CIHR:

Transforming Health Research in Canada

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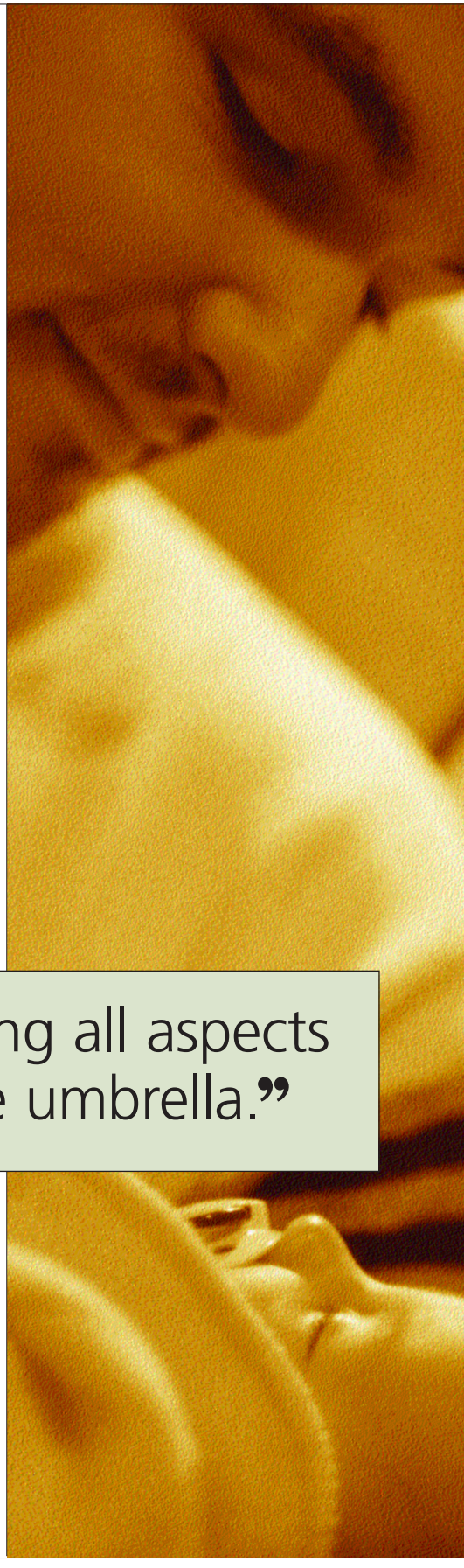
CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Canada

The Canadian Institutes of Health Research: **A Healthy Start**



With the mapping of the human genome, the 21st century is being hailed as the century of health research. It is now possible to determine a person's susceptibility to certain diseases. Soon, through an understanding of the interplay between psycho-social, economic, environmental, cultural and biological factors affecting health science will be able to predict a person's risk of developing common diseases such as diabetes, cancer and mental illnesses.

Canada is in position to meet the challenges of this century in health research. In June 2000, the Canadian Institutes of Health Research (CIHR) was launched to revolutionize Canada's approach to health research. CIHR's mandate is bold and broad. It calls on the health research community to excel in the creation of new knowledge and to share this knowledge with Canadians: those who deliver health services, those who design prevention strategies, and those who are building Canada's knowledge-based society.

And CIHR comes equipped with impressive new tools. With a new integrated, problem-based approach to health research, and a $480-million budget, CIHR not only funds biomedical and clinical research but has expanded its mandate to include health systems and services as well as population health research. The result is that quality-of-life and long-term population studies that examine external factors such as pollution and socioeconomic factors are now being carried out in conjunction with biomedical and clinical studies.

But CIHR's greatest innovation is the creation of 13 virtual institutes that are changing the way researchers work, creating a platform for interdisciplinary health research. These virtual institutes link researchers across the country in categories that Dr. Alan Bernstein, CIHR's inaugural president, calls "quite deliberately a mélange" of disciplines, human systems, diseases and vulnerable groups. These institutes—such as Institutes of Infection and Immunity, Circulatory and Respiratory Health, Cancer Research and Aboriginal Peoples' Health—exist not in a building but in universities, hospitals, community groups and research centres across Canada.

"We were hoping to get around silos and encourage collaboration and cooperation between researchers and institutions," says Bernstein, a world-renowned geneticist. "CIHR's institutes are the meeting ground for researchers under their mandates."

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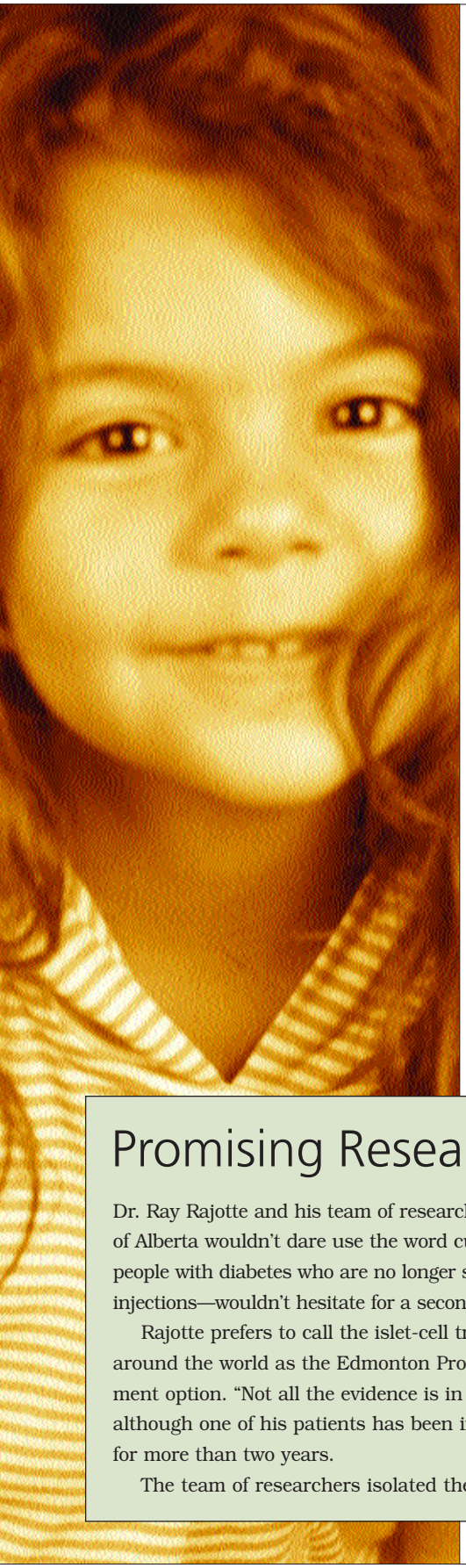
In addition to CIHR's grant-allocating responsibilities, its institutes and their advisory boards are working proactively in partnership with provincial governments, other federal agen-



cies, industry and charities to set research priorities. "The objective is to bring research closer to the health care reality of the new century by integrating everything from basic research to population health," says Dr. Rémi Quirion, scientific director of CIHR's Institute of Neurosciences, Mental Health and Addiction at Douglas Hospital of McGill University.
His institute has undertaken a special multi-disciplinary initiative to investigate smoking that encompasses the neurological process of addiction and involves many of the other institutes—including the Institutes of Aboriginal Peoples' Health, Gender and Health, Cancer Research and Circulatory and Respiratory Health. "We are basically trying to bring all aspects of health research under one umbrella."

Knowledge transfer is essential to gaining the full benefit of research, says Joseph Rotman, founder of merchant bank Clairvest Group Inc. and member of CIHR's governing council. "We want to ensure that intellectual property, whether patentable or not, is transferred into use, and that the economic benefit is realized through health care improvement and jobs in a growing economy."

The Price of Health

Health is priceless, says the adage. But what about ill-health and disability? On that score, we pay a high price.

"It's fair to say the burden of ill health is much more than what we spend to cure disease," says Richard Alvarez, CEO of the Canadian Institute for Health Information.

According to a Health Canada study, in 1993 Canadians spent $71 billion on direct costs of treatment such as physicians' fees, hospitalization, drugs and rehabilitation. But what's often overlooked are the indirect costs, such as lost productivity when workers are absent or die young, and costs related to pain and limited activity. These factors added another $85 billion to the 1993 bill, bringing the total cost to $156 billion.

Taking the biggest bite out of the national wallet were heart disease and stroke at $20 billion, musculoskeletal diseases such as arthritis and osteoporosis at $18 billion, injuries at $14 billion and cancer at $13 billion. "Together," says Alvarez, "these accounted for almost 50% of all costs and in all four cases, indirect costs were much

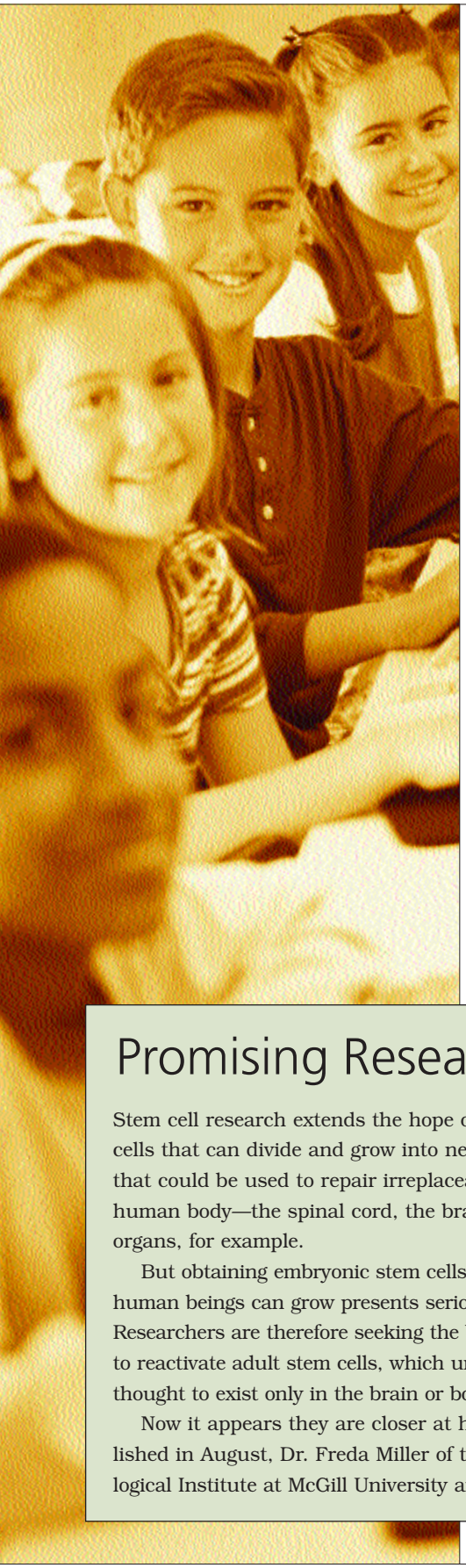
Promising Research: **The Edmonton Protocol**

Dr. Ray Rajotte and his team of researchers at the University of Alberta wouldn't dare use the word cure but his patients—people with diabetes who are no longer slaves to daily insulin injections—wouldn't hesitate for a second.

Rajotte prefers to call the islet-cell transplant known around the world as the Edmonton Protocol a better treatment option. "Not all the evidence is in yet," he cautions, although one of his patients has been insulin-independent for more than two years.

The team of researchers isolated the insulin-producing cells from an organ donor pancreas and transplanted them into patients with diabetes. As well as offering these patients hope for a life free from daily injections, Rajotte says they may also be free from late-stage complications such as blindness and kidney problems because of the better glucose control achieved with an islet transplant.

"Alberta's diabetes advances are a direct result of $17.5 million in long-term Heritage investment which has leveraged other vital funding," says Dr. Matthew Spence, president and CEO of the Alberta Heritage Foundation for Medical Research.



more than direct costs."

CIHR researchers have already produced results that have led to new treatments and prevention strategies, and generated savings to the health system. The potential for health research to further reduce the staggering economic impact of disease is tremendous.

Joining Forces: **Research Partnerships**

The Canadian Institutes of Health Research (CIHR) is always on the lookout for partnerships where the whole is greater than the sum of the parts.

CIHR's unique collaboration with Canada's Research-Based Pharmaceutical Companies (Rx&D)—the organization representing 63 companies that conduct pharmaceutical research—is one such partnership. The CIHR/Rx&D program enables the pharmaceutical industry to channel its growing investment dollars through CIHR's internationally recognized peer evaluation system to fund research that meets the highest levels of scientific excellence. The program is well ahead of schedule in its commitment to significantly increase the amount of collaborative research conducted. In the first five-year phase of the program, CIHR leveraged almost $250 million to fund more than 1,000 projects including 50 clinical trials.

Last year, the program spawned a number of high-profile projects including the internationally acclaimed DREAM study (Diabetes Reduction Approaches with Ramipril and Rosiglitazone Medications), led by world-renowned CIHR investigator Dr. Salim Yusuf, based at McMaster University. Initiated in November 2000, the project brings together CIHR, King Pharmaceuticals, Aventis Pharma Inc., and GlaxoSmithKline to fund a $25 million clinical trial to investigate earlier indications that the drugs ramipril and rosiglitazone can prevent diabetes, a condition that afflicts 142 million people worldwide and costs Canada $10 billion annually.

Pharmaceutical companies benefit greatly from the joint program, says Jean-François Leprince, president of

Promising Research: **Stem Cells**

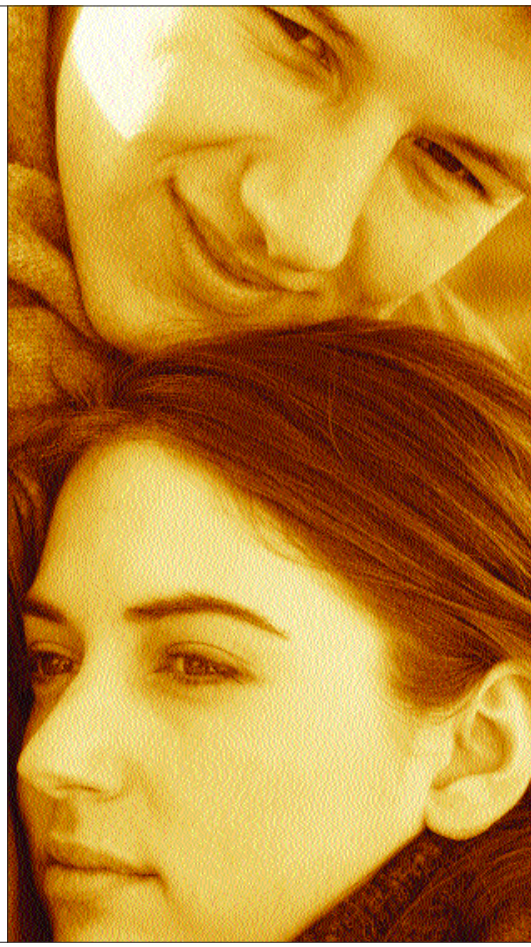
Stem cell research extends the hope of finding special cells that can divide and grow into new human tissue that could be used to repair irreplaceable parts of the human body—the spinal cord, the brain and other organs, for example.

But obtaining embryonic stem cells from which new human beings can grow presents serious ethical problems. Researchers are therefore seeking the biochemical triggers to reactivate adult stem cells, which until recently, were thought to exist only in the brain or bone marrow.

Now it appears they are closer at hand. In results published in August, Dr. Freda Miller of the Montreal Neurological Institute at McGill University announced her CIHR-funded research had discovered adult stem cells in skin.

"It was a radical idea. We hardly talked about it at first," she says. But in her laboratory dishes, skin cells extracted from the dermis of mice grew "in nice round clusters, like grapes." When growth stimulators were removed, they began to differentiate as they attached to proteins that coated the flasks, displaying "markers" indicating neural brain cells, smooth muscle, fat and related tissue.

"We have stumbled onto a way of growing a multipotent cell that can grow into a variety of human tissue," says Miller. The next step: find out how close these cells are to embryonic stem cells. "The boundaries," she says, "may not be that strict."



Aventis Pharma Inc. of Montreal, manufacturer of ramipril. Citing the reputation of Canadian research, he says doctors gain confidence in the product and knowledge about its uses when drug studies are done in Canada, which in turn improves worldwide marketability. Says LePrince: "We create a network and relationship with the main investigators a long time before the product is introduced in commercial form for market."

Collaboration is also instrumental in achieving another key CIHR objective: training a new cadre of highly qualified Canadian researchers. In response to grant applications from pharmacy and medical schools, Rx&D and CIHR make matching grants of about $1 million a year each to train young researchers in significant research studies.

"The public-private partnership has been highly successful," says Murray Elston, president of Rx&D, "and continues to attract high-quality research and establish Canada as a base from which to develop both expertise and international markets."

While partnerships have leveraged more funds for health research, they have also brought about greater focus. CIHR has brought together the health research community to work together to identify research priorities, frame the relevant research questions and contribute financially. As an example, transplants of insulin-producing islet cells are needed to overcome the problem of the patients' immune system destroying the transplanted cells. With joint funding from the Juvenile Diabetes Research Foundation (JDRF) and CIHR, researchers at the University of Alberta successfully accomplished this goal using a new mix of immune-suppression drugs.

"The next step," says JDRF president Ron Forbes, "is how to do without immune-suppression drugs so it can be done for children." Again, JDRF and CIHR, along with other agencies and institutions, are tackling this goal in part through research conducted by Dr. Terry Delovitch at the John P. Robarts Research Institute in London, Ont. "CIHR is the best organization we could be involved with," says Forbes, "because, like JDRF, it is also very tightly focused."

This strategic approach to funding research has brought an enthusiastic response. "It's a hectic pace and there are real challenges on both sides," says Carl Breckenridge, vice-chairman of the research priorities and planning committee of the Heart and Stroke Foundation, which has dedicated $2 million to jointly funded research with CIHR's Institute of Circulatory and Respiratory Health.

He says both CIHR and Heart and

Stroke had to re-examine and negotiate their priorities, but the end result was worth it. With CIHR's participation, Heart and Stroke Foundation exceeded its funding expectations and was able to attract $3 for every $1 they invested. Says Breckenridge: "CIHR really has a lot of momentum."

Spinoffs: **From Research to Development**

The ultimate measure of success for health research is better human health, a healthy health care system and a stronger, more diversified knowledge-based economy.

In knowledge-based industries such as those built around life sciences, employment growth is double that of other industries, according to a 1997 Industry Canada study. In fact, Canada's $36-billion life sciences industry already accounts for 86,000 jobs in Canada, a figure that is expected to grow by 51% to more than 130,000 by 2003.

Canada is also home to the world's second largest biotechnology industry, which largely grew out of research supported by CIHR and its predecessor. In 2000, the biotechnology industry consisted of more then 380 "core" firms, according to Statistics Canada—and about three-quarters employ fewer than 50 people. But the potential for growth is enormous. One in five is traded on public markets, and successes such as BioChem Pharma Inc. and QLT Inc. demonstrate that such firms can grow into global prominence and alliances.

CIHR plays a strategic role in building this pipeline of discovery, moving research from the laboratory to the marketplace. What does the future hold? Here is a selection of promising made-in-Canada biotechnology developments.

Bioniche Life Sciences Inc.: In research funded in part by CIHR, Dr. Brett Finlay made a breakthrough discovery in 1997. He found that pathogens such as *E-coli* infect their host by "harpooning" the intestinal wall with a bacterial protein. Other germs basically attach themselves to existing molecules on the organ's surface.

A professor in the biotechnology lab at the University of British Columbia and one of only 34 CIHR Distinguished Investigators, Finlay decided to tackle human *E-coli* infection, which originates in cattle, at its source. In collaboration

Promising Research: **Spinal Cord Repair**

Severed spinal cords can regenerate, at least to a limited extent, given the right conditions.

In CIHR-backed experiments at the University of Toronto, Dr. Molly Shoichet and Dr. Charles Tator found that severed spinal cords grew into a porous tubular "bridge" implanted in rats. Shoichet, associate professor of chemical engineering and biomedical engineering, made the flexible tubes from hydrogel materials similar to those used in contact lenses. The tubes imitated the flexibility of a spinal cord and allowed nutrients to pass through so that nerves could grow inside.

Describing the tubes, she says "they look like little straws with the consistency of cooked wet spaghetti." The rats' myelinated neurons grew into the tubes over a 3.5 mm gap in about eight weeks and the rats' ability to walk improved, although to a limited extent.

It's too early to declare a solution to spinal cord injury. "Still," says Shoichet, "the results told us the bridge has the right properties because it is allowing tissue to grow, and it may actually be helping."

with Dr. Andrew Potter, associate director of research at the Veterinary Infectious Disease Organization (VIDO) in Saskatoon, he used his discovery to develop an *E-coli* vaccine for cattle. UBC and VIDO share patents related to the vaccine technology.

To conduct wide-scale tests, the Alberta Research Council (ARC) then licensed the technology from UBC and VIDO in order to produce large quantities of the vaccine at its Edmonton facility, a site that is approved by the US Department of Agriculture and Agri-Food Canada.

Early indications showed that Finlay's vaccine dramatically reduced infection from the deadly *E-coli* 0157 bacteria. But any good product needs experienced marketing and distribution. Bioniche Life Sciences Inc. of Belleville, Ont., sub-licensed manufacturing rights from ARC and produced the vaccine this year through its Vetrepharm animal health division. Co-ordinating with ARC and VIDO, Vetrepharm inoculated 75,000 cattle across the country this fall. Trial results should be available by year-end.

If successful, the bovine *E-coli* vaccine may help prevent 50,000 human cases and 500 deaths each year from *E-coli* infections in North America. And considering the losses due to meat recalls, it could save meat producers as much as $5 billion a year.

Says Finlay: "This could become one of the standard vaccinations for cattle."

Fusogenix Inc.: Scientists have long known that drugs and genes can be "packaged" inside a microscopic fatty droplet. It's a way of defending against decomposition or attack before the contents reach their destination in the body. The problem: how to get the contents inside the target cell.

In CIHR-funded research, Dr. Roy Duncan, associate professor of microbiology and immunology at Dalhousie University, began experimenting with certain viruses that cause cell membranes to fuse with other nearby cells. His idea is to use these proteins to merge the packaged droplets—called liposomes—with the cell membrane as a means of treating cancer or infections, or delivering gene therapy or vaccinations to the human body.

If scientifically and commercially

successful, this technology could take aim at the lucrative drug delivery market, estimated at about US$20 billion, or about 10% of the $200-billion prescription pharmaceutical market.

About a year ago, Duncan established Fusogenix Inc. and obtained $285,000 from MedInnova Partners Inc., a technology development company that provides seed funding to develop and commercialize early-stage biomedical discoveries.

The initial investment will sustain the research for about 18 months. "During that time, we have to show that by using our proteins we can effect a more efficient drug delivery inside cells," says Duncan. "If they do work better, we go to the next level." That, he explains, would involve animal models and ex-vivo (not injected) tests that would require another $3-million to $5-million investment from one or a combination of other investors.

SignalGene Inc.: After identifying genes associated with breast cancer and osteoporosis in CIHR-funded research, Dr. François Rousseau, an associate professor of medicine at Laval University, knew that these discoveries could be helpful in creating predictive or diagnostic tests, preventative treatments and genetic therapies for these conditions.

SignalGene Inc. began assisting this research in 1999, along with other genetic research conducted by Vincent Guigère, director of molecular oncology at McGill University. Guigère and Rousseau are now scientific advisors to the company.

SignalGene, with 62 employees under CEO Michael Dennis, has since adopted a "platform" strategy for gene discovery that combines computer-aided drug design with genomic biology and pharmacology. Two acquisitions in 2000 solidified this strategy: GeneScape Inc., a Toronto company that developed a sensitive technology to measure whether gene expression is turned "on" or "off," and Nanodesign Inc., a Guelph, Ont., company that developed computer-assisted drug design software.

These technologies accelerate drug discovery, giving SignalGene the capability of developing numerous drugs and therapies, driving up its potential while spreading risk. SignalGene now has four programs to identify genomic markers and drug targets for breast cancer, osteoporosis, Alzheimer's disease and psoriasis. ■■■

Promising Research: **Cancer Treatment**

Researchers at the University of Calgary have discovered how to use a virus to fight cancer.

Cells begin to show abnormal growth that is characteristic of cancer when a certain biochemical pathway, the RAS pathway, becomes active. In CIHR-enabled research, Dr. Patrick Lee, professor of cancer biology, along with brain oncologist Dr. Peter Forsyth, have found that the commonplace Respiratory Enteric Orphan or REO virus selectively kills cells with highly active RAS pathways.

The research team injected REO virus into human cancers implanted in mice. Results announced last summer showed the virus destroyed not only injected tumours but also tumours in other parts of the body. "We are now seeing whether the virus can work on cancers that have metastasized beyond the initial organ to other organs," says Lee. "This is extremely important, because most cancer patients die from metastatic cancer."

In animal tests, the REO virus effectively attacked colorectal, ovarian, breast and prostate cancers. Small-scale tests on groups of about 50 humans are under way for prostate cancer and in the application stage for brain cancer.