Vaccine and Infectious Disease Organization

VIDO

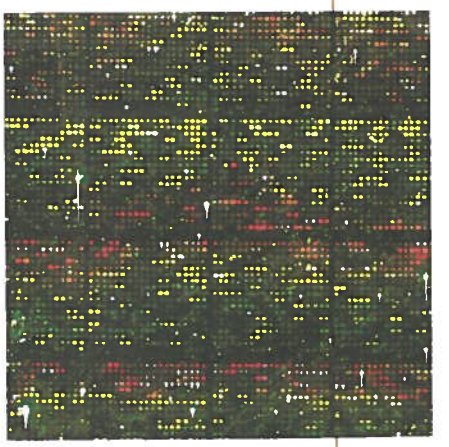
Protecting the world from infectious diseases

2005–2006

A research organization of the

University of Saskatchewan

Contents



Cover: Public health authorities around the world are monitoring avian influenza H5N1, feared to be the harbinger of the next global pandemic.

Our Vision

Protecting the world from infectious diseases

Our Mission

To be a pre-eminent research institute investigating the pathogenesis of infectious diseases and the development of effective therapeutic and prophylactic methods to control infectious diseases of humans and animals

Dr. Lorne Babiuk, Director

With the speed of travel and of global trade, infectious disease in an isolated part of the world can reach all continents in a day.

Securing Your Health in an Era of Emerging Infectious Diseases

Dr. Lorne Babiuk, OC, SOM, PhD, DSc, Director
Canada Research Chair in Vaccinology and Biotechnology

The effects of globalization are being felt everywhere. However, nowhere is this more relevant than in the arena of infectious disease.

It is often stated that infectious agents do not carry passports and so are not restricted to any region. With the speed of travel and of global trade, infectious disease in an isolated part of the world can reach all continents in a day, resulting in infection and significant economic impacts to livestock industries and humans everywhere – including Canada.

No one can feel isolated from infectious diseases occurring in other parts of the world. VIDO has a responsibility to battle these infections. We continue to embrace our mission and vision regardless of where infections may occur.

InterVac and International Collaborations

The majority of emerging or re-emerging diseases – avian influenza H5N1, West Nile virus, tuberculosis – must be studied in Biosafety Level III facilities. Therefore, we have been aggressively pursuing funding to build the International Vaccine Centre (InterVac), a Level III biocontainment facility on the University of Saskatchewan (U of S) campus. InterVac, a $110 million facility, will support research on Level III disease-causing organisms (pathogens) of all species. This facility will be part of the U of S-owned VIDO infrastructure and ensure VIDO is successful in achieving its vision and mission.

Thanks to the support of the Government of Saskatchewan, the Government of Canada through the Public Health Agency of Canada and Western Economic Diversification, the Canada Foundation for Innovation, the U of S, and the City of Saskatoon, the International Vaccine Centre is very close to becoming a reality. These agencies have contributed substantially to this world-class and much-needed infectious disease research facility and we hope to see those investments realized by 2009.

The architectural design is being finalized and will contain 18 large-animal rooms capable of handling a significant number of species at one time. The state-of-the-art facility will exceed regulatory standards for Level III containment, allowing us to work with any emerging or persistent Level III pathogen. Since many of these Level III pathogens are zoonotic (carried by animals but capable of transmission to humans), additional safety measures and operating procedures will be in place to ensure that workers are protected from any exposure to these agents.

Currently, there is a shortage of similar facilities globally. InterVac will be a bridge to international colleagues needing access to such facilities and will enhance opportunities for collaboration and funding. Visiting scientists will be able to participate in joint research programs for mutual benefit. These collaborations should lead to the recruitment of highly trained scientists to Canada. In addition, many international funding agencies require evidence of collaboration between scientists from different disciplines and countries.

National Collaborations in Public Health

The U of S recognizes the importance of public health research. As a result, it is developing a School of Public Health. The school will provide an opportunity for VIDO and the university community to expand our collective expertise through collaboration. VIDO is expected to be an integral part of the School of Public Health and since many of the diseases VIDO is working on are of public health concern, this makes such a relationship extremely valuable.

Building on the School's investigations concerning the epidemiology of public health threats – key to any response to disease – we will also be partners in Canada's national public health infrastructure. VIDO's relationship with the Public Health Agency of Canada as a participant in the National Collaborating Centre on Infectious Diseases allows us to directly contribute to protecting the health of Canadians. In addition, we are participants in the International Centre for Infectious Diseases in Winnipeg. This centre has the mandate to address aspects of infectious diseases on a global scale and to train individuals for research careers= key to Canada's success in battling infectious diseases.

Infrastructure

VIDO currently has state-of-the-art Biosafety Level II laboratory facilities and equipment, including animal isolation facilities and a 160-acre research station to carry out all aspects of research on infectious diseases. This capacity will be expanded significantly with the addition of InterVac, our Level III facility nearing construction.

However, the most important part of our infrastructure is dedicated people. These individuals come from approximately 20 nations and have one common goal – to perform high quality science with relevance to the end users. VIDO's staff of more than 140 individuals in nine programs has embraced the interdisciplinary approach required in today's research environment. This team culture is of paramount importance for VIDO's success. The dedication of VIDO employees is sure to benefit society through novel disease management systems, better diagnostics and, more importantly, better immunization and prophylactic methods for controlling infectious diseases.

VIDO's staff of more than 140 individuals in nine programs has embraced the interdisciplinary approach required in today's research environment.

Commercialization

Both the federal and provincial governments recognize the importance of a knowledge-based economy as the driver of Canada's international competitiveness. As part of this commitment, they continue to increase funding to universities with the goal of increasing commercialization and economic activities in Canada.

VIDO is committed to partnership with different levels of government to contribute to this goal for Canada. In this regard, we aggressively seek partnerships and licensing agreements with local, national, and multi-national biopharmaceutical companies to move research from the bench to the commercial arena. This process is driven by intellectual property – VIDO holds 73 issued U.S. patents with 25 pending. The vaccine technologies represented in these patents and licensing agreements are not only providing revenue to VIDO for continued operations, but are also benefiting society through reduced agricultural input and health care costs, improved productivity and enhanced economic activity.

Infectious disease in developing countries dampens productivity, impacts education, and prevents self-sufficiency. In addition to enhancing commercialization locally, the federal government is targeting support to the developing world to enhance the quality of life globally. In alignment with this commitment and with current society views, several VIDO research projects are directed at reducing the economic burden of disease around the world.

As a wealthy country, Canada has a global responsibility to assist the less fortunate. By reducing the impact of infectious disease around the world, we will not only reduce the

risk of disease transmission internationally, but also enhance economic activity in developing countries, thereby improving stability and prosperity.

Governance

Even as VIDO integrates more closely with the University of Saskatchewan through the School of Public Health, there continues to be a great need for strong governance of VIDO and InterVac. The U of S Board of Governors continues to endorse VIDO's livestock industry-led Board of Advisors that contributes great wisdom and ensures VIDO's programs are focused and delivered.

We are especially grateful to the Board's leadership and advice during the last year of VIDO's evolution to a key partner in the international effort to control infectious disease. Since Board members provide their time and energy on a volunteer basis, their support and numerous hours spent on VIDO business is greatly appreciated. Without their dedication, VIDO could not function at its current level of performance. The Board of Advisors has laid the foundation for our success to date, on which we can build a very successful future.

Financial Partners

Finally, the financial support of our partners is greatly appreciated.

Our partners include:

- Livestock and poultry industries
- Private industries
- Provincial governments of Saskatchewan and Alberta
- The federal government through the Public Health Agency of Canada (PHAC) and Western Economic Diversification (WED)
- Canadian Institutes of Health Research (CIHR) and the Natural Sciences and Engineering Research Council (NSERC)
- The University of Saskatchewan
- The Bill & Melinda Gates Foundation
- The Krembil Foundation

Without this financial support, VIDO would not be able to conduct many of the pivotal research projects that lead to the migration of technologies from the laboratory to the commercial arena. We thank all of our partners for their continued support of VIDO's research efforts. Together, we constitute a powerful opponent to infectious disease.

VIDO Board of Advisors

Front row, left to right: Dr. Robert Kerr, Ms. Catherine McKinley, Dr. W. Ronald Usborne (Chair), Dr. Lorne Babiuk, Mr. Brian Perkins, Dr. Robert Church

Back row, left to right: Dr. Harley Olsen, Dr. Steven Franklin, Mr. Peter Schuld, Mr. Dickson Gould, Dr. Chuck Rhodes, Dr. Gordon Atkins

Absent: Dr. Stanley Alkemade

Dr. Ron Usborne, Chair, VIDO Board of Advisors

InterVac will add another dimension and open broader horizons in VIDO's continuing efforts to protect the health of livestock and humans.

Building on our Foundation of Successful Partnerships

Dr. Ron Usborne, PhD, PAg
Chair, VIDO Board of Advisors

VIDO has had another year of opportunities and challenges. It's amazing how the organization continues to grow, perform, and achieve the high level of excellence it does in the global scientific community. VIDO is an efficient and productive team of scientists, technicians, postdoctoral fellows and graduate students that contributes to the scientific knowledge in the areas of vaccine development, formulation and delivery, and in the modulation of the immune system to capitalize on our natural, or innate, immune responses.

The need for the production and delivery of effective vaccines to combat both existing and emerging contagious diseases is a challenge VIDO vigorously strives to meet. The reward for taking on this challenge is realized in our significant contributions to the safety of our food supply and to the health and well-being of our society. A recent $6.9 million grant from the Bill & Melinda Gates Foundation to work in the area of neonatal immunization is certainly encouragement to take on these societal challenges.

VIDO has operated on the campus of the University of Saskatchewan (U of S) for more than 30 years – an environment that has allowed the organization to grow and partner with the university community. The U of S is unique because it is the only university in Canada with facilities of agriculture and veterinary medicine, as well as all the health sciences, on the same campus. This offers many opportunities for interdisciplinary interactions in research and academic areas. Currently, discussions are underway to enhance these opportunities, which will open even more doors for VIDO to partner with the campus units allied to contribute to societal needs.

The reality of the International Vaccine Centre (InterVac) – a Biosafety Level III large animal containment facility with supporting laboratories – will add another dimension and open broader horizons in VIDO's continuing efforts to protect the health of livestock and humans. The shovel is almost in the ground to launch this valued addition to an already impressive laboratory complex and university infrastructure. InterVac will be available for use to researchers everywhere, from local laboratories to international institutions. The U of S has been extremely supportive of this important project and the Board appreciates this very much.

As chair of the Board over the last 18 months, I have had a great experience participating in the many discussions with fellow Board members, VIDO management, and university officials in trying to help VIDO and the U of S decide on ways and means to make a very good symbiotic relationship even better. Individually, each has great potential, but together, the sky is the limit. I have certainly valued this opportunity to be a little piece of history, witnessing the evolution of VIDO from an already great scientific organization into one of world-class calibre.

Thank you for your support.
Dr. Ron Usborne

International Vaccine Centre (InterVac) Continues to Take Shape

Seventy-five per cent of emerging human diseases – and 60 per cent of all human diseases – have a link to animals. Yet, there is an international shortage of facilities capable of handling large numbers of large animals at the appropriate level of biocontainment.

Many recent emerging diseases have been rated as Biosafety Level III pathogens. Built on VIDO's experience and international reputation and owned by the University of Saskatchewan, the International Vaccine Centre (InterVac) will be a fully secure Biosafety Level III facility suitable for infectious disease research and development, and unique in its capacity to work with large-animal models.

InterVac will offer much-needed research space to partners based locally and around the world. As well, it will join a cluster of life sciences infrastructure and expertise that is unmatched anywhere in North America. This cluster includes Canada's only synchrotron, the Canadian Light Source; VIDO; and the University of Saskatchewan's full array of human, animal and plant health colleges.

Architect's rendering of the International Vaccine Centre (courtesy AODBT in association with Smith Carter

Joyce Sander, Human Resources and Intellectual Property Manager

The human resources at our organization have the potential to become a crucial component in the protection of the world from infectious diseases – but recruitment is very competitive.

Recruiting Scientists for Tomorrow's Fight Against Infectious Disease

Joyce Sander, CIM, PMgr
Human Resources and Intellectual Property Manager

VIDO employs or trains more than 140 people. Taking a team approach, it provides an opportunity for students and postdoctoral fellows to interact with molecular biologists, virologists, bacteriologists and immunologists. VIDO is committed to ensuring that every employee, student and trainee receives the highest level of support, mentoring, and encouragement required to allow them to succeed at what we do best – science.

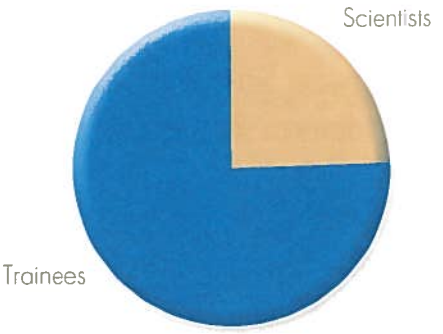
With the advent of antibiotics, health officials were satisfied that infectious diseases were a problem of the past. However, many existing diseases are resurging and new diseases are emerging, due to factors including population growth, increased immune suppression and antibiotic-resistant strains of bacteria.

The human resources at our organization are a crucial component in the protection of the world from infectious diseases, but recruitment is very competitive. A key member of the University of Saskatchewan innovation cluster, VIDO is proactive in attracting scientists from around the world. In order to be successful, VIDO aims to provide job security, ensure job satisfaction, and offer competitive salaries and benefits. To accommodate new talent, we strive for flexibility on many levels – in job descriptions, length of employment terms, pay scales, and in hiring processes.

A Canadian research organization, VIDO will assist in leading Canada in its response to emerging disease. To be effective, VIDO must ensure continued and increased investment in research and research infrastructure – world-class facilities, laboratories and, most importantly, people. The trainees in which we invest become either VIDO employees or, just as importantly, establish careers around the world, benefiting society in various other capacities.

Graduate student Monika Polewicz is a member of VIDO's Neonatal Immunization program.

The Importance of World–class Training at VIDO



"I did my first postdoctoral placement at VIDO from 1989 to 1991, working in the lab of Andy Potter. It was a wonderful experience, personally and professionally, which changed my view on research; the knowledge I gained has been absolutely decisive for my career development. Working at VIDO was a valuable experience for me because the research was conducted at the highest international level with colleagues from all around the world. In particular, the opportunity to meet researchers from different countries and different continents, and with different educational backgrounds, was very stimulating for a young biochemist coming from a small country (Denmark)."

Michael Theisen, PhD, DrMed
Department of Infectious Disease Immunology, Statens Serum Institut
Copenhagen, Denmark

"Having a chance to pursue graduate studies at VIDO greatly helped me prepare for my career. The advanced multidisciplinary research and superb research environment allow the students to learn, discuss, explore and more importantly, open up their perspectives on the 'science and art' of doing research. This environment is essential for preparing for a research career anywhere in the world. Moreover, I am grateful for the Canadian hospitality and friendships that made me feel at home."

Sanipa Suradhat, DVM, PhD
Associate Professor, Faculty of Veterinary Science,
Chulalongkorn University
Bangkok, Thailand

VIDO postdoctoral fellows Dr. Ursla Fernando (left) and Dr. Hong Yu (centre) with scientist Dr. Sasha Zakhartchouk

Dr. Andrew Potter, Associate Director, Research

We recognize that research on global problems requires a coordinated global effort and VIDO has significantly expanded its collaborations, both nationally and internationally.

VIDO Research Focuses on a Healthy Global Community

Dr. Andrew Potter, PhD, Associate Director, Research
NSERC/Bioniche Industrial Research Chair in Food Safety

Despite the widespread use of vaccines and antimicrobials over several decades, infectious diseases continue to be a leading cause of illness and death worldwide in both animals and humans. Emerging diseases and potential threats such as SARS, West Nile virus, pandemic influenza and others have all been in the public eye, but old threats such as non-pandemic influenza and tuberculosis are still important. In addition, our reliance on antibiotics has resulted in the emergence of antibiotic-resistant strains of many common organisms.

VIDO's research programs, outlined on the following pages, have been reorganized during the past year to reflect these issues, with the establishment of two new programs: (1) Emerging diseases and microbial virulence, and (2) Neonatal immunization. This change was made in order to focus related projects into single units to encourage efficient team-based activities and approaches.

We recognize that research on global problems requires a coordinated global effort and VIDO has significantly expanded its collaborations, both nationally and internationally. Typical of all research projects at VIDO, our Pathogenomics program involves a collaboration between four Canadian and three international centres, while our Neonatal Immunization program involves three Canadian centres and one international centre.

In order to respond rapidly to emerging threats, VIDO is also active in the development of technology platforms that can be quickly applied to virtually any disease target. Vaccine-related research has grown tremendously over the past two decades, but much of the effort is still focused on the disease-causing organism, or pathogen. Indeed, the way we formulate and use vaccines has changed little over the past 30 years. Therefore, much of our research is devoted to the development of technologies to improve the formulation, delivery and use of vaccines, and virtually all research programs contribute to this effort.

There has also been significant growth on new vaccine targets, including expanded efforts on zoonotic pathogens affecting both animals and humans as well as animal-specific diseases such as bovine pneumonia, arthritis and most recently *M. tuberculosis* and *M. paratuberculosis*.

Summaries of VIDO's activities are described on the following pages. VIDO also has two additional programs – Clinical Research and Development, and Chemistry and Genomic Services – which support all research programs through activities ranging from animal model development through to antigen purification and peptide synthesis.

I encourage you to visit VIDO's Web site at www.vido.org where more information is available.

Current Research Activities at VIDO

Emerging Diseases and Microbial Virulence

From developing influenza vaccines to investigating the ways bacteria and viruses cause disease, the objectives of this program include responses to emerging and re-emerging diseases that threaten global health.

Influenza is a significant cause of illness and mortality worldwide, causing 36,000 deaths annually in the U.S. alone. In addition, the emergence of new highly virulent strains of avian influenza in Asia has evoked fears of another flu pandemic. VIDO's research on equine influenza, swine influenza and avian influenza serve as excellent models for human disease. We are actively studying how the viruses cause disease (pathogenesis) and developing novel vaccines and testing antiviral compounds against influenza. We are also applying technologies developed in other programs to influenza. For example, immune stimulants can be used as both preventative and therapeutic tools to augment vaccination strategies.

Ultimately, we hope to develop a family of vaccines for animals that will reduce the risk of human infection through contaminated food and water.

The Severe Acute Respiratory Syndrome (SARS) was also associated with the word *pandemic* when the disease first emerged in 2002. A life-threatening pneumonia, SARS caused nearly 800 deaths worldwide and had a significant economic and social impact on Canada. The disease serves as a model for developing rapid responses to previously unknown pathogens. VIDO has been a member of the SARS Accelerated Vaccine Initiative (SAVI), aimed at creating new paradigms for rapid vaccine development, and this coalition of researchers has generated three potential vaccine candidates.

The development of new antimicrobial agents and vaccines requires a sound knowledge of the interaction between the pathogen and its host. We are therefore carrying out more fundamental research in areas such as bacterial cell division and signal transduction pathways by which cells respond to external signals, to create new therapies. Dr. Jo-Anne Dillon's laboratory has pioneered research on how bacteria such as *E. faecalis*, a significant veterinary and human pathogen, and *N. gonorrhoeae*, the causative agent of gonorrhoea, grow and divide. Her laboratory is also engaged in resistance surveillance, molecular epidemiology, and resistance mechanisms of *N. gonorrhoeae*.

VIDO has also initiated a project targeting the use of vaccination to prevent and treat prion diseases of animals such as bovine spongiform encephalopathy (BSE or "mad cow") in cattle and chronic wasting disease in elk. This is an international collaboration being carried out under the umbrella of PrioNet, a new Network of Centres of Excellence.

Bacterial Vaccine Development

Every year, up to 30 per cent of people living in developed countries will develop a food-borne illness, according to the World Health Organization. In North America alone, *E. coli* O157:H7 causes more than 73,000 illnesses from contaminated food or water every year. There are currently few effective measures to control the levels of the principal food- and water-borne pathogens in their animal hosts, the most efficient way to reduce the risk of human infection.

In collaboration with Dr. Brett Finlay at the University of British Columbia, VIDO has developed a vaccine to reduce levels of *E. coli* O157:H7 in cattle that is now being commercialized by Bioniche Life Sciences Inc. (Belleville, Ont.). We are extending this work to protect against other types of *E. coli* and to develop ways of more effectively inducing immune responses in the gut of cattle, where most food-borne pathogens reside.

Human infection with *Campylobacter jejuni* and Salmonella species is often the result of improper handling of contaminated poultry. In the case of *C. jejuni*, infection can have long-term, chronic consequences, including arthritis and Guillain-Barré syndrome. VIDO is currently working on vaccines for both of these pathogens using technologies established during the development of the *E. coli* O157 vaccine. Several vaccine targets have been identified and proof-of-concept has been demonstrated for vaccination against Salmonella infection. Ultimately, we hope to develop a family of vaccines for animals that will reduce the risk of human infection through contaminated food and water.

Also within the Vaccine Development program are projects targeting animal pathogens causing bovine mastitis, pneumonia and arthritis. Mastitis is the most costly infectious disease affecting the dairy industry worldwide and VIDO has developed prototype vaccines against environmental Streptococci such as *S. uberis*. This technology is currently being applied to *Staphylococcus aureus* mastitis as well as pneumonia and arthritis caused by

Mycoplasma. VIDO is part of a new research network in Canada dealing with bovine mastitis and our goal is to optimize methods of stimulating immunity in the mammary gland using novel *S. aureus* vaccine formulations.

Viral Vaccines and Nucleic Acid Technologies

Conventional viral vaccines are composed of live or killed viruses or their individual parts, and have been remarkably successful in disease reduction. Smallpox has been eradicated following international vaccination programs, highlighting the effectiveness of these products. Currently, there are issues associated with efficiency, safety and cost of vaccine production for several viral diseases of humans and animals. Several years ago, it was shown that if nucleic acid (DNA) coding for a protective component of a virus is transferred to an animal or human host, the body is tricked into making the vaccine component, thus reducing concerns due to safety and reducing cost. In addition, nucleic acid vaccines are especially good at creating a type of immune response (cell mediated) critical for the prevention of many viral diseases. This response does not always occur following immunization with killed vaccines.

For example, VIDO researchers have shown in the case of the cattle virus bovine herpesvirus-1 that vaccination with a DNA vaccine results in protection against disease, and the quality of the immune response is similar to that achieved with live vaccines and better than that induced by conventional killed vaccines.

Postdoctoral fellows Dr. Marianela Lopez and Dr. Francois Meurens

Teams are now working to develop additional DNA vaccines against a number of disease-causing organisms of cattle and humans, including bovine viral diarrhea, respiratory syncytial virus, and others. Hepatitis C, for example, is a disease that affects up to 170 million people worldwide. The hepatitis C virus (HCV) can go unnoticed for years and can lead ultimately to liver failure. We are focusing on two vaccine candidates for HCV – one of them a DNA vaccine – and have demonstrated the potential of such a vaccine using mouse model systems.

Impediments to the use of nucleic acid vaccines are the technologies required to formulate and deliver them. Thus, we are investing a significant effort in the development of novel vaccine formulations for both nucleic acid and protein vaccines that can be effectively delivered in a non-invasive fashion.

Neonatal Immunization

Many life-threatening illnesses can occur during the first few weeks of life when the newborn's immune system is not fully developed. Thus, vaccines are required for delivery to very young humans and animals to create strong immune responses at the mucosal surfaces (of the respiratory tract, for example) where most infections occur.

Vaccination of older children with more developed immune systems is one of the most effective means of reducing illness and death. However, few vaccines are available to children in developing countries and nearly two million children die of vaccine-preventable diseases each year (World Health Organization). This is due to issues such as a lack of infrastructure for vaccination programs, transportation issues, and the requirement for multiple vaccinations for most diseases. Conceptually similar problems are also encountered in newborn animals.

VIDO is participating in the Grand Challenges in Global Health initiative of the Bill & Melinda Gates Foundation, an effort targeted at reducing barriers to the prevention of disease in children worldwide. Specifically, we are developing single-dose vaccination technologies for very young children using *Bordetella pertussis*, the cause of whooping cough, as a template system. We have developed a unique model to study this disease in swine and have identified components of mammals' innate, or natural, immune system that are critical to prevention of disease.

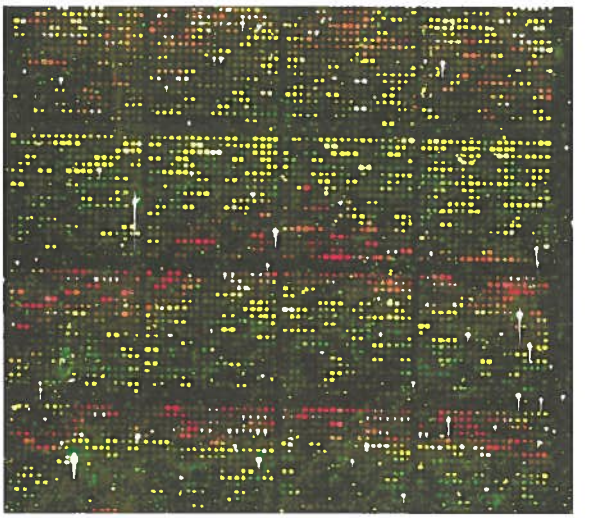
In collaboration with a number of researchers in Canada and Korea, we will be using this model to study the induction of immunity in newborns. With this knowledge, we can develop vaccine formulations and methods of vaccine administration that will be effective in newborns of all species. In addition, strategies to enhance the transfer of immunity from mother to child will be developed as a second method of protecting this high–risk population.

This research effort, while focused on whooping cough, is also applicable to a variety of other diseases affecting young children. The Krembil Foundation is contributing support to the development of early-childhood vaccines at VIDO including whooping cough and similar studies on respiratory syncytial virus (RSV) – the leading cause of respiratory infections in infants worldwide. RSV is also common in young calves, where it is referred to as bovine RSV. There is no licensed vaccine for children and vaccines for cattle are only moderately effective.

Pathogenomics of Innate Immunity

The innate, or natural, immune system is the first line of defence in humans and animals due to its non-specific nature and rapid response. Historically, it was thought to be separate from acquired immunity, the type of response leading to long-term immunity following infection or vaccination. However, we now know that the two systems are linked and the response of the innate system directs the longer-term response. Thus, it is critical to understand the interactions of pathogens with host cells and the relationship of these interactions to innate immune responses.

Genomic technologies, especially microarrays, are powerful tools for the study of how animals respond to infection at the level of gene function. These tools permit the simultaneous measurement of changes in patterns of gene expression or activity for all genes in an organism. In collaboration with researchers in Canada and abroad, we have been using these techniques to define how animals and humans respond to infection, vaccination, or treatment with compounds that modulate the immune system. This has resulted in the identification of gene targets that may be useful for the induction of stronger, longer-lasting immune responses.



A microarray is a grid of thousands of genes. Each dot represents a gene and the colours represent different states of activation (on, off or no change).

More recently, we have expanded this collaboration to include groups at the Sanger Institute (United Kingdom) and the National University of Singapore, and together we are focusing on innate immune responses to Salmonella infection in a variety of species. Target genes are being studied in mice and cattle.

By understanding the innate immune system and the key pathways and decision points involved, VIDO researchers hope to identify control points that can be used to resolve infections more effectively and enhance the efficacy of vaccines through novel formulations which target key pathways.

Immune Modulation

Over the past two decades, we have witnessed the emergence of several pathogens of humans and animals that are resistant to antibiotic treatment, due in part to the widespread use (and abuse) of antibiotics. There has been increasing public scrutiny regarding the routine use of antimicrobials in animal feed, and some countries have banned their use entirely. Thus, there is a clear need for the development of new control strategies.

The immune system has all of the tools necessary to carry out this task by itself, but it needs to be stimulated in an appropriate fashion before its power can be harnessed. Ultimately, we believe that therapies that harness the natural potency of the immune system will be much more sustainable than those that target the pathogen directly.

Over the past two decades, we have witnessed the emergence of several pathogens of humans and animals that are resistant to antibiotic treatment, due in part to the widespread use (and abuse) of antibiotics.

Over the past decade, several molecules capable of carrying out this task have been identified, including synthetic CpG DNA - CpG oligodeoxynucleotides (ODN). These are "signatures" of the presence of pathogens which activate the innate, or natural, immune system, resulting in natural control of the organism. Originally discovered in 1994 by Dr. Arthur Krieg, CpG ODN have been effective in the treatment of many infectious diseases. VIDO has been active in the study of how CpG ODN works using several animal models, and we have shown proof-of-concept for their use in the prevention of infections of poultry and cattle. Due to linkages between the innate immune system and the acquired immune system – the type of response leading to long-term immunity following infection or vaccination – these compounds can also be used to enhance humans' and animals' response to vaccines, both in terms of the quantity and quality of the responses.

In addition to CpG ODN, VIDO is working on another stimulator of innate immunity called host defence peptides. These small molecules are found in all animal species and are key activators of innate immune pathways. In some cases, they can kill microbes directly. In collaboration with Dr. Bob Hancock at the University of British Columbia, we are using engineered molecules he has developed to enhance the effectiveness of vaccines and to use as stand-alone therapeutic compounds for animals.

VIDO is also developing ways to improve stimulation of the innate immune system by studying the interactions between these compounds and host cells, and by studying the effect of targeting different immune response pathways through the combination of different stimulatory compounds.

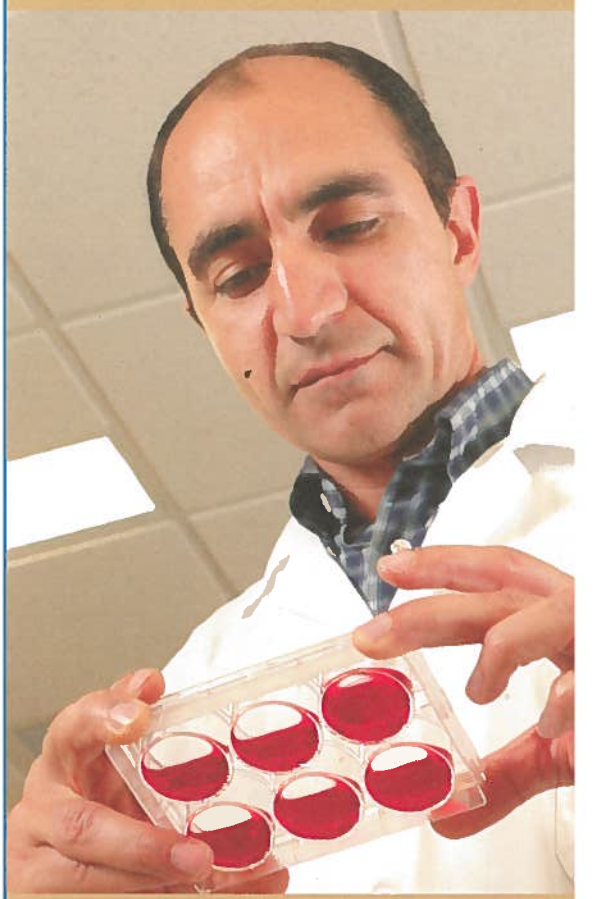
Vectored Vaccines

Live viruses that have been rendered safe by modification of their DNA can be used to deliver a second vaccine antigen – a substance that induces an immune response – from another organism. These viruses can also be used in conjunction with novel diagnostic methods to differentiate vaccinated animals from infected potential carriers of the disease. As vaccine delivery vehicles, the natural infective capability of a virus is co-opted. Live vaccines typically induce a stronger, more balanced and longer-lasting immune response than killed vaccines or vaccines made from part of a pathogen. Live vaccines have many advantages. They can be delivered by needle-free methods, they induce a balanced and long-lasting immune response, they do not require the addition of strong compounds (adjuvants) to bolster the immune response, and they are economical to produce. Furthermore, they are capable of inducing immunity at the pathogen's site of infection due to the vector's natural infection site.

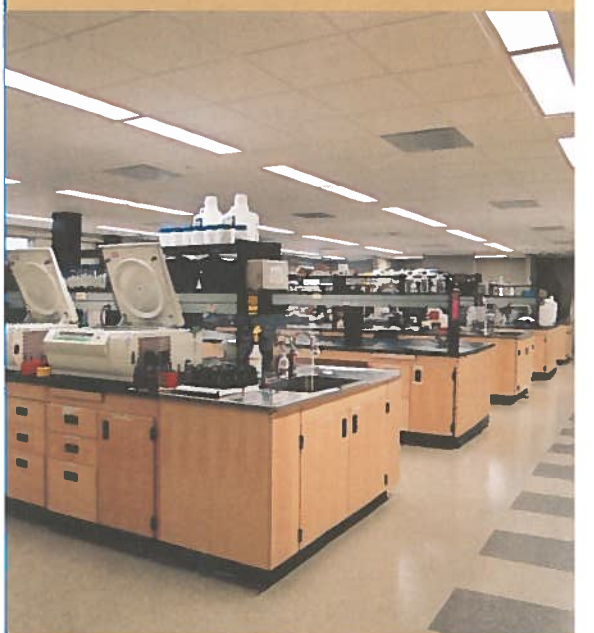
VIDO has worked in this area for the past two decades and we have developed successful strategies for the use of crippled strains of *E. coli* and bovine herpesvirus-1 (BHV-1) as vectors. BHV-1 is part of the bovine respiratory disease complex, which is estimated to cost the North American cattle industry approximately $1 billion per year. VIDO has successfully created a vectored vaccine candidate against bovine herpesvirus-1 that led to significant immune responses when tested in cattle. More recently, we have been developing animal adenoviruses as vaccine delivery vehicles for cattle, swine and humans.

VIDO is also looking to create a vectored vaccine that will protect cattle against intestinal pathogens such as *Cryptosporidium parvum* and bovine coronavirus, which can cause calf scours, a diarrhoeal disease.

Research in swine includes a vector against the swine influenza virus and development of a vaccine against the porcine respiratory and reproductive syndrome (PRRS) virus, which causes severe respiratory distress in young pigs and abortions in the last term of gestation, costing an estimated $600 million annually in the U.S. alone.



Research associate Dr. Shokrollah Elahi



Dr. Paul Hodgson, Associate Director, Business Development

Strong relationships with the livestock producer industry are particularly important given the link between emerging human diseases and animals.

Relationships are Key to VIDO Success

Dr. Paul Hodgson, PhD, MBA
Associate Director, Business Development

In this, my first report as a member of Senior Management, I am pleased to state that 2005 was another commercially successful year for VIDO. I should note that since my start date was January 1, 2006, this success reflects the valued contributions of Dr. Louis Desautels, now retired.

In the past year, VIDO completed 38 new agreements with organizations throughout North America and the world. The majority of these were revenue-generating; however, a large portion focused on setting the groundwork to enhance the international collaborations of our scientists.

Our communications officer, Tess Laidlaw, has been working to convey VIDO's evolving abilities and achievements to our stakeholder groups. Producers remain one of these key stakeholder groups and act as a vital conduit to the livestock industry. We have enhanced connections with producers by dedicating Sherri Hueser as a first-point-of-contact. Strong relationships with this industry are particularly important given the link between emerging human diseases and animals. The link also emphasizes the increased importance of VIDO's research into technologies applicable to multiple species and diseases. These "platform" technologies remain a primary focus at VIDO and will ensure that we remain competitive in research aiming to protect humans and animals.

A personal highlight of the year was my opportunity to meet Bill and Melinda Gates, the world's most financially successful couple and directors of its largest charitable foundation. This opportunity arose through VIDO's success in the Grand Challenges in Global Health initiative of the Foundation. The enthusiasm the Gates portray for research to improve health in developing countries is truly inspiring. In addition, the opportunities and partnerships that will arise from the unique network of investigators united through the Grand Challenges initiative should strengthen research collaborations aimed at improving health in developing countries and enhance the efficiency of research. Ultimately, this initiative will allow biotechnology products to more rapidly enter the marketplace and have a positive impact.

In closing, we remain grateful for the support from federal and provincial governments, the pharmaceutical and livestock industries, foundations, and the University of Saskatchewan. Moving forward, VIDO will continue to nurture relationships with our current funding partners and actively develop long-term associations with new partners. Throughout this process, our best ambassadors are the VIDO employees and alumni who facilitate active relationships with outside organizations.

Members of the VIDO Grand Challenges team speak with Bill Gates in Seattle in November, 2006.

From left, Paul Hodgson, Blake Ball (member of University of Manitoba team), Volker Gerdts and Lorne Babiuk

Carol Martel, Chief Financial Officer

Funding for Researchers Sustains VIDO Objectives

Carol Martel, CMA
Chief Financial Officer

Our position as a leader worldwide in the research and development of vaccine and immunotherapeutic technologies for livestock and humans is supported by an annual budget of approximately $12 million. As a non-profit organization owned by the University of Saskatchewan, we are funded by:

- federal and provincial governments
- livestock industry councils and agencies
- foundations
- competitive grants
- contracts and services, and
- royalties and licensing fees.

The support of foundations, represented by the Bill & Melinda Gates Foundation and the Krembil Foundation, is a new component in our funding structure.

We are also grateful for the support of the University of Saskatchewan, which maintains, as part of its normal operations, various infrastructure services (utilities, caretaking, building maintenance), and financial and administrative functions relating to VIDO.

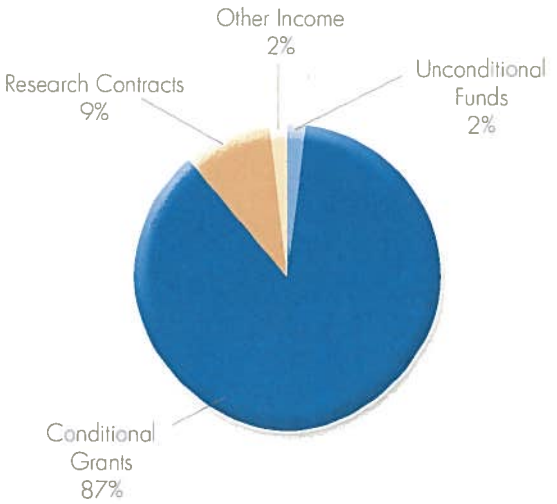
VIDO identifies research objectives and uses a team concept to achieve identified milestones. The objectives become projects requiring an allocation of organizational resources ranging from financial and material to human resources. Successful projects are those that best meet the organization's strategic direction.

The support of our financial partners allows us to pursue objectives ranging from scientific discovery in nine research programs to protect animal and human health; to intellectual property and its application to commercial products; to recruiting and training of more than 140 highly qualified scientists, technicians, postdoctoral fellows, graduate students, summer students and administrative staff.

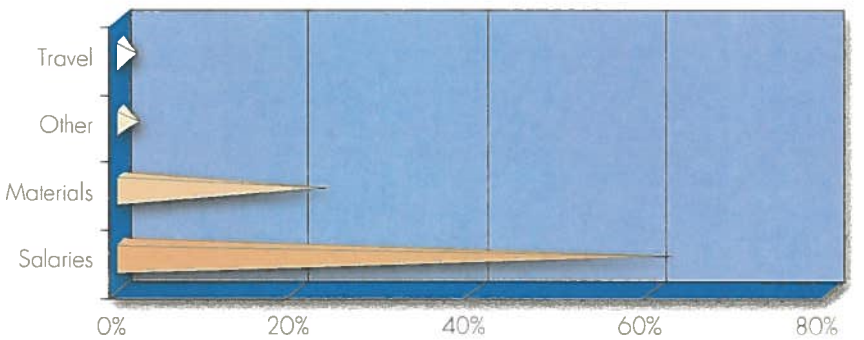
We thank our partners for their support and their faith in our organization.

The $19 million VIDO expansion, opened in 2003, was supported by the Canada Foundation for Innovation, the Province of Saskatchewan, the Province of Alberta, Western Economic Diversification Canada, Genome Canada and the University of Saskatchewan.

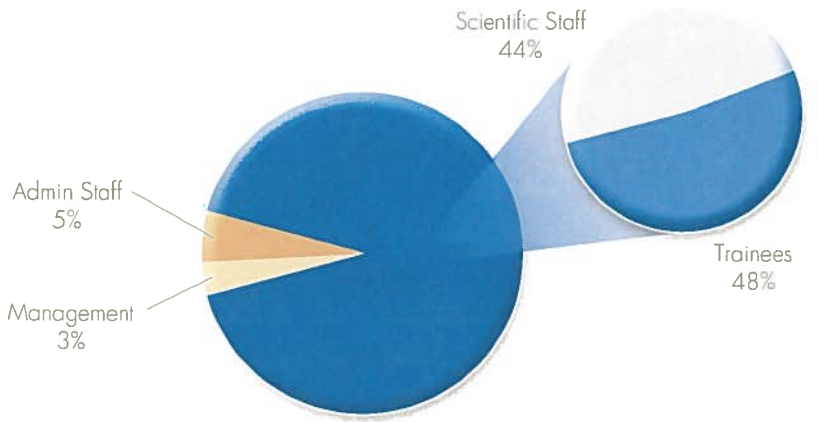
2006 Sources of Revenue

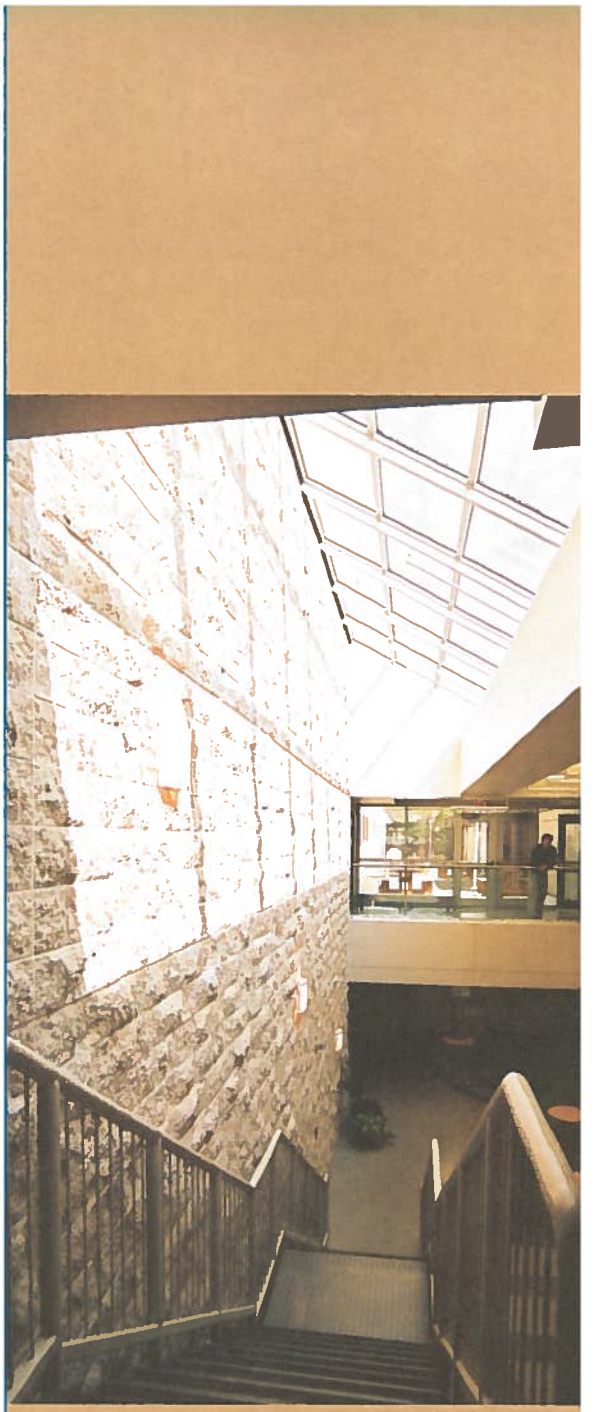


2006 Expenditures by Category



2006 Staff Ratios





Vaccine and Infectious Disease Organization

Contributors

Alberta Agricultural Research Institute (AARI)
Alberta Beef Producers
Alberta Livestock Industry Development Fund Ltd.
Alberta Milk
The Banting Research Foundation
Beef Cattle Research Council
Bill & Melinda Gates Foundation
British Columbia Cattlemen's Association
Canadian Pork Council
Canada Research Chair
Canadian Institutes of Health Research (CIHR)
Canadian Liver Foundation
Cattle Industry Development Council
Centre hospitalier universitaire (CHU) Sainte-Justine
Dairy Farmers of Ontario
Genome Canada
Government of British Columbia - Ministry of Agriculture and Lands
Government of Saskatchewan - Department of Learning
Harvard School of Public Health
Kamloops Stockmen's Association
The Krembil Foundation
Manitoba Pork Council
Michael Smith Foundation for Health Research
National Canadian Research Training Program in Hepatitis C
National Pork Council
Natural Sciences & Engineering Research Council of Canada (NSERC)
Ontario Cattlemen's Association
Ontario Pork
Poultry Industry Council
Province of Manitoba
Public Works & Government Services Canada
Saskatchewan Agriculture, Food and Rural Revitalization
Saskatchewan Cattle Marketing Deductions Fund
Saskatchewan Council for Community Development
Saskatchewan Health Research Foundation
Saskatchewan Horned Cattle Trust Fund
University of Georgia
Western Economic Diversification Canada

Photo Credits

www.debramarshall.ca
University of Saskatchewan, Division of Media and Technology
Stantec

Vaccine and Infectious Disease Organization
120 Veterinary Road
Saskatoon, Saskatchewan Canada

University of Saskatchewan