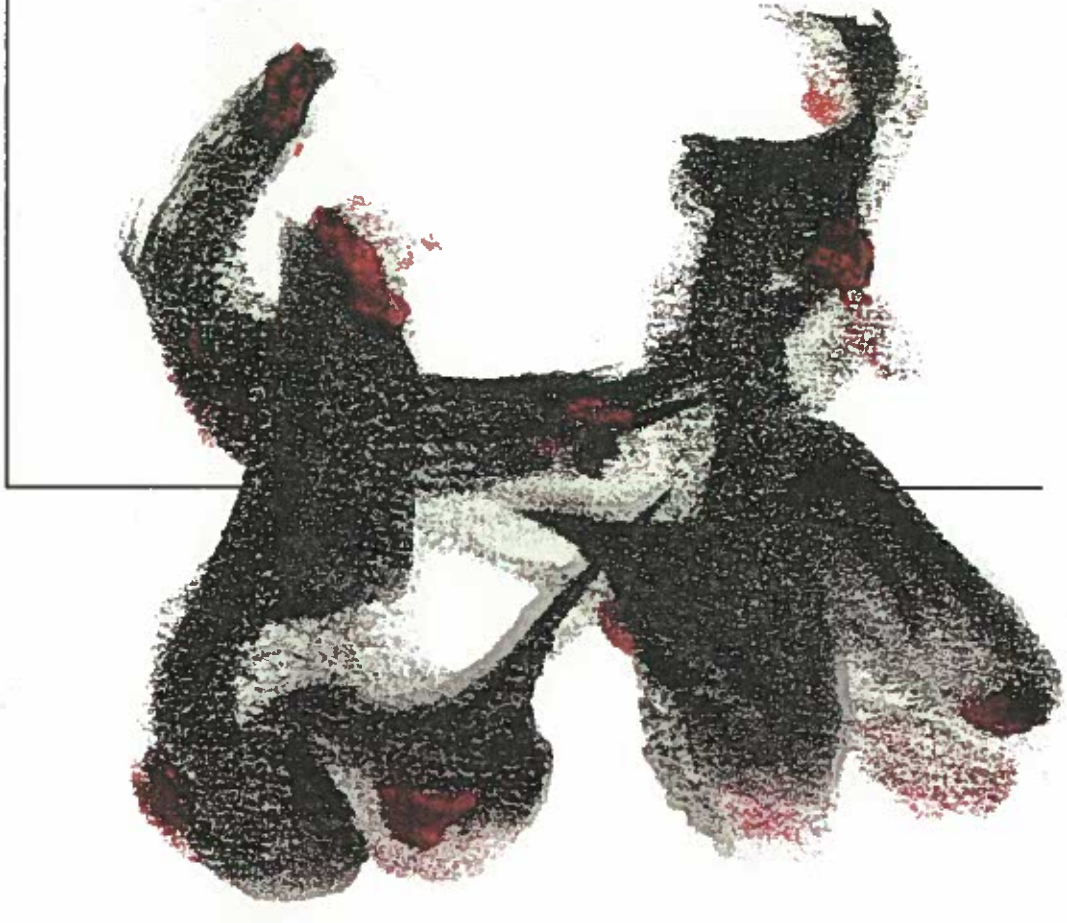
ANNUAL REPORT



2004 | 2005

GenomePrairie

Our cover image this year can be interpreted as showing two phosphorylated protein molecules forming a heterodimer with activating kinase activity. We also see an animated dance of whirling partners, a metaphor for the impending mitosis of Genome Prairie into Genome Alberta and the new GP office that will cover Saskatchewan and Manitoba.

About the artist – Dr. Morley D. Hollenberg

Educated from an early age both in the arts and sciences, Morley began calligraphy-based brushwork in 1985. His free-form calligraphic images are based on the intrinsic energy and visual motifs that can be observed in nature at the macroscopic and microscopic levels. The abstract brushwork forming the images arises from the movement and composition present in traditional Asian calligraphy.

GenomePrairie

Genome Prairie
Suite #115, 3553 – 31 Street NW
Calgary, Alberta
Canada T2L 2K7

This has been another remarkable year for Genome Prairie, with all our nine projects and platform now fully activated, covering research areas of human health, genomic sequencing, agricultural crops, bioinformatics, technology development and GE3LS. This continues to demonstrate the breadth and depth of expertise in the Prairie region as well as our researchers' abilities to work across Canada as a Team.

Together these projects are valued over $110 Million and are generating many patents and publications, training highly qualified personnel, and contributing to public outreach and policy development. We are also laying the foundation for industrial and commercial development as well as next-generation research studies, as Genome Canada moves forward in its renewal process. Considering our projects and corporate office funding together, we have finally achieved full co-funding in contributions, which has been a very important milestone in our growing success.

Our diverse partners include scientists from academic institutions, federal labs and corporations, with researchers located in every region across Canada and multiple collaborative efforts proceeding internationally.

We thank the Province of Alberta, Western Economic Diversification and Genome Canada for helping us maintain and grow our GP Corporate activities. This support for the corporate office, an ongoing issue and concern for the operations of GP, has been critical to our success.

Chair & President's Report

As we look into the immediate future there are two major trends that will have a huge impact on our operations. First, agreement has been reached among our key partners on a move forward strategy with Genome Prairie refocusing its efforts on Manitoba and Saskatchewan and the creation of Genome Alberta to focus on the province of Alberta. We expect this will lead to an overall expanded investment and will have huge impact on genomic research in the Prairie Provinces. Second, Genome Canada and the Regional Genome Centres are beginning our second five-year period of funding, accompanied by Genome Canada's Competition III. There will be new opportunities for exciting research projects and platforms, but also greater expectations for socioeconomic benefits from existing and new programs.

We anticipate new challenges especially with the relocation of the Genome Prairie office to Saskatoon and a proposed satellite office in Winnipeg, as we rebrand and refocus GP. We have much reason to be optimistic since our research teams and our corporate strategy have a proven track record upon which we can build, and clearly this will depend on maintaining and strengthening our partnerships in these Provinces. We are setting even higher goals for Genome Prairie as it enters into the next phase of Genome Canada funding, and look forward to providing our scientists and partners with the best chance to be successful in future opportunities that will add value to Saskatchewan and Manitoba.

Dr. Pete Desai
Chair, Board of Directors

Dr. Randal Johnston
President and CEO

Public outreach activities at Genome Prairie have had considerable success in providing our youth, the general public and the media with opportunities to gain knowledge and understanding of genomics.

Perhaps our most visible impact during this past year has been through the "GEEE! In Genome". This is an innovative and interactive travelling national exhibit that introduces the public to the world of genomics. After earlier events in Ottawa and Vancouver, the exhibit was opened at the Saskatchewan Science Centre in Regina in January, 2004 where over 15,000 people visited the Museum. Winnipeg hosted the exhibit from April to June, and the Provincial Museum of Alberta in Edmonton was host from July to October. A total of seven public forums were scheduled throughout the Prairie region from January to October covering many controversial topics. A number of educational programs accompany the exhibit along with program videos and hands on activities. The GEEE! In Genome" suitcase is a portable exhibit which can be transported to remote, smaller centres. Due to the geographic breadth of the Prairie Provinces, the suitcase exhibit has been extremely popular among teachers and students alike. In total, over 100,000 individuals benefited from the exhibit and associated programs.

Genome Prairie has also been very active in supporting educational programs throughout the Prairies. We offer cash awards at the Regional Youth Science Fairs throughout Alberta, Saskatchewan and Manitoba at the elementary, junior and senior levels. Another national competition that Genome Prairie sponsors and assists with 'in kind' contributions at the regional level is the Aventis Biotech Challenge. This program introduces students to the world of biotechnology by carrying out research projects of their own design. The student teams work with a mentor in their community who provides expert advice and access to equipment and supplies. This competition drives students to broaden their horizons and challenge their intellect. Project specific science programs are also key to our branding success within the education programs throughout the Prairie Provinces, such as the Young Scientist Footstep Award and the Enabling Technologies Proteomics Student Awards. Genome Prairie is recognized as a strong supporter in promoting science within our communities.

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Communications Report

In addition, Genome Prairie was instrumental in establishing the Life Sciences Communicators Network for Saskatchewan, which holds regular scheduled meetings throughout the year to network, share information and promote collaboration. Efforts to establish similar groups for Manitoba and Alberta are progressing.

Genome Prairie coordinates national and international activities with other Genome Centres and Genome Canada to ensure that we have a consistent program of branding and media engagement whenever relevant news items emerge. Our researchers regularly appear in local/regional newspapers, magazines, and television broadcasts. They have been recipients of awards and received noteworthy recognition for their involvement as researchers within their communities and abroad. Given the importance of genetically modified foods in the Prairie agricultural economy, plus continual progress in biomedical research in disease diagnostics and therapeutics, we have regular opportunities to convey our positive and exciting message to the public.

Francophone schoolchildren enjoy the GEEE! in Genome exhibit in Winnipeg.

Building and sustaining relationships with the media, institutions and federal and provincial governments is an ongoing team effort within Genome Prairie. We solicit continual communication and feedback as we move forward in this fast paced environment.

Each year we continue to set the bar higher and achieve greater results as we share the excitement of this scientific arena and roll out the national and regional communication strategies.

Donna Coad
Communications Officer

Chief Scientific Officer's Report

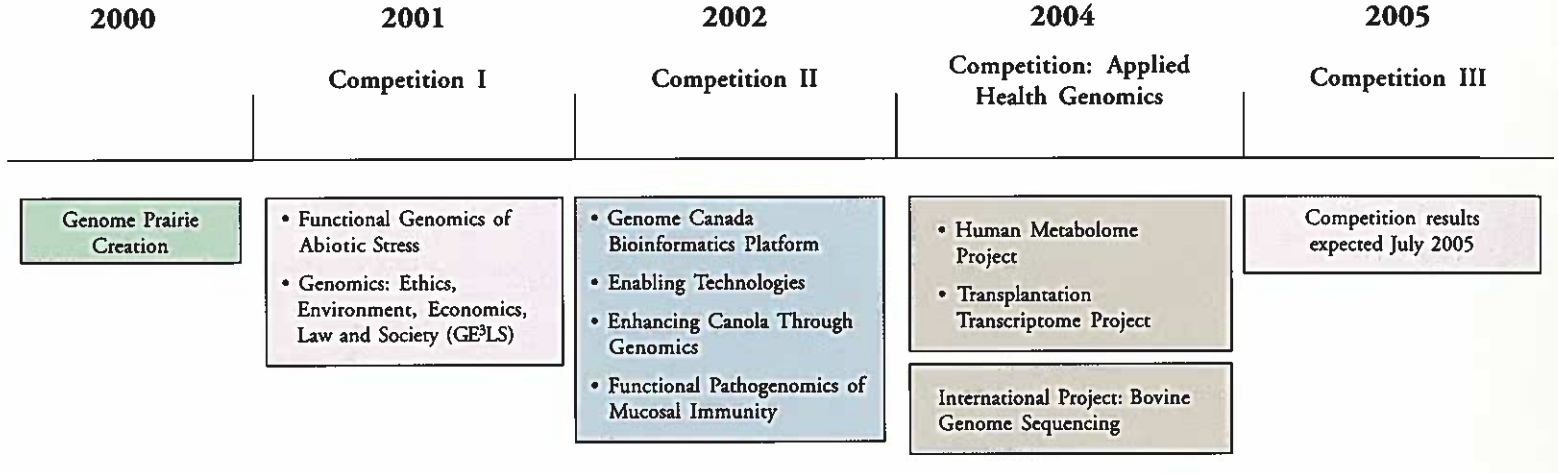
Genome Prairie is in its fourth year of existence and we have made very impressive progress since our inception. All our Competition I and Competition II projects have now undergone and passed the Genome Canada coordinated scientific mid-term review undertaken by an Independent International Scientific Peer Review Panel. Now in the final stretch, these projects are concluding their Genome Canada funded activities between September 2005 and March 2006. During the past year we have seen a gradual shift and evolution in the research focus in our biology projects from genomics resource building to utilization of these resources for the purpose of addressing fundamental biological questions. In the case of our Enabling Technologies project we have seen a further focus on instrumentation technology that has the highest potential for commercialization. This gradual shift resulted in a further increase in peer-reviewed scientific publications and acceleration in the development of Intellectual Property that will result in Socio-Economic Benefits for Canada. These projects have also started to plan their wrap-up activities to celebrate their achievements. Often these celebrations will be in the form of a workshop that brings together the Principal Investigators and as importantly the post doctoral fellows, research associates and graduate students that have been so critical to the success of all of these projects.

While the Competition I and II projects are completing their milestones, the Genome Prairie Applied Human Health Genomics projects and the Bovine cDNA project have been successfully activated this year. Furthermore, Genome Prairie has also been able to secure additional funding for its Bioinformatics Platform to provide additional services to our Human Health Projects.

In July of 2004, Genome Canada announced a Request for Applications for a new competition, called Competition III. We have seen tremendous interest from a large number of Prairie research groups in this Competition. This includes interest from current Genome Canada funded researchers that are interested in further building on the foundation established under previous competitions, plus non-Genome Canada funded researchers. Genome Prairie provided extensive guidance and direction during the application process and in the end a total of 15 Genome Prairie-led Project proposals were submitted to Genome Canada. A Genome Canada commissioned independent panel has carried out a Management and Co-funding Due Diligence review with the result that eleven projects successfully passed review and are proceeding for scientific peer review with results expected in July 2005. In this Competition a stronger emphasis has been placed on the potential of the proposals to realize Socio-Economic Benefits, international collaborations and an integrated GE3LS research plan. Because of our strengths in these areas we feel we are ideally positioned to execute on this refined focus. In our view the submitted proposals are of exceptional quality and we are looking forward to the results of this Competition. The future of genomics on the Prairies looks bright indeed!!

Dr. Gijs van Rooijen
Chief Scientific Officer

Genome Prairie Timeline



Project Team

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EGAS

Studies are underway to identify genes that provide improved resistance to cold and drought in cereal and canola crops.

Functional Genomics of Abiotic Stress

The **FGAS (Functional Genomics of Abiotic Stress)** project exploits a range of genomics and proteomics technologies to decipher the genetic mechanisms that underlie plant responses to various abiotic stresses, particularly cold, but also heat, drought and nutrient stress. Two crops of importance to Canada, wheat and canola, along with the model plant Arabidopsis thaliana, a close relative of canola, are used as experimental systems.

The FGAS research team has made significant progress to meeting the goals. These include the implementation of an array of tools including field genetic resources, protein analytical technologies, DNA sequence databases and genomic resources, that will empower the next project phase concerned with the elucidation of biological mechanisms governing stress adaptation in crops.

With regards to the wheat research on Low Temperature (LT) tolerance, 82,000 Expressed Sequence Tags (ESTs) from specialized libraries have been sequenced and deposited in the public domain as a strategic contribution to the international wheat genomic effort. This data set has been used in the design of a 17,300-feature LT enriched oligonucleotide array in collaboration with 3 international partners. Protocols for high throughput identification of promoters and transcription factors have been developed and protein interaction maps have been constructed. A 1.27 million clone Bacterial Artificid Chromosome (BAC) library has also been produced and provides 5.5X coverage of the hardy wheat cultivar 'Norstar' genome and three 500-loci mapping populations are in place that have been specifically designed to assist in the discovery of key LT tolerance genes.

With regards to the canola research, five custom Arabidopsis Serial Analysis of Gene Expression (SAGE) libraries have been completed and 500,000 tags have been identified. Furthermore, a 25,000-feature Arabidopsis Oligo microarray has been developed. Molecular genetic analyses have revealed over 400 genes differentially expressed upon short-term cold stress. Functional characterization is underway for several candidate genes.

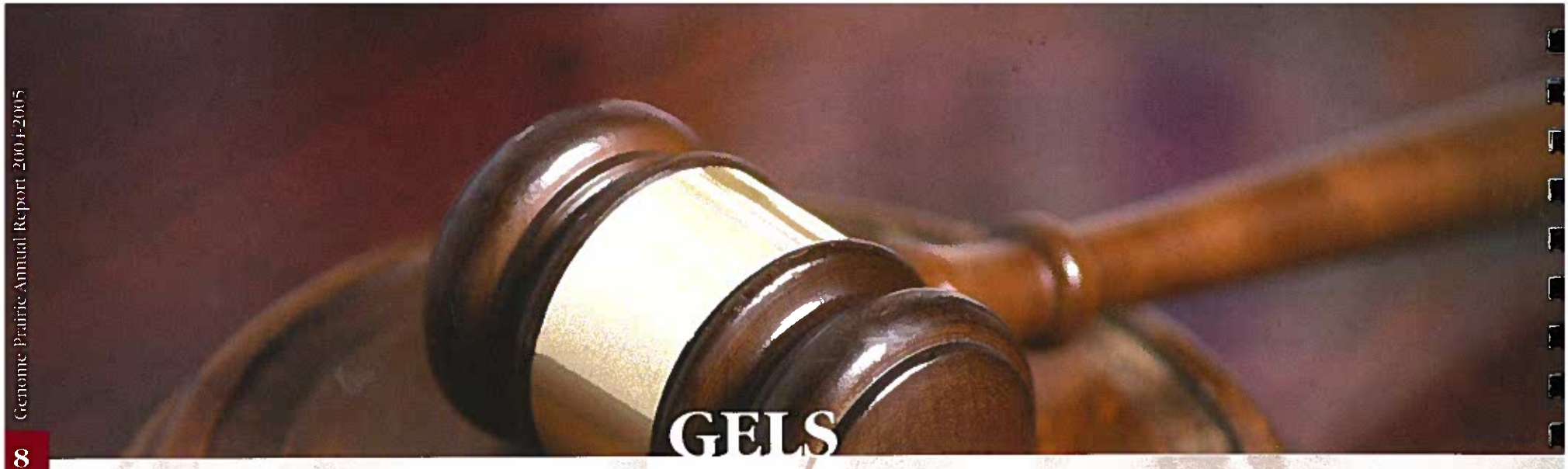
The FGAS team has also implemented an effective informatics infrastructure that permits the secure organization, analysis and exchange of data within and between the 2 project themes.

Genomics data are now being interfaced with proteomics approaches to identify lead-candidate gene products whose expression correlates with cold acclimation in both canola and wheat plant systems. 200 canola proteins which that are differentially expressed under cold treatment have also been identified.

To date, the FGAS team has generated over 100 scientific contributions including publications and scientific presentations directly arising from the project; this number will increase, especially as the project continues to transition from an emphasis on resource development and gene identification to functionality testing.

The FGAS project has established collaborations with organizations such as the US-based NSF-sponsored '2010' program and USDA research network, as well as the researchers at the Australian Center for Plant Functional Genomics, to participate in global efforts in the elucidation of gene function(s) associated with crop stress adaptation. We have also made a significant contribution in the formation of international consortia involving Australia, the USA and the UK, for purposes of jointly developing genomics resources for Wheat and Brassica crops.

The FGAS project has seized the opportunity to develop a highly integrated genomics discovery platform that spans field crop genetics to advanced genomics resource development and bioinformatics. These developments have presented the project with international strategic opportunities in the area of crop genomics of direct relevance and socio-economic benefit to Canada. Knowledge gained from this project has the potential to improve the tolerance of all plants to environmental stresses, to lengthen their growing season and to improve the quality of crops of importance to Canada.



GELS

The advent of genomics technology requires new legal and regulatory approaches to balance benefits and risks to our society.

GE3LS (Genomics: Ethics, Environment, Economics, Law & Society)

Over its three and a half year tenure, the Genome Prairie GE3LS team has become a world leader in identifying and examining the major issues genomics raises in the arenas of intellectual property (IP) management, policy building, and public and stakeholder involvement. Through their success in publishing articles in internationally recognized journals, engaging the media and other stakeholders, and analyzing and informing the policy process, the researchers on our team have made significant contributions to understanding the relationships between genomics and society.

The GE3LS team has been influential in policy development both nationally and internationally. For example, we have contributed policy papers to many groups, including the Canadian Biotechnology Advisory Committee (CBAC), Industry Canada, Health Canada, the Canadian Food Inspection Agency, and Agriculture and Agri-Food Canada nationally, and to the OECD and FAO internationally, on topics ranging from GM food, gene banking, gene patenting and plant molecular farming.

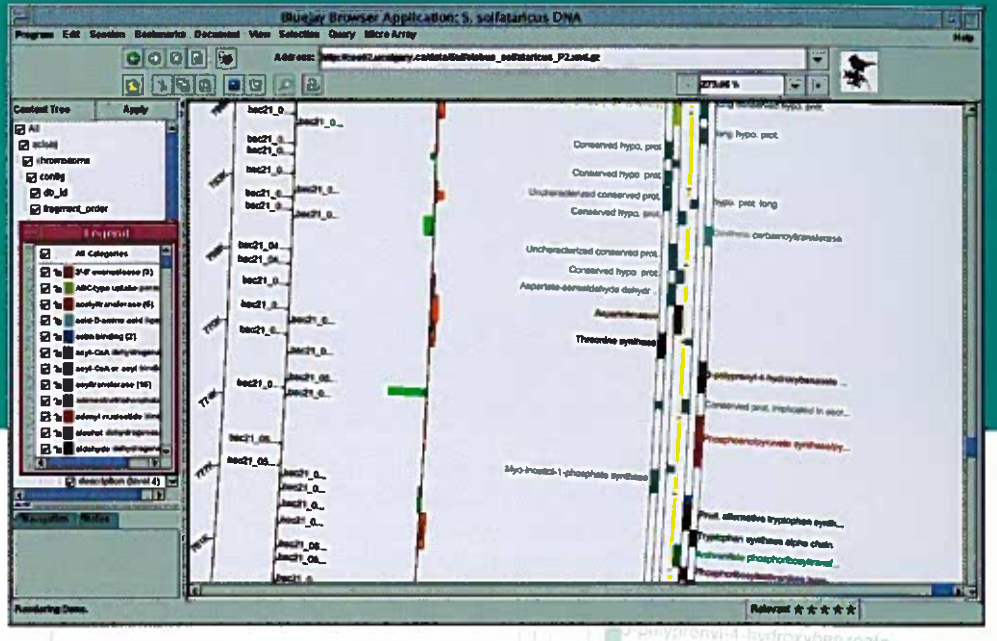
Beyond creating policy papers, we have also participated in policymaking in various other capacities: as members of CBAC and the Canadian General Standards Board Committee on Voluntary Labelling Standards for GM and Non-GM Foods; participation in the Canadian Institutes of Health Research (CIHR) Ad Hoc Working Group to draft new guidelines on stem cell research; providing testimony to the Standing Committee on Health on issues related to stem cell policy; participating in the Canadian Agri-Food Research Council's workshop on policy development for plant molecular farming; advising Health Canada's public consultation on xenotransplantation and FAO's on-line consultation on agricultural biotechnology and rural communities, as well as OECD's discussions on food safety and on human genetic research databases.

To complement this policy work, the GE3LS team has also organized conferences to bring together not only policymakers and GE3LS researchers but also other relevant stakeholders from industry and civil society:

- **"IP Rights and Living Matter: Issues and Assumptions":** Out of this GE3LS-sponsored conference in January 2004, a book manuscript has been developed which offers a framework for analysis of the issues and assumptions that underlie various perspectives on intellectual property management, for example co-existence of GM and organic crops, farmers' rights, technology transfer policies, and traditional knowledge and benefit-sharing, among others.
- **"Crossing Over: Genomics in the Public Arena":** This international conference held in April 2003 examined many facets of genomics in the public sphere - policy development, consumer and other stakeholder perspectives, media coverage, IP and innovation management - and has resulted in a book of the same title to be released in Fall 2005.

The GE3LS team plans to capitalize on the momentum built during this research, through continued collaboration among the principal investigators as well as through an ever-expanding network of national and international collaborators.

Bioinformatics



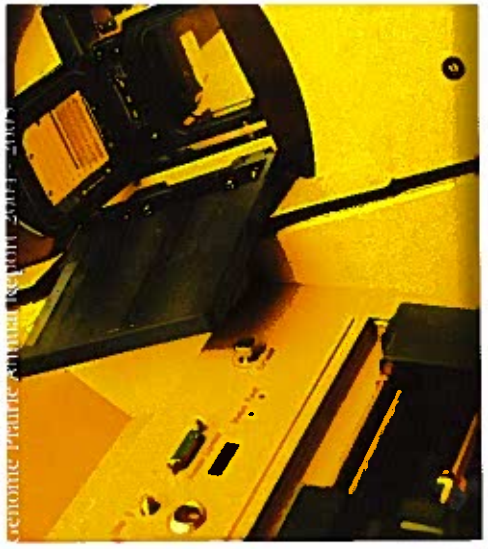
Automated software can analyse and display genomic data and help predict gene function.

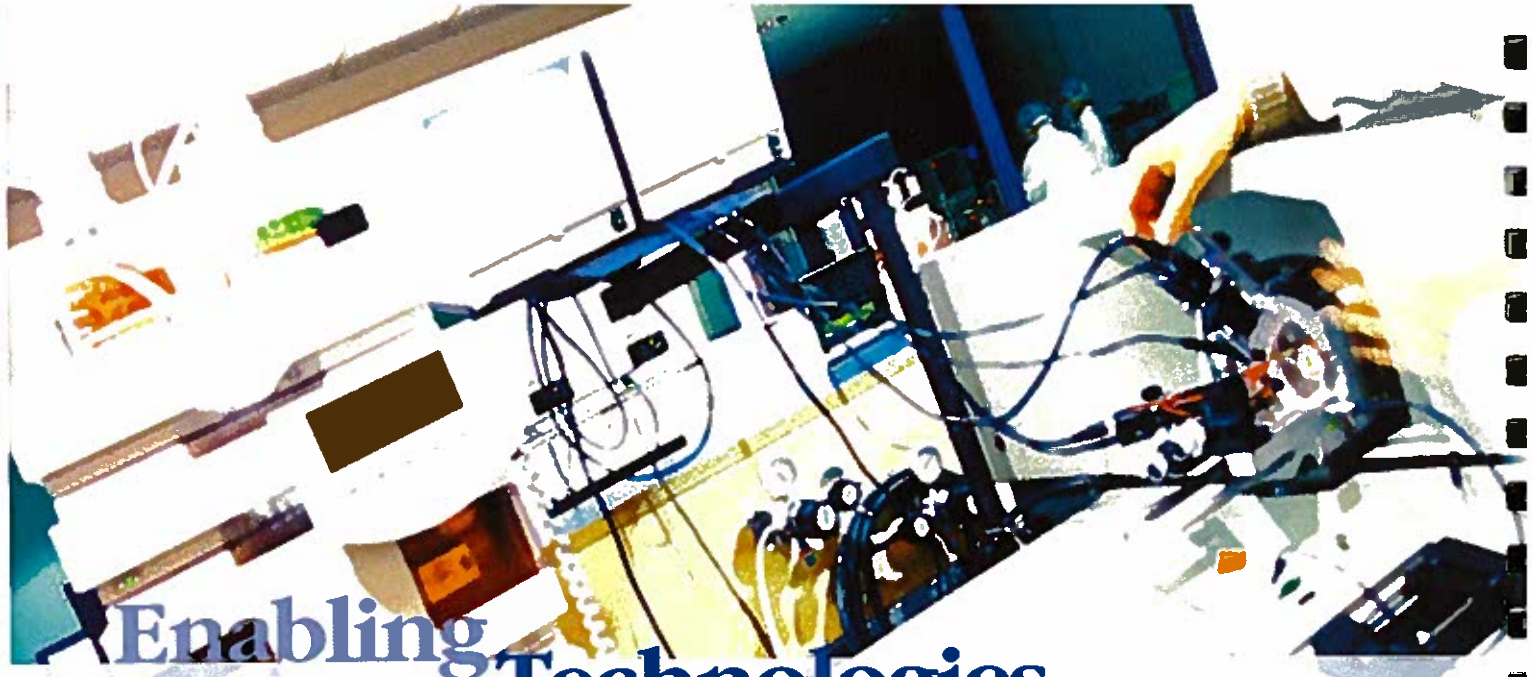
Genome Canada Bioinformatics Platform

The **Genome Canada Bioinformatics Platform** is in its 3rd year of successful operation. Our objective is the creation, through physical and intellectual developments, of a coherent bioinformatics infrastructure for Genome Canada. We are exploring new directions and will continue providing services throughout the next rounds of Genome Canada funding, such as the Platform Expansion that was approved last year and the current Genome Canada Competition III. The Platform Expansion funding will allow for provision of additional Platform delivered bioinformatics services to Genome Canada projects funded through the Applied Genomics and Proteomics Research in Human Health Competition. Projects providing services to the entire community through this initiative are Bluejay and the Help Desk.

There have been many successes within the Platform during 2004-2005 as we expand personnel, service provision, public outreach, and research. Key achievements include:

- Bluejay: A Solaris-powered server cluster provides web-based services to bioinformatics researchers through Bluejay, Magpie, Osprey, Jabiru, Decypher, BlastMachine, and GeneMatcher, receiving over 50,000 page requests a month from across the globe. Bluejay has been released via the web at http://bluejay.ucalgary.ca/ and is fully integrated with BioMOBY services. Since January 2005 Bluejay has had over 1,400 downloads from over 1,100 unique hosts and use is ramping up.
- BioMOBY: Awarded the Carnegie Institute of Canada award to build BioMOBY services connecting DragonDB with TAIR (the Arabidopsis Information Resource). The number of independent BioMOBY service providers has nearly doubled, from 40 to 75. The number of publicly accessible BioMOBY services is 216, almost double last year's count of 121.
- GenQuire: Able to import and export TIGR XML data into GenQuire's database, allowing users to view TIGR (The Institute for Genome Research) data directly, make changes, and output modified data to a community standard TIGR-XML format.
- Database Bias: Presented "Coming to a computer near you: The Genome Canada Bioinformatics Platform" at an Advanced Plant Science Seminar Series through the Department of Plant Science at the University of Manitoba.
- Database Analysis: Delivered 2 lectures at the Nanogenomics conference in Fortaleza, Brazil.
- Help Desk: Close to publishing their 40th bioinformatics newsletter and will soon reach 1,700 subscribers. Over 100 programs can be downloaded at: http://www.gchelpdesk.ualberta.ca/repository/SubmitRealSoftware.php
- Canadian Bioinformatics Resource: Registered user base has grown from 1,200 users in 2001 to over 1,436 in 2004. An integrated system of GRID services and Web services (BioMOBY-based) is being tested between Halifax and Calgary, for release in Summer 2005.
- Training: Successfully completed 4 Applied Computational Genomics Courses, with registration rising, and plans for expanded and updated topics.
- Administration and Funding: Developed leading edge project management methodology with Genome Prairie and leveraged the Genome Canada investment with an additional CAD ~$500K in 2004.
- The Bioinformatics Platform looks forward to continuing its provision of leading edge, integrated, and accessible bioinformatics services to research and industrial communities around the world.





Enabling Technologies

New generations of mass spectrometry instruments will accelerate genomics research.

Enabling Technologies (ET)

The **Enabling Technologies (ET)** Project, supports the development of innovative tools for proteomics research, integrates the activities of academic research teams from Alberta, Manitoba, Ontario, British Columbia and Québec with scientists at MDS Sciex and at Advanced Integrated MicroSystems (AIMS).

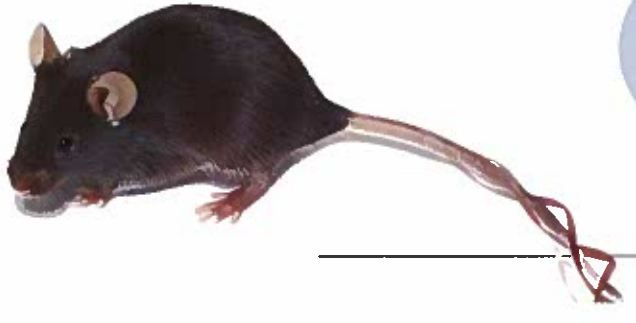
In the Project's second year of operation, important progress was made in four major technology streams: Microfluidics, Nanofluidics, Time Of Flight-Mass Spectrometry (TOF-MS) and Linear Ion Trap MS. The novel scanning modes of a new linear ion trap mass spectrometer were shown to have great utility for high-sensitivity proteomics applications. Equipping such an instrument with a prototype Matrix Assisted Laser Desorption Ionization (MALDI) ion source has further extended these capabilities. A novel combination of liquid chromatography with MALDI mass spectrometry (LC/MALDI-MS) using a heated droplet interface has been used to analyze protein complexes of membranes.

A range of new methodologies has also been developed. This includes a powerful new protein sequencing technique, an accelerated method for the production of labs-on-a-chip from plastics, and improved approaches to coupling these microfluidic devices with mass spectrometric analyzers. Three "Beta Sites" are now online to provide real-world prototype testing and application development for ET Project technologies. The coming year will see an expansion of the Beta Sites' role in demonstrating the broad utility of these tools for improved proteomic analysis.

The level of innovation within the Project is indicated by the intellectual property generated (nine patents filed by March 2004) and the strong publication record. Over twenty research articles have been published in leading journals such as Nature Biotechnology, Analytical Chemistry, and Proteomics. Presentations at international conferences have broadened awareness of the advances made by the Project's award-winning scientists. Closer to home, the Project launched the Annual Symposia on Enabling Technologies for Proteomics (ETP). The 2nd ETP Symposium (Calgary, September 2005) will be a world-class event, featuring recognized thought leaders and innovators discussing the latest developments in proteomic technologies.

In the Project's final year, effort will be focused on accelerating selected technologies of particular scientific and commercial promise to stages of development appropriate for commercialization.

The year following Project wrap-up will see the launch of several new products incorporating these technologies, including consumables and reagents for proteomics workflows; ancillary devices for protein sample handling and preparation; and major instrumentation for improved proteomic analyses. The ET Project is on track to achieve its ultimate objective - the development of novel bio-analytical instrumentation from research concept to mature commercial product, generating jobs, spurring new economic activity, and accelerating research on human health.



Enhancing Canola

Development of a Brassica plant from embryo to seedling.

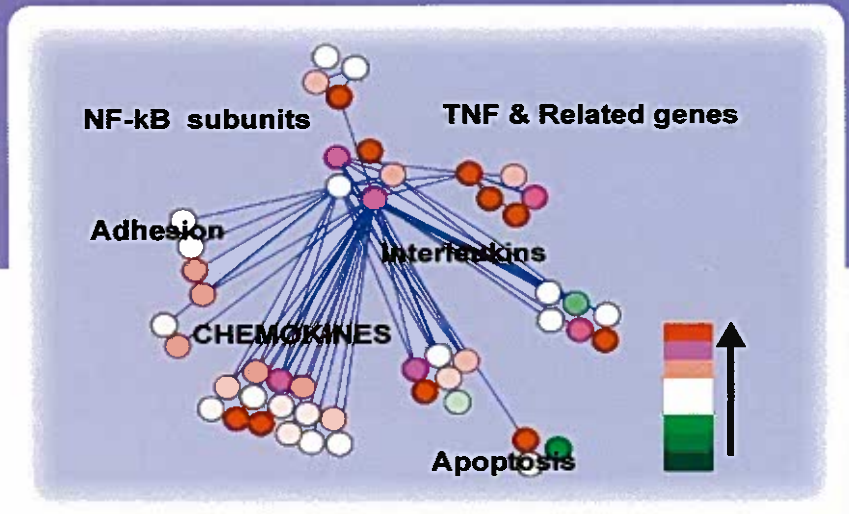
Enhancing Canola Through Genomics

The goal of the **Enhancing Canola through Genomics** project is to develop and employ genomic tools for the study of seed development and composition in Brassica oilseed crops. In the last year, researchers from the National Research Council and from Agriculture and Agri-Food Canada accomplished key objectives within the seed development and composition activities as well as in areas of communications and outreach.

More than 150,000 ESTs related to seed development have been sequenced and annotated since the start of the project. A Brassica cDNA microarray containing 10,000 unique genes is under development. A prototype of the DNA array will be evaluated within the next few weeks and made available to the Brassica research community after validation. Several potential genes that may play an important role in seed development have been identified from the collection of ESTs. These genes are currently characterized and tested in transgenic lines with the goal of developing new prototype cultivars of superior seed quality such as larger seeds. Systems have been developed to reduce/eliminate the expression of native napin and cruciferin thereby allowing the hyper-accumulation of synthetic seed storage proteins or proteins of greater economic or functional importance. A proof-of concept Synchrotron method was developed. This method will enable the rapid screening of Arabidopsis mutant seed libraries to identify genes playing a role in seed composition. Brassica BAC fingerprinting and Arabidopsis homozygous activation tagged lines milestones have been completed (see http://brassica.ca/).

In 2004, 10 papers related to the project objectives were published in peer-reviewed journals. In addition, 34 oral or poster presentations were presented at national and international genomics meetings. The project held two scientific meetings to review progress; the scientific advisory committee members attended one meeting and provided constructive recommendations that are being implemented. The project organized two workshops (www.genomeprairie.ca/canola/workshops.htm). The first dealt with the DNA microarray technology with emphasis in training researchers new to this technology. The goal of the second workshop, entitled "Application of Genomics to Canola Improvement", was to communicate and link with industry and plant breeders. The project successfully passed the Genome Canada midterm review process. Finally, a project newsletter was published and widely disseminated to inform other scientists and the public at large about our project.

With the last remaining year of the project, we expect that we will accomplish all the critical milestones as initially planned, thereby leading to additional original scientific publications and new intellectual property.



Gene expression can be increased (red) or decreased (green) following microbial infection.

Functional Pathogenomics of Mucosal Immunity (FPMI)

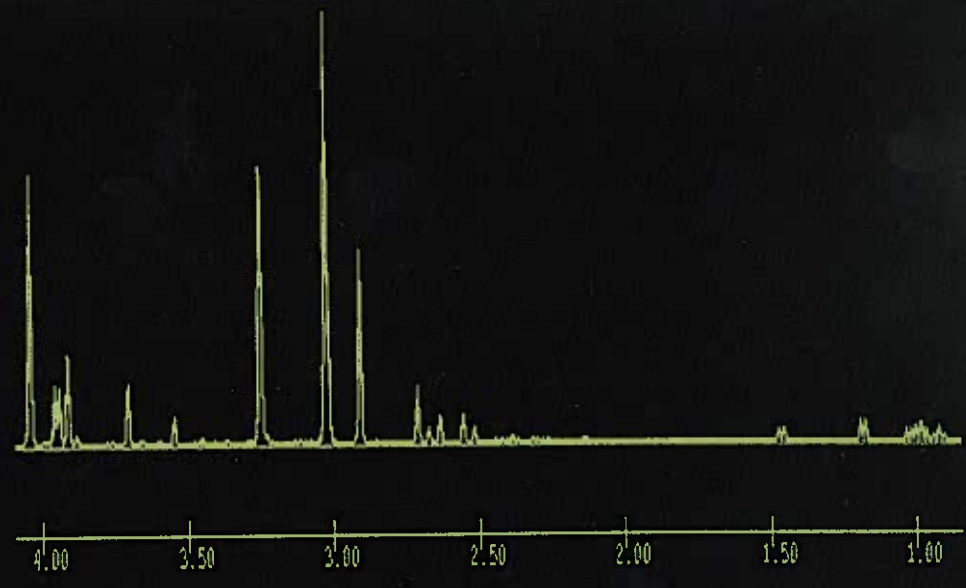
The **Functional Pathogenomics of Mucosal Immunity (FPMI)** program continued to utilize the genomics and bioinformatics expertise of the Vaccine and Infectious Disease Organization (VIDO), Inimex Pharmaceuticals, the University of British Columbia (UBC) and Simon Fraser University (SFU) to provide new information about the processes of disease and innate immunity.

We are pleased to report our major highlights from 2004.

- An International Scientific Review Committee gave the project high commendation for scientific progress and integration among the FPMI research partners.
- We secured substantial new co-funding, received numerous awards and published several manuscripts.
- Our corporate partner - Inimex Pharmaceuticals completed $8 million in Venture Capital financing and created an animal health subsidiary – Inimex Veterinary Research – in Saskatoon, Canada. Their principal scientist, Monisha Scott, was recognized as one of the world's 100 Top Young Innovators in 2004 by Technology Review, MIT's Magazine of Innovation.
- Project Co-Director, Bob Hancock, received the BC Innovation Council's Award for Career Achievement; and Brett Finlay received the Infectious Diseases 2004 Squibb Award and the BC Innovation Council's "Solutions through Research" Award.
- In addition, VIDO was awarded $19.2 million by the Canada Foundation for Innovation to create an International Vaccine Centre (INTERVAC) to protect humans and animals from the threat of emerging diseases.
- Recently, the Prime Minister of Canada visited VIDO to pledge an additional $24 million to this cause.
- Our scientific research has progressed rapidly with four new provisional patents filed. ArrayPipe (www.pathogenomics.ca) our open source microarray analysis tool averaged 80 unique web hits per month and SFU started development of two annotation databases for innate immunity interactions, InteractDB and InnateDB, to facilitate downstream data analysis.
- FPMI also started new collaborations with researchers from Cuba and Ireland to expand understanding of the interaction between bacterial pathogens and immunomodulators on host cells from several species.
- Unique patterns of host cell gene expression were discovered by microarray and PCR analysis in human and bovine systems. We have uncovered specific gene expression patterns and biomarkers associated with potentially fatal bacterial and viral infections in animals. The impact of immunomodulatory agents on these patterns will lead to a greater understanding of their ability to protect against infection of the host.

As we enter the third and final year of research we are focusing on determining the biological significance of altering the innate immunity genes discovered to play a role in host defense.

Metabolomics



Nuclear magnetic resonance spectra can be used to identify compounds in human biological fluids.

Human Metabolome Project

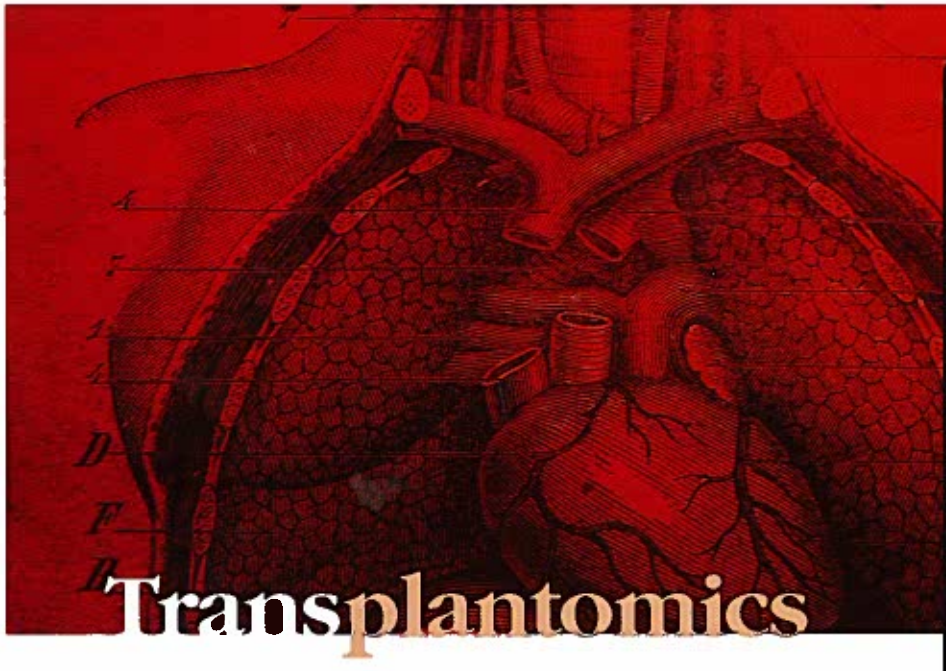
The **Human Metabolome Project** is focused on the rapid, high throughput characterization of the small molecule metabolites found in an organism. Since the metabolome (the whole set of metabolic entities and small pathway motifs in a cell, tissue, organ, organisms, and species) is closely tied to the genotype of an organism, its physiology and its environment, metabolomics offers a unique opportunity to look at genotype-phenotype as well as genotype-envirotype relationships. Metabolomics is increasingly being used in a variety of health applications including pharmacology, pre-clinical drug trials, toxicology, transplant monitoring, newborn screening and clinical chemistry.

A key limitation to metabolomics is the fact that the human metabolome is not at all well characterized. Unlike the situation in genomics, where the human genome is now fully sequenced and freely accessible, metabolomics is not nearly as developed. It is estimated that only _ to _ of endogenous human metabolites in blood or urine have been positively identified. Of those that have been identified, very few have any information on their normal concentration ranges. In contrast to DNA sequences that are publicly available in databases such as GenBank there are no "metabolite libraries" which allow researchers to obtain quantities of rare metabolites from which to standardize their instruments.

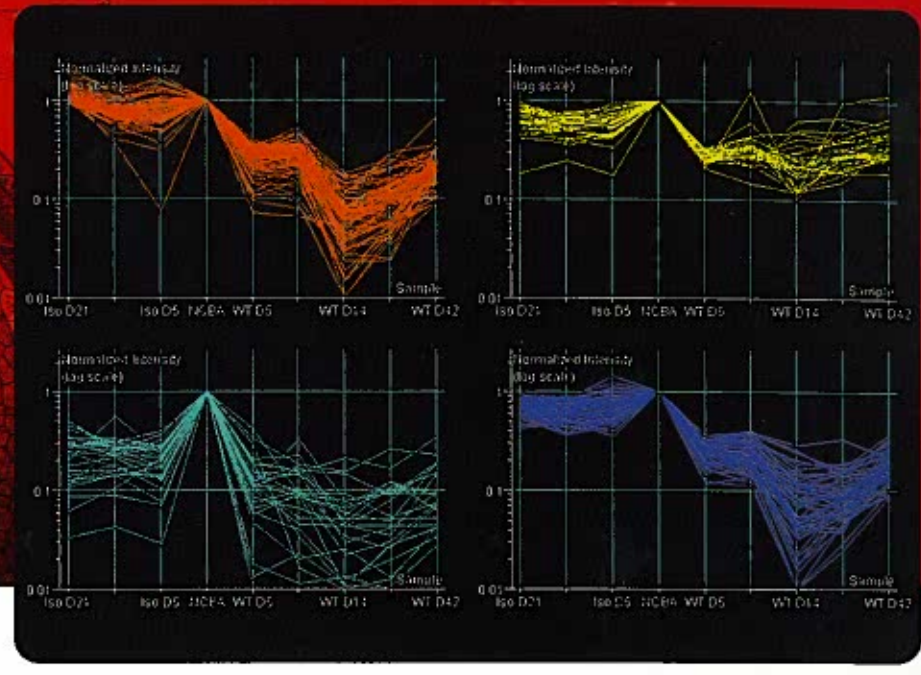
This Genome Prairie co-funded Human Metabolome Project is addressing these issues and is aiming to complete the human metabolome by 2007. This involves identifying, spectroscopically characterizing (via Nuclear Magnetic Resonance and Mass Spectrometry), and quantifying an estimated 1400 endogenous metabolites that can be found in urine, blood, Cerebrospinal Fluid and white blood cells. This project combines high throughput NMR methods along with other analytical techniques to identify and quantify metabolites and their concentration ranges from a large number of human samples. The data and the compounds isolated, synthesized or purchased for this project will be used to create a freely available electronic database - called the human metabolite database (HMDB) and a commercial chemical warehouse - called the human metabolite library (HML) – with quantities of these metabolites.

This project is being led by a team of eight scientists, computer scientists and clinicians from the Universities of Alberta and Calgary. In the first six months we have identified over 900 endogenous metabolites and have collected 200 compounds in our human metabolite library. A publicly accessible human metabolite database has been established and currently has over 150 entries.

The project has made great strides in these first few months and is poised to reach full productivity in the next year. The project is already planning on organizing its first scientific conference in the fall of 2005 and will be presenting at several international conferences. We expect that several novel discoveries will arise from the project including the identification and discovery of biomarkers, novel chemical synthesis and identification techniques, and novel bioinformatics tools for metabolic pathway analysis. This knowledge garnered and disseminated from the Human Metabolome Project will ensure that Canada remains a leader in the emerging field of metabolomics.



Transplantomics



Microarray chip technology can be used to identify gene families that vary together following tissue transplantation.

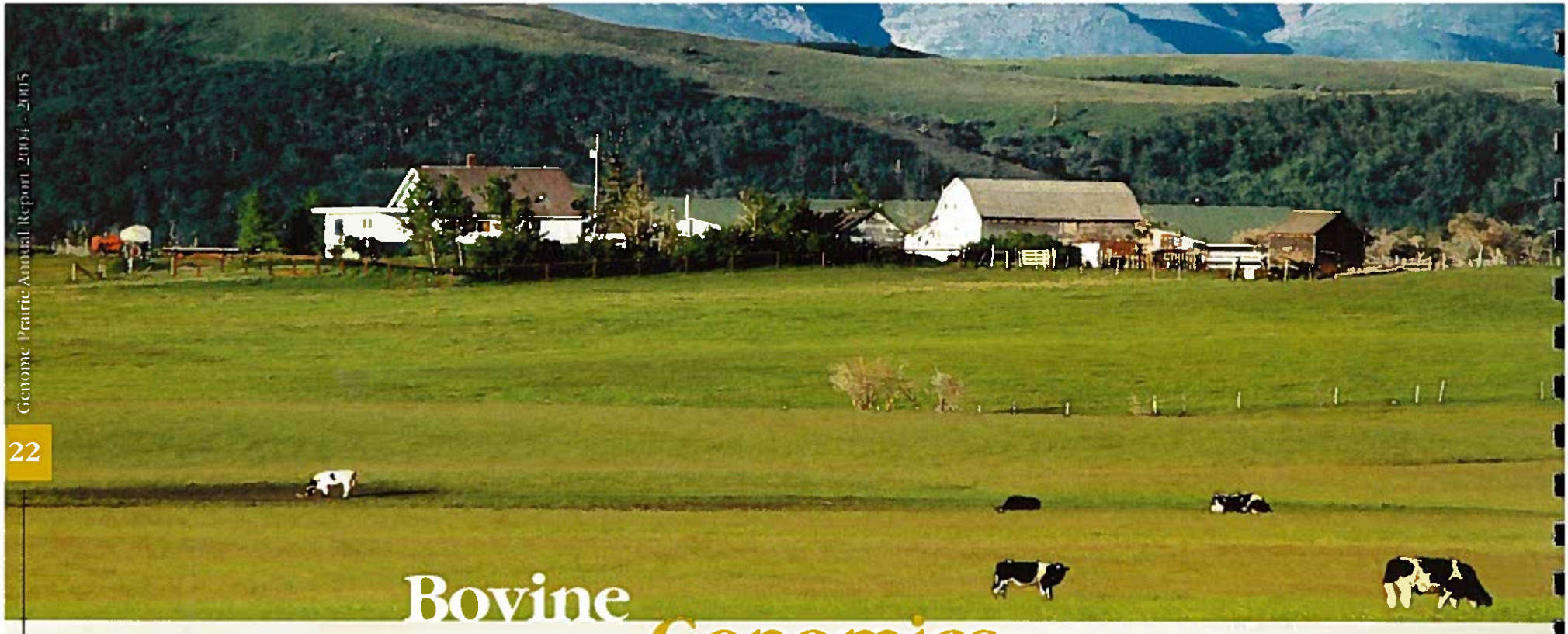
Transplant Transcriptome Project

The **Transplant Transcriptome Project** is devoted to new technologies in the field of organ transplantation, which is the definitive therapy for many forms of end-stage disease of the kidney, liver, heart, lungs, and small bowel, as well as replacement of islet function in diabetes mellitus. Approximately 200,000 people in North America currently have life-supporting organ transplants (kidney, liver, heart, lung), with about 25,000 new transplants performed every year. With modern immunosuppressive therapy, one-year post-engraftment survival approaches 90% for some organs. However, long-term graft survival is not optimal; in the current state of knowledge 20% to 65% of all grafts fail within five years post-transplantation and many others will fail later. Powerful drugs are needed to prevent rejection, and we have not been successful at accurately detecting and measuring rejection. Thus we often over-treat or under-treat.

It is the goal of this project to develop accurate tests that can determine when rejection is present and when it is not so that patients can be managed more effectively with fewer side effects. We also need to discover new drugs based on new understanding of molecular events. We are developing microarrays or 'gene chips' as tests to detect and measure kidney graft rejection mechanisms precisely and will validate these tests in a large-scale international clinical study.

Phase One of our project has begun where we are studying patterns of gene expression in kidney biopsies and blood of patients with rejection to define the patterns that correlate with their clinical problems and their conventional biopsy results. Concurrently, we are defining the patterns of rejection in mice, our model system, where we can analyze mechanisms precisely. Preliminary findings indicate that expression of a subset of gene transcripts preceded the establishment of diagnostic Banff lesions (the current gold standard) and were sustained with little change through day 42 despite massive alterations in the pathology. We believe that changes in transcript levels will establish diagnosis and quantify rejection BEFORE pathology changes and before parenchymal injury occurs. Equally important is the insight into disease mechanisms and potential targets for discovery.

These studies will create a new way of looking at transplant patients that will improve outcomes through more precise diagnosis. Currently the emphasis of this Project is on kidney transplantation rejection, but many of the new insights into mechanisms of rejection will be applicable to other organ diseases as well. This better understanding will aid in drug development and lead to many potential commercial applications in the diagnostic products and services areas.



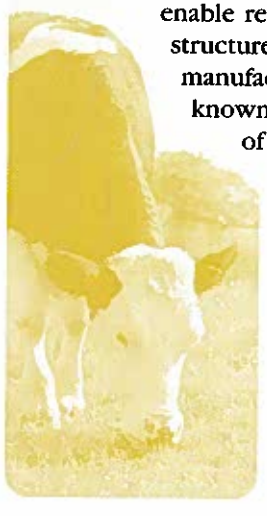
Bovine Genomics

Sequencing the bovine genome will ultimately help improve animal health and meat and dairy production.

Bovine Genome Sequencing

With the completion of the human genome sequence, the opportunities available for acceleration of genomics research activities in cattle have increased dramatically. This is even more valid now that the sequencing of the bovine genome has begun. One shortage that has been identified recently is a lack of adequate numbers of cDNA sequences for cattle which represent the coding regions of the cattle genome (or genes). Full-length cDNA sequences, which contain the entire protein coding sequence of genes, are important in uniquely defining transcribed genes and assigning function to those genes. As a result of the present effort, it will be possible to determine the fine structure of transcripts by providing details as to the position and structure of genes within the bovine genome sequence.

The aim of this project is to produce twenty cDNA libraries from bovine tissues that are suitable for full-length cDNA sequencing, while at the same time addressing a number of issues important to cattle industries in Canada and worldwide. To date seven libraries have been constructed and the first libraries have already entered the cDNA sequencing pipeline established at the Genome Sciences Centre (GSC) in Vancouver. The sequencing project undertaken at the GSC represents Canada's contribution to the international bovine genome sequencing project and will produce up to 600,000 EST reads and up to 412,500 full-length cDNA reads representing approximately 10,000 full-length cDNAs from tissues of importance to beef production. It is expected that at the end of this project, the Canadian contribution will have exceeded its original goals for this Project. The data bank generated will provide an inventory of genes and gene variants in cattle as well as details about the tissue specificity of these variants. Overall this will enable researchers to strengthen linkages between genotype and phenotype and therefore make stronger inferences with respect to structure/function relationships across species. The EST's generated will provide the basis for functional genomics studies through the manufacture of specific cattle microarrays to determine gene expression patterns and infer the function of genes with no previously known function as well as contribute to the identification of key genes relevant to cattle. These genes include those related to traits of interest to animal health, immune response to disease challenges and product quality. In this regard, the effort in Alberta will help establish a web-based interface to a relational database of all EST and full-length sequences, together with information on sequence similarity, tissue specificity and gene ontology.



The setting of goals for the next phase of the bovine genome project and the identification of research partners and funding opportunities to maximize utilization of the sequence information has already begun. On March 29-31 2005 an International Workshop entitled "Bovine Genome Project: The Next Phase" was held in Houston, Texas. This workshop was co-sponsored by Genome Canada and had strong representation from Alberta. We are looking forward to this next phase and hope and expect that Prairie researchers will continue to participate. Furthermore, we expect that this project will also catalyze the participation of other proposed livestock genomics projects such as in the area of porcine genomics. Historically, Genome Prairie has always had a strong interest in Agricultural genomics and we anticipate that this will continue in the future.

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ANNUAL GENERAL MEETING

Meeting held June 25th, 2004, Winnipeg, Manitoba
Next meeting to be held June 24, 2005, Calgary, Alberta

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