Ideas on the Edge

Into the Mysterious Two-Thirds

AN INTERNATIONAL INITIATIVE BASED AT THE UNIVERSITY OF TORONTO IS EXPLORING NEW TERRITORY IN THE FIELD OF HUMAN PROTEINS.

"When you get sick and go to the doctor," says Dr. Aled Edwards of the University of Toronto, "the doctor knows, at best, about a third of what's going on inside you at the molecular level."

Dr. Edwards is referring to the fact that roughly two-thirds of human proteins remain a mystery to science, in terms of what they do and how they work. Since proteins drive every process in our bodies—and since most medications work by interacting with a particular protein—this represents a significant blind spot.

ALED EDWARDS

Now, however, the Structural Genomics Consortium, which Dr. Edwards directs, is helping to draw back the curtain on the hidden world of proteins. Instead of taking the traditional approach of focusing on a known protein and learning more about it, researchers with the consortium synthesize thousands at a time, using data from DNA sequencing. Then they examine the results with exotic technologies like x-ray crystallography and nuclear magnetic resonance to look for proteins with new and unfamiliar three-dimensional structures. These shapes hold vital clues about a protein's function and about the way in which it interacts with potential drugs. If the preliminary examination of a particular structure suggests a key function related to human health, researchers then work out the shape of the "new" protein in detail.

RESEARCH THAT MATTERS

REAL-WORLD BENEFITS FOR ONTARIANS:

- helps make life-saving and life-changing drugs available more quickly
- leads to more jobs and prosperity in future by strengthening province's standing in key global pharmaceutical sector

Given that there are roughly 30,000 proteins at work in the human body, this "shotgun" approach may seem inefficient; it took 22 years for scientists in the 1940s and 50s to isolate and describe the structure of hemoglobin. But advances in imaging, DNA sequencing and information processing now make it possible for the Consortium to identify and describe up to 100 relevant proteins a year. Funding for the sophisticated equipment involved comes in part from the Ontario Innovation Trust.

The structural information being produced by the

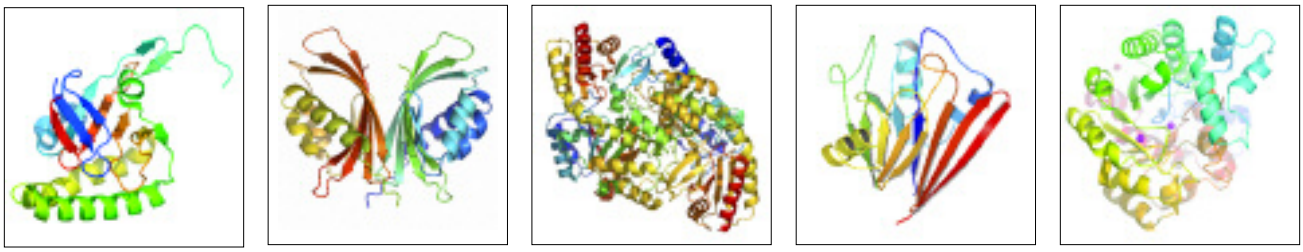
The Power of Partnership

Private support of a public venture

Pharmaceutical giant GlaxoSmithKline (UK) is providing $3 million to support the Structural Genomics Consortium. Why would a corporation support research when there's no return in terms of intellectual property? "They get to provide industry input," Dr. Edwards explains, "on what information companies will find most useful. And when the structures are in the public domain, GSK can use them, too, at a fraction of what it would have cost to do the research themselves. This way, pharmaceuticals can compete with each other in their areas of core competency: chemistry and marketing."

wants," says Dr. Edwards, "is for all this information to be out there, free of charge, no patents, no anything. And that's what we do." The result is faster drug discovery, bringing potentially life-saving drugs to market sooner and more cheaply.

The Consortium's goal is to identify 350 key proteins by the end of its three-year mandate—a significant contribution to a global effort. In fact, in 2005, Consortium researchers were responsible for 20 per cent of all new human proteins whose structures were determined and placed in the public domain. And the breakneck pace continues. Says Dr. Edwards, "We're trying to capture as much information, about as many proteins as possible, in the shortest period of time."



KNOWING THE SHAPE OF A PROTEIN "TARGET" ENABLES PHARMACEUTICAL RESEARCHERS TO DESIGN DRUGS WITH MOLECULES THAT "FIT."

Consortium is vital to the development of new drugs. A medication works by docking at the molecular level with the right protein—like a key fits a lock— allowing it to modify the protein's operation. Knowing the shape of a protein "target" enables pharmaceutical researchers to design drugs with molecules that "fit."

The Consortium is a non-profit venture, and puts its findings into the public domain. This helps provide a level playing field for pharmaceutical companies (see the box "Private support of a public venture"), and also helps avoid situations in which private companies hold patents on important human proteins. "What society

Project: Structural Genomics Consortium
Institution: University of Toronto
Research Discipline: Life Sciences/Genomics
Principal Investigator: Aled Edwards
Trust Investment: $7,198,442
CFI Investment: $7,198,442
Total research investment in infrastructure from all sources: $18,033,106

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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.