

NEWSLETTER

FOR PARTICIPANTS AND FRIENDS OF THE COMPLEX CHRONIC DISEASES STUDY

Welcome!

In 2011, we launched our study with the goal of using state-of-the-art technologies to shed new light on the causes and mechanisms behind complex chronic diseases, such as Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) and what's often described as Chronic Lyme Disease. Our work brings together interested and motivated experts from many different medical and scientific disciplines, and is strongly supported by the BC Ministry of Health and the Provincial Health Services Authority. Our first funding came from the BCCDC Foundation for Population and Public Health and we have since received even more funding from the US National Institutes of Health and ME Research UK to expand our investigations.

Thank you to all participants!

Wonderful people from all walks of life have come to take part in the study – we thank each and every one of you from our case groups (ME/CFS and Chronic Lyme) and our control groups, including healthy volunteers and patients with lupus, who will serve as comparison points. Hearing your stories has been the most touching part of this study – they make it very clear how urgently research into complex chronic diseases is needed. For many of our participants, the act of making a study visit has been no small task and we thank you for your strength and perseverance. We also know that there are others who are unable to attend our study sessions and clinic, and we hope that our findings and future work will touch them too.

Major study paper published

This month, we published an important paper comparing our patient groups to each other and to healthy controls. The paper is free to read at <http://cid.oxfordjournals.org/content/early/2015/06/16/cid.civ470>, and was published in the journal *Clinical Infectious Diseases*, which is a well-respected and widely read journal. In it, we report on the scope of disability we observe among our patient groups, with both ME/CFS and those reporting a diagnosis of Chronic Lyme Disease displaying substantial symptoms that require explanation.

We also report that both patient groups display very similar symptoms - the paper is titled “Lyme Disease Diagnosed by Alternative Methods: A Common Phenotype with Chronic Fatigue Syndrome”. We hope that by clearly demonstrating the similarities between the two diseases, the Lyme community might connect with ME/CFS patients and practitioners, and be included in research studies examining this complex phenotype.

From one discovery platform to three!

When the study was launched, we had enough funding to complete two objectives: compare the patient groups to each other and to healthy controls, and search for microbes that are present in the patient groups but not in our control group. We've completed the comparison (more about that later!) and the microbe search, and have good news – additional funding has allowed us to add new approaches to our study! Here's how things have changed:

Searching for Microbes

Our original platform uses a technique called “metagenomics*” to identify the full array of microbes in a sample – it's like taking a census of the bacteria, viruses, and other microbes that are found in a sample (a sample could be something like blood, tissue, or even a sample from the environment like water or soil). We are using metagenomics to look for microbes that are still present in people that might be contributing to their symptoms; metagenomics can not detect microbes that were previously in a patient, but have since disappeared. We have completed most of our analysis and expect to be speaking about findings at upcoming scientific meetings and community forums.

*To learn more about metagenomics, visit <http://www.ncbi.nlm.nih.gov/books/NBK54011/>

Understanding your Immune System

We are also interested in looking at how peoples' immune systems are acting and whether there are differences between our patient groups. We can study this activity by measuring whether each of the genes in your immune system is being “expressed” – is it being used to make proteins, and what are those proteins doing? We use a technique called RNAseq* to measure these expression levels, and we look for interesting patterns in the data that might point us to explanations for differences between our study groups. When our study was launched, we collected RNA samples from our participants but didn't have the funding to run the tests. However, the intrepid Dr. Patrick Tang forged a partnership with Dr. Charles Chiu at UCSF that has allowed us to move ahead in this area. Dr. Chiu's group has just completed the RNA sequencing, and the data will be analysed in the coming months.

*To learn more about RNAseq, visit <http://rnaseq.uoregon.edu>

Immune Signatures

This is fresh news brought to our attention in recent weeks both by participants (you know who you are!) and by Dr. Jennifer Gardy. For those of you who are familiar with the “Hit and Run” hypothesis for ME/CFS and for persistent symptoms linked to Lyme disease, the concern is that an infection you had in the past may lead to a more permanent imbalance in the body that persists even if the microbe is gone or undetectable through a platform like metagenomics. Now it's possible to look at the full array of past pathogen exposures that leave behind an antibody response – what germs has your immune system seen in your life – and to compare these “immune signatures” between groups. Dr. Gardy has us collaborating with Dr. Stephen Johnston at Arizona State University to see if this approach can be applied to our work*.

*To learn more about the immunosignature approach, visit <http://www.biodesign.asu.edu/news/immunosignaturing-an-accurate-affordable-and-stable-diagnostic>

What's next?

Vancouver ME/CFS Exercise Study

Last year, we banded together with colleagues from the WorkWell Foundation and UCSF to obtain additional funding from the NIH, ME Research UK and the BCCDC Foundation to study changes in host gene expression following exercise in ME/CFS patients. The study is up and running and Dr. Jim Potts at UBC has been working with Staci Stevens' group to fine tune our exercise protocols. Hats off to the brave participants who have been willing to take not one, but two turns on the bike!

Ticks!

Lots of people want to know what infections you can get from a tick bite in BC. The concern is not limited to Lyme disease, as ticks can transmit a broader array of infections if they contain certain microbes. Last fall, Dr. Morshed and colleagues presented data from an extensive study of ticks captured from a variety of sites across southern BC. He used sensitive molecular tests that can pick up the full array of *Borrelia* species that ticks carry, and has found that BC continues to have a low, unchanging rate of *Borrelia burgdorferi* infection in ticks. One in 200 captured ticks carries the pathogen, a rate perfectly in line with what we are finding in ticks submitted by doctors from their patients. This rate is 50-100 times lower than what is currently being reported in the Niagara peninsula and the U.S. Northeast, where the incidence of Lyme disease is much higher. This summer, the team will also apply metagenomics to the ticks to describe the full array of microbes carried by ticks that could be passed to people. This will be one of the first descriptions of the "tick metagenome" and the first from our Pacific North-west ecosystem.

Bringing Research to the

Complex Chronic Disease Clinic

Our study was launched before the clinic at BC Women's Hospital was opened. We've been meeting regularly with the clinic team and other interested scientists to see how clinical research at the hospital can be further advanced.

Kudos, Comings and Goings

We want to make a point of thanking our core study staff, Shoshana Parker (research co-ordinator) and Ruth Miller (post-doc). Shoshana has made these studies happen on the ground. Any of you who meet her know what a positive, compassionate approach she brings to our work.

Dr. Ruth Miller is nearing the end of her term as post-doc with the study. She has borne the brunt of data handling and analysis for the study. We've been very lucky to have someone with such a strong background in both epidemiology and bioinformatics. Please join us in wishing Ruth well.

We were saddened last year when Dr. Alison Bested finished her work at BC Women's Hospital. Alison has been a contributor to the study and is still part of our team as we work toward describing our findings.

We have been able to welcome Dr. Jim Potts to the team. Jim brings a career marrying epidemiology and exercise physiology, so has proved quite integral to the exercise studies.

Other research publication news

The team has previously published on the methods we are employing - you can read these papers for free at the following links:

- Metagenomics for pathogen detection in public health: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3978900/>
- A metagenomic approach to investigate the microbial causes of myalgic encephalomyelitis/chronic fatigue syndrome: moving beyond XMRV: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3835061/>
- Submaximal exercise testing with near-infrared spectroscopy in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome patients compared to healthy controls: a case-control study: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4438583/>

And now for the exciting part!

It looks like the second half of 2015 should be when many of our approaches come to fruition. We hope to get news of the analyses out in a timely fashion, but will also want to make sure we do things right, every step of the way.

Please stay tuned!

Our best to you,
The CCD Study Team

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