GenomeCanada

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BACKGROUNDER

Genomic Applications Partnership Program
Funded Projects – Round 9

The Genomic Applications Partnership Program (GAPP) funds translational research and development projects that address real-world challenges and opportunities as identified by industry, government, not-for-profits, and other "receptors" of genomics knowledge and technology. The following projects have been selected for funding in Round 9 of GAPP, for a total investment of $21 million ($6.7 million from Genome Canada and $14.3 million from co-funding partners including provincial governments, private sector and not-for-profit organizations).

BRITISH COLUMBIA

Antibody therapeutics for Duchenne Muscular Dystrophy

Project leaders: Carl Hansen, AbCellera Biologics, Fabio Rossi & Michael Underhill, University of British Columbia
Genome Centre: Genome British Columbia
Total funding: $6.5 million

AbCellera, a BC-based biotechnology company, will work with the laboratories of Dr. Fabio Rossi and Dr. Michael Underhill of the University of British Columbia to develop new antibody-based therapeutics for the treatment of fibrosis associated with Duchenne Muscular Dystrophy (DMD). The collaboration will use AbCellera's leading antibody discovery and development capabilities to discover and develop therapeutic antibodies against three novel targets for fibrosis. This research builds on new insights in stem cell science from the Rossi and Underhill groups using a combination of innovative genomics tools and unique animal models. An Investigational New Drug (IND) application for a first therapeutic will be made by the end of the project. Two other antibody therapeutics will be advanced to the point of IND-enabling studies, ensuring the research will translate to potential therapies for patients.

Duchenne muscular dystrophy (DMD) is one of the most common congenital diseases in the world, affecting 1 in 3500-6000 males (1 in 3500 in Canada). DMD is caused by mutations in the dystrophin gene that results in progressive muscle degeneration. There are currently no effective treatments for DMD. A major contributor to DMD progression is fibrosis, the accumulation of scarring in muscle tissue, which contributes to progressive muscle stiffness and weakness. Effective treatments that prevent fibrosis would be of great benefit to DMD patients, slowing disease progression and improving quality of

life. Beyond DMD, the same anti-fibrosis therapies have potential for uses in a variety of other high-burden diseases, including fibrosis of the liver, lungs, and heart.

In addition to creating new therapies that address an unmet medical need, this project will promote economic growth in the Canadian biotechnology sector by attracting major investment and new partnerships. The accessible market for new antibody therapies for DMD is estimated at over $900M, and broader application in fibrosis represents a combined market opportunity of over $40B. Over the five years following completion of these studies, this work will contribute to the creation of more than 100 new high-tech jobs in Canada, and will attract between $50-100 million of new foreign investment.

PRAIRIES

Improving on-seed survival and performance of legume inoculants using genome shuffling

Project leaders: Mike Whiting, Lallemand Plant Care, Christopher Yost, University of Regina
Genome Centre: Genome Prairie
Total funding: $427K
Mitacs partnership

Microbial inoculants promote crop yield through biostimulation and biofertilization. The challenge, however, is to develop rhizobial inoculants – inoculants frequently used to promote legume yields– that remain viable on the plant seed during extended periods of storage before planting and perform optimally once seeded several months later, a process called on-seed survival.

Lallemand Plant Care is a global leader in the development and commercialization of microbe-based technologies for use in human health, animal nutrition, wine making, brewing and agriculture. The company is partnering with Dr. Christopher Yost of the University of Regina to create superior rhizobial inoculant strains currently not available to agricultural producers. The strains will improve desiccation tolerance and improve subsequent on-seed survival. To do so, they will use a technique called genome shuffling, which, with appropriate selection pressures, will accelerate normal evolutionary changes.

Such a groundbreaking enhancement would be eminently marketable in Canada and throughout the world, either integrated into existing product lines or as a new branded product. The inoculant could be sold in the United States within a year of the end of the project, while sales in Canada will take another year to meet Canadian Food Inspection Agency registration requirements. Economic benefits from improved soybean crop yields can be realized within three years of the project's end. Farmers will see increased profits while decreasing the use of synthetic nitrogen fertilizer, thus helping farmers to incorporate environmental and economic sustainability within their farming operations.

ONTARIO

Broad-range disease resistance in greenhouse vegetables

Project leaders: Michael Pautler, Vineland Research and Innovation Centre, David Guttman, University of Toronto
Genome Centre: Ontario Genomics
Total funding: $2 million

Canada's greenhouse vegetable industry generates more than $1 billion from retail sales and exports. Its top three crops are tomatoes, peppers and cucumbers, produced mainly in Ontario, British Columbia and Quebec. In an extremely competitive environment, plant diseases are an enormous burden on growers, causing up to 20 per cent crop loss. There is a strong demand for genomics-based technologies to mitigate these losses.

Drs. David Guttman, Darrell Desveaux, and Adam Mott of the University of Toronto have discovered a previously uncharacterized family of genes that allow plants to show broad-range disease resistance against bacteria and fungi. Further, it is extremely difficult for pathogens to overcome the resistance linked to these genes. Now Dr. Guttman and team are working with the Vineland Research and Innovation Centre and its reverse genetics platform (developed with earlier Genome Canada funding) to further develop these Broad Range Resistance genes, as they are known, to protect against multiple pathogens, reduce losses and increase yield. The result will be new varieties of vegetables that give Canadian growers a competitive advantage.

Vineland will take this gene technology from its translation through to the commercial release of new plant varieties with improved disease resistance, within five years of the end of this project. Annual benefits of around $26 million will start to accrue to the Canadian greenhouse industry within the same timeframe. The enhanced competitiveness of Canadian growers will lead to sustained growth, expansion of operations and further job creation. Additional benefits will be seen as Vineland re-invests its licensing revenue from the new vegetable varieties into further research, driving innovation throughout the entire horticultural sector.

Pre-emergence surveillance for reportable influenza viruses at the human-animal interface

Project leaders: Mohammed Qadir, Fusion Genomics, Samira Mubareka, University of Toronto
Genome Centre: Ontario Genomics
Total funding: $791K

It's hard to tell when a virus risks becoming an epidemic – but it's important for risk management, public health and biosecurity. Most companies working in the area, however, focus on diagnostics rather than pre-emergence surveillance. This project's goal is to fill that gap.

Current methods for surveillance, especially before a virus emerges as a danger, are neither timely nor efficient, and a better tool is needed. Next-generation DNA sequencing provides genomic data that can offer insight into the origin, diversity and transmission potential of viruses found in animals, such as avian or swine flu, particularly the likelihood of their making the jump into humans. But there are obstacles to this sequencing being adopting into mainstream surveillance, including pathogen enrichment, sample quantity and computational resources.

Fusion Genomics Corp. is working with the University of Toronto's Dr. Samira Mubareka to further develop its genomic technology, ONETest™ EnviroScreen, which already includes assays for detecting avian influenza, to detect swine flu as well. The result will be a highly sensitive, informative and scalable technology for infectious disease surveillance that harnesses the power of next-generation sequencing. Its ability to provide surveillance in animals before the emergence of an influenza virus will drive a paradigm shift in transmission dynamics, outbreak predictions and vaccine design and production.

The main market for this innovation will be government agencies and institutes charged with pathogen surveillance. Fusion will work with such organizations to validate the technology and bring them on

board as early adopters. Further expansion of its use will happen both nationally and internationally. Use of the technology will enable early outbreak warnings and damage-mitigation efforts. It will also reduce losses among poultry and swine producers and support the growth of a Canadian biotech start-up.

Applying the Adapsyn genomics platform to the identification, isolation and characterization of immune modulators from the human microbiome

Project leaders: Andrew Haigh, Adapsyn Bioscience Inc., Michael Surette and Nathan Magarvey, McMaster University;
Genome Centre: Ontario Genomics
Total funding: $6 million
Mitacs partnership

Adapsyn Bioscience has a proprietary platform whereby it applies patented algorithms, proprietary artificial intelligence, and machine learning to genomic and metabolomic data from microbes to identify and characterize novel natural products that can then be developed as novel therapeutics. The company is working with McMaster University and Dr. Michael Surette and his team to systematically mine the human microbiome – the collection of microbes that colonize the body – for compounds that can be used to treat human disease.

The microbiome contains approximately 100 times as many genes as the human genome, and has been shown to produce antibiotics, vitamins, fatty acids, neurotransmitters such as serotonin, histamine and acetylcholine, and immunomodulators. As a result, the microbiome has the potential to affect the nervous system, suppress pathogen growth, and modulate the immune response to invading pathogens. Dysregulation of the microbiome has been implicated in inflammatory bowel disease, cancer, and neurological conditions, and can affect how people respond to immunotherapies.

Dr. Surette and Adapsyn Bioscience are focusing on the microbes responsible for immunological effects of the microbiome. Their work will lead to personalized medicine based on the composition of the microbiome and new treatments for inflammatory diseases and cancer. Adapsyn has secured financing to ensure future development of the results of this project. The project will also contribute to future partnership opportunities, thus ensuring that the economic benefits of commercialization remain in Canada.

QUÉBEC

Use of Genomics to Manage and Protect Caribou Populations

Project leaders: Réjean Rioux, Protection de la faune du Québec (Québec's Wildlife Law Enforcement Agency), Claude Robert and Steeve Côté, Université Laval
Genome Centre: Génome Québec
Total funding: $3 million

Genomics is a common tool to study the DNA of model organisms and livestock, but it can also be used to protect wildlife, offering great potential for monitoring genetic diversity, identifying populations at risk and managing these populations.

The conservation of caribou is a particular concern in Québec, where some populations are declining rapidly. For example, the George-River herd has declined from more than 800,000 animals in the early 1990s to just 8,900 in 2016, a drop of around 99 percent! The ministère des Forêts, de la Faune et des Parcs (MFFP, Québec's Ministry of Forests, Wildlife and Parks) has put together several action plans to protect caribou populations, and is looking forward to integrate genomics. The inclusion of genome-wide descriptive metrics will allow better herd management decisions and more efficient protection actions. To do so, MFFP will work with the research team, directed by Claude Robert and Steeve Côté from Université Laval, to develop a much-needed genomic tool.

The tool will consist of a SNP (single-nucleotide polymorphism) chip that will allow identifying specific herds based on a simple tissue sample, together with a Web portal to host a registry of caribou genotypes and a data analysis pipeline to support caribou management in Québec. The tool will assist MFFP's wildlife protection officers and biologists in carrying out their mandate to protect and manage the endangered populations of that species and its habitat in a manner consistent with sustainable development and supported by up-to-date knowledge. Caribou is an iconic species not only in Québec, but also in Canada where its sustainability is essential for the stability of the tundra ecosystems and for the food security and economy of Northern communities.

Novel Aminoglycoside Readthrough Therapy for Nonsense Mutations

Project Leaders: Pedro Huertas, MD, Eloxx Pharmaceuticals, Paul Goodyer, MD, McGill University Health Centre
Genome Centre: Génome Québec
Total funding: $2 million

Nephropathic cystinosis is a rare disease affecting infants who inherit two mutant copies of the *CTNS* gene, causing accumulation of cystine in all tissues. At birth, babies appear normal, but growth is impaired by 4 to 6 months and important nutrients leak into the urine. Without treatment, dialysis and transplantation are required by age 10. Other organs deteriorate in the teenage years. In young adults, the muscles, brain and heart are affected and survival beyond 30 years is rare. Current treatment, cysteamine, can delay (but not prevent) renal failure.

In Québec, cystinosis is more common due to a special ("Nonsense") mutation in the *CTNS* gene (W138X) introduced into the French Canadian population by an Irish immigrant. Nonsense mutations instruct the cell to stop production of *CTNS* protein before it is finished. Certain antibiotics (aminoglycosides) can trick the cell to bypass a Nonsense mutation, but are generally too toxic to be used as long-term therapy. In recent years, Eloxx Pharmaceuticals has designed a novel aminoglycoside (ELX-02) that is much less toxic. Studies at McGill University showed that ELX-02 bypasses the W138X mutation in patient cells and shows no toxicity in cells, animals and human volunteers. By restoring production of the normal *CTNS* protein, sustained ELX-02 therapy has the potential to be curative.

Eloxx Pharmaceuticals is now partnering with the laboratory of Dr. Paul Goodyer to screen North Americans for *CTNS* Nonsense Mutations and then move to a Phase II clinical trial. If the trial proves successful, ELX-02 could save up to 5.2 million in the case of cystinosis and would set a precedent for a broad application in other genetic diseases caused by Nonsense Mutations.