



## BACKGROUND

### Structural Genomics Consortium, Phase V

**Project title: Target 2035: WDR Proteins as a Technology Testbed for Illuminating the Dark Proteome**

**Project leader:** Cheryl Arrowsmith, Structural Genomics Consortium

**Lead Genome Centre:** Ontario Genomics

**Genome Canada funding:** \$5,000,000

**Total funding:** \$23,457,198

The Structural Genomics Consortium (SGC) will create a roadmap for Target 2035 – a global initiative that will dramatically increase the translation of genomics into new medicines. This two-year project is part of SGC’s Phase V, which runs from 2020 to 2025. The initial focus is on WD40 Repeat (WDR) domain proteins, one of the largest and most disease-associated protein families in the human proteome. In collaboration with industry, the team will focus on technology optimization, and position Canada as the global leader for Target 2035.

What exactly is Target 2035? The sequencing of the human genome raised great hopes that a new era of genomic therapies would soon follow. Most biomedical research has since focused on only a small fraction of genes and proteins for which accessible research tools exist, resulting in a vast knowledge gap limiting our ability to develop new medicines for debilitating diseases like Alzheimer’s, cancer, and rare diseases. Target 2035 is an ambitious new initiative to address this gap by developing a pharmacological tool for most human proteins by the year 2035, focusing on proteins considered part of the unexplored “dark proteome”. This tremendous task will transform drug discovery but can only be achieved through a coordinated international effort. In partnership with the pharmaceutical industry, the SGC lab at the University of Toronto (SGC-Toronto) is building and leading a Target 2035 global federation of scientists to take on this challenge.

Over the course of Phase V, the team will build directly on the previous success and momentum of the SGC-Toronto, using the platform to create community-enabling pharmacological tools at an unprecedented scale. In the first two years, the project will explore a range of innovative strategies including the application of artificial intelligence (AI), with a focus on WDR proteins, to test and compare technologies for protein production, screening of chemical libraries, and optimization approaches to identify small chemical molecules that bind and/or modulate WDR domains.

The WDR protein family is largely unexplored yet harbours more ‘essential genes’ in cancer than any other protein family, is involved in many other debilitating and rare diseases, and is amenable to pharmacological inhibition. Thus, it is an ideal ‘test set’ to develop protein-based, scalable technologies, workflows and collaborative models.

The two-year pilot phase (2020-2022) will:

- Create drug discovery enabling reagents and know-how for 15–20 WDR proteins that are part of the “dark proteome”;
- Generate 10 highly specific open access chemical compounds or ‘probes’ to disease-relevant WDR proteins that will catalyze the launch of new drug discovery programs; and
- Establish a knowledge translation platform in collaboration with the European EUBOPEN project to manage, integrate and disseminate open-science chemical biology data, reagents and knowledge.

This pilot is an inclusive, pan-Canadian project designed to yield significant benefits. In the near term, this includes training and capacity building, new open data to catalyze AI-driven drug discovery, knowledge and technologies to empower national and global teams, while attracting public and private support. Over the longer term, this includes stronger innovation networks in Canada, inward investment for pre-clinical and clinical trial activities, and new medicines that will have a profound impact on Canadians’ quality of life. SGC aims to replicate their success with WDR5, for which SGC and the Ontario Institute for Cancer Research (OICR) created a chemical probe, which led to a \$40 million investment in Propellon Therapeutic’s leukemia drug discovery program.

Critically, Target 2035 delivers on [Genome Canada’s Strategic Vision](#) to drive high-impact research to benefit Canada. The plan addresses key societal challenges associated with the enormously complex task of developing new drugs. The team will coordinate with other global groups to lead this large-scale, interdisciplinary initiative with line-of-sight to application. The resulting reagents and know-how will lead to new medicines in Canada through translational partnerships with research institutes across the country, five Canadian biotechs and 10 global Pharma companies, and a new cohort of open science spin-offs. Target 2035 is arguably the most ambitious genome effort since the Human Genome Project and will significantly advance Canada’s role in international genomics research, with SGC at the helm.

Related work:

[The Structural Genomics Consortium \(SGC\)](#)  
[Structural Genomics Consortium \(SGC\), Phase IV](#)