



## Hepatitis B Research Leads to New Clues About Virus Progression

### Findings Show Significant Association Between Cirrhosis and Lower/Inactive Disease Activity

In search of factors that may help predict the course of chronic hepatitis B (HBV), California Pacific's Hepatology and Gastroenterology Research Program, in conjunction with Japan's Nagoya City University Medical School, recently conducted a retrospective study to determine virologic and non-virologic factors associated with disease severity.

The study of 84 treatment-naïve patients showed that, contrary to the team's assumptions, cirrhosis negatively influences viral replication and attributes to lower levels of liver inflammation. Of the 48 cirrhotic patients studied (equally divided among Asians and non-Asians), 47% were HBV DNA negative (<2 pg/ml). In contrast, only 20% of the non-cirrhotic patients were HBV DNA negative. Patients excluded from the study include those co-infected with hepatitis C and/or HIV, alcoholics and those previously treated with lamivudine or interferon.

"While additional studies are needed to collaborate our findings, this research may ultimately have implications on the treatment regimen for cirrhotic patients with HBV," says Shahram Javaheri, M.D., a gastroenterology fellow with California Pacific's Hepatology and Gastroenterology Research Program. "Because our findings showed a significant association with cirrhosis and negative HBV DNA, they suggest it may not be necessary to treat patients with Stage 4 cirrhosis if viral replication has already ceased."

The Hepatology Research Team also analyzed the duration of HBV

Fibrosis Stage (biopsy)	Non-cirrhotics	Cirrhotics	P value
<b>N (%)</b>	36 (44)	48 (56)	N/A
<b>Mean ALT</b>	88	85	0.66
<b>HBV DNA negative</b>	20%	47%	0.009*
Disease Activity (Inflammation):			
Active1	47%	33%	0.05**
Active2	33%	21%	
Active3	17%	27%	
Inactive	3%	19%	

\* Among non-cirrhotics, 10% of Asians vs 50% of non-Asians had a negative DNA (p=0.0124); Among the cirrhotics, 58% of Asians vs 33% of non-Asians had a negative DNA (p=0.0822).

\*\*Sub-Analysis of disease activity by stage of disease in Asians, controlling for duration of disease (where duration is presumed to equal age): this observation remains significant (p=0.003).

infection in both cirrhotics and non-cirrhotics to determine its effect on disease activity, with no correlation found between the two factors. Thus, a negative DNA level is not simply due to disease burn-out over time. A similar analysis of the correlation between genotype distribution and cirrhosis showed no significant association.



California Pacific  
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**Seeking men and women 18 years and older with at least 3 months of persistent or recurrent meal-related upper stomach problems.**

**Study:** Tegaserod at three different doses (4mg, 12mg or 24mg) versus placebo in patients with functional dyspepsia (FD) and documented delayed gastric emptying

If you have patients who may be appropriate for this trial, contact Sylvia Borgonovo, RN, at (415) 600-1110 or borgons@sutterhealth.org.

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## Clinical Research Uncovers New Liver Disease and Gastroenterology Therapies



California Pacific's Hepatology and Gastroenterology Research Team includes: (back row from left) Linda Brooks, R.N., Robert Gish, M.D., Micheal Shaffer, Ed Wakil, M.D., Natalie Bzowej, M.D., Ph.D., Peggy Newsom, R.N. (front row) Ohnmar Chan, Annaliza Roque, Anna VonBakonyi, LVN and Sylvia Borgonovo, R.N.

Playing an integral part in the search for better viral hepatitis, hepatocellular carcinoma and gastroenterology therapies, California Pacific's Hepatology and Gastroenterology Research Program currently has more than 100 patients participating in clinical trials at five Northern California locations.

"Our research efforts are a major component of our Liver Program and have contributed to the development of new hepatitis C therapies that have broken through the overall 50% HCV cure rate," explains Ed Wakil, M.D., associate medical director of California Pacific's Liver Disease Management & Transplant Program. "In addition to our clinical research, we are fundraising for an immunology laboratory to study the science behind hepatitis C mutations, the role of T cells, autoimmune hepatitis and other factors that will ultimately provide fertile ground for future discoveries," he adds.

In existence for a decade, the Hepatology and Gastroenterology Research Program has grown significantly in recent years, with eleven full-time staff supporting research efforts at locations in San Francisco, Oakland, Sacramento, Eureka and San Jose.

### Clinical Trial Enrollment

Information on California Pacific's hepatology and gastroenterology trials is frequently sent to physicians and accessible online at [www.cpmc.org/liver](http://www.cpmc.org/liver) under the "research/trials" link.

"Typically, physicians will call the study coordinator of a trial if they have a possible candidate or we will hear from friends of patients who themselves want to participate," says Linda Brooks, R.N., clinical research nurse. "Ultimately, though, we want to hear from a patient directly to make sure the interest is there," she adds.

After receiving further information about the study, a patient will have his or her medical records sent to the research team for review. If the patient meets the pre-screening parameters, a screening visit is scheduled.

"We review the consent form and describe the study procedures, as well as take blood tests during the screening visit," says Brooks. "Consent is the most important part of the study process and we want to make sure patients thoroughly and completely understand their rights and responsibilities." Typically, about 90% of the patients screened for a particular trial are enrolled.

Throughout the clinical trial, patients have regular clinic visits to review the effect of study medication(s), any side effects or illnesses, and to receive blood tests. Most of the studies last for one year and follow-up continues one to six months after the treatment has ended.

"While patients are enrolled in a study, we are continuously reviewing their lab results and progress to examine the treatment's effect and safety," says Wakil. "We are also carefully monitoring for side effects and keeping up-to-date on new information regarding the study drug."

### Research Team Overview

The Hepatology and Gastroenterology Research staff includes four research nurses who are responsible for conducting their particular studies within the Institutional Review Board (IRB) guidelines. A principal investigator—either Robert Gish, M.D., Ed Wakil, M.D. or Natalie Bzowej, M.D., Ph.D.—oversees the trials, traveling to outreach locations for research clinic visits. The team also includes staff fluent in Chinese and Burmese, with translators available for other languages.

"Our patients are introduced to all research team members at the onset of their participation in a clinical trial, and we consider ourselves a team, of which they are part," says Brooks. "Because we interact so closely with patients for a year or more, I develop a little separation anxiety at the end of a study!"

For further information on research trials open for enrollment, visit [www.cpmc.org/liver](http://www.cpmc.org/liver) or contact the Hepatology and Gastroenterology Research Program at (415) 600-1100.



# Hepatology and Gastroenterology Trials Seeking Enrollment

Following is a listing of our Hepatology and Gastroenterology Research clinical trials open for enrollment. If you or a patient are interested in any of these studies, please contact the coordinator listed for further details. Trials with more than one coordinator listed indicate that they are available at an outreach site(s) as well.

Multiple gastroenterology studies are also in development and will be offered in the near future. These studies, which include the use of a new capsule for viewing the intestines in place of endoscopy, Lanreotide for patients with liver disease and gastrointestinal bleeding, and a virtual colonoscopy comparison study will be listed on our Web site as they begin enrollment. Please complete the enclosed card if you wish to be included on our mailing list.

## Hepatitis B

- 1) A phase 3 study of the safety and antiviral activity of Entecavir vs Lamivudine in adult patients with chronic hepatitis B who are positive for hepatitis E antigen
  - Seeking HBV-infected patients with compensated liver disease
  - Treatment lasts 52 weeks with either Lamivudine or Entecavir
  - Pretreatment biopsy required

**Coordinator: Peggy Newsom, R.N. (415) 600-1109; email newsomp@sutterhealth.org**
- 2) A phase 3 study of the safety and antiviral activity of Entecavir vs Lamivudine in adult patients with chronic hepatitis B who are negative for hepatitis E antigen
  - Seeking HBV-infected patients with compensated liver disease
  - Treatment lasts 52 weeks with either Lamivudine or Entecavir
  - Pretreatment biopsy required

**Coordinator: Peggy Newsom, R.N. (415) 600-1109; email newsomp@sutterhealth.org**
- 3) A phase 3 study of the safety and antiviral activity of Entecavir vs Lamivudine in adult patients with chronic hepatitis B who are with incomplete response to current Lamivudine therapy
  - Seeking HBV-infected patients with compensated liver disease and continuing current Lamivudine therapy
  - Treatment lasts 52 weeks with Lamivudine vs Entecavir, plus possible rollover after 52 weeks to combination therapy
  - Pretreatment biopsy required. Participants need to be eAg+ and DNA+

**Coordinator: Peggy Newsom, R.N. (415) 600-1109; email newsomp@sutterhealth.org**
- 4) A phase 1-2 ascending dose evaluation of safety, pharmacokinetics and antiviral activity of a new oral treatment for naïve hepatitis B
  - Seeking HBV-infected patients with compensated liver disease and DNA >100,000 on Roche Amplicor Assay
  - Treatment includes 14 days of therapy and 1 follow-up visit
  - Eligible for phase 2 - 3 trials of the same drug

**Coordinator: Peggy Newsom, R.N. (415) 600-1109; email newsomp@sutterhealth.org**

## Hepatitis C

- 1) An open-label study of Pegasys vs Pegasys plus Ribavirin treatment in hepatitis C patients (WINGS)
  - Seeking treatment naïve and previously treated patients. Must have compensated liver disease with elevated ALT
  - Treatment includes 48 weeks of treatment with 24 weeks of follow-up

**Coordinator: Sylvia Borgonovo, R.N. (415) 600-1110; email borgons@sutterhealth.org**
- 2) Comparison of PEG Interferon with Ribavirin, with or without induction of Intron® A twice a day for 2 weeks for treatment of adult subjects with chronic hepatitis C who failed previous treatment with Interferon
  - Seeking patients with compensated liver disease and elevated ALT
  - Treatment lasts 48 weeks with 24 weeks of follow-up
  - Patients randomized to receive either induction of Intron 5 MU injection twice a day with Ribavirin daily by mouth or PEG-IFN injection weekly with Ribavirin daily by mouth
  - Ribavirin only provided; physician-initiated trial

**Coordinator: Anna VonBakonyi, LVN (415) 600-1107; email vonbaka@sutterhealth.org**  
**Sacramento Coordinator: Mary Hyland, R.N. and Bev Stafford, R.N. (916) 443-0503**
- 3) Comparison of PEG Interferon alfa-2b with Ribavirin given as a fixed dose or on a weight optimized basis for treatment of chronic hepatitis C in previously untreated adult patients
  - Seeking patients with chronic HCV who are naïve to previous therapy
  - Treatment lasts 48 weeks with 24 weeks of follow-up
  - Ribavirin only provided; physician-initiated trial

**Coordinator: Anna VonBakonyi, LVN (415) 600-1107; email vonbaka@sutterhealth.org**  
**East Bay Coordinator: Rosemary Diaz, LVN (510) 208-1777; email eastbayliver@inetmail.att.net**  
**Eureka Coordinator: Loretta Swenson, R.N. (707) 445-9015; email swensol@sutterhealth.org**  
**Sacramento Coordinator: Mary Hyland, R.N. and Bev Stafford, R.N. (916) 443-0503**
- 4) Interferon alfa 2b with induction dosing plus Ribavirin vs standard combination Interferon alfa 2b plus Ribavirin for treatment naïve patients with hepatitis C
  - Seeking patients with HCV who are naïve to previous therapy
  - Treatment lasts 24 or 48 weeks depending on viral genotype with 24 weeks of follow-up

**Coordinator: Rosemary Diaz, LVN (510) 208-1777; email eastbayliver@inetmail.att.net**

- 5) Chronic hepatitis C coinfecting with HIV naïve to Interferon therapy
  - Seeking patients with HCV and HIV coinfection with compensated liver disease and elevated ALT
  - Must have stable HIV and HCV treatment
  - Treatment arms: 1) PEG-IFN + Ribavirin; 2) PEG-IFN + Placebo; 3) Roferon 3 MU TIW + Ribavirin
  - Patients need to have undergone liver biopsy within one year prior to trial start
  - Treatment lasts 48 weeks with 24 weeks of follow-up.

**Coordinator: Sylvia Borgonovo, R.N. (415) 600-1110; email borgons@sutterhealth.org**

## Hepatocellular Carcinoma

- 1) Trial of Zadaxin with transarterial chemoembolization in patients with unresectable hepatocellular carcinoma (HCC)
  - Seeking patients with documented HCC that is unresectable and non-transplantable
  - Moderately compensated liver disease and adequate renal function
  - Treatment consists of chemoembolization with or without Zadaxin therapy for six months

**Coordinator: Sylvia Borgonovo, R.N. (415) 600-1110; email borgons@sutterhealth.org**

## Future Protocols

### Hepatitis C

- Procrit vs placebo to maintain hemoglobin for patients on Interferon + Ribavirin or PEG Interferon + Ribavirin
- Thymosin vs placebo + Pegasys for non-responders; 48 weeks of therapy with 24 weeks of follow-up
- Non-responder to Rebetrone with fibrosis F2 Metavir Score will receive optimal PEG Intron + Rebetrone. Non-responders to this therapy go to one of two long-term studies, PEG-Intron vs Silymarin as maintenance treatment
- Gamma interferon for severe fibrosis or compensated cirrhosis. Non-responders to alfa interferon or alfa interferon contraindicated

### Non-Ulcer Dyspepsia

- Tegaserod at three different doses vs placebo for non-ulcer dyspepsia with delayed gastric emptying

**For the status of these projects call Linda Brooks, R.N. (415) 600-1106; email brooksl@sutterhealth.org**

### Research Staff

<b>San Francisco</b>	(415) 600-1100
<b>Coordinators:</b> Linda Brooks, R.N.	(415) 600-1106
Anna VonBakonyi, LVN	(415) 600-1107
Peggy Newsom, R.N.	(415) 600-1109
Sylvia Borgonovo, R.N.	(415) 600-1110

<b>East Bay</b>	
<b>Coordinator:</b> Rosemary Diaz, LVN	(510) 208-1777

<b>Sacramento</b>	
<b>Coordinators:</b> Mary Hyland, R.N.	(916) 443-0503
Bev Stafford, R.N.	(916) 443-0503

<b>Eureka</b>	
<b>Coordinator:</b> Loretta Swenson, R.N.	(707) 445-9015

<b>San Jose</b>	
<b>Coordinator:</b> Peggy Newsom, R.N.	(415) 600-1109

## Outreach Clinics Offer Clinical Trials in Local Communities

With outreach sites in the East Bay, Sacramento, Eureka and San Jose offering HBV and HCV clinical trials, patients from throughout Northern California can participate in California Pacific's Hepatology Research Program close to home. "Convenience is a factor in clinical trials, and by offering studies in various locations, we are hoping to attract a greater number of patients," says Robert Gish, M.D., medical director.

Numerous trial locations can also offer the opportunity to draw more ethnic diversity. This diversity is especially important when researching treatment for viruses such as HBV that have a high incidence among Asians. "We maintain a database of patients interested in trials—and are always soliciting new patients—so even if one doesn't qualify for a particular study, we can notify them in the future," says Grant Young of the East Bay Liver Clinic. For trial information or details on our outreach sites, contact the location nearest you:

### OUTREACH SITES FOR HEPATOLOGY TRIALS

East Bay Coordinator:	Rosemary Diaz, LVN	(510) 208-1777
Sacramento Coordinators:	Mary Hyland, R.N.	(916) 443-0503
	Bev Stafford, R.N.	(916) 443-0503
Eureka Coordinator:	Loretta Swenson, R.N.	(707) 445-9015
San Jose Coordinator:	Peggy Newsom, R.N.	(415) 600-1109
San Francisco:	Linda Brooks, R.N.	(415) 600-1100

### HEPATOLOGY AND GASTROENTEROLOGY TRIAL SITES



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