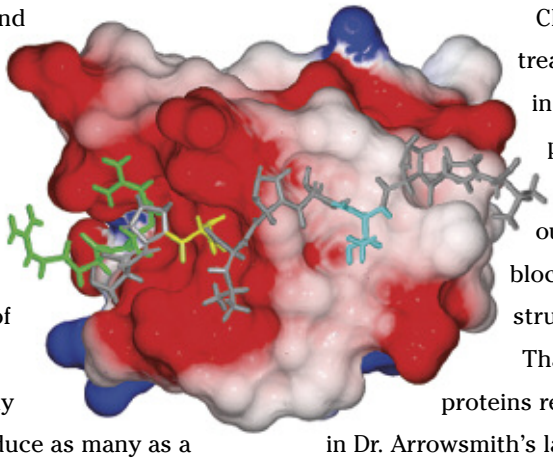
Ideas on the Edge

A Wedge in the Spokes

PROTEINS PLAY AN IMPORTANT ROLE IN CANCER. CHERYL ARROWSMITH AT THE UNIVERSITY HEALTH NETWORK IS LOOKING FOR CLUES IN THEIR SHAPES THAT SUGGEST WAYS TO STOP THEM.

Cancer researcher Dr. Cheryl Arrowsmith uses a memorable image to describe what she does.

"Think of cancer as being like a bike. We're trying to understand what the parts are and how they work, so we can jam a wedge in the spokes. That's what a drug is."



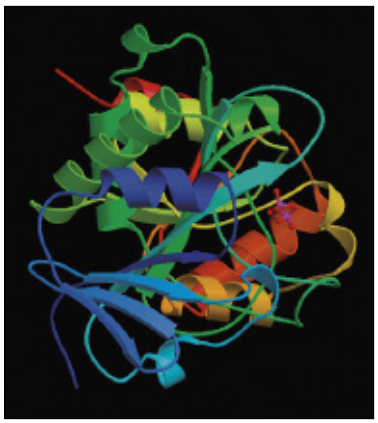
The "parts" Dr. Arrowsmith and her colleagues are trying to understand are proteins. These intricately folded chains of molecules account for up to 18 percent of the weight of a healthy adult. The human body can produce as many as a hundred thousand different kinds, and most of our biological processes are the result of a complex balancing act involving interactions between them.

Proteins are manufactured in our cells using instructions encoded in a gene—a section of the cell's DNA. Damage to a gene can result in the production of too many—or too few—of certain kinds of proteins, or in proteins that are defective. When this happens, the body's balancing act is thrown off. And when it happens to proteins that are part of the system regulating cell reproduction, the resulting interactions can cause runaway growth—cancer.

CHERYL ARROWSMITH

Clearly, one possible approach to treating cancer involves intervening in these interactions. And since proteins interact based on their shapes—think about the ins and outs of children's interlocking plastic blocks—we need to understand their structures.

That's why creating imagery of proteins related to cancer is a central focus in Dr. Arrowsmith's lab, a facility funded in part with an investment by the Ontario Innovation Trust. Just as it's easier to understand how a bicycle works if you have an image rather than a written description of the parts, so it's easier to grasp how proteins



IMAGERY FROM DR. ARROWSMITH'S LAB. ABOVE LEFT: A computer generated 3-D model shows the accessible outer surface of a protein. The stick-like structure is a schematic representation of a second protein bound to the surface of the first protein. ABOVE RIGHT: A "ribbon diagram" provides a schematic view of how the long chains of a protein fold into a unique structure.

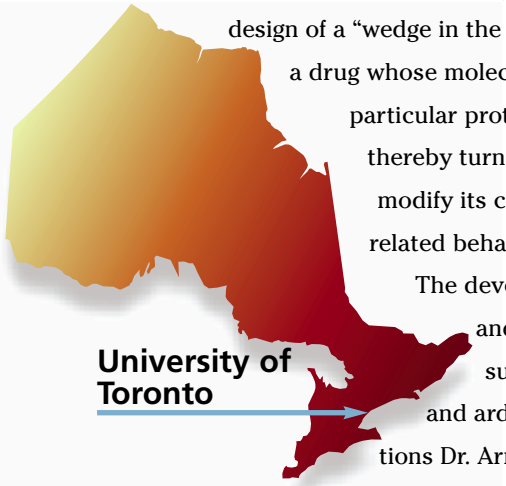
Project: High Throughput Screening of Proteins for Structural Proteomics Research
Institution: University of Toronto
Research Sector: Life Sciences
Principal Investigator: Cheryl Arrowsmith
Trust Investment: $50,000
CFI Investment: $50,000
Total research investment from all sources: $125,000

Dr. Arrowsmith (lower right) and her team, with the nuclear magnetic resonance unit they use in their research.

function if you can see their three-dimensional shapes. "If you have a picture of a bike," explains Dr. Arrowsmith, "you can easily see how you could stick something in the spokes to keep it from moving. In somewhat the same way, visualization helps us understand how proteins interact, and how to block those interactions."

RESEARCH THAT MATTERS
REAL-WORLD BENEFITS FOR ONTARIANS:
- development of powerful cancer-fighting drugs

Dr. Arrowsmith and her colleagues use sophisticated technologies like nuclear magnetic resonance spectroscopy and x-ray crystallography to create the information-rich—and often delightfully colourful—images they need for their research. That information is key to the design of a "wedge in the spokes"—a drug whose molecules "fit" a particular protein, and thereby turn it off or modify its cancer-related behaviour.



The development and testing of such drugs is a long and arduous process, cautions Dr. Arrowsmith. "Clinical trials in the very best of cases take ten years and usually it's longer than that." But each new three-dimensional protein portrait represents a crucial first step in a process that may one day stop the grinding wheel of a cancer dead in its tracks.

Ontario Innovation Trust

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Infrastructure for Innovation
About the Ontario Innovation Trust

The Ontario Innovation Trust was created in 1999 by the Government of Ontario to invest in research equipment and facilities at Ontario's universities, colleges, hospitals and other non-profit research institutions. The Trust is governed by a volunteer Board of Directors, according to the terms of a Trust agreement established by the Ontario government. A small permanent staff looks after day-to-day operations.

Since its inception, the Trust has committed almost $843 million to strengthen Ontario's position in the global marketplace of ideas. This represents more than a third of the $2.44 billion in total funding that has been invested in Trust-supported projects.