The Newsletter of the Hepatitis B Foundation | No. 63 | Spring 2013

B Informed

U.S. Dept. of Justice Strikes Down HBV Discrimination

The Hepatitis B Foundation (HBF) is proud to have played a key role in a landmark settlement by the U.S. Department of Justice (DOJ) on March 5, 2013, which ruled the University of Medicine and Dentistry of New Jersey had violated the Americans with Disabilities Act (ADA) by unlawfully excluding applicants because they have hepatitis B.

The two students involved in the case contacted the HBF for help in 2011 after their acceptances had been revoked due to a positive hepatitis B test on a routine physical exam. Since both had been born in the U.S. and vaccinated as toddlers, they were unaware of their chronic infections.

"The HBF first brought these two cases of hepatitis B-related discrimination to national leaders who could make a difference," explained **Joan Block**, HBF executive director. "And we worked closely with **Nadine Shiroma**, a community civil rights advocate, who contacted the Department of Justice and persisted in making it a civil rights issue."

The settlement was reached based on the strength of the Centers for Disease Control's updated HBV recommendations released in 2012 (*B Informed*, Spring 2012) that clearly state having hepatitis B should not preclude anyone from pursuing studies or a career in health care.

This is the first ever ADA settlement reached by the Justice Department on behalf of people with hepatitis B. "Excluding people with disabilities from higher education based on unfounded fears or incorrect scientific information is unacceptable," explained **Thomas Perez**, U.S. Assistant Attorney General, DOJ Civil Rights Division.

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—Thomas Perez
U.S. Assistant Attorney General
Department of Justice Civil Rights Division

The settlement requires the NJ medical schools to adopt a disability rights policy based on the CDC's recommendations and provide their employees with ADA training. After learning of the DOJ settlement, a student shared with us, "A sense of relief overwhelmed me. The weights on my shoulders were finally lifted and I could pursue my dream to become a doctor with the law behind me."

INSIDE

Cause for a Cure

The Hepatitis B Foundation is a national nonprofit organization dedicated to finding a cure and improving the quality of life for those affected by hepatitis B worldwide through research, education and patient advocacy.

HBF Researchers Target cccDNA.
Read more on page 3

From the Editor's Desk

Joan M. Block, Co-Founder and Executive Director

Making Hepatitis B History

The Hepatitis B Foundation continues to be *the* beacon of hope for those concerned about and affected by hepatitis B and liver cancer. We are guided by our twin goals: to increase awareness about hepatitis B and deliver new discoveries in pursuit of a cure.

Partnerships have been and remain key to our success and future growth. We worked closely with the Centers for Disease Control and Prevention and the U.S. Department of Justice to achieve the amazing advocacy success of striking down hepatitis B-related discrimination for health care students (front page).

With AAPCHO (Association of Asian Pacific Community Health Organizations), we spearheaded the creation of *Hep B United*, the first national campaign that includes more than 15 community-based coalitions from around the country and federal partners. This unique initiative has resulted in the first national community action plan to address the enormous challenge of hepatitis B in the U.S. (page 6).

We are making noise not only in outreach, but also in discovery research. With our academic partner, Drexel University, we have discovered new "lead" compounds with promising activity against hepatitis B and liver cancer, as well as new methods for the early detection of liver cancer (page 3).

As we make progress in advancing our mission through strategic partnerships in the U.S. and abroad (page 6), we are getting even closer to our goal of … *making hepatitis B history.*

Thanks for your donations!

The Hepatitis B Foundation thanks everyone who contributed to our **Annual Fund Appeal** in 2012. We sincerely appreciate your support and donations to help us continue our valuable work in research, outreach, public health and patient advocacy.

HEPATITIS B FOUNDATION

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In the News

HBF's Biotech Center Boosts Economy with $579 Million Impact

The Hepatitis B Foundation's ***Pennsylvania Biotechnology Center,*** which the Foundation established in 2006 to advance its research mission, announced the impressive results of a 2013 Economic Impact Study by Byler Associates, LLC.

From 2009 through 2012, the Center and its affiliated organizations generated $579 million for the Commonwealth of Pennsylvania and 573 jobs.

"We promised we would deliver," said **Dr. Timothy Block**, president of the Pennsylvania Biotechnology Center, HBF and its research institute, and professor at Drexel University.

He added that many of the Center's discoveries are now entering human use studies and can help people. "All of this … [underscores the need for] … continued investment in the Center, since it has prospered during a slow economic period and weathered the most recent economic situation so well."

Jim Greenwood, president and CEO of Biotechnology Industry Organization, and the region's congressman when the Center was established, notes that, "[The Foundation] started with an abandoned warehouse that had lost 140 jobs and converted it into a high-tech incubator of innovation, creating hundreds of jobs and millions of dollars of economic development in a field that brings hope to untold numbers of patients."

Read more at ***www.pabiotechbc.org.***

Targeting cccDNA Could Be a Game Changer

Some of the most exciting work in the field of hepatitis B is happening at the Hepatitis B Foundation's research institute. A team of HBF and Drexel University scientists has identified several compounds that inhibit the formation and activity of covalently closed circular DNA (cccDNA) found inside the chromosome of the hepatitis B virus.

Most scientists think a cure for hepatitis B will require elimination of cccDNA, which is the stable source of all viral replication in the body.

Hepatitis B Foundation researchers have now effectively targeted cccDNA and shown that its formation, expression, and perhaps even stability can all be affected by drugs and cytokines.

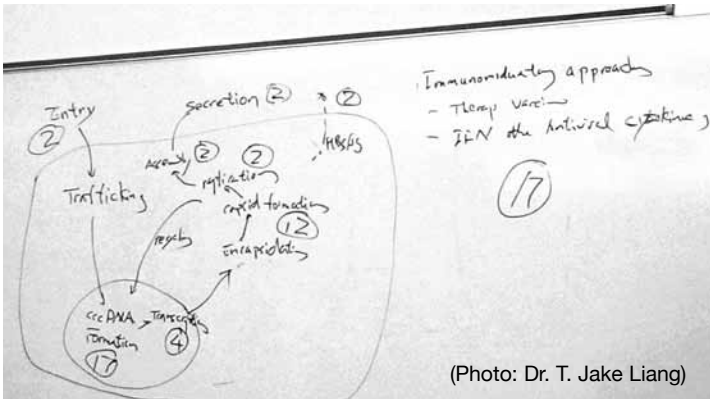
"When you eliminate or silence the cccDNA, you prevent the virus from ever expressing any of its genes. The viral presence, or footprint, goes to zero," says **Dr. Timothy Block**, HBF president and professor at Drexel University.

"The door has now been opened for drug treatments that can stop the disease in its tracks. Rather than just suppressing the virus, these new compounds could actually destroy it," added Dr. Block.

Why cccDNA Is Groundbreaking News

While scientists at the HBF's 2011 Princeton Workshop voted that a cccDNA inhibitor tops the "most wanted" list of new HBV drugs, it remains an elusive goal for now.

One approach to destroying cccDNA without harming the human DNA is being taken by **Dr. Lorne Tyrrell** and his colleagues at the University of Alberta. They are using "zinc finger" enzymes, which are designed to specifically cut HBV DNA sequences without, in theory, targeting the human host.



cccDNA inhibitors win the "Most Wanted Drug" vote during the HBF's Princeton Workshop in 2011.

Why Patients Should Take Note

Many people with chronic HBV must take an oral medication for the rest of their lives, which is not an ideal situation. But by "zapping" the virus with an anti-cccDNA compound, HBF scientists are taking a giant step towards finding a cure.

"Currently, chronic hepatitis B can be medically managed with either pegylated interferons or direct-acting antivirals," says Dr. Block. "But our goal is to eliminate HBV, not just manage it. Targeting cccDNA may take us that much closer to developing a cure. And that could make it a game changer."

Drugs that can target and destroy cccDNA could lower the risk of liver disease and liver cancer significantly. With possibilities such as these, it's no wonder the excitement is spreading from the Hepatitis B Foundation in Doylestown, PA, to the rest of the world.

2012 International HBV Meeting co-chairs with HBF organizers. *L to R: Jackie Corwell and Loretta Molle (HBF); Maila Maini and John Casey (co-chairs); and Peggy Farley (HBF).*

Harry Potter Meets Hepatitis B:
2012 International HBV Meeting in Oxford

The International HBV Meeting, held September 23-26, 2012, and coordinated by the Hepatitis B Foundation, was held in the ancient halls of Christ Church at the University of Oxford, where parts of the popular Harry Potter movies were filmed. The meeting was co-chaired by **Maila K. Maini, MD**, University College London, and **John Casey, PhD**, Georgetown University. After 27 years, it continues to be the definitive scientific meeting for hepatitis B.

The meeting attracted 350 scientists from around the world to meet, present and discuss their research. This was probably the largest turnout in a decade and confirms the distinct feeling that with hepatitis C now curable, there is a renewed interest in hepatitis B, particularly from the commercial world.

See page 5 for the meeting highlights.

HBF Drug Watch

SPRING/SUMMER 2013

HBV Compounds in Development

www.hepb.org/drugwatch

FAMILY/DRUG NAME	MECHANISM	COMPANY	WEBSITE	STATUS, USA
INTERFERONS Mimic naturally occurring infection-fighting immune substances produced in the body				
Intron A (Interferon alfa-2b)	Immunomodulator	Merck, Whitehouse Station, NJ	www.merck.com	FDA Approved 1991
Pegasys (PegInterferon alfa-2a)	Immunomodulator	Genentech, South San Francisco, CA	www.gene.com	FDA Approved 2005
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
Baraclude (Entecavir)	Inhibits viral DNA polymerase	Bristol-Myers Squibb, Princeton, NJ	www.bms.com	FDA Approved 2005
Tyzeka (Telbivudine)	Inhibits viral DNA polymerase	Novartis, Switzerland	www.novartis.com	FDA Approved 2006
Viread (Tenofovir)	Inhibits viral DNA polymerase	Gilead Sciences, Foster City, CA	www.gilead.com	FDA Approved 2008
Clevudine (Levovir)	Inhibits viral DNA polymerase	Bukwang, Seoul, Korea	www.bukwang.co.kr	Approved in S. Korea
MIV-210	Inhibits viral DNA polymerase	Medivir/Daewoong, S. Korea	www.daewoong.com	Phase II
Amdoxovir (DAPD)	Inhibits viral DNA polymerase	RFS Pharma LLC, Tucker, GA	www.RFSpharma.com	Phase II
AG X-1009	Pro-drug of tenofovir	Agenix, Australia	www.agenix.com	Phase I, China
NON-NUCLEOSIDE ANTIVIRALS				
NOV-205 (Bam 205)	Small molecule	Novelos, Newton, MA	http://novelos.com	Approved in Russia
LB80380 (ANA380)	Inhibits viral RNA polymerase	LG Life Sciences, Seoul, Korea	www.lgls.com	Phase II
Myrcludex B	Entry inhibition	Myr-GmbH, Germany	Pending	Phase 1A, Germany
HAP Compound (Bay 41-4109)	Inhibits viral nucleocapsid	AiCuris, Germany	www.aicuris.com	Phase I
REP 9AC	HBsAg release inhibitor	REPLICor Inc., Montreal, Quebec	www.replicor.com	Phase I
Alinia (Nitazoxanide)	Small molecule	Romark Labs, Tampa, FL	www.romark.com	Pre-clinical HBV
dd-RNAi compound	Gene silencing	Benitec, Australia, Biomics, China	www.Benitec.com	Preclinical
ARC520	RNAi gene silencer	Arrowhead Research, Pasadena, CA	arrowheadresearch.com	Preclinical
NEW! NVR-1221	Capsid inhibitor	Novira Therapeutics, Doylestown, PA	noviratherapeutics.com	Preclinical
NEW! IHVR-25	ccc-DNA inhibitor	Institute for Hepatitis & Virus Research, Doylestown, PA	www.ihvr.org	Preclinical
NON-INTERFERON IMMUNE ENHANCERS Boost T-cell infection-fighting immune cells and the body's natural interferon production				
Zadaxin (Thymosin alpha-1)	Immune stimulator	SciClone, San Mateo, CA	www.sciclone.com	Orphan drug approval in U.S. for liver cancer
CYT107 (Interleukin-7)	Immunomodulator	Cytheris, Paris, France	www.cytheris.com	Phase I/IIA
DV-601	Therapeutic vaccine	Dynavax, Berkeley, CA	http://dynavax.com	Phase I
HBV Core Antigen Vaccine	Therapeutic HBV vaccine	Emergent Europe, UK	www.ebse.com	Phase I
GS9260	TLR7-agonist	Gilead Sciences, Foster City, CA	www.gilead.com	Phase I
GI13000	HBV antigen	GlobeImmune, Louisville, CO	www.globeimmune.com	Preclinical with Gilead
POST-EXPOSURE AND/OR POST-LIVER TRANSPLANT TREATMENT				
HyperHEP S/D	HBV immuneglobulin	Talecris, RTP, NC	www.talecris.com	FDA Approved 1977
Nabi-HB	HBV immuneglobulin	Biotest, Boca Raton, FL	www.biotestpharma.com	FDA Approved 1999
Hepa Gam B	HBV immuneglobulin	Cangene, Ontario, Canada	www.cangene.com	FDA Approved 2006

*Sincere thanks to **Timothy Block, PhD** (Drexel U. College of Medicine, Philadelphia, PA), **Nat Brown, MD** (Presidio, San Francisco, CA), **Brent Korba, PhD** (Georgetown U. Medical Center, Rockville, MD), and **Raymond Schinazi, PhD** (Emory U. Medical School, Atlanta, GA) for their regular review of the HBF Drug Watch.*

For More Information...

- **HBV Clinical Trials @ www.hepb.org/clinicaltrials**
- **Resource Round-Up @ www.hepb.org/resources**
- **Hepatitis B Info and Support List @ www.hblist.org**
- **HBV Adoption Support List @ http://health.groups.yahoo.com/group/hbv-adoption/**

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2012 International HBV Meeting Highlights

From the antiviral therapeutic perspective, there is a lot of exciting news to report from the 2012 International HBV Meeting, especially the cccDNA work being done in the Hepatitis B Foundation's research labs.

- cccDNA can be repressed in culture by interferons and even candidate compounds and recombinant cccDNA-destroying proteins *(Lucifora et al., Technische U. of Munchen #35; Arbuthnot et al., U. Witwatersrand #36; Palumbo et al, U. Rome #37; Liu et al, Drexel and HBF #38; Cai et al., Drexel and HBF #50)*
- Use of toll receptor 7 agonists to control HBV has become a viable target *(S. Fletcher, Gilead Sciences)*
- Suppression of HBsAg is becoming a clinical target *(A. Vallient, Replicor)*
- The possibility of targeting HBV RNAseH *(J. Tavis, St. Louis U.)*
- RNAi is back and entering human trials *(Wooddell et al., Arrowhead Research #149)*
- New mouse model for HBV infection might be very useful for therapeutic drug evaluation *(Bility et al., U. North Carolina #96)*

There were a number of other very interesting presentations and topics covered that were more fundamental in nature, rather than serving specific antiviral projects, but were provocative as well.

Register Now!

2013 International HBV Meeting

Meeting to be held in Shanghai

October 20-23, 2013

Visit ***www.HBVmeeting.org***

Hepatitis B Foundation Publication Highlights

Hepatitis B Recommendations for Primary Care Providers

To help primary care providers, who are at the frontline of caring for most people at risk for chronic hepatitis B, the HBF convened a group of leading primary care experts to develop a simple HBV algorithm for screening, diagnosing, and monitoring. To date, the HBF's algorithm and recommendations have been published in four peer-reviewed medical journals: *J. of Family Practice* (2011), *The Female Patient* (2011), *American J. of Medicine* (2012), and *J. for Nurse Practitioners* 2013.

Read the article, ***Internist Diagnosis and Management of Chronic Hepatitis B Virus Infection***, by *McMahon* BJ, *Block* J, *Haber* B, *London* WT, *McHugh* JA, *Perrillo* R, *Neubauer* R, in *Am J Med*. 2012 (Nov);*125:1063-1067* at ***www.hepb.org***.

Chronic Hepatitis B Infection in People Outside of Treatment Guidelines: To Treat or Not to Treat?

Providing new estimates of the age-specific risks of liver-related deaths in people who fall outside the current guidelines, the authors suggest that treatment or other prevention options should be actively explored for such subpopulations, who could particularly benefit from new treatments that are not just targeted at reducing viral loads. *Evans AA, London WT, Gish RG, Cohen C, Block TM. Chronic HBV infection outside treatment guidelines: is treatment needed? Antivir Ther. 2012;Aug 23. doi: 10.3851/IMP2325*. Read at ***www.hepb.org***.

May Is National Hepatitis Awareness Month

In 2001 the CDC designated May as National Hepatitis Awareness Month, which is an important opportunity to increase the visibility of 6 million Americans living with chronic hepatitis B or C infections.

Every year the HBF has been hosting events to draw attention to hepatitis B. Last year **Philadelphia Mayor Michael Nutter** joined our photo flash mob, so this year we hope to see him join our coalition on the "Rocky Run" up the Philadelphia Art Museum steps! In addition, we have our *Philadelphia Hep B Heroes* team *(photo)* ready to go for the gold in the Independence Dragon Boat Regatta, which draws more than 2,000 enthusiasts.

Visit ***www.hepbunited.org*** for events across the country in May.

Capitol News

Hep B United Community Action Plan: A National Resource for Local Coalitions

Hep B United, a national campaign spearheaded by HBF and AAPCHO that supports and leverages the success of community-based hepatitis B coalitions across the country, has developed a community action plan to advance the 2011 Department of Health and Human Services (HHS) Viral Hepatitis Action Plan. The *Hep B United* action plan is the result of a national summit held for coalition and federal partners in August 2012 at the Hepatitis B Foundation's headquarters (*B Informed*, Spring 2012).

By focusing on three priority areas of the HHS Hepatitis Plan—to educate providers and communities, improve testing and linkage to care, and eliminate perinatal HBV transmission—*Hep B United's* action plan has created a national resource with strategies that coalitions can use at at the local level as they combat hepatitis B in their own communities.

For example, with the overarching challenges that include lack of awareness, language and cultural barriers, and funding limitations, local coalitions can serve as a trusted coordinator of services and resources to help people gain access to screening, vaccination, and care, and to reduce perinatal HBV transmission. They can also build partnerships with federal agencies that include the CDC, Office of Minority Health, HHS, and the White House Asian and Pacific Islander Initiative.

There is a lot to do, but *Hep B United* and its coalition and federal partners are working together to implement the community action plan, to define success, and to make a measurable impact on eliminating hepatitis B and liver cancer at both the local and national levels.

Indonesia's Hepatitis B Crisis

By J. Michael Hall, Madison Associates

In 2012, while in Indonesia on a 6-month sabbatical from my government relations business in Washington, DC, I interviewed Indonesia's leading health officials and experts in liver diseases to understand the scale of Indonesia's public health problem posed by hepatitis B.

An estimated 10% of Indonesia's population of 239 million is infected with the hepatitis B virus, ranking Indonesia third in the world in terms of the number of people infected by hepatitis B.

Dr. Poernomo Boedi, chairman of Internal Medicine at Airlangga University in Surabaya, reported that most people in Indonesia are unaware that they have hepatitis B until its later stages. There have been no public health campaigns to increase awareness or to encourage testing, especially among pregnant mothers, because of the expense.

And most Indonesians are unaware that hepatitis B treatment is covered under the national health care insurance, according to **Dr. Rino Gani**, chairman of the Indonesian Liver Research Association. Compounding the lack of awareness is the low immunization rate in Indonesia. **Mohammad Subuh**, director of the Communicable Diseases Department at the National Health Ministry, observed that very few newborns are vaccinated at birth, a critical means of stopping perinatal hepatitis B transmission.

Dr. Boedi believes major improvements in Indonesia's public health system are possible with more resources, so he and others at Airlangga University Medical School have begun discussion with **Dr. Timothy Block**, president and co-founder of the Hepatitis B Foundation and its research institute. They are also exploring a possible collaborative initiative that could qualify for funding from the University Partnership Program offered by the United States Agency for International Development (USAID).

A joint venture with USAID and the HBF could provide Indonesia with critical assistance as it tackles the enormous public health challenge of hepatitis B in an era of effective vaccines and treatments.

Chronic Hepatitis B or C: Which Is Worse?

W. Thomas London, MD, Board Member and Medical Advisor, Hepatitis B Foundation
Professor Emeritus, Fox Chase Cancer Center

Recently a group of investigators from Johns Hopkins University published a paper with the title "*Comparative Risk of Liver-Related Mortality from Chronic Hepatitis B Versus Chronic Hepatitis C Virus Infection*." They found that hepatitis B is more likely to cause liver-related death than is hepatitis C. Unexpectedly, studies related to the acquired immune deficiency syndrome (AIDS) epidemic brought the authors to this conclusion.

"…Hepatitis B, which was already a worse disease than hepatitis C before the new therapies for hepatitis C, is now a much more important unsolved health problem."

AIDS was first reported in the United States in 1981. The deadly disease affects all populations, but men who have sex with men (MSM) accounted for most of the early cases. MSM also had been identified in the 1970s as having a high incidence of hepatitis B.

Fast-forward to 1984. Before the human immunodeficiency virus (HIV) causing AIDS was clearly identified, several researchers suggested that a variant of the hepatitis B virus was the cause. Researchers proposed a prospective study of MSM who had been tested for hepatitis B and a newly reported anti-HIV antibody, but who did not have immune deficiency disease. By following the men over time, the researchers wanted to observe which infection—HIV or HBV or a combination of both—led to AIDS.

Between 1984 and 2002, the Multicenter Cohort Study enrolled 6,972 MSM from four U.S. cities. The men were studied until 2010, on average for more than 8 years. Serum samples were collected every 6 months, frozen, and stored. Although the hepatitis C virus (HCV) had not yet been identified in 1984, all the samples were later tested for HIV, HBV, and HCV. All deaths, including liver-related deaths, were recorded.

The results were surprising. Comparable numbers of men were infected with HBV and HCV, but men with chronic HBV were twice as likely to die a liver-related death as the men with chronic HCV.

After carefully accounting for the treatments of the hepatitis viruses and HIV used during the study, the investigators found that immunodeficiency further increased the risk of liver-related death in the men with chronic HBV over that in the men with HCV.

The study showed that in the two and a half decades after 1984, hepatitis B infection was more serious than hepatitis C.

Now this difference is even greater. HCV has become a curable disease. Chronic HBV is manageable, but not yet curable. This means that hepatitis B, which was already a worse disease than hepatitis C before the new therapies for hepatitis C, is now a much more important unsolved health problem.

Calendar of Events 2013

May 18-21 **Digestive Disease Week 2013 (DDW)**
Sponsored by AASLD, AGA, ASGE, SSAT
Orange County Convention Center
Orlando, FL
www.ddw.org

May 19 **National Hepatitis Testing Day**
Centers for Disease Control and Prevention
Events held across the USA
www.cdc.gov/hepatitis

May 29 **World Digestive Health Day 2013**
World Gastroenterology Organisation
Special Focus on Liver Cancer
www.wgofoundation.org/wdhd-2013.html

Oct 20-23 **2013 International HBV Meeting**
Organized by the Hepatitis B Foundation
Shanghai Medical College, Fudan University
Shanghai, P.R. China
www.hbvmeeting.org

Nov 1-5 **The Liver Meeting 2013**
American Assoc. for the Study of Liver Diseases
The Walter E. Washington Convention Center
Washington, DC
www.aasld.org/livermeeting

Dec 8-12 **HEP DART 2013**
The Fairmont Orchid
Kohala Coast, Big Island, Hawaii
www.informedhorizons.com/hepdart2013

Liver Cancer Webinar Series

Available During May: Hepatitis Awareness Month

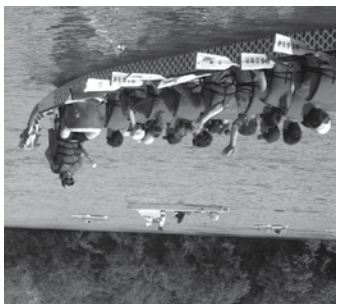
HBV and Liver Cancer — Dr. Robert Gish
HCV and Liver Cancer — Dr. Douglas LaBrecque
Fatty Liver and Liver Cancer — Dr. Kenneth Rothstein

Download the free webinar recordings at ***www.LiverCancerConnect.org***, a dedicated program of the Hepatitis B Foundation.

Find HBF on your favorite social media networks and join the conversation.

facebook.com/hepbfoundation twitter@hepbfoundation HEP B BLOG wp.hepb.org youtube.com/hepbfoundation

B Informed **and all back issues are available online at *www.hepb.org/newsletters.***



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