



GenomeCanada

Released June 12, 2017

BACKGROUND

Structural Genomics Consortium, Phase IV

Project leaders: Aled Edwards, Cheryl Arrowsmith, Structural Genomics Consortium

Genome Centre: Ontario Genomics

Total funding: \$33 million

The estimated 100,000 different human proteins constitute the key functional and structural components of our and indeed all species; they are critical to normal development and health. Each protein, which is actually a long linear chain of amino acids, is folded into an exact three dimensional shape. This, the so called protein structure, is essential data when thinking about creating molecules such as drugs that bind and modify protein function.

Since 2004, the Structural Genomics Consortium (SGC) has been working to determine the three-dimensional structure of proteins relevant to human diseases. These structures are made available online in the public domain, without restrictions on their use by industry or academia, to support early-stage drug discovery.

To date, and with ongoing support from Genome Canada and other partners, the SGC is responsible for internationally leading 13 per cent of all solved human protein structures. The SGC also leads an international program in partnership with other scientists, research agencies and pharmaceutical companies, that generates small inhibitor molecules, called chemical probes, against proteins and makes them available in the public domain. The chemical probes help researchers understand the role of a protein in normal and disease physiology and play an essential role in the early drug-discovery process.

A key area of focus for the SGC is proteins that regulate epigenetics, the study of heritable modifications to gene expression. Understanding how proteins turn specific genes on and off is important for developing therapies to treat many debilitating diseases, such as cancer and neurodegenerative and inflammatory diseases. Based on SGC science, there are now more than 25 clinical trials ongoing, including in Canada.

Another example is when, because of genetic mutations, proteins are misinformed, resulting in one of the estimated 7000 different rare diseases which affect approximately one million

Canadians. Here, SGC's ability to define protein structure can make all the difference. Care 4 Rare, a Genome Canada-funded large-scale applied research project, working with the SGC has identified the structure of a protein which may hold the key to therapy for a rare seizure disorder as well as discovering small molecules which bind to this protein, potentially serving as drugs; more recently the world's first genetic model of the condition has been created and is now poised to perform pre-clinical testing of the SGC-enabled theory.

The SGC is considered a leader in open science. By sharing all research results and output with no restrictions on use, SGC's open science ethos protects against waste and duplication of effort, and strengthens collaboration and innovation by facilitating scientific exchange that is unencumbered by intellectual property considerations.

In its current phase, the SGC is expanding its open science collaborative network to include disease and patient foundations. The SGC is also partnering with clinicians and research hospitals to test its chemical probes on patient samples, a more predictive approach to validating new targets for drug discovery. The project will also provide training for the next generation of Canadian researchers in early-stage drug discovery.

The Canadian arm of the SGC is co-supported by eight pharmaceutical companies and the Ontario Ministry of Research, Innovation and Science (MRIS). SGC has also established a robust collaborative research and training network among Canadian institutions with support from hospital research institutes, the Bill and Melinda Gates Foundation, the Natural Sciences and Engineering Research Council (NSERC), Canadian Institutes of Health Research (CIHR) and the Mitacs program.

The wider research program includes sister SGC sites at Oxford University (UK), the University of Campinas (Brazil), the Karolinska Institute (Sweden), the University of North Carolina (USA) and Goethe University Frankfurt (Germany).