

#### AT A GLANCE

Founded: 2005

Most recent renewal: 2010

Program Directors: Charles Boone, University of Toronto, and Frederick P. Roth, University of Toronto

Fellows and advisors: 17

Institutions represented: 9, in 2 countries

Fields and subfields represented: genetics; biochemistry and molecular biology; computational biology and bioinformatics; cell, evolutionary and systems biology; pathology; immunology; biotechnology

Interaction meetings: 2; in St. Louis, USA, and Toronto, Canada

Relevant knowledge user groups: human clinical geneticists; policy-makers interested in the impact of genomic technologies and personalized genomic medicine; organizations managing patient medical records

# GENETIC NETWORKS

**Devoted to mapping the biological networks that translate genomes into complex traits and improving our fundamental understanding of biological systems to enable new treatments and preventive measures.**

The program in Genetic Networks experienced a diverse range of activities over the past year. The program underwent a planned leadership change to have Senior Fellow **Charles Boone** serve as Program Co-Director with **Frederick Roth**. The program also held two program meetings: one at Washington University in St. Louis, USA, and the other in Toronto, Canada, both of which had strong participation of graduate students and postdoctoral fellows. Program fellows used these meetings as an opportunity to discuss the program's future scientific plans as they near the end of their current five-year research

term. The program has decided to pursue a stronger integration of human genetics. Their goal is to leverage the knowledge obtained through their investigation of genetic networks in model organisms and apply the approaches, understanding and methodologies to better understand the genetic underpinning of human disease. As such, the fellows used their meetings as a strategic opportunity to engage researchers from the human genetics community. Program meetings were also used as a strategic opportunity to enhance the program's ties with the Japanese genetic networks community by inviting several Japanese researchers from RIKEN and the University of Tokyo.

The program also underwent a five-year external review to assess its achievements over its second full program term. To assess the program and its proposal for renewal, an international review panel consisted of subject-matter experts from the United Kingdom, the United States, Germany and Canada.

## Research

- Fellows **Charles Boone**, **Brenda Andrews** (both University of Toronto) and **Chad Myers** (University of Minnesota) finished mapping genetic interactions between more than 20 million double mutant strains in yeast. The analysis encompassed over 95 per cent of all genes in the yeast genome and identified about one million interactions, providing the first complete genetic interaction map for any organism. The mapped network reveals a hierarchical model of cell function, as well as general principles of genetic networks. As such, it is expected to serve as an atlas for mapping analogous networks in more complex biological systems. This work is currently submitted for publication.
- Fellows **Jason Moffat** and **Frederick Roth** (both University of Toronto) and collaborators worked on a research project that switched off nearly 18,000 human genes, or approximately 90 per cent of the human genome, allowing the researchers to identify particular genes essential for cell survival. The results of this study were published in *Cell*.
  - > Hart T, Chandrashekhar M, Aregger M, Steinhart Z, Brown KR, MacLeod G, Mis M, Zimmermann M, Fradet-Turcotte A, Sun S, Mero P, Dirks P, Sidhu SS, **Roth FP**, Rissland OS, Durocher D, Angers S, **Moffat J**. 2015. High resolution CRISPR screens reveal fitness genes and genotype-specific cancer liabilities. *Cell*. 163(6): 1515-1526.
- Fellows **Andrew Fraser**, **Brenda Andrews**, **Charles Boone**, **Jason Moffat** (all University of Toronto), **Philip Hieter** (University of British Columbia) and **Chad Myers** (University of Minnesota) initiated a major new collaboration. Using insights from the complete yeast genetic network and a combination of genetic and chemical tools, the team will select genes to screen for genetic interactions in *C. elegans*, a human haploid cell line, and in different cancer cell lines.

## Other notable publications

- Bailey ML, Singh T, Mero P, **Moffat J**, **Hieter P**. 2015. Dependence of human colorectal cells lacking the FBW7 tumor suppressor on the spindle assembly checkpoint. *Genetics*. 201: 885-895.
- Sun S, Yang F, Tan G, Costanzo M, Oughtred R, Hirschman J, Theesfeld CL, Bansal P, Sahni N, Yi S, Yu A, Tyagi T, Tie C, Hill DE, Vidal M, **Andrews BJ**, **Boone C**, Dolinski K, **Roth FP**. 2016. An extended set of yeast-based functional assays accurately identifies human disease mutations. *Genome Res*. 26(5): 670-680.

## IdeasExchange

- At their program meeting in Toronto, fellows invited Dr. Hanna Faghfoury, a physician from the University of Toronto medical school responsible for the medical genetics undergraduate curriculum, to discuss how knowledge and insights emerging from the program could contribute to medical school curriculum development. The program has also begun developing the framework for a workshop that will aim to better understand how to extract meaningful data from personal genomes.

## Global Academy

- The program regularly integrates graduate students and postdoctoral fellows into its meetings. Fellows' trainees, as well as trainees from the local academic community hosting a Genetic Networks program meeting, are invited to participate by presenting a poster or talk.

To learn more: <https://www.cifar.ca/research/genetic-networks/>

The "Daisy" model of gene essentiality. Image provided by CIFAR Senior Fellow Jason Moffat.

