HCV ADVOCATE WEEKLY NEWS REVIEW

Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights

Alan Franciscus
Editor-in-Chief

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In This Issue:

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Presence of drugs doesn't stop transplants

http://www.metrowestdailynews.com
By Peter Reuell
DAILY NEWS STAFF

Maxsuel Medeiros' organs could still save the lives of as many as a half-dozen people, despite the fact that the Framingham man had cocaine in his system when he died this week.

Medeiros died Tuesday, more than a week after he became ill following his arrest by state police on two outstanding warrants.

But while the presence of the drug in his system raises new questions in the investigation into the circumstances of his death, Sean Fitzpatrick, director of public affairs for the New England Organ Bank, said it wouldn't hold up the decision to donate his organs.

"There are no hard and fast automatic rule-outs for donation," he said. "Those types of decisions are best made by individual transplant surgeons with a particular recipient in mind."

Earlier this week, his family said they had agreed to donate his organs.

Potential organ donors, Fitzpatrick said, must go through a rigorous screening process, which begins with tests for more than a half-dozen communicable diseases, including Hepatitis B and C, syphilis and HIV.

"If a family says yes, we want to donate, part of that consent process includes them consenting to a (communicable disease) panel," Fitzpatrick said. "The reason why you do the communicable disease test is because you don't want to transplant a particular disease to the recipient."

With organ recipients also taking immunosuppressive medication to make sure their bodies don't reject the new organ, they are particularly susceptible to disease risk, he added.

Prior to their organ donation, Fitzpatrick said, most patients undergo toxicology screening which would reveal the presence of drugs and/or alcohol in their system.

"After we get consent from the family to go forward, we receive the medical records of a potential donor," Fitzpatrick said. "Toxicology screens are usually already in the chart."

Medical staff will also run a series of tests on the organs themselves, to ensure they function properly, Fitzpatrick said.

The final stage in the process is for officials from the Organ Bank to meet with family members to go over a donor's medical history.

"That is sitting down with the family and going into great detail about the person," Fitzpatrick said. "Did they smoke and how much, did they drink and how much, did they use recreational drugs and how much?"

Armed with that information, the Organ Bank will then produce a list of potential recipients and begin contacting transplant surgeons.

"All that information is provided to the transplant surgeon, so the transplant surgeon can make an assessment as to the health and function of the organ and any potential risks," Fitzpatrick said.

"The surgeon uses his or her medical judgment whether they'll accept an organ."

Though it's not uncommon for organs to be rejected by a surgeon, Fitzpatrick said the decision rarely has anything to do with whether the donor might have drugs in their system.

"If you're in need of a liver or a heart, and you have a couple days to live, the fact that a person might have traces of drugs in their system is less important than your dire need for a heart," he said.

Even testing positive for disease doesn't rule out an organ donation.

"I might have a patient who is waiting for an organ who is already Hepatitis B positive, or HIV positive," Fitzpatrick said.

More often, the decision is based on the health of the recipient.

Since potential recipients are often so ill, doctors may opt not to perform the dangerous transplant surgery until a person's condition improves, meaning they may have to pass on an available organ.

"Nothing is really an automatic rule-out," Fitzpatrick repeated. "What we want to do is gather the information, and then allow the surgeon to determine whether or not it's a good match for their patient."

(Peter Reuell can be reached at 508-626-4428 or at preuell@cnc.com.)

September 16th, 2007

Hepatitis-promoting protein caught in the act

http://www.news-gazette.com
By Greg Kline

When your body, or a nasty virus invading it, cooks up a batch of genes, helicases – an enzyme, or type of catalyzing protein molecule – appear to be bigger than Betty Crocker in the kitchen.

The tasks performed by the proteins apparently include the unwinding of the tightly coiled ribbonlike DNA and RNA molecules containing the instructions for gene making.

Those chains of nucleic acids – the "N" and "A" in DNA and RNA and the basic building blocks of life – are then read by another type of protein molecule, called a polymerase.

But the genetic cookbook has to be cracked open by helicases first, and scientists have been of two minds on how that happens.

Some structural studies of helicases frozen in place seemed to suggest they work one page – or base pair, the basic unit of DNA and RNA strands – at a time.

Meanwhile, biochemical studies indicated that helicases sometimes work over three base pairs at once.

University of Illinois Professors Sua Myong and Taekjip Ha might have resolved the conflict. Their theory, backed by research using a technique developed by Ha to capture the movement of single molecules, is that it's both.

Helicases have three domains, or legs, as Myong described it recently. Two of those legs step along the acid chains, a base pair at a time during the unwinding process. The third leg remains anchored behind and gets stretched out until enough tension builds that it snaps lose and ahead three pairs. Ha, a UI physics professor, likened its movement to a spring.

"When we saw it, it made a lot of sense," said Myong, a professor at the UI Institute for Genomic Biology and the lead author of a paper on the study in the journal Science.

While interesting biologically, the information also has the potential to play into medical breakthroughs.

The UI researchers and collaborators at Yale University and the Maryland-based Howard Hughes Medical Institute looked at a helicase from the hepatitis C virus, which affects hundreds of millions of people worldwide – and for which there is no vaccine.

The helicase and its unwinding job are necessary for the virus to replicate, which makes the protein a potential target for new hepatitis C treatments.

That is undoubtedly a ways off and presents some challenges. For one thing, it appears that many helicases, including those of benefit in the human body, might function in a similar manner. A treatment would need to hone in on the hepatitis C helicase while leaving others alone, said Ha, a biological physicist who's also an affiliate of the Institute for Genomic Biology and of the Hughes Institute.

Besides their role in hepatitis C propagation, helicases have been implicated in human maladies such as cancers and in premature aging diseases, Ha said.

"If they don't function properly, then you can get into trouble," he said.

In their study of the hepatitis C helicase, the researchers found that the protein is powered by a lot of energy – and plenty of a cellular fuel called adenosine triphosphate, or ATP, to generate it. Ha said that makes a helicase more like an SUV than an economy car in this instance.

But gas guzzling could be a good thing here, Ha and Myong said. The nucleic acid chain road is a rough one, full of bumps and twists and turns and possibly obstacles to be cleared, such as other proteins interacting with the DNA or RNA molecules. The helicases might need an SUV's power and off-road capability, a lot more than most SUV owners do, to get their job done.

To track the tiny protein as it moves, Ha's lab uses a method called fluorescence resonance energy transfer, FRET for short, in which the researchers attach, through a biochemical process,

fluorescent dye markers at various locations.

The sample is exposed to laser light, which makes the dye glow, and glow in different colors depending on its proximity to another marker.

Those light signals can be captured and interpreted to understand how a helicase is moving, at a resolution that allows not only pictures but animations to be created from the data.

The study was funded by the National Institute of General Medical Sciences at the National Institutes of Health.

Next, the researchers need to look at other helicases in action, Ha said. Myong has a plan to contrast the hepatitis C helicase with a helicase involved in putting the body's immune system on a battle footing in response to invaders like the hepatitis virus.

Liver cancer in Bexar County a puzzle

http://www.mysanantonio.com
Don Finley
Express-News Medical Writer

Vilma Moran seemed an unlikely candidate for cirrhosis of the liver, which her doctor said explained her swollen abdomen and yellowing eyes. In her 60 years of life, she had consumed probably 10 alcoholic beverages. She didn't smoke, didn't have hepatitis.

She was diabetic, which is a risk factor. But when it was found later that she had liver cancer, the surgeon asked if she'd ever worked in a chemical plant. The type of cancer she had suggested a chemical exposure, he said. No, she told him, she worked with special education children at Lowell Middle School.

Then she and her husband recalled a letter they had received four years earlier, inviting them to a neighborhood meeting to discuss a plume of contaminated groundwater linked to the shuttered Kelly AFB. They had ignored the invitation. She had lived near Kelly almost all her life. Her father had maintained the base golf course.

In February 2006, Moran attended another neighborhood meeting from her wheelchair. She listened as Tim Aldrich of East Tennessee State University, an expert in cancer clusters, announced he had been hired to look into reports of elevated liver cancer in neighborhoods surrounding Kelly.

Last month, Aldrich's report was quietly released to the San Antonio City Council. A planned meeting to announce the results to people living in those neighborhoods never was held.

The report noted that while 14 ZIP codes that roughly encompass the plume of polluted groundwater indeed did have high rates of liver cancer, so did all of Bexar County. In fact, when adjusted for age differences, the liver cancer rates in those 14 ZIP codes over several years actually were lower than for the county as a whole.

"Whatever is the process for Bexar County to think about its liver cancer risk, in my opinion they must keep in mind that they have more communities with elevated liver cancer risk than just the one near" Kelly, Aldrich said by phone.

Despite those findings, the high rates in those 14 ZIP codes fit the definition of a cancer cluster, Aldrich said. Examine them over shorter periods of time, or in other ways, and they do stand out. That justifies a more in-depth look comparing the cases in those ZIP codes with a comparison group somewhere else.

The ZIP codes are 78201, 78204, 78205, 78207, 78211, 78214, 78221, 78224, 78225, 78226, 78227, 78228, 78237 and 78242.

Local, state and federal health officials have criticized the report and its conclusions. Although they agree the rates in those neighborhoods are high compared with the state and the nation, they disagree with Aldrich that a major study of liver cancer cases in those 14 ZIP codes is feasible — noting only five survivors were willing to be interviewed.

And they strongly disagree with one particular statement in the report: that after statistically excluding the other possible causes — hepatitis, alcohol-related cirrhosis, smoking and diabetes — 11.5 percent of the liver cancers in those 14 ZIP codes "may be attributable to residing over the Kelly ... plume."

A cancer puzzle

For years, experts have puzzled over Bexar County's high rates of liver cancer, particularly the large number of cases that plague the modest neighborhoods to the south and west of downtown. Between 1999 and 2002, Bexar ranked no lower than seventh each year in liver cancer death rates among all 254 Texas counties, for both men and women, according to the Texas Cancer Registry. Hispanics ranked no lower than fourth. Only much smaller counties had higher rates.

There was good reason for concern. No cancer drug is FDA-approved for liver cancer. Most patients are diagnosed with advanced disease, when surgical options — including a liver transplant — often have a poor prognosis.

Worldwide, liver cancer is the fourth biggest cancer killer, with 80 percent of new cases taking place in developing countries. The most common causes in those countries are hepatitis B and food-borne toxins — primarily aflatoxin, a mold that grows on corn, peanuts and other grains.

In fact, while rates for many cancers have declined, liver cancer rates have gone up in the United States and other wealthy nations, fueled instead by hepatitis C, alcohol consumption and diabetes.

Some experts warn the worst lies ahead.

"That's the way we view it," said Dr. Melanie Thomas, assistant professor of gastrointestinal medical oncology at the University of Texas MD Anderson Cancer Center in Houston. In a 2005 paper, she and a co-author described liver cancer as "a looming epidemic for which the medical oncology community is largely unprepared."

The federal Agency for Toxic Substances and Disease Registry first identified liver cancer as a major concern in 1999 after studying the neighborhoods around the base at the request of the late U.S. Rep. Frank Tejeda.

Residents had a laundry list of health complaints that many blamed on contamination from the base. A number of studies since then have confirmed high rates in those neighborhoods and countywide.

Health officials have argued the polluted shallow aquifer beneath the neighborhoods wasn't used for drinking or watering lawns, and people weren't exposed. They noted the lag time between exposure and cancer can be decades.

Aldrich points out that the 14 ZIP codes in his study share another characteristic besides the plume. Nearly half of Bexar County's Hispanic population lives in them. Across the country, Hispanics — particularly Hispanic men — are more prone to liver cancer than other groups.

Hispanics are slightly more likely to have hepatitis C, and some research has shown the virus progresses more rapidly in Hispanics. Diabetes, an epidemic in the Hispanic community, causes a condition known as fatty liver disease, which can progress to a form of cirrhosis called NASH — non-alcoholic steatohepatitis — and liver cancer. Having diabetes doubles the risk of liver disease and liver cancer.

Then there's the question of alcohol use. A 2004 study in the American Journal of Public Health, which looked at survey data from the late 1990s, found San Antonio had the highest percentage of binge drinking among 120 U.S. cities. Twenty-four percent of adults here — and more than a third of all men — had consumed five or more alcoholic beverages in one occasion within 30 days of being asked. Nationwide, the median was 14.5 percent. Those researchers found no statistically significant differences between racial or ethnic groups. Those with lower education levels were slightly more likely to be binge drinkers.

With funding from the Air Force, the Metropolitan Health District commissioned a feasibility study through HealthCare Resolution Services Inc. of Laurel, Md., which hired Aldrich as a consultant. The study was to examine rates of primary liver cancer — cancer that began in the liver, excluding cancer that might have begun in another part of the body and spread to the liver — in those 14 ZIP codes to see if a large, comprehensive study might be justified.

With the help of Metro Health staff, the study grew beyond its initial scope — including a survey of neighborhood veterinarians to see if they had diagnosed liver cancer in dogs, which might suggest an environmental cause. They hadn't.

In his report, Aldrich estimates that when you apply Bexar County's rates of hepatitis, smoking, diabetes and other causes to those ZIP codes, that still would leave 11.5 percent of cases unexplained. He's unapologetic for stating those cases "may be" related to living over the plume, saying the report was written to guide the health department as it considers studying the matter further.

"I'm trying to explain to the health department, if they do a study, how many of the people

they've studied will they be able to say, it looks like your liver cancer was the result of living over this plume," Aldrich said. "Their study should be designed to find this many cases."

"We do not agree," said Dr. James Wittmer, a local environmental health consultant to the Metropolitan Health District. "It's a firm conclusion of all the people who have read this report, the professionals and the reviewers, that this is an unfounded statement."

Other possible causes

In any case, health officials are looking at other causes. A still-unpublished study of 800 liver cancer death certificates between 1996 and 2005 by the health district and University of Texas Health Science Center researchers found little they didn't already know. Hepatitis was more common in Hispanics than in Anglos, but about the same as in blacks. Diabetes — probably the least understood cause of liver cancer — was much more common in Hispanics who died of liver cancer.

"Was diabetes a contributing factor in the progression to cirrhosis? We couldn't make that conclusion," said Roger Sanchez, an epidemiologist with the health district.

In 2004, Houston researchers published the strongest evidence to date on diabetes and liver cancer involving more than 800,000 VA hospital patients.

They estimated diabetes doubles the risk of liver disease and liver cancer. While the link had been known, some had questioned whether diabetes caused liver disease, or the other way around.

Under way is still another study, and perhaps the biggest long shot yet. Some researchers looking at the high Hispanic rates have wondered whether food-borne toxins might play a role, as they do in other parts of the world.

Aflatoxin and fumonisins contaminate corn, peanuts and other grains. Contamination levels can rise and fall depending on seasonal weather patterns that put stress on plants — drought in particular. And South Texas is drought prone.

Hispanics might consume more corn, the theory goes, and they might buy less expensive corn products, which might be more prone to contamination.

A lot of mights. Researchers at Texas A&M and Texas Tech universities, together with the health district, are targeting three ZIP codes with some of the highest liver cancer rates — 78207, 78228 and 78237, which lie north of U.S. 90 on the West Side. The researchers have sophisticated tests that can detect byproducts of the toxins in blood and urine going back a year from ingestion.

The study is hoping to recruit 500 residents — a number that would provide the strongest statistical evidence of a cause. About 100 have volunteered so far. To learn more about the study, call (210) 434-0077.

For Vilma Moran, it's less important to find what caused her own liver cancer than it is to prevent it from developing in someone else.

"I've already gone through it, however bad it was," she said. "But maybe it will be helpful for someone else. I'm concerned for my son and the other people in the area."

dfinley@express-news.net

Living with 'silent killer' hepatitis C

http://icnewcastle.icnetwork.co.uk
by Pauline Holt, *Sunday Sun*

BODY SHOP founder Anita Roddick, who died earlier this week from a brain haemorrhage, had been living with hepatitis C since having an infected blood transfusion following the birth of her youngest daughter in 1971.

As a patron of the Hepatitis C Trust, Anita helped stamp out the stigma surrounding sufferers such as Wayne Taylor, who tells PAULINE HOLT why her awareness raising campaign must continue.

AS a young man of 27, long distance lorry driver, Wayne Taylor became concerned about his health after repeatedly falling asleep at the wheel.

"It got to the point where it was only the rumble strips keeping me — and other road users — alive," said Wayne from South Shields, South Tyneside. "I'd pull over for a rest but, within an hour and a half or so, I'd have to nap again."

Wayne, now 53 and a father and grandfather, went to his GP to complain about his chronic fatigue and was diagnosed with depression. He said: "It was about 1991. I was feeling very tired and my mood was very low and aggressive, which weren't normal traits for me.

"I was prescribed various antidepressants. I would take them for six weeks and then the side effects would outweigh any benefits.

"This went on year after year, and I was struggling and struggling all the time, until I listened to a Radio 4 programme in 1997 discussing a new virus called hepatitis C. Until then, I'd never heard of it."

Hearing the case histories, Wayne silently ticked off his shared symptoms and promptly returned to his GP.

He said: "I couldn't just turn up and say, 'I want this test for an illness I have never heard of' so I made up a story that an ex-partner had died of hep C and I didn't know what it was but thought it would be sensible to get tested." His GP immediately asked if he was an intravenous drug user.

Wayne said: "Everyone then assumed you must be a drug user or homosexual to get it."

He took the test, which proved positive. He explained: “I said, ‘What do I do now?’ and my GP said, ‘I don’t know, you’re the first person I’ve ever diagnosed.’ He didn’t have any advice, didn’t say, ‘You’re a married man with two children . . . we should have them tested’ and there was no counselling.”

Wayne said: “I felt as though I was a leper. In those days, everyone thought you must be a junkie. No one could give me any information.”

He was relieved, though, to find his illness was not just in his head and, after being referred to Professor Margaret Bassendine at Newcastle’s Freeman Hospital, he began interferon and ribovirin therapy, which can wipe out the virus in at least 50 per cent of patients.

Sadly, despite three gruelling treatment cycles, Wayne’s virus persisted and, today, he remains on anti-depressants because of his illness. He has also lost both his job and his marriage.

But, on a positive note, Wayne has a new partner and now volunteers with the charity LIVErNORTH which supports people with all kinds of liver disease.

Wayne believes hepatitis C is a timebomb waiting to explode. He said: “It’s been called the ‘silent killer’ because you can go years without any symptoms. It’s estimated nine out of 10 of people who have hep C don’t know they’ve got it.

“So I’d like to see people in my age group — in their 40s, 50s, and 60s who think they might have been exposed either through blood transfusion or unsterilised equipment like syringes and needles — to see their GP because the sooner you know you have it, the more effective the treatments.”

**World Hepatitis Awareness Day takes place on October 1 and anyone interested in finding out more can go to www.hepc.nhs.uk There is also a free helpline on 0800-451 451.

Ways to contract the disease
HEP C is a virus that can damage the liver and affect its ability to function correctly.

Like many sufferers, Wayne still doesn’t know how he got it. He said: “It’s a continual battle because you just want to know how it happened, how this life-changing event could have happened and you not know about it.

“I was told I’d probably had it since 1976 but wasn’t diagnosed until 1997, by which time I had a wife and two children who had to be tested. Waiting for those results was horrendous but, thankfully, they were clear.”

The virus is mainly spread through contact with infected blood but can also be passed on via other body fluids, although this is less common.

People who had blood transfusions before September 1991, or blood products — such as clotting agents — before 1986, may be at risk.

Injecting drug users who share needles are also at risk. Less commonly, hep C can also be passed on by the following:

- An infected mother to her baby, before or during birth.
- Unprotected sex with someone who has the virus.
- Medical and dental treatment abroad where unsterile equipment may be used.
- Tattooing, ear or body piercing or acupuncture with unsterile equipment.
- Sharing razors, toothbrushes or other toiletry equipment which may have been contaminated with infected blood.

September 17th, 2007

HIV Patients Now Have the Option of Organ Transplants

http://www.associatedcontent.com
By Sussy

No Evidence to Suggest Transplants Cause Progression to AIDS

Only recently has organ transplantation, specifically liver and kidney, been considered an option for HIV-infected individuals. A Sept. 15 press release states that new developments and clinical approaches have resulted in good outcomes in an increasing number of transplanted HIV-positive patients. Further, there is no indication that HIV-positive patients are at an increased risk to progress to AIDS.

As HIV-infected and AIDS patients are living longer - said to be the result of anti-HIV drug combinations - other complications have come to the forefront. Many patients are now experiencing kidney and liver disease related to both hepatitis B and C. Reportedly, the anti-HIV drug combinations can exacerbate the damage to the liver because of their toxic effects.

The anti-HIV drug combinations, known as "highly active aniretroviral therapy" (HAART), have no doubt given many people infected with HIV a new lease on life. But there have also been some long-term problems, experts says.

According to the Alberta Reappraising Aids Society (ARAS), HAART therapy is prescribed to many HIV-positive people, even before they develop symptoms of AIDS, even though the "list of side effects...is so long that it is impossible to categorize all of them." The ARAS quotes from a Feb. 2006 study (Wyatt CM et al. Acute renal failure in hospitalized patients with HIV: risk factors and impact on in-hospital mortality. *AIDS*. 2006 Feb 28;20(4):561-5) that says "kidney disease has emerged as a leading cause of death among HIV-infected patients in the HAART era...In addition, chronic kidney disease and acute or chronic liver disease were strongly associated with both acute renal failure and in-hospital mortality among patients with HIV, suggesting a need for more aggressive management of chronic kidney disease and hepatitis virus co-infection in the setting of HIV."

Dr. Michelle E. Roland, Assistant Professor of Clinical Medicine at the University of Calif., San Francisco (UCSF), specializes in antiretroviral drug resistance and organ transplantation in HIV-infected patients. She and Dr. Peter G. Stock, Professor of Surgery in Residence at UCSF, wrote that the "blanket exclusion (for organ transplantation) of HIV-infected patients can no longer be

justified based on the early results demonstrating the safety and efficacy of transplantation in this group of patients."

The doctors report that progress has been made in several areas, according to studies at UCSF and elsewhere. The ability to control HIV infection using HAART and improvement in preventing other infections have made liver and kidney transplants an increasingly viable option for HIV-positive individuals. For example, their study of the 3-year survival rate for HIV-positive liver transplant patients was 73 percent, which is similar to patients not infected with HIV.

Although Drs. Stock and Roland say more research is still needed, there is no evidence thus far to suggest that the risk of progression to AIDS is increased in HIV-positive patients who undergo organ transplantation. Therefore, it's "imperative that HIV-positive patients, HIV health care providers, and the transplant community are aware that transplant is a viable option for the HIV infected patient," the doctors conclude.

A summary of the newest organ transplant developments for HIV-infected individuals can be found in the Sept. 15 issue of the *Transplantation* journal.

Sources:
Press release, Transplants for HIV-Positive Patients?;
http://www.newswise.com/articles/view/532923/

ARAS; http://www.aras.ab.ca/haart.html

Hawaii hepatitis project to aid newly released inmates

http://the.honoluluadvertiser.com
Advertiser Staff

A new project to educate recently released inmates infected with hepatitis is being created by the Hepatitis Support Network of Hawaii.

A new office has been set up at River of Life Mission, where both newly released prisoners and the homeless are offered free screenings, vaccinations for Hepatitis B and other services.

Information or to volunteer: Eddie Ochoa: 845-9944.

Idera Pharmaceuticals Initiates Phase 1 Trial of IMO-2125 in Hepatitis C

http://www.genengnews.com
News source: Business Wire

Idera Pharmaceuticals (AMEX: IDP) today announced that the first patient has been dosed in a Phase 1 trial evaluating **IMO-2125** for the treatment of patients with hepatitis C virus (HCV)

infection. IMO-2125 is a novel agonist of Toll-like Receptor (TLR) 9.

"IMO-2125 is a TLR9 agonist that Idera designed to induce endogenous interferon-alpha along with other immune response factors to treat hepatitis C," said Sudhir Agrawal, D. Phil., Chief Executive Officer and Chief Scientific Officer. "IMO-2125 is the second novel TLR9 agonist from our portfolio to enter the clinic following IMO-2055 for cancer. We generated both of these drug candidates using our chemistry-based drug discovery approach which allows us to design TLR-targeted drug candidates which act as agonists for TLR7, 8 or 9 or as TLR antagonists for a broad spectrum of indications."

"The preclinical data that we have generated, including data demonstrating potency in the HCV replicon assay of cytokines and chemokines present in the blood of non-human primates treated with IMO-2125, provides a strong rationale for evaluating IMO-2125 in patients with HCV infection," commented Robert Karr, M.D., President.

The Phase 1 trial evaluating IMO-2125 is being conducted in HCV patients who have failed to respond to previous combination therapy with ribavirin and pegylated interferon-alpha. The trial is designed to assess the safety and tolerability of IMO-2125 at different dose levels as well as determine the effect of IMO-2125 on HCV RNA levels and parameters of immune system activation. Four doses of IMO-2125 are being investigated. IMO-2125 will be administered subcutaneously once a week and treatment will continue for four weeks. The target enrollment for the trial is 40 patients with ten patients per cohort. Of the ten patients per cohort, eight are randomized to receive IMO-2125 treatment and two are randomized to receive placebo treatment. The trial is expected to be conducted at five or more U.S. sites. The lead investigator of this trial is John McHutchison, M.D., Associate Director, Duke Clinical Research Institute and Director, GI/Hepatology Research Program and Professor of Medicine, Division of Gastroenterology, Duke University School of Medicine.

About IMO-2125
IMO-2125 is a novel DNA-based TLR9 agonist being evaluated for the treatment of HCV. IMO-2125 was designed to induce endogenous interferon-alpha along with other immune response factors to treat hepatitis C. In preclinical studies, IMO-2125 induced high levels of endogenous interferon-alpha, as well as other cytokines and chemokines, in non-human primates and in human immune cell cultures. The cytokines induced by IMO-2125 in human immune cell cultures and in non-human primates have shown potent activity in inhibiting HCV replication in an in vitro assay (HCV replicon assay).

About Idera Pharmaceuticals, Inc.
Idera Pharmaceuticals is a drug discovery and development company that is developing drug candidates to treat cancer and infectious, respiratory, and autoimmune diseases, and for use as vaccine adjuvants. Idera's proprietary drug candidates are designed to modulate specific TLRs, which are a family of immune system receptors. Idera's pioneering DNA chemistry expertise enables it to identify drug candidates for internal development and creates opportunities for multiple collaborative alliances. Idera's most advanced clinical candidate, IMO-2055, is an agonist of TLR9 and is currently in a Phase 2 trial in oncology and in a Phase 1/2 chemotherapy combination trial in oncology. Idera's second TLR9 agonist, IMO-2125, is currently in a Phase 1 trial for the treatment of hepatitis C virus infection. Idera is collaborating with Novartis

International Pharmaceutical, Ltd. for the discovery, development, and commercialization of TLR9 agonists for the treatment of asthma and allergy indications. Idera is also collaborating with Merck & Co., Inc. for the use of Idera's TLR7, 8 and 9 agonists in combination with Merck's therapeutic and prophylactic vaccines in the areas of oncology, infectious diseases, and Alzheimer's disease. For more information, visit www.iderapharma.com.

Forward Looking Statements
This press release contains forward-looking statements concerning Idera Pharmaceuticals, Inc. that involve a number of risks and uncertainties. For this purpose, any statements contained herein that are not statements of historical fact may be deemed to be forward-looking statements. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects," "estimates," "intends," "should," "could," "will," "may," and similar expressions are intended to identify forward-looking statements. There are a number of important factors that could cause Idera's actual results to differ materially from those indicated by such forward-looking statements, including whether results obtained in early clinical studies or in preclinical studies such as the studies referred to above will be indicative of results obtained in future clinical trials or warrant additional trials; whether products based on Idera's technology will advance into or through the clinical trial process on a timely basis or at all and receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether, if the Company's products receive approval, they will be successfully distributed and marketed; whether the Company's collaborations with Novartis and Merck will be successful; whether Idera's cash resources will be sufficient to fund product development and clinical trials; and such other important factors as are set forth under the caption "Risk Factors" in Idera's Quarterly Report on Form 10-Q filed on August 1, 2007, which important factors are incorporated herein by reference. Idera disclaims any intention or obligation to update any forward-looking statements.

September 18th, 2007

NM Hepatitis C program wins international competition

http://www.bizjournals.com/

New Mexico Business Weekly - Project ECHO, a Hepatitis C program developed by the University of New Mexico Health Sciences Center and the state's Health and Corrections departments, won first place in an international competition designed to identify programs that change the way medicine is practiced.

The Robert Wood Johnson Foundation chose the New Mexico project out of 307 entrants from 27 countries.

Project ECHO (Extension for Community Healthcare Outcomes) was developed in 2003. It uses teleconferences, telemedicine and the Internet to help providers throughout the state care for patients suffering from the disease.

Dr. Sanjeev Arora, project director and executive vice chairman for the department of medicine at the UNM Health Sciences Center, said the goal of the project is to bring specialty care to patients living in rural areas who do not have access to specialists.

More than 34,000 people in New Mexico are infected with Hepatitis C and 40 percent are uninsured, according to a UNMHSC news release.

The key component of the ECHO model is an innovation called a Knowledge Network in which the expertise of a single specialist is shared with several primary healthcare providers, each of whom sees numerous patients. Since June 2004, the project has conducted 205 Hepatitis C Knowledge Network clinics and provided 2,316 consultations for patients.

Statewide partners include the New Mexico Primary Care Association and Indian Health Services.

Distributed computing tackles dengue, hepatitis

http://arstechnica.com
By John Timmer

IBM has announced the latest project for their World Community Grid distributed computing effort, and it has the potential to be a significant one: a search for molecules that block the reproduction of flaviviruses. That obscure name represents a number of very obvious health issues, as this family of viruses causes dengue fever, yellow fever, hepatitis C, and West Nile disease. The new effort brings together resources from a variety of institutions in the hope of combating these deadly diseases.

The project is being coordinated by the University of Texas Medical Branch, and its home page lists some sobering statistics about the significance of these viruses: two percent of the global population harbors hepatitis C infections, while 1.5 million people annually are treated for dengue fever. Currently, there are no drugs that specifically target any of them.

The Grid hopes to change that. The members of this family of viruses have an unusual structure that presents the opportunity to design therapies that specifically inhibit their infection. In contrast to many other viruses, which have individual genes that encode the proteins needed for their spread, flaviviruses produce a single, large protein that's then chopped up into individual functional parts (a more detailed description is available in this Open Access publication). The virus itself encodes two proteins, called proteases, which help to break the initial protein into the smaller, functional pieces—one of these proteases has now become the target for the World Community Grid.

The Grid's work builds on the determination of the physical structure of the NS3 protease, which has been obtained for both the dengue virus and hepatitis C virus. With the structure in hand, researchers have identified the active site, where the enzyme catalyzes the splitting of the viral protein. The Grid will search for small molecules that fit into the active site in the hope that one of them will block the interaction between the protease and its targets.

That search will leverage ZINC, a free database hosted by the University of California, San Francisco that contains over 4.6 million structures of commercially available chemicals. Individual computers on the Grid, given the protease structure and the structure of a chemical from ZINC, can calculate the energy of association between the two. Two rounds of screening,

based on separate pieces of software developed at the Scripps Research Institute and Harvard, will allow researchers to identify the chemicals with the highest specificity of binding to the protease. Those chemicals will then be forwarded to biologists, who will determine how well they protect cells from viral infection.

Overall, the project seems like a great way to contribute to a goal that's a bit more concrete than those of other distributed computing projects. It's also a great demonstration of how essential information sharing is to scientific progress, as the project leverages a combination of data, software, and open information from many individuals and institutions.

The University Of Nottingham In The British Midlands Announces Development Of Possible Hepatitis C Vaccine

http://www.medicalnewstoday.com

The British Midlands Development Corporation announced that the University of Nottingham in the British Midlands has released a statement promoting the development of a possible Hepatitis C Vaccine.

The United Kingdom is home to Europe's largest biotechnology sector, generating revenues in excess of $8.6 billion per year. In central England is the British Midlands region, which is at the heart of the UK's biopharma and medical device industries.

The British Midlands is one of Europe's premier locations for the advancement of medicine and life sciences. All of the region's 18 universities have unique areas of scientific expertise, which fuel the region's record of innovation in the field.

Some of the twentieth century's most important innovations in medicine took shape in the British Midlands. Magnetic resonance imaging (MRI) was invented by The University of Nottingham's Sir Peter Mansfield. The Birmingham Children's Hospital leads the field in treatments for congenital heart disease and developed the world's smallest successful heart pacemaker in a three-day old infant.

Just last week, another potential breakthrough was announced by the British Midlands' University of Nottingham, which released a statemet claiming the discovery of a possible vaccine which can be used in the treatment of Hepatitis C.

Dr. Alexander Tarr, a Research Fellow at Nottingham's Institute of Infection, Immunity and Inflammation, presented a paper titled 'Human Antibodies to Hepatitis C Virus - Potential for Vaccine Design', at the Society for General Microbiology's 161st meeting which was held at The University of Edinburgh two weeks ago.

The research group had recently analyzed antibodies that can successfully prevent infection with many diverse strains of Hepatitis C virus in laboratory models.

Dr. Tarr made a statement saying, "The clinical potential of this work cannot be overstated. Historically, successful vaccines against viruses have required the production of antibodies, and

this is likely to be the case for Hepatitis C virus. Identifying regions of the virus that are able to induce broadly reactive neutralizing antibodies is a significant milestone in the development of a HCV vaccine, which will have distinct healthcare benefits for hepatitis sufferers, and could also help us design vaccines for other chronic viral diseases such as HIV."

"We are also currently exploring the possibility of improving liver transplantation success rates by passively infusing people with these antibodies," said Dr. Tarr, "Additionally we are using the information gained by identifying and characterizing the antibody responses to Hepatitis C virus to design new ways of making vaccine candidates. If the antibodies we have discovered can be reproduced by vaccination, control of the disease might be possible."

The Hepatitis C virus affects over 180 million people worldwide. Infection with the virus can lead to liver cancer, and is the most common reason for liver transplantation in the United States and the United Kingdom.

About The British Midlands Development Corporation
The British Midlands Development Corporation is the North American economic development agency for central England. The Midlands region is located just one hour north of London and includes the major commercial centers of Birmingham, Nottingham, Coventry and Northampton.

As an agency funded by the UK Government, The British Midlands Development Corporation provides specialist advice and support to North American companies seeking to establish a presence or expand a current operation in the region. The British Midlands Development Corporation provides access to business networks, details about sources for grants and funding, business support services, and information to help companies identify opportunities to develop and grow.

The British Midlands Development Corporation is based in Chicago with branch offices in Boston, Washington DC and San Jose.

For more information, please visit our website at http://www.thebritishmidlands.com

The British Midlands Development Corporation
http://www.thebritishmidlands.com

Liver Cancer Marker Could Yield Blood Test For Early Detection

http://www.sciencedaily.com/
Source: American Association for Cancer Research

Science Daily — In the face of an emerging liver cancer crisis in Asia, researchers at the Chinese University of Hong Kong have developed a test that could help millions.

Due to widespread hepatitis B virus (HBV) infection, nearly 10 percent of China's population is at high risk for hepatocellular carcinoma (HCC), a liver cancer with low survival rates if not detected and treated early.

Researchers report on a new blood screening technique that could make it possible to detect early-stage liver cancer and predict how well a patient will do following treatment. They present their data September 18 at the American Association for Cancer Research's Second International Conference on Molecular Diagnostics in Cancer Therapeutic Development, in Atlanta, Georgia.

According to their report, the Chinese team has detected an altered version of RASSF1A, a tumor suppressing gene, in the blood of HCC patients and in 58 percent of HBV-infected test subjects. Healthy subjects showed no signs of the altered gene. They also found that patients treated for HCC with high blood levels of the gene were more likely to have a relapse of the disease.

"A large portion of the population throughout Hong Kong and China are carriers of hepatitis B, so many people are at risk for hepatocellular carcinoma," said K.C. Allen Chan, MBBS a professor at the Chinese University of Hong Kong. "And we hope that this will form the basis of an effective clinical test for early detection of hepatocellular carcinoma."

Hepatocellular carcinoma is one of the deadliest forms of cancer in China and throughout Asia, according to the researchers. In the West, liver cancer is usually a secondary cancer, caused by the spread of tumor cells from elsewhere in the body. In China, however, liver cancer mainly manifests as HCC, a primary cancer, which has been linked to hepatitis B and C infection and cirrhosis. Noticeable symptoms do not usually appear until the cancer has progressed, so it is rarely caught early, when intervention would be most effective, and survival rates are typically low, said Chan.

Currently, ultrasound and CT scans are the gold standard for detecting HCC. However, they are too expensive to be an effective mass screening tool, the researchers said. About 70 percent of patients exhibit a detectable increase in bloodstream amounts of alphafetoprotein, but a screen for this protein would miss many potential patients. "We need a new biomarker for hepatocellular carcinoma, something that can be used to screen large populations of at-risk people for follow-up studies," Chan said.

RASSF1A is a good candidate, according to Chan. Researchers have known that the DNA of HCC tumor cells lack a functioning copy of RASSF1A. In these cells, RASSF1A is "hypermethylated," meaning the RASSF1A gene has been physically altered by cancer-related processes that added clusters of carbon and hydrogen atoms, called methyl groups, to portions of the DNA within the gene. Hypermethylation is epigenetic -- the gene is altered by environmental circumstances and is not inherited. Since the cell's protein making system can't access the gene, hypermethylation effectively knocks out the tumor-suppressing RASSF1A gene, which is then unable to stop cells from becoming cancerous.

While hypermethylated RASSF1A would make a useful biomarker for HCC, methylation-specific PCR -- the polymerase chain reaction used to specifically amplify and detect methylated DNA -- destroys about 85 to 93 percent of the DNA in a blood sample. Together with the fact that tumoral DNA is only present at very low concentrations in blood during early stages of HCC, this method has not been sensitive enough to detected altered RASSF1A in blood for the purpose of early cancer detection, Chan said.

To compensate, Chan and his colleagues invented a new technique that they call "methylation-sensitive enzyme-mediated real-time PCR," which combines real-time PCR, a technique that enables researchers to simultaneously detect and amplify a given gene, with an enzyme that breaks unmethylated DNA apart. With this new technique, Chan's team was able to separate out the altered methylated DNA, thus developing a more sensitive technique for detecting and quantifying hypermethylated RASSF1A derived from cancer cells in blood.

To test the relationship between altered RASSF1A and HCC -- as well as test the new detection technique -- Chan and his colleagues conducted two studies involving HCC patients. In the first, they matched 63 pairs of patients, one with HCC and the other a chronic HBV carrier by age and sex, along with 30 healthy volunteers. They detected hypermethylated RASSF1A in 93 percent of the HCC patients, 58 percent of the HBV carriers and none of the healthy patients. The median RASSF1A levels for the HCC patients were 770 copies per milliliter and 118 copies per milliliter for HBV carriers.

"The respective levels of the gene for HCC patients and HBV carriers, is consistent with what we already know about the progression of the disease," Chan said. "The gene is altered very early in the procession of malignant transformation, and so we can see that the levels of the altered gene increase as the cancer process progresses."

In the second study, the researchers looked at 22 pairs of sex- and age-matched patients who had been enrolled in a HCC surveillance program involving 1018 HBV carriers. For the 22 HBV carriers who subsequently developed HCC, there was a significant increase in circulating RASSF1A levels from the time of enrollment to the time of cancer diagnosis. On the contrary, there was no significant change in RASSF1A levels over the same period for the 22 matched subjects enrolled in the same program who didn't develop HCC.

"As we refine the process of detecting hypermethylated RASSF1A, we hope to have a functioning test for hepatocellular carcinoma," Chan said. "A significant number of people will develop this cancer and it is only through early screening and detection that we can hope to help them."

Note: This story has been adapted from a news release issued by American Association for Cancer Research.

What Baby Boomers, Seniors Need to Know About Hepatitis C

http://www.associatedcontent.com
By Pamela Green

The Virus May Be Lurking in a Liver Near You

According to the Center for Disease Control, more than four million people in the United States have hepatitis C; that's more than five times as many people infected with HIV. And in article, Newsweek's senior medical editor Geoffrey Cowley wrote, "Now thousands of people are getting sick. By 2010, it may strike down more Americans each year than AIDS."
Through the fall of 2001, a wave of us across America received a life changing letter from the

American Red Cross informing us that the blood we donated after 9/11 tested positive for the hepatitis C virus (HCV). Discovered in 1988, the virus invisibly incubates in the liver for decades possibly causing cirrhosis, cancer, and liver failure. Or one can live their lives never knowing they have the disease. Boomers are being hardest hit, because of the timing, some are learning they have hep C when the get their life insurance physical results.

"Those people who got it in the late 70s, early 80s, are now at the point where that five percent (of the four million with HCV) is showing up. Death rates are going to increase because those people who have been marching along, are now hitting the time where they're at risk of death," noted Dr. Fredric Gordon, liver transplantation director at Lahey Clinic in Burlington, Mass.

It wasn't until 1992 that blood used for transfusions was tested for the presence of HCV, putting those who had transfusions or organ transplants before then at risk. Since then, new cases of the disease have declined. However, keeping in mind that the virus takes twenty or more years to become symptomatic, if at all, that takes those most at risk back to the 70s.

It was an era of an emerging counter culture. People were protesting the Vietnam War, experimenting with intravenous drug use, and living communally sharing peace, love, toothbrushes, razors, and nail clippers, creating opportunities for the virus to spread. According to Dr. Gordon, hepatitis C can live for four days in the blood residue left on shared surfaces. Sharing syringes with an HCV infected person may have shot the virus directly into the veins.

After the stunning events of 9/11, many of us functioned in a state of numbness. Despite the brilliant sunlight illuminating the fiery reds, oranges and yellows of the leaves on an autumn New England day, my view of the world had become a two dimensional display of muted shades of gray. My melancholy mist enveloped me for weeks.

Relenting, admitting that this sadness wasn't going anywhere soon, I took the anti-depressant my doctor prescribed. Looking back, the pills were a layer of protection against the deep depression that was a possible side effect of the then experimental drug cocktail I would take to treat hep C.

After I learned about my infection, I began researching on the Internet. I stumbled onto a new test that measures the virus' activity in the body. I called the manufacturer and got the name and phone number of the sales person for my area. He told me about another drug, Pegasys, his company had in clinical trials to treat the disease and gave me the names of doctors at hospitals conducting studies. That conversation created the sequence of divinely guided steps of a journey that changed my spiritual perceptions, physical being, and marital status.

From February through March 2002, I was blood tested, liver biopsied and introduced to a hospital culture previously unknown to me and with which I became intimately familiar. On April 12, with my then husband and list of questions, I met my doctor to review the results.

Smart, highly regarded, and impeccably dressed, he stood at a white board, explaining numbers to us with diagrams and charts that he drew with dry markers. Sitting down, Dr. Gordon said that the disease had damaged my liver, but because it scars and deteriorates the tissue slowly, I would probably die of something unrelated to HCV. However, I would still have this virus loitering in my liver. The numbers showed scarring and required monitoring or I could pursue treatment - the

choice was mine.

A proactive patient, I continued researching, contacting experts to get their opinion of Pegasys. After sharing the gathered information with my doctor, I asked for his input. The side effects range from none, mild flu-like symptoms or most unpleasant, including hair loss, fatigue, depression, suicidal thoughts, and anemia. (After I started, the drug study nurse told me that due to side effects 15 to 20 percent dropout). At twelve-week intervals, tests would determine if the drugs were working and if so, I would continue taking them for another 12 and then, 24 weeks. If the results continued to show no viral detection, I would take the drugs for a total of 48 weeks - a long time. Leaving Lahey, my head throbbed from so much information. I had to decide - to treat, or not to treat.

Like a comforter that's been around for years, lovingly stitched together in places that had ripped apart, my marriage was frayed. Because of his job, my husband was often absent. I wrote for a newspaper part-time, while caring for our son, Sam, and taking him to his seasonal athletic games and practices.

With grandparents in Florida, no family nearby except for a few close friends, who would be there for him during the next 48 weeks if the side effects were extreme? Who would be there for me? Bombarding myself with questions for days, I got my answer one night on the tag of an herbal tea bag, "Now is the time, the time is now." I pay attention to those kinds of messages. Evaluating the circumstances, I knew that at 48 years old, my healing abilities were ebbing away with age, I had a superb doctor, and knowing I would eventually treat; I decided that the time was now.

My chiropractor found an immune building regimen of vitamins and herbal supplements, which I began taking after clearing them with Dr. Gordon. Further study of alternative medical treatments naturally led me to the guru of integrative medicine, Dr. Andrew Weil. While reading *Spontaneous Healing,* I learned he didn't favor the chemotherapy-like treatment for HCV. However, toward the end of the book, I found Weil's Seven Strategies of Successful Patients. Number six was to "regard illness as a gift."

Weil wrote, "Because illness can be such a powerful stimulus to change, perhaps the only thing that can force some people to resolve their deepest conflicts, successful patients often come to regard it as the greatest opportunity they have ever had for personal growth and development - truly a gift." I re-read that sentence throughout my treatment and it became my rallying cry for a period in my life that I refer to as Revolution #6.

On Friday, June 14, 2002, I injected myself with the first weekly dose of Pegasys. Along with the daily doses of ribaviron, the internal pharmaceutical war began. The battle included weekly, then monthly trips south on Route 3 to Burlington to meet with the study nurse, answer the drug company's study questionnaire rating my side-effects, and then sit in the large waiting room where they draw blood, until I hear my name being called. The entire spectrum of American society sat in that room. From well dressed to threadbare, people of all ages and degrees of healthiness waited - some in wheelchairs with clear thin plastic tubes taped to their noses. If the Democratic National Committee continues its quest for a more diversified primary than New Hampshire's, they should have it in that phlebotomy waiting room.

As I have done throughout my life, I kept a journal. After the first five weeks, I wrote, "It is so foreign and frightening to feel like this. Is it good that I do? Are the drugs working? Is this just the massive initial attack on the virus and then things will settle into a steady simmer?

"Walking up or down steps makes me dizzy and out of breath. Standing too long makes me break into a sweat. My body is here and my mind is floating over there. I may look and sound normal, cognitively astute, but I assure you, mentally I am in a thick fog. My brain is a big cotton ball."

On Sunday of the seventh week, I seriously contemplated quitting the study. Nauseous, achy, and mentally disjointed, I was in emotional turmoil and during a tearful telephone conversation with my father; he encouraged me to hang in there.

"Anxiety envelops me. Red patches of psoriasis cover my body, my hair is falling out, and the ebb and flow of energy makes me feel like a dog on a choke chain, just about to run. Start, stop, start, stop. I removed my jewelry. There is no desire for adornment. In fact, I wish I could function invisibly," I wrote.

Fatigued, I read Neale Donald Walsch's *Conversations with God*. The trilogy contains God's responses to Walsch's questions. God told him, "I am always with you, in all ways." According to Walsch, all I had to do was start the conversation, pay attention, and God's response comes in the next song I hear, movie I see, or tea bag tag I read. In those days of isolation, I had many silent conversations."

On September 29, 2002, a huge crowd of 150,000 protesters in London held signs, "Don't Attack Iraq." Our government's war chatter grew louder and seemingly, a simultaneous transmission of Thunderclap Newman's song, "Something in the Air," reached the planet: "Call out the instigators/Because there's something in the air/We've got to get together sooner or later/Because the revolution's here, and you know it's...right/And you know that it's right/We have got to get it together/We have got to get it together...Now".

My qualitative and quantitative numbers in October showed that the drugs were working, so despite the fatigue, constant sadness, and physical maladies, I continued the treatment, writing, "I am withering. I feel ugly and am spiritually depleted. I summon energy for my Revolution #6 and remind myself to regard illness as a gift, while wondering if my marriage will survive this ordeal.

"Bill is gone again and I have to take Sam to basketball tryouts. Some people have two or three chins. I have three eyelids. They are so swollen that when I blink, the skin rolls under the next soft rounded layer. The skin under my eyes is dry, flaky, and reptilian textured - no more eye make-up for me. Barry Reynold's song, "I Scare Myself" comes to mind."

When I walked into the crowded gym with Sam, I saw the other parents whom I knew from years of Sam's participation in different seasonal sports. Although no one said a thing, I felt the penetrating visual examinations. It was the most psychologically uncomfortable moment I'd experienced since starting this process. Dying inside, I wanted to hide. But this wasn't about me - it was about the promise I made to myself to keep Sam's life as routine as possible.

Always self-sufficient, for Sam's sake I learned how to ask for help. After dropping him off for basketball or soccer practices at night, his coaches kindly brought him home. Exhausted, I got into bed and read or meditated until Sam returned. During this time, I refused to think of myself as a victim. I saw myself as a pioneer in the search of a cure for hep C, consciously choosing hope instead of anger at my circumstances. Lying in bed alone again, I tried to figure out what to do with these feelings of being a leper. The message came that I am not my body - I am my soul.

The dying leaves and shorter spans of sunlight signaled it was time to prepare for hibernation during the harsh New England winter. As the drugs seeped further into my body, my mental clarity and ability to breathe decreased. An asthma inhaler was added to my medications. Like a whale diving deep below the surface of the sea for long periods of time, I was going under and there was nothing I could do except go with the flow.

I found solace in music. It became my lifeline. Hearing it reassured me that there was still someone inside able to hear sound and make a connection with the notes. Rhythmically, Peter Gabriel, Paul Simon, and Pete Townsend fanned my flickering flames. In Rosanna Arquette's documentary about music, All We Are Saying, she interviewed many artists including punk priestess, Patti Smith, who said, "Music is such a powerful force. Music is the only way ... that collectively, we all can understand. Music can heal."

Echoing that concept, Sting noted, "It's a kind of religion and religion essentially is about reconnecting. Music is one of the ways we can connect with the world of spirit, with something I don't even pretend to understand. But I know it's there, and I know it's very important to people on the planet." Amen.

A new year, a new phase of this drug induced state. I'm being sucked dry from the inside, starting from my head. I just thought it was time for new glasses, however, after scanning my eye, the doctor said it was so dry that the surface of the cornea was cratered - a condition called viral keratitus. I started using viscous eye drops that when dry, created spider-like webs in my eyelashes.

My dry lips required frequent chap stick applications. I put together a hydration bag filled with saline nasal spray, hand lotion, lip balm, and eye drops. Wearing it over my shoulder, so that the thin strap crossed my chest and back, the bag went everywhere with me as I crept around the house. I wondered how many other lab rats in this study were experiencing similar reactions.

Watching me succumb to the effects of the drugs, Sam was having a tough time emotionally and acting out in school. Wondering whether it was puberty or the fact that his father is rarely around and his mother has become a female version of Ozzie Osbourne, complete with unsure movements and spaciness, I sent an e-mail to his teachers explaining the current circumstances and enlisted their help - it takes a village.

Heavy hearted, I woke up at six a.m. one morning to get Sam ready for school. Bill was in Rochester and then heading to Utica. It's cold, Sam is unhappy with me because I questioned him about the television being on before he was fully ready for school. After reading our agreement regarding morning television, he retorted, "Dad let's me." Great....

After Sam left, I sat downstairs in the living room, put my headphones on, and listened to Pete Townshend sing, "Let my love open the door." All I have to say is, 'come on in'. I looked at my name printed in the magazine's masthead listing me as assistant editor. I recall driving around town interviewing people, writing articles on deadline, and happily reading the published results. Where is that woman? Where is the energy that allowed me to function? Where's my hair?

"A permanent tint of what looks like diluted dried blood colors my eyelids and a dark smudge defines the area between my eyes and cheeks. Fluids of varying thickness seep from the openings in my face. I must constantly peer into a mirror to clean the dried excess of lubricating drops required to ease the viral keratitus that resides in my eyes or the dried skin around my nostrils and lips.

Peter Gabriel sings, "...in your eyes/the light the heat/in your eyes/I am complete..." I can't imagine what people see in my eyes. When I stand in front of the mirror, two dull, lifeless eyes look back at a woman I no longer know. "I am not the person I was...perhaps a good thing - a new Pam in the making. I am Frankenstina," reads a February journal entry.

Cold came in from every seam of the house. Usually, I put the storm windows in and although it is painfully apparent that it would have reduced the cold, I just didn't have the energy. Bill isn't around enough to notice the temperature. I felt so wasteful, knowing that we could have done more to insulate, saving precious energy.

I missed the Sonoran desert and the intense heat of the sun that I left behind years ago to be with Bill on the East Coast. The effort to will the warmth and serenity I felt in Tucson eluded me. And so I curled into a ball under blankets in my bed listening to Hot Tuna play, "Sunny Day Strut," an instrumental piece that makes my soul soar - until it ends.

Reduced to a blubbering mass of molecules, I allow myself to wallow in the frustration of my limitations. It's not a frequent indulgence. Today however, despite the emptiness in my heart, I am full of tears, and my body is numb from the cold that surrounds me. A tornado of sadness swirls inside. Removed from the living, I forced myself to write through the physical fatigue and mental haze. Paul Simon sings, "Why deny the obvious, child?" Resisting is futile.

As January ends, the war drums were beating. The Buffalo Springfield song "For What it's Worth" an anthem of the 60s, resonates with relevance today: "There's somethin' happening here/What it is ain't exactly clear/There's a man with a gun over there/Tellin' me I gotta beware/I think it's time we stop/Hey, what's that sound/Everybody look what's going down." Gathered in cities around the world people protested the possibility of war. This administration has provided only rhetoric, no substance, and no evidence to justify a preemptive strike. It's insanity.

The first virtual antiwar demonstration on February 26, 2003 allowed me to join the protest from my bed. The e-mail from moveon.org asked us to call our Congressional representatives and one Senate leader. Although alone, I felt like I was a part of something.

The meditation for March in my *One Spirit Book of Days* is the Energizing Shower, appropriate considering my dried insides. Sitting, breathing deeply, "...imagine cleansing spring water pouring into the crown of your head, flowing deep into your being, and then pouring out through

your feet..." Mentally my parched insides soak in the imaginary water like a sponge - making me momentarily moist like ripe fruit.

Opening my eyes, I was still the being that required hydration for my eyes, nose, and cracked, cold sore marred lips. I swished L-Glutamine inside my mouth, a non-essential amino acid that my drug study nurse suggested, to get rid of the sores on the sides and bottom of my tongue. Then for the next half an hour, I grab tissue after tissue, catching the fluids that flowed from eye sockets, nasal cavity, and mouth. Charming.

Seven more weeks on these wacky drugs. I think back to the encouraging phone call from my father on the seventh week at the beginning of this treatment. Like a desert cactus, this lab rat has learned to survive on so little and for that I am grateful. I no longer hoped for warmth from my husband, who checked out emotionally, long ago. Physically depleted, there is nothing I can do. Accept, accept, accept.

From my journal, "Mornings begin with muscle spasms, banging headaches and feeling like I am moving through mud. With five weeks left, mental clarity eludes me, tiredness envelops me, and yet, sleep denies me. I sustain myself with hugs from Sam, and my silent conversations with God, whose responses I know when I see or hear them."

On May 16, 2003, I took my final shot. Although proud of myself for finishing the trial, I felt like I was sitting at the bottom of a ravine rubbing my throbbing head trying to figure out how I got there and with a groan, looked at the terrain I had to climb to get back to level ground.

Within months, Bill asked for a separation and moved to an apartment. I cried, nodded, and stepped aside, believing that everything happens for a reason. My heart was broken, but I blessed his decision, because isn't that what love does?

I spent the summer recuperating physically and emotionally. As part of rebuilding my obliterated immune system, essential in strengthening a body's defense against illness, I went back to Spontaneous Healing. The book opened to the page marked with a worn, bright pink post it. Seeing "6. REGARD ILLNESS AS A GIFT," I closed my eyes, took a deep breath, and silently chanted my mantra. When I opened them, my eyes fell on: "5. DO NOT HESITATE TO MAKE RADICAL LIFE CHANGES."

Continuing, I read, "Many of the successful patients I have known are not the same people they were at the onset of illness. Their search for healing made them aware that they had to make significant changes in their lives: changes in relationships, jobs, places of residence, diet... In retrospect, they see these changes as steps that were necessary to personal growth, but at the time, the process was wrenching. Change is always difficult; major change can be very painful. Illness often forces us to look at issues and conflicts in their lives that we have ignored in the hope that they would disappear. Continuing to ignore them may block any possibility of spontaneous healing, while willingness to change may be a strong predictor of success." Hmmmm.

Healing has been a turbulent journey, including counseling and drugs for Sam, then 16, and me. After nearly a year of minimal human contact, I made my social re-entry by getting involved in

New Hampshire's first-in-the-nation-presidential primary, ultimately becoming the New Hampshire correspondence director of retired General Wesley Clark's campaign.

Bill took a second chance on marriage with his first love from high school. The once white walls in our house, the only color Bill allowed, were repainted with colors of the desert. Sam is growing into a kind, responsible human being, and together we share a love of Matisyahu's music. Performing music described as Hasidic reggae, Matisyahu's songs are soul inspiring and great for dancing. I heard "King without a Crown" on the radio a couple weeks before leaving for a Caribbean vacation and was stunned by the joy and hope that I felt in his music.

It was my first vacation as a single woman - my celebration of survival. The island sun sparked my sputtering spirit; life pulsated through me as I danced to reggae rhythms in the crowded beach bars. It was my bon voyage to the diminishing dissonant note of disease and treatment. Although relevant to the whole song, its tonal contributions are muted in relation to the barely perceptible sound of the next note. I endured and am able to physically and emotionally function in the world again. Still wobbly, I am getting stronger and surer of who I am becoming.

Evidenced by four media mentions since September 25, 2006, news of hep C is seeping into our cultural mainstream. Steven Tyler, lead singer of Aerosmith, announced that three years ago he was diagnosed and treated for hepatitis C. Stan Miller, a 51-year-old news anchor for Channel 8 in San Diego was talking about the disease and treatment on the air,[1] and in my mind, the most significant reference was in the opening of the October 29 episode of Desperate Housewives when Susan describes Edie as, "Just a neighbor. She visits Mike after her hepatitis C treatments." [2]

I recently had a physical and the blood test revealed that after four years, I remain hep C free. The disease is real and many people are living their lives unaware that this insidious virus is lurking in their liver, silently scarring its healthy tissue. A simple blood test confirms its presence and like many other diseases, early detection is critical as it may prevent the catastrophic need for a liver transplant. Get tested and if positive, you will have to decide to treat or not to treat. And the beat goes on.

[1]http://www.signonsandiego.com/uniontrib/20061021/news_7m21bell.html

[2] http://dynamic.abc.go.com/streaming/landing, 7:40/43:03

New film puts hepatitis C in the picture

http://www.nursinginpractice.com

A powerful new film to raise awareness of hepatitis C and how to avoid it among prisoners, and encourage those at risk to get tested, was previewed on Monday at the annual Health Protection Agency Conference.

Created by the Department of Health, the film provides a gritty insight into the virus including how it can be transmitted, with a particular focus on the risks of intravenous drug use. With estimates showing that more than 50% of prisoners have a history of using drugs, the film aims

to educate a crucial audience with a high potential risk of being infected.

Hepatitis C patients, including those with a prison background, explain what the virus is, its varied transmission routes, and how it can be diagnosed and treated. Their real-life testimonials are interspersed with dramatised scenes of the impact of the virus in a prison setting.

Vicky Putt, public health improvement specialist for prisons and NW Health prisons co-ordinator, said: "This film will be an essential resource for prison health professionals, drug teams and education staff involved in educating prisoners on this critical health issue. The film has been tested in a variety of prisons and feedback from prisoners and staff has been overwhelmingly positive. Getting to this audience is always going to be tough but using patient stories with a realistic portrayal of the prison environment appears to be effective in engaging the prison population."

It is estimated that around 200,000 people in England have hepatitis C and of this number, the majority are probably unaware of their condition. Testing "at-risk" people as well as carefully managing those already diagnosed is essential to reducing the prevalence of the disease and ensuring that those infected have access to treatment.

Launched in December 2004, the Department of Health's hepatitis C awareness campaign "FaCe It"aims to raise awareness of the virus and its prevention, diagnosis and treatment, while tackling the stigma often attached to it.

Further information on hepatitis C is available on the website, which can be found at www.hepc.nhs.uk . The film is expected to be distributed to all prisons across England towards the end of the year.

September 19th, 2007

Research from Metabasis Therapeutics, Inc. yields new data on hepatitis C virus therapy

http://www.newsrx.com

(NewsRx.com) -- A report, "Liver-targeted prodrugs of 2'-C-methyladenosine for therapy of hepatitis C virus infection," is newly published data in *Journal of Medicinal Chemistry*.

According to recent research from the United States, "2'-C-Methyladenosine exhibits impressive inhibitory activity in the cell-based hepatitis C virus (HCV) subgenomic replicon assay, by virtue of intracellular conversion to the corresponding nucleoside triphosphate (NTP) and inhibition of NS5B RNA-dependent RNA polymerase (RdRp). However, rapid degradation by adenosine deaminase (ADA) limits its overall therapeutic potential."

"To reduce ADA-mediated deamination, we prepared cyclic 1-aryl-1,3-propanyl prodrugs of the corresponding nucleoside monophosphate (NMP), anticipating cytochrome P450 3A-mediated oxidative cleavage to the NMP in hepatocytes. Lead compounds identified in a primary rat hepatocyte screen were shown to result in liver levels of NTP predictive of efficacy after intravenous dosing to rats. The oral bioavailability of the initial lead was below 5%; therefore,

additional analogues were synthesized and screened for liver NTP levels after oral administration to rats," wrote S.J. Hecker and colleagues, Metabasis Therapeutics, Inc.

The researchers concluded: "Addition of a 2',3'-carbonate prodrug moiety proved to be a successful strategy, and the 1-(4-pyridyl)-1,3-propanyl prodrug containing a 2',3'-carbonate moiety displayed oral bioavailability of 39%."

Hecker and colleagues published their study in the *Journal of Medicinal Chemistry* (Liver-targeted prodrugs of 2'-C-methyladenosine for therapy of hepatitis C virus infection. Journal of Medicinal Chemistry, 2007;50(16):3891-6).

For additional information, contact S.J. Hecker, Metabasis Therapeutics, Inc., Departments of Biochemistry and Medicinal Chemistry, 11119 North Torrey Pines Road, La Jolla, CA 92037 USA..

Publisher contact information for the *Journal of Medicinal Chemistry* is: American Chemical Society, 1155 16th St., NW, Washington, DC 20036, USA.

This article was prepared by NewsRx editors from staff and other reports.

CEL-SCI Presents Data for CEL-1000 as a Vaccine Adjuvant with Recombinant Hepatitis B Virus Protein

http://biz.yahoo.com

VIENNA, Va., Sept. 19 /PRNewswire-FirstCall/ -- CEL-SCI Corporation (Amex: CVM - News) announces that its CEL-1000 immunomodulator was shown to be able to jump start the immune response against the recombinant hepatitis B virus protein more quickly than did other vaccine adjuvants. This effect in the mouse model was seen within 14 days, most pronounced with a single dose of CEL-1000 at day 0 and resulted in up to a 40% increase in antibody signal at day 28. Also, the timing of the CEL-1000 administration had significant impact on the type of immune response that was created, as well as its strength.

The significance of this data lies in the fact that CEL-1000 appears to be able to mount a faster immune response, something that is absolutely necessary for a bio defense or a pandemic flu setting, as well as the potential ability to create more effective immune responses through the use of CEL-1000 as an adjuvant. The data were presented by Dr. Daniel H. Zimmerman, Senior Vice President of Research, Cellular Immunology at CEL-SCI and involved a collaboration with scientists at several other institutions including Drs. Kenneth S. Rosenthal Professor of Microbiology and Immunology at Northeastern Ohio Universities Colleges of Medicine and Pharmacy (NEOUCOM), Rootstown, Ohio, Frank Klotz of Biocon, Rockville, Maryland, Peter Blackburn and Steve Grimes of Mercia-Pharma, New York. The data were presented at the 47rd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Chicago, Illinois.

Dr. Zimmerman said, "These findings are important not just for our CEL- 1000 adjuvant, but also for any adjuvant because our work has shown that the timing of the use of the adjuvant and

how often it is given have significant influence on the type and strength of the immune responses elicited."

In challenge studies, CEL-1000 has also previously been shown to protect animals against infection against viruses and unrelated diseases, specifically herpes simplex virus, viral encephalitis and malaria.

CEL-1000 appears to activate innate (very early stage) and Th1 type (cellular) immune responses to induce a broad-spectrum protection against infection in animal models. The innate immune system is generally accepted to be the first line of defense against infectious agents.

CEL-1000, derived from the beta chain of human MHC-II, is a modified version of a human immune-based protein known to bind to both human and mouse immune cells and appears to act by enhancing the host's protective immune response.

About CEL-SCI Corporation:
CEL-SCI Corporation is developing products that empower immune defenses. Its lead product is Multikine®. In Phase II clinical trials Multikine was shown to be safe and well-tolerated, and to improve the patients' overall survival by 33% at a median of three and a half years following surgery. The U.S. Food and Drug Administration (FDA) gave the go-ahead for a Phase III clinical trial with Multikine in January 2007 and granted orphan drug status to Multikine in the neoadjuvant therapy of squamous cell carcinoma (cancer) of the head and neck in May 2007.

Multikine, a patented defined mixture of naturally derived cytokines, is the first immunotherapeutic agent in a new class of drugs called "Immune SIMULATORS". Immune SIMULATORS simulate the way our natural immune system acts in defending us against cancer. As opposed to other immunotherapies which are designed to target a single or limited number of specific antigens or molecules, Immune SIMULATORS are multi-targeted; they simultaneously cause a direct and targeted killing of the specific tumor cells and they activate the immune system to produce a stronger anti-tumor attack on multiple fronts.

Multikine is also the first immunotherapeutic agent being developed as a first-line standard of care treatment for cancer. It is administered prior to any other cancer therapy because that is the period when the anti-tumor immune response can still be fully activated. Once the patient has advanced disease, or had surgery or has received radiation and/or chemotherapy, the immune system is severely weakened and is less able to mount an effective anti-tumor immune response. Other immunotherapies are administered after the patient has received chemotherapy and/or radiation therapy, which can limit their effectiveness.

The Company has operations in Vienna, Virginia and Baltimore, Maryland. CEL-SCI's other products, which are currently in pre-clinical stage, have shown protection against a number of diseases in animal tests and are being tested against diseases associated with bio-defense and avian flu.

Source: CEL-SCI Corporation

Dynavax's HEPLISAV(TM) Hepatitis B Vaccine Maintains Full Immunogenicity at 50 Weeks in Phase 3 Trial

http://www.examiner.com/

BERKELEY, Calif. (Map) - Dynavax Technologies Corporation (Nasdaq: DVAX) announced today that the seroprotection of HEPLISAV at 50 weeks after the first vaccination remained at 100% while the seroprotection of the comparator, GlaxoSmithKline's Engerix-B(R); vaccine declined.

The data show that after three doses, HEPLISAV provided seroprotection (anti-HBsAg antibodies greater than or equal to 10 mIU/mL) to 100% of subjects versus 68.6% for Engerix-B ($p < 0.0001$) as measured at 50 weeks.

These data were reported in a poster at the 47th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Chicago, IL. Primary endpoint data from this Phase 3 study in a difficult-to-immunize population of older adults were reported in November, 2006. The primary endpoint is seroprotection four weeks after the third vaccination.

According to Eduardo Martins, M.D., D.Phil., Vice President, Clinical Development, "These results demonstrate HEPLISAV's long-term superior immunogenicity over conventional hepatitis B vaccine as measured at 50 weeks. These data confirm earlier clinical studies showing that HEPLISAV has superior immunogenicity and comparable tolerability to Engerix-B. The overall results suggest that HEPLISAV elicits a faster immune response, higher rates of seroprotection and a more durable immune response than conventional vaccine."

The Phase 3 trial enrolled more than 400 seronegative subjects, 40 to 70 years of age, at study sites in Singapore, Korea and the Philippines. One group of subjects received three doses of Dynavax's HBV vaccine; the other group received three doses of Engerix-B.

Dynavax reported in mid-July 2007, that an international Phase 3 trial in Europe and Canada had completed enrollment. Data from the pivotal Phase 3 trial plus lot-to-lot consistency trials will contribute to a safety database of approximately 4,000 subjects for a planned BLA submission in 2008. Dynavax's HBV vaccine is based on its proprietary immunostimulatory sequence (ISS) that specifically targets Toll-Like Receptor 9 (TLR9) to stimulate an innate immune response. Dynavax's HBV vaccine combines ISS with HBV surface antigen (HBsAg) and is designed to significantly enhance the level, speed and longevity of protection. Dynavax indicates that as a result of its acquisition of Rhein Biotech in April 2006, the company has secured manufacturing capabilities in Dusseldorf, Germany for producing both clinical and initial commercial quantities of the hepatitis B surface antigen component of the vaccine.

About Dynavax
Dynavax Technologies Corporation discovers, develops, and intends to commercialize innovative TLR9 agonist-based products to treat and prevent infectious diseases, allergies, cancer, and chronic inflammatory diseases using versatile, proprietary approaches that alter immune system responses in highly specific ways. Our TLR9 agonists are based on immunostimulatory sequences, or ISS, which are short DNA sequences that enhance the ability of the immune system to fight disease and control chronic inflammation. Our product candidates

include: HEPLISAV, a hepatitis B vaccine in Phase 3; TOLAMBA(TM), a ragweed allergy immunotherapy; a therapy for non-Hodgkin's lymphoma (NHL) in Phase 2 and for metastatic colorectal cancer in Phase 1; and a therapy for hepatitis B also in Phase 1. Our preclinical asthma and COPD program is partnered with AstraZeneca. The National Institutes of Health (NIH) partially funds our preclinical work on a vaccine for influenza. Symphony Dynamo, Inc. (SDI) funds our colorectal cancer trials and our preclinical hepatitis C therapeutic program. While the NIH and SDI provide program support, Dynavax has retained rights to seek strategic partners for future development and commercialization. For more information, please visit http://www.dynavax.com.

This press release contains forward-looking statements that are subject to a number of risks and uncertainties, including statements about clinical trials for HEPLISAV, the potential timing of the planned HEPLISAV BLA submission and the superiority of HEPLISAV. Actual results may differ materially from those set forth in this press release due to the risks and uncertainties inherent in our business, including difficulties or delays in development, initiation and completion of clinical trials, the results of clinical trials and the impact of those results on the initiation and completion of subsequent trials and issues arising in the regulatory process; achieving our collaborative and licensing agreement objectives and obtaining regulatory approval; the scope and validity of patent protection and the possibility of claims against us based on the patent rights of others; our ability to obtain additional financing to support our operations; and other risks detailed in the "Risk Factors" section of our Quarterly Report on Form 10-Q. We undertake no obligation to revise or update information herein to reflect events or circumstances in the future, even if new information becomes available.

September 21st, 2007

Roche puts hold development of hepatitis drug MAXY-alpha - US partner Maxygen

http://money.cnn.com

ZURICH, Sep. 21, 2007 (Thomson Financial delivered by Newstex) -- Roche Holdings AG has put a hold on further clinical development of MAXY-alpha, a treatment for hepatitis C and B virus infections, the Swiss pharma giant's US partner Maxygen Inc (NASDAQ:MAXY) said.

During a phase I trial MAXY-alpha was shown to be less effective in the majority of patients who received two doses of the drug. Roche is currently assessing those results, Maxygen said in a statement.

Russell Howard, Maxygens chief executive officer, said he was surprised by the findings, adding: We dont yet know how this will impact the future timing or advancement of the program.'

Roche was not immediately available for comment.

In March, Roche and Maxygen ended part of their partnership on developing products to treat uncontrolled bleeding, but said collaboration would continue on developing treatments for hepatitis B and C.

Congress OKs Drug Safety Bill

http://www.therapeuticsdaily.com/

WASHINGTON_Congress sent President Bush legislation Thursday giving the Food and Drug Administration new powers to ensure the safety of prescription drugs.

The Senate passed the FDA bill by voice vote Thursday, a day after the House approved it by an overwhelming margin. Bush is expected to sign the bill.

Broadly, the bill renews for five years two programs to collect fees from drug and medical device manufacturers to defray the FDA's expense in reviewing products seeking agency approval. The FDA had warned if the fees programs were not renewed by Friday, it would be forced to begin sending layoff notices to nearly 2,000 of its employees. That now appears unlikely.

Legislators used the bill as a vehicle to add to the FDA's powers to police drug safety – a response to the withdrawal of the painkiller Vioxx three years ago.

"This bill will meet the challenges of protecting American consumers and patients and usher in a new era of drug safety," said Sen. Mike Enzi, R-Wyo.

While the FDA's focus traditionally has been on the approval of new drugs, its handling of emerging problems with Vioxx and other drugs already on the market has earned it sharp criticism in recent years.

The bill would give the FDA the power both to require drug companies to further study the safety of medicines if needed and to mandate new label warnings, when problems do appear. The FDA would be able to fine companies to ensure compliance with those two new authorities. The legislation also would require companies to publicly release results of all clinical trials that show how well their drugs performed, although the level of disclosure remains to be determined.

The FDA also would gain the ability to fine drug companies for not completing follow-up studies on their drugs after they've won government approval. Those studies now often remain undone, often leaving important safety questions unanswered.

"This important bill should give every American greater peace of mind every single day – every time we eat, take our medicine or see our doctor," said Sen. Edward M. Kennedy, D-Mass.

The bill calls for drug companies to pay $393 million, and medical device makers $48 million, in fees next year.

The legislation also would force the FDA to further step up its active surveillance for new safety issues with drugs. That system traditionally has been largely passive. The manufacturers of certain new drugs would have to draft for each a so-called "Risk Evaluation and Mitigation Strategy" that can include medication guides distributed with each prescription to ensure the medicine's safe use.

On food, the bill calls for the setting up of a registry to log incidents where adulterated food could pose a health risk. It also would require the FDA to set pet food ingredient and processing standards – a provision born of the massive dog and cat food recalls of earlier this year.

FDA Commissioner Andrew C. von Eschenbach said in a statement that the agency was pleased Congress had approved the bill, which he said reauthorized programs that were "vitally important to the agency and its continued ability to protect and promote the public health."

The trade association representing the drug industry, the Pharmaceutical Research and Manufacturers of America, called passage of the bill "a crucial step to make our nation's drug safety system – which already is the best in the world – even better."

ICAAC: Cross-resistance to 3TC and FTC develops slowly with entecavir monotherapy

www.aidsmap.com
Derek Thaczuk

Resistance to FTC and 3TC emerges slowly and does not occur in all HIV-positive patients if they are exposed to the hepatitis B drug entecavir (Baraclude) when not taking anti-HIV therapy, researchers reported this week at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy in Chicago.

Entecavir is a nucleoside analogue drug (a guanosine analogue) used as an antiviral treatment for hepatitis B. As entecavir was originally thought to have selective activity against hepatitis B virus (HBV) polymerase only, it has been the recommended therapy for HBV treatment in people with HIV-HBV coinfection.

However, a research team from the Johns Hopkins University School of Medicine recently reported that entecavir is also an inhibitor of HIV reverse transcriptase (RT), after observing HIV viral load drops in coinfected patients who began entecavir treatment.

In some such patients, entecavir use has selected for the M184V mutation in HIV, conferring cross-resistance to 3TC (lamivudine) and FTC (emtricitabine). The manufacturer Bristol-Myers Squibb has issued a press release and added a black box warning to the package insert regarding this danger.

In their presentation this week, the same group of Johns Hopkins researchers further investigated the evolution of drug resistant HIV in HBV-HIV co-infected patients who took entecavir monotherapy. HIV variants were obtained and sequenced for phylogenetic analysis using RT-PCR and cloning. The phylogenetic analysis documented the emergence of the M184V mutation associated with 3TC and FTC resistance in the HIV reverse transcriptase (RT) gene in these patients.

Dose response showed that, above a certain point, increasing plasma concentrations of entecavir do not result in increased anti-HIV effect. The significance is that entecavir is, at best, a partial inhibitor of HIV, creating selective pressure and a favourable environment for HIV resistance to

develop, even at high entecavir concentrations.

In the in vitro studies, significant minority viral populations with the M184V mutation emerged after 92 days of culture and grew to half the viral population by 180 days.

In vitro studies suggested that, compared to wild-type HIV, virus with the M184V mutation has only a modest advantage in replicative fitness at entecavir concentrations that would be encountered in clinical use (Cmax, 30 nM).

The researchers suggest that "this may not only explain why the M184V mutation arises slowly in vitro but also why some patients, after several months of entecavir monotherapy, do not have the M184V mutation." They also suggest that different cellular factors affect the viral response to entecavir.

The study team concluded that "these data provide an explanation for the variable rate at which M184V variants emerge in patients on entecavir monotherapy[,] highlight the clinical significance of the anti-HIV activity by entecavir and provide a basis for understanding the evolution of drug resistant HIV in patients taking entecavir."

Reference

McMahon MA et al. Evolution of drug resistant HIV-1 variants during monotherapy with the hepatitis B drug entecavir. 47th Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, abstract H1018, 2007.