



NCRTP-HepC E-Newsletter

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Program Director's message

When I was chosen to become the NCRTP's new Program Director, I knew it would not be an easy job but I also knew that a fantastic amount of work had already been done to make this program highly successful. I believe that the NCRTP's biggest challenge continues to be fostering a transdisciplinary and collaborative approach to research.



While initiatives like our multidisciplinary course and liver clinic visits have broadened our trainees' horizons, we must continue to encourage their explorations into other fields of research. It is not only our trainees who must grow. Even scientists and researchers like myself must remember that our specialties are not mutually exclusive. We must explore the possibilities of collaborative projects and see how we can interweave our research to lead to better results in all facets of hepatitis C research. Furthermore, we should also be leaders in exporting our program structure outside Canada, aiming to develop mutually rewarding collaborations.

The NCRTP's number one goal remains to train students to become high quality researchers. However, all subsequent goals concentrate on fostering a collaborative transdisciplinary network whose ultimate goal is to eliminate the hepatitis C virus.

With a strong team of mentors already in place and with support from our sponsors, I am positive that the NCRTP can continue to grow and more effectively reduce the impact of hepatitis C. I look forward to working with the program over the next 6 years.

Sincerely,
Marc Bilodeau

Former Program Director's message



I am a firm believer that no one should remain in the same capacity for too long and that we must eventually pass the torch to another. This is why I have relinquished directorship of the program to Dr. Marc Bilodeau. Dr. Bilodeau was selected by his peers within the program and I am confident that he will foster its continued growth and further development.

When I first conceived of the NCRTP I never anticipated how overwhelmingly successful it would become. Although we got off to a rocky start with our 2002 grant application being rejected by CIHR, our subsequent application was accepted and we have grown not only in sheer numbers but also personally by leaps and bounds. Over the past 6 years we have added 10 new mentors to our ranks. We have also expanded from an initial 4 trainees to a whopping 24 and have graduated 9 people from the program – the majority of whom have stayed in the field, thereby fulfilling one of the major goals of the strategic training initiatives.

My greatest pride in the program has been the students. I am continuously impressed by their quality and the work they produce. It is extremely fulfilling to see them mature as researchers and know that we have had a direct impact on their growth. Additionally I see that the mentors have all "opened their eyes" to new different approaches and issues. The degree of collaboration between both the mentors and students is just wonderful to observe.

I would like to thank everyone who has made this program a success over the past 6 years. Without your generosity and support, the NCRTP could never have succeeded. I am excited for the program's future growth and look forward to seeing how it will evolve next.

Sincerely,
Jenny Heathcote

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Updated Program Objectives

In November 2008 the NCRTP submitted its application for renewed funding. Dr. Marc Bilodeau prepared the application which explained the NCRTP's procedures, requirements, etc. The application also listed proposed improvements and changes that would be implemented in the program. Included in the application was an updated listing of the program's objectives. They are:

1. To attract and train high quality graduate students (both national and international) to become independent researchers and leaders in the field of hepatitis C
2. To consolidate, enhance, and ensure sustainability of the multidisciplinary approach of the network of mentors and to translate it to trainees, relevant individuals, and the general public
3. To help and support all aspects of HCV research from epidemiology, prevention, infection control, diagnostics, health economics, to vaccine development, viral resistance, immune response, pathogenesis, and psychology
4. To become a central forum for discussion, thinking, and orientation with regards to the political, social, economic and research issues in hepatitis C
5. To build on the now established international recognition of the program by continuing to attract foreign students and experts and to promote international collaborations
6. To eradicate hepatitis C

2009 Trainee Retreat and PAC Meeting

The NCRTP returned to Banff, AB for its 2009 Trainee Retreat and PAC Meeting. From February 27 – 28, members and industry representatives met and discussed program issues and their research. Guest speakers included Dr. Norah Terrault from the University of California, San Francisco, Dr. Peter Singer, an ethicist from the McLaughlin-Rotman Centre for Global Health and Dr. Rudi Balling from Germany's Helmholtz Centre for Infection Research.

Guest lectures:

- "Clinical trial design: relevance to the evaluation of new agents in the treatment of hepatitis C," Dr. Norah Terrault
- "From Lab to Village: Bioethics & Global Health," Dr. Peter Singer
- "The Need for Mathematical Modeling in the study of infectious diseases," Dr. Rudi Balling

The Trainee Retreat was very successful. The trainees decided to play a mini-speed research dating game amongst themselves. (The speed dating game was introduced at the 2008 NCRTP PAC meeting.) Because many trainees were taking part in the *Transdisciplinary Studies in Infectious Disease* class, they spent time discussing their collaborative research projects. Finally, the trainees and administrative coordinator held a brainstorming session to create a



"wish list" of changes and improvements they want implemented in the program.

On the second day of the retreat, trainees met

with mentor Aled Edwards to discuss the real-life implications of pursuing a post-graduate degree.

Afterwards Melanie Kearns, VP of Marketing &

Communications for the Canadian Liver Foundation, held a workshop on Knowledge Translation.



The PAC meeting started off with Dr. Jenny Heathcote reviewing the changes made in the NCRTP-HepC since the program's inception in 2003. The group then went through various aspects of the program including its finances, educational programs, internal challenges, etc. After discussing internal program workings, representatives from Boehringer-Ingelheim, Novartis, Hoffmann-La Roche, Schering-Plough, the Canadian Liver Foundation, and the Public Health Agency of Canada each gave short presentations on what innovations their organizations were pursuing with regards to Hepatitis C research and awareness.

After the PAC meeting, Dr. Terrault gave a talk on "Clinical Trial Design: relevance to the evaluation of new agents in the treatment of hepatitis C." Next, trainees set up their research posters and mentors circulated, anonymously judging the works. Following the poster presentations, Dr. Peter Singer held a discussion entitled, "From Lab to Village: Can life sciences (help) save the world?" Unfortunately due to bad weather, Dr. Rudi Balling was unable to make it to the PAC Meeting. Instead he gave his lecture, "The Need for Mathematical Modeling in the study of Infectious Diseases," via teleconference.

New NC RTP Members

The NC RTP is pleased to welcome its newest members to the program:

- Mohamed Abdel-Hakeem (PhD) University of Montreal Mentor: Dr. Naagla Shoukry
- Amir Mohajerani (PhD) University of Alberta Mentor: Dr. Norm Kneteman
- Mahra Nourbakhsh (PhD) University of Alberta Mentor: Dr. Norm Kneteman
- Patricia Poulin (Post-doc) University of Ottawa Mentor: Dr. Louise Balfour
- Yiming Qian (Masters) University of Ottawa Mentor: Dr. John Pezacki
- Julia Thorpe (Masters) McGill University Mentor: Dr. Marina Klein

The new members were all evaluated and interviewed at the PAC meeting. In addition, Selena Sagan and Jason Grebely received extensions on their student stipends.

Trainee Poster Presentations

Below is a list of the posters that trainees presented at the 2009 PAC meeting.

Name	Abstract Title
Stephen Barry	Elucidating The Mechanism of DNA Unwinding by the HCV Helicase
Christine Cabrera	Differential impact of multiple facets of stigma in men and women living with Hepatitis C
Limin Chen	USP18 promotes HCV replication and blunts the antiviral effect of IFN α in a protease-independent fashion
Ran Chen	Studying of HCV and HBV infections in chimeric mouse model.
Wendong Chen	Population-derived estimates of direct medical costs among late-stage hepatitis C patients with diabetes
Jason Grebely	Partial Protective Immunity Against Hepatitis C Virus Reinfection in Humans
Candice Jackel-Cram	Involvement of Akt in the up-regulation and processing of sterol responsive element binding protein-1 by HCV-3a core protein
Ava John-Baptiste	Improvements in quality of life and work productivity following successful antiviral therapy for chronic hepatitis C virus infection are lasting
Liang-Tzung Lin	Replication of hepatitis C virus in rodent cells deficient in IRF-3/IRF-9 that express putative receptors and co-receptors for the virus
Sonya MacParland	Decreased Interferon Alpha Expression in T Lymphocytes In Vitro Exposed to Wild-Type Hepatitis C Virus
Sandy Pelletier	Natural Killer Cells Activation Following HCV Exposure
Megan Powdrill	Establishment of a Fluorescence Resonance Energy Transfer Based System for the Characterization of Non-Nucleoside Inhibitors of the Hepatitis C Virus NS5b Polymerase
Selena Sagan	Examining the influence of genome structure on siRNA target site accessibility using native hepatitis C virus RNA.
Mohammed Sarhan	CD5 – A Molecule Potentially Mediating Susceptibility of T Lymphocytes to HCV infection
Kenneth Seaman	Proposal of methods for assessing the systemic consequences of mitochondrial alterations caused by HCV
Bahareh Vali	T-Cell Cross-Reactive Recognition of HLA-A2-Restricted HIV-GAG: SLYNTVATL And HCV-NS5B: ALYDVVSKL Epitopes
Sarah Welbourn	Investigation of a role for lysine residues in NS2/3 and NS2 degradation and hepatitis C virus assembly
Li Zhao	Dendritic Cells Can Kill T Cells During Chronic HCV Infection

2009 Award Winners



The following trainees won prizes at the NC RTP PAC and the Canadian Association for the Study of Liver Disease meetings.

- Li Zhao (University of Alberta) – 2009 CASL Student Prize
- Ava John Baptiste (University of Toronto) – 2009 NC RTP Best Clinical Science Presentation
- Mohammed Sarhan (Memorial University) – 2009 NC RTP Best Basic Science Presentation

NCRTP featured in Knowledge Translation Casebook

In 2008 the Canadian Institutes of Health Research (CIHR) called for various organizations to provide examples of knowledge translation activities they participate in. The program's previous administrator, Cathy Chau, submitted the NCRTP to the contest and it was one of 10 organizations selected to be showcased. In February 2009, CIHR released [Knowledge to Action: A Knowledge Translation Casebook](#). Look for the NCRTP's entry in the section entitled, "[Bringing Liver Disease Home: NCRTP-HepC.](#)"



Farewell to Dr. Sherman Morris

The NCRTP would like to bid farewell to Dr. Sherman Morris. Dr. Morris has been a mentor within the program since 2004. Although he is no longer officially affiliated with the NCRTP you can expect to hear from him in the NCRTP's new graduate course. (Expected launch date: September 2010.)

External Funding Awarded

Congratulations go out to Selena Sagan for winning a post-doctoral fellowship from the Natural Science and Engineering Council of Canada. The fellowship is worth \$40,000 per year for 2 years. Selena will complete her post-doc with Dr. Peter Sarnow at Stanford University. She will maintain links with the NCRTP via her new NCRTP mentor, Dr. Nahum Sonenberg from McGill University. Selena is currently in Scotland completing her research elective.

International conferences

NCRTP trainees have presented at a variety of international conferences in the past year. Below are the conferences for which the NCRTP has provided financial support for trainees to attend:

- *10th International Hepatitis C Conference, Derby, UK*
Angelique Myles
- *15th International Symposium on Hepatitis C Virus and Related Viruses, San Antonio, TX, USA*
Candice Jackel-Cram, Megan Powdrill, Selena Sagan, Sarah Welbourn, Li Zhao
- *30th Annual Meeting of the Society for Medical Decision Making, Philadelphia, Pennsylvania, USA*
Ava John-Baptiste
- *59th American Association of Study Liver Disease (AASLD) annual meeting, San Francisco, USA*
Wendong Chen
- *The 5th Annual Canadian Association for the Study of the Liver Winter Meeting, Banff, AB*
Jason Grebely

Upcoming conferences

The 16th International Symposium on Hepatitis C Virus and Related Viruses

Date: October 3 – 7, 2009

Location: Nice, French Riviera

Abstract submission deadline: June 30th, 2009

Website: <http://www.hcv2009.org>

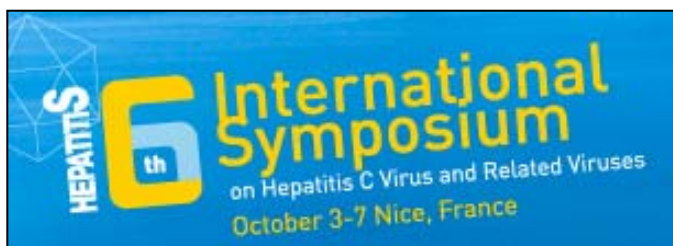
The American Association for the Study of Liver Diseases' 60th Annual Meeting

Date: October 30 – November 3, 2009

Location: Hynes Convention Center in Boston, MA.

Abstract submission deadline: June 8, 2009.

Website: <http://www.aasld.org/thelivermeeting/>



Trainee and Alumni Publications

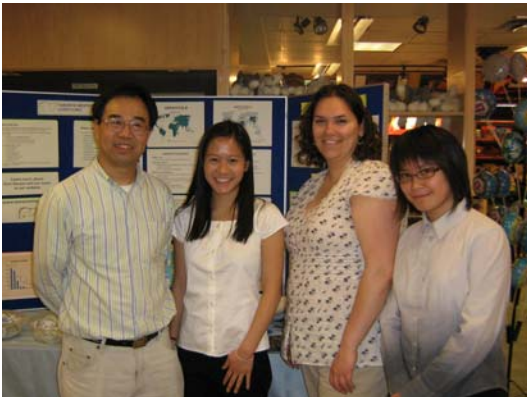
Below is a list of publications that our trainees and alumni have published in the past year.

- Borozan I, **Chen L**, Paeper B, Heathcote JE, Edwards AM, Katze M, Zhang Z, McGilvray ID. *MAID: an effect size based model for microarray data integration across laboratories and platforms*. BMC Bioinformatics. 2008;9:305.
- Selzner N, **Chen L**, Borozan I, Edwards A, Heathcote EJ, McGilvray I. *Hepatic gene expression and prediction of therapy response in chronic hepatitis C patients*. J Hepatol. 2008;48(5):708-13.
- **Grebely J**, Knight E, Genoway KA, Viljoen M, Khara M, Elliott D, Gallagher L, Storms M, Raffa JD, DeVlaming S, Duncan F and Conway B. *Optimizing assessment and treatment for hepatitis C virus infection in illicit drug users: a novel model incorporating multidisciplinary care and peer-support*. European Journal of Gastroenterology and Hepatology 2009. In Press. (Original Research, IF 1.83)
- **Grebely J**, Raffa JD, Lai C, Kraiden M, Kerr T, Fischer B and Tyndall MW. *Low uptake of treatment for hepatitis C virus infection in a large community-based study of inner city residents in Vancouver*. Journal of Viral Hepatitis 2009; 16(5):352-58. (Original Research, IF 2.97)
- Tossonian HK, Raffa JD, **Grebely J**, Rashidi B, Viljoen M, Mead A, Khara M, McLean M, Krishnamurthy A, DeVlaming S, Conway B. *Primary drug resistance in chronically infected antiretroviral naïve injection drug users*. International Journal of Infectious Diseases 2008 Dec 24 [Epub ahead of print] (Original Research, IF 2.06)
- **Grebely J**, Duncan F, Viljoen M, Khara M, DeVlaming S and Conway B. *Current Approaches To HCV Infection in Current and Former Injection Drug Users*. Journal of Addictive Diseases 2008; 27(2):25-35. (Invited review, IF NA)
- Matthews GV, **Grebely J** and Dore GD. *The role of reinfection in determining rates of spontaneous clearance after hepatitis C exposure*. Journal of Hepatology 2008 49(3):305-7. (Invited Commentary, IF 6.07)
- **John-Baptiste A**, Tomlinson G, Hsu P, Kraiden M, Heathcote J, Laporte A, Yoshida E, Anderson F, Krahn M. *Sustained responders have better quality of life and productivity compared to treatment failures long after antiviral therapy for hepatitis C*. American Journal of Gastroenterology. Manuscript in press.
- **John-Baptiste A**, Varenbut M, Lingley M, Nedd-Roderique T, Teplin D, Tomlinson G, Daiter J, Krahn M. (2009). *Treatment of hepatitis C infection for current or former substance abusers in a community setting*. J Viral Hepat. 2009 Feb 23. [Epub ahead of print]
- **MacParland SA**, Pham TN, Guy CS, Michalak TI. *Hepatitis C virus persisting after clinically apparent sustained virological response to antiviral therapy retains infectivity in vitro*. Hepatology. 2009 May;49(5):1431-41.
- **Panessa C**, Hill WD, Giles E., et al. (2009). *Genotype D amongst injection drug users with acute hepatitis B virus infection in British Columbia*. J Viral Hepat. 16(1):64-73.
- Lightfoot B, **Panessa C** and Hayden S, et al. (2009). *Gaining insite: Harm reduction in nursing practice*. Canadian Nurse. Volume 105, Number 4.
- Pezacki JP, **Sagan SM**, Tonary AM, Rouleau Y, Belanger S, Supekova L, and Su AI. *Transcriptional profiling of the effects of 25-hydroxycholesterol on human hepatocyte metabolism and the antiviral state it conveys against the hepatitis C virus*. BMC Chem. Biol. (2009) 16(9):2.
- Davis M, **Sagan SM**, Pezacki JP, Evans DJ, and Simmonds P. *Bioinformatic and Physical Characterisation of Genome-Scale Ordered RNA Structure (GORS) in Mammalian RNA Viruses*. J. Virol. 2008 Sep; 82 (23):11824-11836.
- **Thein HH**, Yi Q, Heathcote EJ et al. *Prognosis of hepatitis C virus-infected Canadian post-transfusion compensation claimant cohort*. J Viral Hepat 2009.
- **Thein HH**, Yi Q, Dore GJ, Krahn, MD. *Natural history of hepatitis C virus infection in HIV-infected individuals and the impact of HIV in the era of highly active antiretroviral therapy: a meta-analysis*. AIDS. 2008;22: 1979-1991.
- White, B, Day, C, **Thein, HH**, Doab, A, Bates, A, Holden, J, van Beek, I, Maher, L. *Acceptability of hepatitis C virus testing methods among injecting drug users*. Drug Alcohol Rev 2008; 1-5.
- **Thein, HH**, Yi, Q, Dore, GJ, Krahn, MD. *Estimation of stage-specific fibrosis progression rates in chronic hepatitis C virus infection: A meta-analysis and meta-regression*. Hepatology 2008; 48:418-431.
- Day CA, White B, **Thein HH**, Doab A, Dore GJ, Bates A, Holden J, et al. *Experience of hepatitis C testing among injecting drug users in Sydney, Australia*. AIDS Care 2008;20:116-123.
- **Welbourn, S**, Jirasko, V., Breton, V. Reiss, S., Penin, F., Bartenschlager, R. and Pause A. *Investigation of a role for lysine residues in non-structural proteins 2 and 2/3 of the hepatitis C virus for their degradation and virus assembly*. J. Gen. Virol. 90 (2009) pp.1071 – 1080
- **Yu H**, Jiang X, Shen C, Karunakaran KP, Brunham RC. *Novel Chlamydia muridarum T cell antigens induce protective immunity against lung and genital tract infection in murine models*. J Immunol. 2009 Feb 1;182(3):1602-8.
- **Yu H**, Babiuk LA, van Druenen Littel-van den Hurk S. *Strategies for loading dendritic cells with hepatitis C NS5a antigen and inducing protective immunity*. J Viral Hepat. 2008 Jun;15(6):459-70.
- Jiang X, Shen C, Rey-Ladino J, **Yu H**, Brunham RC. *Characterization of murine dendritic cell line JAWS II and primary bone marrow-derived dendritic cells in Chlamydia muridarum antigen presentation and induction of protective immunity*. Infect Immun. 2008 Jun;76(6):2392-401.

World Hepatitis Day 2009

May 19th, 2009 was the second annual World Hepatitis Day. Groups and organizations around Canada, including the NCRTP-HepC, promoted public awareness of Hepatitis B and C. For its part, trainees in the NCRTP set up booths across the country to distribute promotional items.

- In Toronto, Ava John-Baptiste and Limin Chen worked with Toronto Western Hospital's Liver Clinic. Man Wah Yeung and Victoria Leung, NCRTP summer students, also contributed to the team effort.
- Montreal trainees Stephen Barry, Megan Powdrill, Sandy Pelletier, and Sarah Welbourn spent the day on McGill University's campus raising awareness among the students, staff, and public.
- Mohamed Abdel-Hakeem, one of the NCRTP's newest trainees in Montreal, arranged an event at the hospital center of Université de Montréal - Campus St.-Luc to raise the public awareness about the methods of prevention and the clinical aspects of viral hepatitis B and C. Speakers at the event included Dr. Marc Bilodeau, Dr. Naglaa Shoukry and Dr. Nebal EL-Tanbouly from the Egyptian Council for Cultural and Educational affairs.
- Li Zhao and Ran Chen worked with members of Dr. Tyrrell's lab in Edmonton. They distributed the promotional items among patients and their families at the liver clinic.
- Ken Seaman based in Fredericton, set up a booth on his campus to promote the internationally recognized day.
- Similar to last year, trainees in St. John's , NL set up a booth at the Health Sciences Centre. The trainees included Sonya MacParland, Mohammed Sarhan, as well as alumni Dr. Tram Pham. They set up the booth with help from the local CLF chapter and worked alongside other members of their supervisor's lab and volunteers from neighbouring labs.
- Liang-Tzung Lin worked with Halifax's IWK Health Centre and its Research Office to distribute promotional items for the day



- Our trainee in Australia, Jason Grebely, worked with nurses and clinic staff at the Rankin Court Treatment Centre (an opiate pharmacotherapy clinic). Together they set up a morning tea and information session on hepatitis C. Jason also helped out at a special drop-in HCV clinic run by Dr. Greg Dore and one of his Hep C nurses.
- For World Hepatitis Day, Ottawa trainee Christine Cabrera and the Behavioural Medicine Infectious Disease Lab of the Ottawa Hospital attended a talk held by the Canadian Liver Foundation. The talk was entitled "Hepatitis B and C: Management and Treatment" and was geared towards patients and health professionals who are concerned with liver health.

Alumni

Since our last publication, several trainees graduated from the NCRTP. They include:

- Ivan Borozan - Ivan is now a postdoc in Dr. Zhaolei Zhang's computational biology group in the Donnelly Center for Cellular and Biomolecular Research of the University of Toronto.
- Angelique Myles – She is now working as a Research Assistant at the Primary Healthcare Research Unit in Memorial University.
- Wael Soliman - After graduating from the NCRTP, Wael returned to the University of Minya in Egypt as a hepatologist
- Rineke Steenbergen - Post-NCRTP, Rineke continues her post-doctoral studies at the University of Alberta. Her research project is entitled, "Viral entry of HCV, in vivo and in tissue culture."
- Rosie Thein - Rosie has obtained a position as a lecturer with the University of New South Wales' Viral Hepatitis Clinical Research Program.



NCRTP graduate course

The NCRTP recently completed its third ever graduate course. The course, run out of the University of Toronto and entitled, "Transdisciplinary Studies in Infectious Disease (using Hepatitis C as a model)," spanned a total of 26 lectures. Eight of the twelve students in the course were from the NCRTP.

The end of term project required that the students work in multi-disciplinary teams to create mock grant proposals. The students learned all about the grant writing process and how to create a CIHR common CV. In the end, they produced the 3 grants below:

1. The effect of microbial translocation on liver fibrosis in HIV/HCV co-infected patients
 - John-Baptiste, Ava (Toronto)
 - Chen, Ran (Edmonton)
 - Pelletier, Sandy (Montreal)
 - Amir Mohajerani (Edmonton)
2. Investigating host-virus interactions during Hepatitis C virus particle assembly
 - Powdrill, Megan (Montreal)
 - Mahra Nourbakhsh (Edmonton)
 - Cabrera, Christine (Ottawa)
 - Sagan, Selena (Ottawa)
3. Influences of Hepatitis C Virus on Mitochondria: Molecular, Cellular, and Systemic Impacts
 - Seaman, Ken (Fredericton)
 - Non-NCRTP student (Saskatoon)
 - Sarhan, Mohamed (St. John's)
 - Non-NCRTP student (Toronto)

Partner Notices

The Canadian Liver Foundation held its inaugural LIVERight Gala on April 4th, 2009. It was a unique and remarkable evening offering parents *and their teens* an evening of non-stop, jaw dropping exciting entertainment and activities.

Co-hosted by celebrated media personalities, Sabrina Jalees and Daryn Jones, the gala offered a host of activities, including the Gibson Guitar Jam Zone, Crush Vintage Booth, Temporary Tattoo Parlor, Laser Graffiti Wall, photo booth, tarot card reader, silent/live auctions and raffle.

The spectacular line-up of entertainment, including an up close and personal performance from Tokyo Police Club, a dazzling dance number featuring heartthrob Nico Archambault, winner of So You Think You Can Dance Canada, a red-hot fashion show featuring Guess?, Ed Hardy, gsus, PUMA and Roxy, an original hip-hop performance by Twisted Ankles Crew, and an astonishing BMX Bike and Skateboard demonstration that left the audience clamouring for more.

Most importantly, the evening provided the Canadian Liver Foundation the perfect platform to reach young people (who probably don't think of their liver too often) and explain that certain activities like getting a tattoo or piercing, experimenting with drugs, alcohol and sex all carry inherent liver health risks. It was a great opportunity to inform the young and the young-at-heart about ways to LIVERight for liver health.

The NCRTP and the CLF hope to see you at next year's LIVERight Gala!

NCRTP Sponsors

