there is a good deal of success to be reported on the vaccination side, the treatment side has been slow to turn up new therapies - a problem that could be blamed on the limited research power in the HBV arena right now.

Anna Lok, MD, director of Clinical Hepatology at the University of Michigan adds, "Yes, we have a vaccine for HBV and yes, there are more options for HBV treatment than there were, say, 10 years ago, but current treatment is really only a stop-gap measure, to suppress symptoms. We need to do better than that, if we really want to go forward. Research is going forward, certainly, but not as quickly as one would like."

London adds, "The perception is that there is a vaccine for HBV, so no further research is needed. We don't have vaccines for HCV or HIV, so these are considered more pressing." Block concurs, "I think there is a sense of complacency in the research community, that there's a vaccine in place, and that we have treatments. However, we have not seen much of an advance in those treatments in the last few years. We need to be doing more."

Block continues, "It is difficult to say how much money is needed to solve the HBV problem. Moreover, since advances may come from other fields, it is even difficult to completely determine which is HBV funding and which is not. As a rule, scientists will be attracted to a field if it is important, interesting, tractionable, and, of course, if it is funded. HBV certainly meets the first three of those criteria."

There is, however, one troubling public health trend that underscores the need for further aggressive research on

HBV - the substantial increase in liver cancer incidence. According to the *Journal of the National Cancer Institute*, most cancers decreased over the 10-year period between 1992 and 2001. Distressingly, the incidence of liver cancer went up.

It is partly for that reason - liver cancer is on the rise, of which 80% of cases are due to HBV - that in 2003 the NIH created the Liver Disease Research Branch to focus and accelerate research on liver disease. Part of its mission was to create an Action Plan for Liver Disease Research, which was just released in January 2005, to address the challenges in the next decade (see page 8). **Jay H. Hoofnagle, MD**, director, NIH Liver Disease Research Branch, explained, "The major focus of this Action Plan is to stimulate translation of basic research findings to practical and effective means of prevention and control of liver diseases, including such important conditions as hepatitis B and C...[and] liver cancer."

The primary challenge for HBV research today is to compete for the same dollars that HCV and HIV are getting. In addition, biodefense is a new funding consideration added since our last report five years ago.

"We have to acknowledge the budget deficit and how that will impact funding," London said. "Right now, funding is flat, but you'll see in the next few years that funding from the NIH is actually going to go down, and that there will be a lot of fighting for a much smaller piece of the pie."

Elizabeth Lipp, science writer from Oreland, PA.

"Yes, we have a vaccine for HBV and yes, there are more options for HBV treatment than there were, say, 10 years ago, but current treatment is really only a stop-gap measure, to suppress symptoms. We need to do better than that, if we really want to go forward." Anna Lok, MD.

Number of Infected Individuals

	HBV	HCV	HIV
Chronically Infected, Worldwide	>350 million	170 million	40 million
Chronically Infected, U.S.	1.2 million	2.7 million	850,000-900,000

Sources: Centers for Disease Control and Prevention and the World Health Organization

Total NIH Funding

	HBV	HCV	HIV	Biodefense
2000 Est.	\$27 million	\$34 million	\$2 Billion	-
2003 Act.	37.2 million	112 million	2.7 Billion	\$370 million
2004 Est.	39 million	118 million	2.8 Billion	>1.3 Billion
2005 Est.	40 million	130 million	2.9 Billion	1.6 Billion

Source: NIH Budget Office, Dec. 2004

Nucleonics Poised To Make Advances Against Hepatitis B

When **Cathy Pachuk, PhD**, and **C. Satishchandran, PhD**, decided to leave Wyeth-Lederle in 2000 after it acquired Apollon, a Malvern-based biotechnology company at which they had been studying DNA vaccines, they had a plan.

While at Apollon, they had made discoveries involving what was called "post-transcriptional gene silencing," or RNA interference (RNAi), a technique to essentially turn off genes. In RNAi, genes are prevented from making certain proteins. They thought the technology had potential for treating human disease, but needed time, effort and resources to be developed.

By chance, they found a kindred spirit in HBF president Timothy Block, PhD, who was director of the then-Jefferson Center for Biomedical Research, which is now the Drexel Institute for Biotechnology and Virological Research (*B Informed*, Fall 2004). He invited the pair of scientists to join the center and discussed continuing their RNAi research with an HBV twist.

Block admits today that at the time, the notion of using gene silencing to treat disease seemed more science fiction than science. Gene silencing was new and had all sorts of technical problems. But Pachuk and Satishchandran had already established a company, Nucleonics, Inc., now in Horsham, PA, in January 2001, by the time they joined the Jefferson Center and became Jefferson Medical College faculty later that year.

"Cathy and Satish had provocative theories on how genes are regulated," Block says. "We were interested in curing HBV and HCV and in nurturing translational research. It seemed a good match."

It was. Today, Nucleonics' goal is to develop RNAi-based therapeutics for diseases, and for now, is focusing on HBV and HCV, says Pachuk, who is the company's vice president for preclinical research. But the company's mission is broader. "We won't be limited to viral disease," she notes. "We're also interested in cancer, autoimmune disease - any disease that can be ameliorated by shutting off genes."

Both Pachuk and Satishchandran, who is the company's senior vice president for research and development, think RNAi will prove to be the best therapeutic bet against HBV.

"Many of the HBV drugs currently on the market are polymerase inhibitors, which can decrease virus amounts to very low levels," notes Satishchandran. "But clinicians have told us that the drugs seemed to have reached a ceiling. When they take away the drugs, the virus comes back." Then there's the problem of drug resistance. While some antivirals

have been tried in combination with other agents, such as interferon, nasty side effects can get in the way.

The Nucleonics technology also reduces viral antigen, something no antiviral currently does, says Pachuk, and is a key to reducing liver inflammation and the development of liver cancer.

RNAi is a natural process; cells use it to turn off genes. Pachuk and Satishchandran use an abbreviated version - short interfering RNA, or siRNA. siRNAs as drugs have huge potential - RNAi was dubbed *Science's Breakthrough of the Year in 2002*. Companies are rushing to make siRNAs, which are synthetic strings of nucleotides that bind to messenger RNA, blocking transcripts of genes from making proteins.

Pachuk and Satishchandran's technique is different. Rather than attempting to get pre-made RNAs into cells to do the job, they are using a DNA vector to produce siRNAs within target cells. That is, this "expressed interfering RNA," or eiRNA, is made by the patient's cells. Once the vector is inside the cell, the cell churns out siRNAs like a factory. In contrast, pre-made siRNA is used up by the cell more quickly, is less stable, and can have toxicity.

Block, who was recently appointed to the scientific advisory board of Nucleonics, is a believer. "This is a kind of designer gene approach," he says, adding that in theory, the technology can target any HBV gene product. He thinks Nucleonics' approach will be "therapeutically successful."

The company has made believers out of investors and the federal government as well. Nucleonics recently received \$50 million from venture capitalists and another \$1.6 million from the National Institute of Allergy and Infectious Disease.

But challenges remain. While the technology has been successful in the laboratory and in mouse HBV studies, difficulties in delivery - getting the interfering RNA sequence into the liver cell - is still a hurdle to overcome.

Still, Nucleonics is preparing to file an investigation of new drug application for chronic HBV with the U.S. Food and Drug Administration later in 2005 - a prelude, it's hoped, to clinical testing.

"No one is in the clinic yet with eiRNA," notes Pachuk. "We anticipate we will be the first."

Steve Benowitz, science writer from Philadelphia, PA.



Drs. Cathy Pachuk (left) and C. Satishchandran are scientific co-founders of Nucleonics, Inc. (Dec. 2004)

There is also a growing consensus that reliance upon eAg status (or conversion) as a milestone of therapy may be too limited. HBV DNA levels (or, perhaps, reduction during therapy) may be a better marker. Ultimately, it will probably be a combination of markers that serves the purpose of prognosis best.

Reduction in cccDNA levels, if they could be determined, might lead to an excellent indicator of favorable outcome. However, detection of cccDNA is very difficult for technical reasons. Perhaps sAg, which is made from the cccDNA template and easily detected in the blood, could be a good surrogate for cccDNA.

In many individuals, reductions in HBV DNA levels can be achieved with antiviral therapy, and the DNA levels will remain low indefinitely - even in the absence of presumably useful immunological activations. What holds the DNA level down? Are there innate cell defenses, some type of cell sensor that does this? The group heard evidence that liver cells harboring HBV are "resistant" (refractory) to re-infection, and that this may be related to the viral envelope proteins.

It is unclear if cccDNA in liver cells can be reduced without harming the cell in which it is housed. cccDNA is difficult to study since it exists, usually, in very low amounts (except in the case of the duck system). There is conflicting evidence about control of cccDNA. Some think its fate is integrally linked to that of the cell in which it is housed (you have to burn the house down to destroy the cccDNA) and others believe there is good data suggesting cytokines or other immune modifiers, factors that influence cell cycle state, can significantly reduce its abundance without harming the cell.

Clearly, this is one of the most important frontiers in HBV research, with tremendous implications for therapy as well as for basic science - since how cells manage small "foreign" DNA (a family to which cccDNA belongs) is a key question in what is now fashionably called "innate host defense from infection."

Can the interferons affect cccDNA stability? When effective, interferons can certainly serve to "turbo charge" the infected individual's immune system, forcing immune cells to take a look at HBV and see it as "foreign." In addition, interferons can apparently work directly on the infected cell, perhaps by influencing HBV capsid stability. Can they take a direct whack at cccDNA? This is controversial.

The new wave of HBV antivirals coming up for testing is generating a great deal of excitement. Although several have a mechanism similar to the currently approved oral HBV drugs, some of the new drugs - entecavir, telbivudine, or perhaps clevudine - are extremely potent, generate little resistance, and may be so potent that they might result in therapeutic reductions in cccDNA. That is, if they can be taken for long enough without generating resistance.

If the approved drugs and the new antivirals coming up can't do the job alone, perhaps combination with another

therapeutic that complements their mechanism of action will do the trick. It will hopefully become realistic to use cytokine or even therapeutic vaccine type approaches that may correct HBV antigen levels, while the antiviral drugs reduce DNA levels.

Finally, perhaps gene silencing holds the most exciting, if uncertain, promise, since it can selectively reduce the level of almost any viral gene product, by simply altering the design of the gene silencer (see page 7). In combination with a drug that controls viral reproduction and another that activates the immune system, a powerful cocktail might be created. Now that is something we could all drink to (non-alcoholic, of course!).

The bottom line for the hepatitis B community is to not give up. We must not become complacent or satisfied with therapeutics that only reach a limited population and may leave the rest as if nothing has ever been done.

NIH Action Plan for Liver Disease Research

On January 5, 2005, the National Institutes of Health (NIH) released its *Action Plan for Liver Disease Research*, a comprehensive ten-year plan aimed at decreasing the burden of liver diseases, which accounts for about 46,000 deaths each year and ranks 9th in overall causes of death in the U.S.

"The major focus of this Action Plan is to stimulate translation of basic research findings into practical and effective means of prevention and control of liver diseases, including such important conditions as hepatitis B and C..." said **Jay Hoofnagle, MD**, founding director of the NIH Liver Disease Research Branch, which initiated the action plan. "Acute and chronic liver disease affects people of all ages, with the greatest burden among minority individuals and persons between the ages of 40 and 60."

A total of 214 specific goals are outlined for reducing the frequency and burden of liver disease, along with an implementation plan and specific steps needed to achieve each goal. Some specific goals for hepatitis B focus on the development of new therapies (i.e. a therapeutic vaccine), and defining the basis for antiviral resistance.

Representatives from 17 NIH institutes and approximately 250 experts in liver disease including researchers, physicians, patients, and non-profit members participated in the development of the Action Plan. **Timothy Block, PhD**, HBF president, and Drexel University professor, brought his research expertise to the NIH planning session in Bethesda, MD, where Dr. Hoofnagle highlighted the *HBV Research Priorities*, identified at the Hepatitis B Foundation's Princeton Workshop in 2000, as important guidelines in establishing the Action Plan for Liver Disease Research.

To download the Action Plan, visit www.niddk.nih.gov (search for "liver action plan").

Foundation at the Forefront

American Gastroenterological Association President Gives Lecture at HBF



Dr. Emmet Keeffe (left) receives the *Distinguished Bruce Witte Lecturer* award from HBF co-founders **Janine and Paul Witte** (Nov. 2004).

There was standing room only to hear **Emmet Keeffe, MD**, president of the American Gastroenterological Association, professor of Medicine and chief of Hepatology at Stanford University Medical Center, speak about "Chronic Hepatitis B: Evolving Treatment Strategies" as the HBF's 5th Annual *Bruce Witte Distinguished Lecturer* on November 30, 2004. Dr. Keeffe is a world renowned liver specialist and lead author of "A Treatment Algorithm for the Management of Chronic Hepatitis B in the U.S." (*B Informed*, Summer 2004).

Major highlights of Dr. Keeffe's excellent overview of hepatitis B treatment strategies included the following: it appears patients who are in the "immune-active" phase will respond best to treatment (for example, they have high DNA and high ALT levels); early liver fibrosis (the stage before cirrhosis) is reversible with antiviral therapy; genotype has not been predictive in lamivudine or adefovir studies; pegylated interferon is on the "fast track" for approval for chronic hepatitis B; entecavir is very potent and looks very promising; and that combination therapy appears to help reduce the risk of viral mutations, but doesn't seem to improve DNA reduction, therefore, insurance companies don't want to pay for two drugs (lamivudine costs about \$150/month and adefovir about \$450/month).

What does the future hold? Dr. Keeffe believes that despite the high cost of combination therapy, it appears to be the key to success; pegylated interferon will make an impact, especially for chronic hepatitis B eAg-negative infections; and that genotypes will play a larger role in tailoring treatment choices in the future.

The *Bruce Witte Distinguished Lecturer* was established by HBF co-founders **Paul and Janine Witte**. Previous Witte Lecturers include **Prof. Raymond Dwek, Dr. Raymond Schinazi, Dr. John Gerin, and Dr. Frank Chisari**.

HBF Testifies at Social Security Hearing on Liver Disease

More than 50 people attended the Social Security Administration (SSA) public hearing on liver disease in Cambridge, MA, on November 17, 2004. The hearing focused specifically on proposed changes in the medical criteria used to evaluate disability claims, such as liver transplantation, liver biopsy, cirrhosis, and other complications, related to chronic liver disease.

Panelists included **Ms. Mollie Conti** (HBF vice president for community outreach), **Dr. Leonard Seef** (NIH), **Ms. Chris Kukka** (hepatitis B advocate), and other prominent clinicians and disability law specialists. Several patients provided compelling personal testimony throughout the hearing as well.

"This hearing was a unique opportunity for the HBF to share our knowledge and deep concern about the enormous problem of hepatitis B in this country with policy leaders at the SSA," said Ms. Conti. "Our presence is vital to ensure that hepatitis B is not forgotten in the national discussion about viral hepatitis."

According to experts at the hearing, an estimated 2.5 million Americans apply for disability each year and 60% are denied. Of those denied, less than 50% will appeal the decision because the process can take up to 24 months. But for those who persist and reapply, almost 70% of those applicants are granted disability benefits.

For more information, visit <http://policy.ssa.gov>.

The HBF was invited to participate in the **THINK B Leadership Conference**, held Nov. 12-14 in New York, NY, and sponsored by the American Liver Foundation. The focus was "Hepatitis B Prevention and Management in Asian Americans." HBF co-founder and senior advisor **Joan Block, RN**, and HBF medical advisor **Hie-Won Hann, MD**, each chaired workshop sessions.



Joan Block (center) with conference co-chairs **Dr. Anna Lok (left)** and **Dr. Eddie Cheung (right)** (Nov. 2004).



The **40th Anniversary Celebration of the US-Japan Co-operative Medical Science Program**, held Dec. 7-10, in Kyoto, Japan, included 40 scientists from each country. The Imperial Crown Prince and Princess of Japan officiated at this historic meeting. HBF president **Timothy Block, PhD**, was invited to give a special presentation on hepatitis B during the conference.

Foundation at the Forefront

Meet Our New Vice President for Institutional Advancement



In October, **Daniel M. Schulster** joined the Hepatitis B Foundation as the new Vice President for Institutional Advancement. He will be responsible for raising funds to support our growing research and outreach programs, and leading the effort to raise the national profile of the foundation and its important mission.

Mr. Schulster brings valuable experience and expertise from both the non-profit world and the for-profit business sector. He started his career in Florida, relocated to California, and finally, settled down in Pennsylvania. His move from the sunshine states to the keystone state has already resulted in good things for the foundation!

Mr. Schulster kicked off the New Year with a strong annual appeal (thank you to everyone who made a donation!) and the launch of our *Benefactor's Society*. In his spare time, Mr. Schulster enjoys life with his wife and three young boys, tennis, music, and good books.



A Donor's Note of Appreciation

"Dear Dan, I would love to be able to contribute millions to the cause if I could do it! Your organization has been a huge help to me and my family over the years. I have taken the B-Informed newsletter with me to doctor's visits so that I could be sure the doctor had the most current information. I am especially happy about the new research effort underway. Please tell all of the researchers that hepatitis B is a very important issue - that young lives are depending on them to persevere and find an effective way to cure the disease."

Email message received 1/13/05

Please Join the HBF's New Benefactor's Society

There is an exciting new fundraising program underway at the Foundation to help support the good work we do through our research and outreach activities. We are proud to announce the creation of our **Benefactor's Society**, a program to raise major funds to advance our mission.

Within the first two months of launching this new program, we have had a generous response from many people nationwide. Today, we invite our readers (and friends) to join as an Individual or Corporate **Sponsor** with an annual gift of at least \$1,000. Annual commitments of \$5,000 or more provides membership to our **President's Circle**, while gifts of \$10,000 and above offer membership in the **Trustees Council**.

This program is a unique opportunity to support the Hepatitis B Foundation and to make a significant impact in advancing our mission. As a member of the *Benefactor's Society*, you can become our partner in finding a cure and improving the quality of life for those affected by hepatitis B worldwide!

All members of our *Benefactor's Society* will be acknowledged prominently throughout the year in various publications and will be honored at our annual Crystal Ball Gala. We hope you will join us and the growing list of members in our Benefactor's Society.

To join, or to request additional information, please email **Dan Schulster at dan@hepb.org or call (215) 489-4900.**

Mr. Charles Sigety Joins the HBF Board of Directors

The HBF Board welcomes **Mr. Charles Sigety**, president and CEO of Sigety Family Businesses. He is a prominent businessman who brings tremendous experience, acumen, and commitment to help advance our mission. Mr. Sigety made a substantial donation and joined the HBF's new *Benefactor's Society* (see article above).



Trained as an attorney, with degrees from Yale, Harvard and Columbia, he is a Baker Scholar, served on various White House Conferences including those on Aging and World Economics, frequent lecturer at numerous universities and colleges, and recipient of the prestigious *Navy Supply Corps Distinguished Alumnus Award*.

Hepatitis B Foundation 2004 Donors' List

Thank you to all of the individuals and organizations that have generously supported the Hepatitis B Foundation through donations, grants, matching gifts, memorials, and attendance at our annual gala celebration and golf tournament.

Thank you also to those who have made in-kind gifts of time and talent this past year. We truly appreciate your generosity in contributing to our *Cause for a Cure!*

The Benefactor's Society

TRUSTEES COUNCIL (≥\$10,000)

Mr. & Mrs. Charles Sigety

PRESIDENT'S CIRCLE (\$5000 - 9999)

Dr. & Mrs. Timothy Block
Elkins Family
Gunst Charitable Trust
Robert and Maria Lin Fund
Mr. & Mrs. Paul & Janine Witte

SPONSORS (\$1000 - 4999)

Mr. & Mrs. Warren Axelrod
Mr. & Mrs. Stanley Broadbent
Mr. & Mrs. Stephen Chang
Ms. Hannah Cohn
Mr. & Mrs. Stephen DeAngelis
Drexel University Health Sciences
Esterly Family Fund of
The Pittsburgh Foundation
Fox Chase Cancer Center
Ms. Dale Kindregan
Mr. Hyun Koo Lee
Mr. John Lyons
Samuel P. Mandell Foundation
Mr. & Mrs. Joel Rosen
Mr. & Mrs. Adrian Simon
The Souder Law Firm
Tulchin Family Foundation
Univest Corporation
W.E. Lahr Company

PATRONS (\$500 - 999)

Mr. & Mrs. Michael Bodisch
Mr. Alan Braverman
Drs. Patrick & Beverlee Ciccone
Composition LLC
Senator & Mrs. Joseph Conti
Prof. Raymond Dwek
Fidelity Investments
Ms. Janet Findley
Mr. & Mrs. Daniel Fox
Mr. & Mrs. Curt Friehs
The Glenmede Trust Company
Mr. Mike Isco
Dr. Emmet Keeffe
Mr. & Mrs. Paul Nelson
Mr. David Schulster
Dr. Christopher Williams
and Ms. Janis Nussbaum

FELLOWS (\$250 - 499)

Ms. Barbara Bailey
Mr. Russel Bechtloff
Mr. Joe Benning and
Ms. Mary Anne McDonald
Blasenheim Family
Ms. Joyce Block
Ms. Barbara Chimicles
Mr. & Mrs. Steven Choen
Mr. Michael Conway
Dr. & Mrs. Joshua Feldstein
Mr. & Mrs. Alan & Irma Freedman
Mr. & Mrs. Robert Frey
Mr. Paul Galvin

Mr. H. McIntyre Gardner
Mr. Douglas Green
Mr. & Mrs. Brian Hillard
Mr. & Mrs. Peter Hoekstra
Ms. Donna Holseth
Mr. John Jennings
Dr. Amy Jessop
Dr. & Mrs. Donald & Kim Jungkind
Dr. & Mrs. Barry Kahn
Ms. Alison Kingsley
Mr. David Lambertsen
Ms. Anna Lee
Mr. Raymond Lee
Mr. & Mrs. Adam B. Levitt
Dr. & Mrs. W. Thomas London
Mr. & Mrs. Robert Loughery
Mr. & Mrs. John Maida
Dr. & Mrs. Anand Mehta
Mr. & Mrs. Shanti Mehta
Mr. Larry Nolt
Mr. & Mrs. Glenn Petterson
Dr. Srinivasa Rao
Mrs. Myra Recchia
Ms. Gail Reinard
Mrs. Jennie Rosen
Senator Robert Tomlinson
Ms. Christine Tourville
Triumph Brewing Co
Mr. Ron & Dr. Vail Unterberger
Dr. Thomas Vernon
Wells Fargo Community Support
Campaign
Mr. Stephen Wong
Ms. Aileen Marie Yu

SUPPORTERS (\$100 - 249)

Mr. & Mrs. William Antheil
Dr. Clement Au
Mr. & Mrs. David Austin
Mr. & Mrs. James Baker
Ms. Susan Bellaire
Dr. & Mrs. Baruch Blumberg
Mr. Michael Carr
Center for Advanced Medical
Education
Young Cha Chong
Mr. & Mrs. Hong Taek Chung
Countrywide Home Loans, Inc.
Ms. Joyce Craft
Mr. David Crane
Mr. & Mrs. Joseph Crilley
Mr. & Mrs. James & Carol Curry
Mr. & Mrs. William & Linda Deeter
Se Jong Ding
Mr. Paul DiVito
Mr. Michael Drago
Mr. & Mrs. Kevin Drake
Ms. Sandra Esner
Mr. Gregory Farkas
Mr. Steven Feiles
Mr. & Mrs. Leonid Feller
Dr. Lawrence Friedman
Mrs. Kathleen Garcia
Mr. & Mrs. Matthew Gesicki
Mr. & Mrs. Carl Giombetti
Dr. & Mrs. Robert Goldberg
Mr. & Mrs. William Goldman
Mr. Jesus Gomez-Navarro

Dr. Joseph Gonnella
Mr. Gregory Gore
Dr. & Mrs. Charles Grezlak
Ms. Terry Grundman
Dr. Baohua Gu
Harleysville Insurance Co.
Mr. Phillip Hasegawa &
Ms. Anne Drouin
Mr. Harry Hicks
Ms. Joyce Huber
Mr. & Mrs. Kevin & Virginia Jameson
Mr. & Mrs. Chris Jarvis
Dr. Margaret Keenan
Sang Joo Kim
Mr. Anthony Klockenbrink
Mr. Jeremy Klopfer
Ms. Karin Koelle
Ms. Theresa Lai
Mr. & Mrs. Peter Lamberts
Mr. & Mrs. Michael Landis
Anh Le
Dr. Manuel Lee
Mr. & Mrs. Wooyoung &
June Ja Lee
Dr. Young Bin Lee
Mr. & Mrs. Abraham Leibson
Yao Hu Liao
Dr. Karen Lindsay
Ms. Beatrice Liu
Mr. Jeffrey Markowitz
Dr. Cynthia Matossian
Ms. Karen McCusker
Mr. & Mrs. Ed Meyers
Ms. Jean Miller
Mountainview Enterprise Inc.
Mr. & Mrs. Stephen Muzekari
Delaware Valley College
Mr. Barth Norton
Mr. Brian O'Connor
Ms. Irene Ong Hai
Ms. Dorothy Orlando
Dr. Catherine Pachuk
Mr. & Mrs. Steve & Candice Pelland
Mr. Edward Peritz
Mr. Del Reddy
Mr. & Mrs. Alan Rosenberg
Mr. & Mrs. Richard Rosenberger
Mr. & Mrs. Ronald Sanderson
Mr. & Mrs. Joe Sanguillano
Dr. C. Satishchandran
Mr. & Mrs. Daniel Schulster
Ms. Kathleen Scullion
Mr. & Mrs. Richard Senker
Mr. James Shapiro
Mr. Thomas Shaw Stiffel
Ms. Nancy Sidun
Mr. Stephen Skoczylas
Mr. Gary Smoot
Mr. Timothy Stack
Ms. Susan Stehman
Mr. Jan H. Steiner
Major Harriet Stenzel
Ms. Jill Tarabar
Mr. & Mrs. William Taylor
Mr. & Mrs. Curtis Thomsen
Ms. Kappy Touhill
Ms. Eva Tsai
Mr. Wayne Tuan

Hepatitis B Foundation 2004 Donors' List

Ms. Sharon Victor
Ms. Kathleen Wallace
Mr. & Mrs. Dietmar Weselin
Dr. David West
Ms. Claire Wilson
Mr. & Mrs. Donald & Helen Wise
Mr. Frank Wiswell
Mr. David Woody
Mr. & Mrs. Douglas Youngers
Mr. & Mrs. Rosendo Yu

FRIENDS (up to \$99)

Ms. Leticia Adams
Dr. Ishola Adeyemo
Mr. Matthew Adlai-gail
Mr. Thomas Aiken
Mr. Charles Akinmade
Mr. Jeffrey Albert
Mr. & Mrs. G. Arnold & Kathy Bardall
Mr. Paul Beck
Mrs. Patricia K. Benham
Ms. Danise Bianchi
Mr. & Mrs. Earl Bierman
Ms. Amy Binks
Mr. Shawn Blank
Mr. & Mrs. Thomas Block
Mr. Anthony Blomert
Mr. & Mrs. George Bondra
Mr. & Mrs. John Dillon Bray
Mr. & Mrs. William Bretzfelder
Mr. & Mrs. Russell Brown
Mr. Leonard Bryant
Ms. Marianne Buzby
Ms. Dorothy Carter
Mr. Garrett Chang
Mr. Hong Chartrand
Mr. Henry Chuang
Mr. & Mrs. William & Rita Clark
Mr. & Mrs. Herman Cler
Mr. & Mrs. Nate Cohler
Mr. Joe Conklin
Mr. & Mrs. James Copp
Ms. Margaret Davey
Mr. & Mrs. Chris David
Mr. Paul Davis
Ms. Yonas Demissie
Mr. Salvatore Digianno
Ms. Bin Ding
Mr. & Mrs. Thien Do
Mr. & Mrs. William Donaldson
Ms. Patricia Donovan
Mr. Barry Durst
Ms. Paulina Essieh
Mr. John Estok
Ms. Shandra Evans
Mr. & Mrs. Allan Fehser
Mr. Allen Fisher
Mr. & Mrs. Frank Follmer
Ms. Susan Gabai
Mr. & Mrs. Matthew Ganis
Mr. Andres Gentry
Mr. Daniel Gerety
Dr. & Mrs. Richard Gesser
Mr. Richard Gittleman
Ms. Anny Gonzalez
Mr. James Granelli
Mr. & Mrs. David Griffith
Mr. & Mrs. Richard Haliburton
Mr. David Harper
Mr. Greg Hatala

Mr. Marc Helman
Mr. & Mrs. Richard Herder
Mr. Thomas Hines
Mr. & Mrs. Michael Horn
Mr. & Mrs. Alfred How
Mr. Paing Huang
Ms. Alice Carter Huston
Ms. Aubrey Huston
Mr. Leonard Hutner
Mr. Joseph Iassogna
Mr. & Mrs. Joseph Iervolino
Ms. Patricia Johnson
Mr. David Johnson
Mr. Barry Josepher
Ms. Sandra Jung
Dr. Alexander Karasev
Mr. & Mrs. Craig Keumpel
Reeran Kim
Mr. Joseph Kim
Ms. Tracy Korman
Mrs. Susan Kressly
Mrs. Helen Kuntz
Mr. Archie Kwan
Mr. Jack Leonard
LFD Family Services
Mr. Athanasio Liakopoulos
Mr. King Liang
Mr. Gary Lin
Mr. & Mrs. Michael Line
Mr. Nicholas Machado
Dr. Robert Maigetter
Menominee Indian Tribe Wisconsin
Mr. & Mrs. Reggie A. & Neema Chong Michaud
Ms. Nancy Middleton
Mr. & Mrs. John Miller
Mr. & Mrs. James Molnar
Mr. Paul Monaghan
Mr. Christopher Morgan
Mr. Frank Murphy
Mr. & Mrs. Joseph Napolitano
Mr. Fred Naslund
Mr. Fai Hung Ng
Mr. Peter Nguyen
Ms. Joan Odonnell
Ms. Debra Olander
Mr. & Mrs. John Oldani
Mr. & Mrs. Donald Page
Ho-Hyun Park
Mr. & Mrs. Yoon Ja Park
Ms. Susan Peck
Mr. John Perez
Mr. & Mrs. Charles Pisano
Mr. Ron Potts
Ms. Carol Prevost
Mr. James Price
Mr. David Profito
Ms. Annabelle Radcliffe-Trenner
Mr. & Mrs. Edward Ravitch
Mr. David Reed
Regency Hualalai Namakua LLC
Ms. Carol Rico
Drs. Mark & Lori Rosolowsky
Mr. Mark Sandifer
Mr. Sal Savioni
Mr. Stephen Schaller
Mr. Leon Schiffer
Mr. Michael Schwartz
Ms. Helene Zucker Seeman
Ms. Anna Sever
Mr. Yeh-Heng Sheng

Ms. Ingrid Sheriff
Phurba Sherpa
Mr. John Sherwin
Mr. & Mrs. Michael Short
Ms. Vicki Shteir-Dunn
Sperling & Slater
Ms. Joan Stack
Ms. Susan Stillinger
Mr. Yi Su
Ms. Kara Sullivan-Cowan
Mr. & Mrs. Bruce Szal
Mrs. Priscilla Taylor
Ms. Judy Taylor
Mr. Robert Thran
Ms. Nancy Tolle
Ms. Idamae Trenner
Mr. Nelson Trenner
Ms. Kathryn Trenner
Mr. & Mrs. Thomas & Jessica Truong
Mr. & Mrs. Harry C. Tse
Mr. C. Theodore Tucker
Mr. Ron Uroda
Mr. Chuck Valley
Mr. Michael Vallone
Ms. Elizabeth Walsh
Rendi Wardhana
Dr. David Weiner
Mr. Greg Winter
World Reach Inc.
Ms. Mary Yee
Mr. Kevin Zhang

CORPORATE CONTRIBUTIONS

Bristol-Myers Squibb
Gilead Sciences, Inc.
GlaxoSmithKline
Idenix
Merck Community Foundation



YOU'RE INVITED !

*Hepatitis B Foundation
Crystal Ball Gala*

Saturday April 30, 2005

The *Distinguished Founders' Award*
will be presented to
*Dr. Bill Stephenson, Vice Provost
and Drexel University*

Fine Dining and Dancing at Occasions, New Hope, PA
The Courtney Colletti Orchestra

For more information, please call 215.489.4900

*We apologize for any errors or omissions in the donor list despite our best efforts to be as accurate as possible.
Please contact us so that we can print any corrections in our next newsletter. Thank you!*



Speaking Personally

Steve Bingham

Co-Owner of the Internet Hepatitis B Information and Support List (HB-L)

Carl's Job

My friend Carl, 51 years, is a salesman who had worked for an Ohio investment company for seven years. He had kept his chronic hepatitis B a secret at work, but the time came when he felt he had to tell his boss about his situation.

Increasing fatigue caused him to miss work occasionally, and his blood test reports indicated that his body had reached an ideal condition to start rigorous treatment. His hepatologist recommended that Carl begin six months of pegylated interferon (Carl's doctor prescribed this "off-label" since peg interferon is only approved in the U.S. for hepatitis C).

Carl went to his supervisor well-prepared to explain how the disease and the treatment might temporarily impact his work. He had even translated his medical situation into a spreadsheet for the meeting, because he knew that businessmen understand spreadsheets.

Two weeks later Carl received a letter of termination from his company. Carl's story illustrates the dilemma we "hepBers" face at work. On one hand, we are under no obligation to tell a potential or current employer about our hepatitis B. In fact, the *Americans with Disabilities Act (ADA)*, signed into law in 1990, makes it crystal clear that employers can't ask about infectious diseases, unless it could pose a risk in the activities expected to occur in one's job.

On the other hand, there are circumstances, such as Carl's, where we decide it is time to disclose our hepatitis B diagnosis. Surprisingly, Carl found out afterward that if he hadn't told his employer about his hepatitis B before he was fired, he may not have been eligible for legal protection.

The lesson being, if there comes a time when you know your performance is going to be affected by either hepatitis B or treatment side effects, then it's time to let your boss know. The only legal protection you have is whether you can show they fired you because of the disease.

The best thing to do if you face job discrimination is to contact your local office of the Equal Employment Opportunity Commission, the federal agency that enforces the ADA. Its local offices are listed at the agency's website at www.eeoc.gov. You can also learn more about the ADA at the federal website www.disability.gov.

My friends have also found the Department of Labor to be helpful at www.dol.gov/esa/whd/fmla, which includes links and telephone numbers for information and advice con-

cerning the Family and Medical Leave Act and other labor laws.

Unfortunately, even if you have a good legal case in your favor, taking your employer to court might not be worth the trouble. Court cases can take years to resolve, and the accompanying stress can be damaging to your health. And who wants to win a job back where the people you work with want to get rid of you?

Carl knew he had a good case, but he decided to settle with his ex-employer out of court. He had quickly found a new job, so money wasn't as much a motivating factor as the emotional blow of suddenly going from "valued employee" to "pariah". But he insisted on one stipulation: that the money from his settlement would be donated directly by his employer to the Hepatitis B Foundation.

Thank you Carl for turning a lemon of a story into lemonade.

Best Wishes, Steve

Hepatitis B Foundation Sponsors the 5th Annual B Informed Conference A Gathering of Friends

July 9 - 10, 2005
Doylestown, PA

The Hepatitis B Foundation and the Hepatitis B Information and Support List invite you to join us for a lively two-day conference focusing on the care and treatment of those living with chronic hepatitis B.

Patients, families and all those concerned about hepatitis B are invited to participate.

Learn from each other and the experts in a relaxed and supportive environment.

For more information, or to register, contact the Hepatitis B Foundation at info@hepb.org or call 215.489.4900.

Visit www.hepb.org to read about our past conferences (select "Patients & Families").

Hepatitis B Foundation HBV Clinical Trials
www.hepb.org/clinicaltrials

National Institutes of Health Clinical Trials
www.clinicaltrials.gov

Centerwatch Clinical Trials
www.centerwatch.com/studies/cat79.html

NEW Entecavir for Chronic HBV: An Early Access Program

The purpose of this research study is to provide entecavir to subjects with chronic hepatitis B infection who have failed or who have demonstrated intolerance of marketed therapies or for those in whom use of these agents is contraindicated and have no other available treatment options. Patients 16 years or older are eligible to apply. Contact: Bristol-Myers Squibb tollfree at 1-866-892-1BMS, ext. 127.

NEW Adefovir Dipivoxil in Children and Adolescents with Chronic Hepatitis B

The purpose of this study is to investigate the efficacy and safety of adefovir for the treatment of chronic hepatitis B in children and adolescents (age 2 to 17 years) compared to placebo following 48 weeks of treatment. Additional goals include - to evaluate the number of eAg and sAg seroconversion following 48 weeks of adefovir or placebo; to evaluate the development of resistance to adefovir; and to evaluate the long-term safety and efficacy in children and adolescents over an additional 4-year follow-up period including assessment of growth and renal function. Study started June 2004 and will enroll approximately 150 individuals. Contact: Anant Jain, Gilead Sciences at 650-522-5523 or ajain@gilead.com.

NEW Comparative Trial of Entecavir versus Adefovir in the Treatment of Chronic Hepatitis B Infection

The purpose of this study is to evaluate antiviral activity and efficacy of entecavir (phase III drug) compared to adefovir (an HBV approved drug) in adults with chronic hepatitis B who have not been treated yet with an antiviral medicine. Contact: Bristol-Myers Squibb tollfree at 1-866-892-1BMS, ext. 150.

NEW Safety of and Immune Response to a HBV Vaccine Given with a Booster (CpG7909 ODN) in HIV Infected and HIV Uninfected People

The purpose of the study is to determine the safety of and immune response to a hepatitis B virus vaccine series given with a boosting agent, CpG7909 oligodeoxynucleotides (ODN), in HIV infected and HIV uninfected individuals who previously failed to develop a response to hepatitis B vaccine. Healthy volunteers accepted, too. Study started Dec. 2004 and will enroll 30 individuals. Study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). Contact: Kathy M. Burgner, BSN, at 216-844-8136 or burgner.kathy@clevelandactu.org, Cleveland AIDS Clinical Trials Unit.

LdT (Telbivudine) versus Lamivudine in Adults with Compensated Chronic Hepatitis B

To evaluate how safe and effective LdT (Telbivudine) is in the treatment of chronic hepatitis B infection in comparison to results for patients taking lamivudine, which is an approved HBV drug. Contact: Barbara Fielman, RN, MS, PNP, at 617-995-9812 or fielman.barbara@idenix.com.

Lamivudine and Adefovir to Treat Chronic Hepatitis B

This NIH study will evaluate the safety and effectiveness of lamivudine plus adefovir versus adefovir alone to treat chronic hepatitis B infection. Candidates may not have received lamivudine treatment in the past 6 months or prior treatment with adefovir and must not be taking other anti-viral treatments for their hepatitis. Contact: NIH Patient Recruitment at 1-800-411-1222 or email prpl@mail.cc.nih.gov

Telbivudine versus Lamivudine in Adults with Decompensated Chronic Hepatitis B and Evidence of Cirrhosis

Idenix Pharmaceuticals is conducting this research study to see if the investigational medication, LdT (Telbivudine), is safe and effective in the treatment of decompensated hepatitis B infection over two years. The results for patients taking LdT will be compared to results for patients taking lamivudine (EpiVir-HBV). Contact: Gloria Dubuc at 617-995-9814 or email dubuc.gloria@idenix.com

Evaluate Efficacy, Safety and PK of Adefovir Dipivoxil Liquid Suspension in Patients with Chronic Hepatitis B

Gilead Sciences is sponsoring a multi-center phase 3, open-label, parallel-group study designed to evaluate the efficacy, safety and pharmacokinetics of adefovir dipivoxil liquid suspension in patients with chronic hepatitis B and varying degrees of renal impairment. Contact: Anant Jain at 650-522-5523 or email ajain@gilead.com

Comparison of Entecavir to Adefovir in Chronic HBV Patients with Hepatic Decompensation

A Phase IIIb comparative study of entecavir vs. adefovir in patients who have chronic hepatitis B and hepatic decompensation for up to 96 weeks. Contact: Bristol-Myers Squibb toll-free at 1-866-892-1BMS.

Prevention of Recurrent HBV After Liver Transplantation

Eligible patients for this study MUST be on a liver transplant waiting list or have already received a liver transplant for hepatitis B. HBIG, EpiVir-HBV and Hepsera will be evaluated. Contact: Doug Armstrong at darms@umich.edu or call 734-936-1712 at the Univ. of Michigan Medical Center.

Pegylated Interferon to Treat Chronic Hepatitis D

This NIH study will evaluate the effects of pegylated interferon, given once weekly, on hepatitis D (HDV) and hepatitis B. HDV is often severe and progressive and only infects people who already have hepatitis B infection. Patients with chronic hepatitis D over 6 years old may be eligible for this study. Patients who improve with treatment may continue therapy long-term. Contact: NIH Patient Recruitment Office at 1-800-411-1222 or email prpl@mail.cc.nih.gov

Resource Roundup



Hepatitis B Foundation

215-489-4900

www.hepb.org

info@hepb.org

Comprehensive website dedicated to hepatitis B. Facts, Drug Watch, clinical trials, liver specialist directory, and responsive email. Includes *Chinese, Vietnamese, Korean, and Spanish Language Chapters*. Subscribe to our free e-newsletter *B News You Can Use*.

American Liver Foundation

1-800-GO-LIVER

www.liverfoundation.org

Information about all liver diseases, including viral hepatitis.

Asian Liver Center at Stanford University

650-725-4837

<http://livercancer.stanford.edu>

Educates people about hepatitis B and liver cancer among Asians and Asian-Americans.

Centers for Disease Control, Hepatitis Division

1-888-443-7232

www.cdc.gov/ncidod/diseases/hepatitis

The national authority for viral hepatitis information.

CDC Hepatitis Immunization Hotline

1-800-232-2522 (English)

www.cdc.gov/nip

1-800-232-0233 (Spanish)

Hepatitis B Research List

To subscribe, send a blank email to:

HBV_Research-on@mail-list.com

A free electronic research list maintained by Sheree Martin.

Hepatitis B Research Archive Website

http://archive.mail-list.com/hbv_research.

Archived research bulletins from the Hepatitis B Research List.

HCV Advocate

www.hcvadvocate.org

HCV website that also includes hepatitis B information.

Hep C Connection

1-800-522-4372

www.hepc-connection.org

Comprehensive information about hepatitis C.

Hepatitis Foundation International

1-800-891-0707

www.hepatitisfoundation.org

Information about viral hepatitis, support groups and research.

HepLink

www.heplink.org

A search engine that gathers viral hepatitis information.

Hepatitis Magazine

1-800-310-7047

www.hepatitismag.com

The only print magazine about hepatitis published bi-monthly.

HepTrec

1-866-HEPTREC

www.heptrec.org

The Delaware Valley Hepatitis Treatment, Research and Education Center (HepTREC) in the greater Philadelphia area.

HIV and Hepatitis Treatment Advocates

www.hivandhepatitis.com

Professional online publication with free e-mail updates.

Immunization Action Coalition

651-647-9009

www.immunize.org

www.vaccineinformation.org

www.hepprograms.org

Comprehensive source of immunization information. The first website is for health professionals, the second is for the general public and the third highlights preventive programs. "IAC Express" and "HEP Express" are free e-mail announcement services.

Memorial Sloan Kettering "About Herbs"

www.mskcc.org/aboutherbs

Scientific information about herbs, their side effects and drug interactions. Maintained by experts at Memorial Sloan Kettering.

Nat'l Center for Complementary and Alternative Medicine

1-888-644-6226

www.nccam.nih.gov

Sponsored by the National Institutes of Health (NIH).

Parents of Kids with Infectious Diseases

1-877-55-PKIDS (toll-free)

www.pkids.org

An excellent resource for parents and professionals.

Internet Support Groups



Hepatitis B Information and Support List

www.hblist.org

To subscribe, send a blank email to:

hepatitis-b-on@mail-list.com

Well-supervised list with useful information and lively exchanges between supportive members. For those with HBV, their caregivers, and anyone interested in or affected by HBV are invited to participate.

HBV Adoption Support List

www.onelist.com/community/hbv-adoption

For adoptive or biological parents of children with HBV.

This is a restricted list to protect the privacy of parents and children, and requires pre-approval by the list owner to join.

New! PKIDs Lists for Children and Teens

www.pkids.org/listserve

Children (8-12 years) and teens (13-19 years) living with hepatitis B or C can now talk with each other on two separate lists that are well supervised.

Calendar of Events



- April 30** **Crystal Ball Awards Gala**
Hepatitis B Foundation
Occasions, New Hope, PA
www.hepb.org
- May 9-14** **Aim for the B Awareness Week**
Bristol-Myers Squibb, Hepatitis B Foundation
A Nationwide Media Campaign
www.hepb.org
- May 15-18** **Digestive Disease Week**
AASLD, AGA, ASGE, SSAT
McCormick Place, Chicago, IL
www.ddw.org/
- June 23-26** **Clinical Care Options for Hepatitis**
iMed Options
Co-Chairs: Drs. DiBisceglie,
Schiff, Lindsay, et al.
Bacara Resort & Spa, Santa Barbara, CA
<http://clinicaloptions.com/go/ccohep2005/>
- July 9-10** **5th B-Informed Patient Conference**
Hepatitis B Foundation
Delaware Valley College, Doylestown, PA
www.hepb.org
- Sept. 18 - 21** **International Meeting of the
Molecular Biology of HBV**
Co-Chairs: Drs. Block and Urban
Kirchoff Institute, Heidelberg, Germany
www.hbvmeeting.org
- Sept. 21 - 24** **43rd Interscience Conference on
Antimicrobial Agents and
Chemotherapy**
American Society for Microbiology
Morial Convention Center, New Orleans, LA
www.icaac.org
- Oct. 6-8** **Hepatitis B Conference**
European Association for the Study
of Liver Disease
Istanbul Convention Center,
Istanbul, Turkey
www.easl.ch/hbv2005
- Oct 28 - Nov 2** **70th ACG Annual Meeting**
American College of Gastroenterology
Honolulu Convention Center, Honolulu, HI
www.acg.gi.org
- Nov. 11-15** **56th Annual AASLD Meeting**
American Association for the Study of
Liver Diseases
Moscone West Convention Center,
San Francisco, CA
www.aasld.org
- Dec. 5-9** **National Viral Hepatitis Prevention
Conference**
Centers for Disease Control and Prevention
Capitol Hill Hyatt Regency Hotel,
Washington, DC
www.cdc.gov/hepatitis
- Dec. 11-15** **HEP DART 2005**
Co-Chairs, Drs. Schinazi,
Sommadossi, and Rice
Fairmont Orchid, Kohala Coast, HI
www.informedhorizons.com



Giving Hope to Millions Is As Easy As Giving...

... And We've Made It Easier! Secure Credit Card
Donations Can Be Made Online.

The growing number of people seeking information and support each year continues to affirm the importance of the HBF's *Cause for A Cure* since we rely on the generosity of individual donations, we need your help to continue our work. Thank you!

Yes! I wish to join the *Cause for A Cure*. Enclosed is my tax deductible gift.

Name _____ \$50 Friend
Address _____ \$100 Supporter
City _____ \$250 Fellow
State _____ Zip _____ \$500 Patron
 \$1,000 Leader
 Other

Check MasterCard Visa Card # _____
Name on card _____ Exp. Date _____
Signature _____

Please make checks payable to: Hepatitis B Foundation
700 East Butler Avenue, Doylestown, PA 18901
**Contributions will be acknowledged in our Winter newsletter
unless otherwise requested.**

A copy of the official registration and financial information may be obtained by calling the Pennsylvania Department of State toll-free within PA at 800-732-0999 or out-of-state at 717-783-1720. Registration does not imply endorsement.



HEPATITIS B FOUNDATION
700 East Butler Avenue
Doylestown, PA 18901-2607

*We are a national non-profit organization dedicated to
finding a cure and improving the quality of life
for those affected by hepatitis B worldwide.*

Tele 215-489-4900 • Fax 215-489-4920
email: info@hepb.org • website: www.hepb.org

- Board of Directors**
Chair & President: Timothy M. Block, Ph.D.
Vice Chairs: Robert Goldberg, Ph.D.
Gurney Sloan, Esq.
Treasurer: Richard Rosenberger, Esq.
Secretary: Janine Witte
- Steven Bingham, M.Ed.
Joan M. Block, R.N., BSN
Thomas Block
Stanley Broadbent
Patricia David, Esq.
Jamie Fox
Kim Jungkind, R.N., MPH
Dale Kindregan
Maria C. Lin, Esq.
W. Thomas London, M.D.
Joel Rosen, Esq.
Charles Sigety, Esq.
- Scientific and Medical
Advisors**
Harvey Alter, M.D.
Baruch Blumberg, M.D., Ph.D.
Marianne Buzby, R.N., MSN
Raymond Dwek, D.Phil., FRS
Lawrence Freidman, M.D.
Hie-Won L. Hann, M.D.
Eric Maller, M.D.
Kenneth Rothstein, M.D.
Mark Zern, M.D.
- Vice President
Community Outreach**
Molli C. Conti
- Editor**
Joan M. Block

Layout & Design: Laser Ad & Print Works

The newsletter **B Informed** is a free publication of the Hepatitis B Foundation. The information provided is solely for educational purposes and is not intended to serve as medical advice or endorsement of any product or company. Readers should discuss all personal questions and decisions with a qualified health care provider.