GenomeCanada

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BACKGROUNDER

Genomic Applications Partnership Program
Funded Projects – Round 5

The Genomic Applications Partnership Program (GAPP) funds research projects that address real world challenges and opportunities as identified by industry, government, not-for-profits, and other "users" of genomics research. The following five projects have been selected for funding in the fifth round of GAPP. Backgrounders on previous projects funded under the program are available on Genome Canada's website.

Microbial Genomics for De-risking Offshore Oil and Gas Exploration in Nova Scotia

Project Leaders: Casey R. J. Hubert, University of Calgary (academic); Adam MacDonald, Nova Scotia Department of Energy (user)
Project Managers: Offshore Energy Research Association of Nova Scotia
Administrative Co-Lead Genome Centres: Genome Atlantic, Genome Alberta
Total Project Funding: $4.9 million
Mitacs partnership

Atlantic Canada's petroleum industry has a significant impact on the region's economy. Since 1995, it has generated investments of $37 billion and more than 12,000 direct jobs. But offshore drilling is expensive. A critical component to Nova Scotia's ongoing ability to attract interest is a comprehensive set of tools to help de-risk the exploration process. This project offers microbial genomics as one of those tools.

To put it simply, some bacteria thrive on hydrocarbons and can be found around seeps—areas where petroleum naturally bubbles up out of the seabed. These bacteria can provide an indication of petroleum trapped beneath the surface.

Dr. Hubert's team will develop new genomics-based tools to identify aerobic, anaerobic and thermophilic bacteria associated with seeps. Adam MacDonald will lead the core sample collection, geochemical analysis, and integration of the results to deliver a deeper

understanding of the characteristics and origins of the petroleum. This adds a valuable layer of information to more conventional geological data to de-risk offshore exploration.

The project will initially focus on the southwestern to central Scotian Slope and then extend to other areas off the coast of Nova Scotia. Results will expand the understanding of offshore petroleum resources developed through the original Play Fairway Analysis conducted by the Department of Energy in 2011. That initiative helped to attract over $2 billion in new exploration commitments.

This project is intended to develop new analytical techniques and data that will provide additional insights to heighten industry interest, enhance exploration activity and increase the dollar value of work commitments arising from future licensing rounds. This could lead to job creation, royalties and taxes that benefit both Nova Scotia and Canada as a whole.

Second Generation Diagnostics: iMALDI-based Assays for Protein Activity to Improve Patient Selection for Therapeutic Akt Inhibitors in Cancer Treatment

Project Leaders: Christoph Borchers, University of Victoria, McGill University – Jewish General Hospital, Segal Cancer Centre; and Gerald Batist, Segal Cancer Centre, Jewish General Hospital, McGill University (academic); AstraZeneca (user)
Administrative Co-Lead Genome Centres: Génome Québec, Genome British Columbia
Total Project Funding: $3.3 million
Mitacs partnership

Cancer, research is discovering, is not the monolithic disease it was once thought to be. In fact, most cancer types have many sub-types, each with its own distinct molecular signature. In some instances this molecular signature determines whether or not a particular drug therapy will be effective.

AZD5363 is an anti-cancer drug in clinical development by AstraZeneca, which has been shown to stop tumour cell growth by inhibiting a protein called Akt. AstraZeneca and the clinical community want to be able to understand more accurately which patients are likely to respond best to this drug and is conducting exploratory research on tumour tissue as well as blood to address this challenge. New technology developed by Dr. Christoph Borchers, called immunoMALDI (iMALDI), uses antibodies and mass spectrometry to monitor for multiple forms of the Akt protein in a single assay. The clinical trials ongoing with AZD5363 provide the opportunity to validate iMALDI and proteomics in samples from patients with mutations in the PI3-kinase/Akt pathway and to test the concordance of iMALDI with other types of mutation testing for molecular signatures.

If iMALDI demonstrates clinical utility, the test may be used to identify patients with specific types of protein and pathway activation to enrich clinical trials with those patients most likely to benefit from the trial treatment, and to determine who will respond best to Akt inhibitors

once approved. If successful, this project may lead to the development of a diagnostic test that will be commercialized by Victoria-based MRM Proteomics Inc.

The ability to use proteomic tests such as iMALDI to identify those most likely to respond to particular treatments will also help Canada attract millions of dollars in biopharma investment to further develop protein-based biomarkers.

A Genetic Toolbox for Tomato Flavour Differentiation

Project Leaders: Dr. Charles Goulet, Université Laval (academic); Dr. David Liscombe, Vineland Research and Innovation Centre (user)
Administrative Co-Lead Genome Centres: Ontario Genomics, Génome Québec
Total Project Funding: $1.8 million

Tomatoes, it is said, are the quintessence of summer in a bite. They are also responsible for more than half a billion dollars in annual farm gate sales and are Canada's biggest fresh vegetable export. Canadian growers are facing competition due to lower production costs in other regions, leading to difficulties maintaining their market share. Canadian producers need to innovate in order to offer a differentiated product that will give them a competitive edge.

Generally, plant breeding programs focus on production traits, such as yield or disease resistance. Vineland Research and Innovation Centre (Vineland) is working with Dr. Charles Goulet of Université Laval to ensure new tomato varieties possess these traits, in addition to something more important to the consumer – flavour. Flavour is a complex trait, reflecting sugar, acid and aroma, as well as texture. Because aroma is defined by more than 30 volatile chemicals and dozens of genes, genomics can greatly facilitate breeding with much greater precision than ever before. This project will use variation in aroma-related genes to develop new tomatoes with differentiated flavour. The resulting plant lines will be used to breed tasty tomatoes at Vineland, and will be made available to other tomato breeders. The first varieties should be commercially available within three years of the project's completion.

The development of locally-adapted, flavourful tomato cultivars will give Canadian greenhouse producers a clear advantage in a competitive consumer market, with total direct economic benefits estimated at more than $30 million per year.

Scale-up of Bioaugmentation Cultures and Development of Delivery Strategies and Monitoring Tools for Anaerobic Benzene and Alkylbenzene Bioremediation

Project Leaders: Elizabeth A. Edwards, University of Toronto (academic); Sandra Dworatzek, SiREM (user)
Administrative Lead Genome Centre: Ontario Genomics
Total Project Funding: $950,000
Mitacs partnership

BTEX compounds – benzene, toluene, ethylbenzene and xylenes – are natural components of crude oil and petroleum and are used in the synthesis of a wide range of useful materials and chemicals. They are also toxic, and benzene in particular is a known human carcinogen. As a result of extraction, transportation and refining processes, as well as accidental spills and leaks, BTEX compounds frequently pollute groundwater in all industrialized regions of the globe.

In Canada and elsewhere, remediation of contaminated sites is difficult and costly. When possible, affected soils are dug up and treated or disposed of offsite. Dr. Elizabeth Edwards of the University of Toronto is working with SiREM, a Canadian leader in bioremediation, to scale up and commercialize anaerobic bioaugmentation cultures for in situ BTEX remediation. These cultures were developed in Dr. Edwards' lab where genomic knowledge was used to identify novel benzene-depleting microbial strains. Bioaugmentation, or the injection of specific microbes into contaminated sites, could significantly accelerate the rate of biodegradation, leading to the cleanup of these sites. How well the cultures perform this biodegradation should be understood in 1-3 years, leading to a cost-effective approach for cleanup of BTEX-contaminated sites.

If successful, this project would be the first commercial application of bioaugmentation for anaerobic BTEX degradation. It would lead to more widespread cleanup of contaminated sites where currently technologies are not feasible or too expensive. It will enable remediation of soils in-place, as opposed to excavation and removal. There are also significant economic benefits, as the global bioremediation market was conservatively estimated at $1.5 billion in 2009 and is now probably greater than $10 billion and continuing to grow.

Preclinical Development of Drugs for Intracerebral Hemorrhage (ICH)

Project Leaders: Xiao-Yan Wen, St. Michael's Hospital (academic); R. Loch Macdonald, Edge Therapeutics, Inc. (user)
Administrative Lead Genome Centre: Ontario Genomics
Total Project Funding: $5.9 million

Intracerebral hemorrhage (ICH) is a form of brain hemorrhage responsible for 10 per cent of all strokes. It affects about 90,000 people in North America each year, more than half of whom either die or are disabled. Anywhere from one-quarter to 44 per cent of those who survive have recurring ICH. The annual economic burden of ICH is estimated at $300 million to Canada and $6 billion to the United States. Apart from treating hypertension, which is one of the causes of ICH, there is currently no way to prevent recurrent ICH.

Dr. Xiao-Yan Wen, director of the Zebrafish Centre for Advanced Drug Discovery (ZCADD) and his team at St. Michael's Hospital, used genomics-driven research tools to identify several existing drugs that are already approved by the US Food and Drug Administration (FDA) that have shown the ability to prevent ICH in zebrafish models. In this project, Edge Therapeutics is partnering with Dr. Wen to perform preclinical studies on the most potent anti-ICH molecules known as EZF-0100 for treatment of ICH and brain microhemorrhages (BMH). Depending on the

results of these studies, Edge may explore the use of its Precisa™ technology to develop a way to administer the drug in a sustained release profile and may also synthesize and test analogs of EZF-0100 to determine the best drug candidate for preclinical development and clinical study in Canada and the US.

The project will reinforce ZCADD's leadership in drug development, attracting new partnerships, investment and revenue generation for the Centre. It will also train next-generation scientists and entrepreneurs and create new jobs for Canadians.