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Follow the Leaders

CELEBRATING CANADA'S BIOTECHNOLOGY INNOVATORS

SECOND EDITION

Canada

FOLLOW THE LEADERS

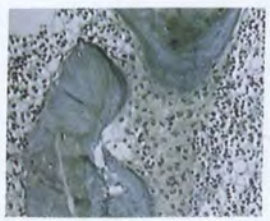
Virus research that lets persons with HIV/AIDS lead productive lives. Molecular science that draws medicinal and industrial products from natural, renewable resources. Protein investigation that probes beneath the surface of genomic discovery.

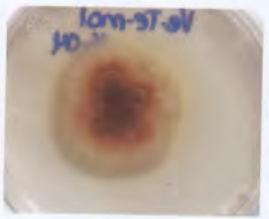
Behind each of these novel ideas stands a Canadian who is out front, exploring the promise of biotechnology on the frontiers of human knowledge.

Follow the Leaders

Second Edition

CELEBRATING CANADA'S BIOTECHNOLOGY INNOVATORS

The Government of Canada is proud to present new and updated stories highlighting how Canadian innovators are touching lives, generating economic benefit, and laying foundations for future discovery. Stories that demonstrate why Canada is a great place to bring innovation to life.

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Fifty years ago, the phrase 'double helix'
entered our vocabulary and expanded our horizons.
The discovery by James Watson and Francis Crick
was hailed as one of the most important in the history of science,
but it is doubtful that anyone could have predicted
the enormous, transformative effect it would have on biology,
on medicine and on our understanding of life itself.
Fewer still would have predicted that it would give rise
to a whole new branch of science—biotechnology.

GENOME CANADA

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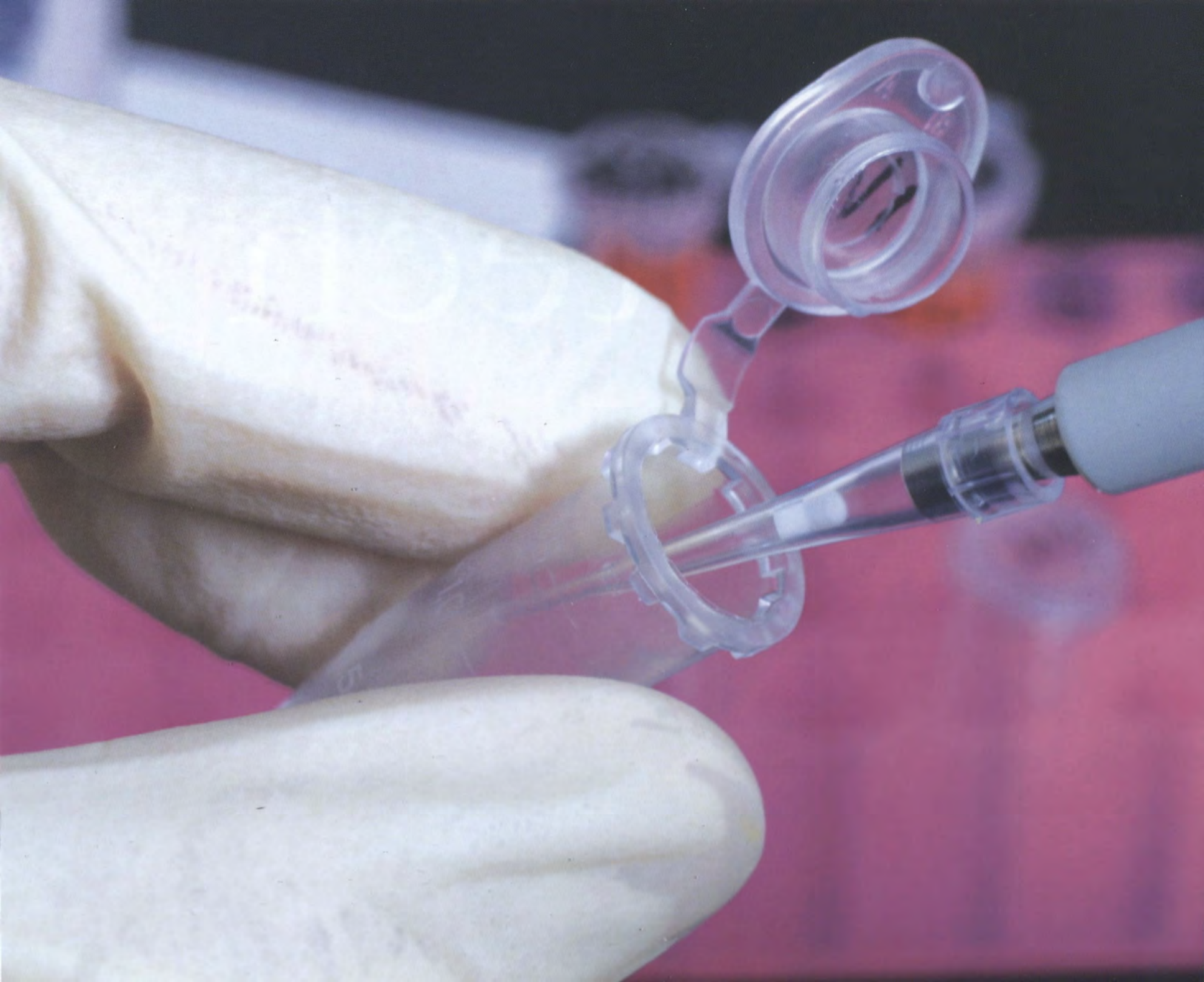


CANADA:
A GLOBAL LEADER
in Biotech
research

In 2000, scientists completed the first working draft of the human genome, ushering in a new era of scientific discovery. As part of the global team that worked on the Human Genome Project, Canadian scientists were proud contributors to one of the most fascinating and promising discoveries in human history. More recently, in April 2003, Canadian scientists announced their compilation of the complete DNA sequence of human chromosome 7, using fifteen years of their own data combined with public and private databases created as a result of the Human Genome Project.

In Canada, scientific breakthroughs seem to happen almost daily. For example, on April 12, 2003, scientists at the British Columbia Genome Sciences Centre completed the first publicly available draft sequence for the coronavirus implicated in Severe Acute Respiratory Syndrome (SARS). This information is expected to lead to the development of definitive diagnostic tests for SARS.

In the not-so-distant future, we will see vaccines for cancer, cures for diabetes and AIDS, regeneration of spinal cords, and food enriched for nutritional and medicinal purposes. The enabling power of biotechnology promises to create entirely new approaches to feeding the planet, treating illnesses and disease, and providing a sustainable supply of renewable raw materials and energy for economic development.

At the same time, Canada understands that the pace of change in this field demands an increased responsibility on the part of government to ensure that biotechnology is used wisely and safely—to strike an appropriate balance between the detection and management of risk and the development of new discoveries.

The Government of Canada is dedicated to seeing Canada become one of the top five countries in the world for biotech research and development by 2010. This commitment is helping to energize our industry, which is gaining increased levels of research investment from both the private and public sectors. The Canada Foundation for Innovation, a creation of the Government of Canada, has invested almost $2 billion in Canadian universities and research institutions. As well, the Government of Canada established the Canada Research Chairs Program in 2000 to provide $900 million for the creation of 2,000 university research chairs by 2005. Additional federal support includes $375 million for Genome Canada from 2001-2006, an annual investment of more than $460 million in biotech research by federal labs and granting councils, $123 million for seven life science-related Networks of Centres of Excellence, and more than $70 million in annual support to biotech development and commercialization by the private sector.

Canadian universities are also rising to the challenge of making Canada a global leader in biotech research. Programs that are designed specifically to grow in partnership with government and industry are continuing their long history of excellence in research. To help train the scientists of tomorrow, more academic programs are providing legal, business management and marketing skills to support both the scientific practice of biotechnology and the commercialization of innovations.

Indeed, Canada is now a global 'hot bed' for biotechnology. With about 375 core biotechnology firms projecting research and development activity of $1.5 billion and revenues of $3.6 billion in 2004, the biotech sector in Canada remains an important part of the foundation of a diversified economy. In its 2002 international study, *Competitive Alternatives: Comparing Business Costs in North America, Europe and Japan*, KPMG cited Canada, for the third consecutive time, as both the lowest-cost industrialized country for conducting business and the number one country in which to conduct biomedical research and development.

Canadians are already reaping the benefits of biotechnology and the powerful results of collaboration in this sector. Over the next decade or two, biotechnology will change our world in ways limited only by our imagination. Canada's commitments to fostering innovation and attracting investment will ensure that Canada delivers biotechnology to the world.

ALLAN ROCK
MINISTER OF INDUSTRY

PIERRE S. PETTIGREW
MINISTER FOR INTERNATIONAL TRADE

Canada...the right place to bring biotechnology to life

SUCCESS IN BIOTECHNOLOGY DEMANDS THE RIGHT BLEND OF TALENT, CREATIVITY AND OPPORTUNITY—A MIX EASILY FOUND IN CANADA. BOASTING ONE OF THE WORLD'S BEST FISCAL ENVIRONMENTS, PROVEN LOW BUSINESS COSTS, A TALENTED AND DEPENDABLE WORKFORCE, AND A BUSINESS AND REGULATORY ENVIRONMENT COMMITTED TO FOSTERING SUCCESS WHILE PROTECTING THE PUBLIC INTEREST, IT'S NO WONDER CANADA IS HOME TO MANY OF THE WORLD'S TOP BIOTECHNOLOGY RESEARCHERS AND FIRMS.

AS THE WORLD FORGES AHEAD INTO THE 21ST CENTURY, CANADA IS STAKING ITS CLAIM AS A COUNTRY WITH ENORMOUS POTENTIAL TO LEAD THE WAY IN KEY AREAS OF BIOTECHNOLOGY: HUMAN AND ANIMAL HEALTH, AGRICULTURE AND THE ENVIRONMENT, AND GENOMICS AND PROTEOMICS. IN FACT, CANADA IS ALREADY HOME TO THE SECOND-LARGEST NUMBER OF BIOTECHNOLOGY COMPANIES IN THE WORLD. AND THOSE COMPANIES ARE ALREADY CAPTURING WORLD MARKETS IN EVERYTHING FROM MEDICAL DEVICES AND BIOINFORMATICS, TO ENVIRONMENTAL ASSAYS AND INDUSTRIAL PROCESSES.

THE SECRET IS OUT

The costs of doing business in Canada are low. In fact, a 2002 international study by KPMG—which compared the basic costs of doing business across the G-7 countries, Austria and the Netherlands—concluded that Canada enjoys a substantial and constant cost advantage over the United States in all industries, particularly those requiring a large proportion of skilled workers. But that's only one aspect of an incredible range of benefits. In reality, what sets Canada apart is its combined advantages in scientific expertise, a balanced economy projected to weather the current economic storm, access to U.S. markets, and low labour and production costs. Add an excellent quality of life and a world-respected regulatory system, and it's not hard to see why Canada is one of the best places in the world to do business in biotechnology.

SCIENTIFIC EXPERTISE

Canada has cornered the market when it comes to the greatest asset in a knowledge economy: people. With the highest percentage of post-secondary graduates, Canada offers an exceptionally high ratio of skilled workers. Still, the Government of Canada believes it can improve an already good situation. In 2002, the Government of Canada announced an innovation strategy that provided a vision for improved access to higher learning, knowledge online, and the ability to gain new skills. Considering that Canada already has the highest percentage of population with Internet access among G-8 countries, it's no wonder Canada's workforce is considered a valued asset.

The future of science and technology is both highly specialized and necessarily multidisciplinary. To support such demands, the Government of Canada established the Canada Foundation for Innovation (CFI). An independent corporation, the CFI's goal is to strengthen the capability of Canadian universities and research institutions to carry out world-class research and technology development. The CFI targets its investments in research infrastructure projects in health, science, engineering and the environment. As well as helping to improve the quality of life of Canadians, these projects help protect the environment. Advances in many areas of science translate into potential economic growth.

Canada also recognizes that talent is located all over the world. Researchers from around the globe are welcome to come to Canada to explore new ideas and opportunities in a dynamic environment. Canada's fast-track immigration system for skilled workers helps universities and firms attract top talent and grow their core competencies. A diversity of culture and depth of knowledge are key factors in understanding and responding to global and niche needs.

INDUSTRY SUPPORT

Recognizing biotechnology's vital role in the future, Canada has established an innovation system supporting collaboration between scientific and business communities. The Networks of Centres of Excellence (NCE) program fosters powerful partnerships among university, government and industry to develop Canada's economy

and improve the quality of life for Canadians. World-class, regional technology clusters support the growth of significant concentrations of innovative companies around R&D facilities such as those found in universities and leading-edge government laboratories.

Montréal, home to firms such as Neurochem and Nexia, hosts the world's largest cluster of pharmaceutical research and development organizations. The bio-agriculture cluster in Saskatoon, home to VIDO, continues to attract interest and investment from all corners of the globe. Toronto's medical research community ranks among the top four in North America, attracting firms such as Aventis Pasteur.

These successes reflect a key fact: Canada understands the corporate sector's need to keep an eye on the bottom line. By 2005, firms in Canada will have almost a 4.5 percentage point corporate income tax advantage over U.S. firms. In fact, Canada's top rate on capital gains is now lower than the typical top rate in the United States. Canada's capital tax will be reduced in stages, and by 2008 will be eliminated. And it's not just corporate taxes that are falling; by 2004-2005, federal personal income taxes will have been reduced by 21 per cent on average. When you add to these the most generous tax credits for R&D in the G-7 countries, you have a tax system that is more than competitive.

A highly efficient regulatory system helps companies bring products to market faster, while Canada's 20-year patent protection plan ensures they realize rewards over an extended period. In addition to low labour and production costs, Canada's first-rate telecommunications infrastructure helps reduce the everyday costs of doing business in a global market.

Through the North American Free Trade Agreement (NAFTA), Canada has paved the way for domestic companies to gain direct access to vital sectors of the massive U.S. market. In fact, Canada is already the largest U.S. trading partner with the total value of Canada-U.S. trade standing at $696 billion in 2001.

QUALITY OF LIFE

Canada has an enviable reputation for repeatedly capturing the United Nations' designation as one of the best countries in the world in which to live. In addition to offering an acclaimed health care system, superior universities and safe communities, Canada enjoys the lowest cost of living among G-8 nations. It all adds up to making Canada a great place to work and to live.

NET RESULTS

Canada's many benefits make it possible for this country to develop, attract and retain the best and brightest minds, the most innovative entrepreneurial spirits, and the most savvy investors.

This book provides a snapshot of Canadian innovation in biotechnology at a critical point in time—the beginning of a new century in which technological advances are heralding the next industrial revolution. Read the stories of some of our most prominent and innovative scientists and business leaders and see for yourself why Canada is such a great place to bring innovation to life.

HEALTH RESEARCH

THE GROWTH SECTOR OF THE 'NEW ECONOMY'

AS THE 21ST CENTURY UNFOLDS, THE HEALTH SECTOR IS EMERGING AS THE LARGEST AND MOST IMPORTANT DRIVER OF THE GLOBAL ECONOMY. SOME INDUSTRY ANALYSTS PREDICT THAT THE GROWTH RATE IN HEALTH-RELATED KNOWLEDGE IN THE CENTURY AHEAD WILL EXCEED THE GROWTH RATE THAT THE INFORMATION TECHNOLOGY SECTOR EXPERIENCED IN THE 20TH CENTURY. IN FACT, SUCH PREDICTIONS ARE THE LOGICAL ENDPOINT OF THE RECENT CONVERGENCE OF HEALTH SCIENCE AND INFORMATION TECHNOLOGY, WHICH IS DRIVING RECENT ADVANCES IN BIOTECHNOLOGY.

TODAY, CANADA'S BIOTECHNOLOGY SECTOR IS THE SECOND LARGEST IN THE WORLD. CANADIAN HEALTH RESEARCHERS ARE BRINGING BETTER HEALTH FOR ALL CANADIANS AND PEOPLE AROUND THE WORLD. IN THE PROCESS, THEY ARE CONTRIBUTING TO ECONOMIC DEVELOPMENT THROUGH COMMERCIALIZATION AND JOB CREATION, AND GENERATING SIGNIFICANT RETURNS FOR INVESTORS.

CANADIAN INNOVATION
IN HEALTH BIOTECHNOLOGY

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Aventis Pasteur Limited is harnessing the canarypox virus in experimental vaccines designed to boost the human immune system against cancer. Unlike traditional vaccines, these vaccines aim to defeat (treat) cancer rather than prevent it.

Page 26

In the 1920s, Canadian scientists brought insulin injections to the world. Now, they're revolutionizing diabetes treatment again. A University of Alberta team has successfully transplanted islets (the cells that produce insulin), offering diabetics a new lease on life.

Page 34

Dr. Harold Jennings of Canada's National Research Council invented the world's first conjugate vaccine that effectively protects infants against Group C meningitis—a potentially fatal infection of the fluid and lining of the brain and spinal cord.

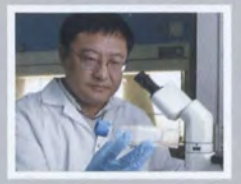
Dr. Molly Shoichet is the co-founder of two biotechnology firms that aim to develop specially designed polymers for tissue engineering applications. She hopes to achieve spinal regeneration by creating a biocompatible device that encourages nerve regrowth.

Page 18

A pioneer in photodynamic therapy, Vancouver-based QLT Inc.'s flagship product, Visudyne®, helps maintain the vision of patients with age-related macular degeneration (AMD). Visudyne had the world's most successful launch for a new ophthalmology drug.

Page 30

Millenium Biologix Inc. was launched in 1993 to develop and market Skelite™, a skeletal repair material. Skelite is used as implantable bone grafts and tissue engineering scaffolds on Earth, and has also been tested in space by NASA to learn why micro-gravity induces bone density loss.



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The world is in the midst of a profound revolution in health research—a revolution driven by the rapidly emerging understanding of the molecular basis of life. As with prior scientific revolutions, this one draws upon the convergence of diverse disciplines.

As genetics, molecular biology, small molecule and surface chemistry uncover new areas of discovery, information technology makes it possible to collect, store and analyse enormous volumes of data. As well, epidemiology, health economics, bioethics and the humanities provide the impetus to consider new developments from both individual and global perspectives.

Historically recognized throughout the world for scientific excellence, Canadian health researchers play a key role in this revolution. In a very real sense the biotechnology revolution started in 1921, when Canadian researchers Dr. Frederick Banting and Charles Best discovered insulin, showing that a protein could be used as a new therapeutic. Recently, Dr. Ray Rajotte and his University of Alberta team pioneered the 'Edmonton Protocol', eliminating the need for insulin injections in some people with Type I diabetes. In the emerging fields of genomics and proteomics, Canadians are demonstrating their leadership in areas such as cell signaling, developmental biology and bioinformatics. For example, the work of Dr. Tony Pawson, one of the world's leading experts in cell circuitry and proteomics, provides a foundation for novel approaches to drug discovery in the 21st century.

It is clear that advances in human and animal health will be realized by integrating current knowledge with multidisciplinary expertise. The accelerating pace of the health research revolution is driven by significant global commitments—of both human and financial capital—from the public and private sectors. The Government of Canada understands that success in the commercial arena depends on public investment in health research and innovation.

Through the Canadian Institutes of Health Research (CIHR), the Government of Canada is leading the way in establishing a national health research agenda and funding academic health research. CIHR's objective is to excel in the creation of new knowledge and its translation into improved health, more effective health services and products, and a strengthened Canadian health care system. Through 13 'virtual' Institutes, CIHR embraces four pillars of research: biomedical science; clinical research; health services and systems; and the social, cultural and other determinants of health.

The Networks of Centres of Excellence of Canada (NCEs) further enhance Canada's health research infrastructure. Each NCE links scientists from across the country, allowing collaboration on research in areas such as arthritis and stroke, genetic and bacterial diseases, vaccines and immunotherapies, protein engineering and stem cells.

The Canada Foundation for Innovation (CFI) strengthens the research capacity of Canadian universities, colleges, research hospitals, and other not-for-profit institutions. The Canada Research Chairs Program is the most ambitious initiative of its kind. Established in the year 2000, the Program is providing $900 million to fund 2,000 world-class researchers at Canadian universities by the year 2005. A key element of the Government of Canada's *Innovation Strategy*, the Chairs Program is enabling Canada's universities to attract and retain some of the world's best and brightest minds. Genome Canada is developing and implementing a national strategy in genomics research. In addition, Technology Partnerships Canada encourages private-sector investment in innovative biopharmaceutical R&D.

These programs are part of the Government of Canada's commitment to make Canada one of the top five countries in the world investing in R&D. They also seek to create strong ties among research organizations, universities and industrial partners, facilitating the translation of research discoveries into health benefits and economic gain.

Canada provides an exceptional environment for scientific enquiry and innovation in health research, and a regulatory system acknowledged as one of the best anywhere. To conduct scientific research in Canada is to make a statement of excellence. We invite you to take a closer look at what Canada offers as a home for health research that is paying both health and economic dividends.

Tissue engineering

BRINGS NEW HOPE FOR SPINAL CORD REPAIR

DR. MOLLY SHOICHET TACKLES THE PROBLEM OF SPINAL REGENERATION FROM A NEW ANGLE: CREATING A BIOCOMPATIBLE DEVICE THAT ENCOURAGES NERVE REGROWTH.

One of a new breed of scientists, Dr. Molly Shoichet, Canada Research Chair in Tissue Engineering, combines chemistry, biology and engineering into the emerging field of tissue engineering.

An expert in the creation and modification of polymers, Dr. Shoichet is the co-founder of two biotechnology companies that aim to develop specially designed polymers for neuro-regeneration and cardiovascular applications. She holds 12 patents, including two for processing technologies that form the basis of her companies.

As a young girl she aspired to be a medical doctor. But making her 'first polymer' in a university chemistry class eventually changed the course of Dr. Molly Shoichet's career. Today, the Associate Professor of Chemical Engineering and Chemistry at the University of Toronto is pushing the frontiers of science forward, inventing new technologies that may one day be used by the physicians of tomorrow.

Her research touches on both materials science and regenerative medicine—modifying and making new polymers for medical applications. The potential applications for such designer polymers—which can be formed into virtually any size, shape and texture—are many and varied.

"Our bodies have lots of internal plumbing, which polymers can be used to mimic," says Dr. Shoichet. "For example, polymers could be used for vascular grafts or other applications that require tubes. A simpler application would be using them to coat medical devices, such as pacemaker leads, to make them more biocompatible."

Dr. Shoichet and her team are developing polymers that are biodegradable and others that will elicit specific cellular responses. "A big area of tissue engineering is guided regeneration to encourage tissue to grow in specific areas rather than sporadically," she says. Dr. Shoichet is also developing a minimally invasive drug delivery strategy using injectable polymers, which could one day be used to treat spinal cord injuries. "The drugs are dispersed in a polymeric solution that gels quickly once injected into the subarachnoid space at the site of injury. So far we've demonstrated that this method is safe."

MARKETING BIOENGINEERED PRODUCTS

To help commercialize her inventions, Dr. Molly Shoichet has co-founded two biotechnology companies: matREGEN and BoneTec.

matREGEN focuses on the development and commercialization of products for the cardiovascular and nervous systems. Dr. Shoichet launched the Toronto-based company in 2002 with $1 million in seed capital from Genesys Capital Partners of Toronto. The company's platform technology—SpinFX—is a technique for making polymer-based porous tubes, composites and coatings. The market for such resorbable implants is estimated to reach $6 billion by 2008.

BoneTec—a bone tissue engineering company—is also founded on a processing technology developed by Dr. Shoichet. The company received its initial funding from University Medical Discovery Inc.

RECOGNITION FOR EXCELLENCE

Academic, researcher and entrepreneur, Dr. Molly Shoichet wears many hats and has received wide recognition for her research and innovation. She holds the Canada Research Chair in Tissue Engineering, and in 2003 was awarded the prestigious Steacie Fellowship by Canada's Natural Sciences and Engineering Research Council.

In 2002, Dr. Shoichet received the Canadian Institute for Advanced Research's Young Explorers Award (to the top 20 scientists under age 40 in Canada). She is also a recipient of Canada's Top 40 under 40 Award (for innovation and leadership).

The technologies being developed by Dr. Shoichet and her team have many potential medical applications. However, she has gained particular attention for her research on spinal cord regeneration, one of the ultimate challenges in tissue engineering.

Several problems have hindered traditional nerve transplants from restoring body movement and sensation. These include: not enough nerve cells grow; the transplanted nerves don't grow in the central nervous system; and surgeons must cause a second injury by removing a nerve from another part of the body. Research also indicates that the central nervous system actually inhibits nerve growth.

With these challenges in mind, Dr. Shoichet is tackling the problem from a different angle: developing a device to encourage nerve regrowth. "Nerve fibres need a pathway to grow along, molecules to encourage growth, and signals to guide them in the right direction," she says. "Our efforts are geared to developing a device that will meet these needs."

Applying her expertise in polymer science, Dr. Shoichet and her team are designing polymers to make artificial tubes that mimic the structure and feel of spinal cord tissue.

"The tubes, also called hollow fibre membranes, look like a soft white straw made out of wet spaghetti," she explains. "They're a hydrogel, which means they swell in water, and the walls are porous to allow nutrients to cross it."

The tubes—made using a processing technology that she invented—are then implanted across a break in the spinal cord, providing support and directional guidance for new nerve cells to grow along. While the tubes have the properties of soft tissue, they are strong enough to withstand compression at the site of implantation.

In preclinical trials, the tubes were implanted into the spinal cords of paraplegic rats then infused with neural growth factors, resulting in the growth of new nerve tissue and some restored movement. "What's encouraging about our findings is that we're starting to get some of the right cells to regenerate," says Dr. Shoichet. "The results show promise, but there is still a lot of work to do."

These and other technologies form the basis of two biotechnology companies that Dr. Shoichet has co-founded—matREGEN and BoneTec. matREGEN is a start-up biomaterials company based on a platform technology called SpinFX—a processing technology that can be used to create porous coatings, tubes and composite structures. The advantage of the SpinFX process is that it can be used to create very small diameter tubes and coatings (about 100 micrometres in diameter), which is important for capillary-based sensor applications.

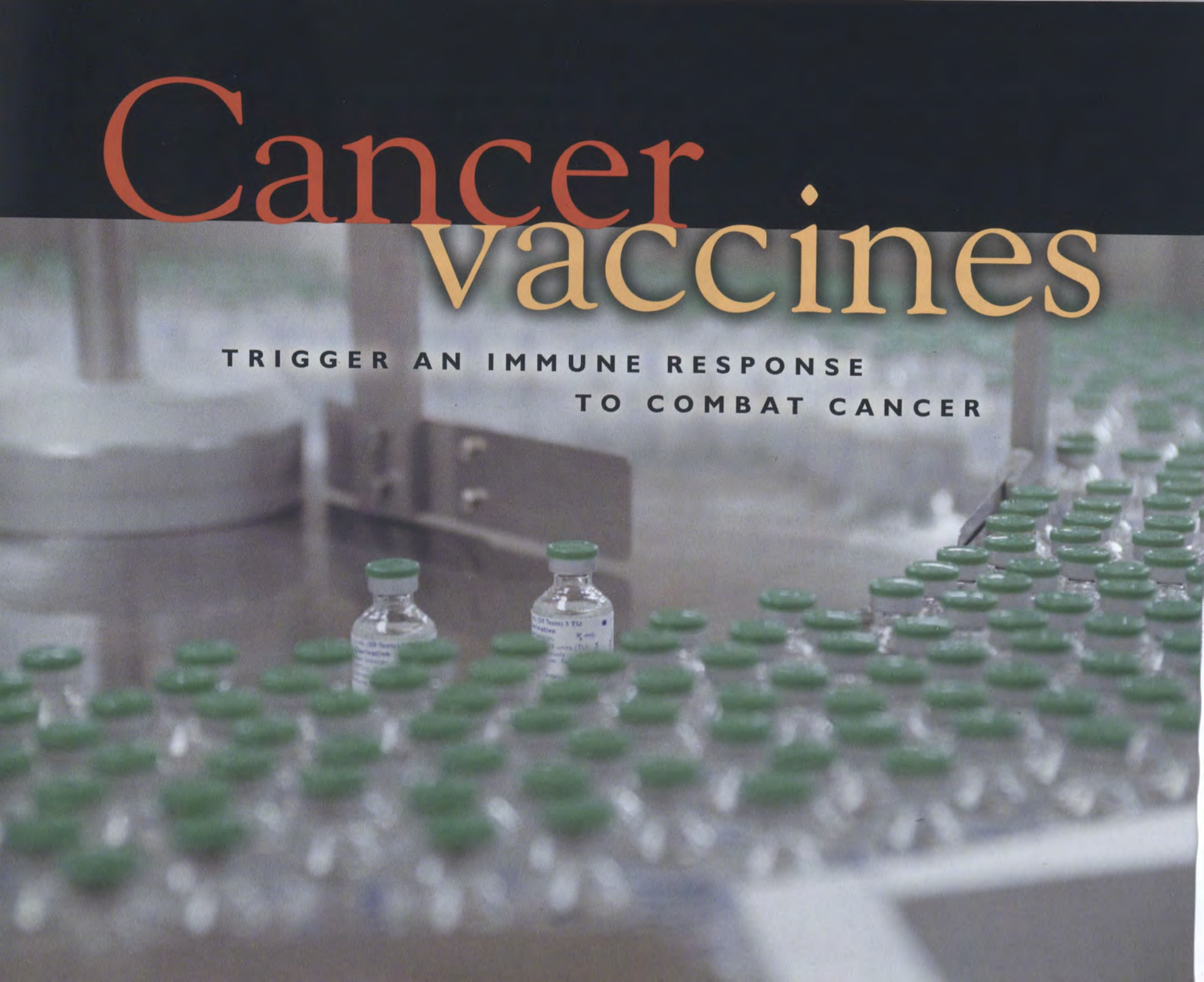
"What's so promising about regenerative medicine is there could be a whole paradigm shift in terms of the way we treat people," says Dr. Shoichet. "The challenges are incredible."

Right now we treat diseases, but the potential of regenerative medicine is to overcome them. That's what's so exciting. We're applying this to spinal cord repair. Others are applying it to bone defects or burn wounds.

DR. MOLLY SHOICHET, ASSOCIATE PROFESSOR,
CHEMICAL ENGINEERING AND CHEMISTRY,
UNIVERSITY OF TORONTO

Cancer vaccines

TRIGGER AN IMMUNE RESPONSE
TO COMBAT CANCER



AVENTIS PASTEUR LIMITED IS LEADING A GLOBAL INITIATIVE THAT COULD CHANGE THE WAY WE TARGET CANCER.

In the battle against cancer, the future could rest with a tiny virus.

The canarypox virus ordinarily infects and grows in canaries only, but Aventis Pasteur is harnessing it in experimental vaccines designed to help the human immune system fight back and win against cancer.

These therapeutic vaccines—intended to treat cancer rather than prevent it—may soon join the arsenal of weapons used to control the recurrence of cancer, enhance quality of life, and offer new hope.

As a supplement to traditional treatments, such as surgery or chemotherapy, therapeutic vaccines show great promise in boosting the immune system.

Frustration with the lack of improvement in survival rates in certain cancers led Dr. Neil Berinstein to seek more innovative approaches to the foe with many faces. While training as a medical oncologist two decades ago at the University of Toronto, Aventis Pasteur Limited's program director for cancer became fascinated by the potential of the human immune system to battle disease.

As head of the Aventis Pasteur global Cancer Vaccine Program, Dr. Berinstein now oversees a collaboration involving Aventis Pasteur and top cancer researchers in Canada and around the world, which aims to harness the immune system against cancer.

The program began in June 1997 when Aventis Pasteur announced it would spend up to CAD$350 million over 10 years to develop therapeutic vaccines for cancer. Already, Aventis Pasteur has shown great success in establishing the new concept of therapeutic vaccines as a viable approach to cancer treatment. The program is currently focusing on two main targets—colorectal cancer and melanoma—with further research underway on breast cancer. In North America and Europe, about 300,000 new cases of colorectal cancer and 50,000 new cases of melanoma are diagnosed each year.

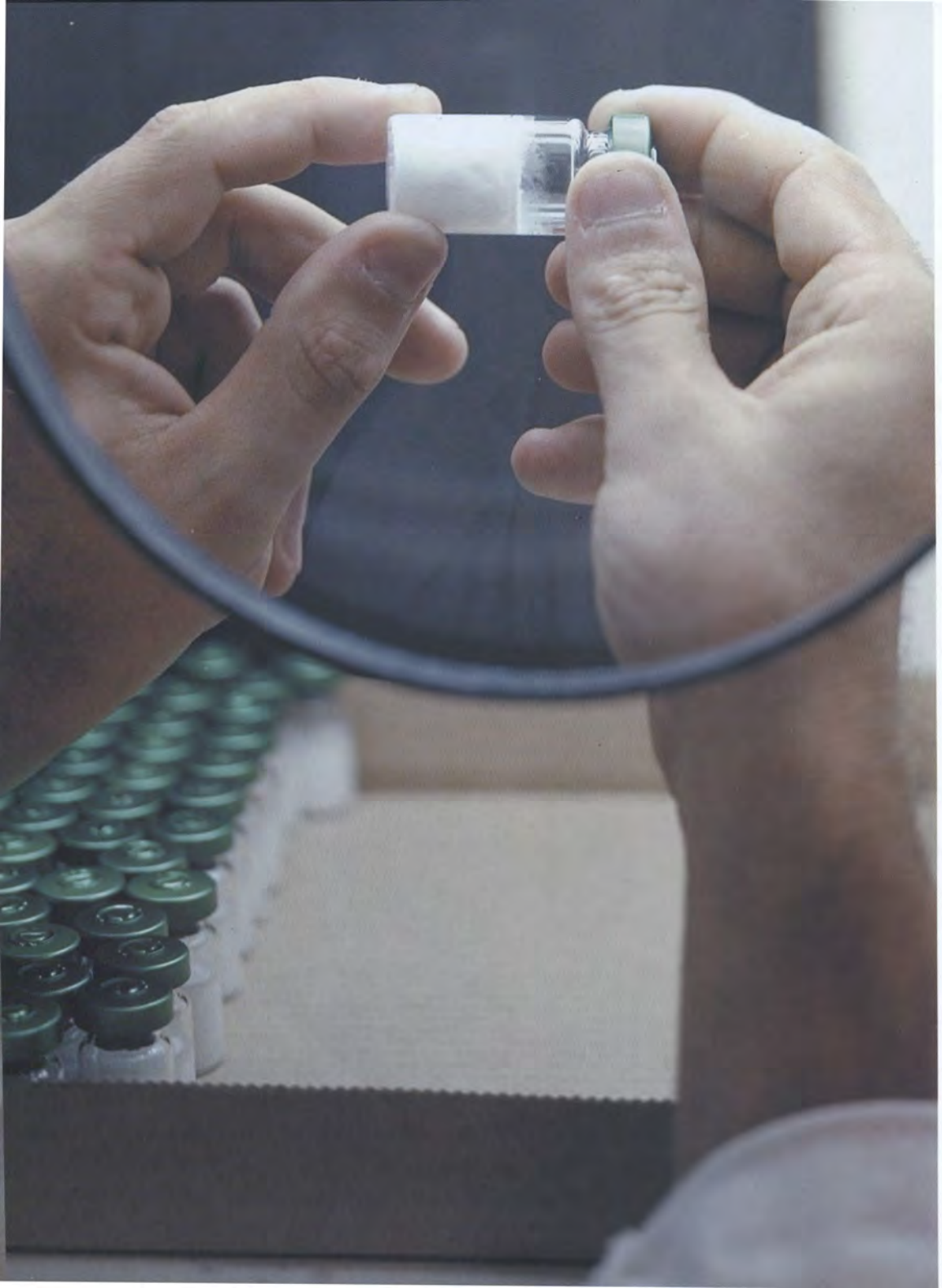
"The science has evolved to the point where this is really possible," says Dr. Berinstein. "The idea of a therapeutic cancer vaccine isn't just a dream; it finally is something that is potentially within our grasp."

A PROUD HISTORY OF INNOVATION

When Dr. John G. Fitzgerald founded Connaught Laboratories in 1914, his first success story was diphtheria antitoxin, formulated in an old stable that is still preserved on Aventis Pasteur Limited's Connaught Campus in Toronto. This was soon followed by insulin, polio vaccine and, more recently, the gold standard in immunization, Pentacel™—a combined vaccination against five diseases, which is now given to all Canadian children.

Today, the company is part of pharmaceutical giant Aventis SA. With 1,000 employees in Toronto, Aventis Pasteur is Canada's largest vaccine company, manufacturing or distributing 30 vaccines and immunotherapeutic products, which protect against 17 infectious diseases and common illnesses.

Aventis Pasteur invests almost 40 cents of every sales dollar into research and development in Canada.



In the usual sense, a vaccine prevents disease by preparing the immune system for a possible attack at a later date. Therapeutic cancer vaccines, on the other hand, would be used to 'turn on' the immune system of people who already have the disease and to increase the potential power of current treatments (such as chemotherapy) to fight recurrence.

The research program uses Aventis Pasteur's 'prime-boost' approach to stimulate an immune system attack on tumour cells. "The prime-boost technology first tells the immune system which targets to attack and then revs it up into overdrive for the assault," says Dr. Berinstein. This approach activates both arms of the immune system—the cellular arm, which hunts down and kills target cells, and the humoral arm, which produces antibodies. Both arms must be active for an immune response to succeed against an attacker.

"Unlike conventional vaccines, which turn on the immune system to prevent disease, our vaccines will, it is hoped, stimulate an immune response against a cancer that has already started," says Dr. Berinstein. "We are confident that, in combination with other therapies, this will improve the chances of beating the disease."

Aventis Pasteur has already had an opportunity to test its theories. In 1999, clinical trials of its vaccine against melanoma began at Sunnybrook and Women's College Health Sciences Centre and Cancer Care Ontario/Toronto-Sunnybrook Regional

Cancer Centre. It is here, on two floors of a research building, that Aventis Pasteur runs its global Cancer Vaccine Program.

Clinical trials for colorectal cancer are underway in six Canadian cities. Cancer treatment centres in the United States are also involved in clinical trials involving an Aventis Pasteur candidate vaccine for colorectal cancer, one of the most common forms of cancer. In Canada alone, colorectal cancer is the second most common type of cancer for both men and women. Approximately 17,200 Canadians are diagnosed with colon cancer every year, and about 6,400 people die from it. Despite many advances in cancer research, the overall survival rate of patients with colorectal cancers—especially of the bowel—has improved little in recent years. Initial studies will examine the safety of the vaccine when administered with chemotherapy.

Canada is an ideal environment for innovation. This country offers a critical mass of world-class talent working at internationally recognized research institutes.

MARK LIEVONEN,
PRESIDENT, AVENTIS PASTEUR LTD.

Aventis Pasteur is already exploring other cancers that might benefit from the vaccine approach to treatment. "That doesn't mean there isn't a lot of hard work ahead and there won't be some setbacks, but conceptually this is possible now, and I don't think it was 10 years ago," says Dr. Berinstein.

CANADA'S FUTURE LOOKS BRIGHT FOR CANCER VACCINE DEVELOPMENT

As a renowned vaccine leader, Aventis Pasteur Limited is set to put Canada on the global map with its research into therapeutic cancer vaccines.

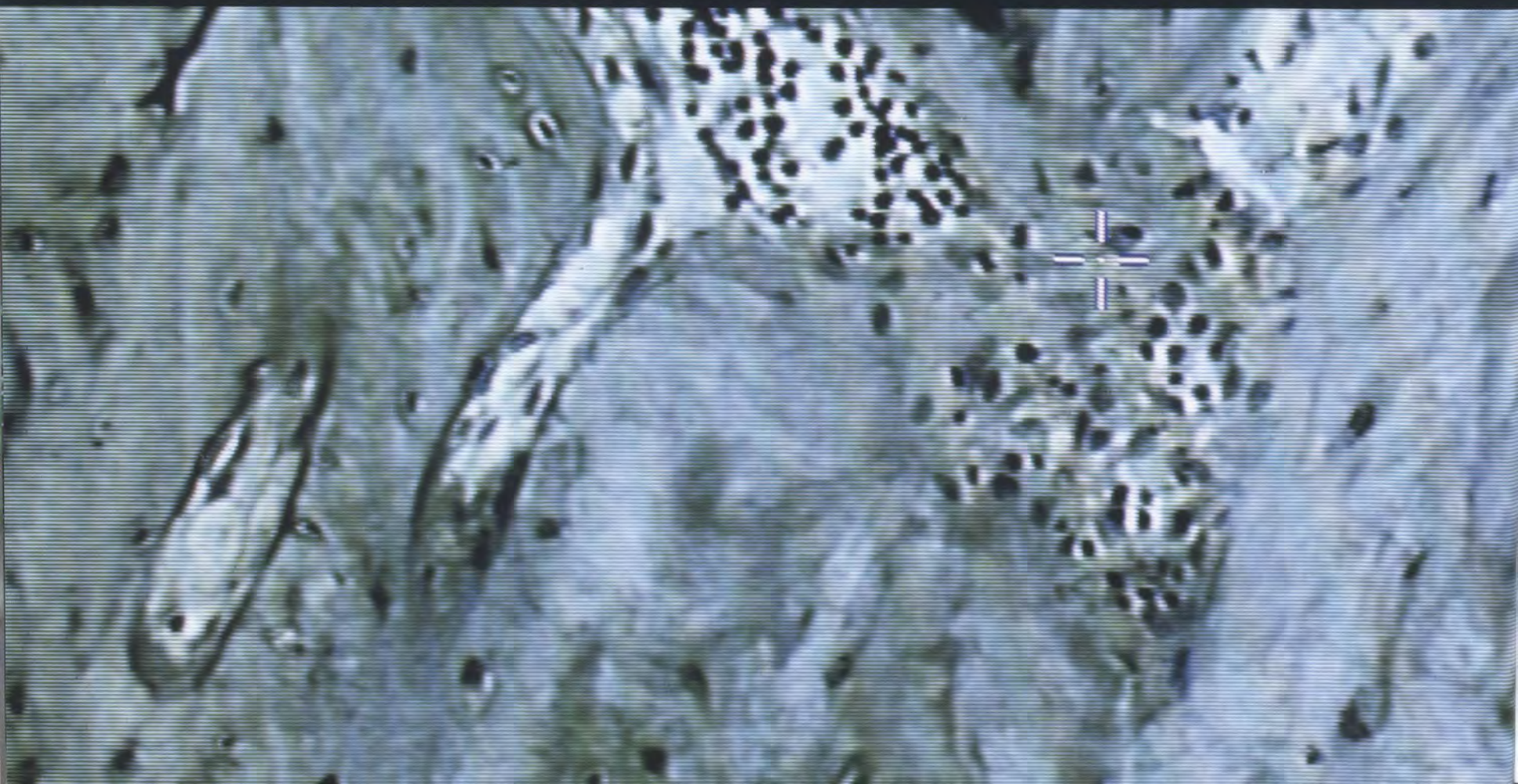
Aventis Pasteur just completed construction of a state-of-the-art, high-technology facility dedicated to its cancer vaccine program. The $19 million centre on the company's Toronto campus will house researchers, cancer experts and vaccine technicians, as well as Canada's first robotic arm for the explicit use of vaccine production.

"The new facility is the result of recognizing that therapeutic cancer vaccines require a serious research and development commitment," says Mark Lievonen, President.

"Researchers and technicians located there will focus on the development and clinical manufacture of these vaccines, which promise enormous benefits for Canada and the world."

Bone-building molecule

PUTS BACK WHAT'S BEEN LOST



A NEW TREATMENT HELPS BUILD BONE MASS QUICKLY AND SAFELY FOR PEOPLE WITH ADVANCED OSTEOPOROSIS.

The World Health Organization has named osteoporosis second only to cardiovascular disease as the world's most common health care problem. An estimated 100 to 200 million people worldwide have this quiet disease, but most won't know it until significant bone loss leads to a fracture. By then, the damage is done.

Existing treatments—such as estrogen therapy—help to slow bone loss, but until recently there has been no way to put that missing bone back.

New hope comes from innovative treatments derived from parathyroid hormone (PTH). A product called Ostabolin-C™—developed by Zelos Therapeutics Inc.—promises to rebuild bone quickly, and without the side effects of other PTH therapies.

Osteoporosis steals bone slowly, chipping away over the years until one day a simple fall means a broken hip or fractured wrist. Most victims are post-menopausal women; one in two women will have an osteoporosis-related fracture during their lifetime. Among men, the proportion is one in eight.

The costs in human life and health care are enormous. Hip fracture is the number one reason for entering long-term care facilities. Almost a quarter of hip fracture patients die within a year. The health care cost of osteoporosis is estimated at US$13.8 billion/year, and with an aging population, is only expected to rise.

The World Health Organization has declared osteoporosis to be the world's #2 health problem, behind only cardiovascular disease.

Using technology licensed from Canada's National Research Council, a new company called Zelos Therapeutics Inc. has developed a powerful 'bone building' product called Ostabolin-C™. The treatment is derived from parathyroid hormone (PTH), a naturally occurring hormone that regulates calcium levels in the body.

The natural hormone is a chain of 84 amino acids. "What we've done is take a fragment

HEALING SKIN AND BONE

Zelos Therapeutics Inc. has found a surprising application for its bone-building hormone—treating psoriasis. "It turns out that the receptor for this molecule is found not only in bone but also in the skin," says Dr. Paul Morley, Chief Technical Officer for Zelos.

Psoriasis causes skin cells to grow so quickly that they don't have time for differentiation: the process whereby cells stop growing and put down a layer of keratin, the outer layer of the skin. "PTH slows down that cycle of accelerated growth and allows that normal keratinization process to occur," says Dr. Morley.

Zelos is investigating a topical cream treatment for psoriasis based on the hormone.

The incidence of osteoporosis is the same as breast, ovarian and uterine cancer combined.

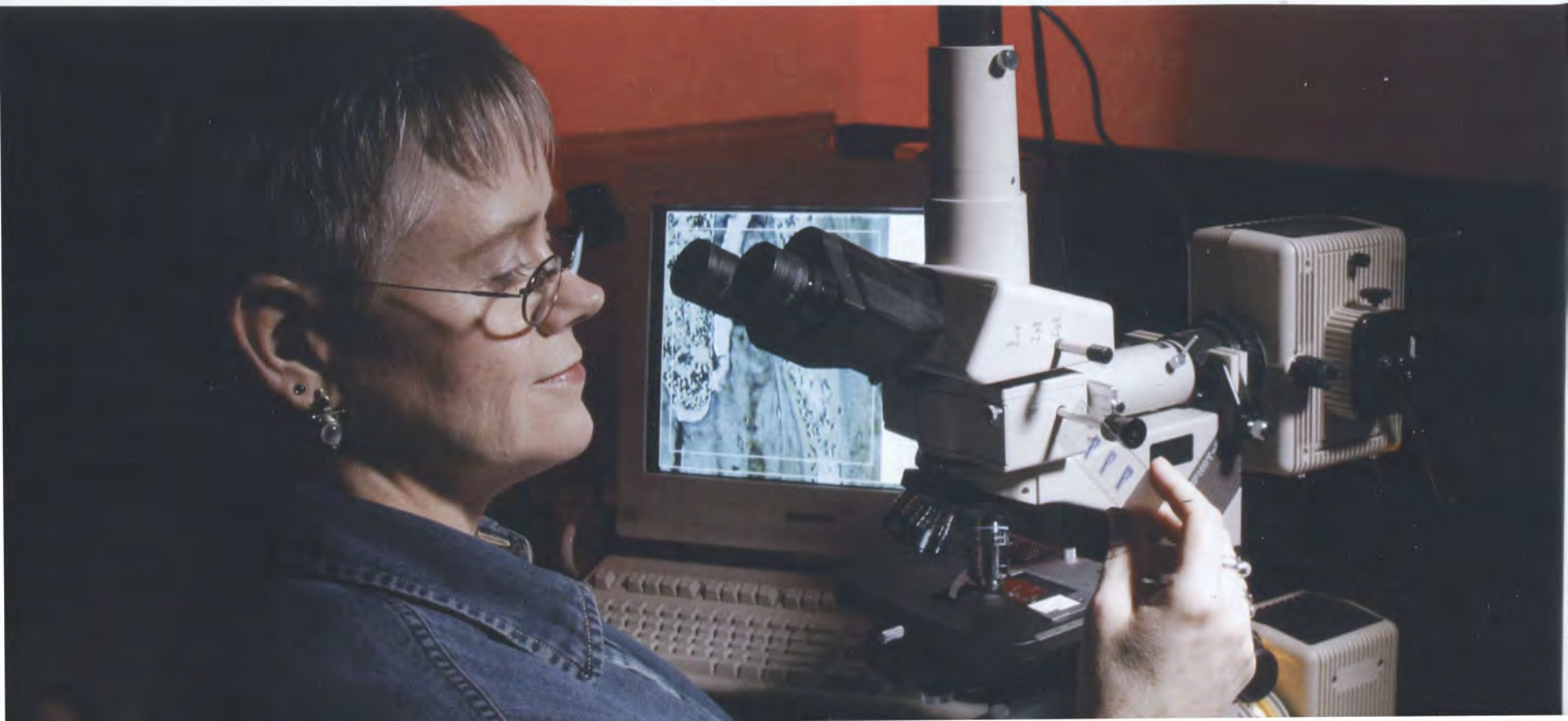
consisting of the first 31 amino acids and modify it to make it both safer and better at building bone," says Dr. Paul Morley, Chief Technical Officer for Zelos.

Ostabolin-C affects the two cell types that regulate bone density: osteoblasts, which build bone mass, and osteoclasts, which tear it down. "You reach your peak bone mass at age 30, then you start to lose it quite slowly," says Dr. Morley. "Throughout life, estrogen acts like a brake on osteoclast cells. But after menopause, when estrogen levels go down, bone loss accelerates quickly."

Ostabolin-C stimulates the osteoblast cells to build more bone. At the same time, it inhibits the bone-destroying osteoclasts.

The product holds greatest promise for advanced osteoporosis patients, whose bone mass is so reduced that existing 'antiresorptive' treatments—which slow further bone loss—offer limited help.

It also avoids the side effects caused by other PTH molecules, of which the most serious is hypercalcemia—an elevation of calcium in the blood. "Calcium is one of the most tightly controlled variables in the body," says Dr. Morley. Elevated blood calcium can cause mild to severe



symptoms such as nausea, vomiting, headaches, fatigue and kidney stones.

Early testing has shown that, unlike other molecules, Ostabolin-C has no effect on blood calcium levels. "So we can use a higher dose of our molecule, which will build the bone back faster but without the dangerous side effects," says Dr. Morley.

Zelos has attracted strong interest from investors, with CAD$14 million already in place. Clinical trials are set to begin in the fall of 2003. Right now, the company is looking at a product that patients inject daily, like insulin. But the long-term goal is to develop a more patient-friendly form of the drug. "The holy grail for these types of drugs is an alternative delivery form. This basically means a pill, which patients can take easily," says Dr. Morley.

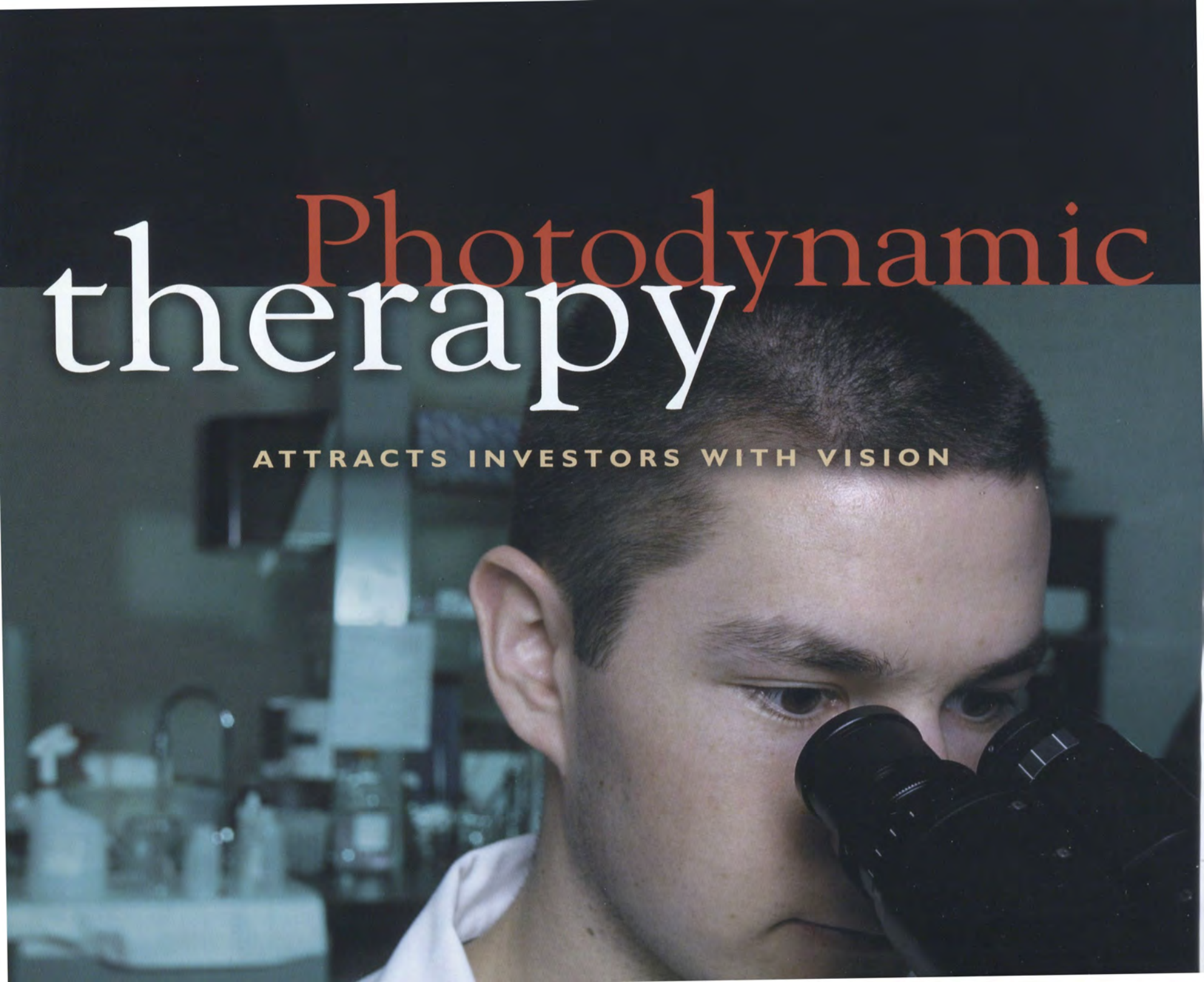
PTH has potential for many other bone-related ailments. For patients with hip or knee replacements, the bone around the implant often deteriorates. PTH could help stimulate bone growth around the implant and hold it in place, delaying or preventing the need for more surgery.

Another target group is patients who take high doses of steroids for chronic inflammatory diseases, such as inflammatory bowel disease. "Those molecules destroy bone," says Dr. Morley. "But if the patient takes PTH as well, we might be able to prevent that bone loss from occurring."

PTH could also help in the simplest bone injury, such as a broken leg. "You could get somebody out of a cast two or three weeks sooner, and the healed bone would be just as strong, if not stronger," says Dr. Morley.

Photodynamic therapy

ATTRACTS INVESTORS WITH VISION



QLT INC.'S FLAGSHIP PRODUCT, VISUDYNE®, HAD THE WORLD'S MOST SUCCESSFUL LAUNCH FOR A NEW OPHTHALMOLOGY DRUG.

One could say QLT's success began when a company founder noticed that her son sometimes had a strange rash after playing in nearby fields. A colleague suggested that it could be caused by a toxic enzyme found in cow parsley—an enzyme that is inactive unless struck by sunlight.

A group of scientists from the University of British Columbia in Vancouver then began thinking about using light wavelengths to activate drugs. In 1987, six years after QLT was formed, the company acquired the rights to Photofrin™—a light-activated cancer drug. The company shepherded the drug through clinical trials, and made it the first photodynamic therapy to hit the market.

By then, the company had turned its attention to another serious condition that ultimately led to a medical breakthrough and even greater success for QLT.

QLT Inc. founder, Past President and CEO Dr. Julia Levy knew little about age-related macular degeneration (AMD) before 1985, the year her mother began to go blind. At the time, QLT was focused on cancer treatment.

"But when your parent is losing her vision, especially when you're a scientist, you become very aware of a disease," she says. A year later, she heard an ophthalmologist hypothesize that photodynamic therapy (PDT)—QLT's specialty—could treat tumours in the eye. Dr. Levy immediately made the connection between PDT and AMD.

By 1994, that connection—combined with the work of QLT researchers and others—had culminated in clinical trials of a new drug: verteporfin, now marketed as Visudyne®.

For the AMD patient, this photodynamic therapy is a 20-minute process that begins with a pinprick. After an intravenous injection, the drug quickly travels through the bloodstream, adhering preferentially to the walls of abnormal blood vessels such as those in the damaged retina. Fifteen minutes later, an ophthalmologist delivers an 83-second burst of non-burning laser light to activate the drug, thereby converting normal oxygen in the cell into a highly energized form called 'toxic singlet oxygen'. The singlet oxygen immediately disrupts normal cellular functions, causing targeted cells to curl into

VISUDYNE'S SUCCESS SUPPORTS LONG-TERM GROWTH

Formerly called Quadra Logic Technologies Inc., QLT Inc. was founded in 1981. The company initially focused on antibody research, but soon shifted its attention to photodynamic therapy (PDT).

In 1987, QLT bought a subsidiary of Johnson & Johnson and acquired the rights to Photofrin™, a light-activated cancer drug. QLT shepherded Photofrin through clinical trials that led to its approval for the treatment of lung, bladder, cervical and esophageal cancers.

In April 2000, QLT received approval for Visudyne in the United States, and two months later sold the rights to Photofrin to Axcan Pharma Inc. Visudyne went on to become the most successful new ophthalmology product ever and still has tremendous untapped potential. Sales of Visudyne have not only made QLT profitable, but have also allowed it to move into new areas of research with other exciting therapeutic prospects.

unusual shapes—a reaction known as 'beading'. This transformation tricks the body into thinking that the vessel is about to hemorrhage. Seeking to avoid a rupture that could damage surrounding tissue, the body quickly destroys the distressed cell.

Because plenty of healthy blood vessels remain to nourish the retina, destroying these abnormal blood vessels does not harm vision. Rather, the therapy effectively eliminates the risk of abnormal cells leaking excess protein or forming scar tissue, the two processes that damage the retina in AMD.

When Visudyne underwent worldwide clinical trials, the results were superb. One year after treatment, 60 per cent of AMD patients showed treatment benefit; in fact, approximately 20 per cent experienced improved vision. Virtually all the patients receiving the photodynamic therapy fared better than AMD sufferers who received no treatment. In a four-year follow-up, many recipients enjoyed complete stabilization of their vision.

Visudyne received full regulatory approval for the treatment of predominantly classic AMD in 2000 and has since been used to treat more than 200,000 people worldwide. Sales of the drug reached US$287 million in 2002. More recently, the drug was approved for treating abnormal retinal blood vessels in patients with

AMD: FACTS AND FIGURES

Age-related macular degeneration (AMD) is the leading cause of blindness among men and women over 50 years of age, striking an estimated 500,000 new victims worldwide every year.

Wet AMD—the condition's more severe form—results from the growth of abnormal blood cells across the macula, or central area of the retina. These blood vessels progressively leak fluid and create scar tissue. Within months, the sight of AMD sufferers starts to deteriorate, becoming increasingly foggy in the centre of their field of vision.

Without treatment, AMD invariably leads to blindness.

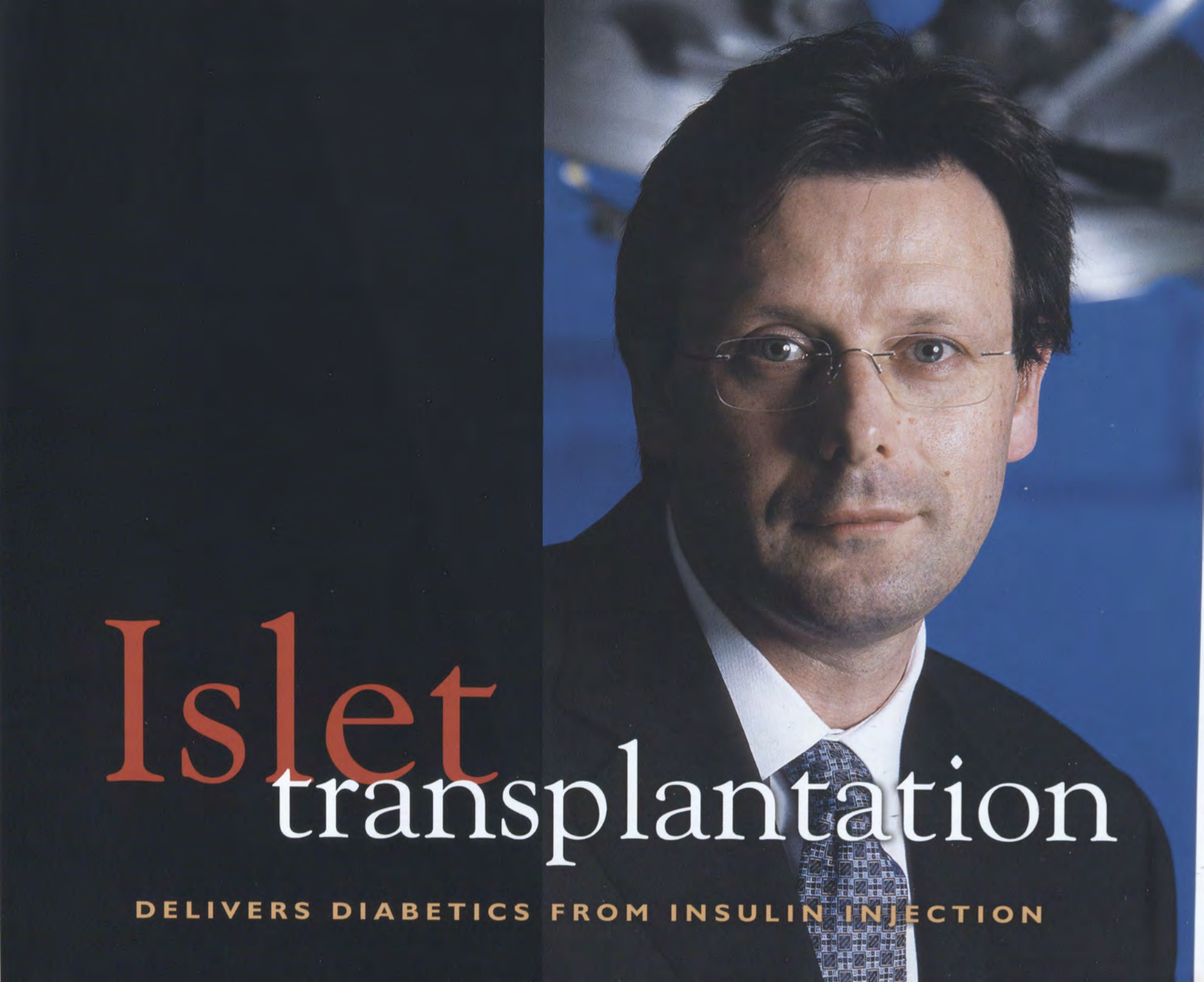
pathologic myopia and ocular histoplasmosis syndrome, a fungal disease of the retina. Visudyne was also approved in Europe and elsewhere for the treatment of the occult form of AMD, which progresses less quickly and is harder to diagnose.

Visudyne's success has propelled QLT into an elite class—making it one of only a handful of biotech companies in North America to operate at a profit. After successfully taking not one but two products from bench to market, QLT—now led by Paul J. Hastings—may spur other Canadian researchers to turn their work into clinical and commercial success. Mr. Hastings, an American, agrees with Dr. Levy that academic research in Canada is "first rate and among the best in the world" but that too many researchers turn their ideas over to U.S. or European firms to develop into commercial products.

In fact, QLT has once again bucked that trend by acquiring the development and North American marketing rights to a cancer treatment developed by a British firm. The treatment, called tariquidar, could be QLT's next big success story. It has the potential to be both the first and best in its class as an inhibitor of P-glycoprotein, a membrane protein that pumps out cancer-fighting drugs from tumour cells, thus preventing accumulation of these drugs and reducing their effectiveness. Tariquidar is now in late-stage clinical trials for non-small cell lung cancer; QLT anticipates that it will file for regulatory approval of the drug in 2005.

QLT is a company that is always looking forward. We're a team of leaders moving together in one direction. Our significant clinical talents are focused on building a robust development pipeline that will form the basis of the company's growth in years to come.

PAUL J. HASTINGS,
PRESIDENT AND CEO, QLT INC.


Islet
transplantation
DELIVERS DIABETICS FROM INSULIN INJECTION

BIOMEDICAL ENGINEERING, PHYSIOLOGY AND TRANSPLANT SURGERY CONTRIBUTED TO THE EDMONTON PROTOCOL—A NOVEL TREATMENT THAT ELIMINATES INSULIN DEPENDENCY.

For the second time in medical history, a diverse team of Canadian scientists is revolutionizing diabetes treatment.

The insulin injection arose from canine experiments conducted by physician Frederick Banting and medical student Charles Best, under the supervision of University of Toronto professor J.R.R. Macleod. But it was James Collip, a visiting biochemist from Edmonton, who isolated a pure enough 'dose' of the hormone to perform the first successful treatment.

Just footsteps from Dr. Collip's old lab at the University of Alberta, another team of disparate scientists has pooled their expertise to successfully transplant islets—the cells that produce insulin. Unlike an injection regimen, which only postpones the ravages of the disease, the Edmonton Protocol gives diabetics a new lease on life.

It takes a lot of determination to stick to your convictions when a paltry 8 per cent of patients realize any benefit from your efforts. But with diabetes, the alternative—a slow and painful system shutdown—is unacceptable. And so it is that Dr. Ray Rajotte at the University of Alberta has spent almost 30 years working in the area of islet transplantation—the most physiological way to give insulin to a diabetic patient.

Type I diabetes is the end result of an immune system attack on islets—specialized cells in the pancreas that produce insulin. The body needs this hormone to convert food into energy. Without it, sugars pile up in the bloodstream and are eliminated through the kidneys while tissues throughout the body starve to death.

At best, Type I diabetes can be managed through insulin injections and a strict diet. At worst, it leads to serious complications such as kidney failure, blindness, nerve damage, heart attack, and stroke. But best always deteriorates to worst: on average, diabetes cuts 15 years off a person's lifespan. Type II diabetes, in which the body produces insulin but uses it poorly, is less severe and more manageable but still reduces quality of life.

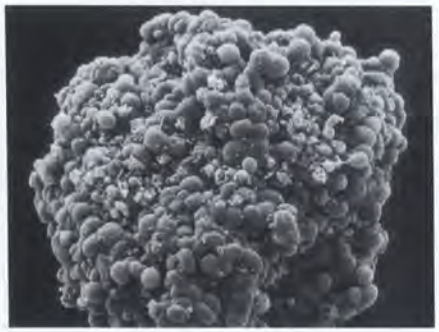
To a biomedical engineer such as Dr. Rajotte, the concept of replacing the broken part in the insulin production plant seemed an obvious

BIRTH OF A NEW RESEARCH CENTRE

The University of Alberta will soon be home to a new institute that plans to tackle all aspects of diabetes treatment. The success of the islet transplant team helped the university win CAD$11.5 million from the Canada Foundation for Innovation to build the Alberta Diabetes Research Centre (ADRC).

"It will be a state-of-the-art facility focused on trying to cure this disease," says Dr. Ray Rajotte, project leader for the ADRC. "We already have outstanding diabetes researchers across campus, from nutritionists to molecular biologists, and the new institute will attract even more talent."

In November 2001, the Edmonton team also received CAD$23.7 million (over five years) from the U.S. Juvenile Diabetes Research Foundation—one of the largest grants ever awarded by the Foundation. The funds will be directed toward establishing a new clinical centre and advancing islet transplantation research.



TOP: *(SEM) Scanning Electron Micrograph of human islet.*

BOTTOM: *Encapsulated dog islet—capsule open to see islet inside.*

solution. In 1990, he convinced Jonathan Lakey, a graduate zoology student, to do a Ph.D. on improving the isolation of islets from the pancreas to support transplants.

Their work progressed, but like other islet transplant teams, their clinical success was minimal. Transplanted islets simply didn't survive in the recipient's body—most likely because of the anti-rejection drugs used. By the late 1990s, about 450 islet transplant procedures had been attempted worldwide; fewer than 40 patients showed islet function one year after surgery.

In 1993, British surgeon Dr. James Shapiro relocated to Edmonton to do a transplantation fellowship with Dr. Norman Kneteman. Drs. Rajotte and Kneteman soon realized they had found the right person to lead the clinical team as it moved forward with a refined protocol now known as the 'Edmonton Protocol'.

"Islets are quite remarkable," says Dr. Shapiro, Director of the Clinical Islet Transplant Program. "Each one is made up of more than 2,000 cells. They look like tiny snowflakes, smaller than a pinhead, but those cells contain the entire endocrine orchestra. They perfectly control insulin release."

The Edmonton team tried again—this time using fresher islets and more of them. In fact, the team requires two donor pancreases to harvest enough cells for a single transplant. The team also chose to work with healthier patients, bypassing individuals who had already undergone kidney transplants because it was evident that anti-rejection steroids compromised the incoming islets. Finally, the team tried out a new immunosuppressant drug to protect the foreign islets from the patient's immune system.

"The results have been fantastic," says Dr. Rajotte. "The problem is we can't do enough transplants. In Canada, there are only 400 donor pancreases available, but 6,000 new Type I diabetics per year. At best, we can perform transplants on 10 per cent of diabetic patients."

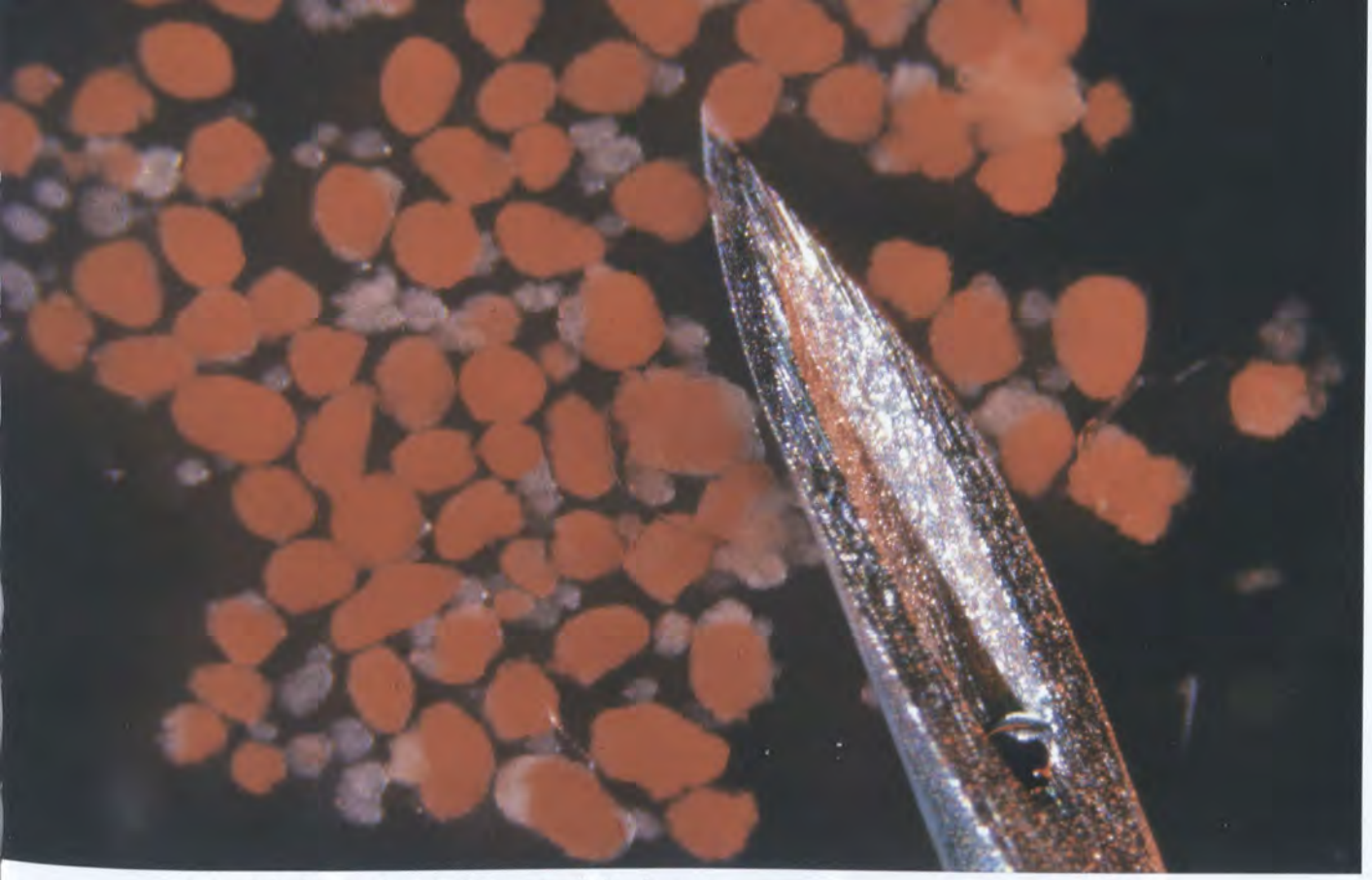
The team has identified two final hurdles to overcome before islet transplantation becomes a widespread treatment option. Once again, they are on the hunt for additional expertise and looking to the biotechnology community for input.

"First, there will never be enough human pancreases to treat all diabetics, so we need to develop alternative sources of islet tissue," says Dr. Rajotte. Dr. Greg Korbutt at the University of Alberta has shown that neonatal pig islets can be isolated, and the Edmonton team is exploring the possibility of using human stem cells to grow new islets in culture.

Second, patients who receive islet transplants must go on a lifelong regimen of immunosuppressant drugs. Dr. Rajotte hopes biotech companies will be able to develop drugs that induce tolerance or find new methods to protect transplanted islets so no drugs are needed.

Riding the wave of attention generated by their success, the Protocol team is ready to expand by establishing the Alberta Diabetes Research Centre and recruiting new staff. The researcher collaborators believe they have every reason to anticipate future triumphs.

"We put the jigsaw pieces together because the right people were around at the right time in the right environment," says Dr. Shapiro. "Canadian scientists have shown they can really excel and lead the field when that happens."



ABOVE: *Isolated human islets—tip of 20-gauge needle for reference.*

LIVING PROOF OF THE EDMONTON PROTOCOL'S EFFICACY

Since being diagnosed with diabetes in his early teens, Edmonton lawyer Bob Teskey estimates that he has stuck a hypodermic needle into his arm more than 40,000 times. He has also monitored his diet with the utmost care.

But his low blood sugar episodes became more erratic—and more dangerous. After blacking out in several boardroom meetings, he adopted a policy of always eating a large meal before driving. Sometimes he awoke in the middle of the night, surrounded by the paramedics his wife had summoned when she found him unconscious in bed.

By 1999, conventional therapies ceased to offer any hope, and Mr. Teskey resigned himself to an increasingly rapid decline. Then he agreed to try the Edmonton Protocol.

"The effect has been dramatic," says Mr. Teskey. "For all intents and purposes, I now function as a normal, non-diabetic. I don't have to worry about the highs and lows, about when or whether I eat. I can do pretty much as I wish."

His needles stowed for almost three years, Mr. Teskey now sleeps without fear. Of the 31 transplant patients in Edmonton, 80 per cent remain off insulin after a year. Other researchers have copied the Protocol and achieved similar success.

We are very fortunate to have world-class researchers, people who were attracted to Alberta by stable research funding and the quality of the university and the research establishment. Researchers who set themselves apart from others because they have that spark of creativity.

BOB TESKEY,
ISLET TRANSPLANT RECIPIENT

Skeletal repair products

MARK THE CONVERGENCE OF
BIOLOGY AND ENGINEERING

THROUGH THE LABORATORY PRODUCTION OF 'LIVING' BONE AND CARTILAGE, MILLENIUM BIOLOGIX INC. IS TRANSFORMING ORTHOPAEDICS AND TISSUE ENGINEERING—AND SUPPLYING AN EFFECTIVE TEST BED FOR DRUG DISCOVERY.

In the early 1990s, a graduate student was experimenting on bone cell cultures in Dr. Michael Sayer's physics lab at Queen's University in Kingston, Ontario. A serendipitous mistake led to the discovery of a unique synthetic substance that acts like natural bone mineral—to the point that normal cells accept its implantation without hesitation.

Building on the work of Dr. Sayer's team, Millenium Biologix Inc. was launched in 1993 to develop and market the material, dubbed 'Skelite™', for rapidly growing markets involved in the research, diagnosis and treatment of skeletal diseases. Currently available as both implantable bone grafts and tissue engineering scaffolds, the material is now part of a growing family of innovative products and services. As Millenium earns recognition as a pioneer in the repair and replacement of skeletal tissue, Skelite is receiving invitations to travel into outer space to help NASA study why micro-gravity induces bone density loss.

Almost everyone experiences a loss of bone density and joint degeneration over the course of a lifetime. The combination of an aging population and more physically active lifestyles means there is greater need for therapeutic products to treat degenerative bone diseases such as osteoporosis, and joint diseases such as osteoarthritis.

"The global market for synthetic bone replacement and cartilage tissue products is US$5 to $6 billion," estimates Sydney Pugh, President and CEO of Millenium Biologix Inc. of Kingston, Ontario. "Our primary products— Skelite™, the Osteologic™ research line, and Cartilogic™, a total system for clinical tissue engineering—stimulate natural bioprocesses to safely and reliably produce living tissue, and also support pharmaceutical R&D."

Currently, most skeletal implants are constructed of relatively inert metals. Although such devices may be mechanically strong, they are not biologically active. They generally fail to integrate with natural tissue and ultimately malfunction at the point of connection to the skeleton. Furthermore, although the risk of toxicity or immune system rejection is minimal, metal implants are not truly compatible with human systems.

LIVING BONE IN OUTER SPACE

Astronauts may lose up to 10 per cent of their bone mass during a single month in space. Scientists have yet to determine why this happens or—more importantly—how to minimize the risks associated with longer space missions.

Since the early 1990s, Millenium Biologix Inc. has provided both the proprietary bioactive materials and the integrated OSTEO™ hardware needed for scientists to carry out various studies on bone cell function, growth, and tissue engineering for in-orbit missions. OSTEO has laid the foundations for Millenium's advanced clinical tissue engineering systems, which are now close to commercialization on Earth.

The company is involved in joint projects with the Canadian Space Agency, the European Space Agency and NASA, including another payload of Skelite™ on the space shuttle Columbia's STS-107 mission that was launched in the summer of 2002.

"Skelite is biocompatible so it is not rejected by the body," says Mr. Pugh. "But it is also bioactive, which means that it is naturally reabsorbed and replaced through ongoing bone growth."

Millenium Biologix offers multiple Skelite lines that easily surpass the limitations of current synthetic bone implants. Current products range from powders and granules, which are designed to fill small, irregular bone voids at common fracture sites, to large porous synthetic scaffolds that can repair problems such as badly damaged limbs or collapsing spines.

Skelite's similarity to normal bone spans both its chemical makeup and its detailed physical structure. Following the initial healing phase, the normal cell-mediated remodeling process gradually replaces Skelite devices with natural tissue.

Because it can be manufactured at low cost in various function-specific configurations, Skelite satisfies critical needs in a variety of medical and biotechnology applications. It belongs in a class of materials called bone graft substitutes that's already recognized and well accepted by international regulatory agencies.

In 1996, Millenium Biologix entered into an agreement with Mississauga-based Allelix Biopharmaceuticals Inc. to develop that company's novel extracted bone cell stimulating factor (BCSF), which accelerates natural bone growth. Since Allelix's merger with NPS Pharmaceuticals of Salt Lake City, Utah, a division of Millenium Biologix continues to operate within the NPS Allelix facility in Mississauga.

"Millenium Biologix has taken BCSF and further developed it into a family of synthetic, small molecular weight peptides with demonstrated activity in bone and cartilage," says Mr. Pugh. "These

ABOVE: *The OSTEO-2 (Osteoporosis Experiment in Orbit-2) payload was launched on NASA's STS-107 mission in July 2002. Using technology developed by Millenium Biologix, OSTEO-2 aims to better understand bone loss during space flight.*

are at various stages of development, and clinical trials are expected to begin in the near future."

In addition, Millenium Biologix has developed the Osteologic line of products for medical and pharmaceutical research; these are marketed worldwide by the New Jersey-based medical technology firm, Becton Dickinson. Osteologic provides a unique bone cell assay technique to measure the effects of new drugs. The technology uses a sub-micron film of synthetic bone in one format, and small three-dimensional macroporous constructs in a second format, which can be exposed to various treatments and then analysed using the Microst Image Analyzer™—produced by Millenium Biologix.

Well-educated and creative people, an appetite for excellence, and a strong competitive spirit propel our drive towards leadership in clinical tissue engineering.

SYDNEY M. PUGH, PRESIDENT AND CEO, MILLENIUM BIOLOGIX INC.

The company's products already generate strong revenues by creating valuable new market opportunities and by offering competitive advantages in existing markets. Millenium Biologix has R&D and production facilities in Canada and Switzerland, as well as an extensive network of international partners.

REDUCING RISK IN BONE REPAIR AND REPLACEMENT

Millenium Biologix Inc. is the world leader in turn-key human autologous tissue engineering—a technique that prevents the rejection of bone implants by eliminating the need to introduce foreign tissue in the patient's body.

Instead, early-stage bone cells are harvested from the patient and seeded onto a synthetic scaffold in a laboratory setting to create a natural mineralized matrix. The result is a 'hybrid bone graft' that can be inserted to repair or replace damaged or diseased bone without the risk of stimulating an immune system attack.

These hybrid grafts can serve as a 'time release' drug delivery system. Millenium Biologix is also exploring the idea that such tissue could be stored in 'bone banks' for broader human use.

Transforming natural bio-polymers

TO PREVENT POST-SURGICAL COMPLICATIONS

CHITOGENICS LTD. OFFERS A WAY TO REDUCE POST-SURGICAL ADHESIONS USING A POWERFUL BIO-ADHESIVE DERIVED FROM THE SUBSTANCE THAT GIVES SHRIMP SHELLS THEIR STRENGTH.

When processed the right way, a substance found in shrimp shells can be transformed into NOCC—a white, odourless, soluble powder with the potential for use in medical applications, including drug delivery and post-surgical adhesion prevention.

Developed initially by three professors in Nova Scotia, NOCC and its derivatives form the platform technology for Chitogenics Ltd., a Dartmouth, Nova Scotia-based biotechnology company. With its first product scheduled for market in 2005, Chitogenics is set to tap into an estimated $4 billion global market for anti-adhesion products.

Considered one of the leading complications of surgery, post-surgical adhesion can cause pain, infertility, bowel obstruction, restricted range of motion, and even death. "It's one of the great unmet surgical problems," says Marina Zazanis, President and Chief Executive Officer of Chitogenics Ltd.

Chitogenics believes that its anti-adhesion products—made from N,O carboxymethyl-chitosan (NOCC)—will reduce the incidence of post-surgical adhesions. Chitin, the bio-polymer from which NOCC is derived, comprises about 15 per cent of shrimp shells and is also found in other shellfish. To make NOCC, chitin is first processed to make chitosan, and then carboxymethylated. The resulting substance is a water-soluble powder, which to the limit of detection of the testing methods shows that it contains no proteins that can cause allergies.

NOCC has many properties that make it suitable for use in medical applications. "Based on toxicological tests, we know it's biocompatible, so it doesn't cause any side effects," says Dr. Agis Kydonieus, Senior Vice-President, Research and Development, Chitogenics. "It has a very high molecular weight, so you only need about 1 per cent in water to produce a viscous material much like honey. It is also a good lubricant, so it's suitable for use in eye products."

In addition, NOCC is bioresorbable—ultimately breaking down into sugars that can be excreted in the urine. Last but not least, it's an excellent bio-adhesive that works on both soft and hard tissues, which makes it ideal for preventing post-surgical adhesions.

STRATEGIES FOR SUCCESS

With only 11 employees, Chitogenics Ltd. is nonetheless 'a global company' with a multinational reach. The firm's strategic partner—a Fortune 500 medical company—has invested $5 million in Chitogenics' research and for milestone payments. Chitogenics has also received $4 million in funding from four institutional investors.

Money aside, how does a small company harness a technology with so much potential? "We work a lot with consultants, such as Dr. Michael Diamond, an international expert in post-surgical adhesions," says Marina Zazanis, President and CEO, Chitogenics. "We have directors from two of the world's leading pharmaceutical companies—Merck and Schering-Plough. And we collaborate with some of the top scientists in the world."

Post-surgical adhesions occur when the blood left behind from an operation causes fibroblast cells, which help repair the wound, to release collagen. This process can cause separate organs to adhere to one another. For example, the abdominal wall could stick to the intestines and cause continuous pain. "The NOCC in our product prevents those cells from attaching to any surface that is coated with it. Preventing the cells from attaching helps prevent adhesion from taking place," says Dr. Kydonieus. "And when you use this product at a surgical site, you want it to stay where you put it, so its bio-adhesive property is very important."

Chitogenics is currently in Phase III clinical trials for a product designed to prevent adhesions following gynecological surgery. "The product has two components—a solution of 2 per cent NOCC and 98 per cent water, and a gel made by cross-linking the polymer so it lasts longer. Both components would be used in one operation," says Dr. Kydonieus.

The global market for products to address post-surgical gynecological adhesions alone is about $800 million a year. And for all the other adhesion products—spine, tendon, cardiac, abdominal, nasal—the global market is approximately $3 billion a year.

MARINA ZAZANIS,
PRESIDENT AND CHIEF EXECUTIVE OFFICER,
CHITOGENICS LTD.

These trials are scheduled for completion by the end of 2004. Chitogenics expects to obtain regulatory approval to market this product in Europe by early 2005, and in the United States by late 2005. Meanwhile, Chitogenics has completed preclinical research for abdominal and cardiac adhesion products.

Besides preventing post-surgical adhesions, NOCC and its derivatives have other potential applications. Chitogenics currently has two agreements with major pharmaceutical companies interested in using its compounds for eye products. A company is also interested in using NOCC as an anti-inflammatory agent for a bowel disease.

"Another big potential market involves using our material to supplement sinovial fluid, which cushions the body's joints," says Dr. Kydonieus. "Sinovial fluid tends to dissipate with age, so supplementation by injection would be beneficial."

Chitogenics is also conducting research on the oral delivery of peptides and proteins, in collaboration with the University of Leiden in the Netherlands. "This is the holy grail of drug delivery. Many therapies such as insulin and most peptide drugs can only be administered by injection because enzymes in the stomach and intestines would break them down," says Dr. Kydonieus. "Oral delivery is a much easier and less expensive method of administering a drug. We have very early but promising results."

NOCC'S ROOTS

N,O carboxymethylchitosan (NOCC) was originally developed by three Nova Scotia professors—Dr. Clive Elson and the late Drs. Ernie Hayes and Don Davies. "Their research came from the heart," says Dr. Agis Kydonieus, Senior Vice-President, Chitogenics Ltd. "They wanted their work to accomplish two things: prevent the dumping of shrimp shells into the ocean, and develop a technology that would eventually provide jobs for the children of Nova Scotia."

In 1987, the three researchers formed NovaChem and patented NOCC, envisioning it as a potential preservative for fruit. In 1993, NovaChem merged with Neogenics, whose CEO, Marina Zazanis, saw NOCC's potential for the health care sector. Ms. Zazanis became CEO of the newly formed Chitogenics, which now holds seven patents and develops products based on the original technology.

Testing healing powers

OF NATURAL HEALTH PRODUCTS

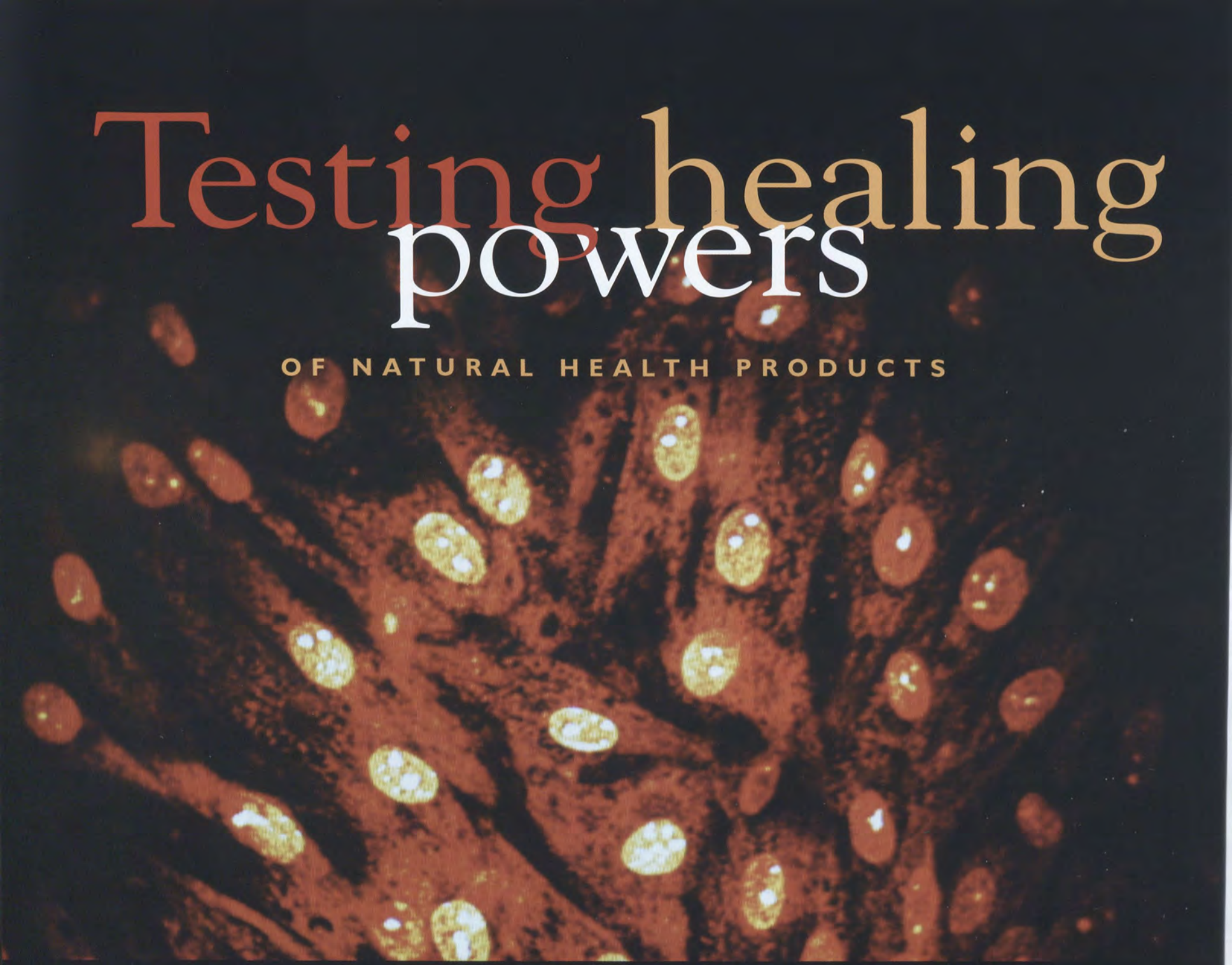


Image from a confocal microscope of vascular smooth muscle cells. The nuclei have been stained as a standard for a live/dead assay™.

THE NATIONAL CENTRE FOR AGRI-FOOD RESEARCH IN MEDICINE EXPLORES THE POTENTIAL OF NUTRACEUTICALS AND FUNCTIONAL FOODS TO FIGHT HEART DISEASE, CANCER AND OTHER DISEASES.

Dr. Grant Pierce hates to see people wasting billions of dollars on nutraceuticals and functional foods, betting on unproven health claims. Coming from the Director of the National Centre for Agri-Food Research in Medicine (NCARM), this might sound like heresy.

But Dr. Pierce believes that before these food products can play a useful role in health care—a role he believes could be revolutionary—they must first prove themselves all the way from the lab bench to high-enrolment clinical trials. That's exactly what NCARM, coupled with the new I.H. Asper Clinical Research Institute next door, intends to do.

Consider cod liver oil. For generations, mothers, grandmothers and the occasional zealous father have tipped spoonfuls of the vile stuff into resentful gullets. Unless they are all part of a sadistic conspiracy, these people must believe that good will result.

Once people hear about food products like this, scientists need to accumulate enough clinical evidence to prove—even to doubters—that the health benefits are real, says Dr. Grant Pierce, Professor of Physiology at the University of Manitoba, and Director of the Stroke and Vascular Disease Division at St. Boniface General Hospital Research Centre. "If you believe this stuff isn't snake oil, that it actually has an effect on heart disease, cancer, or whatever other ailment you hope to address, then you are going to buy it," he says. "That means overall consumption will go up, which also means that the price of the product will rise as the demand increases."

This is the argument Dr. Pierce pitched to the Agri-Food Research & Development Initiative (ARDI)—that nutraceuticals and functional foods will generate a boom in agriculture and biotechnology only after their health benefits are known. ARDI agreed and provided $3 million in funding, and the National Centre for Agri-Food Research in Medicine (NCARM) was born in 1999.

NCARM's star candidate at the moment is flax, which contains a variant of the omega-3 fatty acids that give cod liver oil its benefit against heart disease. Although NCARM gives priority to agricultural products that can be produced in Canada's prairie provinces, that

FLAXSEED'S TRIPLE THREAT

When people get heart attacks, it's the arrhythmia that usually kills them. Flaxseed (also known as linseed) contains omega-3 fatty acids that help to keep the heart in rhythm. Flaxseed also contains a lignan that may protect against plaque formation in blood vessels. Finally, flaxseed has fibre that is known to reduce cholesterol levels.

Canada is the global giant in flaxseed production, accounting for up to 80 per cent of the world export market.

isn't the only reason Dr. Pierce decided to research flax rather than cod liver oil.

"Our goal is not so much to produce great science, although we want to do that," he says. "But also to produce science that is going to be applied to the human situation. Cod liver oil is a classic example. Your mother has been telling you since day one to eat it, but you're not going to because it tastes awful. You need to be convinced of its medical benefit, you need enough of the compound to have health benefits, and you also need it in a form that you will take regularly."

The big advantage of nutraceuticals and functional foods is that we can use them to prevent or slow down a disease... Those are the major trials that need to be done. They will be extremely expensive and long-term, but they will have a huge potential impact on how much money we spend on health care and on quality of life.

DR. GRANT PIERCE, PROFESSOR OF PHYSIOLOGY, UNIVERSITY OF MANITOBA; AND DIRECTOR OF THE STROKE AND VASCULAR DISEASE DIVISION, ST. BONIFACE GENERAL HOSPITAL RESEARCH CENTRE

When Dr. Pierce looks out his window, he can see what makes NCARM unique. For starters, of all the research groups that focus on nutraceuticals and functional foods, NCARM is the only one in Canada located within a medical research facility: the St. Boniface General Hospital Research Centre (SBRC). Next door is St. Boniface General Hospital itself, one of two teaching hospitals at the University of Manitoba. And across the street, construction is underway on the I.H. Asper Clinical Research Institute.

"That makes NCARM not only unique nationally but unique internationally," he says. "As soon as it's finished we'll have access to a state-of-the-art, Phase 1 through Phase 3 clinical research facility."

RESEARCH INSTITUTE COMPLETES 'VIRTUOUS CIRCLE'

"Industry was crying for more involvement in clinical trials by Canadian academic institutions," says Dr. John Foerster, Director of Research for the St. Boniface General Hospital Research Centre (SBRC). One result is the new I.H. Asper Clinical Research Institute, which will help SBRC complete what he calls the 'virtuous circle': problems encountered on hospital wards are addressed by basic scientists, solutions are tested in model systems, and then therapies are introduced to the wards following clinical trials.

The Asper Foundation—founded by Winnipeg media mogul Izzy Asper—is an enthusiastic supporter of this vision, and donated CAD$5 million towards the $25 million, 100,000-square-foot facility. According to Dr. Foerster, several international biotechnology companies are eager to start using the Institute when operations begin in the spring of 2004.

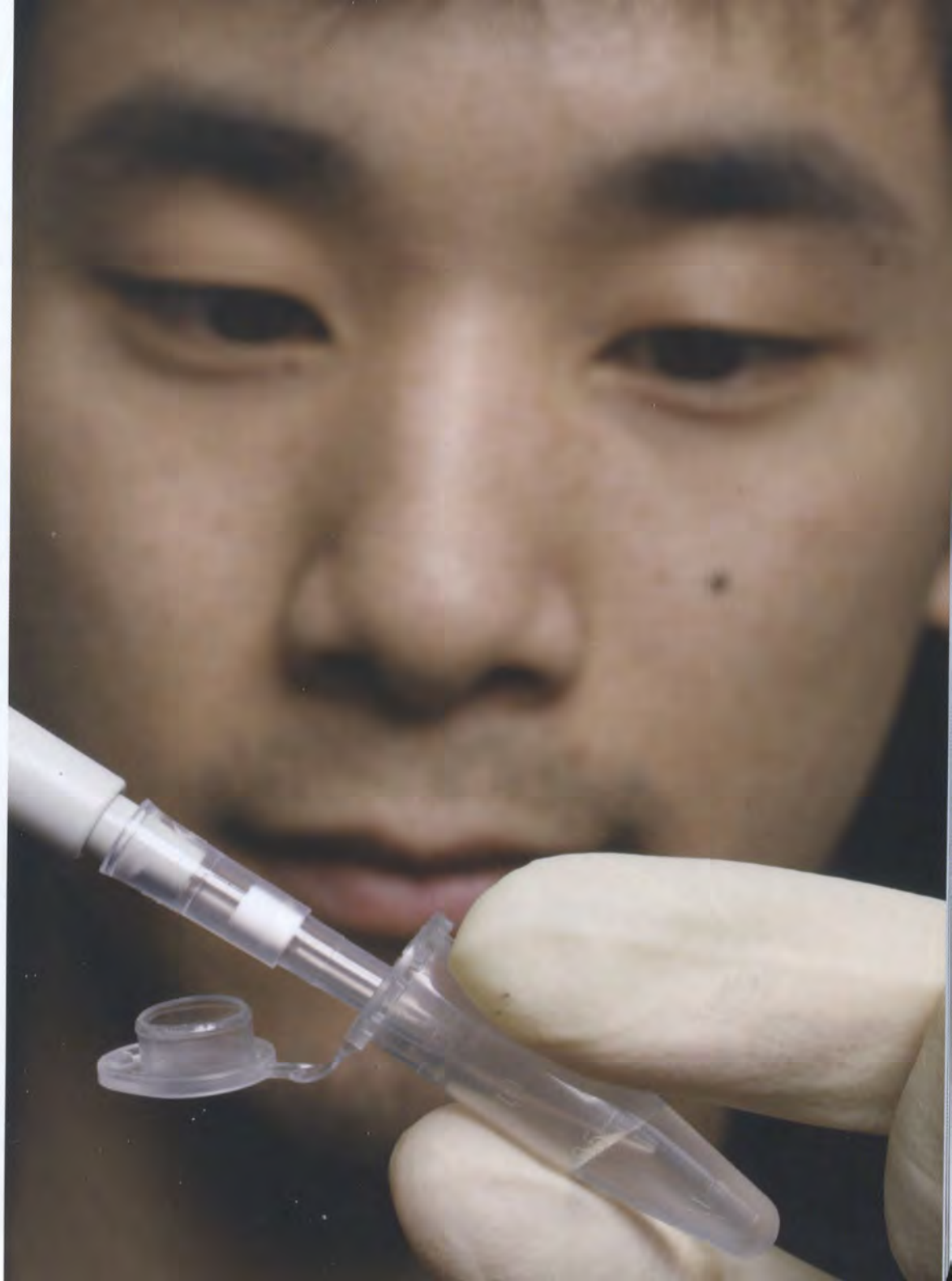
NCARM is also linked to the University of Manitoba's Faculty of Agriculture and Food Science—a faculty with plenty of expertise in plant breeding, biotechnology and food processing. "We don't want to duplicate that, but we do want to collaborate with it and gain every advantage we can—and they from us," says Dr. Pierce.

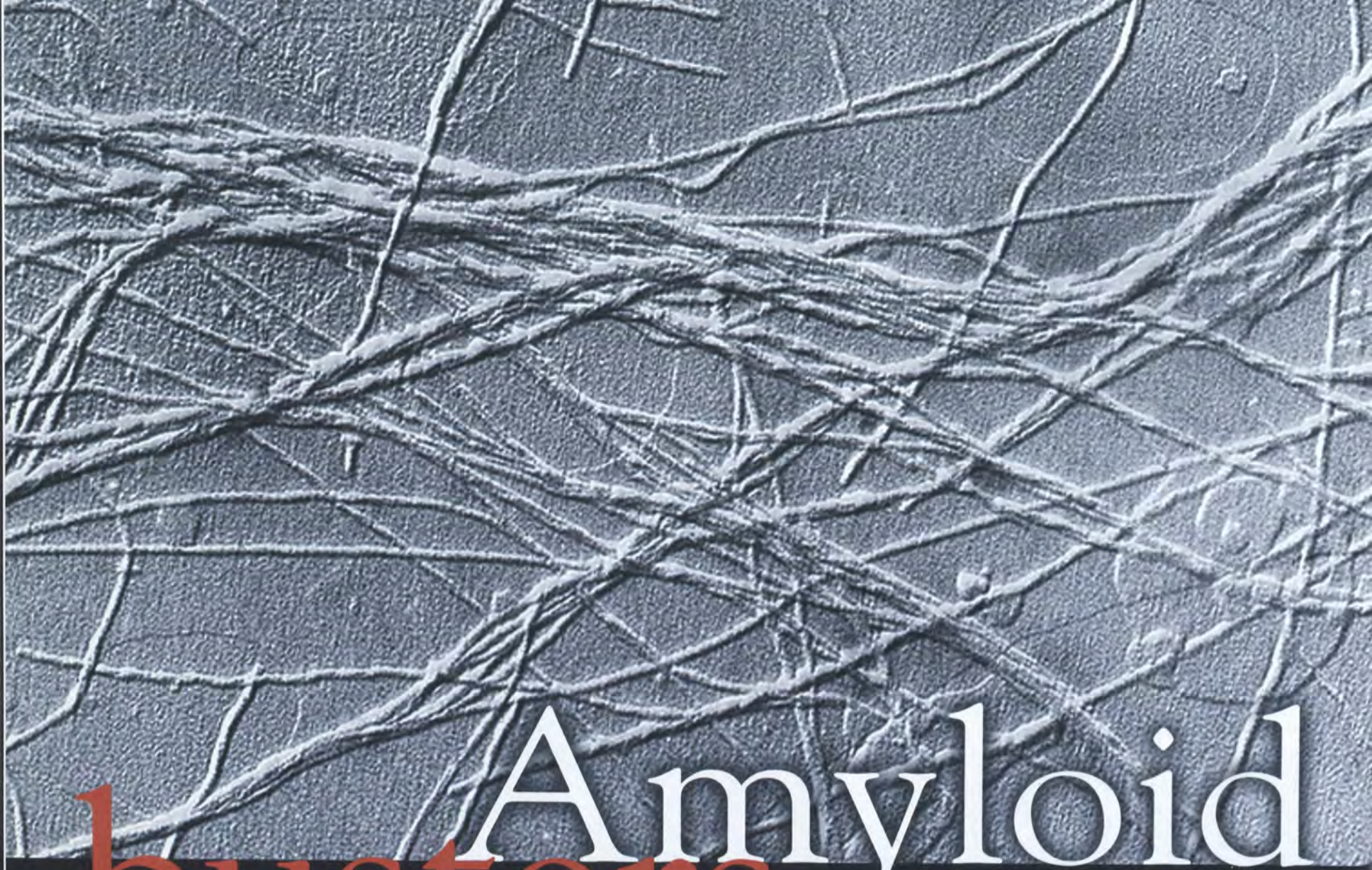
For his part, Dr. Pierce already has an outstanding track record researching cardiovascular disease, with pioneering work on ion channel blockers and vascular disease in diabetics, says Dr. John Foerster, Director of Research for SBRC.

"He came to functional food research after studying cardiovascular disease," says Dr. Foerster. "He recognized that if you add a fair amount of flaxseed to your cereal in the morning, that flaxseed contains substances that are at least as effective as the most expensive medications you can take for lowering cholesterol. So research on vascular diseases and functional foods fits together."

"Dr. Pierce is an example of our attempt to reverse the brain drain," adds Dr. Foerster. "We recruited him back from Southern California. We've had to work very hard to keep him here—he received many offers—but he found we have the most exciting vision for future programs."

In Dr. Pierce's own vision of the future, people will be much more certain about the health effects of food products. "We'll know a lot more about whether these compounds really work. We'll know a lot more about their side effects and their drug interactions. And I think we'll have the confidence to say this one works and this one doesn't."





Amyloid busters

COMBAT DEGENERATIVE BRAIN DISEASES

Electron micrograph of fibrillar human amyloid protein. In the case of Alzheimer's disease, amyloid fibrils are toxic to surrounding cells, which contributes to severe neurodegeneration.

A MONTRÉAL BIOTECH FIRM IS WINNING CONVERTS WITH ITS APPROACH TO TREATING ALZHEIMER'S, WHICH SUGGESTS THAT AMYLOID FIBRILS ARE INTIMATELY RELATED TO THE DEVELOPMENT OF THIS DISEASE.

In 2002, Montréal-based Neurochem Inc. attracted widespread attention for its groundbreaking work on degenerative illnesses.

In April 2002, the business magazine, *Forbes*, singled out the biotech company in an article on potential treatments for Alzheimer's disease. Then Neurochem was invited to present at the prestigious International Geneva/Springfield Symposium on Advances in Alzheimer's Therapy.

"There was a biopharmaceutical company from Canada at centre stage," says Neurochem Chairman and CEO Dr. Francesco Bellini. "Alzheimer's disease is in need of a treatment with great potential. We had positive results to report."

In the early 1990s, three professors at Queen's University in Kingston launched a biotech company based on the then radical idea that amyloid fibrils—clusters of deformed proteins that accumulate in diseased brains—are the culprit behind several major diseases that afflict the central nervous system and other organs.

Today, as this theory gains wider acceptance, the firm they created is considered one of the front-runners for an early treatment for Alzheimer's and other degenerative diseases, such as Amyloid A (AA) amyloidosis. It is well documented that up to 170 million people in the world may suffer from some sort of amyloid-related illness.

With a solid pipeline of products already in clinical trials for diseases such as Alzheimer's, hemorrhagic stroke and AA amyloidosis, the Montréal-based company appears to be on the brink of commercial success.

Neurochem's mission is to develop innovative therapeutics for neurological diseases and amyloid-related disorders. The company's drug candidates specifically target structures called glycosaminoglycans (GAGs), which play a role in converting amyloid protein fragments into destructive fibrils. By blocking GAGs, the firm's synthetic molecules may prevent fibril formation.

In December 2000, Neurochem researchers demonstrated that Alzhemed™—a therapeutic

THE IMPACT OF ALZHEIMER'S

More than 364,000 Canadians—one in 13 over age 65—now suffer from Alzheimer's disease or a related dementia, resulting in a total annual health care cost of CAD$5.5 billion.

In the United States, Alzheimer's and related diseases affect about 4 million people today, with the number of patients expected to rise to 14 million by 2025. Alzheimer's disease is already the third most expensive disease in the United States, and the direct and indirect costs could escalate to more than US$100 billion by 2025.

Amyloid fibrils result from the buildup of proteins that normally occur in the body in a benign, soluble form, but which are transformed in the disease process into an insoluble toxic form. In Alzheimer's, the accumulation of these deformed proteins poisons brain cells and prevents associated brain pathways from functioning properly.

DR. FRANCINE GERVAIS,
VICE-PRESIDENT, RESEARCH AND DEVELOPMENT,
NEUROCHEM INC.

candidate for treating Alzheimer's—effectively reduces the advance of the disease in genetically engineered mice. In March 2003, Alzhemed completed a Phase II human clinical trial.

Dr. Francesco Bellini, Chairman and CEO of Neurochem Inc., believes the company is only about five years away from making a significant impact in the fight against Alzheimer's—a sentiment shared by many investors. Since its inception,

the company has raised almost CAD$80 million, which includes a successful Initial Public Offering in June 2000. In 2002, Neurochem attracted a strategic investment of more than $15 million with Picchio Pharma, a joint venture between Dr. Bellini and Power Corporation of Canada.

Neurochem now employs more than 100 people in research and management.

According to Dr. Bellini, the company received considerable help in its early years, including strong academic support and government financial assistance in the form of research contributions and R&D tax credits. "Scientifically, Canada is a strong country—better than most," he adds. "There's a tremendous amount of scientific know-how and brainpower here."

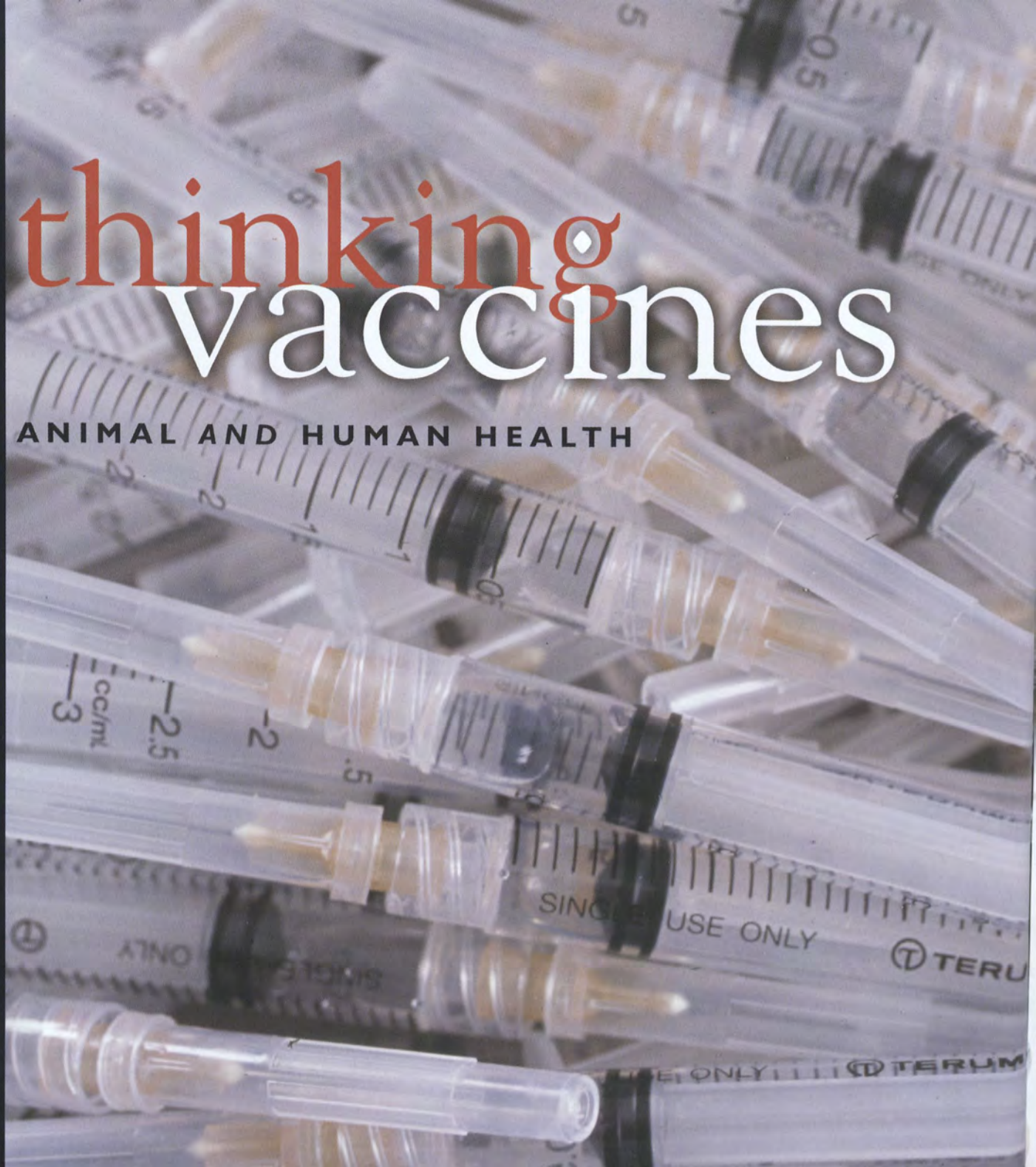
FIBRILLEX™ OFFERS HOPE FOR TREATING AA AMYLOIDOSIS

By 2006, Neurochem Inc. expects to market its drug Fibrillex™ for AA amyloidosis—a serious condition with a very poor prognosis and no treatment at this time. The most common cause is the chronic inflammation that occurs such as in rheumatoid arthritis, juvenile arthritis and spondyloarthropathies. The inflammation leads to: the formation and deposition of amyloid fibrils in major organs of the body; morbidity due to end-stage renal disease; and ultimately, death.

Neurochem is currently completing a pivotal Phase II/III clinical trial to assess the safety and efficacy of Fibrillex for treating AA amyloidosis. The company has successfully recruited all the patients in 27 clinical centres in the United States, Europe and Israel, and expects to complete the study in early 2005. In addition, Fibrillex has been designated an 'orphan drug' in the United States and Europe. Neurochem thereby benefits from the long market exclusivity and other incentives offered to the makers of drugs developed to treat relatively rare diseases.

Rethinking vaccines

TO IMPROVE ANIMAL AND HUMAN HEALTH



OVER THE PAST 25 YEARS, VIDO HAS BUILT ITS REPUTATION BY CHALLENGING THE NOTIONS OF WHEN, WHERE, WHY AND HOW VACCINES ARE DELIVERED.

The Vaccine and Infectious Disease Organization (VIDO) is a world leader when it comes to pushing the envelope of vaccine development. Expertly bridging the great divide between academia and industry, the Saskatoon-based research institute has recorded a series of impressive firsts: an enteric (intestinal) combination vaccine for cattle, a genetically engineered vaccine for shipping fever, and now an animal vaccine designed to protect humans from a deadly *E. coli* strain.

In the process, VIDO has forced regulators and industry to consider new questions and come up with new answers.

"Our vision is to be doing things today that other people think about doing five years from now," says Dr. Lorne Babiuk, Director of the Vaccine and Infectious Disease Organization (VIDO). "We are very opportunistic. We scour the literature. We look at new ideas and concepts, and we capitalize on them."

Dr. Babiuk and his colleagues at VIDO have a long history of exploring new territory. Ever since the creation of VIDO in 1975 by the University of Saskatchewan, this one-of-a-kind research institute has been pushing the limits of what's possible. Consider its impressive track record.

In the early 1980s, VIDO introduced the world's first enteric combination vaccine for cattle—a triple-threat vaccine that controls 'calf scours' or diarrhea by protecting against bovine rotavirus, coronavirus, and *E. coli* K99. VIDO scientists also developed a technique for growing rotavirus, which has been widely adopted by biopharmaceutical firms around the world. Later in the decade, VIDO created the world's first genetically engineered vaccine for any animal species. The pioneering vaccine prevents shipping fever, a disease that costs the North American cattle industry US$0.5 to $1 billion per year.

In the late 1990s, VIDO made its first foray into human health. By collaborating with scientists at the University of British Columbia, scientists developed a cattle vaccine against the *E. coli* 0157:H7 strain. Although this organism is harmless to cattle, it leads to the deadly 'hamburger disease' in humans. The vaccine is currently undergoing field trials.

CONTROLLING FOOD- AND WATER-BORNE PATHOGENS

When the Vaccine and Infectious Disease Organization (VIDO) helped develop a successful cattle vaccine against the *E. coli* 0157:H7 pathogen, it presented a unique problem for the Canadian Food Inspection Agency and the U.S. Department of Agriculture.

"One of the main criteria for licensing an animal vaccine is to show that it reduces disease," says Dr. Lorne Babiuk, Director. "The *E. coli* vaccine fails this test because the bacteria doesn't make cows sick."

VIDO explained that using the vaccine reduces the amount of *E. coli* shed by cattle and that lower levels of environmental contamination indirectly reduce the chance of human exposure and disease.

Regulators bought the argument, and VIDO has since launched an ambitious food and water safety program. It is now developing vaccines against the Cryptosporidium parasite, which infects cows and humans, and the *Campylobacter* bacteria, which is spread by chickens.

PROTECTING THE FETUS FROM INFECTIOUS DISEASE

Herpes simplex, HIV, Group B streptococcus and hepatitis B—just a few of the life-threatening diseases infants can contract in the birth canal or shortly after birth. Every year, millions of infants worldwide die of such infections before age one. Consider the case of genital herpes.

"If the child is born through the birth canal to a mother who has active genital herpes, there's a 90 per cent chance that the child will get infected," says Dr. Lorne Babiuk, Director, VIDO. "And there's about a 90 per cent chance that it will die or have very serious long-term consequences."

VIDO's pioneering method for vaccinating the fetus could eliminate the current practice of delivering at-risk babies by Cesarean section and protect against infections that occur when the mother's water breaks early and viruses swim up the birth canal.

VIDO recently chalked up another first by successfully vaccinating a fetal lamb against viral infections that often occur during labour and delivery. Some day, this groundbreaking technique may protect human infants against a wide range of potentially fatal diseases that can be passed from mother to child in the birth canal.

"We started out as a veterinary infectious disease organization," says Dr. Babiuk. "As we evolve, we're capitalizing on the convergence of human and animal health. So in March 2003, we changed our name from the Veterinary Infectious Disease Organization to the Vaccine and Infectious Disease Organization."

What hasn't changed, however, is its recipe for success. Wholly owned by, and based at, the University of Saskatchewan in Saskatoon, VIDO was one of the first Canadian research institutes created to bridge the divide between academia and industry. Its *raison d'être* is to turn sound research ideas into viable commercial concepts—which then generate economic benefits.

One of VIDO's current preoccupations may seem well beyond the mandate of an animal health research institute, but it is bound to be of huge interest to both pharmaceutical companies and health care providers—across many species.

"All of our children's vaccines today are given with needles. This can be very unpleasant for both the children and their parents," Dr. Babiuk deadpans. "We're looking into needle-free delivery of vaccines for both humans and animals. We're developing a family of vaccines, some of which can be delivered through the skin, intra-nasally, or orally, using little tablets."

VIDO's ability to pursue such a breadth of research reflects its unique structure. Although not a legal entity, VIDO operates at arm's length from the University of Saskatchewan. The university has the final say on major decisions, but VIDO generates revenue and has a board of directors. Unlike most academic research units, it retains total control over its intellectual property and keeps all the royalties.

In fact, VIDO holds more patents (52 at last count, with another 27 pending) and earns more royalties than the entire university. All of its private-sector revenues support further research. VIDO also receives funding from provincial, national and international sources, as well as the livestock industry. In 2002, the organization received $26.9 million from Genome Canada, the Province of Saskatchewan, Western Diversification, and the private sector to investigate how immunity to infectious diseases works as well as develop prevention strategies for human and animal infections.

This investment is helping to fuel a massive expansion that will see its current staff of 100 increase to more than 140 people within the next two years. When complete, VIDO may rank as the world's largest 'discovery team' in veterinary medicine and infectious diseases.

"Large biopharmaceutical companies don't do much 'discovery' work. They focus on development work. We don't do much development work, so we partner with companies to bring our discoveries to commercial realization," Dr. Babiuk concludes.

In 1984, Dr. Lorne Babiuk was awarded the first Industrial Research Chair in Biotechnology, sponsored by the Natural Sciences and Engineering Research Council of Canada. Dr. Babiuk held the Research Chair for more than 10 years.

Targeting AIDS

AT KEY POINTS IN THE VIRAL LIFE CYCLE

NOT CONTENT TO BASK IN ITS PREVIOUS SUCCESSES, THE McGILL AIDS CENTRE TAKES AIM AT THE ELUSIVE HUMAN IMMUNODEFICIENCY VIRUS, BETTER KNOWN AS HIV.

AIDS—acquired immune deficiency syndrome—is projected to become the world's leading cause of death within the next five years. At present, almost 50 million people worldwide are infected with the human immunodeficiency virus (HIV); at least 18 million have already died.

New drugs have gone a long way towards helping AIDS patients live longer and more productive lives. But HIV is an elusive foe; the virus mutates constantly, developing resistance to the same drugs that once slowed it down.

Dr. Mark Wainberg, founding director of the McGill AIDS Centre, is searching for new angles of attack against HIV. The question is, how do you hit a moving target?

Since 1996, drug cocktails have transformed the diagnosis of the human immunodeficiency virus (HIV) from a death sentence into a manageable condition. In industrialized countries where patients have access to combination drug therapy, almost 1.5 million people live with HIV. By effectively staving off full-blown acquired immune deficiency syndrome (AIDS), the therapy has given many AIDS patients a second chance to lead full, productive lives.

Although treatment has come a long way, the virus seems to be always one step ahead. "One of the biggest problems is that HIV is mutating all the time, and so becomes resistant to drugs," says Dr. Mark Wainberg, Director of the McGill AIDS Centre at McGill University (Montréal, Québec). "So we need to find newer drugs, and we need to identify novel targets in the viral life cycle that these drugs can be active against."

Long before AIDS became a household word, Dr. Wainberg was studying how viruses, such as the common cold virus, can temporarily suppress the immune system. "I had always been

AN EARLY BREAKTHROUGH

While working in collaboration with BioChem Pharma Inc., Dr. Mark Wainberg was the first independent researcher to demonstrate the anti-HIV properties of 3TC—one of the key drugs used in the highly successful AIDS combination therapies or 'cocktails'. Like AZT and other AIDS-cocktail drugs, 3TC works by attacking the enzyme that initiates reverse transcription—the conversion of viral RNA into DNA.

Over the past decade, more than a million people have taken 3TC, which is still the leading AIDS drug in worldwide sales. Dr. Wainberg, Director of the McGill AIDS Centre, counts the development of 3TC among his proudest achievements. "It's a contribution that has helped save the lives of hundreds of thousands of people throughout the world," he says. "Nothing tops that."

fascinated by how these tiny little things could do so much damage," he says.

When the AIDS epidemic broke in the early 1980s, Dr. Wainberg was the first scientist in Canada to isolate the virus—which directly attacks the immune system—and begin research on possible treatments. In fact, his lab was the first in the world to demonstrate the anti-viral properties of the breakthrough AIDS drug called 3TC and among the first groups to identify the problem of HIV drug resistance. For his groundbreaking work, Dr. Wainberg received the Order of Canada—the country's highest honour for lifetime achievement.

With HIV, people are infected for life, and the virus is mutating all the time. That's a pretty lethal combination.

DR. MARK WAINBERG,
DIRECTOR, McGILL AIDS CENTRE

Now one of the world's leading AIDS researchers, Dr. Wainberg—who is also Research Director at Montréal's Jewish General Hospital—is looking for new ways to keep HIV in check. One promising new target is TAT, a protein involved at multiple points in the HIV life cycle. TAT enhances the synthesis of viral RNA, and also seems to promote reverse transcription—the process whereby viral RNA is copied into a host cell's DNA and HIV reproduces itself.

"TAT is something that the virus absolutely needs for its replication," says Dr. Wainberg. "If we could come up with drugs that will attack it, then viral replication might come to a standstill."

In Dr. Wainberg's lab at the McGill AIDS Centre, researchers are screening tens of thousands of compounds for antiviral activity. They hope to find key ingredients that keep TAT from supporting HIV synthesis and replication. It may be something as straightforward as a compound that blocks TAT from binding to another protein. Or it may involve finding out how several compounds interact.

In one sense, the key is to try everything. "When we get hits, then we keep working to see if this compound could be used as a drug," says Dr. Wainberg.

Although new and improved treatments offer promise for slowing growth of the virus, Dr. Wainberg doesn't think there will be a cure for HIV any time soon. This highlights the need to constantly pursue new drug development, for which Canada offers an ideal environment.

"The Canadian talent pool is second to none, and the costs of doing research and development in Canada are far lower than in the U.S. and Western Europe," he says. "The proof is in the pudding. We've already participated in successful drug development, not just for HIV but for other diseases as well."

In the future, Dr. Wainberg hopes to generate new insights and new drugs that will make a difference for HIV patients. He says that being part of the drug discovery process has been a wonderful experience. "It enables you to feel that you've been part of saving people's lives. I don't know what could be more meaningful."

AFRICA AT WAR WITH AIDS

Of the almost 50 million people infected with HIV, at least 30 million live in sub-Saharan Africa. "In terms of prevention, we've made progress in North America and Europe, but in the developing world we're absolutely losing the battle," says Dr. Mark Wainberg, Director of the McGill AIDS Centre.

The new AIDS drugs that are prolonging lives in North America are largely unavailable in poor African countries. Dr. Wainberg is encouraging governments in developed nations to take an active role in establishing funds that will make these drugs available in developing countries.

Newfoundland genes

IDENTIFY PROMISING NEW THERAPIES

CANADA'S HIGH REGULATORY STANDARDS AND NEWFOUNDLAND'S LARGE VOLUNTEER POOL GIVES NEWLAB CLINICAL RESEARCH INC. A COMPETITIVE EDGE IN THE CLINICAL TRIAL BUSINESS.

The province of Newfoundland and Labrador is an important resource for genetic research. Many residents' ancestors were among the original 20,000 European immigrants who settled in tiny, isolated communities. Today, they share a common gene pool that can help researchers to understand hereditary diseases.

This fertile genetic ground gives a competitive advantage to NewLab Clinical Research Inc., a St. John's-based company that performs clinical trials on new dermatological treatments for conditions such as psoriasis. A high proportion of Newfoundlanders suffer from psoriasis, so NewLab benefits from a large and willing group of patients eager to try out new therapies for this debilitating disease.

Residents of Newfoundland and Labrador are known for their generosity, donating more money per capita to charities than most other provinces. They're also very generous with their time, which aids NewLab Clinical Research Inc. The St. John's-based company recruits volunteers to participate in Phase II, III and IV clinical trials of pharmaceutical companies' new dermatological treatments.

In Canada, roughly 1 to 2 per cent of people have psoriasis, a chronic and painful build-up of flaky skin that can force some patients to walk with a cane or be hospitalized. But the disease afflicts between 5 and 10 per cent of people in Newfoundland and Labrador, making the province 'the world capital for psoriasis' and the ideal place for NewLab to find volunteers.

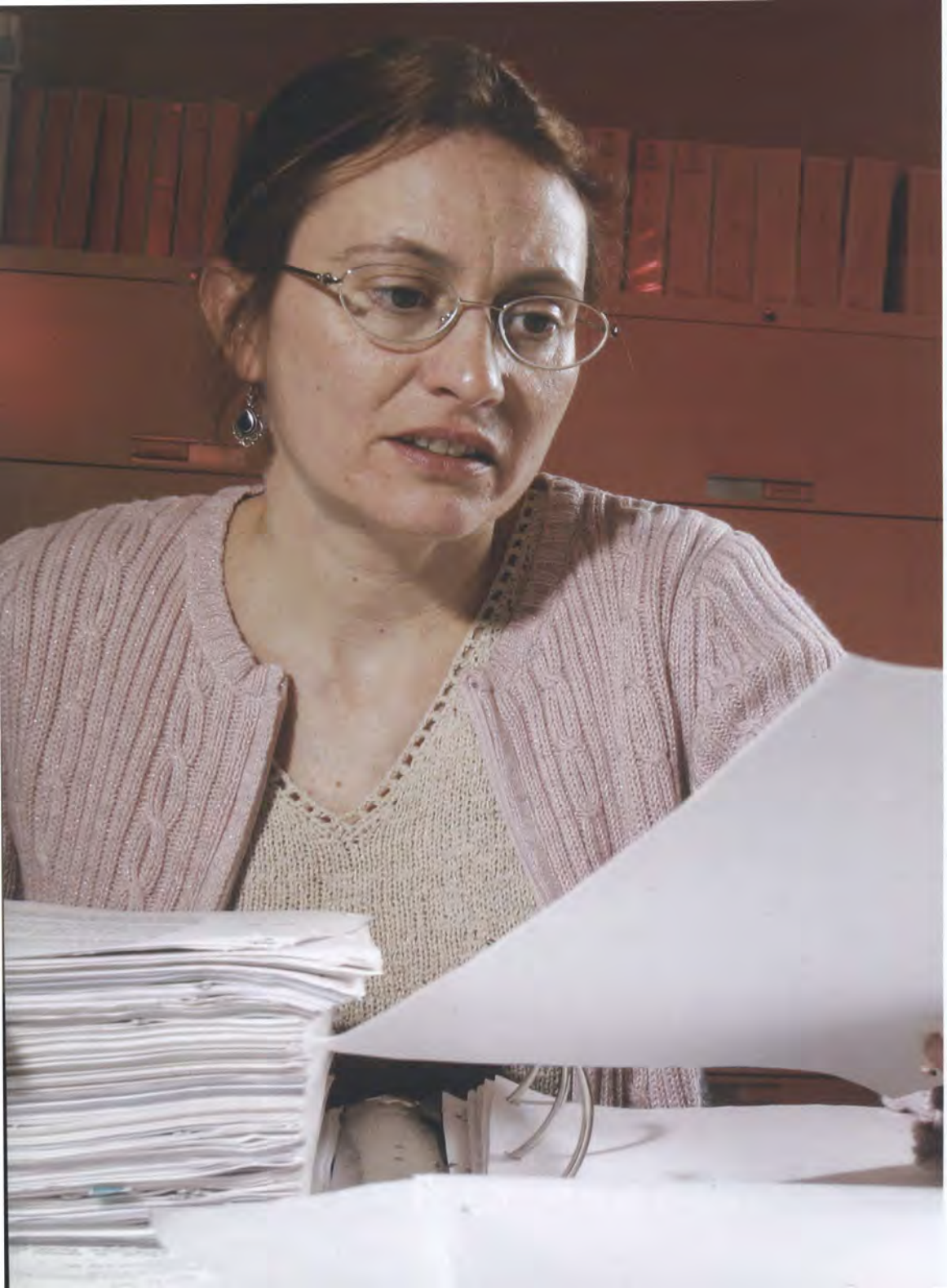
"We tend to recruit very quickly and in high numbers, which brings clinical trials to completion earlier," says Dr. Wayne Gulliver, NewLab Chairman and Medical Director. "That means a pharmaceutical company can get their drug to market faster. It also gives them more time in terms of patent protection," the dermatologist adds.

NewLab competes with many U.S. firms performing clinical drug trials, which pay their patients. Often, such 'professional' patients

PLANS FOR EXPANSION

Dr. Wayne Gulliver's medical specialty is dermatology, which is why most of NewLab Clinical Research Inc.'s trials involve treatments for skin conditions such as psoriasis, eczema, leg ulcers, and acne. But with the facilities, process and staff already in place, NewLab could also conduct trials of treatments for other conditions with a high prevalence in Newfoundland including diabetes, inflammatory bowel disease, Crohn's disease, ulcerative colitis, rheumatoid arthritis, lupus and certain cancers.

NewLab is also discussing the formation of partnerships to perform drug trials with universities and other biotechnology companies—many of them in Ireland.



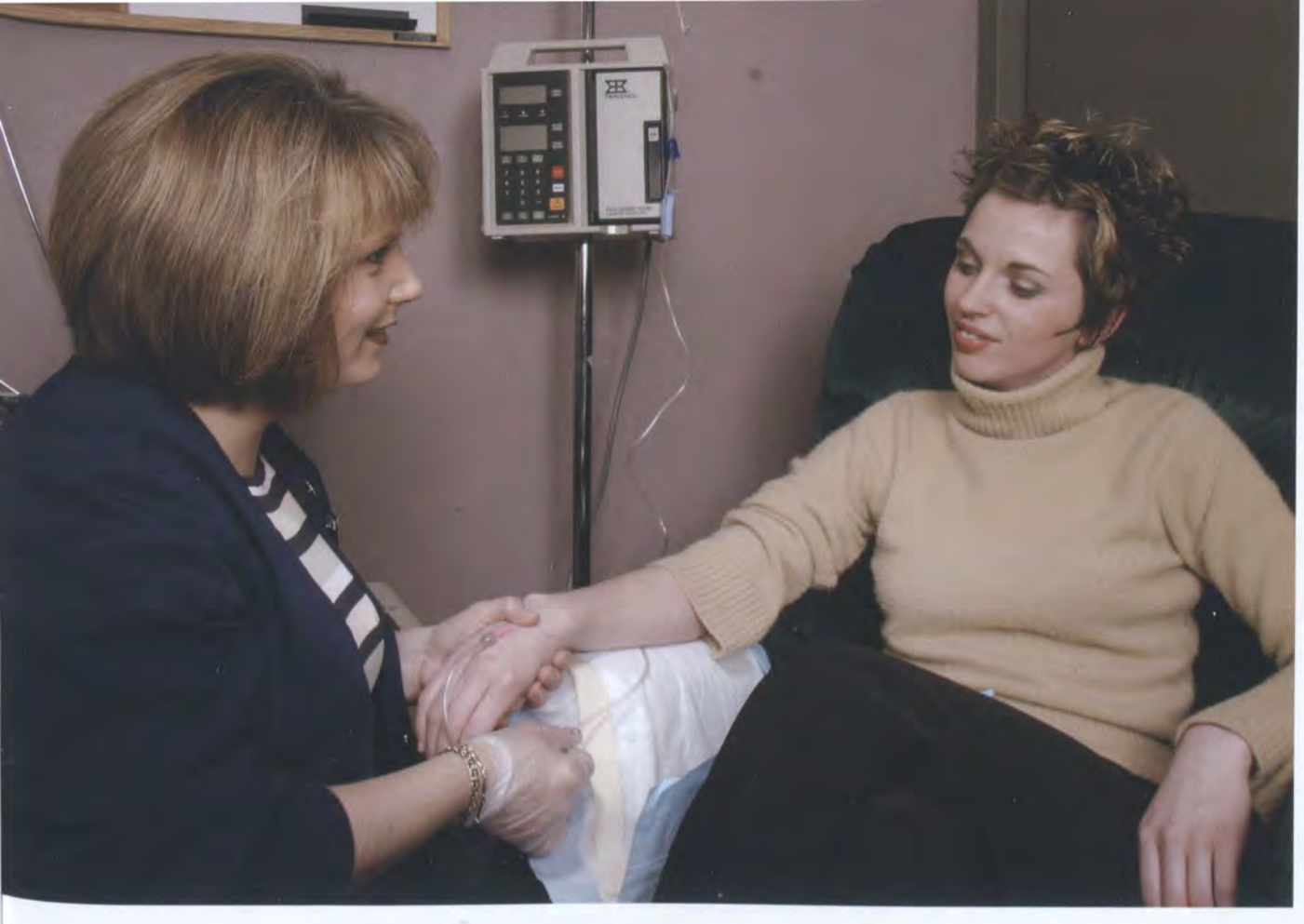
participate in more than one study and hence are exposed to several drugs. But NewLab rarely uses the same people for more than one trial, so its data are more reliable, says Dr. Gulliver.

"Our other big advantage, which a lot of people aren't aware of, is that Canadian data are accepted by both the U.S. Food and Drug Administration and the European Union," whereas U.S. studies are not accepted in Europe, notes Dr. Gulliver. This means that drug companies can do one study at NewLab to satisfy regulatory authorities on both continents. Most of NewLab's clients are pharmaceutical companies in the United States and Europe, with a few in Canada.

Dr. Gulliver founded NewLab in 1997 when the clinical trials he performed at his own dermatology practice outgrew his office. So he started one of the first private firms in Canada—and still the only one in Newfoundland and Labrador—to conduct clinical drug trials, a process normally done in hospitals, universities, or physicians' offices.

Dr. Gulliver continues to maintain his dermatology practice beside the NewLab facilities, and sometimes invites his patients to enrol in NewLab trials if other therapies aren't working. NewLab also gets volunteers from other doctor referrals and by advertising. It has roughly 15,000 volunteers in its database. A few other physicians assist in conducting the NewLab trials.

A privately held company, NewLab has been profitable since its creation, says President and CEO Debbie Reynolds. The company has



grown so quickly, conducting more than 75 trials to date, that it recently doubled its space, moving into an 8,000-square-foot building.

NewLab has received federal business development loans but is otherwise self-sufficient—a selling point for venture capitalists if the company ever decides to raise capital, says Ms. Reynolds.

But the real return on investment is helping improve the lives of people suffering from psoriasis—including one woman who couldn't wear a short-sleeved dress to her brother's summer wedding for fear of offending the guests.

Even if a drug doesn't prove to be the one that controls these terrible diseases, patients will often say, 'Look, if it doesn't work for me, at least my child or grandchild won't have to go through what I went through.'

DR. WAYNE GULLIVER,
CHAIRMAN AND MEDICAL DIRECTOR,
NEWLAB CLINICAL RESEARCH INC.

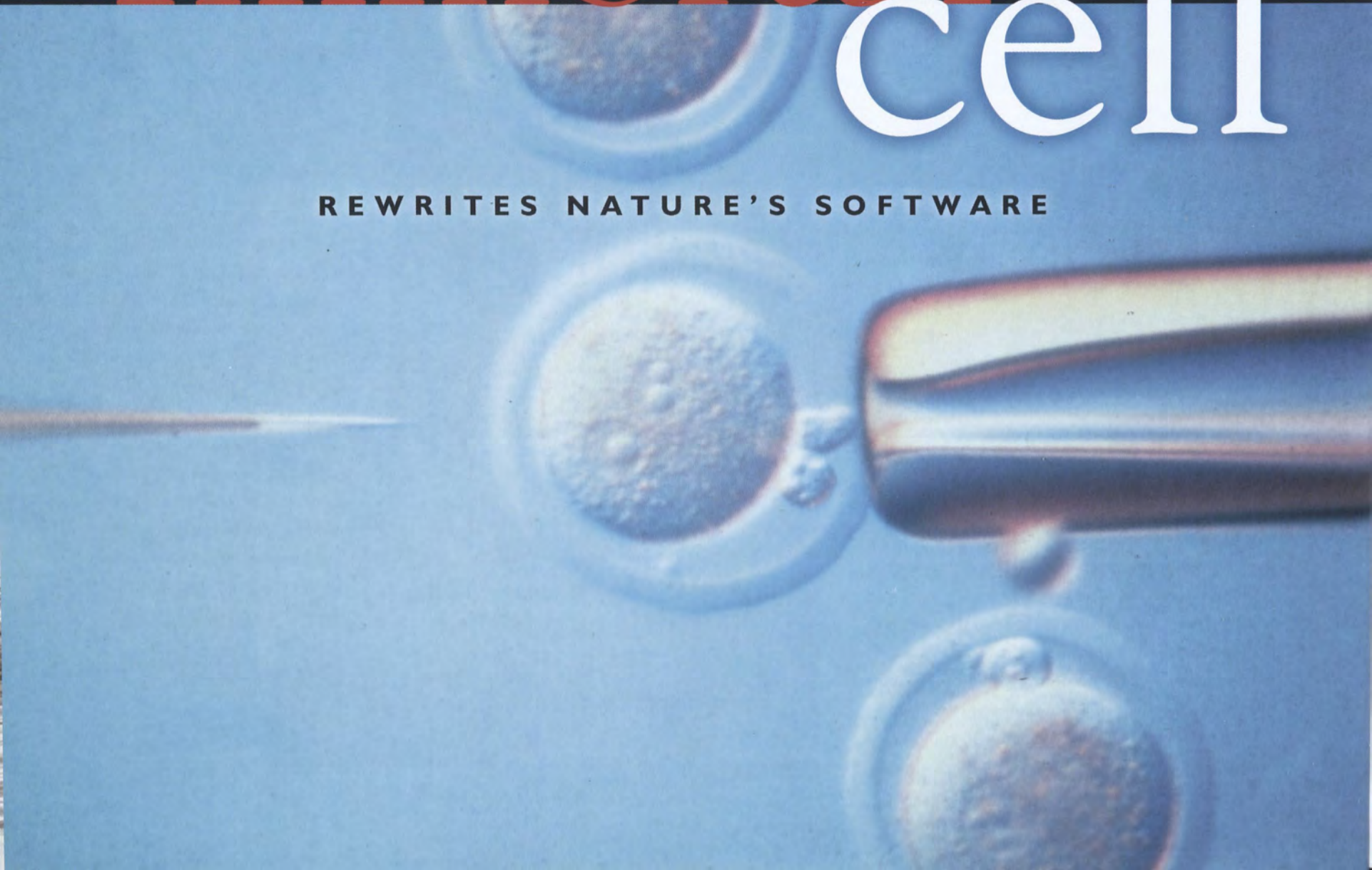
NEW USES FOR OLD DRUGS

Soon, NewLab hopes to expand from clinical drug trials into pharmacogenomics research: determining which genes make some people susceptible to hereditary diseases such as psoriasis and diabetes, and identifying existing drugs to help them.

The trick is finding which drug will work for which diseases. "If you line up susceptibility genes against drugs that attack, react with, or somehow change the proteins being produced by those susceptibility genes, you may find a drug already on the market that's being used for another disease," says NewLab Chairman and Medical Director Dr. Wayne Gulliver. NewLab could then apply for patents on new applications of these drugs—avoiding the several years and hundreds of millions of dollars it costs to develop new drugs.

Immortal cell

REWRITES NATURE'S SOFTWARE



DR. MARC-ANDRÉ SIRARD SEEKS THE GENETIC CODE THAT CAN ERASE A CELL'S HISTORY AND REPROGRAM ITS DESTINY.

The oocyte—an unfertilized egg cell—is the only cell in the body that does not age or die, remaining frozen in time until a sperm triggers its transformation into an embryo.

Oocytes also have the unique capacity to turn back time in other cells. Dolly the sheep—the cloning project of scientists in Edinburgh, Scotland—is the product of fusing a mammary cell from one adult ewe and an oocyte from another. The oocyte reversed the mammary cell to time zero: the starting point of a new individual.

No one knows how the oocytes do it, but one thing is certain: it's all in the genes. Dr. Marc-André Sirard, Canada Research Chair in Animal Reproductive Applied Functional Genomics, is hot on the trail.

Unlocking the secret of the oocyte's immortality could lead to new treatments for human diseases—from Parkinson's to diabetes to cancer.

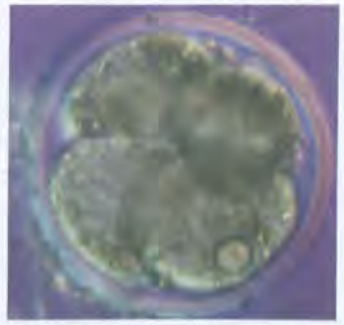
In the world of cells, the oocyte is huge. A full 100 microns in diameter, or about the size of the smallest speck of sand visible to the naked eye, it is the largest cell in the human body. Within that speck rests the power to decide when life begins, to make old cells new again, or to erase a cell's memory and program it for a new role.

Dr. Marc-André Sirard has spent more than 20 years studying the oocyte, which he calls "a wonderful and immortal cell." His research has answered questions about why some oocytes become embryos, while others don't. Thanks to this groundbreaking research, Canada is now a leader in bovine genetics.

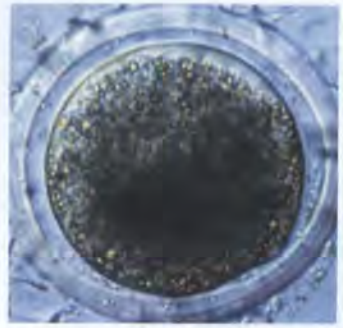
But for Dr. Sirard, the real treasure is hidden in the genes: somewhere in the oocyte's DNA is the genetic coding that tells a cell how to stay young, or reverses an adult cell back to the embryo stage. That genetic code could bring radical new treatments for a wide range of human diseases.

During a 10-year research partnership between Semex Alliance and Laval University (Québec City, Québec), where he directs the Research Centre in Reproductive Biology, Dr. Sirard focused on increasing egg quality in livestock. He found that the hormones administered to cows during *in vitro* fertilization caused rapid growth of the follicles—the small balloons in which oocytes grow.

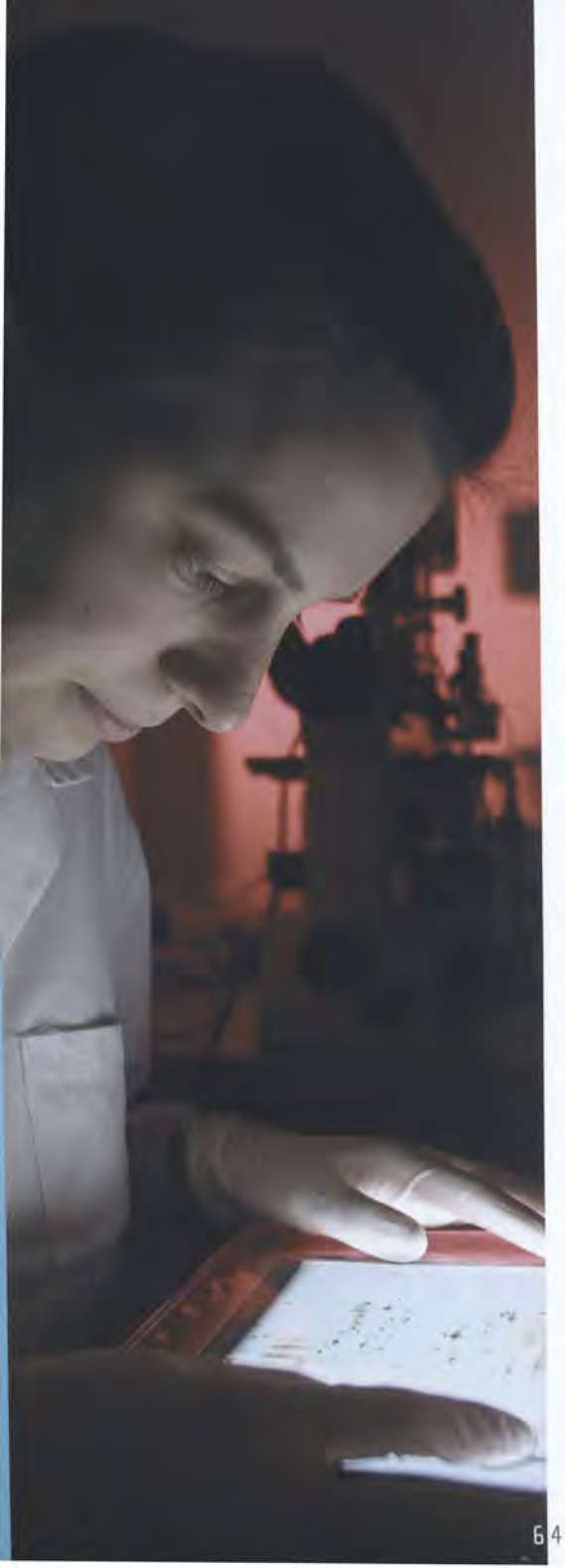
ABOVE: *Human embryo one day after fertilization*



ABOVE: *Bovine embryo two days after fertilization*



ABOVE: *Porcine embryo six days after fertilization*



However, the follicles grew so quickly that the developing oocytes could not keep up. The result: a windfall of oocytes, but many too weak to survive.

By modifying the hormones to create a 'plateau', or resting phase, for the follicles, Dr. Sirard was able to increase the number of successful embryos from 35 to 85 per cent, a success rate achieved nowhere else in the world.

"It's not because we found a magic bullet," he says. "It's because we took the time to understand how the ovary works, and how it influences the oocyte to become an embryo."

Companies around the world now use Dr. Sirard's procedure to breed better animals more quickly. Researchers on human fertility are also taking notice. "They're looking at the work we've done in animals, and they're realizing that maybe they also need to allow time for the follicles to differentiate, and produce better oocytes, not just more of them," he says.

With a solid understanding of what oocytes do, Dr. Sirard now wants to know how they do it. The oocyte is the only cell that can reverse the natural process of differentiation, whereby generic embryonic cells become specialized. It can then reprogram the same cell to take on a new role.

"If we understood how this works, we could reverse the differentiation process in skin cells, for example, to the point where we could transform them into neurons, or into liver cells," he says.

I want to understand this system, built in by nature, that makes us age, while the oocyte does not.

DR. MARC-ANDRÉ SIRARD, DIRECTOR, RESEARCH CENTRE IN REPRODUCTIVE BIOLOGY, LAVAL UNIVERSITY

The secret lies in the oocyte's genes, which carry the instructions that regulate cell development and function. As the Canada Research Chair in Animal Reproductive Applied Functional Genomics, Dr. Sirard is using gene mathematics and comparative studies to isolate the genes in question.

"Very simply, we take all the genes that are in the oocyte of a cow, and subtract the genes expressed in the liver, kidney and other tissue," he says. "We end up with a small portion of genes that are unique to the oocyte, but there are still more than a thousand of them."

By comparing genes from the oocyte of a cow with those of other animals, Dr. Sirard hopes to isolate the genes that are expressed in the oocytes of all animals, including humans. Then he can sequence those genes and determine their role in the body.

The research has many applications for treating disease and rebuilding cell tissues. "For people with Parkinson's, you need to reprogram the nerve cells to secrete dopamine, a chemical substance that affects movement, emotional response, and the ability to experience pleasure and pain," he says. "People who are diabetic need their pancreatic cells engineered to stabilize insulin production and function."

Eventually, oocytes could even regrow pieces of our bodies using our own cells. "We could rebuild your kidney, instead of trying to get one from a donor," says Dr. Sirard.

With the strong support that I receive from Canadian governments, I can do fundamental research that will create applications. It's normally there that we create the highest value in new intellectual property.

DR. MARC-ANDRÉ SIRARD, DIRECTOR, RESEARCH CENTRE IN REPRODUCTIVE BIOLOGY, LAVAL UNIVERSITY

A BETTER MEDIUM FOR PROTEIN PRODUCTION

Most companies that make recombinant proteins use the mammary glands of cows, sheep or goats as manufacturing plants. In a new application of an existing technology, TGN Biotech—founded by Dr. Marc-André Sirard and his colleague Dr. François Pothier—has found a way to use the seminal glands of pigs.

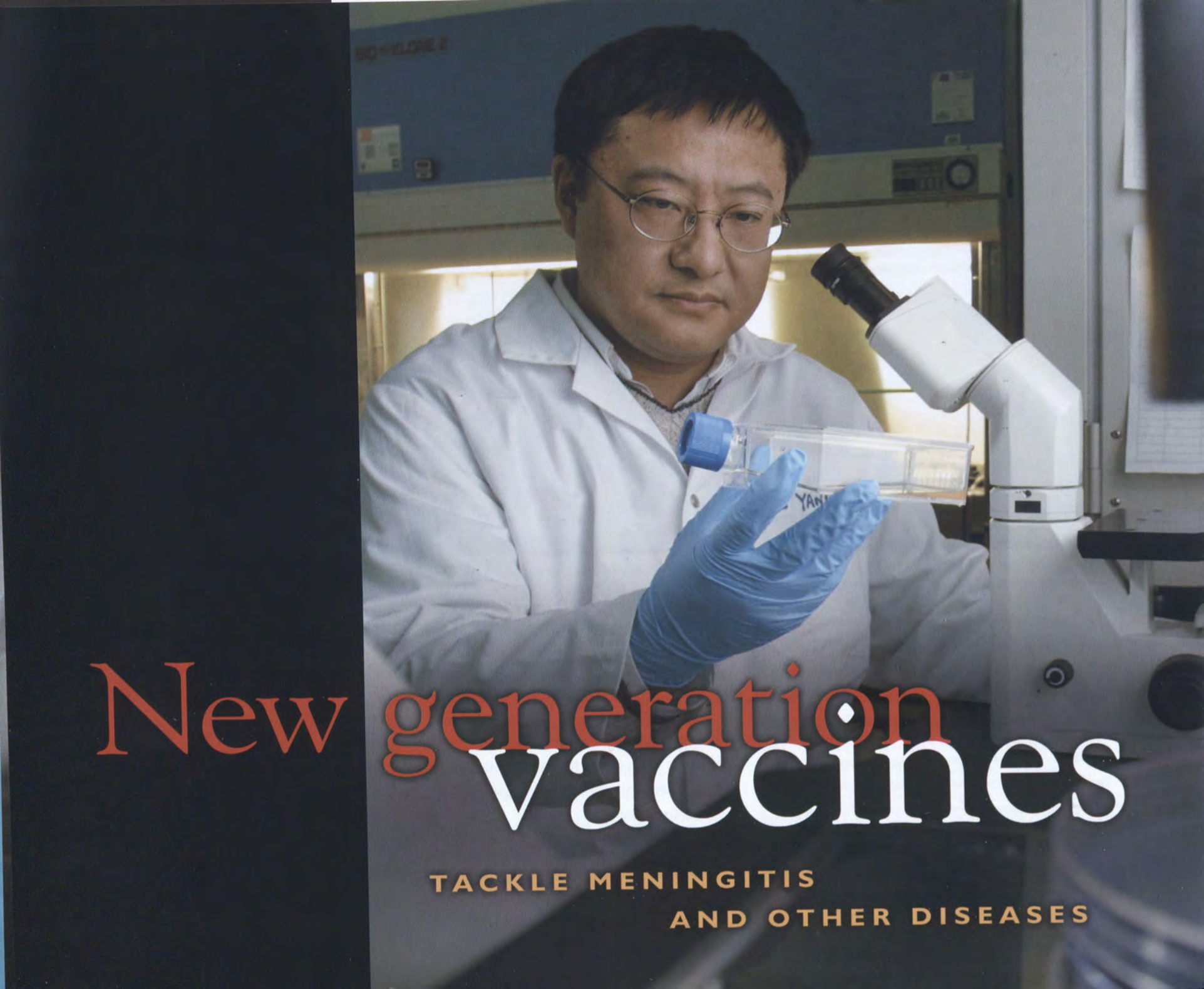
The technique, called Semenesis, uses transgenic technologies to modify the pig's seminal vesicle gland to produce a desired protein in the semen. The semen is then collected and the specific protein purified.

"It's better than milk—it's very clean, there is no bacteria," says Dr. Sirard. "The liquid is very soft on proteins because it's there to protect sperm cells."

The technique is also economical, because pigs are inexpensive to raise and produce 200-500 ml of semen per day. The semen is harvested painlessly, and much more easily than harvesting milk from a sow.

Dr. Sirard originally founded the company to keep young scientists from going to the United States to seek work, but also sees a significant global market for the Semenesis technology.

"There is a huge shortage worldwide in the capacity to produce complex proteins for drug manufacturing," he says. "It's very timely for a company to provide this expertise."


New generation vaccines
TACKLE MENINGITIS
AND OTHER DISEASES

DR. HAROLD JENNINGS' PIONEERING VACCINE RESEARCH HELPED GREAT BRITAIN TO VIRTUALLY WIPE OUT GROUP C MENINGITIS IN ONLY TWO YEARS.

Dr. Harold Jennings of Canada's National Research Council invented the world's first conjugate vaccine, now known as NeisVac-C, that effectively protects infants against Group C meningitis—a potentially fatal infection of the fluid and lining of the brain and spinal cord.

Great Britain, the first country to use the vaccine in a mass immunization program, reduced the incidence of Group C meningitis by 75 to 85 per cent in the first year alone. Now the innovative techniques that Dr. Jennings pioneered to develop NeisVac-C have spawned a new generation of vaccines that hold promise for a wide variety of diseases including pneumonia and some types of cancer.

Dr. Harold Jennings has been fascinated by chemistry since his boyhood, when he spent hours experimenting with his home chemistry set. That curiosity about molecules ultimately led him to develop a meningitis vaccine that is now saving hundreds of children's lives each year.

As a principal research officer for the National Research Council's Institute for Biological Sciences (NRC-IBS), Dr. Jennings earned an international reputation for his detailed knowledge of the structures and functions of polysaccharides—purified complex sugars used in many industrial processes. Building on this foundation, Dr. Jennings and his team developed new techniques for determining the structure of bacterial polysaccharides.

That research caught the attention of Dr. Emil Gotschlich, who developed the first polysaccharide vaccine for Group C meningitis some 30 years ago. "Through Dr. Gotschlich we learned that there were serious weaknesses in the performance of that vaccine," says Dr. Jennings. "The most serious problem was that it wasn't effective in infants." Half of the cases of Group C meningitis occur among children less than 2 1/2 years of age.

Many people carry the meningococci bacteria, but their bodies have built up immunity against it. For those who are not immune, one to two people out of every 100,000 exposed will develop a serious illness such as meningitis. If not treated with antibiotics, meningitis can kill within 24 hours. Of those who survive, many suffer serious

PERSISTENCE PAYS OFF

Today, NeisVac-C is marketed in Canada by Shire Biologics and sold elsewhere by Baxter Healthcare Corporation, which now owns the vaccine technology developed by Dr. Harold Jennings. The vaccine is licensed in more than 25 countries, and more than 8 million doses have been sold. The British immunization program resulted in sales of CAD$86 million in the first year alone. So far, the National Research Council's Institute for Biological Sciences has received $10 million through its licensing agreement.

After nearly 25 years of researching, developing and bringing NeisVac-C to commercialization, Dr. Jennings' greatest rewards can be measured in lives saved as well as the potential to develop vaccines for other devastating diseases. But his dedication and innovation have also been recognized in other ways: in 2002, he was selected to receive the prestigious Manning Award. And he has become the highest royalty-earning researcher ever in a Canadian government laboratory.

CONJUGATE FUTURES

"Conjugate vaccines have been the most important development in the vaccine industry during the past 15 years," says Dr. Harold Jennings, Principal Research Officer, National Research Council of Canada. "The technology we developed for the Group C meningitis vaccine can be applied to any encapsulated pathogen."

Successful conjugate vaccines have also been produced for *Haemophilus influenzae* type b, and *Streptococcus pneumoniae*. And Dr. Jennings has used the same technique to develop a new Group B meningitis vaccine.

Dr. Jennings is also collaborating with Dr. Dennis Kasper of the Harvard Medical School to develop a conjugate vaccine for Group B *Streptococcus*, the main cause of neo-natal meningitis. And he is exploring ways to adapt the vaccine technology for cancer. "Some cancer cells, such as those found in small cell lung cancer and Wilms tumour, are covered by the same polysaccharide as Group B meningococci," Dr. Jennings explains.

ABOVE: *Molecular structure of meningitis*

health complications such as permanent brain damage, hearing loss and intellectual impairment. The global incidence of this disease is estimated at 500,000 cases each year, but can reach much higher numbers if an epidemic occurs.

The failure of the Group C polysaccharide vaccine to stimulate infants' immature immune systems captured Dr. Jennings' interest. "I knew that protein vaccines protected infants against diseases such as diphtheria, tetanus and whooping cough," he explains. "So we hypothesized that the solution for Group C meningitis was to find a way to combine the complex sugars covering the bacteria with a protein to make a safe, effective vaccine."

In 1978, using a new coupling technique they developed, Dr. Jennings and his team became the first to produce a conjugate Group C meningitis vaccine, later called NeisVac-C. It was patented in 1982.

At first, attracting solid commercial interest in the vaccine was difficult, but Dr. Jennings persisted. In 1986, he met Dr. Francesco Bellini of the Montréal-based biotechnology firm BioChem Pharma. Dr. Bellini eventually co-founded North American Vaccine (NAVA) and invested in the commercial development of NeisVac-C and other conjugate vaccines being developed by Dr. Jennings. NAVA was eventually bought by Baxter International Inc., which now sells NeisVac-C around the world.

In 2000, Baxter Healthcare Corporation successfully launched NeisVac-C when Great Britain, faced with outbreaks of Group C meningitis, launched an immunization campaign for

The success of conjugate vaccines has had a considerable influence on the comeback of vaccine research, and applications of this technology to other diseases are inevitable. New approaches to vaccine development are also likely as our basic knowledge in the genetics of pathogens improves.

DR. HAROLD JENNINGS, PRINCIPAL RESEARCH OFFICER,
INSTITUTE FOR BIOLOGICAL SCIENCES,
NATIONAL RESEARCH COUNCIL OF CANADA

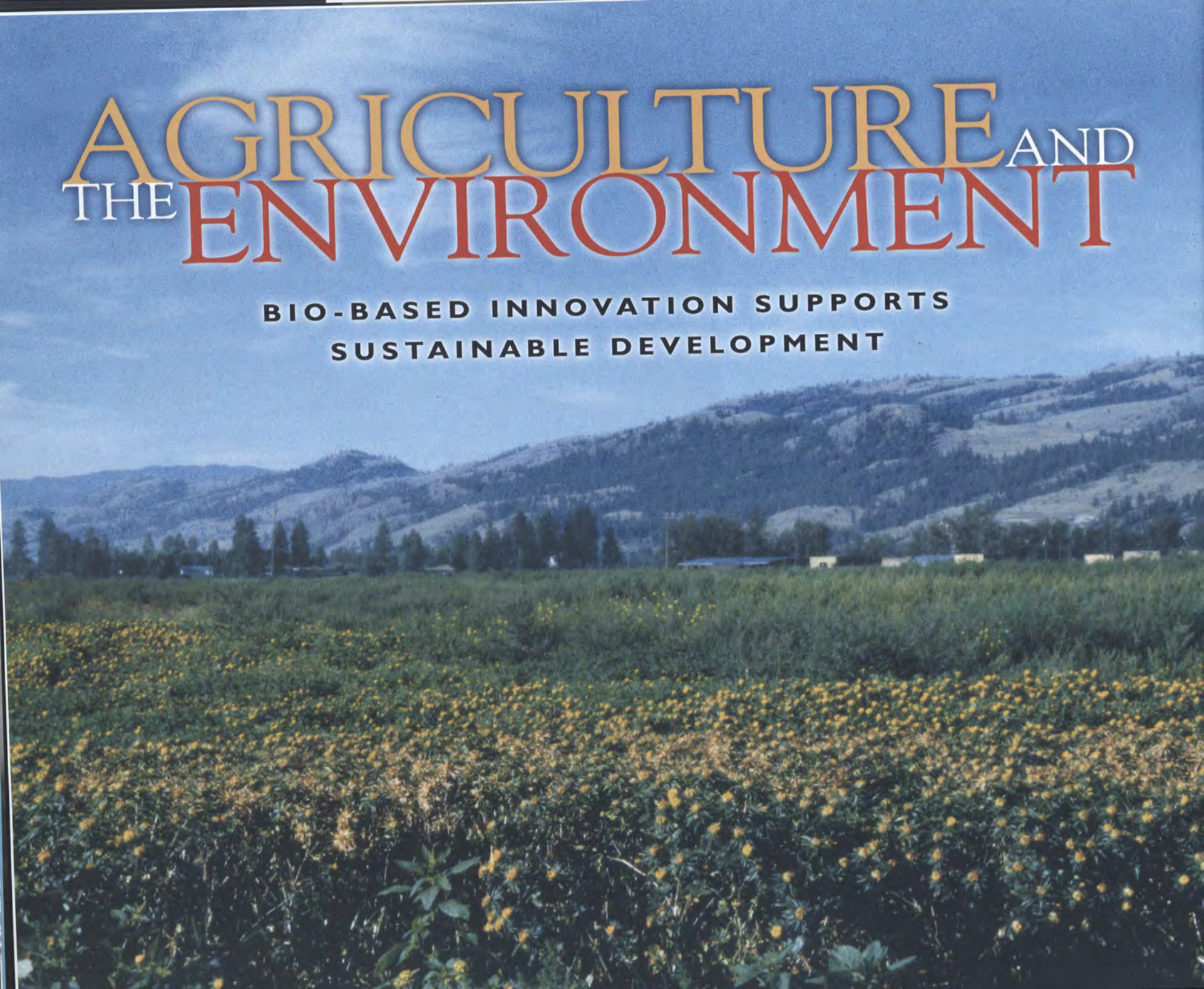
infants and people under 18 years of age. "The program virtually wiped out Group C meningitis in Britain in two years," says Dr. Jennings. In Canada, Québec became the first province to put a routine meningococcal immunization program in place, followed by Alberta. "There's no doubt in my mind that Canadians stand to realize a similar health benefit from NeisVac-C as seen in the UK," says Dr. Jennings.

The innovative techniques that Dr. Jennings pioneered also hold promise for developing a new generation of vaccines for a variety of diseases, including some types of cancer and pneumonia. In fact, he and his colleagues have already developed a promising new conjugate vaccine for Group B meningitis, which is expected to go into clinical trial sometime in 2003.

"Currently, there is no effective vaccine against Group B meningitis, which accounts for 50 per cent of all cases of meningococcal meningitis in developed countries," says Dr. Jennings.

AGRICULTURE AND THE ENVIRONMENT

BIO-BASED INNOVATION SUPPORTS SUSTAINABLE DEVELOPMENT



WITH ITS LARGE LANDMASS AND STRONG AGRICULTURAL TRADITION, CANADA IS WELL EQUIPPED TO TAKE A LEAD POSITION IN THE GLOBAL BID TO DEVELOP NEW PLANT VARIETIES THAT BENEFIT FARMERS AND CONSUMERS.

BUT CANADIAN SCIENTISTS APPROACH AGRICULTURAL BIOTECHNOLOGY FROM A MUCH BROADER PERSPECTIVE—ONE THAT ENCOMPASSES ENVIRONMENTAL SCIENCE AND INDUSTRY REQUIREMENTS. SINCE THE MID-1900s, CANADA HAS TAKEN A KEEN INTEREST IN HARNESSING CROP PLANTS, PLANT AND FORESTRY RESIDUES, AND OTHER SOURCES OF BIOMASS TO MANUFACTURE VALUABLE INDUSTRIAL PRODUCTS INCLUDING PHARMACEUTICALS, ENERGY SOURCES, POLYMERS AND STRUCTURAL FIBRES, LUBRICANTS AND FINE CHEMICALS. SUCH PRODUCTS ARE INHERENTLY RENEWABLE, SUSTAINABLE AND OFTEN NON-POLLUTING.

CANADIAN INNOVATION IN AGRICULTURE AND THE ENVIRONMENT

Page 74

Bacteria beware! Warnex Inc. offers Genevision™, a fast and reliable way to ensure the quality of processed foods before they reach the supermarket. What once took up to seven days to test can now be done in 24 hours or less using Genevision.

Page 82

Calgary-based SemBioSys Genetics Inc. is harnessing oilseeds to slash the production costs of genetically engineered proteins used in the pharmaceutical, cosmetics, nutritional products and other industries.

Page 94

Iogen Corporation's plant on the outskirts of Ottawa can turn 40 tonnes of agricultural waste into bioethanol fuel. Iogen's enzyme-induced process extracts energy from agricultural leftovers while leaving the cream of the crop for food production.

Page 78

Dragline silk, the single-protein thread found in the radiating spokes of a spider web, is five times stronger by weight than steel. But spiders won't spin silk in cramped quarters. Dr. Jeffrey Turner asked: *what if you produced the protein in a different factory?*

Page 86

By identifying and mapping genes in red and black spruce, scientists in Atlantic Canada will help the forestry industry select and breed trees that are well adapted to climate change. The science positions Canada as a global leader in forestry genomics.

In the 1950s, Canadian scientists responded to a shortage of edible oils by extracting seed oils from plants such as rapeseed and flax. By developing and applying the advanced technologies of the day, they eventually developed a rapeseed variety with low erucic acid in the seed oils, making it suitable for human consumption, and low glucosinolates in the meal, thereby creating a non-toxic alternative for animal feed. They dubbed the new variety *canola*, which today generates annual economic activity of more than CAD$2 billion.

More recently, Canada has produced numerous plant varieties with novel traits that benefit farmers such as increased yield, resistance to insect or fungal pests, and tolerance to herbicides. Other varieties have traits that benefit consumers such as healthy oil profiles, easy-to-digest fibre, and enhanced nutritional value. Most of these new plant varieties are grown for consumption by humans or domestic animals. In addition, Canadian researchers have been applying genetic technologies to prevent infectious diseases in livestock and improve animal production.

At the same time, Canada's agricultural and environmental research and industrial sectors have been actively pursuing an alternative direction. The aim of this work is to harness the biological and chemical energy of living things, rather than to continue expending non-renewable resources. Today, plants and animals are being used to produce valuable consumer and industrial products—including pharmaceuticals, medical products, fuels, lubricants, and industrial fibres.

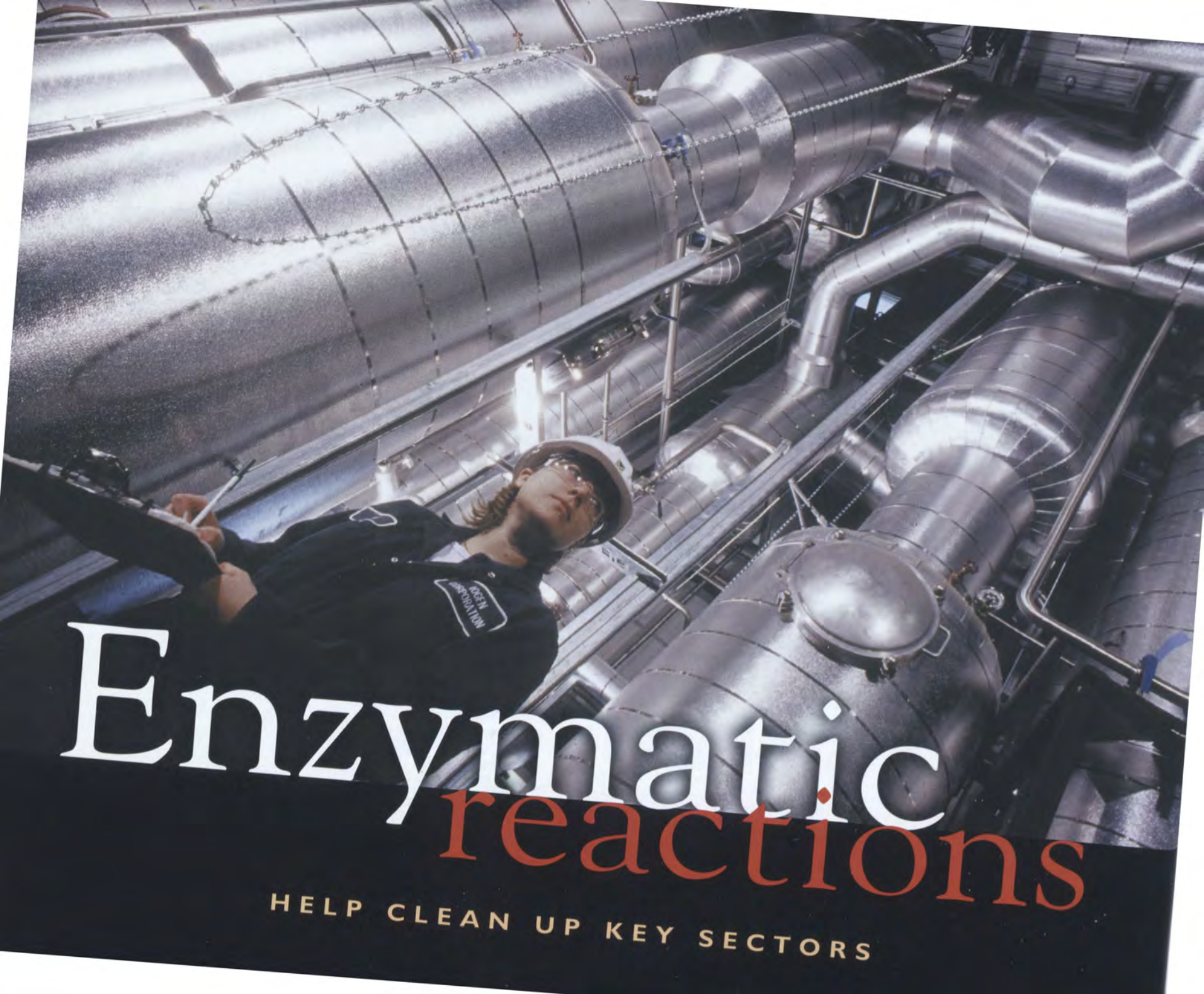
Fueled by the growing public awareness that non-renewable, carbon-based resources are limited, and that alternative sources of raw materials must be found to sustain future global development, R&D activity in these areas is expected to increase significantly in coming years.

The Government of Canada supports innovation in these vital fields through a number of departments and agencies. Collectively, Natural Resources Canada, Agriculture and Agri-Food Canada, the National Research Council, and Environment Canada are exploring new opportunities in biomass conversion, industrial uses for plants and animals, and processes that reduce greenhouse gas emissions and atmospheric carbon dioxide.

As the Canadian bio-based products industry becomes more fully developed, it will generate tremendous economic benefits for farmers, forest product companies, energy producers and chemical manufacturers. Rural areas will benefit as bio-based manufacturing facilities are established near supply sources, providing new revenue streams for farmers and cash flow for other rural development initiatives. Moreover, biotechnology will allow more of Canada's land base to be used for industrial and environmental purposes. Scientists have already developed plant varieties, such as hybrid poplar and switch grass, that thrive in marginal agricultural areas and low-grade forest regions.

Modern biotechnology has an important role to play in the emerging economy, as plants are engineered to: produce components that are easier to extract and purify; provide valuable industrial compounds such as polymers; and thrive in marginal conditions. The advent of more bio-based products will help ensure a continuous supply of renewable raw materials and energy, while reducing the environmental impact of many petroleum-based products.

At the current rate of consumption growth, the world's known and estimated petroleum reserves will be exhausted within the lifetime of the current generation. In addition to improving food and feed sources, Canada is well on its way to demonstrating the viability—and sustainability—of alternative sources of energy. Turn the page to see how we are doing it.



Enzymatic reactions

HELP CLEAN UP KEY SECTORS

AFTER 30 YEARS OF SUCCESS IN DEVELOPING INDUSTRIAL ENZYMES, RENEWED INTEREST IN CLEAN FUELS ALLOWS IOGEN CORPORATION TO RETURN TO ITS ROOTS.

Iogen Corporation has taken the idea of separating the wheat from the chaff to heart. Every day, its plant on the outskirts of Canada's national capital can turn 40 tonnes of agricultural waste—wheat, barley and oat straw as well as stalks of corn—into EcoEthanol™, a bioethanol fuel. Iogen's enzyme-induced process extracts energy from agricultural leftovers while leaving the cream of the crop for food production.

The concept of using ethanol fuel has existed for almost as long as the internal combustion engine. But the clear benefits of EcoEthanol—including a 99 per cent reduction in greenhouse gas emissions*—have been overshadowed by high production costs associated with grain ethanol and the controversy of using vital food sources to create fuel resources.

Until now.

Driven by issues such as rising oil prices, heavy reliance on foreign sources, and environmental concerns, petroleum producers and consumers alike are eager to see cleaner options at the gas pump. For Iogen Corporation, it means the time for their initial *raison d'être* has finally come.

In the mid-1970s, with the world on the verge of a fuel shortage, Iogen responded by proving that enzymes could break down the sugars in plant fibre to produce clean-burning ethanol fuel. When oil prices fell and interest in alternative sources waned in the 1980s, the company looked for ways to apply its knowledge in other sectors. Iogen built an international reputation for enzyme products that improve the digestibility of animal feed and significantly reduce the environmental impact of both the pulp and paper and textiles industries.

Now, with an economically viable process in place, the world's first bioethanol demonstration plant in operation, and blueprints for a full-scale commercial plant on the table, Iogen is undeniably the centre of global attention.

Iogen never let go of its bioethanol dream. Ever aware of the need to generate a secure, domestic energy supply, the company took a serious look at raw materials and further refined its active

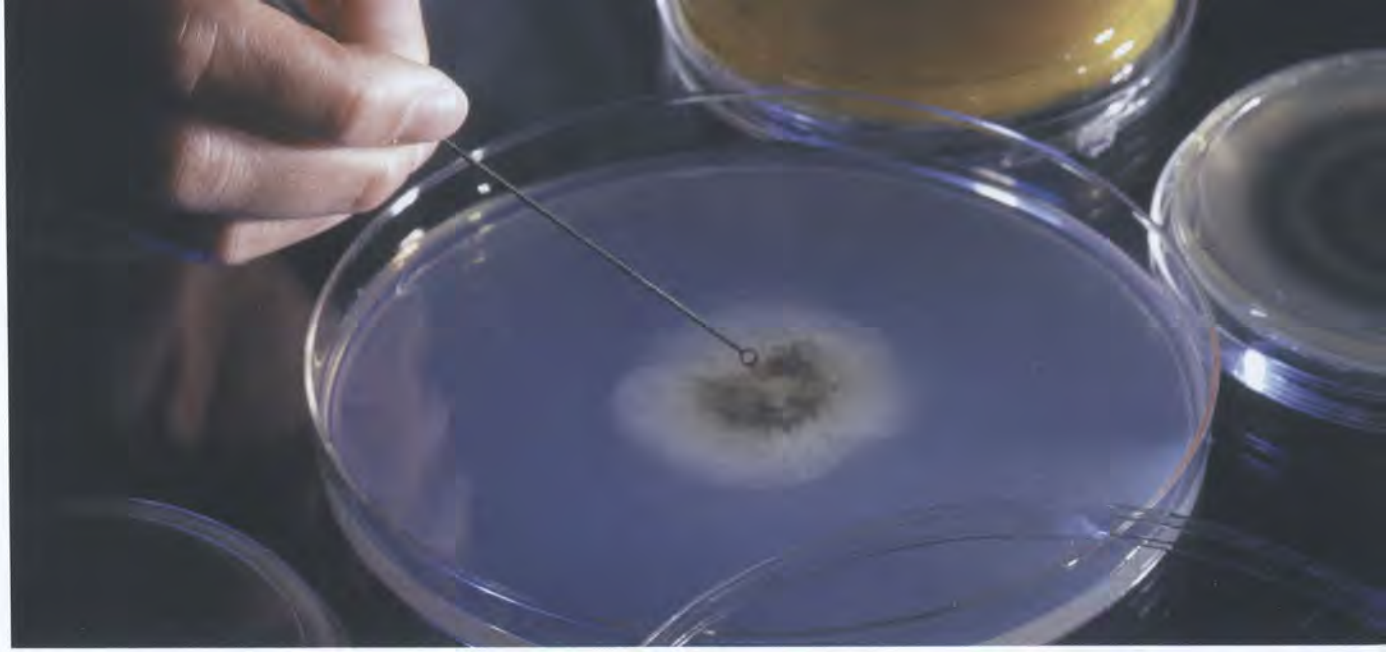
THE BENEFITS OF ECOETHANOL™

EcoEthanol™, made from Iogen's unique bioethanol process, provides practical solutions to many energy and environmental issues such as dwindling energy supplies, global climate change, and consumer demand for greener choices.

This alternative fuel makes virtually no contribution to greenhouse gas emissions. Because it contains 35 per cent oxygen, bioethanol burns more efficiently and produces up to 30 per cent lower toxic carbon monoxide emissions than regular gasoline. In fact, EcoEthanol actually reduces smog and local air pollution.

Because it is produced from existing agricultural residues that are widely available in Canada, EcoEthanol is poised to become a viable domestic source of energy. Moreover, large-scale production plants will revitalize rural communities by creating a new market for farmers and generating business opportunities for local communities.

* *U.S. Department of Energy Life-cycle Analysis*



IOGEN CLEANS UP ON BLEACHING AND STONEWASHING

Today's consumers know they want white paper and faded jeans. What they don't know is that Iogen enzymes have helped producers of both products clean up their act by replacing environmentally detrimental processes.

Iogen Corporation's BioBrite® xylanase product line helps pulp and paper companies produce high-quality products with less chlorine bleach. The active enzymes break down fibrous raw material, making it more accessible to a smaller amount of chlorine. In the process, BioBrite reduces the release of toxic dioxins known to pollute rivers and streams.

The Denabraide® cellulase line allows textile manufacturers to provide the softer, more faded jeans that consumers prefer without the environmental impact caused by pumice stones and chlorine bleaches.

Iogen supplies 90 per cent of the xylanase enzyme used in Canadian pulp mills and 10 per cent of the world supply of fading agents in the blue jeans industry.

ingredient. Iogen now starts with the fibrous portion of plants—essentially the bio-waste of farming and food production, which is much cheaper than the grains themselves but still a readily available, renewable resource. In addition, it developed a cellulase enzyme that accelerates the conversion of these plant fibres into sugars, which are then fermented and distilled into ethanol. Together, these factors put to rest the argument that bioethanol is too impractical and costly to manufacture.

That vital leap forward captured the attention of Canada's largest petroleum producer. In 1997, Petro-Canada invested in Iogen to support the development of a bioethanol validation facility. Just three years later, these two partners received additional funding from the Government of Canada to establish the world's only bioethanol demonstration plant. This plant is designed to validate equipment performance and to identify and overcome production problems prior to the construction of a $300-million full-scale commercial plant in 2004.

In May 2002, Iogen announced a $46-million investment by the Royal Dutch/Shell Group in the form of a strategic partnership. This investment gives Shell a 22 per cent stake in Iogen and expands Iogen's global reach.

People usually think of bioethanol when they think of us, which is just fine. But if you read magazines or books, drink fruit juices or beer, or wear jeans or T-shirts, there's a good chance Iogen has made direct contact with some part of you during most days of your life.

BRIAN FOODY,
PRESIDENT, IOGEN CORPORATION

Such broad-spectrum success comes from Iogen's careful cultivation of one of the world's fastest-growing organisms. The company's Ottawa-based facilities house huge vats of fungus, which replicate quickly to supply a steady stream of enzymes. Through in-depth research of these biochemically active proteins, Iogen has found ways to dramatically increase the rate of naturally occurring biochemical reactions.

Iogen's enzymes fall into two broad classes: cellulases, which target a plant fibre constituent called cellulose; and hemi-cellulases, which modify hemi-cellulose. Within these classes, Iogen produces a wide array of task-specific enzymes that can be delivered in liquid or powder form. Depending on how they are selected and used, Iogen's enzymes can help industrial clients meet technical specifications for their products, improve processes to reduce operating costs, and increase yields from individual batches. For example, an enzyme additive may prevent fibrous material from clogging production systems or deliver an end product (such as apple juice) with greater clarity.

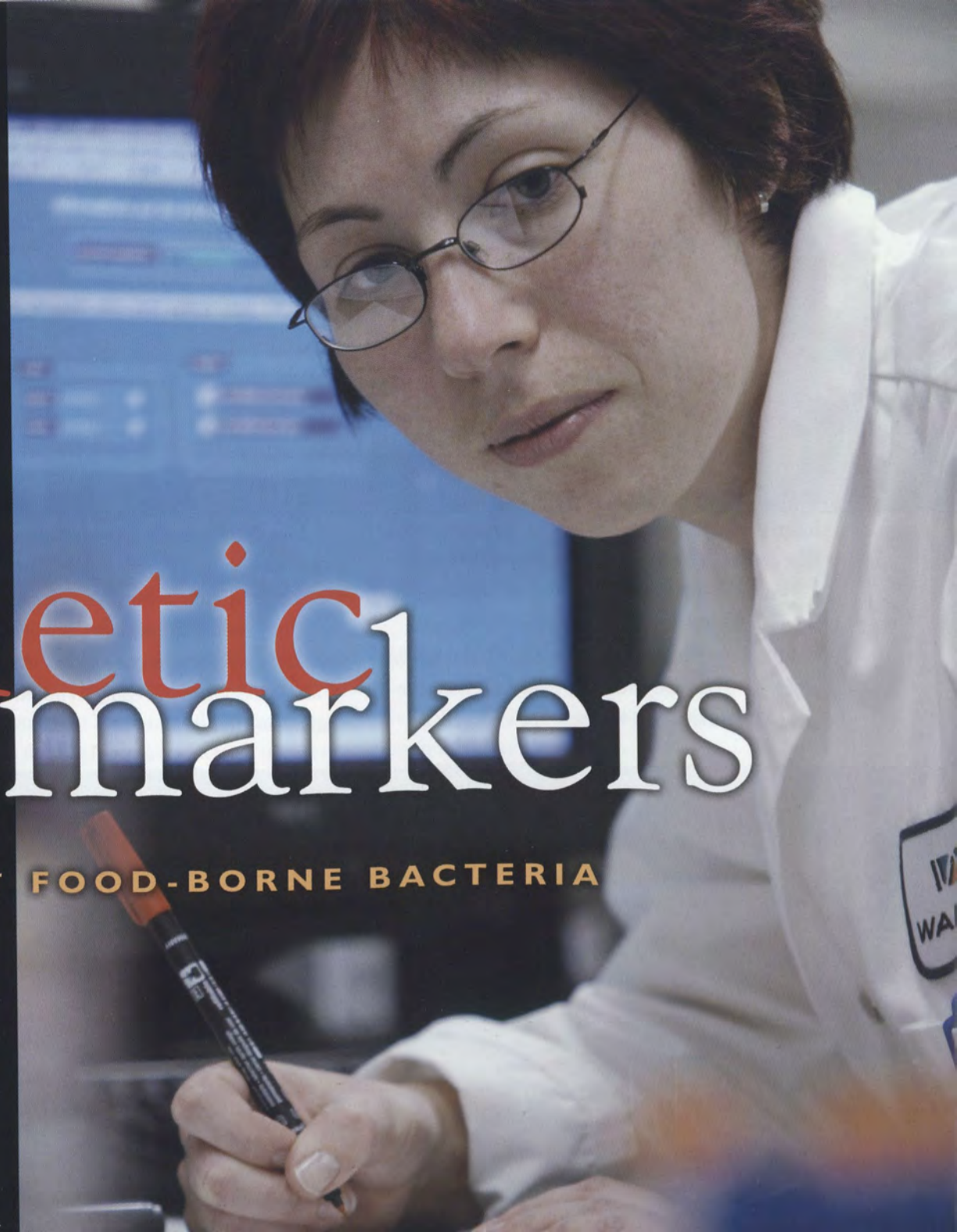
But Iogen's commercial offering doesn't start and end with enzymes. In recent years, the company expanded its business base by developing specialized enzyme application equipment and testing processes for the pulp industry. Iogen's remotely operated control systems regulate enzyme and acid addition in production plants across the country while also collecting vital data, used to generate productivity and quality assurance reports for individual clients.

Iogen's full-service approach ultimately leads to production improvements that directly affect the bottom line in key industry sectors—all while responding to consumer demands that include cleaner streams and rivers, lower levels of air pollution, and overall environmental improvements.

ABOVE: *a more environment-friendly and economical way to produce bleached pulp. In 2002, more than 2 million tons of brown pulp produced from wood chips were pretreated using xylanase enzyme before the bleaching process. This led to a decrease in the use of bleaching chemicals and a reduction in harmful chlorinated byproducts.*

Genetic markers

HUNT FOOD-BORNE BACTERIA



GENEVISION™ OFFERS A FAST AND RELIABLE WAY TO ENSURE THE QUALITY OF PROCESSED FOODS BEFORE THEY REACH THE SUPERMARKET.

"The days of the Petri dish are numbered," proclaims the website of Warnex Inc. Based in Laval, Québec, this genomics-based quality control company is known for Genevision™—a revolutionary new technology that detects and identifies pathogenic bacteria.

Applying existing state-of-the-art technology combined with proprietary molecular markers and unique software, Genevision can detect harmful micro-organisms found in everything from cheese to ground beef. What once took up to seven days to test using traditional microbiological methods can now be done in 6 to 24 hours using the Genevision technology.

Genevision will allow agri-food facilities to rapidly and accurately monitor product quality, preventing costly recalls and potential food poisonings.

About one in four North Americans get food poisoning every year. These unlucky people now have an ally in Dr. Christian Archambault, a molecular biologist and the inventor behind the Genevision™ rapid detection technology.

Although he can't recall exactly how the idea for Genevision arose, his knowledge of forensic applications played a part. "DNA has become a very good forensic tool to identify criminals. In our case, the criminals are bacteria," says Dr. Archambault, Executive Vice-President and Chief Operating Officer of Warnex Inc.

Genevision uses proprietary DNA markers to detect various organisms. Warnex's initial focus has been on developing and validating markers for *Salmonella*, *Listeria* and *E. coli*, at both the genus and species level. Additional markers are being developed for other pathogens, beneficial

TESTING FOR GENETICALLY MODIFIED ORGANISMS

Warnex Inc.'s Genevision™ technology can identify anything that contains DNA, including genetically modified organisms (GMOs). Genevision uses a DNA marker to find the matching DNA in a GMO. This technology can be applied either to certify that certain foods are GMO-free, or to ensure that GMO products do in fact contain the genetic modification that agri-food companies claim.

For example, in the near future some genetically modified rice may contain an anti-cholesterol agent. "I would rather eat an extra helping of rice than take my cholesterol medication every day," says Mark Busgang, Warnex President and CEO. "And if I'm paying a premium price, I'd like to be sure I'm getting what I paid for."

BIRTH OF WARNEX INC.

Beginning as a Junior Capital Pool Corporation on the Alberta Stock Exchange in 1996, CEO Mark Busgang and Chairman Richard Lafferiere have created a solid success story.

With more than 100 employees and a market capitalization of $57 million, Warnex migrated to the Toronto Stock Exchange in early 2003. In 2002, its analytical services group generated more than $6 million in revenues—providing substantial cash flow to help cover the company's corporate overhead and contribute to its research and development.

Following the June 2000 acquisition of the Genevision™ technology from Dr. Christian Archambault, Warnex has invested more than $5 million in its development. The company is beginning to commercialize the technology and is planning a major commercial rollout for the second half of 2003.

organisms and genetically modified organisms (GMOs). Warnex can customize its test kits to meet clients' needs—for example, a poultry processor may want to test for *Salmonella*, while a brewer may want to confirm the presence of specific yeasts that give a beer its unique flavour.

When a marker encounters complementary DNA from a target organism, fluorescent light is emitted, which is then detected by a Real-Time PCR. The results are analysed by Warnex's proprietary Virtual QA software, which translates the data into easy-to-interpret results: an organism is present or it isn't; a sample meets government safety standards or it doesn't. All this takes just 6 to 24 hours.

Genevision has many practical applications, says Warnex President and CEO Mark Busgang. The company's primary target market is the processed food industry. Ensuring quality control in foods is worth $5 billion per year worldwide. If manufacturers hold onto a shipment of food for just the few hours required to obtain test results, they can save themselves millions of dollars in potential recall costs—as well as incalculable damage to their reputation.

The technology can also improve the safety of fresh food, which is rarely tested for harmful bacteria because it takes too long using conventional microbiological techniques. And in the

pharmaceutical industry, speedy results from quality control tests allow products to be shipped earlier. "When you're carrying $10 million worth of inventory, the savings are huge," says Mr. Busgang.

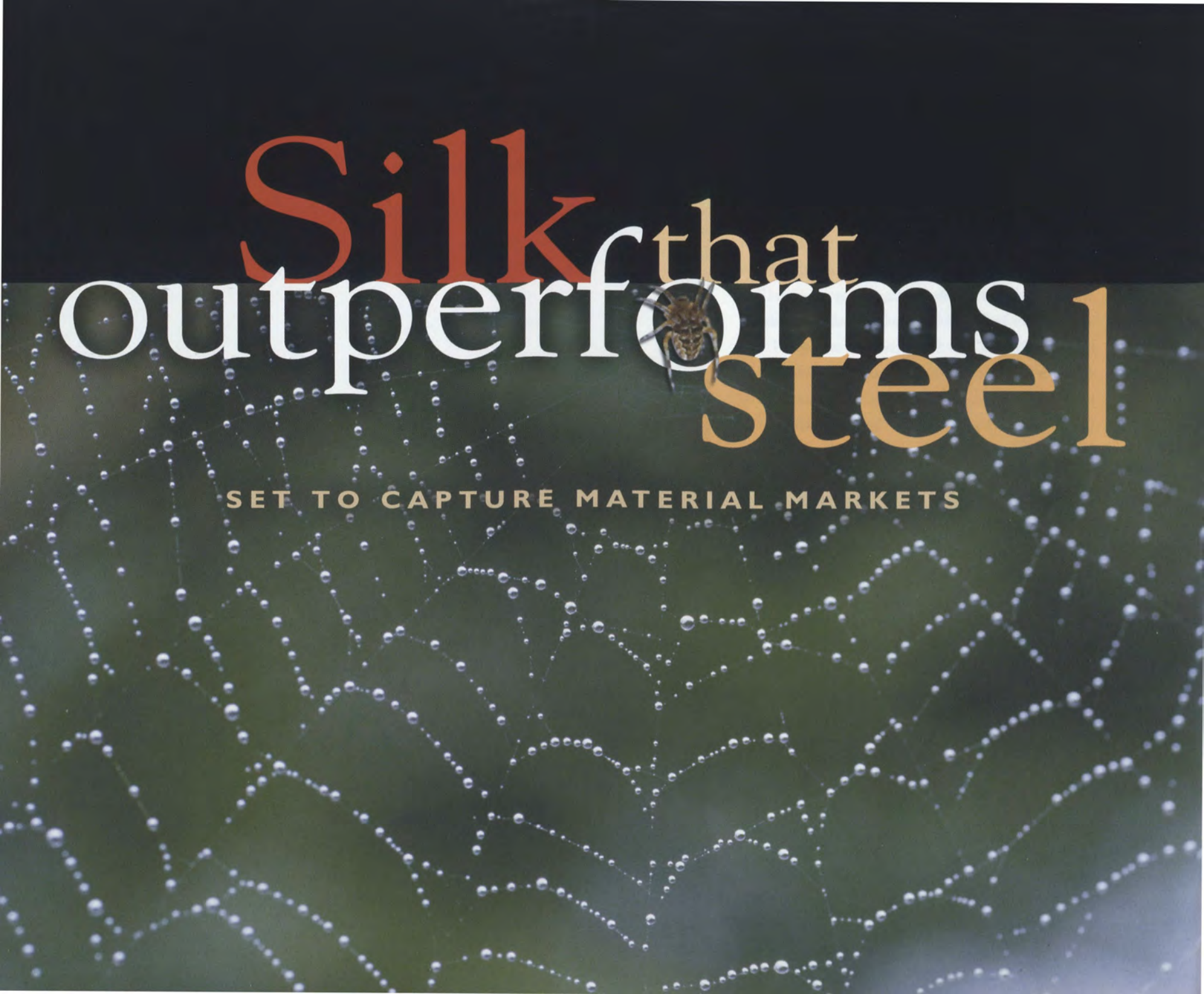
In future, Genevision may also be used to test water supplies or fresh flowers. It could help detect food allergens such as peanuts and antibiotics. One of the most exciting potential applications is the Molecular Bar Code. Warnex has applied for a patent for this technology, which involves manufacturing unique DNA strands for adding to factory-made products. Like a fingerprint, Molecular Bar Codes can label a product, manufacturer or lot number—even the production day.

Molecular Bar Codes can be added into liquids or sprayed dry onto products without damaging them. "Labelling a litre of milk or juice would cost just one-ten thousandth of a cent," says Mr. Busgang. "It is the most economical and inexpensive way to trace products from the farm to the fork."

Molecular Bar Codes can also prevent fraud. Imitation perfumes, for example, are often sold in bottles identical to the real thing. By spraying their products with bar codes before they leave the factory, perfume makers could easily prove if bottles sold in the market are genuine or fake. "You can also add it to printer's ink to mark bonds, dollar bills and the like. It's the ultimate in terms of traceability and anti-counterfeit protection," says Mr. Busgang.

Silk that outperforms steel

SET TO CAPTURE MATERIAL MARKETS



MOLECULAR GENETICIST DR. JEFFREY TURNER, FOUNDER AND CEO OF NEXIA BIOTECHNOLOGIES INC., FINDS A WAY TO SPIN CELLULAR SIMILARITY TO HIS ADVANTAGE.

With an inherent genius for engineering, a spider spins seven types of silk: one for wrapping eggs, one for wrapping prey, and five for web construction. Dragline silk, the single-protein thread used to create the web's radiating spokes, has a tensile strength of 400,000 pounds per square inch and is five times stronger, by weight, than steel.

But the territorial and aggressive nature of spiders severely limits the supply of spider silk. Unlike silkworms, spiders will not produce in cramped quarters. Dr. Jeffrey Turner looked at the potential market for spider silk and asked a basic question: *what if you produced the protein in a different factory?*

"Spider silk is a material science wonder—a self-assembling, biodegradable, high-performance nanofibre structure one-tenth the width of a human hair that can stop a bee traveling at 20 miles per hour without breaking," says Dr. Jeffrey Turner, the founder, President and CEO of Nexia Biotechnologies Inc. "Spider silk has dwarfed man's achievements in material science."

Spider silk is considered a fine 'denier' fibre—a yarn weighing only one gram for each 9,000 metres.

The properties of proteins first captured Dr. Turner's attention while he was teaching molecular biology—an area of science that focuses on finding patterns in fine detail—at McGill University (Montréal, Québec). It is only at this level that orb spiders (which weave orb-shaped webs) and Nigerian dwarf goats reveal their similarities. By some whim of nature, spider silk glands and goat mammary glands both contain epithelial cells that manufacture and secrete large amounts of complex, water-soluble proteins. In the spider's case, an additional 'spin cycle' makes the previously soluble proteins insoluble—and the resulting fibres even more desirable.

With this in mind, Dr. Turner founded Nexia in 1993 and started building Canada's first transgenic farm animal facility. He shifted his attention to finding the gene that codes for silk protein production, then began the quest for another living system that could decipher

BREEDING SUCCESS

In January 2000, Nexia Biotechnologies Inc. announced the birth of two male BELE® goats, which have since been used to sire a growing herd of silky milk producers. The acronym stands for 'Breed Early, Lactate Early' and reflects the desired qualities of an organic spider silk factory: short generation times, multiple births, and good milk production.

The company has first-generation female BELE goats producing BioSteel® milk and recently confirmed that the silk-producing gene has been successfully transferred to the second generation of the new breed.

the spider's genetic instructions to deliver the desired product. By 1999, the company achieved its first critical milestone: Nexia's patented MAC-T mammary cell lines successfully produced fully soluble silk protein in a laboratory setting.

This encouraged the company to forge ahead with the concept of using a milk-producing herd to house Nexia's silk protein factory. The Nexia team added a single gene to the 70,000 others that regulate all aspects of goat life, in such a way that the spider gene lies dormant in every cell except the critical epithelial cells found in female mammary glands. The end result is a goat breed, known as the BELE® (Breed Early, Lactate Early) system, that produces silky milk.

But producing silk protein is only the first step in manufacturing Nexia's proposed BioSteel® product line. Once extracted from the milk, the syrupy liquid of silk proteins must be spun into fibres. Again, Nexia's aim is spider-like: the company wants to optimize its spinning processes to create a range of spider silks with different properties. Each type of spider silk is composed

It's incredible that a tiny animal found literally in your backyard can create such an amazing material using only amino acids, the same building blocks that are used to make skin and hair.

DR. JEFFREY TURNER, PRESIDENT AND CEO,
NEXIA BIOTECHNOLOGIES INC.

of specific proteins coded by specific genes, which means Nexia has at least six more genes to explore. Dragline silk is coveted for its tensile strength, but 'capture silk' is stickier and can stretch up to three times its length before breaking. Ergo, Nexia sees commercial potential for several BioSteel product lines.

But it's not only the end product that holds appeal. "Using these water-based BioSteel solutions for large-scale fibre spinning would be much more environmentally friendly than using the harsh solvents typical of most synthetic fibre manufacturing," says Costas Karatzas, Nexia's Senior Vice-President of Research and Development.

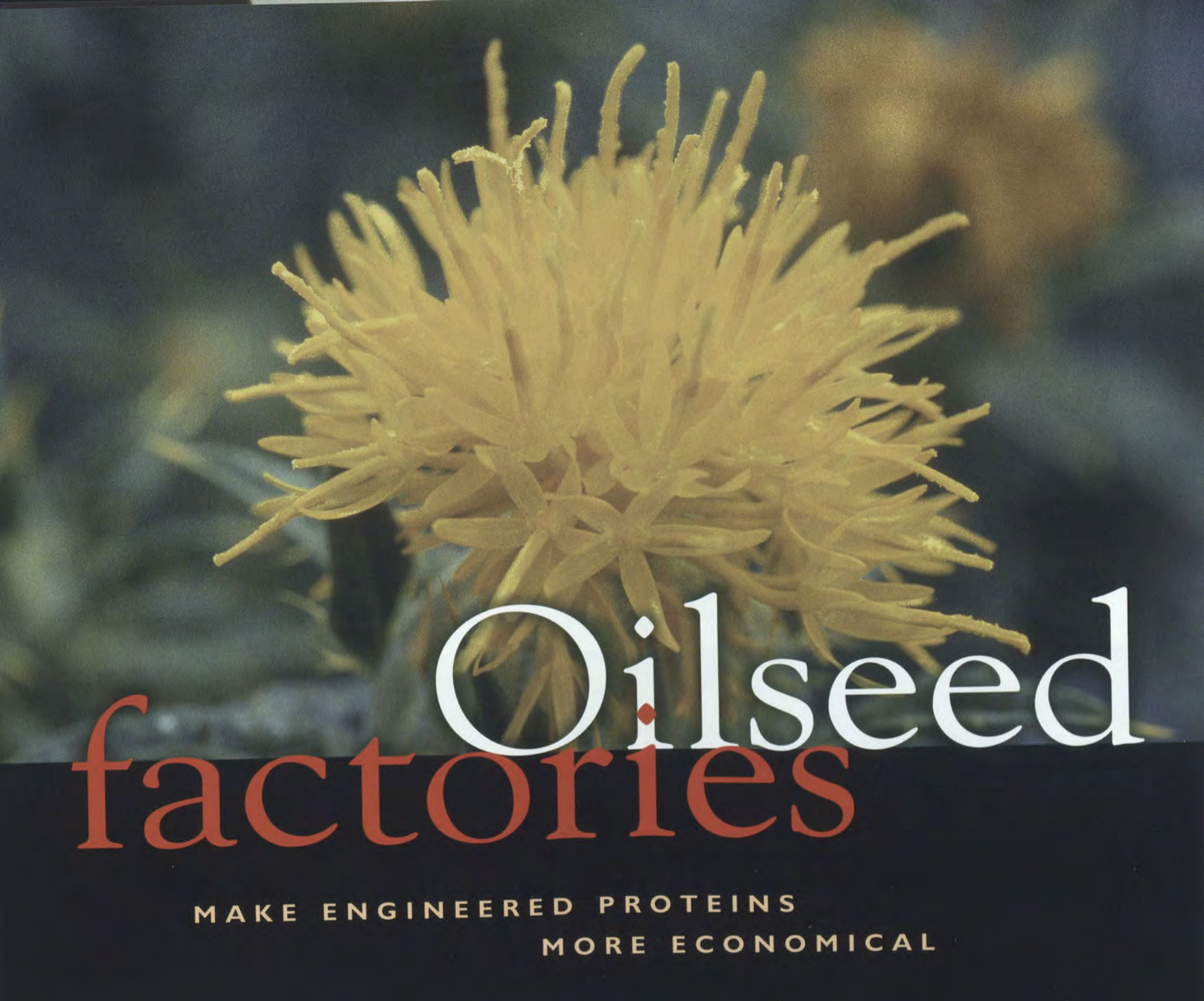
Commercial spider silk is still a year away, but Nexia is already weaving an impressive web of support. The company raised $42.2 million in Canada's largest biotech Initial Public Offering and now trades on the Toronto Stock Exchange as NXB. It has received approximately $24.7 million of private funding from prominent investors such as MDS Capital Corp., the Ontario Teachers' Pension Plan, Société Innovatech du Grand Montréal, Royal Bank Ventures Inc., Sofinov (a subsidiary of the Caisse de dépôt et placement du Québec), the Canadian Medical Discoveries Fund, and four Asian investor groups. Nexia now has 65 highly trained employees, a centralized office and laboratories in the Montréal suburb of Sainte-Anne-de-Bellevue, and three production farms (two in Québec and one in upstate New York).

Nexia's product pipeline includes Protexia™, which is a medical pre-treatment for military and civilian personnel that's designed to counter the toxic effects of chemical weapons, particularly nerve agents. Protexia is the recombinant human bioscavenger compound, butyrylcholinesterase, which is expected to be manufactured in commercial quantities in the milk of Nexia's transgenic goats.

FROM MEDICAL DEVICES TO MILITARY GEAR

The size, tensile strength, and biodegradability of BioSteel® make it an ideal material of the medical device market: wound closure systems and ligament prosthetic devices. Nexia's next product from transgenic technology is expected to be Protexia™—a medical countermeasure to combat the toxic effects of chemical weapons such as nerve agents.

BioSteel holds equal appeal for the U.S. Army (Soldier and Biological Chemical Command) and the Canadian Armed Forces (Defence Industry Research Program of the Department of National Defence). Both groups are working with Nexia to create protective clothing such as softbody armour.



Oilseed factories

MAKE ENGINEERED PROTEINS MORE ECONOMICAL

A MOLECULAR FARMING METHOD DEVELOPED BY DR. MAURICE MOLONEY EXPLOITS BASIC PHYSICS TO REVOLUTIONIZE THE PRODUCTION AND PURIFICATION OF COMMERCIAL PROTEINS.

Scientific advances have dramatically increased the number of proteins with commercial potential, but the protein products pipeline isn't flowing the way it should. For smaller biotech firms in particular, the daunting costs of building production facilities—combined with expensive purification processes—slow the pace of bringing proteins to market.

SemBioSys Genetics Inc.—a Calgary firm built upon Dr. Maurice Moloney's love affair with oilseeds—has found a way to slash the costs of manufacturing genetically engineered proteins used in the pharmaceutical, cosmetics, nutritional products and other industries. The company believes it has a globally applicable solution to help biotech companies lower production costs, based on the unique properties of oilseeds.

Around the world, genetic engineering is accelerating the development of novel proteins with commercial potential. But for the companies that need genetically engineered compounds, splicing a protein gene into a host bacterium, plant or animal species is just the first step. In many cases, the most fiscally challenging part—accounting for 80 to 90 per cent of total production costs—involves isolating and purifying the end product.

Enter SemBioSys Genetics Inc., which is pushing the frontiers of plant biotechnology to deliver cost-effective protein production and purification services across the biotech industry. The privately owned, 45-employee company has developed a new approach—the StratoSome™ Biologics System—in which recombinant proteins are grafted to oilseed proteins found in safflower. After harvest, the desired proteins are easily extracted with the safflower oil.

This technique promises to substantially lower the cost of producing, collecting and purifying commercial peptides and proteins that other companies require to generate vaccines, pharmaceuticals, industrial enzymes, cosmetic ingredients and nutritional products. In the process, SemBioSys' technology may create exciting opportunities for oilseed farmers.

"We think that we'll be able to rewrite the whole story of manufacturing drugs," says

PUTTING SAFFLOWER ON DOUBLE DUTY

Traditionally harvested for its oil, the safflower seed may someday be better known as the ideal protein factory.

Firstly, safflower is readily available. It thrives in both the northern and southern hemispheres. With few weed varieties found in the western hemisphere, safflower is also easy to contain—which reduces the risk of any foreign genes being carried through the environment.

According to Dr. Maurice Moloney, Chief Scientific Officer of SemBioSys Genetics Inc., the safflower is easy to modify in the lab; as well, studies show that genetically engineered proteins are stable in transgenic safflower seeds for long periods of time.

MOLECULAR FARMING OPENS VAST NEW MARKETS

With its promise of higher revenues per hectare and immunity from unpredictable commodity markets, molecular farming offers a bright future for the rural economy. The emerging agribusiness aims to transform traditional crop plants into manufacturing facilities for products such as industrial oils, enzymes, plastics, therapeutic proteins and vaccines.

"If plant molecular farming replaces some forms of conventional manufacturing, it could easily become a $10- to 15-billion business in 10 years," predicts SemBioSys founder Dr. Maurice Moloney. "Producers are very enthusiastic."

Dr. Maurice Moloney, the company's founder and Chief Scientific Officer. "There are hundreds of exciting new medications in development, but they're very expensive to produce. That's where we come in. Using our technology, we are confident that protein production facilities can be built for a fraction of what they cost now."

As a result, SemBioSys is confident about its future. "Five years from now, we want to be the world's leading supplier of transgenic proteins for the pharmaceutical market," says Andrew Baum, SemBioSys President and CEO. "In ten years, we want to be recognized as a leading, fully integrated biopharmaceutical business. We believe our technology is that powerful. A lot of companies are involved in the transgenic production of proteins. But we're the only one that simultaneously addresses both the purification and bulk production of proteins, while offering other benefits such as enhanced protein formulations for oral and topical applications."

SemBioSys was founded in 1994 as a spin-off from the University of Calgary, where Dr. Moloney holds the Industrial Research Chair of Plant Biotechnology, sponsored by the Natural Sciences and Engineering Research Council of Canada and Dow AgroSciences. After several years in the 1980s with the U.S. firm Calgene Inc., Dr. Moloney came north to teach and conduct university research. SemBioSys emerged from his early analysis of the inner workings of

canola seeds. "When I was with Calgene, I got very attached to canola seeds. Later, we found that safflower shared canola's virtues but had other advantages, so now I love it even more."

Although most plant proteins tend to be water soluble, oleosin proteins found in oilseeds have a higher affinity for oil. The role of oleosins is to collect the oil droplets produced by crops such as safflower and canola. Dr. Moloney discovered that when recombinant protein genes are spliced to oleosin genes, the expressed proteins end up adhering to oleosins inside safflower seeds. And because oil is lighter than water, it's relatively easy to extract and isolate oleosins—along with any attached proteins—in a purified form.

"When the plants mature, we simply harvest the seeds, and collect and purify the protein in much the same way as you would separate cream from milk," explains Mr. Baum. So far, SemBioSys has demonstrated this technology with more than 25 different proteins including anti-obesity compounds, cosmetic ingredients, therapeutic products, and proteins used in aquaculture.

With its efficient, cost-cutting technology, SemBioSys has had little trouble attracting interest and capital from both private and government sources. Current investors include Bay City Capital, BDC Venture Capital, Dow AgroSciences, RBC Capital Partners, the University of Calgary, and Ventures West Capital Ltd.

What's more, SemBioSys is already staking its claim in the market. So far, its clients include the agribusiness giant Syngenta and a multinational fine chemicals manufacturer.

Forestry byproducts

SERVE UP NATURAL HEALTH BENEFITS

WHERE INDUSTRY INSIDERS SAW ONLY WASTE, ORGANIC CHEMIST DR. JAMES KUTNEY RECOGNIZED ENORMOUS POTENTIAL.

When Dr. James Kutney made British Columbia his home, he realized that the largest industry in the province was burning and burying a tremendous asset. Each time the pulp and paper mills processed a log, they threw away raw materials that could be used to produce important, and lucrative, biologically active compounds.

"Everyone knows that this is one of the drawbacks of the forestry industry—they don't know how to use the byproducts they produce," says Dr. Kutney.

With visions of tapping into a readily available resource, Dr. Kutney helped establish the science department at Forbes Medi-Tech Inc. in 1993. The company now holds several patents—to produce everything from cholesterol-busting food additives to prescription drugs—and boasts a strong track record for innovation in unconventional areas.

While his colleagues in the University of British Columbia's chemistry department ordered fine-grade reagents for their research, Dr. James Kutney excitedly cracked open large barrels of fatty, pungent sludge.

The shipments came from local pulp mills, where the process of digesting wood chips to create pulp creates a frothy white substance known as 'soap' or 'tall oil'. The byproduct is cheap and plentiful: the average mill produces thousands of tonnes of tall oil per year.

"This stuff was just being burned, and I thought this was a real waste," says Dr. Kutney, Past Vice-President of Scientific and Research Development, Forbes Medi-Tech Inc., and now a consultant. "Tall oil contains high concentrations of plant sterols—called phytosterols—that have great pharmaceutical potential. I realized there could be considerable revenues derived from these byproducts."

Dr. Kutney knew something forestry workers didn't: bacteria could degrade phytosterols to create the raw materials for steroid-based drugs, such as birth control pills and anti-inflammatories. Throughout the 1980s, he toiled to perfect processes for extracting and bioconverting phytosterols.

During that period, an even more audacious —and potentially lucrative—idea occurred to

EMERGING MARKETS FOR FUNCTIONAL FOODS AND NUTRACEUTICALS

Calcium-fortified orange juice and Echinacea drops are two hot products in our increasingly health-conscious society.

Functional foods are defined as recognizable, conventional foods containing ingredients that provide additional health benefits—such as calcium to reduce the risk of osteoporosis. Nutraceuticals are health-benefiting products isolated from foods and delivered in a medicinal form, which covers a broad range of herbal products.

"The growing popularity of functional foods and nutraceuticals is driven by increasing health care costs and people's perceptions about how to improve their longevity and quality of life," says Charles Butt, President and CEO of Forbes Medi-Tech Inc.

Statistics for these young industries are difficult to establish, but Agriculture and Agri-Food Canada estimates the current market at $1 to $2 billion in Canada, and likely more than $15 billion in both the United States and Europe.

We're showing that there is more and more you can do with the byproducts of the forestry industry. I think this is exciting, since Canada has traditionally been more primary resource-based but lacking in secondary industries.

DR. JAMES KUTNEY,
CONSULTANT AND PAST VICE-PRESIDENT,
FORBES MEDI-TECH INC.

Dr. Kutney. He remembered that in the early 1950s, the pharmaceutical giant Eli Lilly and Company briefly marketed phytosterols to combat high cholesterol. The concept was relatively simple: phytosterols help stabilize plant cell membranes in much the same way as cholesterol stabilizes human cell membranes, and both molecules have nearly identical structures. Eli Lilly found that phytosterols could be used to block absorption in the small intestine, ultimately reducing the amount of cholesterol circulating through the bloodstream and clogging arteries.

Knowing that at least half of North Americans have elevated cholesterol levels, Dr. Kutney saw an excellent opportunity to revive the idea. In 1993, he was approached by Tazdin Esmail and Egon Novak, two colleagues who indicated an interest in developing both aspects of phytosterol production. Forbes Medi-Tech was established with two business objectives: to produce raw materials for steroid-based drugs, and to create cholesterol-fighting food additives.

"The Eli Lilly product failed because you had to take so much of it, at least seven grams a day, to get a real effect," says Dr. Kutney. "We found that our phytosterols were much more potent—you only needed 1.5 grams to get a cholesterol-lowering effect."

Forbes ran a clinical trial in 1999, supplementing the diet of hypercholesterolemic men with a 1.8g daily dose of Reducol™—the brand name of their cholesterol-fighting phytosterol. By the end of one month, the average LDL-cholesterol levels of subjects dropped by 15 per cent. This low-density lipoprotein cholesterol is known as 'bad' cholesterol because of its tendency to form plaque deposits that restrict arterial blood flow.

"Phytosterols are clinically proven for reducing LDL and total cholesterol, and therefore cardiovascular disease," says Jerzy Zawistowski, Forbes' Vice-President of Functional Foods and Nutraceuticals. "I'm not aware of any other

manufacturer of a functional food in Canada with solid support from clinical trials."

In addition to its potency, Reducol has another major advantage over competitor products. Unlike other cholesterol-lowering sterols, it doesn't have to be incorporated into fat-based matrices such as margarine or salad dressings, which is important for consumers looking to avoid high-fat products. Rather, Forbes opted to include the sterols in daily staples and briefly partnered with Novartis to test the product line.

"The test market results of our cereals and cereal bars were good in terms of consumer uptake and consumer perception," says Charles Butt, Forbes' President and CEO. Unfortunately, when Novartis decided to get out of the functional food business, "the product line became a classic, corporate orphan child."

Reducol is now being marketed in the United States by dietary supplement companies such as Pharmavite and Twin Laboratories, but Forbes remains confident of the product's broad potential and is looking for other major partners. In a joint venture with Chusei (U.S.A.) Inc., a subsidiary of Chusei Oil Co. Ltd., Forbes recently built one of the largest sterol-production facilities in the world—a 1,000-tonne capacity plant near Houston, Texas.

As a follow-up to the functional foods line, Forbes is also venturing into the pharmaceutical industry with a cholesterol-lowering compound named FM-VP4. Pre-clinical studies show that FM-VP4 has tremendous potential; Phase II clinical trials at the University of Amsterdam are scheduled for completion by the end of 2003.

Over the past 20 years, Dr. Kutney has received considerable support from government granting agencies such as the Natural Sciences and Engineering Research Council of Canada and the Science Council of British Columbia.

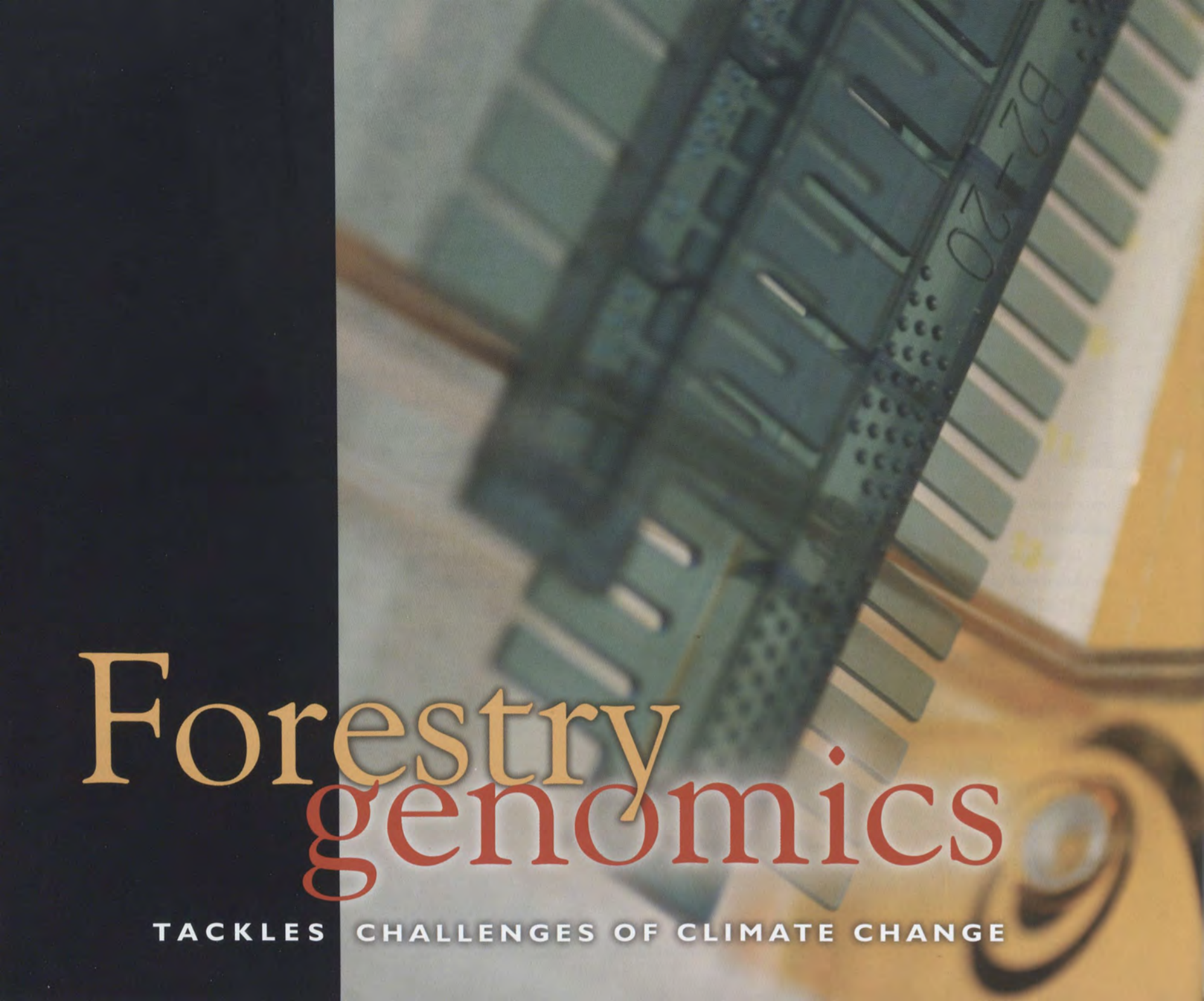
The nutraceutical and functional food market will definitely increase. There are three hot areas right now—cardiovascular, digestive, and women's health. We have a strong product for cardiovascular health, so the future looks good.

CHARLES BUTT,
PRESIDENT AND CEO, FORBES MEDI-TECH INC.

REDUCOL™ APPROVED FOR U.S. MARKETS

Phytosterols—and Reducol™ in particular—stand out in the functional food market because of the clinical data supporting their cholesterol-reducing claims. In fact, nearly 100 clinical studies worldwide have delivered positive results.

In May 2000, Reducol was cleared for sale in the United States by the Food and Drug Administration (FDA) under the *Generally Recognized As Safe* notification process. The FDA subsequently issued an interim rule allowing foods fortified with 'sterol esters' to make health claims on their labels. Forbes Medi-Tech Inc. recently received a letter from the FDA allowing the company to advertise the health benefits of Reducol.



Forestry genomics

TACKLES CHALLENGES OF CLIMATE CHANGE

AN ATLANTIC CANADA TEAM HAS LAUNCHED A PIONEERING SPRUCE GENOMICS PROJECT TO ENSURE THE SUSTAINABLE MANAGEMENT OF CANADA'S MOST IMPORTANT SOFTWOOD TREE.

Scientists in Atlantic Canada are studying the genetic makeup of one of Canada's most precious natural resources, the spruce. By identifying and mapping genes in red and black spruce, they will help the forestry industry select and breed trees that grow and adapt better to elevated carbon dioxide levels, warmer weather, less moisture, and other effects of climate change.

The science positions Canada as a global leader in forestry genomics—and Atlantic Canada as a Centre of Excellence for Spruce Genomics.

Like humans, trees can become stressed by their environment, particularly extreme conditions. A three-year, spruce genomics research project underway in Atlantic Canada aims to identify and map the genes and genetic factors that help spruce trees cope with climate change, drought, pollution and other stressors. The pioneering project, which joins researchers at Dalhousie University and the Canadian Forest Service's Atlantic Forestry Centre (AFC), will ultimately help sustain Canada's most important softwood tree—even as the climate changes.

Spruce is the most abundant tree in Canada, and the primary species of the Boreal forest which stretches from coast to coast. "It's the backbone of the forest industry and forest ecosystems in Canada," says project leader and principal investigator Dr. Om Rajora, an internationally recognized molecular geneticist and genomics expert. An Associate Professor of Biology at Dalhousie University and Adjunct Research Scientist at AFC, Dr. Rajora's collaborators are John Major and Dr. Alex Mosseler at AFC, and Dr. Tom Noland at the Ontario Forest Research Institute.

"We picked spruce because it's the most widely distributed species in Canada and the most important softwood across Canada, particularly for Atlantic Canada," adds Mr. Major, an internationally leading ecophysiological geneticist. "Forestry is also important worldwide. To be able to contribute in even a small amount to improving the industry will have a huge value economically."

GLOBAL FORESTRY LEADER

Canada is the world's largest exporter of forest products, with 21 per cent of the global market share and 10 per cent of the world's forests.

Canadian exports of forest products exceeded $41 billion in 2001, with spruce and other softwood lumber accounting for $11 billion. The United States is Canada's largest customer, representing 77 per cent of export sales.

Canada's forest industry sustains 353,000 direct jobs and another 700,000 indirect jobs.

Red spruce and black spruce are Canada's most widely distributed tree species, and the most important softwood trees for lumber and pulp production in Atlantic Canada.

FUELING SCIENTIFIC EXCELLENCE

Dalhousie University is Atlantic Canada's leading research university, earning more than $68 million in grants and contracts in 2001-2002. The Forest Genetics and Biotechnology program, directed by Dr. Om Rajora, is the largest research program in Dalhousie's Biology Department and one of the three largest forest tree genomics programs in Canada.

The Atlantic Forestry Centre (AFC) is one of five research centres of the Canadian Forest Service, a sector of Natural Resources Canada. AFC has locations in Fredericton, New Brunswick and Corner Brook, Newfoundland and Labrador.

The research partnership between Dalhousie University and AFC is fueling Atlantic Canada's emergence as an international centre of excellence for spruce genomics.

In Canada, elevated carbon dioxide (CO_2) levels and rising temperatures create frequent drought-like conditions for the country's largest forests. By identifying, mapping and characterizing which genes enable a spruce tree to absorb more CO_2 and require less water, researchers can select trees that adapt more easily to the changing environment. "Drought is always going to be a factor for trees, but the severity is going to increase with climate change," says Mr. Major.

The first step of the project is to develop a basic genetic blueprint for the spruce. This is an ambitious goal that involves sequencing approximately 100,000 Expressed Sequence Tags or ESTs (sequences used to quickly find and extract entire genes from chromosomes), 40,000 gene-rich region clones, and 10,000 full-length cDNA clones; and then identifying genes expressed differentially in response to stresses caused by climate change.

The second step is to identify and map genes and quantitative trait loci (QTLs) that influence how spruce trees cope with different environmental stresses. The result? The creation of the world's first large-scale gene sequence database, and genetic and QTL maps for red and black spruce.

"Having this spruce genomics information is like having the black box deciphered from an airplane," says Dr. Rajora, who also holds the StoraEnso Senior Chair in Forest Genetics and Biotechnology at Dalhousie University. "Genomics research allows us to identify and map genes and genetic factors controlling traits or characteriztics such as growth, and adaptation to high levels of CO_2, drought or freezing. We can then map genes, molecular markers, and genomic regions controlling specific traits onto a genetic map. That opens the door for selecting and breeding trees that can absorb more CO_2, grow better, or be more tolerant to drought or freezing."

Dr. Rajora and Mr. Major say the results of their research will begin making a difference to forest conservation and sustainable management programs almost immediately.

Genomics information and technology have tremendous potential. Scientists all over the world are eager to see the results of our spruce genomics project, especially the ESTs, genomic sequencing and gene discovery. Not only will it apply to spruce, it will also have relevance to other tree species. What we're doing here in Atlantic Canada will have far-reaching consequences around the world.

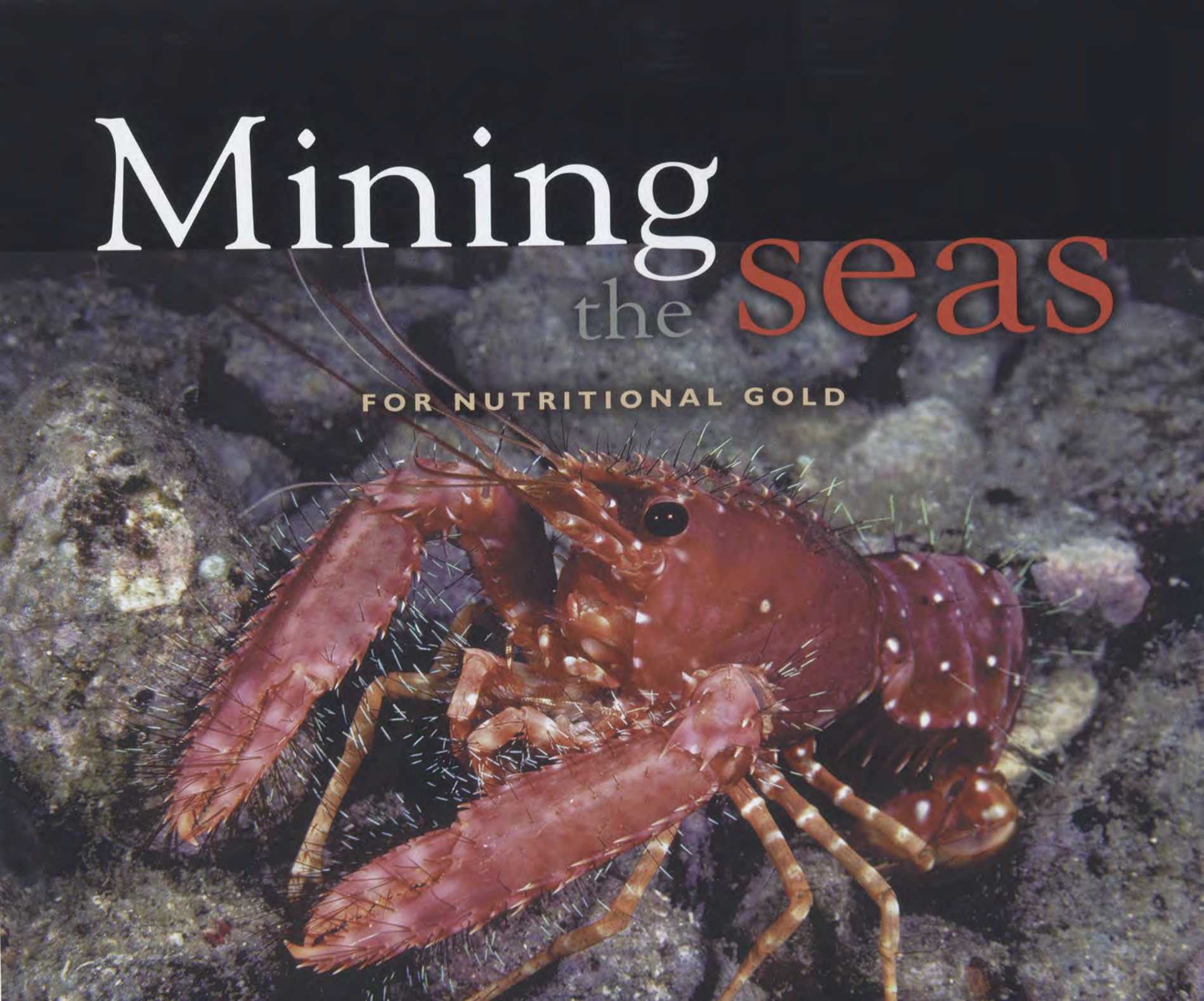
DR. OM RAJORA, ASSOCIATE PROFESSOR OF BIOLOGY, DALHOUSIE UNIVERSITY; AND ADJUNCT RESEARCH SCIENTIST, ATLANTIC FORESTRY CENTRE




The spruce genomics project has received $4.26 million in funding from Genome Canada, including matching contributions from Natural Resources Canada, the Ontario Ministry of Natural Resources, and StoraEnso Port Hawkesbury Ltd.

Mining the seas

FOR NUTRITIONAL GOLD



OCEAN NUTRITION CANADA GOES UNDERWATER TO DISCOVER NEW BUSINESS OPPORTUNITIES.

With its coastal Nova Scotia locations, guaranteed access to fresh raw materials, and talented research team, Ocean Nutrition Canada is in an ideal position to dominate the emerging marine-based nutritional ingredients industry. The young biotech firm is one of the world's first to recognize the commercial potential of fisheries byproducts with therapeutic properties such as omega-3 fatty acids. And Ocean Nutrition is actively searching for more natural products with healing powers. Because only a tiny fraction of marine compounds have been identified and characterized, the ocean's the limit when it comes to the company's future growth.

Imagine getting the health benefits of eating two fish per week from everyday staples such as bread, orange juice, soup or salad dressing. That's the kind of heady vision driving the rapidly growing 'functional foods' industry—estimated to be worth up to $57 billion worldwide by the year 2004—and one that Nova Scotia-based Ocean Nutrition Canada is poised to exploit.

Launched in 1996 by Clearwater Fine Foods, the largest privately held seafood company in Canada, Ocean Nutrition Canada was conceived by Clearwater's owner and CEO, John Risley. In the early 1990s, Mr. Risley started wondering about the commercial potential of fisheries byproducts. When the U.S. television show *60 Minutes* produced a documentary alleging that shark cartilage had anti-cancer benefits, Mr. Risley hired two scientists to find out whether the medical claims had

any validity. It turns out they didn't: shark cartilage supplements have no impact on human cancers.

But this exercise helped persuade Mr. Risley that the fisheries waste stream may contain other marine compounds with real nutritional or therapeutic value. In the mid-1990s, a Nova Scotia Crown corporation called InNOVAcorp introduced

OCEAN NUTRITION CANADA'S SEASIDE APOTHECARIES

"Early on, we realized the need to ensure the safety and efficacy of our products," says Robert Orr, President of Ocean Nutrition Canada. "To support that requirement, we have assembled a highly competent group of people including research scientists, engineers and technical production professionals."

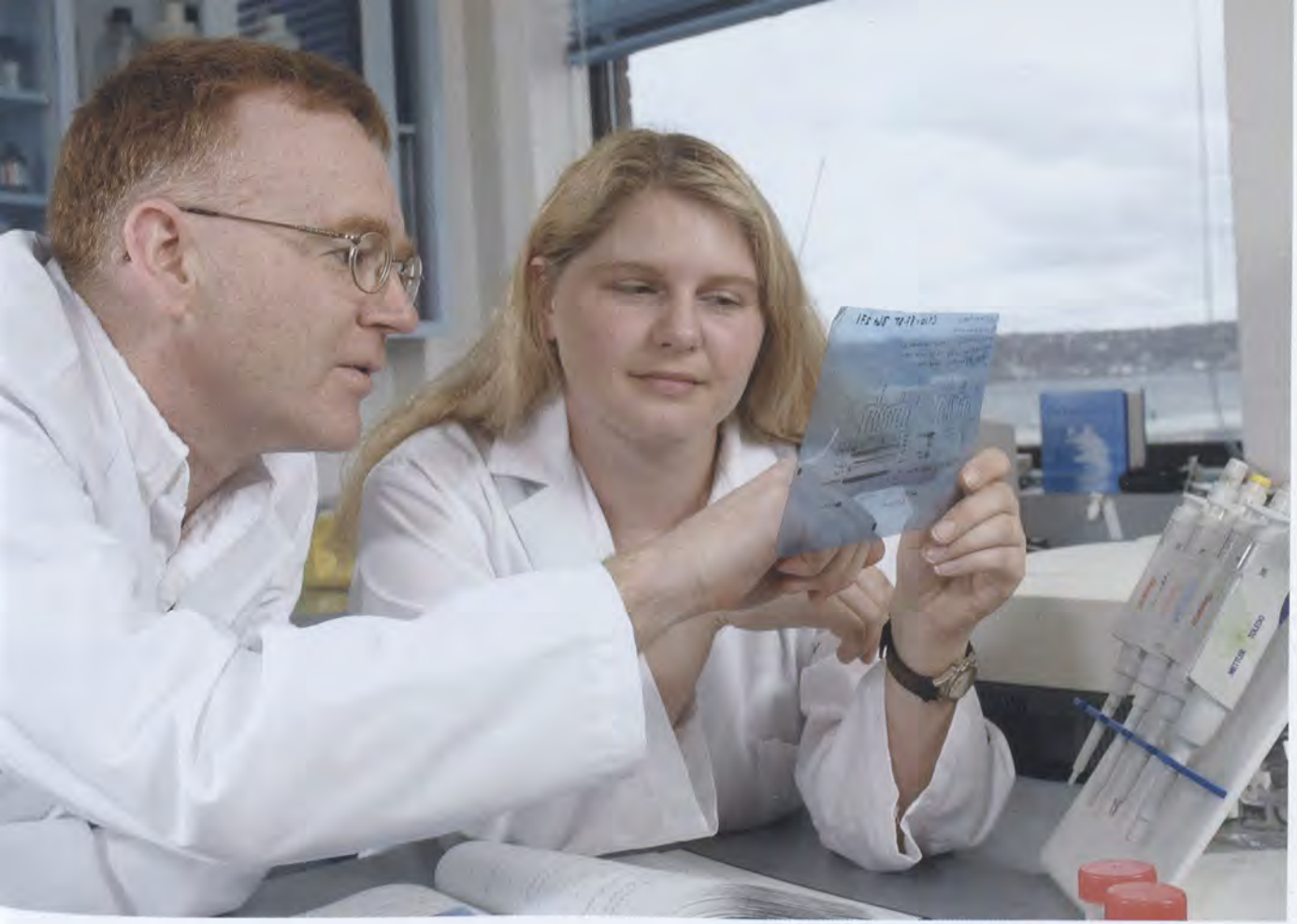
Ocean Nutrition boasts the most advanced privately owned facilities for analysing marine natural products in North America, which allows the company to apply a pharmaceutical model to the development of its marine compounds.

"When we isolate and characterize bioactive compounds, we know what works, how it works, and we can ensure that the right amount of bioactive material is there every time," Mr. Orr says. "Our ability to control the active compound in any extract is critically important, especially for toxicological or human clinical trials."

him to Laer Products Ltd., a Cape Breton-based manufacturer of omega-3 fish oils for the veterinary market. Mr. Risley ended up buying Laer Products as a jumping-off point for his new business strategy.

Today, Mr. Risley's dream is a reality. Drawing on a wealth of human resources in the Halifax area, such as the National Research Council's Institute for Marine Biosciences and Dalhousie University Medical School, Clearwater has built a 200-employee company with a team of 40 marine scientists. Ocean Nutrition Canada claims to be the "world's leading researcher, manufacturer and marketer of marine natural products to the global marketplace," a position strengthened by its steadily climbing sales of dietary supplements and functional food applications. The company's three primary products are: heart-healthy omega-3 fish oils, harvested from salmon, sardines and anchovies; a blood pressure lowering product derived from fish protein; and an immune-modulating product derived from marine algal extract. Ocean Nutrition sells its marine compounds mainly to nutritional products companies and major food suppliers.

And unlike its competitors, Ocean Nutrition Canada is actively mining the oceans for more natural compounds with potential health and nutritional benefits. "No one else in the world is doing what we're doing," says President Robert Orr. "We have competitors worldwide, but no one else is taking the same scientific approach to finding new products: screening compounds, testing them, then isolating and characterizing their properties."



Ocean Nutrition Canada focuses on key 'Western society' medical conditions such as diabetes, cardiovascular diseases, high blood pressure and arthritis. "We're looking for natural compounds with no side effects that have a positive impact on these diseases," explains Mr. Orr. The company currently has about a dozen products at various stages of development including compounds that boost the immune system, lower cholesterol, reduce blood pressure, and simultaneously impact both cholesterol and triglycerides.

"Our goal is to sell these ingredients as dietary supplement ingredients in the short term," says Mr. Orr. "But over the longer term, we believe in promoting a more natural approach to maintaining wellness by incorporating these nutrients into the food system—such as with calcium-fortified orange juice. For example, maybe we can introduce completely safe ingredients into the favourite foods of people with hypertension, which will allow them to lower their blood pressure through their diet so they don't have to pop pills every day."

IN PRAISE OF OMEGA-3

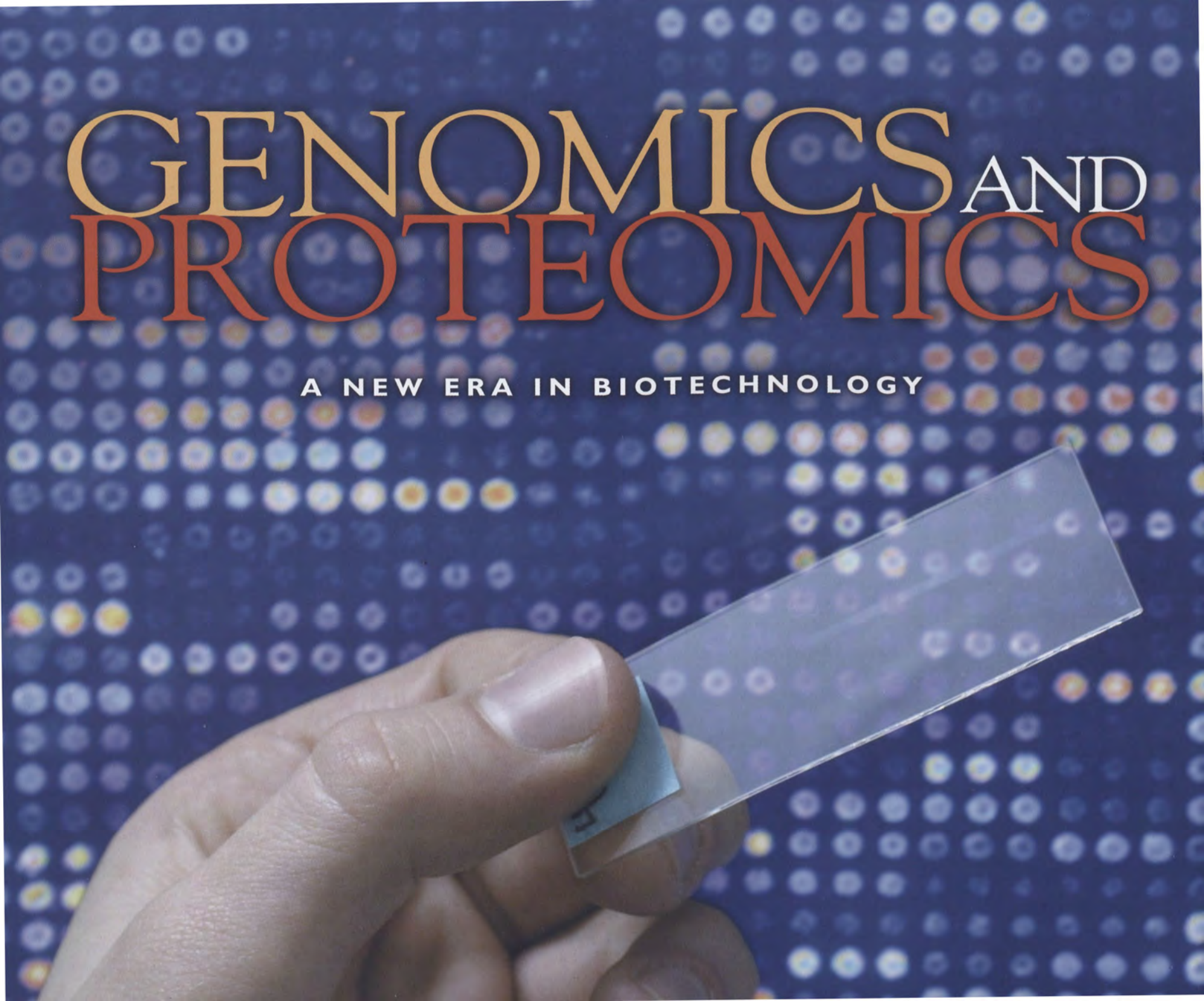
"Omega-3 from fish oil can reduce the risk of sudden cardiac death by up to 81 per cent," declares the *New England Journal of Medicine* (April 2002). "Eating fish cuts heart attack risk, studies show," declares *The Globe and Mail*, while CNN asks, "The benefits of fish without the fish?" Such headlines routinely trumpet the benefits of Ocean Nutrition Canada's main product.

Scientific studies suggest that omega-3 fish oils decrease triglyceride levels, reduce blood clotting, lower blood pressure, decrease blood viscosity, help prevent arrhythmia, and reduce joint and muscle inflammation. They also appear to reduce the risk of brain disorders and may even enhance memory, cognition, awareness and mood.

According to the *Journal of Nutrition*, "The North American diet lacks adequate levels of omega-3 fatty acids to provide optimum health because they are not present in most common foods." For Ocean Nutrition Canada, this all translates into great expectations of a healthy bottom line.

GENOMICS AND PROTEOMICS

A NEW ERA IN BIOTECHNOLOGY



THE HUMAN GENOME CONTAINS ABOUT 35,000 DIFFERENT GENES THAT COLLECTIVELY DETERMINE PROTEIN STRUCTURE, DIRECT GROWTH AND DEVELOPMENT, AS WELL AS CONTROL BIOLOGICAL FUNCTIONS. OUR 'PROTEOME' IS EVEN LARGER, ENCOMPASSING ABOUT 300,000 DIFFERENT PROTEINS, WHICH SERVE AS THE STRUCTURAL FOUNDATION OF CELLS AS WELL AS THE BODY'S 'WORKER BEES'. BETWEEN THEM, THE TWIN DISCIPLINES OF GENOMICS AND PROTEOMICS ARE TRANSFORMING BIOTECHNOLOGY AT A RAPID PACE—WITH HUGE IMPLICATIONS FOR MEDICINE, AGRICULTURE, NATURAL RESOURCE MANAGEMENT, AND THE ENVIRONMENT.

CANADA IS AT THE FOREFRONT OF THIS SCIENTIFIC REVOLUTION. WITH AMPLE PUBLIC-SECTOR SUPPORT, OUR RESEARCHERS ARE PLAYING A MAJOR ROLE IN MAPPING, SEQUENCING AND CHARACTERIZING THE HUMAN GENOME AND PROTEOME—AS WELL AS THE GENES AND PROTEINS OF OTHER LIVING SPECIES.

CANADIAN INNOVATION
IN GENOMICS AND PROTEOMICS

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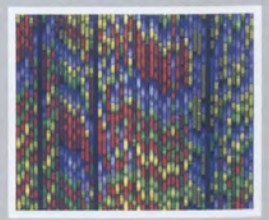
The ascension of proteomics to the leading edge of drug discovery has placed a premium on researchers with the requisite expertise to push the research envelope. MDS Proteomics Inc. has assembled an all-star, all-Canadian management team that rivals the world's best.



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DNA Genotek expands the horizons of DNA collection with an easy-to-use kit that indefinitely preserves DNA from saliva. The kit is attracting the attention of medical research organizations and others that conduct large DNA population studies.

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The BC Cancer Agency's Tumour Tissue Repository and Genome Sciences Centre are about to point the way toward more effective cancer therapies by giving researchers the tools to study how cancer differs between individuals.

Page 114

The McGill University and Génome Québec Innovation Centre is one of the world's first research facilities to integrate genomics and proteomics in one cluster. This integration will help researchers cross paths and share information, leading to rapid-fire discoveries.

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Caprion Pharmaceuticals Inc. creates protein maps of subcellular bodies to help detect abnormal patterns that distinguish healthy from diseased cells. This approach may lead to new ways to diagnose, treat and possibly prevent a range of human diseases.

In the late 1980s, a major transformation in biotechnology gave birth to the science of genomics. This involved a dramatic shift from a focus on single genes to the exploration of thousands of genes, and from a molecule-by-molecule approach to a computer-aided bioinformatics approach.

Genomics is the study of genes and the role they play, individually and collectively, in determining protein structure, directing growth and development, and controlling biological functions. Human genomics includes genome mapping, gene sequencing, and functional characterization of the traits controlled by the genetic material found in human chromosomes.

The Human Genome Project, launched in the 1990s, is genomics research on a grand scale. The project's main goals are to identify all of the approximately 35,000 genes found in human DNA and determine the entire sequence of the 3 billion chemical base pairs that make up human DNA. Several types of genome maps have already been completed, and a working draft of the entire human genome sequence was announced in June 2000. As part of the global team involved in this project, Canadian scientists made a significant contribution toward mapping the genome.

Canadian researchers are now applying genomics to find better ways to diagnose, treat and prevent disease. In addition to its potential medical benefits, genomics is being used to develop: new energy sources; improved crop varieties resistant to disease, insects or drought; more nutritious foods; and healthier, more productive livestock and fish species.

While genomics is making huge strides, the science of proteomics is emerging as the next big wave in biotechnology. Proteomics involves the identification and study of the proteome—the complete set of proteins made in a given cell, tissue or organism—including their amino acid sequence, function inside cells, and interactions with each other. In humans, the proteome is much larger than the genome because a single gene may code for up to 50 different proteins.

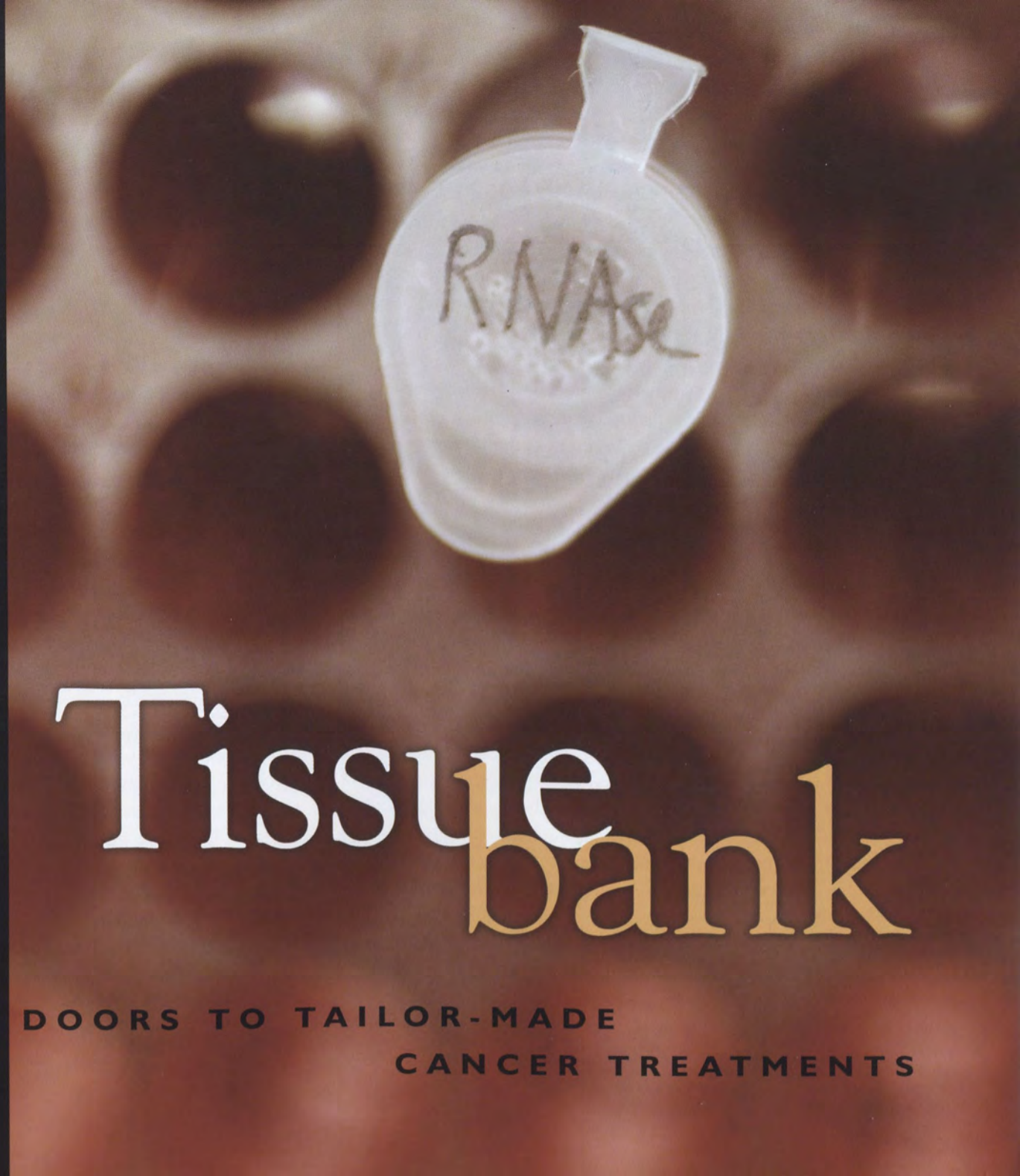
Proteomics is essential to understanding the molecular mechanisms of disease. The key aim of proteomics in medical research is to determine how proteins behave in diseased cells versus healthy ones. Because diseased cells often manufacture proteins that healthy cells do not, every protein that is associated with a particular disease is a potential marker for diagnosis and a potential target for treatment.

In Canada, genomics and proteomics research receives broad support from all sectors. Genome Canada—a private, not-for-profit corporation—works closely with partners such as federal institutions, provincial governments, the private sector, the financial community, and national and international foundations to ensure that Canada becomes a world leader in genomics and proteomics research. Genome Canada funds large-scale genomics and proteomics research projects in key selected areas such as agriculture, bioinformatics, environment, fisheries, forestry, health and technology development. It also supports research projects aimed at studying and analysing the ethical, environmental, economic, legal and social issues related to genomics research.

The Government of Canada's Genomics Research Initiative provides funding for projects led by the National Research Council of Canada, Agriculture and Agri-Food Canada, Natural Resources Canada, Environment Canada, Fisheries and Oceans Canada, and the Canadian Institutes of Health Research (CIHR). Through CIHR and the Natural Sciences and Engineering Research Council of Canada (NSERC), the government also funds genomics and proteomics research at Canadian universities.

The Canadian Networks of Centres of Excellence program is a key ingredient in this support. Each network allows scientists from across the country to collaborate on research. The program includes the Canadian Protein Engineering Network, the Canadian Bacterial Diseases Network, the Canadian Genetic Diseases Network, the Canadian Network for Vaccines and Immunotherapeutics, and the Stem Cell Network, among others.

Today, dozens of companies across Canada are involved in genomics and proteomics R&D. The following stories highlight some of the exciting work underway.



Tissue bank

OPENS DOORS TO TAILOR-MADE CANCER TREATMENTS

THE BC CANCER AGENCY'S TUMOUR TISSUE REPOSITORY AND GENOME SCIENCES CENTRE (AUTHOR OF THE WORLD'S FIRST SARS SEQUENCE) ARE ABOUT TO POINT THE WAY TOWARD MORE EFFECTIVE CANCER THERAPIES.

Scientists have advanced our understanding and treatment of cancer by studying models that mimic the disease. "But to move forward you can't just use animal models and cell lines. You have to go into the real world," argues Dr. Juergen Vielkind.

Dr. Vielkind is Director of the new Tumour Tissue Repository (TTR), a research department of the BC Cancer Agency. The TTR will store tumour tissue and molecular data on each tumour. What sets it apart is the Agency's access to 19,000 new cases a year and five decades of data on patients, pathologies, treatments and outcomes. The TTR will give researchers the tools to study how cancer differs between individuals, and how therapies can be personalized.

Cancer occurs when our biology goes awry. Just as no two people are exactly the same, no two tumours are identical. This uniqueness has serious implications for the effectiveness of cancer treatment. Pharmaceutical companies may discover, to their dismay, that products successful in small-scale trials fail when applied to larger, more heterogeneous populations. For example, a therapy that worked for one lung tumour might not work against the same tumour type in a different patient.

"If you know more about particular tumours—and combine that with life history and other patient information—you will know better how to treat them," says Dr. Juergen Vielkind, Director of the BC Cancer Agency's Tumour Tissue Repository (TTR). "That will save money, it will save time, and it means a better experience for the patient."

From his melanoma research on the tropical fish *Xiphophorus*, Dr. Vielkind realized the strengths as well as the limitations of using animal models for cancer. Although it has been 15 years since he started lobbying for a facility like the TTR, he is convinced that now is the right time to start the TTR.

"A lot of new and essential techniques have become available during the past few years, mostly triggered by the human genome sequencing," Dr. Vielkind explains.

AN INFORMATION GOLD MINE

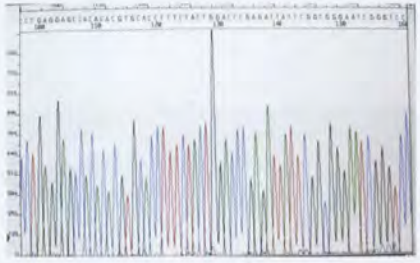
In late 2003, tissue samples will start to arrive at the Tumour Tissue Repository (TTR), based in the BC Cancer Agency's research centre in Victoria. The databank will store: patient data (such as medical and surgical history, lifestyle, family cancer incidence and demographic profile); diagnostic imaging and other pertinent data; and blood samples (taken before the operation) and tumour tissue samples (harvested for protein, RNA and DNA). Storage of these data and samples will be based on patient consent and ethical approval.

To manage the vast amounts of data produced, the TTR partnered with IBM to develop a database that can store, rank and search information of different formats.

WORLD'S FIRST SARS SEQUENCE

Researchers around the world turned to the Genome Sciences Centre (GSC) website on April 12, 2003 to view the first publicly available draft sequence of a coronavirus implicated in Severe Acute Respiratory Syndrome (SARS). A high-throughput genomics lab, the GSC received one millionth of a gram of purified viral genetic material from the National Microbiology Lab in Winnipeg. Once the material was prepared for sequencing, it took less than six hours to determine the 30,000 base pair genome.

"Something like SARS is of broad significance to everybody, including cancer patients," says GSC Director Dr. Marco Marra. This feat will add to GSC's international reputation for decoding the genomic sequences of more complex organisms such as humans and mice.



The TTR is partnered with one of Canada's premier genomics research facilities—the Genome Sciences Centre (GSC), another BC Cancer Agency research department. The GSC will take the lead in the genomic profiling of TTR specimens, as well as molecular profiling of RNA and protein expression. Bioinformatics experts at the GSC will scour this data for unique identifiable patterns.

A database this extensive, with this wide a range of data and tumour types, simply is not anywhere out there right now.

DR. JUERGEN VIELKIND, DIRECTOR, TUMOUR TISSUE REPOSITORY, BC CANCER AGENCY

"We'll be looking for changes in the DNA or gene expression that correlates with either cancer or with differential response to therapy," says Dr. Marco Marra, Director of the Genome Sciences Centre. "You know, there are lots of things we can imagine doing in collaboration with the TTR. It would be very difficult to name any area of research that might not be touched by it."

Because every cancer patient in British Columbia receives standardized care through the BC Cancer Agency, the TTR has access to a large population that is not biased toward any particular group, genetic type, lifestyle or ethnicity. As a result, the databank

will allow researchers to study cancer at both the population and individual tumour levels.

"That puts Canada in a unique and privileged position," says Dr. Samuel Abraham, Director of the BC Cancer Agency's Technology Development Office. "In the United States, there is a revolving door in terms of patient treatment and care. There exists no longitudinal database of information on outcomes. Socialized medicine has generated something that nobody predicted at the time it was created—that it would have this impact on genomics and cancer research."

Researchers from outside the BC Cancer Agency will be able to access different types of information through the TTR. Some will want to get their hands on the actual tissue material, while others will be more interested in genomics data derived from it. (Future research projects for TTR data and samples are not pre-determined when samples are collected, therefore systems are in place to ensure patients' confidentiality is protected, and that their consent for every research project meets all legal and ethical standards.)

Dr. Brian Weinerman, Regional Vice-President of the BC Cancer Agency for Vancouver Island, believes that interest in the tissue bank will come from both academic and commercial researchers.

Drug companies could use the data to develop new treatments. "Many drug trials today are limited by the fact that large randomized trials don't show benefits seen in the smaller trials," says Dr. Weinerman. "It's possible that in the small trial you got lucky with the group—they had a particular genetic profile, but were diluted out in the large trial. So the TTR should allow researchers to identify the particular type of patient who would benefit."

With the Tumour Tissue Repository, it's the patients of the future who will benefit. Take screening procedures. We now screen all women over 50 using mammograms—maybe we can save many of them that discomfort and worry, and focus on a much smaller group who should be screened regularly regardless of their age.

DR. BRIAN WEINERMAN, REGIONAL VICE-PRESIDENT, BC CANCER AGENCY FOR VANCOUVER ISLAND

Start-up funding for the TTR came from Western Economic Diversification Canada, the BC Cancer Foundation and Genyous Life Sciences Ltd., a private company that will act as a vehicle to commercialize TTR discoveries. The TTR will operate on a cost-neutral basis, charging researchers for the collection and processing of material.

"The major benefit will go to the researcher who finds something," says Dr. Vielkind. "The TTR itself won't be the owner of all research results that arise from its samples. I'm already aware of researchers who are waiting for this thing to open so they can use it."

STAR power

UNCOVERS NEW DRUG TARGETS

ALETHIA BIOTHERAPEUTICS INC. IS APPLYING A POWERFUL AMPLIFICATION TECHNIQUE TO IDENTIFY THE SPECIFIC PROTEINS THAT CAUSE DISEASE.

What do breast cancer, ovarian cancer and osteoporosis have in common? All are diseases that affect mainly women. All require more effective treatments than what is currently available. And most importantly, research suggests that they may have common underlying mechanisms.

By studying these three disorders simultaneously, researchers at Montréal-based Alethia BioTherapeutics Inc. believe they can find new, highly specific molecular targets for the diagnosis and treatment of these serious health problems.

When looking for potential drug targets, you can never be too focused. At least that's what Montréal-based Alethia BioTherapeutics Inc. is banking on with an innovative new technique for identifying highly specific drug targets to treat women's diseases such as breast cancer, ovarian cancer and osteoporosis.

"Once you've identified a specific target protein in a cell, you can design a way to inhibit its function," says Dr. Mario Filion, Chief Operating Officer of Alethia and head of a Québec-based genomics research program for women's health. "This kind of specificity leads to improved treatments, lower drug failure rates, and faster clinical trials and approvals."

Quick, smooth drug deliveries certainly attract the attention of pharmaceutical companies—and they're not the only ones. For the first time ever, Génome Québec (one of Genome Canada's five genome centres) has taken a stake in a startup in exchange for funding. The deal is worth $10 million over three years, but the return on investment could be much, much more.

Alethia's innovative approach to drug discovery relies on its STAR (Subtraction Transcription-based Amplification of mRNA) target identification technique. This approach focuses on identifying 'differentially expressed' messenger RNA sequences (mRNAs) that may play a role in disease development—and that cannot be identified using any other method on the market. Dr. Lawrence Malek, Chief Scientific Officer, was the creator of STAR.

"When disease occurs, changes in the activity of genes in a cell cause changes in the

BRIDGE OVER TROUBLED WATERS

Alethia BioTherapeutics Inc. takes a corporate-minded approach to science—it's how they plan to weather today's turbulent biotech market.

Dr. Lawrence Malek, Chief Scientific Officer, is a 'career inventor'. Alethia has 19 employees, all of whom are involved in research. And it's focused on an area—breast cancer, ovarian cancer and osteoporosis—that has a big need for effective treatments and a high profit potential for pharmaceutical companies.

If the opportunity arises, the company will add flexibility to its list of growth strategies. "Although our current focus is on women's diseases, we are ready and able to explore collaborations in other areas," says Alethia's Chief Operating Officer Dr. Mario Filion.

condition of the cell," says Dr. Filion. These changes result in certain mRNAs (the mediating template between DNA and proteins) being 'turned on' or 'turned off'. 'Differential expression' is the term used to describe changes in gene activity, as measured by the mRNAs present in different cells.

Determining which mRNAs are differentially expressed between two or more cells can be a formidable task. A typical human cell expresses about half of the genes in the human genome as distinct mRNA molecules, of which 86 per cent are present in low amounts and considered rare. Unfortunately, most key regulators of disease are found among low-abundance mRNA, which means sifting through many, many individual sequences.

This is where STAR comes in. The technique simplifies the task of searching through cellular mRNA by eliminating sequences that are unaffected by disease, while selectively enriching sequences that are implicated in a disease. Involving two or more clinical samples, the process uses the RNA sequences from one sample to subtract the common mRNA sequences from another sample. It then amplifies the remaining mRNA sequences.

In addition, STAR gives Alethia an enormous advantage over its competition because through amplification, the company can generate 10,000 times more research material than the

WOMEN'S HEALTH FIRST

Montréal is the place to be for women's health research. Funded by Genome Canada and Génome Québec, a group of scientists from industry and academia have formed the 'Integrated Genomics for Women's Health Program'.

Integrated genomics blends the information from different tools and approaches—including clinical research, discovery platforms and bioinformatics—to reach a better understanding of disease processes. The Montréal group will focus on breast cancer, ovarian cancer and osteoporosis.

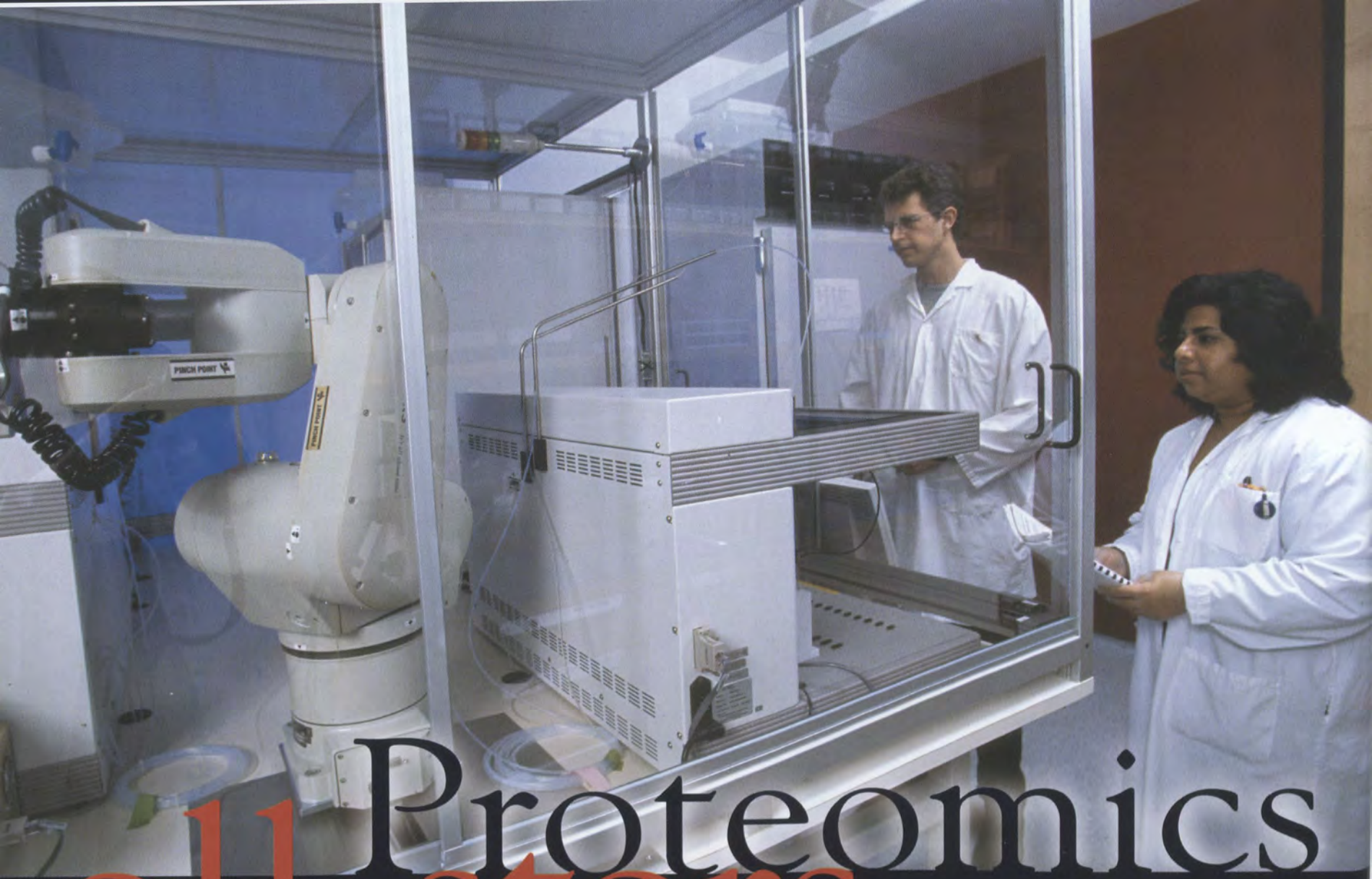
The group includes Alethia COO Dr. Mario Filion, who heads the program; breast cancer researcher Dr. Morag Park of McGill University Health Centre; ovarian and breast cancer researcher Dr. Patricia Tobin of Montreal General Hospital; and ovarian cancer researcher Dr. Anne-Marie Mes-Masson.

By generating as complete a catalogue of mRNA as possible, STAR maximizes our chances of identifying all key regulators in the sample tissue. By identifying all key regulators, we improve our chances of finding usable targets.

DR. MARIO FILION, CHIEF OPERATING OFFICER,
ALETHIA BIOTHERAPEUTICS INC.;
AND HEAD OF A QUÉBEC-BASED GENOMICS RESEARCH
PROGRAM FOR WOMEN'S HEALTH

original tissue sample contained. This is useful for studying diseases such as breast cancer for which tissue samples tend to contain a mixture of cancerous and non-cancerous cells, making it hard to obtain enough usable cancerous cells for research. With the amplified mRNA, researchers can look at the mechanisms of diseased cells in minute detail.

"Validation of our osteoporosis targets should be complete in 18 months. In 24 months, we'll be set to start validating our breast and ovarian cancer targets," says Dr. Filion. "At that point, we'll be more than ready for strategic alliances with pharmaceutical companies to bring drugs based on these targets to market."



Proteomics all-stars

PUSH DRUG RESEARCH FRONTIERS

WITH A SOLID TECHNOLOGY PLATFORM, MULTI-TALENTED TEAM AND PARTNERSHIPS WITH MAJOR PHARMACEUTICAL FIRMS, MDS PROTEOMICS INC. HAS THE FORMULA IT NEEDS TO SUCCEED IN THE GLOBAL MARKETPLACE.

With the human genome now mapped, scientists have turned their sights on the exploding field of proteomics to develop new disease-fighting drugs. The ascension of proteomics to the leading edge of drug discovery has placed a premium on researchers with the requisite expertise to push the research envelope.

One Toronto company has assembled an all-star, all-Canadian management team that rivals the world's best. And the world is taking notice.

MDS Proteomics Inc. (MDSP) is combining the power of biology, bioinformatics and analytical chemistry to fight some of our most serious health problems. In its short four-year history, the MDSP team has developed a reputation for its success in matching research talent to areas with the most scientific and commercial need.

Proteomics researchers strive to learn how proteins work together to make cells function in an organism. Exploring the proteome—the complete set of proteins expressed by a cell, tissue or organism—is the first step in the process. By studying the range of proteins produced by a cell, researchers can make distinctions between healthy and diseased cells, and determine the start or progression of a disease state.

Drug researchers believe that proteomics holds the key to future drug development. Analysis at the molecular level can help to identify new drug targets, decide if a potential drug is effective, and cut drug development times. The result could be faster identification and application of more effective treatments for cancer, AIDS, diabetes, depression and other diseases.

MDSP is in the business of hypothesis-driven proteomics research—a method of finding out which proteins are involved in biological or toxicological processes. By marrying its core expertise of applying mass spectrometry to study proteins with the power of bioinformatics, MDSP has developed a coveted portfolio of technologies.

What pharmaceutical firms need—and what MDSP delivers—are technologies that can

REPRESENTING CANADA ABROAD

Early in 2003, MDS Proteomics Inc. (MDSP) was one of 40 global firms and the only Canadian company chosen to participate in the World Economic Forum's prestigious Technology Pioneer's Program. The event showcases the important roles that cutting-edge technology and management vision play in achieving medical breakthroughs and stimulating economic growth.

"We are proud to represent Canada," says Dr. Mike Moran, Senior Vice-President and Chief Scientific Officer. "The criteria for selection further validate our revolutionary technology. The MDSP approach to proteomics has direct application to enhancing the discovery and clinical development of antibody and small molecule therapies."

rapidly map changes in how proteins interact within complex networks, detect changes in protein expression levels, measure changes in protein phosphorylation, and identify protein targets of small molecule drugs.

The privately held Toronto company recently landed its first major research collaboration with Cephalon of West Chester, Pennsylvania. The multi-year collaboration will help Cephalon identify and validate disease-relevant therapeutics targets, particularly in the area of the neurosciences. Using MDSP's technology, Cephalon will also be able to expand the potential disease indications for its development compounds, maximize the potential of its proprietary chemical library, and identify novel targets related to diseases of the central nervous system.

MDSP already has joint pilot projects underway with Eli Lilly and Company and two other major pharmaceutical firms. Dr. Mike Moran, MDSP's Senior Vice-President and Chief Scientific Officer, describes these pilots as "testing the waters, to prove MDSP can do what it says it can do."

MDSP has spent several years developing technologies in the areas of protein mapping and profiling. Now we're moving to commercialization. In the short term, we're entering research collaborations with pharmaceutical companies but in the medium to long-term we're generating value by building an early-stage pipeline.

DR. MIKE MORAN, SENIOR VICE-PRESIDENT AND CHIEF SCIENTIFIC OFFICER, MDS PROTEOMICS INC.

Over the past four years, MDSP has built an impressive management team, attracting a strong roster of scientific and management talent—all Canadians—from both home and abroad.

Dr. Daniel Figeys, Vice-President Systems Biology and Lead Profiling, personifies the

MDSP'S TALENT ROSTER

Dr. Daniel Figeys, VP Systems Biology and Lead Profiling, is a leading researcher in proteomics. He isn't the only shining light at MDS Proteomics Inc. Anil Amlani, Executive VP and Chief Financial Officer, has a strong background in tax and strategic planning, acquisitions, mergers and business analysis. And Shane Climie, Senior VP Research Collaborations and co-founder of MDSP in 2000, previously held managerial roles at Allelix Biopharmaceuticals Inc.

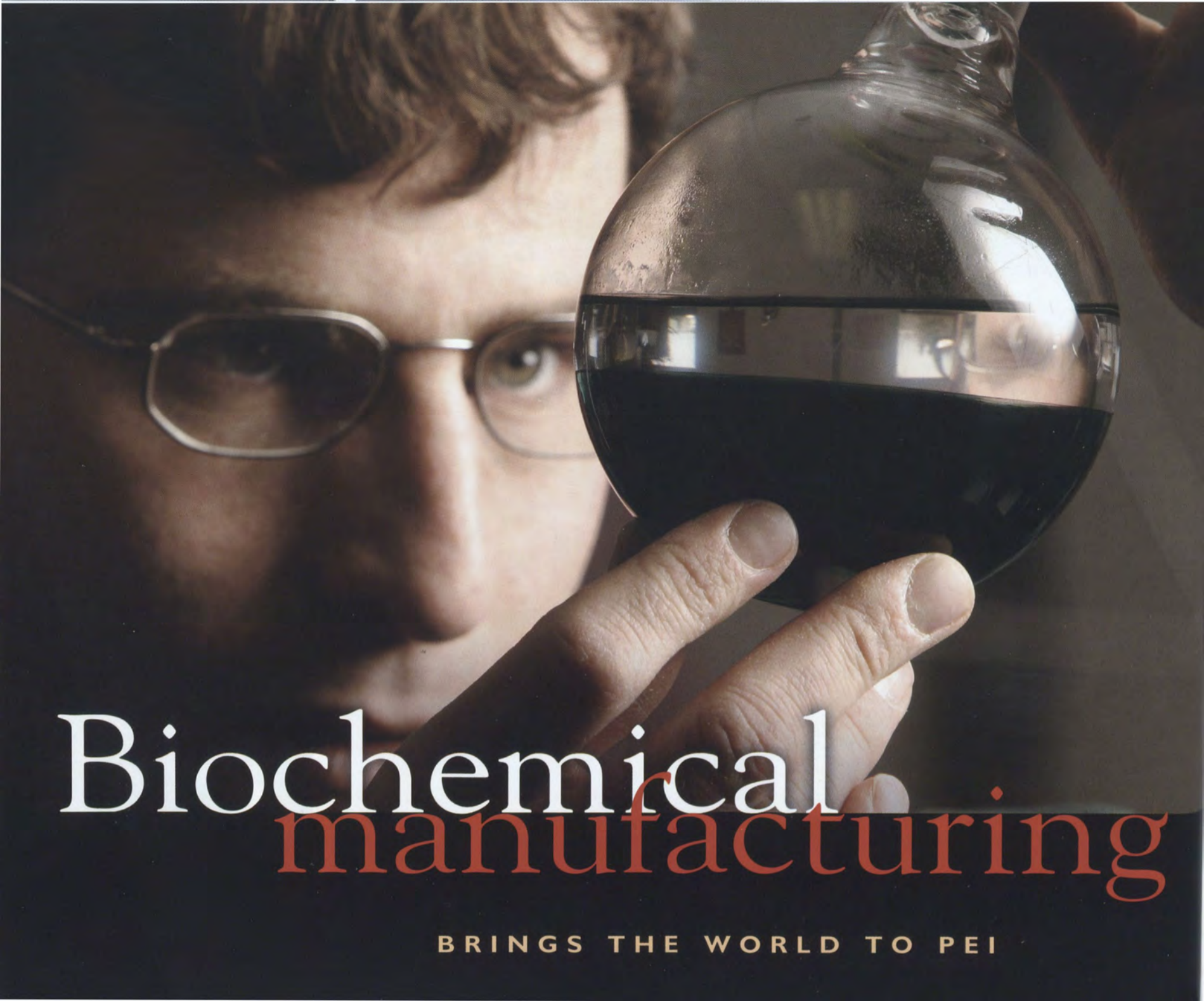
Franco Rossetto, VP Intellectual Property, served as patent counsel for Aventis Pasteur Limited before joining MDSP in 2000. Thodoros Topaloglou, VP Bioinformatics, worked in the United States for the pioneering bioinformatics companies GeneLogic and Incyte Genomics. And Dr. Mike Moran, Senior VP and Chief Scientific Officer, spent a decade as a University of Toronto professor before co-founding MDSP.

high-calibre talent that MDSP has attracted. Dr. Figeys joined MDSP in 2000 after working at the National Research Council of Canada, where he ran a research laboratory involved in industrial applications of proteomics. A prolific author, he completed his doctoral work under the internationally renowned Dr. Norman Dovichi, a Professor of Chemistry at the University of Alberta.

"Dr. Figeys' research in proteomics leads the world," says Dr. Moran. "He wants to work for a leading-edge proteomics company and has become an integral part of our senior management team."

Looking ahead, MDSP is planning to further bolster its in-house research capacity. By generating revenues and building an early-stage pipeline of products, MDSP management believes its winning formula will keep Canada at the forefront of the proteomics revolution.

ABOVE: *To mine the vast amounts of data it generates, MDS Proteomics uses an IBM 'cluster' supercomputer and its proprietary bioinformatics toolset.*


Biochemical manufacturing
BRINGS THE WORLD TO PEI

WITH A PERSONALIZED APPROACH, BIOVECTRA DCL HAS DEVELOPED AND MANUFACTURED MORE THAN 500 CHEMICAL COMPOUNDS WITH ITS CLIENTS, RANGING FROM MILLIGRAM TO MULTI-TONNE QUANTITIES.

When it comes to making pharmaceuticals, you can't pick up the ingredients at your local supermarket, and you certainly don't want to shop at the cut-rate outfit on the Internet.

So what to do? More and more, drug companies worldwide are coming to Prince Edward Island to do their shopping. In fact, 70 per cent of the "big pharmas" and 50 per cent of the "big biotechs" do business there.

Why? Because the small island off Canada's east coast, known mainly for potatoes and Anne of Green Gables, is also home to BioVectra DCL, an up-and-coming biochemical manufacturer.

In a condensed, competitive market, Charlottetown-based BioVectra DCL understands that there's one sure way to stay in business: keep in touch with your customers and take care of their needs. The company even has a name for it: customer closeness and care. But for BioVectra, formerly the Biochemical Division of Diagnostic Chemicals Limited, this catch phrase is more than just a marketing slogan—it's a business way of life that extends its small-town roots worldwide.

"Approximately 10 pharmaceutical companies in the world are responsible for 60 per cent of the industry's drug sales. The same goes for the biotechnology industry," says BioVectra CEO Dr. Tony Lucas. "We don't have thousands of customers, so we go out of our way to give the ones we do have personalized service, whenever and wherever we can."

This personalized approach—and the competitive advantage it brings—influences every aspect of the company, including its products and services, its innovations, and its manufacturing and quality standards.

BioVectra develops and manufactures a range of specialty and fine chemicals, advanced intermediates, enzymes and biomolecules both in research and process-scale quantities. The company also provides custom synthesis and manufacturing services for the pharmaceutical industry—in person from one of its branch offices in the United States, if necessary.

IF YOU BUILD IT, THEY WILL COME

In 1970, Dr. Regis Duffy, then Chairman of the University of Prince Edward Island's Faculty of Science, started a business called Diagnostic Chemicals Limited (DCL). Essentially, he set up a lab in his garage to help keep homegrown chemists in the province.

Little did he know he was starting one of the earliest examples of innovation and entrepreneurship in Canada. Over the past 30 years, DCL has grown to employ more than 200 people in Prince Edward Island.

The company has also produced a successful spin-off in BioVectra DCL, a biochemical manufacturer that is now firmly established as a leading supplier in the pharmaceutical and biotechnology industries.

THE CANADIAN BRAND

What makes Canadians Canadian? Courtesy? Helpfulness? An ability to keep the peace? It's probably each of these things, plus a little bit more.

For Dr. Tony Lucas, CEO of BioVectra DCL, based in Charlottetown, Prince Edward Island, it's a sense of fair dealing that he calls the "Canadian brand."

"When an organization requires a custom-made molecule, we work hard with them to establish a technology-intensive dialogue," says Dr. Lucas. "We need to exchange information to come up with a molecule that will do what it's supposed to do."

The personal approach has paid off. To date, BioVectra has developed and manufactured more than 500 chemical compounds with its clients, ranging from milligram to multi-tonne quantities and at every step in the drug approval and marketing cycle.

Cued by customer needs, BioVectra has come up with a number of innovations to solve manufacturing problems, both in the company's own labs and those of its customers. One notable example is a protein-folding catalyst.

"Sometimes, when proteins are produced by recombinant methods, they aren't in the correct shape to work biotherapeutically," says Dr. Lucas. "Why this happens is one of the great unsolved problems in protein science."

These misfolded or unfolded proteins form insoluble aggregates known as inclusion bodies, which must be isolated, denatured and refolded into the native, active state of the protein. To aid in this process, BioVectra developed Vectrase™, a proprietary small molecule that promotes the correct folding of these proteins to make them biologically active.

Similarly, to assist with on-site monoclonal antibody and protein production, BioVectra developed VectraCell™ single-use bioreactors for its clients. The bioreactors are made using a gas-permeable plastic that reduces the opportunity for microbial contamination, eliminates the need for high-humidity environments, and results in better yields compared with traditional methods of cell culture.

I've found that people expect quality and integrity when they're dealing with Canadians. It's definitely an advantage of doing business in Canada, especially in the pharmaceutical and biotech industries, where quality is so important.

DR. TONY LUCAS,
CEO, BIOVECTRA DCL

"Our clients have found that using VectraCell is an economical and time-efficient method for cell culture," says Dr. Lucas. "The product also eliminates the demanding cleaning and validation process that is necessary with more-traditional methods."

To ensure these custom-made products and solutions are of the highest standard possible, BioVectra takes a proactive approach to quality control in its manufacturing operations. The company has been ISO-9001 accredited for the past 10 years, but has also continued to grow and evolve in its quality control procedures.

For example, the company adheres to the current Good Manufacturing Practices (cGMP) followed by pharmaceutical and biotechnology firms. These guidelines ensure that the products a company makes meet specific requirements for identity, strength, quality and purity.

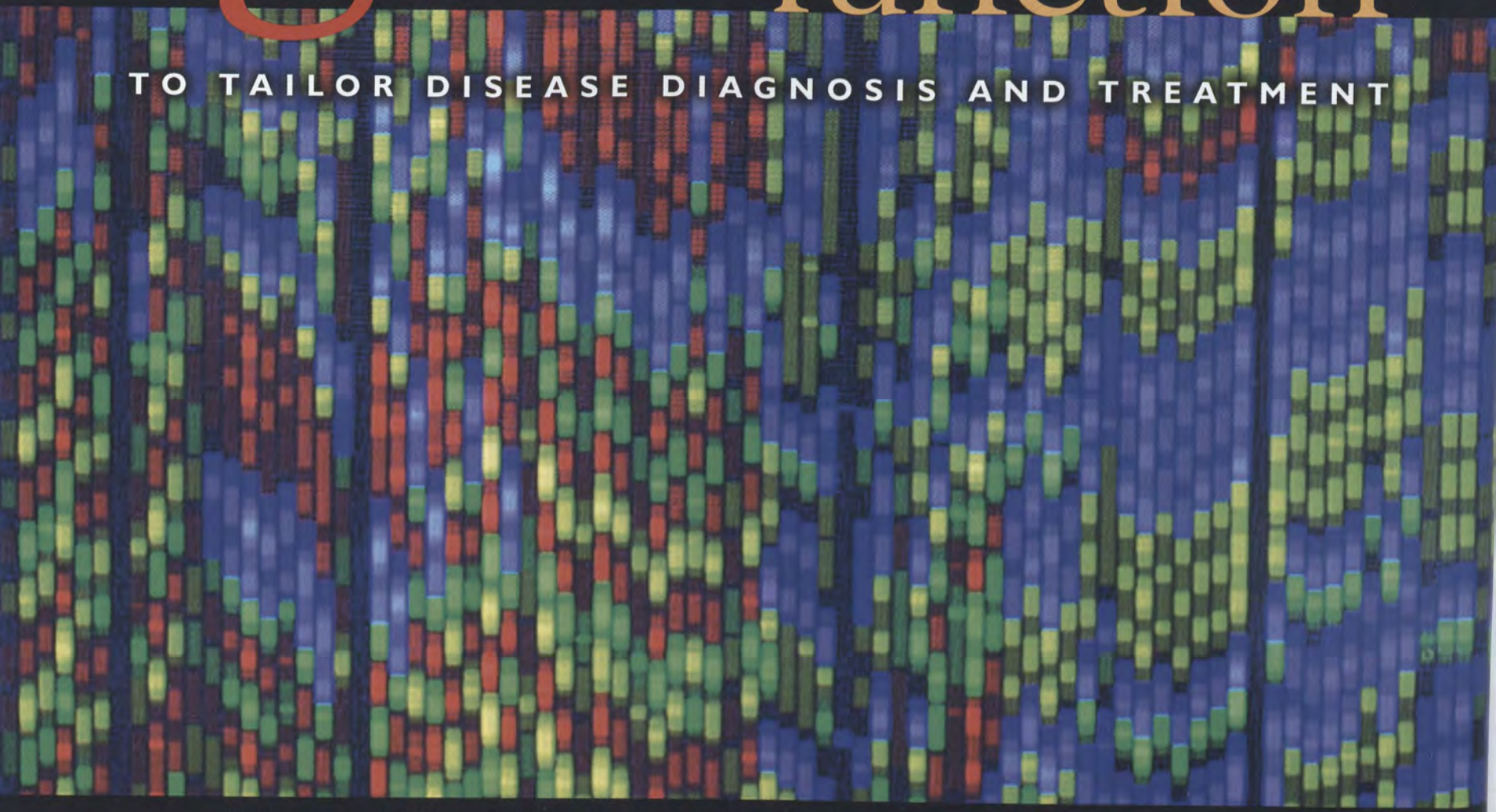
"By adhering to cGMP, we are subject to and invite audits of our quality standards by regulatory bodies," says Dr. Lucas. "In fact, we're waiting to start a series of U.S. Food and Drug Administration audits so we can be approved to manufacture drugs marketed in the U.S."

Considering that 90 per cent of BioVectra's sales now come from outside Canada—and the majority of these from the United States—this will be a welcome development.

ABOVE: *BioVectra's cGMP Manufacturing Facility for Active Pharmaceutical Ingredients contains three product isolation suites that can be maintained as a Class 100,000 Clean Room.*

Probing gene function

TO TAILOR DISEASE DIAGNOSIS AND TREATMENT



This image contrasts the DNA sequences of different human patients at a specific gene. Each colour represents one of the four different nucleotide bases (adenine=green, thymine=red, cytosine=blue and guanine=yellow) which make up DNA.

THE McGILL UNIVERSITY AND GÉNOME QUÉBEC INNOVATION CENTRE USES FUNCTIONAL GENOMICS TO LAY THE FOUNDATION FOR MEDICAL BREAKTHROUGHS.

There's strength in numbers: approximately 35,000 genes in the human genome, about 300,000 proteins in the human proteome, and now one research facility in Canada that combines the study of both.

Since January 2003, the McGill University and Génome Québec Innovation Centre has been one of the first research facilities in the world to integrate genomics and proteomics in one cluster. This co-location will allow researchers to cross paths and share information, thereby spurring each other to rapid-fire discoveries.

And in the two principal fields driving biomedical research, faster is definitely better.

With the first draft of the human genome now complete, Dr. Tom Hudson's role as Assistant Director of the Whitehead Institute/ Massachusetts Institute of Technology Center for Genome Research has come to an end. But there is still plenty to do. Aside from accepting the position of Director of the McGill University and Génome Québec Innovation Centre, Dr. Hudson holds the titles of geneticist, immunologist, allergist, physician, researcher and teacher.

Dr. Hudson joined the Whitehead Institute in 1991 and became leader of the team that generated the first physical map of the human genome in 1995. He also played an important role in developing the DNA chip, an exciting new technology that allows researchers to study tens of thousands of DNA samples simultaneously.

Such outstanding accomplishments made Dr. Hudson a natural choice to head the McGill University and Génome Québec Innovation Centre. After juggling multiple roles and commuting weekly between Montréal and Boston for five years, Dr. Hudson made Montréal his full-time base in 2001. By then, he had established his practice as an asthma specialist at the McGill University Research Centre. He now continues his research into the genetic causes of disease and teaches in the departments of medicine and genetics at McGill University. In part, it is this degree of breadth and depth that drew Dr. Hudson back to Canada.

THE WORLD OF A CELL ON A SLIDE

Imagine miniaturized laboratories the size of a postage stamp. Welcome to the amazing new world of genomics research using DNA chips.

DNA chips—also called biochips, gene chips, and DNA microarrays—allow researchers to study tens of thousands of genes in a matter of seconds. Laid out in rows and columns on a microscopic slide, the genes dot an area one-centimetre square.

Researchers expose these 'gene probes' to different biological conditions, such as a disease or a drug. Then, using a specially designed microscope, they observe which genes have been turned 'on' or 'off' as a result.

"With DNA chips, researchers are like astronauts," says Dr. Tom Hudson, Director of the McGill University and Génome Québec Innovation Centre. "We become observers of everything that goes on in a cell, essentially studying problems using a global approach."

The study of genomics is like popcorn: right now, we're seeing the first kernels cracking, but in 10 to 20 years, the changes will be visible to everyone.

DR. TOM HUDSON, DIRECTOR,
McGILL UNIVERSITY AND GÉNOME QUÉBEC
INNOVATION CENTRE

"Canadian scientists have had to fight to create a research environment that can compete with the United States," he says. "We've done that, and now Canada and Québec are very competitive in the area of genetics. I was anxious to come back and be part of it."

Many scientists believe the infrastructure is now in place to take a lead position in functional genomics—the quest to determine what all these sequenced genes actually do.

Through its research activities and strategic alliances, the McGill University and Génome Québec Innovation Centre will be a key component of this infrastructure. In addition to housing the technology platform of Génome Québec, the Centre collaborates with this not-for-profit investment agency to conduct three of the 15 large-scale projects in its portfolio. These initiatives include Dr. Hudson's research on genetic regulators and haplotypes (highly structured blocks contained in the genome that explain the vast majority of all genetic variation), as well as Dr. John Bergeron's proteomic studies associated with creating cell maps, using assays to validate protein interactions, and analysing the structures of key proteins. The partnership will increase scientific contributions from Québec researchers, support economic spin-offs, and enhance Genome Canada's ability to renew and diversify its sources of funding. The joint facility will also provide vital services such as sequencing, genotyping and biochip analysis to researchers across the province, as well as throughout Canada and the United States.

With its recent move to a new building on the McGill campus, the McGill University and Génome Québec Innovation Centre is increasing its staff to 150 people. They use genomic information to study as many as 20 major diseases, including asthma, ovarian and breast cancer, multiple sclerosis, hypertension and diabetes. Collectively, the staff sequences large stretches of chromosomes, examines DNA markers in a large number of patients to map genetic variation, and reclassifies diseases according to specific causes at the genetic level.

"Reclassification is one of the first steps that has to happen before genetics information can really affect medicine," says Dr. Hudson. "For example, where we now have asthma, we will eventually identify Type I, Type II, Type III asthma, and so on. Once we know the specific causes, we can begin to develop better, more-effective treatments."

In the Centre's future scenario, people with a particular sub-type of asthma will receive a treatment tailored to the type of disease they have. This will be a vast improvement over the current trial-and-error approach in which physicians administer various treatments until they find one that works. The ultimate winner will be the patient.

"If we can identify the underlying cause of a patient's disease through their genes, we can give them the treatment they will respond to from the first try," says Dr. Hudson. "This will be a major advance."

IMPROVING ACCESS TO GENOMICS DATA

Not long ago, the use of DNA chips in genomics research was limited to elite companies and organizations. Now, thanks to the McGill University and Génome Québec Innovation Centre, the technology is widely available.

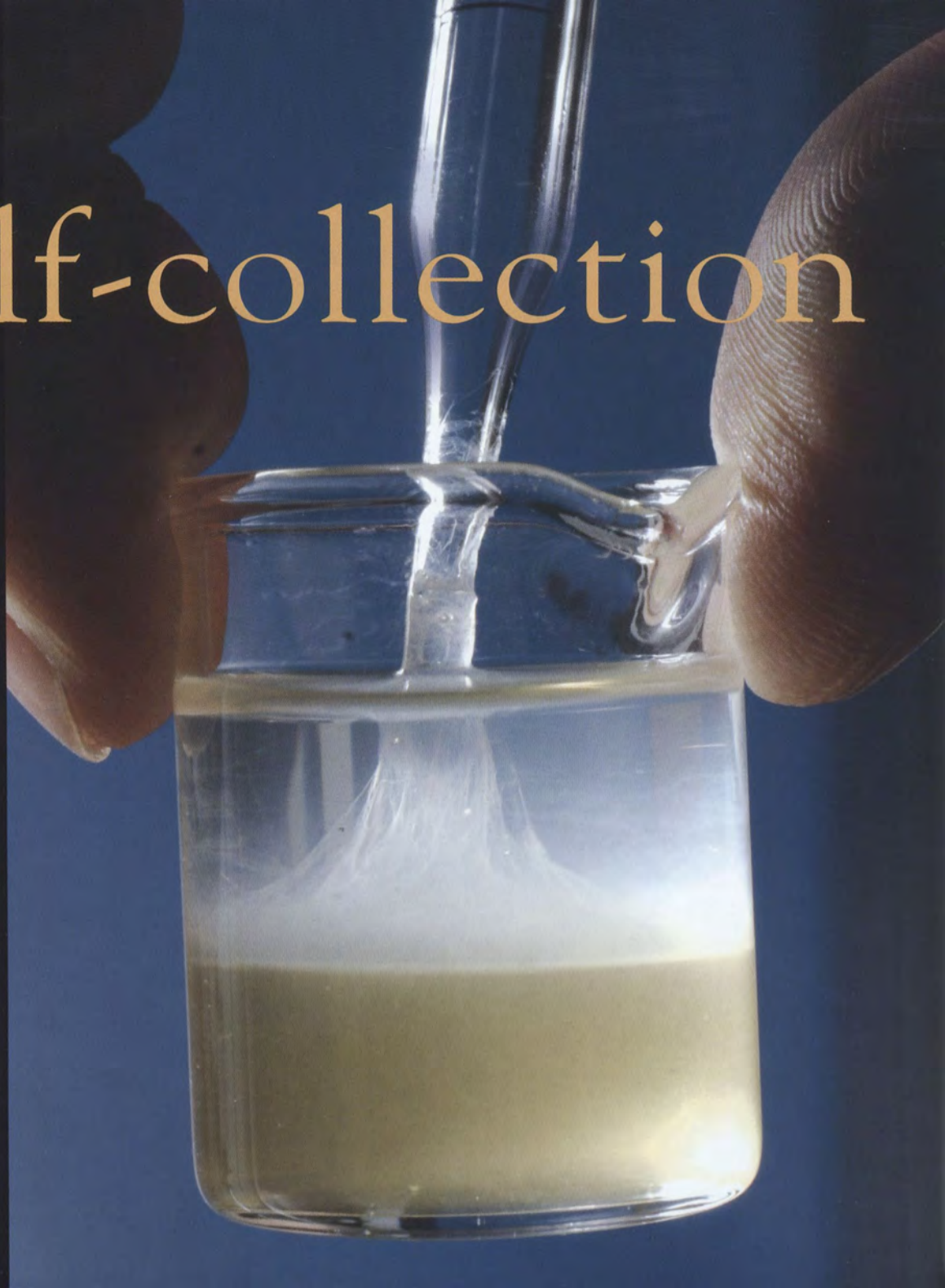
"For the cost of making the DNA chip, any group can bring their genes here to study them using our advanced technology," says Centre Director Dr. Tom Hudson.

In 2001 alone, more than 100 groups used the service. Approximately two-thirds were based in Québec, but research centres from across Canada and the United States, and from as far away as Israel and New Zealand, also benefited.

"Our work in giving access to core facilities is as important as our research achievements," says Dr. Hudson. "We see it in the publications."

DNA self-collection

SO SIMPLE
A CHILD CAN
DO IT



DR. CHAIM BIRNBOIM EXPANDS THE HORIZONS OF DNA COLLECTION WITH AN EASY-TO-USE KIT THAT INDEFINITELY PRESERVES DNA FROM SALIVA.

DNA samples provide valuable information for a wide range of applications, including DNA banking and determining predisposition to disease. However, collecting and analysing the samples can be costly and time-consuming. For those providing the DNA, the requisite needle to collect blood may seem invasive. For those seeking to preserve samples, careful chemical processing and temperature control is necessary to ensure the DNA doesn't degrade before it's analysed.

DNA Genotek Inc.—an Ottawa-based biotechnology company—is tackling these and other hurdles with its new DNA self-collection, preservation and purification kit. Oragene™ promises unprecedented ease-of-use, high-yield and high-quality DNA, long-term stability of samples at room temperature, and simplified, cost-effective purification. Little wonder that it's attracting the attention of medical research organizations and others that conduct large DNA population studies.

"Just spit, and that's it." That may well become the catch phrase for the latest DNA preservation technology to come out of DNA Genotek Inc.'s labs. Billed as the world's simplest and most reliable DNA self-collection kit, Oragene™ replaces the pain of needles with a special vial and chemical solution for collecting, preserving and purifying one's own DNA from saliva.

"It's so easy, even a child can do it," says Ted McClelland, Vice-President of Marketing and Sales. People need only rinse their mouths, spit some saliva into the vial, and screw the cap on. A mechanical system then breaks the seal that initially separates the Oragene solution from the saliva sample. Shake to mix the solution with the saliva, and DNA preservation and purification begin.

The Oragene solution preserves DNA at room temperature indefinitely, removing the time urgency for shipping, freezing or processing samples. "It's changing the way we think about collecting DNA samples," says Dr. Chaim Birnboim, DNA Genotek's Chief Scientific Officer.

Dr. Birnboim, a long-time senior scientist at the Ottawa Regional Cancer Centre, first attracted the scientific community's attention in 1979 with a paper describing an effective plasmid DNA purification process. That process has become a standard method used in labs around the world.

ORAGENE™ GOES TO AFRICA

Dr. Ruth Ballard knows just how tricky collecting DNA can be. In the summer of 2001, the biology professor at California State University ventured to northern Tanzania to collect DNA samples from the Masaai people—part of an ongoing study to analyse DNA markers from various populations. Dr. Ballard brought with her buccal swabs, the *de facto* standard at the time for non-blood DNA collection. Back in California, however, she found that degradation due to lack of refrigeration had completely ruined more than half of her samples.

The loss of valuable data led Dr. Ballard to DNA Genotek Inc. The company suggested she try Oragene™. In August 2002, Dr. Ballard returned to Tanzania to collect more samples using Oragene, and shipped them back to the United States under the same demanding time and temperature conditions. This time, 97% of the samples yielded complete genetic profiles, while the remaining 3% yielded almost complete profiles.

The DNA purification process took less than 45 minutes for the Oragene samples, compared to six hours for buccal swab samples. The Oragene samples yielded 30 times more DNA, a major benefit for population studies.

For years, the 'gold standard' for collecting DNA samples for tests has been based on blood. We know our Oragene technology will do the job better, and make these procedures less stressful for people.

TED McCLELLAND, VICE-PRESIDENT, MARKETING AND SALES, DNA GENOTEK INC.

In 1993, Dr. Birnboim developed GenoFix™, a technology for preserving DNA from tissue samples, and the impetus for establishing DNA Genotek. GenoFix, combined with industry contacts, served as a springboard to the development of Oragene. "It has been known for years that there's DNA in saliva, but there were problems using it as a source," says Dr. Birnboim. "We identified the problems, overcame them, and developed the mechanical vial system to make it all work."

"We've invented a new technology that improves on the chemistry and economics of existing DNA sampling methods," says Mr. McClelland. "Applications requiring DNA are many and growing very rapidly; however, there are a number of areas where it's not practical or cost-effective to get DNA from blood." Oragene is a high-tech, yet down-to-earth, alternative that is already making DNA collection easier and more reliable for those who have put it to the test.

Moreover, Oragene provides a high quantity and quality of DNA, which is important for many

fields of genomics research. "Oragene is also cost-effective," adds Mr. McClelland, "because the donor supplies the labour, and it's significantly cheaper to ship and process the sample. These are where the big cost efficiencies come in."

Such advantages are why the technology is initially attracting attention in fields that require low-cost, high-reliability DNA self-collection for large populations. "We are in the early stages of working with the world's largest cancer research institutes, with major pharmaceutical companies involved in pharmacogenomics research [the fusion between pharmaceutical and genomics research], and with major predictive medicine companies. All have shown great interest," says Dr. Birnboim. And recently, the company attracted financing from a group of seasoned investors.

Oragene also has many other potential applications, including: forensics (collecting DNA from convicted felons, for example); the consumer identification market (paternity tests, genealogy, child find programs, personal DNA banking and family records); and eventually the point-of-care market (insurance companies, health care maintenance organizations, and even doctor's offices).

Although the product hasn't been formally launched, Oragene is ready for market and is regulatory approved for use in Canada, the United States and Europe. The company has patents pending on both the Oragene solution and the vial system.

"There's a multibillion-dollar world market for nucleic acid testing and diagnostics, and it's growing rapidly," says Mr. McClelland. "Our mission is to establish DNA Genotek as the global standard for self-administered DNA collection preservation and purification solutions."

MARKETING ORAGENE™

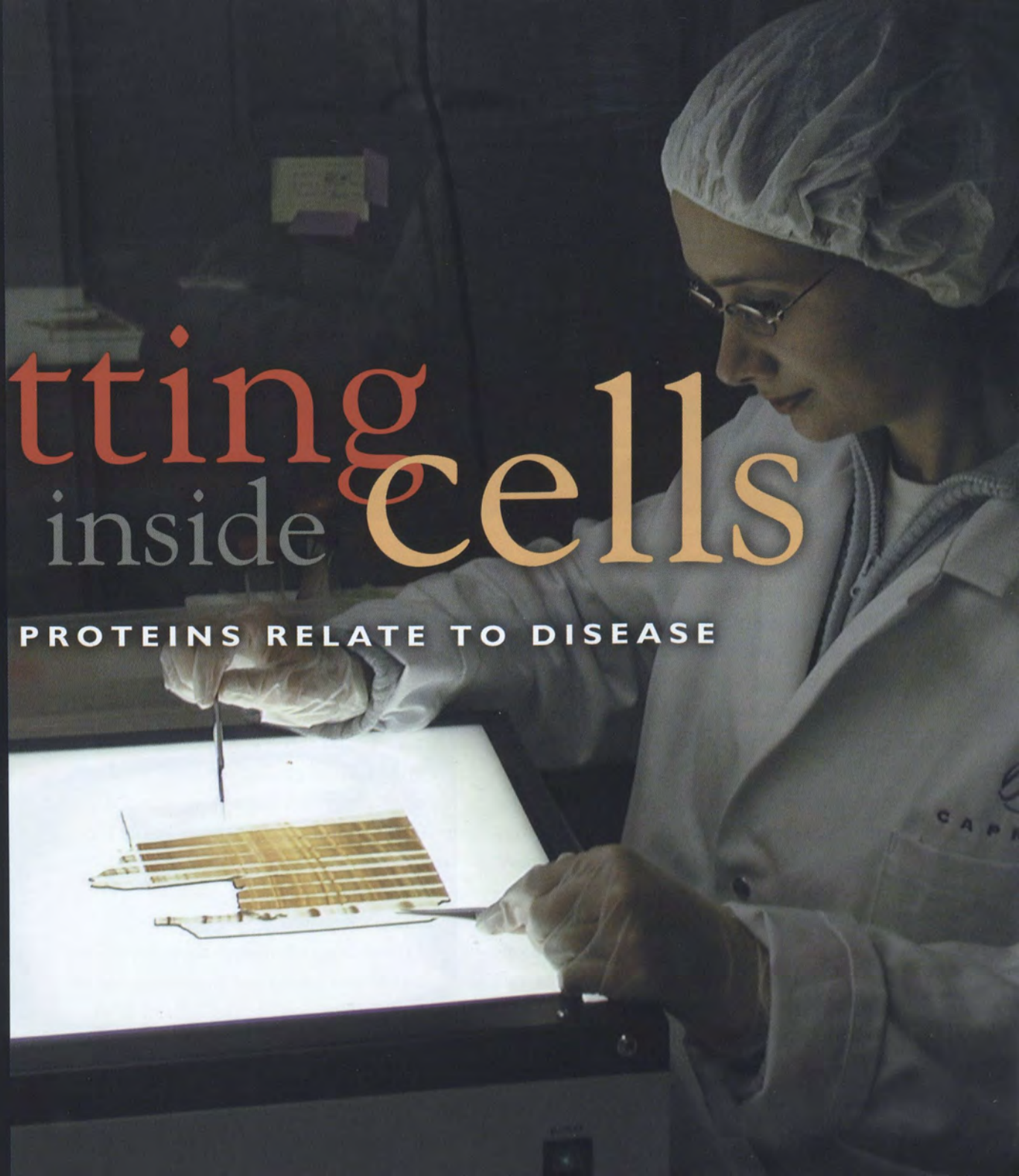
DNA Genotek Inc. is initially targeting Oragene™ to markets that conduct large DNA population studies—molecular epidemiology, predictive medicine, pharmacogenomics, and DNA banking. "These are fields that typically need DNA samples from larger numbers of people and it's often not practical or cost-effective to get blood samples," says Ted McClelland, DNA Genotek Vice-President.

Molecular epidemiology requires DNA from hundreds or often many thousands of people. "Because of the number of people and their geographical dispersion, researchers typically try to collect samples by mail," says Mr. McClelland. They need people to volunteer, so a non-invasive method is preferable.

Predictive medicine also depends on DNA samples from large populations to unearth genetic markers that indicate predisposition to various ailments. And once a marker is found, people who want to know if they're at greater risk for a particular disease need to provide a DNA sample to test if they carry the marker.

Getting inside cells

TO SEE HOW PROTEINS RELATE TO DISEASE



CAPRION PHARMACEUTICALS INC. TAKES A HIGH-TECH, PROTEOMIC APPROACH TO DIAGNOSING AND TREATING HUMAN DISEASE.

CellCarta™, a discovery platform developed by Caprion Pharmaceuticals Inc., maps the protein levels found in organelles, enabling researchers to detect abnormal protein patterns that distinguish healthy cells from their diseased counterparts.

Using CellCarta, Caprion is charting the frontiers of drug discovery. CellCarta provides a technological basis for a deeper understanding of the subcellular basis of disease—leading to more-effective therapeutic and diagnostic products.

Proteins are the building blocks of all human cells. To date, researchers have identified only a subset of the proteins found in human cells—they know even less about what these proteins do and where they're located. Hence, a comprehensive protein-based understanding of most disease states is not currently possible. New technologies now being applied have only recently allowed scientists to identify and study a significant complement of the proteins that comprise a cell.

The human genome provides a 'blueprint' for all of the proteins made by human cells. Because many of the 30,000 genes in our genome code for multiple proteins, scientists estimate there may be as many as one million different human proteins. A 'proteome' is the unique set of proteins present in an organelle, cell or tissue. Its complexity and function are modulated by the movement of proteins throughout the cell, the modification of proteins after they're made, and interactions between proteins or with other biomolecules. Consequently, an unprecedented level of biological information is required to discover and decipher the proteomic basis of human diseases.

Caprion Pharmaceuticals Inc. has pioneered a unique approach—called CellCarta™—to proteomics research that promises to unearth protein 'gold' in the fastest, most efficient way possible. CellCarta integrates proprietary technologies for fractionating human tissue specimens, enriching organelles and disease-related proteins, and determining the relative levels of proteins. Other distinctive components of this approach are analytical and bioinformatic tools that map the identity and level of proteins, and accurately compare those maps to discover proteins that are involved in a particular diseased state. CellCarta enables

DISCOVERING PROTEINS ONE COMPARTMENT AT A TIME

If human cells were factories, then the subcellular components called organelles represent the machinery. Each organelle has a specific role to play–the nucleus contains and manages the genetic blueprint, while ribosomes make the proteins and mitochondria generate energy that drives all of the activity within a cell.

Isolating cells from tissues and organelles from cells, while conserving the proteins they contain, takes great skill and years of experience. Caprion's scientists are leading experts in organelle isolation using a wide variety of cell types and tissues. They have innovated scalable and adaptable methods based on a variety of techniques—including centrifugation and immunoprecipitation—to produce the highly purified organelle preparations needed to make protein-based disease discoveries.

IDENTIFYING NEW AGENTS OF INFECTION

Until recently, the known causes of infectious diseases were limited to viruses, bacteria, fungi and parasites. But in the process of examining a newly discovered protein-based source of infection, Caprion Pharmaceuticals Inc. is charting new market potential.

Proteinaceous infectious particles—or 'prions'—are mutant proteins believed to cause several neurodegenerative diseases. Collectively called Transmissible Spongiform Encepharlopathies (TSEs), the group includes Mad Cow Disease and variant Creutzfeldt-Jacob Disease, the human equivalent.

At present, it is impossible to test for prions in humans or animals and therefore impossible to diagnose carriers of these fatal diseases. However, Caprion has developed antibodies that specifically recognize the mutant prion. In partnership with Ortho-Clinical Diagnostics (a division of life sciences giant Johnson & Johnson), the company aims to develop the first human blood-screening test for mutant prions—and capture a stake in a worldwide market estimated at US$500 million.

a disease-focused, multi-dimensional analysis of human proteins including the identity, level, subcellular location and movement of proteins.

"By focusing at the subcellular level, Cell*Carta* detects an unprecedented number of proteins and provides unique insights into protein function relevant to drug discovery," says Lloyd M. Segal, Caprion's President and CEO. Caprion's mission is to generate the most comprehensive profiles of disease proteomes under study to leverage their distinctive capabilities. The company's ongoing drug discovery programs are focused on tumour antigens and biomarkers.

Not surprisingly, Cell*Carta* generates vast quantities of disease-relevant information, all of which must then be managed and stored. Caprion has collaborated with Sun Microsystems, Oracle Corporation, and the information technology services firm CGI to create one of the world's largest dedicated protein computer farms. This cluster of high-performance servers and storage systems can process up to 100 terabytes of information per year, the equivalent of five billion pages of information.

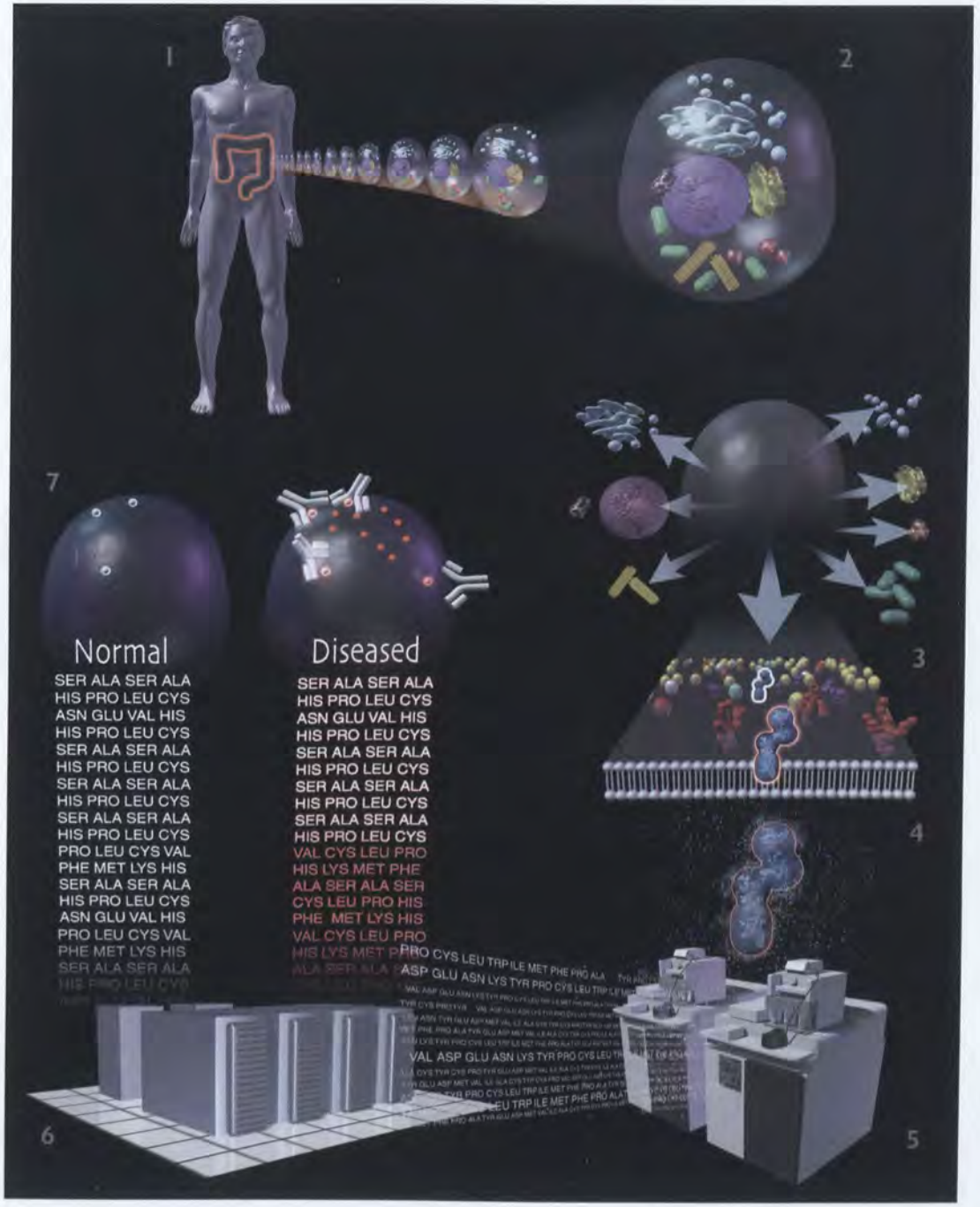
Caprion undertakes focused research and development collaborations with biopharmaceutical companies in areas of strong commercial interest. In September 2002, the company formed its first proteomics alliance—with IDEC Pharmaceuticals—for the discovery of novel tumour antigen targets for colorectal cancer. Caprion is actively seeking additional partnerships in three research areas. First, tumour antigen discovery focuses on identifying protein targets for antibody, vaccine and diagnostic applications. Second, biomarker discovery identifies protein candidates for diagnostic and prognostic applications. The third area, subcellular study of compound mechanisms, aims to identify novel and more effective therapeutic approaches and methods for evaluating drug efficacy.

Caprion's collaborations and partnerships will generate both revenues and retained rights to valuable drug targets. As its technology and business evolves, Caprion will seek complementary assets and technologies to build and mature its pipeline. The company currently has product

alliances with Ortho-Clinical Diagnostics to develop a blood screen for variant Creutzfeldt-Jacob Disease (vCJD), and with IDEXX Laboratories to develop a diagnostic test for Mad Cow Disease. Caprion also has strategic technology alliances with Micromass UK Ltd., Sun Microsystems, Oracle Corporation, and CGI.

"Caprion has a leading technology platform, strong corporate and academic partnerships, plus the facilities and technological infrastructure required to successfully compete as a global proteomics-based drug discovery company—and lead to the advancement of medicines worldwide," says Mr. Segal.

Since its founding in 1998, Caprion has raised more than CAD$100 million in financing; attracted international experts in cell biology, mass spectrometry and bioinformatics; grown to more than 80 employees; and built a 54,000-square-foot, CAD$31 million research facility in Montréal, Québec. On the research side, Caprion is collaborating with Micromass UK Ltd. to pursue mass spectrometry-based proteomic discoveries, and with McGill University to generate innovations in organelle proteomics.



RIGHT: *Caprion's CellCarta approach involves taking fresh human tissue samples from colon cancer biopsies (1) and using highly skilled cell fractionation (2) and organelle isolation (3) to obtain pure plasma membranes (4). The membranes are separated using two-dimensional liquid chromatography, and the membrane proteins are introduced into mass spectrometers (5) to determine protein masses and sequences. Once the data are processed (6) by custom-developed bioinformatics algorithms, CellCarta generates lists of differentially expressed protein targets. These targets, which are localised to the plasma membrane, can then be used as the basis for developing antibody therapies (7) to treat colon cancer.*

WORLDWIDE VENTURE CAPITAL FUNDING FOR BIOTECHNOLOGY

	YEAR	TOTAL VC	VC BIOTECH	BIO %
Canada	2001	$4.9 B	$842 M	17.3%
Europe	2000	$49.0 B	$1,073 M	2.2%
U.S.	2000	$160.0 B	$4,600 M	2.9%

Sources: Canadian Venture Capital Association (Mary MacDonald), NRC/IRAP, European Venture Capital Association, Genetic and Engineering News, 2002

Canada...
an investment in success

CANADA'S PUBLIC AND PRIVATE SECTORS CAPITALIZE ON BIOTECHNOLOGY'S POTENTIAL

INVESTORS ARE LOOKING AT CANADA AS A KEY PLACE TO INVEST FOR BIOTECHNOLOGY. THE NUMBERS TELL A COMPELLING STORY: BIOTECHNOLOGY ACCOUNTS FOR ROUGHLY 17 PER CENT OF ALL VENTURE CAPITAL FUNDING IN THE COUNTRY.

CANADA OFFERS A PORTFOLIO OF FINANCING TOOLS FOR BIOTECHNOLOGY, RANGING FROM ANGEL INVESTORS TO VENTURE CAPITAL TO PUBLIC SOURCES. THESE RESOURCES ARE SOLIDLY ESTABLISHED AND SUPPORT LONG-TERM GROWTH, MAKING CANADA AN IDEAL PLACE TO UNDERTAKE RESEARCH AND GET READY FOR COMMERCIAL DEVELOPMENT.

VENTURE CAPITAL FUNDING

Canada offers two main sources of venture capital funding for biotechnology: direct venture capital funds and labour-sponsored venture capital corporations (LSVCCs).

In addition to the funds listed below, a number of other groups have life sciences interests: the Business Development Bank of Canada, Milestone Medica of Ontario, Royal Bank Ventures, and Ventures West in British Columbia.

FUND	LOCATION	$CAD	FOCUS
BioCapital	Québec	$55 M	Human & environment
CPD Sofinov	Québec	$47 M	Multiple
Foragen	Ontario/Saskatchewan	$43 M	Agriculture
GeneChem	Québec	$100 M	Human
MDS Health Ventures	Ontario	$30 M	Human
MSBI	Québec	$26 M	New—links 3 universities

Source: NRC/IRAP, 2002

Labour-Sponsored Venture Capital Corporation Funds

Labour-Sponsored Venture Capital Corporation Funds (LSVCCs) are offered to individual investors, who obtain special federal and, in some cases, provincial, tax benefits. Canadians have invested more than $3.7 billion in LSVCCs. Some of these funds—which have a specific or significant investment in life sciences—are listed below:

FUND	$CAD
VenGrowth Investment Fund (I+II)	$889 M
Working Opportunity	$526 M
Working Ventures Canadian	$335 M
Canadian Medical Discoveries Fund	$351 M
University Medical Discoveries Fund	$335 M

Source: NRC/IRAP, 2002

GOVERNMENT SUPPORT

The Government of Canada is committed to creating a supportive environment for the biotechnology industry. Through a wide range of programs, the government supports research in federal organizations, universities and the private sector.

Support to federal organizations and universities

The National Research Council of Canada had the largest federal allocation to biotechnology at $83 million (out of a total budget of $640 million) in 2001-2002. Another major departmental involvement is Agriculture and Agri-Food Canada, which spent $57 million on biotech R&D in 2000-2001.

Both the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Canadian Institutes of Health Research (CIHR) support considerable levels of biotech research in universities. NSERC spent $40 million on biotech R&D in 2000-2001, while CIHR spent $133 million. Part of the funding from these organizations supports the 22 Networks of Centres of Excellence, which link university researchers across Canada. Seven of these centres are in the health sciences.

Genome Canada—a major new activity—is an arm's-length foundation with $300 million in federal funds. This support will be matched by provincial and industrial funding.

The Canada Foundation for Innovation (CFI) has capital of $3.15 billion—with leverage from partners—to support infrastructure in universities. It covers a wide range of sectors, including biotechnology.

Support to the private sector

The four main sources of federal funding available for industry are:

- Technology Partnerships Canada (TPC) makes strategic investments in innovative private-sector research and development initiatives. From 1997 to March 2002, TPC has approved $263 million in conditionally repayable contributions for 18 Canadian biotechnology R&D projects. These investments

are supporting development of leading-edge biotechnology applications in the environmental, medical and agricultural sectors.

- The National Research Council of Canada's Industrial Research Assistance Program provides about $5 million/year in biotechnology support to small and medium-sized firms.
- Agriculture and Agri-Food Canada's Matching Investment Initiative Fund spent $11 million in 2001-2002 on agricultural/food biotechnology research conducted in collaboration with firms.
- The Natural Sciences and Engineering Research Council's Research Partnerships Programs support academic research in collaboration with industry. In 2001, the budget allocation was $117 million, of which about 20 per cent was spent to support biotechnology.

Research tax credits

Canada has one of the most extensive systems of research tax credits for industry. There is a 20 per cent federal tax credit for research and experimental development, which rises to 35 per cent for Canadian-controlled private corporations. These credits totaled more than $1.5 billion in 2000, and a further $500 million (estimated) from the provinces.

The provincial governments also have specific initiatives to assist life sciences. One of the first was the Alberta Heritage Foundation for Medical Research (AHFMR), which was set up with a $300 million endowment from the Alberta government. AHFMR primarily funds university and hospital-based research, but some funds are also linked to industry.

In 2000, AHFMR's success inspired the Government of Alberta to create the Alberta Heritage Foundation for Science and Engineering Research. The Foundation supports 172 researchers, and the endowment is valued at $1 billion.

The province of Ontario has provided $20 million to set up or expand three technology centres in London, Ottawa and Toronto. In its 2002 budget, the province of Québec announced a new $100 million loan program to help firms access non-Québec based funds.

BUSINESS FINANCING FOR BIOTECHNOLOGY

In many countries around the world, business bio-financing peaked in 2000—and Canada was no exception. In that fiscal year alone, Canadian industry raised more than $3.3 billion. The following figures provide an overview of worldwide investment, and of Canada's place in the global scheme.

YEAR	WORLD FINANCING ($US)	CANADA %
2001 (9 months)	$10.8 B	21% (estimate)
2000	$36.8 B	9%
1999	$7.6 B	14%
1998	$6.1 B	13% (estimate)
1997	$5.8 B	9%

Sources: Biotech, BioCentury and NRC/IRAP; Nov/Dec 2001

INVESTMENT PARTNERSHIPS CANADA

Companies considering investing or expanding in Canada can benefit from Investment Partnerships Canada (IPC), which provides a wide range of assistance in assessing investment opportunities:

- Site selection data
- Advice on programs, regulations, transportation and taxation
- Introductions to key government and private-sector contacts

Through linkages with Canadian diplomatic missions around the world and investment advisors at the national, provincial and municipal levels, IPC is well positioned to assist companies in their investment decisions.

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APPENDIX I

The Government of Canada's Biotechnology Infrastructure

Biotechnology, with its immense promise and potential benefits, is a priority within Canada's industrial strategy. The sector's impact will be dramatic and far-reaching, with the capacity to improve human and animal health, the environment, and quality of life in general. In addition to a world-class regulatory regime, the Government of Canada has developed a comprehensive strategy to maximize the benefits, and reduce the risks, that may flow from these cutting-edge technological advances. A diverse range of initiatives—undertaken by several dedicated departments, bodies and agencies—ensures that Canadian industry remains a leader in the responsible development and use of biotechnologies, now and into the future.

Companies, both domestic and foreign, are realizing the commercial benefits provided under the Government of Canada's strategy. We invite you to explore the following programs and services supporting biotechnology innovation in Canada and how they are spurring researchers, scientists and private industry to technological and commercial success.

SUPPORT FOR RESEARCH AND DEVELOPMENT

With an annual budget of $617 million, the **CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)** is Canada's leading agency for health research. CIHR and its 13 institutes play a strategic role in building the pipeline of discovery, moving research from the laboratory to the marketplace through programs such as CIHR/SME and CIHR/R&D Research Programs, Proof of Principle and Intellectual Property Management. CIHR currently funds more than 5,000 researchers and thousands of research trainees in academic institutions across Canada. CIHR and its institutes are leading the way in building national research agendas, fostering excellence, and building capacity across Canada.
For more information: **www.cihr-irsc.gc.ca**

GENOME CANADA is the primary funding and information resource relating to genomics and proteomics in Canada. Dedicated to developing and implementing a national strategy in genomics and proteomics research for the benefit of all Canadians, it has so far received $375 million from the Government of Canada. Genome Canada has established five Genome Centres across the country (Atlantic, Québec, Ontario, Prairies and British Columbia) and has as a main objective to ensure that Canada becomes a world leader in genomics and proteomics research. Together with its five Genome Centres and with other partners, Genome Canada invests and manages large-scale research projects in key selected areas such as agriculture, bioinformatics, environment, fisheries, forestry, health and technology development. Genome Canada also supports research projects aimed at studying and analysing the ethical, environmental, economic, legal and social issues related to genomics research (GE3LS). To date, Genome Canada has invested more than $294 million across Canada. With funding from other partners, this amounts to an investment of $588 million in 56 innovative genomics and proteomics research projects and science and technology platforms.
For more information: **www.genomecanada.ca**

The National Research Council's **GENOMICS AND HEALTH INITIATIVE (GHI)**, in collaboration with other federal agencies, industries and universities, makes key contributions to national efforts to exploit advances in the areas of genomics and health. With an annual budget of $25 million, NRC is advancing fundamental and applied technical research in areas such as the diagnosis of disease, aquaculture, human pathogens, agricultural crop enhancement, environmental remediation of pollution, cancer, and neurobiology. These contributions build upon NRC's expertise in its biotechnology research institutes, as well as regional innovation networks across the country.
For more information: **www.nrc-cnrc.gc.ca**

THE NATIONAL RESEARCH COUNCIL (NRC) is one of Canada's most powerful resources for creating science- and technology-based innovation in every region of Canada. NRC makes key contributions

to the economy in aquaculture and marine sciences, agriculture, medical diagnostics, and health sciences working in partnership with industry, governments and universities across the research and innovation spectrum. NRC's biotechnology-related activities are conducted by five core research institutes:

- NRC Biotechnology Research Institute
- NRC Institute for Biological Sciences
- NRC Institute for Marine Biosciences
- NRC Institute for Biodiagnostics
- NRC Plant Biotechnology Institute

NRC's biotechnology activities are supported by several key partner institutes and programs:

- NRC Institute for Information Technology
- NRC Steacie Institute for Molecular Sciences
- NRC Institute for Microstructural Sciences
- National Institute for Nanotechnology
- NRC Industrial Research Assistance Program
- NRC Canada Institute for Scientific and Technical Information

For more information: **www.nrc-cnrc.gc.ca**

THE CANADA FOUNDATION FOR INNOVATION (CFI) is an independent, not-for-profit corporation established by the Government of Canada in 1997 to strengthen the capacity for innovation in Canadian universities, colleges, research hospitals, and other non-profit institutions. A significant portion of its $3.65 billion budget supports biological research.
For more information: **www.innovation.ca**

THE NETWORKS OF CENTRES OF EXCELLENCE (NCEs) represent an innovative approach to R&D by connecting, across the nation, the highest-quality research in government, university and industry in specific problem areas. Of the 22 currently funded NCEs, seven undertake work with biotech dimensions, including:

- The Canadian Bacterial Diseases Network
- The Canadian Genetic Diseases Network
- The Protein Engineering Network of Centres of Excellence
- The Canadian Network for Vaccines and Immunotherapeutics (CANVAC)
- The Canadian Arthritis Network
- The Canadian Stroke Network
- The Stem Cell Network

For more information: **www.nce.gc.ca**

AGRICULTURE AND AGRI-FOOD CANADA (AAFC) operates 19 national research centres that act as catalysts for industry growth, providing expertise and attracting investment. AAFC and industry collaborate on more than 700 research projects each year, producing a steady stream of products for markets around the world.
For more information: **http://www.agr.gc.ca**

THE NATURAL SCIENCES AND ENGINEERING RESEARCH COUNCIL OF CANADA (NSERC) funds more than 9,000 university researchers every year as well as the advanced training of highly qualified people through scholarships and fellowships. In addition, NSERC supports innovation by sharing with industry the costs and the risks of research conducted in partnership with universities. NSERC invests more than $600 million annually in university-based research in the natural sciences and engineering. It provides financial support for university research in biotechnology through discovery grants and project grants that include:

- Strategic Projects
- Collaborative R&D
- Nanotechnology Innovation Platform

For more information: **www.nserc.ca**

DEFENCE R&D CANADA (DRDC), Canada's leader in defence and national security research and development, provides science and technology (S&T) leadership to the Department of National Defence, the Canadian Forces and the Canadian industrial base. Through its R&D programs, DRDC forges strong partnerships and collaborations with industry, government and university partners and clients in Canada and abroad. DRDC advances leading-edge S&T expertise in three key sectors: sensors and information technology, combat systems, and human systems. The human systems include biochemical defence, systems integration, and system performance and protection. DRDC is a national network of six defence research centres with an annual budget of $200 million and a staff of 1,400 people.
For more information: **http://www.drdc-rddc.gc.ca**

THE TECHNOLOGY DEMONSTRATION PROGRAM (TDP) demonstrates technologies fostered by Defence R&D Canada and Canadian industry in the context of real and potential future Canadian Forces capabilities, concepts, doctrine, operations and equipment.
For more information: **www.drdc-rddc.gc.ca/business/tdp/tdp_e.asp**

THE CANADIAN FOREST SERVICE (CFS) advances sustainable forestry in Canada and internationally by generating knowledge about, and exploring the applications of, biotechnology to improve forest regeneration and protection methods. CFS plays a key role in defining strategic research orientations, advising on environmental regulations, developing skilled workers, increasing public awareness of forest biotechnology, and coordinating activities with industry, academia, and other governmental departments and agencies.

Biotechnology research is conducted at CFS laboratories in the Pacific, Northern, Great Lakes, Laurentian, and Atlantic centres and is integrated nationwide through the **FOREST BIODIVERSITY NETWORK**, the **FOREST HEALTH NETWORK**, the **INTEGRATED PEST MANAGEMENT METHODS NETWORK**, and the **FOREST BIOTECHNOLOGY NETWORK**.
For more information: **www.nrcan.gc.ca/cfs-scf**

CANADA ECONOMIC DEVELOPMENT FOR QUÉBEC REGIONS (CEDQ) is a key player among the federal stakeholders working for the economic development of Québec's regions. The federal agency focuses on two main areas of activity: enterprise development and improving the environment for the economic development of the regions. With its partners, CEDQ offers the following services: information, advice, skills acquisition and funding.
For more information: **www.dec-ced.gc.ca**

THE ATLANTIC INNOVATION FUND, administered by the Atlantic Canada Opportunities Agency (ACOA), focuses on R&D projects in the area of natural and applied sciences, as well as social sciences and the humanities where these are explicitly linked to the development of technology-based products, processes or services, or their commercialization. Focusing on small and medium-sized enterprises, ACOA's Business Development Program offers access to capital in the form of interest-free, unsecured, repayable contributions for a breadth of activities including construction, machinery and equipment acquisition, marketing, training, innovations, product/quality improvement, and development and commercialization of technology-based products, processes or services.
For more information: **www.acoa.ca**

WESTERN ECONOMIC DIVERSIFICATION CANADA (WD) is the lead federal department for economic development and diversification in Western Canada. WD's strategic priorities include Innovation, Business Development/Entrepreneurship, and Sustainable Communities. WD focuses on strengthening the western Canadian innovation system through strategic investments in key sectors, including: life sciences (genomics/proteomics, health technologies, neutraceuticals and biotechnology), information technologies (new media, wireless and micro-technologies), and other technologies (synchrotron, climate change technologies, design engineering and fuel cells). More than half of WD's new approvals for financial support are directed to innovation initiatives and are targeted at key activities such as technology commercialization, addressing gaps in R&D and infrastructure, community innovation, and facilitating linkages. WD works in partnerships with federal, provincial, university, industry and other innovation system players to identify priorities and lever new investments.
For more information: **www.wd.gc.ca**

INVESTMENT INITIATIVES

INVESTMENT PARTNERSHIPS CANADA (IPC) is the Government of Canada's one-stop centre for investment services. IPC offers: assistance in assessing investment opportunities, including site selection data, advice on programs, regulations, transportation and taxation; or introductions to key government and private-sector contacts. Through Canadian diplomatic missions around the world, and with direct access to investment counsellors at national, provincial and municipal levels within Canada, IPC is well positioned to support companies in their investment decisions.
For more information: **www.investincanada.gc.ca**

Innovation is essential in the increasingly knowledge-based global economy of the 21st century. **TECHNOLOGY PARTNERSHIPS CANADA (TPC)** was established in 1996 to help position Canada as a leading player in that economy. TPC has played a key role as a technology investment program to contribute to the achievement of Canada's objectives such as increasing economic growth, jobs and wealth creation, and supporting sustainable development.

TPC advances and supports government initiatives by investing strategically in research, development and innovation in order to encourage private-sector investment, and so maintain and grow the technology base and technological capabilities of Canadian industry. TPC also encourages the development of small and medium-sized businesses in all regions of Canada.

As of March 31, 2003, TPC has approved 524 projects across Canada worth more than $2.3 billion leveraging in excess of $9.5 billion.
For more information: **tpc.ic.gc.ca**

THE NRC INDUSTRIAL RESEARCH ASSISTANCE PROGRAM (IRAP) (NRC-IRAP) provides financial assistance for promising early-stage opportunities, access to business and technical expertise, and valuable access to international networks. NRC-IRAP is active in 90 communities across Canada, helping to increase the innovation capacity of small and medium-sized enterprises.
For more information: **irap-pari.nrc-cnrc.gc.ca/**

THE MATCHING INVESTMENT INITIATIVE increases collaborative agri-food research activity between the private sector and Agriculture and Agri-Food Canada. The department can match up to one-for-one industry R&D contributions to collaborative research projects.
For more information: **res2.agr.ca/indust/mii/index_e.htm**

THE DEFENCE INDUSTRIAL RESEARCH PROGRAM (DIR) is a cost-sharing industrial program that promotes and improves the research and technological capabilities of Canadian defence companies in order to strengthen the defence industrial base. DIR projects are initiated by industry and jointly funded by Defence R&D Canada and Canadian industry.
For more information: **www.drdc-rddc.gc.ca/business/dirp/dirp_e.asp**

THE SCIENTIFIC RESEARCH AND EXPERIMENTAL DEVELOPMENT (SR&ED) PROGRAM of the Canada Customs and Revenue Agency provides financial assistance, through investment tax credits, to individuals and corporations that conduct scientific research and experimental development in Canada. The program encourages companies to do work that will lead to new, improved or technologically advanced products or processes.
For more information: **www.ccra-adrc.gc.ca/taxcredit/sred/menu-e.html**

NSERC's **COLLABORATIVE RESEARCH AND DEVELOPMENT PROGRAM** shares the costs and risks with industry of collaborative research conducted in partnership with universities. The program stimulates industry investment in university research and exposes students to real-life challenges and opportunities in industry.
For more information: **http://www.nserc.ca/guide/b3_e.htm**

CIHR's **UNIVERSITY-INDUSTRY PROGRAMS** build on CIHR's research programs by facilitating strategic partnerships that better enable research to be carried through to delivery. Over the past three years, more than $170 million has been invested through these programs, stimulating infrastructure and recruitment for health research.
For more information: **www.cihr-irsc.gc.ca/**

THE GOVERNMENT OF CANADA'S BUDGET 2003 continued Canada's prudent management of the nation's finances; it was this government's sixth consecutive balanced budget. Canada is enjoying the benefits of a thriving economy. More than 560,000 new jobs were created in 2002, and Canada led the G-7 countries in economic growth in 2002. Both the IMF and the OECD predict that Canada will again lead the G-7 countries in growth in 2003. Tax rates continue to fall; by 2005, firms in Canada will have almost a 4.5 per cent corporate income tax advantage over U.S. firms. Canada's top rate on capital gains is lower than the typical top U.S. rate, and Canada's capital tax will be eliminated by 2008. Tax credits and accelerated R&D deductions are among the most generous in the world.
For more information: **www.fin.gc.ca/budtoce/2003/budliste.htm**

EXPORTING CANADIAN EXCELLENCE

Agriculture and Agri-Food Canada's **AGRI-FOOD TRADE SERVICE** component of Team Canada provides strategic and practical assistance to exporters of agri-food products and services to give innovative Canadian companies a competitive edge in international markets.
For more information: **atn-riae.agr.ca**

THE CANADIAN TRADE COMMISSIONER SERVICE of Foreign Affairs and International Trade Canada helps Canadian companies assess their export potential and identify key international contacts, and provides them with the market intelligence they need to succeed in business abroad. With a network of 500 professionals working in 140 cities around the world, the Canadian Trade Commissioner Service also provides assistance and support to international clients by matching their needs with the appropriate sources of Canadian products, services and technology.
For more information: **www.infoexport.gc.ca**

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Canada Research Chairs Program
www.chairs.gc.ca

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CANADIAN INNOVATION IN BIOTECHNOLOGY

It takes all kinds of innovators—scientists and engineers, entrepreneurs and investors—to transform new ideas into products and services with global appeal.

The Government of Canada is proud to present new and updated stories highlighting how Canadian innovators are touching lives, generating economic benefit, and laying foundations for future discovery. Stories that demonstrate why...

Canada is a great place to invest and bring innovation to life.

TO FIND OUT MORE ABOUT INVESTMENT OPPORTUNITIES IN CANADA:

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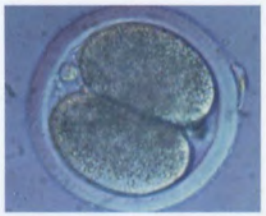


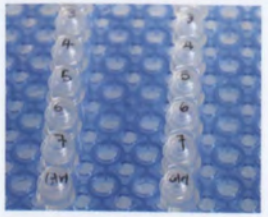

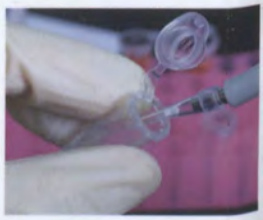

PLEASE CONTACT YOUR LOCAL CANADIAN DIPLOMATIC MISSION OR WRITE TO US AT:

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