Reaching for the Cure

PBC Connections

A Canadian PBC Society Newsletter

SUMMER 2009

YOUR DONATIONS PUT TO WORK!

'Thank you,' from the Liver Clinic at Toronto Western Hospital.

The very generous donation from the PBC Society, as always, will greatly facilitate our studies on the genetics of Primary Biliary Cirrhosis. This support will be put towards our "Family Studies in PBC" study database. Our longtime goal to have a clinical database on patients with PBC is now approaching reality. Dr. Teru Kumagi (Hepatologist from Japan) and Dr. Nadia Al-Harthy (Fellow from Oman) played a key role in collating routine clinical data for all patients with PBC who attend/attended the Liver Clinic in Toronto. Our goal now is to collect the clinical data for all participants in the Genetics study.

Your generous donation will be used to collate routine clinical information from the collaborating centers.

Eventually we hope to publish another important paper on PBC and its cause. This work, as before, is so dependent on our patients and their generosity.

If you have PBC and you are interested in participating in a study, you can always contact Barbara Badstober, by email, at pbcsociety@yahoo.ca

Dr Gideon Hirschfield accepting the cheque from Barbara

Dr. Teru Kumagi & Dr. Nadia Al-Harthy

UNRAVELING THE GENETIC BASIS OF PRIMARY BILIARY CIRRHOSIS

Katherine Siminovitch,MD,FRCPC
Mount Sinai Hospital/University Health Network

The fundamental causes of PBC are unknown, but genetic factors play key roles in development of this autoimmune disease. Until relatively recently, identification of the genes conferring risk for PBC has been frustrated by lack of sufficiently powerful gene discovery tools. This situation changed dramatically with completion of the Human Genome Project, an achievement that provided unprecedented gains in knowledge and technology that have made it possible to identify the genetic causes of even the most complex diseases.

Capitalizing on these new technical capabilities, our group embarked upon a search for PBC risk genes. This endeavor began about six years ago with an invitation to PBC patients from across this country and to their physicians to participate in our project. Since then, over 700 individuals with PBC have enrolled in this study. This exceptional response from the PBC patient and physician community allowed our group to begin, two years ago, hunting down the genes for PBC. This hunt involved screening genetic (DNA) samples from 500 PBC patients and 800 healthy individuals (controls) with over 300,000 genetic markers. Patients and controls were then compared with respect to their marker profiles.

To our delight, the gene screen was remarkably successful, identifying at least fifteen genetic regions that contribute to risk for PBC. Importantly, three of the very top hits that surfaced from the screen are genes that regulate the immune system, a system with critical roles in development of autoimmune diseases such as PBC. These three genes normally allow our immune cells to make three proteins that work together to help our immune cells fight infection. However, activity of these three proteins needs to be carefully regulated – too much or too little activity of any of the three can unbalance the immune system, potentially causing immune cells to overreact and mistakenly attack cells in the body causing tissue damage and disease. Our screen revealed PBC to be associated with gene variants that likely alter the functions of these proteins in a manner that leads to defective immunity.

Importantly, medicines that target several of the PBC proteins identified in our study are already being tested for treatment of other diseases. Thus, by demonstrating the link between these proteins and PBC, our study paves the way for a new, more effective PBC therapy that will improve outcomes for all PBC patients. Our goal now is to make such therapy a reality. Our results also have a more general significance – providing direct evidence of the potential for genetic screens to impact on clinical management and outcomes of chronic diseases. We will now focus on defining the cell pathways linking PBC risk genes/proteins to disease and on establishing the extent to which available drugs can repair these pathways so as to ameliorate disease. We will also continue our genetic studies so as to pin down all the major genes conferring risk for PBC. This research will therefore require continued recruitment of PBC patients into our study and the development of animal models of PBC that allow selected drugs to be screened for ability to delay or halt disease onset and progression.

Importantly, a project of this scope cannot be carried out by just one or even a few individuals - it takes a village. On behalf of Drs. Gideon Hirschfield and Jenny Heathcote who direct this research with me, I thank the many hepatologists and clinical coordinators across this country, our technologists, statistical analysts and international collaborators, and the Canadian PBC Society, Canadian Institutes for Health Research and Ontario Research Fund for their generosity in participating and supporting our ongoing effort to improve diagnosis, treatment and outcome of PBC.

Volunteers

Help from a Young Friend

When 10-year-old J heard that her aunt had PBC, she wanted to help. When offered an opportunity to support a charity through a school project, J decided to use her new skill at making bead jewellery to raise funds for the Society by selling bracelets and necklaces to her family, friends and classmates.

She also brought a selection to our Woodbine fundraiser, where it proved very popular. Most people left wearing a new piece of jewellery or carrying some intended as gifts. One 92-year-old who received two bracelets loved them so much that she wouldn't take them off.

In total, J raised $380 for the Canadian PBC Society. Thank you, J, for your donation and caring.

We cannot use J's full name because of her age.

Group News

ATLANTIC GROUP

The PBC Atlantic Group ended the year with an informative talk from **Dr. K. Peltekian** on the genetic research project that we participated in. Approximately 20 attended the meeting and we look forward to the possibility of further treatment options being developed based on the findings of this study. PBC note cards were presented as a gift of appreciation for the presentation.

Our bingo bowling will be held in the fall as the previous presentation constituted our June meeting and we do not meet over the summer.

Next meetings:
Sept. 17 and Nov 12, guest speakers to be announced. For further information contact Judi Pemberton at 902.798.5554 or atlantic@pbc-society.ca

ALBERTA

We set the date for the **3rd Annual Fall Barbeque** and Garry and Saule have generously offered to host again:
Saturday, September 19th at 2pm

Any members, from any region, and family and friends, as well as anyone with an interest in PBC, are most welcome. Put this date on your calendars to set it aside and we'll be sure to remind you ahead of time. Garry will have his BBQ and smoker going for meat and fish. Bring a dish to share: an entrée or appetizer or salad or dessert etc. Also bring your own beverages AND a lawn chair.

If you're coming from out of town and need a place to stay let us know and someone will billet you!

For more information contact Shauna, 780-962-6217 or email: vwell@shaw.ca

BRITISH COLUMBIA

The BC group are meeting for a luncheon at 12 noon on **Saturday, September 26th 2009**. **Boathouse Restaurant at The Quayside.** 900 Quayside Drive, New Westminster, BC V3M 6G1, Restaurant Phone: 604.525.3474

If you would like to join us, please contact Kathryn Swift at kswift@shaw.ca or 604-988-4030 to be added to reservation. All are welcome.

Canadian PBC Society

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