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## **Genomics-Enhanced Forecasting Tools to Secure Canada's Near-Term Lignocellulosic Feedstock Supply for Bioenergy using the Mountain Pine Beetle System**

<b>Sector</b>	Environment
<b>Genome Centre</b>	Genome British Columbia
<b>Project Leaders</b>	Jorg Bohlmann, UBC / Janice Cooke, U. of Alberta
<b>Budget</b>	Total budget = \$7,795,145 / GC contribution = \$3,691,649

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### **Project Description**

The recent mountain pine beetle outbreak in British Columbia, now spreading into Alberta, has caused unprecedented damage to the Canadian forest industry. The current infestation has affected more than 14 million hectares of pine forests and is the largest such epidemic in recorded history. Conifer forests are Canada's largest renewable source of ligno-cellulose, used for energy production, paper and wood products. Understanding the biology of the mountain pine beetle in order to use that knowledge for anticipating and helping to control future outbreaks is an important contribution to Canadian forest economics, particularly related to energy production. Although massive amounts of dead timber from the mountain pine beetle epidemic have created an unexpected surplus of potential energy feedstock, this will not necessarily provide a sustainable feedstock supply in the future. Before strategic investments are made in the forest industry, current methods of predicting feedstock need to be improved.

The mountain pine beetle infestation has three interacting components: the host trees, lodgepole pine and jack pine, the beetle itself and multiple beetle-associated tree-killing fungal species. Our study has four parts. First, we will carry out extensive genomic studies of all three organisms, with an emphasis on genes that are important in their interaction. Second, we will use this information to build a map that shows the inter-relationships of populations of these organisms in relation to geographic location, time, environment and climate. Third, we will use the above information to create models that could forecast the likelihood of a mountain pine beetle outbreak in any location at a particular time. Finally, we will use all of this information to make an analysis of the economics of forest use for energy production. A unique aspect of this project is our ability to combine all the genetic and genomic data with geographic and economic information to provide a detailed picture of the threat of a mountain pine beetle outbreak.

The overall goal of our applied genomics project is to generate new genomics-based information and tools for improved prediction of renewable energy feedstock supply from conifer forests, using the current mountain pine beetle epidemic as an example of an important host-pest-pathogen system.



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## **Bridging Comparative, Population and Functional Genomics to Identify and Experimentally Validate Novel Regulatory Regions and Genes for Crop Improvement**

<b>Sector</b>	Agriculture - Crops
<b>Genome Centre</b>	Genome Quebec
<b>Project Leader</b>	Thomas Bureau, McGill University
<b>Budget</b>	Total budget = \$4,594,596 / GC contribution = \$2,182,189

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### **Project Description**

Genomic methods, pioneered in studies of simple, single-celled organisms, are being applied with great success to important crop plants. Genomics provides a way to examine and analyze all of the genes (i.e., the genome) that define the crop with a view to enhance yield and productivity, while reducing production costs.

In recent years it has become clear that the genome is more than the sum of genes that code for cellular proteins. Indeed, the regions (“non-coding DNA”) between the protein-coding genes are important for regulating their activity. Studies in plants, humans and other animals now suggest that many of these non-coding DNA regions may have profound significance, harbouring the very elements that regulate genes or provide novel functionality. Our goal is to use genomics as a means to identify, characterize and validate non-coding DNA regions that have a direct role in determining characteristics that are important for Canadian crops.

We have chosen to concentrate on a plant called Arabidopsis for two reasons. First, more is known about the genetics and genomics of this plant than any other in the world. Second Arabidopsis is a close relative of several crops important to the Canadian economy (e.g., canola). Thus, through the comparison of Arabidopsis with other plants, we can identify important non-coding DNA regions, including those relevant for Canadian crops.

We will approach this by determining the whole-genome sequence of several close relatives of Arabidopsis and canola, using this information for within species and between species comparative studies. Non-coding DNA regions will be identified by computer-based predictions and will be validated by experiments that use population genetics and genomic methods. Important findings will be protected for further exploitation.

We anticipate that our project will identify non-coding DNA regions that will have proven potential for crop improvement. We will also generate valuable data, expertise and trained personnel that will provide the basis for future crop-improvement applications.



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## **BEEM: Bioproducts and Enzymes from Environmental Metagenomes**

<b>Sector</b>	Environment
<b>Genome Centre</b>	Ontario Genomics Institute
<b>Project Leaders</b>	Elizabeth Edwards, U. of Toronto / David Major, Geosyntec Consultants (Guelph)
<b>Budget</b>	Total budget = \$10,942,642 / GC contribution = \$5,045,990

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### **Project Description**

Today's global economy is based upon the production of fossil fuels. But increasingly, as we grapple with the depth of the environmental footprint that the production and use of those fuels leaves, we are searching for sustainable alternatives. One of the most exciting alternatives involves using plant-based material to produce biofuels.

An economy based on the use of these renewable resources will depend upon products made from agricultural crops, feedstock and waste materials. This bio-economy will revolve around new processes that transform low-cost materials into high-value products, while minimizing the release of carbon dioxide and other contaminants into the environment.

Our team of chemical engineers, biologists and policy experts will apply our knowledge of gene sequencing and computer modelling to identify, screen, analyze and clone new proteins. We will determine their potential as catalysts to transform low-value plant residues and waste products into valuable bioproducts. We will screen for communities of microbes that are essential to the fermentation of renewable agricultural or waste materials to convert them into fuel. We will also search for microbial communities that we can use to restore contaminated land and water, by understanding their natural function as one of nature's recyclers to break down the pollution at contaminated sites. We will carefully assess the viability of new biotransformation processes considering economic, policy and regulatory constraints.

We have already worked with pulp and paper mills to develop microbial processes that have reduced the harmful byproducts they produce and generated energy to help power their operations. We have also developed and commercialized a microbial community, called KB-1<sup>®</sup>, that is already being used to clean up sites contaminated with solvents. In this project, we plan to apply our basic research knowledge and skills to develop other microbial-based processes to transform, reuse, recycle and remediate contaminants and byproducts from common industrial and agricultural processes. Our goal is to contribute to the sustainability of the biorefineries of the future.



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## Synthetic Biosystems for the Production of High Value Plant Metabolites

<b>Sector</b>	Environment
<b>Genome Centre</b>	Genome Alberta
<b>Project Leaders</b>	Peter Facchini, U. of Calgary / Vincent Martin, Concordia U.
<b>Budget</b>	Total budget = \$13,602,100 / GC contribution = \$6,443,100

### Project Description

It has been said that plants are the world's best chemists. They can synthesize an immense diversity of molecules based on innumerable chemical- backbone structures and combinations of chemical-functional groups. The unparalleled biosynthetic capacity of plants has long been exploited through their use as traditional medicines and more recently the medical and commercial application of pure plant metabolites: pharmaceuticals (e.g. codeine, vinblastine, taxol); flavours (humulone, nootkatone, carvone); fragrances (jasmine, rose oil); pigments (carotenoids, anthocyanins, betalains); insecticides (pyrethrins), and other fine chemicals. The metabolic diversity of these compounds reflects the fundamental mechanisms that drive the evolution of plant natural products; plants interact with their environment mainly through chemical means and metabolites play diverse physiological roles from pathogen defence to pollinator attraction.

Plants produce these chemical products through metabolic biochemistry, relying on a staggering number of enzymes for biosynthesis. This catalytic diversity has remained largely untapped for the industrial production of high-value products.

We will use genomic tools coupled with analysis of metabolic products to identify genes from over 75 plants that can catalyze the synthesis of potentially important chemical compounds. Our principal tool will be ultra-high-throughput DNA sequencing to find interesting genes, followed by detection of chemical products synthesized under the direction of these genes. This will give us a "parts catalogue" of functional components. These components will be assembled into enzymatic pathways inside ordinary baker's yeast cells, which can then be used for the production of new biological processes with specific industrial applications.

The main outcomes of this project are: (1) a public resource of genomic and metabolic information for 75 plants that produce a huge number of important natural products; (2) yeast strains that produce high-value natural plant products; (3) a catalogue of new enzymes for use as catalysts in synthetic biology applications; (4) the invention of functional-genomics methods for describing metabolic pathways and identifying unknown biosynthetic genes from plants; and (5) an analysis of regulatory, ethical, and economic subjects, which will help to ensure sound and responsible plant-technology development.



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## Genomics in Agricultural Pest Management

<b>Sector</b>	Environment
<b>Genome Centre</b>	Ontario Genomics Institute
<b>Project Leader</b>	Miodrag Grbic, University of Western Ontario
<b>Budget</b>	Total budget = \$6,390,093 / GC contribution = \$2,789,939

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### Project Description

Greenhouse vegetable production is a growing industry in Canada, with Ontario alone home to more than 1700 acres of greenhouse vegetables – the largest concentration in North America. These crops make a significant contribution to the province's economy, with greenhouse tomatoes, cucumbers and pepper crops bringing in a combined gate of more than \$550 million in 2006-2007. But a tiny mite that can reproduce every seven days during the hot summer months is poised to wreak havoc on this industry. Already, insects and mites destroy 13 percent of all potential crops.

Spider mites feed on more than 1000 different plant species, causing yellow flecks on the surfaces of leaves that can reduce the yield from those plants. Currently, many growers use chemical pesticides to try to eradicate the pests – a major source of environmental pollution that contributes to the destruction of wildlife. These pesticides are also becoming less effective, as the spider mites' resistance to major pesticides is growing. As global warming intensifies, researchers expect spider mites to pose a serious threat to crops grown in the fields, as well as those housed under glass.

This project will create tools and technologies to control spider mites, based on our success in mapping the entire genome of this mite. Our team combines expertise in genomics, bioinformatics, genetics, biochemistry, population biology, plant biotechnology and plant breeding. We will use high-throughput genomic technologies to analyze plant resistance to spider mites, and we will evaluate the consequences to the pests of eating resistant and susceptible plants. By studying the interaction between plant genes and pest genes, our goal is to combine pest and plant genomics, inserting pest-resistant genes in plants so that they can resist spider mites. We will also develop tools to turn off pest-specific genes, opening up a new tool for pest control, and will develop new strategies to reduce the ability of these pests to reproduce.

Creating this new, environmentally sound approach will negate the use of chemical pesticides and decrease energy consumption in agriculture, by employing this sustainable pest-control strategy. Our project will increase Canada's competitiveness in this vital aspect of our knowledge-based economy.



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## Microbial Genomics for Biofuels and Co-products from Biorefining Processes

<b>Sector</b>	Environment
<b>Genome Centre</b>	Genome Prairie
<b>Project Leaders</b>	David Levin, U. of Manitoba / Richard Sparling, U. of Manitoba
<b>Budget</b>	Total budget = \$10,470,715 / GC contribution = \$4,877,141

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### Project Description

As the world faces the reality of peak oil, serious efforts are being made to develop renewable energy sources that can displace our dependence on fossil fuels. One promising alternative fuel source is biological production (biofuels), in which fuels such as ethanol are produced from a wide variety of agricultural feed stocks. Current production of ethanol involves microbial fermentation of the sugars derived from sugarcane (in Brazil) or the starch from grain (predominantly corn in the US and eastern Canada, and wheat in the prairie provinces of Canada), followed by distillation of the ethanol from the fermentation broths. However, the long-term prospects of grain-based ethanol production is in question because the cost of the feed stocks makes up a large fraction of the total costs of production, and the use of food grains has very negative implications for food prices. Thus, abundant, low-cost feed stocks from other sources are essential for the commercial viability of biofuel production.

Sources of cellulose-containing biomass (ligno-cellulosics) are a potential feed stock for synthesis of fuels, and are typically waste products from forestry (e.g., wood chips) or agricultural (e.g., straw from wheat, flax and hemp) sources. However, processes that produce only ethanol from ligno-cellulosics are not economical. One way to overcome this limitation is to co-synthesize high-value products, such as lignin for resins and adhesives, along with the production of biofuels and plastics from cellulose.

The focus of our research is on the bacteria that accomplish the conversion of the ligno-cellulosics to ethanol, hydrogen, and plastics. We aim to increase the economic potential of the refining processes by developing well-characterized cultures of bacteria that can carry out these industrially important specific enzymatic reactions. This requires detailed understanding of both the genes (and their function) and metabolism of bacteria that use cellulose to make fuels and other products.

We will carry out a full genomic characterization of known and new bacteria that are selected for their ability to contribute to a variety of metabolic processes. On the basis of this information we will produce metabolically engineered bacteria with enhanced fuel and co-product synthesis characteristics. We will combine appropriate bacterial strains to create communities (or "consortia") of microorganisms for industrial application. The aim is to enable biorefineries to generate products (ethanol, hydrogen, and co-products) from relatively low-cost feed stocks of ligno-cellulosics, thus increasing their economic-viability. The goal is to help establish Canada as a leader in the production of biofuels and bioplastics.



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## Grape and Wine Genomics

<b>Sector</b>	Agriculture - Crops
<b>Genome Centre</b>	Genome British Columbia
<b>Project Leaders</b>	Steven T. Lund, UBC / Hennie J.J. van Vuuren, UBC
<b>Budget</b>	Total budget = \$3,440,481 / GC contribution = \$1,629,701

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### Project Description

Wine brings pleasure and is also becoming an important Canadian agricultural product. The Canadian wine industry, accounting for about \$4.2B in sales each year, began to thrive on the world stage in the 1990s following a switch from the native Labrusca grapes to the European Vinifera varieties. Exports of Canadian wine, primarily to the U.S. and Taiwan markets, accounted for \$832M. Canadian wine making creates many jobs among the growers, suppliers, distributors, and service providers that comprise the industry.

Wine making traditionally has been regarded as more of an art than a science, subject to the vagaries of nature and insulated from the advantages of scientific study. This is changing rapidly. The application of new genomics and related techniques now make it possible to uncover fundamental gene functions in wine grapes and yeasts. These methods are already leading to the development of protein biomarkers that can assist viticulturists to monitor how the vine and berries respond to natural and human-made environmental changes along each season, ultimately allowing greater consistency in high value wine grape production.

Yeast has been studied as a model organism for more than 40 years and was the first eukaryote whose genome was fully sequenced. The functions of 5,000 of the 6,000 genes in *S. cerevisiae* have been elucidated. During wine making, yeasts are exposed to many stress conditions such as osmotic pressure, nutrient limitation and ethanol. We have recently discovered that yeast cells adapt to wine making stress conditions by switching on 62 genes of unknown functions which we named Fermentation Stress Response genes. Our objective is to discover function for each of these 62 genes.

Our project will apply genomic and genetic techniques to the study of important wine varieties. Specifically, we will do the following: 1) clarify how nitrogen fertilization affects hormone regulation of metabolic pathways important for berry ripening, chemical composition and wine quality; 2) determine the relationship between gene expression patterns and variation in amino acid composition at maturity in ripening berries; 3) develop biomarkers for vineyard monitoring of vine water stress. 4) use a systems biology approach to identify functions for each of the genes involved in the fermentation-stress response and the regulation of molecular sugar and amino-acid transporters during wine fermentation; and 5) deliver knowledge that leads to understanding the complex scientific, policy, industry and public issues involved in the application of genomics to the wine industry.



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## Value Generation through Genomics

<b>Sector</b>	GE <sup>3</sup> LS (Ethical, Environmental, Economic, Legal & Social Implications of Genomics Research)
<b>Genome Centre</b>	Genome Prairie
<b>Project Leaders</b>	Peter Phillips, U. of Saskatchewan / David Castle, U. of Ottawa
<b>Budget</b>	Total budget = \$5,413,101 / GC contribution = \$2,553,656

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### Project Description

Methods of genome research have come to permeate almost all areas of biological studies. This includes agriculture, which has great importance for the well being of Canadians. Agricultural genomics is concerned with studying the entire sets of genes and their function in organisms of agricultural importance, such as wheat, flax, beans, tomatoes, canola and corn.

We have assembled a national research team to study how Canada can benefit from applying genomic research to agriculture. The project focuses on three important factors for removing roadblocks to innovation in Canada's bio-based economy.

First, we will examine the role of intellectual property such as patents, copyright and trade secrets in moving laboratory discoveries toward practical application. This research will investigate how these legal tools are used currently and their effects on innovation. We will also investigate what changes in intellectual property law, university and government policies and scientific practices might be needed in order to enhance agricultural innovation in Canada.

Second, we will study whether there are new ways of regulating important new agricultural technologies and products. This will involve examining both global networks of regulators and private management of supply chains. The aim is to ensure that publicly supported research is used in the best possible way for the benefit of Canadians and to find ways to evaluate and accept (or reject) new agricultural products as quickly as possible.

Third, we will adapt and test a wide range of engagement tools with the Canadian public to learn how to determine more effectively their interests, fears and attitudes concerning new technologies. Our aim is to provide meaningful ways for Canadians to participate in decisions about how we choose to use new agricultural technologies and products.

Our research team will use up-to-date social science research methods in pursuing these goals. Our results will be communicated to other academic researchers through professional articles, conferences and workshops. We will communicate with the Canadian public, governments and the private sector through a mix of publications, public events and news media.



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## Genomics of Sunflower

<b>Sector</b>	Agriculture
<b>Genome Centre</b>	Genome British Columbia
<b>Project Leader</b>	Loren Rieseberg, University of British Columbia
<b>Budget</b>	Total budget = \$10,481,589 / GC contribution = \$4,964,963

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### Project Description

The sunflower family (Compositae; so-called because their flowering heads are made up of many tiny flowers), is the largest plant family on earth, with over 24,000 described species, roughly 10% of all flowering plant species. They include economically important crops (sunflowers, lettuce, artichokes), beautiful wildflowers (daisies), common allergens (ragweed, goldenrod), valuable medicinals and costly invasive plants and rangeland weeds (thistles, dandelions). Despite the wide diversity and economic importance of plants in this family, there is no genome sequence for any of these species, or even any plants from closely related families. This has delayed genetic research and crop breeding.

Despite the rather large genome size of Compositae, recent advances in DNA sequencing technology (so-called “next-generation” sequencing) now make it practical to sequence their genomes. Our project will use both these new technologies along with more conventional sequencing methods to obtain the DNA sequence of the entire cultivated sunflower genome.

Having an entire genome sequence will facilitate scientific research across this diverse plant family, with applications ranging from crop improvement to weed control to the development of wood-producing sunflower varieties. For example, it will allow us to characterize genetic and morphological variation among domesticated sunflower lines, relating genetic differences to important crop characteristics. This will facilitate molecular breeding programs for the improvement of commercial crops. A second application will be the development of sunflower as a new fuel (biofuel) source with unique advantages as an annual woody plant. Biofuel development will exploit wood-producing ecotypes of two extremely drought tolerant, wood-forming, desert-dwelling wild species: silverleaf sunflower (*H. argophyllus*) and Algodones dune sunflower (*H. tephrodes*). This will allow farmers to grow small, woody trees (a source of biofuel) in a single year while simultaneously using the sunflower seeds for edible oil. Such a dual-use crop has great economic potential.

Our project will increase the speed and precision of sunflower-breeding programs by identifying molecular markers for beneficial genes that encode important agricultural traits such as seed-oil content and flowering time. We will exploit Canada’s strong genomics infrastructure and leadership in Compositae genomics and use this infrastructure and expertise to full advantage in collaboration with experts world-wide.



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## Total Utilization Flax Genomics

<b>Sector</b>	Agriculture - Crops
<b>Genome Centre</b>	Genome Prairie
<b>Project Leaders</b>	Gordon Rowland, U. of Saskatchewan / Sylvie Cloutier, Agriculture & Agri-Food Canada
<b>Budget</b>	Total budget = \$11,976,146 / GC contribution = \$5,645,463

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### Project Description

Flax is becoming a very popular food ingredient. For example, flax seed is rich in omega-3, which is implicated in human brain functions, reducing “bad” cholesterol, and moderating the risk of heart disease. Flax seed is also a rich source of plant-estrogens, which are associated with reduced risks of some cancers. Flax seeds are used in many industrial processes, including linoleum, solvents, paints, car panels and composites. Flax is an unusual crop in that it yields two different kinds of product—seed and fibres. The straw produces a strong and long-lasting fibre that is used to make linen cloth, one of its ancient applications; flax fibre is also used to replace fibre-glass in composites, and in the manufacture of fire logs, paper and other similar products.

Our project—Total-Utilization Flax Genomics—aims at enhancing the usefulness, and versatility of flax by developing strong genomics research as a base for enabling flax breeding and improvement. Canada is the world’s largest producer of flax, which places the onus on us to lead flax research and development. Our goal is to help develop flax as a dual-purpose crop providing both seeds and straw products of unmatched quality and high value.

Our project will develop genomic research methods that will be used to study important questions regarding the biology and technology of flax growth. We will determine the DNA sequence of the entire flax genome, the largest such contribution by any Canadian research team. We will develop genetic and physical maps outlining the position and relationship of genes that are important for improved flax usefulness. This research will be conducted by a team of experts located across Canada. A second team will perform data analysis and management, and will develop software to preserve and present the new data, which will be made available to the international research community in order to foster and stimulate flax research all over the world.

We expect that this research project will create information and genomic tools that will accelerate flax research and create opportunities for advancements on flax yield and applications that were undreamt of only a short while ago.



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## Genozymes for Bioproducts and Bioprocesses Development

<b>Sector</b>	Environment
<b>Genome Centre</b>	Genome Quebec
<b>Project Leader</b>	Adrian Tsang, Concordia University
<b>Budget</b>	Total budget = \$17,422,953 / GC contribution = \$8,139,013

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### Project Description

To move from a fossil-fuel based economy to a bioeconomy based on converting plant material into energy, researchers need to isolate the proteins involved in the process that converts woody biomass (lignocellulose) into simple sugars. Those sugars are the basic blocks required to build the advanced biofuels and biochemicals that can turn agricultural and urban waste into products and energy.

Fungi play a natural role in decomposition. They break down woody biomass, which includes limbs, tops, needles, leaves, bushes and shrubs, into sugars. That makes fungi an ideal natural laboratory where we can search for the proteins involved in this process, which we aim to harness and duplicate.

Our project will use the massive amounts of information available from genome research to identify, analyze and develop potential enzymes in fungi that we could use as catalysts to produce biofuels and other plant-based products. We will map the genome of important fungi and identify the enzymes, or proteins, they use to break down the biomass. We will build a database of the genes and genomes of various types of fungi, as well as the enzyme families and the properties and applications for those proteins. We will clone and express these proteins in the large volumes needed for industrial use. We will also modify promising enzymes to adapt their properties to the requirements of industrial settings. We will use them to develop new fuels, chemicals and novel processes for pulp and paper manufacturing and the production of cattle feed. We will also establish new standards to measure the sustainability of converting woody biomass to biofuels and other products. Finally, we will develop effective communications strategies to engage the Canadian public in a conversation about issues associated with using biomass as a key source of chemicals and fuels in the future.

Once we have developed new enzymes, they will become the cornerstones for the development of large-scale industrial biorefineries that process biomass into biofuels and biochemicals. We also plan to develop enzyme supplements to use in cattle feed, reducing the amount of grain necessary to ensure a nutritious feed product. That development would stabilize the cost of feed for farmers and could cut food costs overall. The enzymes we develop will also help the pulp and paper industry reduce the amount of energy it requires and the pollution the pulping process generates.



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## **Metagenomics for Greener Production and Extraction of Hydrocarbon Energy: Creating Opportunities for Enhanced Recovery with Reduced Environmental Impact**

<b>Sector</b>	Environment
<b>Genome Centre</b>	Genome Alberta
<b>Project Leader</b>	Gerrit Voordouw, University of Calgary
<b>Budget</b>	Total budget = \$11,584,423 / GC contribution = \$5,358,605

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### **Project Description**

Canada recognizes the necessity to transition global energy production towards renewable resources. But until the technologies exist to make it economically feasible to do so, Canada's oil, gas and coal must be extracted in the most environmentally friendly way possible. This project is designed to minimize the environmental impact of oil sands production, by decreasing its use of water and emission of greenhouse gases and by enhancing the extraction of clean burning gas from coal beds.

We will develop a database to describe and harness the genetic potential of the microorganisms, genes and biological processes that exist naturally in microbial communities in our oil sands and coal beds. By identifying the genes, bioprocesses and bacteria in the old sands and coal beds, we will improve our understanding of how methane in hydrocarbon resources is generated and identify the enzymes involved in the natural cracking of hydrocarbons that produce methane and carbon dioxide.

We will use these organic bioprocesses to decrease the water used and land lost in mining operations and manage the methane emissions from tailings ponds. The publicly accessible knowledge generated by this project will also help other researchers harness the power of the processes present in Canada's deep biosphere to resolve other important research questions. In addition to the database, this project will also create publicly accessible genetic and microbial tools that scientists can use to create greener energy and feedstock production.

By designing new biotechnologies that decrease the energy and water required currently for oil sands extraction and by enhancing methane production from coal beds this project will help to ensure that both Canada and the world's current energy requirements are met with the smallest environmental impact possible. The accomplishment of this aim will help Canada's energy production become an environmentally sustainable enterprise.