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BC's Hepatitis C News Bulletin

"Promoting HCV Wellness"

November 1996

DAVE'S COLUMN

by David Smith

Last November I was invited to attend the first annual general meeting (AGM) in Toronto. Not knowing anyone, I was feeling quite unsure of myself, and besides that, I had only been post-transplant about 3 months, and I was still suffering from post-traumatic symptoms. However, I had been assured that my presence was required, and that I would be able to contribute to the proceedings. Well, folks, this is my call to you.

The AGM is being brought to Victoria because we are the biggest and best organized Hep C support group in the country. This is why we have been chosen to host the AGM, so let's all of us endeavor to make it a memorable event for everyone.

We have a core group of 35 to 40 members who attend our regular monthly meetings, and we have about 120 to 130 others who are on our mailing list. Some of you are paid up national members, and perhaps some of you aren't currently aware of your status in this regard. Remember, if we want to get things done with respect to recognition of our disease on a national level, then we must realize that we are more that just a local support group, but that we are also a national body, worthy of recognition and respect for what we endure physically, psychologically, and spiritually, regardless of how we acquired the disease. Look at what the AIDS coalition has done in the last 15 years, and there are 10 times as many transfused Hep C victims (I shudder to use that word) as there are HIV.

So let's look at making the best show possible for our group and have as many people attend the proceeding possible. This is a way of having our group take a collective look at itself and to see its potential as a force capable of making changes to the Health Care System and to how diseases of this nature are viewed by the general public.

What is this AGM about? It is being held at Royal Roads University on the 8th and 9th of November. We will have meetings of the board members, general meetings, workshops, guest speakers, and nominations and elections of the new National board. As well, we'll have lunch and dinner on both days, and on the Saturday we will have a string quartet serenade us at dinner, and then afterwards we will have a dance. Yes, a *dance*. I think it's about time we cast aside our doom and gloom, as well as our chairs, and had some fun. So, as well as taking care of business, we will also do a fair amount of socializing.

There will be many people coming from as far away as the east coast and the states, as well. Not including our own group, there is an estimated 35-40 people coming from else where, and by the beginning of November, there may be many more.

So we'll be phoning you, our members, around Nov. 1st, to get an estimate on how many will be coming. See you there!

The deadline for any contributions to next issue of hepc.bull is November 23rd. Please contact Joan Diemecke at Tel. 479-5290.

MEMBERSHIP DESK

In this issue there are details of the AGM being hosted by the Victoria Chapter, here at Royal Roads University on Nov. 8th. and 9th./96. Please make note, because members of HeCSS in good standing, (in possession of a current membership card issued by Toronto office) who plan on attending, will be able to enjoy some benefits. Enclosed with this issue is a Membership Application form, used for New and Renewal Membership, which, on completion and mailed to the Toronto office, will ensure your being a paid-up member in good standing. It is even more important now that we rally together as members in good standing to give more emphasis when delivering submissions to the likes of both Federal

and Provincial Public Health Ministries, applications for funding, etc. Please give this matter some thought to help us, your steering committee, in being able to wield more clout. Please attend to it today. I look forward to meeting you at the AGM

I also want to say a big thank you to my fellow co-chair-persons, committee members and the number of volunteers who have attended to the running of the Support Group while I have been away this last three months. I'm happy to say that as of today all my record keeping is up to date, thanks to your diligence and attention to details. Makes doing this job so much easier. Thanks.

Reminder:- Any change of address, phone number, (area codes have been changed where necessary), or postal code, please let me know at your earliest. Thanks.

Jim Lodge 386-8227
Co-chairperson, Membership Chair

FREE PCR and GENOTYPING?

Here's something some of you might wish to investigate further. Please inform us of any further information that comes from your research. This comes from the Internet, from a fax from Jeremiah Donovan, University Of Nebraska Medical Center - home, by the way, of the Liver Transplant Foundation set up by the Redfords(as in Robert, the actor, etc.) - His numbers are: 402-559-4938, and fax: 402-559-6132)

"...I would suggest that rather than using Univ. of Washington (which is a good lab, I agree) there is a better way to go....I would suggest that you do a PCR and Genotype at National Genetics. I have two reasons as to why I say they are better:

1. They were involved in the clinical trials of Roferon, and consensus interferon. Their lab seems to be very well run and they have a very large reference number of patients to draw from. With regards to their PCR technique they do a quantitative assay that is accurate to 100 copies/ml.

2. Also, they will not bill you or me for the test, but rather have recently been bought by Schering (20%) and this allows them to use a write off system, that if they can bill your insurance, they will, but if they can't, then they bill Schering's patient assistance program. They will do genotyping .... (On the phone he had confirmed that it was the 'Commitment To Care' program from Schering.)"

The numbers for **National Genetics** are:

Toll Free Help Line:
888-4NGI LAB (888-464-4522)
Toll Free Fax:
888-PCR TEST (888-727-8378)
or Mail To:
National Genetics Institute
(attn: Jack Barritt - for shipment of blood samples in dry ice)
5839 Green Valley Circle, Suite 104
Culver City, CA, USA 90230

HOWEVER...National Genetics confirmed ...that they are NOT the people to contact.

The "Commitment To Care" forms should be filled out by the physician's practice (or in this case UNMC) for pre-approval of the free testing.

"Commitment to Care" has a toll free 800 number at:
1-800-521-7157

(Note: the 800 number for CARE in Canada is 1-800-363-3422 Ext. 2000)

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NEW HOPE

An article appeared in Friday's Wall Street Journal announcing that Vertex Pharmaceuticals and Agouron Pharmaceuticals both announced separately that they had identified the protein structure crucial to the reproduction of the HCV virus. "The starting gun has been fired and the race has begun" says Vertex CEO Joshua Boger. If the protease (protein molecule) is disabled, the hepatitis virus would be unable to reproduce itself and, scientists hope, the disease would be cured. Identifying a hepatitis C drug will now take at least two or three years of intensive research, Vertex and Agouron said. The prize "an effective drug could rack up $2 billion to $3 billion a year in sales."

Vertex Pharmaceuticals Researchers Report Three-Dimensional Structure of Hepatitis C Protease Enzyme
Cambridge, MA, October 18, 1996 -- Researchers from Vertex Pharmaceuticals Incorporated
have solved the three-dimensional atomic structure of the hepatitis C virus NS3 protease, an enzyme that plays a key role

in viral replication. The achievement is described in a paper, "Crystal Structure of the Hepatitis C Virus NS3 Protease Domain Complexed with a Synthetic NS4A Cofactor Peptide," published in the 18 October 1996 issue of the journal *Cell*.

The publication follows the first presentation of the hepatitis C protease structure by Vertex at the 36th Interscience Conference on Antimicrobial Agents and Chemo-therapy (ICAAC) held 16 September 1996. Vertex is using the structural information to design hepatitis C protease inhibitors as new antiviral drugs to treat hepatitis C infection.

(The article goes on to give basic information and statistics about hepatitis C.)

"The NS3 protease of hepatitis C plays a fundamental role in the replication of virus, similar in function to the role that HIV protease plays for the HIV virus, and therefore represents a key target for therapeutic intervention," said Dr. Vicki Sato, Senior Vice President of Research and Development and Chief Scientific Officer of Vertex. "Our experience and success in designing VX-478, a potent, well-tolerated and orally administered HIV protease inhibitor in Phase II clinical trials, make us well-positioned to undertake the challenge of designing a protease inhibitor to treat hepatitis C infection."

Vertex scientists determined the three-dimensional structure of hepatitis C NS3 protease complexed to part of another protein in the viral genome, NS4A, using X-ray crystallography. This biophysical technique determines accurately the position of every atom of the complex. Vertex used X-ray diffraction data with the aid of supercomputer-based modeling and computational techniques to construct a high-resolution (2.5 Angstroms) electron density map of the complex. The map locates the active site of the enzyme, as well as details of the architecture of the NS3/NS4A complex, and the location of a tightly bound metal ion that is important for the enzyme's activity.

"One of the most interesting features of the structure is that NS3 wraps around its cofactor protein, NS4A, in a manner that stabilizes the complex. This architecture explains a wealth of biochemical data characterizing the interaction between the two proteins," said Vertex crystallographer, Dr. Joseph Kim. "In addition, our structural analysis reveals that there is a bound zinc ion located away from active site. This structural element also appears important for enzyme stability and activity."

Dr. John Thomson, Vertex Senior Scientist and Project Head - Hepatitis Research, added, "The structure of the hepatitis C NS3 protease shows, in atomic detail, several unique features of this enzyme that we believe will provide opportunities to accelerate our ongoing efforts to design a potent and specific compound against hepatitis C."

AGOURON SCIENTISTS SOLVE STRUCTURE OF FOURTH VIRAL TARGET: HEPATITIS C PROTEASE

LA JOLLA, Calif., October 18, 1996 - Agouron Pharmaceuticals,Inc., (Nasdaq-NM: AGPH) today announced that its scientists have solved the three-dimensional atomic structure of the protease enzyme encoded by the human hepatitis C virus (HCV). HCV is a virus that causes illness that ranges from a mild flu-like disease to progressive liver disease, cirrhosis and primary liver cancer. Solution of the HCV protease structure opens the way to the design of a new class of anti-viral drugs that block the HCV protease and disrupt the HCV life cycle.

The solution by Agouron scientists of the NS3 protease structure from HCV at a resolution of 2.4 Angstroms was reported in today's issue of the scientific journal Cell, Vol. 87, No. 2. The HCV protease is the fourth viral protease structure to be solved over a period of six years by Agouron scientific teams consisting of molecular biologists, protein biochemists and protein crystallographers. An Agouron research team solved the structure of the HIV protease in 1990.

VIRACEPT (nelfinavir mesylate), an Agouron anti-HIV drug now in pivotal clinical trials was designed on the basis of the HIV protease structure. In 1994, an Agouron scientific team solved the structure of the 3C protease enzyme from rhinovirus--the most frequent cause of the common cold. Agouron is now carrying out pre-clinical evaluation and optimization of several potent rhinovirus protease inhibitors and intends to commence development of one such compound in 1997.

Six weeks ago, Agouron scientists reported their solution of the structure of the protease encoded by cytomegalovirus (CMV)--a virus that causes degeneration of vision in immuno-compromised patients. A major program to design specific inhibitors of the CMV protease is now in progress at Agouron. Agouron is conducting development of Viracept, as well as design of inhibitors of proteases from CMV and HCV in collaboration with the pharmaceutical division of Japan Tobacco Inc. (JT).

"With the structure of the HCV protease in hand, we know of no other company in the pharmaceutical industry in possession of so deep and diversified a structural data base covering proteases as anti-viral drug targets," said Peter Johnson, Agouron's president and chief executive officer. "As a result we expect that Viracept will ultimately prove to be only the first of a series of viral protease inhibitors from Agouron that make important contributions to anti-viral therapy."

NOTE:

CALENDAR OF EVENTS:

HeCCS NATIONAL ANNUAL GENERAL MEETING

Victoria has the honor of hosting this important event. The dates are **November 8th and 9th,** at **Royal Roads**. Please mark your calendars now. There will be a dinner/dance the evening of November 9th. More information will be included in your next phone committee message.

NEXT MEETING: Wednesday, November 20, 1996

1 - 3 PM, and again at 7-9 PM
St. John the Divine ChurchLounge
1611 Quadra St.
Our guest speaker will be Arnold Porter, who will talk about acupressure and the liver meridians.
(Entrance through the rear, marked Annex)

COORDINATING COMMITTEE -- VICTORIA CHAPTER

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