GenomeCanada

January 23, 2018

BACKGROUNDER

Results of the 2017 Large-Scale Applied Research Project Competition: Genomics and Precision Health

Genome Canada, in collaboration with the Canadian Institutes of Health Research, and project co-funding partners, is pleased to announce an investment of approx. $162 million over four years in 15 new genomics and precision health projects. These projects – spanning multiple disease areas – demonstrate how genomics-based research can contribute to a more evidence-based approach to health and thereby improve health outcomes for patients, as well as enhance the cost-effectiveness of Canada's health-care system.

BRITISH COLUMBIA

Silent Genomes: Reducing health-care disparities and improving diagnostic success for Indigenous children with genetic disease

Project leaders: Laura Arbour (University of British Columbia), Nadine Caron (University of British Columbia), Wyeth W. Wasserman (BC Children's Hospital Research Institute)
Genome Centre: Genome British Columbia
Total funding: $10.4 million

First Nations, Inuit and Métis' populations, collectively known as the Indigenous Peoples' of Canada, face strikingly similar health challenges with global Indigenous Peoples'. Inequities include barriers to healthcare access that produce poorer health outcomes compared to non-Indigenous groups.

Whereas genomic technologies are advancing health care by allowing medical treatments to be tailored to the specific needs of individual patients ('precision medicine'), this 'genomics revolution' is widening the health inequities gap. In particular, compared to what is becoming routinely available to other Canadians, Indigenous populations often have little or no access to genomic technologies and the research that drives them, hence intensifying the 'genomic divide'.

A key concern in the growing genomic divide is the lack of background genetic variation data for Indigenous populations living in Canada and globally. This prevents accurate diagnosis because the reference data are needed for precise genetic diagnosis. Notably, standard genomics resources are **silent** with respect to First Nations (FN), Inuit and Métis'. ***Silent Genomes*** *will address the genomic divide by reducing access barriers to diagnosis of genetic disease in Indigenous children.*

Silent Genomes, is a game changing partnership with First Nations, Inuit and Métis Peoples that will:

- establish processes for Indigenous governance of biological samples and genome data,

- lead to policy guidelines and best practice models, bringing equitable genomic testing to Indigenous children in Canada with suspected genetic diagnosis, and
- develop an Indigenous Background Variant Library (IBVL) of genetic variation from a diverse group of First Nations in Canada.

Silent Genomes will improve health outcomes by enhancing equitable access to diagnosis, treatment, and care while assessing cost effectiveness of precision medicine

Genomic and outcomes database for pharmacogenomics and implementation studies (Go-PGx)

Project leaders: Bruce C. Carleton and Colin J. Ross (University of British Columbia)
Genome Centre: Genome British Columbia
Total funding: $9.9 million

Adverse drug reactions (ADRs) are a major problem in modern medicine, leading to withdrawal of treatment, non-compliance with medication, permanent disability and death. This is particularly true for cancer treatment, with its potent medications. The vision of Go-PGx is to save lives and improve the quality of life of children with cancer, by using genomics-based precision health strategies to reduce the most common and serious ADRs in these children.

It is increasingly evident that genetic differences in patients can affect the likelihood of their developing an ADR. Drs. Bruce C. Carleton and Colin J. Ross, both of the University of British Columbia, are working to prevent these ADRs by developing lab tests to predict the likelihood of a childhood cancer patient developing an ADR and tools to incorporate these tests into clinical practice. Through Go-PGx, they will analyze more than 6,125 DNA samples and corresponding medication use and ADR outcome data to discover biomarkers that will reveal genetic susceptibility to ADRs and develop tools to educate and inform physicians and patients, beginning with five of the most severe ADRs in childhood cancer. They will also develop a comprehensive database linking clinical and genetic data as an accessible resource for researchers throughout the world. With the data they generate, they will begin providing testing at 10 pediatric cancer centres across Canada, while studying barriers and facilitators to the uptake of ADR screening in the health-care system, as well as the economic implications of introducing this kind of testing into clinical practice. The team will also develop peer-reviewed clinical practice guidelines before the project's end and publish them within a year post-project.

Precision Medicine CanPREVENT AMR: Applying precision medicine technologies in Canada to prevent antibody-mediated rejection and premature kidney transplant loss

Project leaders: Paul Keown (University of British Columbia), Ruth Sapir-Pichhadze (McGill University), Timothy Caulfield (University of Alberta), Stirling Bryan (University of British Columbia)
Genome Centres: Genome British Columbia (administrative lead), Génome Québec, Genome Alberta
Total funding: $9.7 million

Transplantation is the treatment of choice for patients whose kidneys have failed, providing superior survival, better quality of life and lower health-care system costs (<$20,000/year vs. > $90,000) compared with dialysis. However, a severe form of rejection (known as antibody-mediated rejection, or AMR) causes premature loss of the transplant kidney in as many as 30 per cent of transplant recipients, or 500 Canadians every year, prompting a return to dialysis and often early death.

The team led by Drs. Paul Keown and Stirling Bryan of the University of British Columbia, Ruth Sapir-Pichhadze of McGill University and Timothy Caulfield of the University of Alberta, which includes over 70 scientists and clinicians from 22 universities in Canada, the US, the UK and the EU, will use genomic technologies to reduce the risk of AMR. These will enable better matching of patients and donors, precise monitoring of the immune response after transplantation to better predict AMR, and the use of personalized drug treatments to prevent rejection while avoiding infection or cancer. The team will also engage patients, providers and health care payers to study the legal, ethical, societal and economic considerations of introducing these strategies into clinical practice.

The goals of the research program are to reduce the frequency of AMR by at least 50 per cent and in so doing to benefit first the patient and his or her family through improved survival and quality of life, reduced caregiver burden and personal health costs; second to minimize demand on the health-care system by reduced costs through decreasing dialysis and re-transplantation, and third to improve societal care of a major chronic disease by increasing productivity and streamlining the management of chronic kidney failure.

Deciphering the genome biology of relapsed lymphoid cancers to improve patient management

Project leaders: Christian Steidl, Marco Marra and David Scott (BC Cancer Research Centre and University of British Columbia)
Genome Centre: Genome British Columbia
Total funding: $11.9 million

Lymphoid cancers, which start in the immune system and include Hodgkin's and non-Hodgkin's lymphoma, myeloma, lymphocytic, and lymphoblastic leukemia, are the fifth-most-common cancers in both men and women and affect people of all ages. Every year in Canada, 16,000 people are diagnosed with a lymphoid cancer and 6,000 die from them. Death most often happens when disease relapses after an initially successful treatment, making treating and controlling the symptoms of relapsed disease the most pressing need for patients suffering from lymphoid cancers.

Because the causes of relapse are not known, and because relapsed cancer differs considerably from the initial cancer, there are no clinical tests to provide information on the prognosis for individual patients and likely treatment outcomes, or to provide guidance to physicians and patients on the use of alternative therapies, such as small molecule drugs or immunotherapy. Relapses and associated treatments cost the Canadian health-care system more than $315 million each year, about 10 per cent of the expected cancer drug budget in 2022, and the lack of clinical tests means many of these expensive treatments are applied without adequate guidance.

Drs. Christian Steidl, Marco Marra and David Scott of the BC Cancer Research Centre are developing genomics-based clinical tests to improve patient outcomes and quality of life, and working to integrate the tests in the health-care system. To do so, they will sequence relapsed tumours to identify novel biomarkers. They will undertake economic analyses to better understand the cost-effectiveness and health-system impact of genomics-informed management of relapsed disease. They will also develop an e-health application to assist patients with shared decision-making.

The results of this project will be novel clinical tests that will provide decision aids for physicians and patients, help policy makers in implementing personalized treatment approaches for relapsed lymphoid cancers and reduce the costs of treating relapsed lymphoid cancers.

Childhood asthma and the microbiome – precision health for life: The Canadian Healthy Infant Longitudinal Development (CHILD) study

Project leaders: Stuart Turvey, Michael Kobor, Brett Finlay (University of British Columbia), Padmaja Subbarao (The Hospital for Sick Children)
Genome Centres: Genome British Columbia (administrative lead), Ontario Genomics
Total funding: $9.1 million

Asthma is the most common chronic disease of childhood, affecting one in seven Canadian children (and more than three million Canadians of all ages). It is the most common reason for children to be admitted to hospital and for them to miss school. It is also expensive, costing more than $2 billion per year in Canada. Treatments can manage symptoms, but there is no cure, only the slight hope that children will "grow out of it."

Dr. Stuart Turvey, his team at the University of British Columbia and the CHILD study team are focusing on early diagnosis and prevention, two factors that can reduce the personal and economic toll of asthma. Their sample of choice comes from dirty diapers: by using powerful genomics technologies to analyze stools, they may be able to predict which infants will go on to develop asthma. The reason? Evidence has shown that babies who go on to develop asthma tend to be missing key microbes in their intestines (the microbiome, as it is known) in the first few months of life. Beyond predicting who may develop asthma, thus enabling early diagnosis, the research will guide the ethical development of ways to replace these microbes, to prevent asthma from developing at all.

GenCOUNSEL: Optimization of genetic counselling for clinical implementation of genome-wide sequencing

Project leaders: Alison M. Elliott (BC Provincial Health Services Authority), Bartha Knoppers (McGill University), Larry Lynd (University of British Columbia), Jehannine Austin (University of British Columbia)
Genome Centres: Genome British Columbia (administrative lead), Génome Québec
Total funding: $4.2 million

Genome-wide sequencing (GWS; whole genome or exome sequencing) is a powerful new genetic test that analyzes a person's entire genetic make-up. While valuable, it can be problematic, by revealing disorders or disease risk factors unrelated to the original reason for testing, or by generating complex findings that are difficult for non-expert health providers to interpret. While not currently routinely available, genome-wide sequencing will soon be in more widespread use for patients who need it – increasing demand for genetic counselling, to which access is already limited in Canada.

Genetic counsellors provide education and emotional and decisional support to patients and families, helping them to make informed decisions about genetic testing and its results. Because of lack of legal recognition of genetic counsellors in Canada, most of them are found in academic centres rather than in the community.

GenCOUNSEL, which brings together experts in genetic counselling, genomics, ethics, health services implementation and health economics research, is the first project to examine the genetic counselling issues associated with clinical implementation of GWS. It will determine the most efficient socio-economic, clinical, legal and economic methods of providing genetic counselling once GWS is available in the clinic. It will create an understanding of current and future needs for genetic counselling, develop

best practices for the delivery of genetic counselling, improve access to the counselling, particularly for underserved patient populations, and study the feasibility of different models of legal recognition of genetic counsellors. The result will be increased access, patient satisfaction and cost-efficiency while helping to make genetic counselling available to all Canadians who need it.

ALBERTA

Reducing the global burden of infectious diseases through precision population health

Project leaders: Ian Lewis (University of Calgary) and Deirdre Church (Calgary Laboratory Services)
Genome Centre: Genome Alberta
Total funding: $11 million

Antibiotic-resistant bacteria are a serious problem, with nearly half of all infection-causing bacteria now resistant to front-line drugs and superbugs emerging that cannot be killed by *any* drug. If these superbugs take hold in our health-care system, all kinds of procedures, such as hip replacements chemotherapy and organ transplants will become too risky and Canadians' life expectancy could be reduced by as much as 20 years. Fighting these superbugs is a moral imperative if future generations are to benefit from the health care we take for granted.

One of the major reasons for this growing risk is the one-size-fits-all approach we take to treating infections, which encourages overuse of antibiotics. Different strains of bacteria can be radically different in the risks they pose, but the limitations of technology mean we can't take these differences into account in making treatment decisions. Drs. Ian Lewis and Deirdre Church are leading an international team of experts to develop a new approach to treating infection. They will identify the significant biochemical traits present in different strains of bacteria, create an analytical system and database to predict the potential risks posed by different infections, and implement a new Precision Infection Management (PIM) strategy that will allow physicians to match each patient to the level of antibiotic therapy needed to cure the infection.

PIM will reduce antibiotic use and may preserve the lifespan of critical front-line drugs, while ensuring that people with particularly aggressive infections such as flesh-eating disease get aggressive therapy faster. PIM will allow these health improvements while saving money to the health-care system and, most importantly, saving lives.

ONTARIO

Care4Rare Canada: Harnessing multi-omics to deliver innovative diagnostic care for rare genetic diseases in Canada (C4R-SOLVE)

Project leaders: Kym Boycott (Children's Hospital of Eastern Ontario Research Institute), Michael Brudno (The Hospital for Sick Children), François Bernier (University of Calgary), Clara van Karnebeek, (University of British Columbia)
Genome Centres: Ontario Genomics (administrative lead), Genome Alberta, Genome British Columbia
Total funding: $12.9 million

There are more than 7,000 rare genetic diseases in Canada, which have a devastating impact on some one million Canadians and their families: two-thirds of these diseases cause significant disability; three-quarters affect children; more than half lead to early death; and, almost none has any targeted

treatment. Further, more than one-third of these diseases remain unsolved (their genetic cause is unknown). Building on the work of the Care4Rare Canada Consortium, the C4R-SOLVE project is working to identify the genetic cause of unsolved rare diseases and make genomic sequencing available to Canadians for rare disease diagnosis. Genomic sequencing will speed up the diagnostic process, thereby ending or even preventing years of diagnostic testing and visits to multiple specialists. Providing a timely diagnosis improves the care and wellbeing of patients and their families and reduces unnecessary healthcare spending.

Key to C4R-SOLVE's success will be new sequencing technologies and improved worldwide data sharing. In addition, the group will work with provincial ministries of health to determine how best to include genomic sequencing as a clinical test to diagnose rare diseases, beginning with Alberta and Ontario. In doing so, C4R-SOLVE will more than double our ability to diagnose unsolved rare disease, while building the infrastructure and tools needed to improve rare disease diagnosis worldwide. Accurate and early diagnosis will optimize care, improve the wellbeing of patients and their families, provide new insights into these devastating diseases, and potentially save at least $28 million/year in health-care spending.

Personalized therapy for individuals with cystic fibrosis

Project leader: Felix Ratjen (The Hospital for Sick Children)
Genome Centre: Ontario Genomics
Total funding: $10 million

Cystic fibrosis (CF) is the most common fatal genetic disease, affecting 4,000 Canadians and 80,000 people throughout the world. The debilitating disease causes difficulties in breathing, recurrent lung infections and digestive disorders before killing those who suffer from it, at a median age of 35 in Canada. Currently, treatments can ease the symptoms of the disease, but there is no cure. Newer drugs today can address the underlying genetic defect that causes CF, but only some patients respond positively to them, while others do not – and there is no way for clinicians to know in advance which category a patient will fall into. Given the side effects of these drugs and their cost (more than $300,000/year per patient for a drug that needs to be administered lifelong), there is a pressing need for robust predictors of who will respond to what treatment.

Dr. Felix Ratjen of the Hospital for Sick Children and his team are developing predictive tools that will help clinicians determine the right medicine for the right patient. The team will examine how genetic factors, which can be assessed from a non-invasive blood test, can help predict individual treatment responses. They will also examine if drug testing on patient-derived tissue samples can be used to inform the potential clinical response to drugs by each patient. The team will work with industry partners, patient organizations and the Ontario Ministry of Health and Long-Term Care to integrate these strategies into patient care once they have been shown to be effective.

The result of the team's work will be a paradigm shift toward individualized treatment for CF, assistance for clinicians in making treatment decisions, guidance for policymakers on reimbursement for the most cost-effective care and better health outcomes for patients.

Microbiome-based precision medicine in inflammatory bowel disease

Project leaders: Alain Stintzi (University of Ottawa), David Mack (Children's Hospital of Eastern Ontario and University of Ottawa)
Genome Centre: Ontario Genomics
Total funding: $9.1 million

Inflammatory bowel disease (IBD) results from gut inflammation and leaves sufferers with serious health issues due to this chronic inflammation. Canada has one of the highest rates of IBD in the world, with more than 10,200 new cases each year, for an estimated total of 233,000 patients (including 5,900 children) and a cost to the Canadian economy of $2.8 billion/year. There is no cure for this lifelong condition and its cause remains unknown, although it seems to be tied to an imbalance of key beneficial and deleterious intestinal microbes.

Treating IBD can be unpredictable raising concerns of using too-aggressive treatments for some patients and risking doing more harm than good while using insufficiently aggressive treatments might not help. Drs. Alain Stintzi and David Mack will use genomics to characterize, identify and quantify the microbes that change in IBD patients during treatment. They will use this information to design simple and quick tests to reveal the optimal treatment for each affected patient, allow for personalized treatment plans based on each patient's characteristics and be used to easily monitor each patient's progress and modify treatment plans if needed. These tests will help clinicians use the right drug at the right time for the right patient. The researchers will also unravel the mechanisms underlying IBD development and identify new targets for future drug development. Their work will set the stage for future clinical trials aimed at restoring IBD patients' microbes to a healthy state.

The project will reduce long-term disability and enable patients to reach deep and long-lasting remission, thereby improving quality of life and significant cost savings.

UCAN CURE: Precision decisions for childhood arthritis

Project leaders: Rae S. M. Yeung (The Hospital for Sick Children), Susanne M. Benseler (University of Calgary)
Genome Centre: Ontario Genomics (administrative lead), Genome Alberta
Total funding: $10 million

Arthritis – it's not just for seniors. More than 24,000 children in Canada live with the painful, chronic disease that can cause fevers and permanent destruction of joints, leading to a life of permanent disability. A class of powerful drugs called biologics can dramatically reduce joint inflammation and pain and prevent joint damage in the longer term. The drugs cost as much as $400,000 per year, though, and children may only qualify after traditional treatments have failed, by which time permanent damage has occurred. Evidence shows that early short-term biologic treatment, even for as little as three months, can result in long-lasting disease control in the most severely affected children, possibly even curing the disease.

UCAN CURE will let doctors and families quickly know who needs biologics, which biologic will work best for an individual child, and when the biologic can be safely stopped. The team will develop the first genomics-based, low-cost biomarker blood test to rapidly identify the best treatment for each child, thus completely transforming the treatment of childhood arthritis. A smartphone- and web-based

system of eHealth apps will give children and their families a powerful voice and establish an integrated network of patients, physicians and researchers. An updatable model of the risks, benefits and costs of biologic therapy will help inform health-policy decision makers.

The research is expected to have immediate impact on treatment for children with arthritis, improving their health and the quality of life for themselves and their families.

QUEBEC

PEGASUS-2: Personalized Genomics for Prenatal Abnormalities Screening Using Maternal Blood: Towards first tier screening and beyond

Project leaders: François Rousseau (Université Laval), Sylvie Langlois (University of British Columbia)
Lead Genome Centres: Génome Québec (administrative lead), Genome British Columbia
Total funding: $12.2 million

The discovery that fetal DNA is present in the mother's blood during pregnancy has led to the development of a genomics-based maternal blood test called NIPS (non-invasive prenatal screening), which is a very reliable test for Down syndrome. In part due to its cost, NIPS is currently only used as a second-tier test, after a mother has tested positive on less costly and less accurate tests, to confirm the finding prior to resorting to amniocentesis.

Making NIPS the entry-level test for Down syndrome could benefit women by more accurately detecting an affected pregnancy with less chance of a false positive result and by providing that result several weeks earlier in the pregnancy. As well, because NIPS can detect other chromosomal abnormalities, its use could enable screening for more conditions. The PEGASUS-2 project's goal is to provide high-quality evidence to support the use of NIPS instead of traditional screening tests by comparing its use as a first-tier and second-tier test in a large cohort of pregnant women. The project will also study the cost effectiveness of expanding screening to other conditions and the ethical, social and legal implications of doing so. It will also provide strategies to promote shared decision-making between couples and health-care professionals. Finally, it will further develop the NIPS technology to reduce its costs by 50 percent and expand its ability to detect other anomalies, as well as ensuring quality control for clinical NIPS testing in Canada and worldwide.

PEGASUS-2 will enable publicly funded access to a promising genomics technology for all interested pregnant women, while ensuring that couples have access to web-based tools to help their decision-making and that all health-care professionals are trained in shared decision-making for prenatal screening.

Tackling childhood brain cancer at the root to improve survival and quality of life

Project leaders: Nada Jabado (Research Institute of the McGill University Health Centre; McGill University), Michael Taylor (The Hospital for Sick Children, SickKids), Jacek Majewski (McGill University)
Genome Centres: Génome Québec (administrative lead), Ontario Genomics
Total funding: $13 million

Brain cancer remains a lethal and disabling disease, the leading cause of cancer-related deaths among children under age 20 and the third-leading cause in young adults aged 20-39. This is in contrast to childhood leukemia and other blood cancers, where survival and quality of life

have improved markedly based on improved classification and novel targeted therapies implemented at diagnosis. There are particularly aggressive forms of brain cancer, with barely 10 percent of children and young adults surviving three years after diagnosis, and other forms where those who do survive suffer severe lifelong disabilities due to the life-saving therapies they receive.

The research teams of Drs. Nada Jabado and Jacek Majewski of McGill University and Dr. Michael Taylor at SickKids have previously discovered that many pediatric brain tumours are driven by mutations in genes that play a significant role in brain development. They also provided tools to improve the diagnosis and better classify these brain cancers in children, promoting more effective treatments. To decrease the burden of survivorship and improve survival rates, this project will fast track the use of treatments targeting specific genetic alterations early at diagnosis. The team will also perform innovative investigations of the tumour genome and transcriptome, including at the single-cell level, to identify new alterations and specific vulnerabilities that can be targeted for therapy. The team will ensure treatments are validated through relevant disease models and fast-track meaningful clinical trials to tackle refractory brain tumours during this grant; the goal is to work closely with health-care providers and regulators to ensure the rapid translation of validated treatments to the bedside.

Ultimately, the team's work will improve the survival rate and quality of life for children and young adults with brain cancer, both during and after treatment.

Interrogating and implementing Omics for precision medicine in acute myeloid leukemia

Project leaders: Guy Sauvageau (Institute for Research in Immunology and Cancer (IRIC) of the Université de Montréal), Josée Hébert (Hôpital Maisonneuve-Rosemont)
Genome Centre: Génome Québec
Total funding: $12.8 million

Acute myeloid leukemia (AML) is one of the leading causes of cancer-related deaths in young adults and a highly lethal disease in older adults. Most AML patients do not survive longer than two years after diagnosis, due to a lack of effective treatment options and inadequate molecular tools to monitor disease prognosis. Treating patients considered favourable (with chemotherapy) or adverse (stem cell transplant) is relatively straightforward. It is the patients who fall into the middle, intermediate, category who present the most problems.

In 2009, the team leads for this project, Drs. Guy Sauvageau (Université de Montréal) and Josée Hébert (Hôpital Maisonneuve-Rosemont) launched the Leucegene project, today an international leader in deciphering the genetic abnormalities present in AML. Leucegene's work has led to the imminent worldwide implementation of a new prognostic test, enabling physicians to predict responses to available AML therapies for patients. Nonetheless, physicians are not able to identify optimal treatment for fully 30 percent of AML patients.

This project's goal is to reduce that number to less than 10 percent by using new, state-of-the-art genomic technologies to identify previously unknown genetic variants and to develop new prognostic tests based on this knowledge. The team will also identify key vulnerabilities in AML that can be targeted by existing drugs not currently used in AML treatments, enabling the identification of appropriate therapies for more patients.

Results from this research will be made available on a public web portal to facilitate further work by other researchers and make information available to patients and physicians. The team will create strict ethical

and legal guidelines for the portal. It will also analyze the costs arising from the novel tests developed, compared to the costs saved and years of productivity gained through better AML treatment strategies.

Personalized risk assessment for prevention and early detection of breast cancer: Integration and Implementation

Project leaders: Jacques Simard (Université Laval), Anna Maria Chiarelli (Cancer Care Ontario, University of Toronto)
Genome Centres: Génome Québec (administrative lead), Ontario Genomics
Total funding: $15.5 million

Breast cancer is the most common cancer and second leading cause of cancer death in Canadian women. Women face one-in-eight chances of developing breast cancer in their lifetime. Current screening recommendations are that all women aged 50-74 have a mammogram every two-to-three years. Personalized risk assessment using a combination of genomic profiling and other breast cancer risk factors would allow tailored prevention and screening recommendations based on individual risk to improve the balance of benefits to harms.

This research project will provide evidence that can significantly extend the benefits of current population age-based screening programs by supporting the transition to a risk-based approach. The evidence generated will also improve genetic counselling about screening and risk reduction strategies for women with a family history of breast cancer who are seen in cancer genetic clinics.

The research team, led by Drs. Jacques Simard of Université Laval and Anna Maria Chiarelli of Cancer Care Ontario and the University of Toronto, will study very large cohorts of women using high-throughput genomic technologies, together with statistical and epidemiological methods, to develop and validate a multi-gene panel test based on genetic variations associated with breast cancer. The team will also assess the acceptability, feasibility and outcomes of risk-based screening using a new, comprehensive risk-prediction web-based tool and a genomic profiling test within existing mammography centres.

Improved personalized risk assessment will enable earlier detection and treatment of breast cancer, saving lives and providing health and socio-economic benefits.