Roadmap 2.0

“The Time is Now for Personalized Medicine in British Columbia”
Table of Contents

Summit Partners ............................................................................................................. 2
Executive Summary ........................................................................................................ 4
Why Is Personalized Medicine Important? ..................................................................... 6
  Why is Personalized Medicine Happening Now? ......................................................... 7
  What Are Examples of Personalized Medicine? ......................................................... 8
  What Are the Barriers to Implementing Personalized Medicine? ............................... 9
How Can We Implement Personalized Medicine in BC? ............................................. 11
  1. Make A Provincial Government Leadership Commitment .................................... 12
  2. Form A Collaborative Implementation Organization ............................................. 14
  3. Leverage Our Assets ............................................................................................... 15
  4. Generate Omic Data-Clouds for 25,000 British Columbians ............................... 18
  Conclusion .................................................................................................................. 19
Appendix ......................................................................................................................... 20
  i. Glossary .................................................................................................................... 20
  ii. Personalized Medicine Resources in BC ............................................................... 22
  iii. Details on Other Omic Initiatives .......................................................................... 23
  iv. References ............................................................................................................. 25
  v. Contacts ................................................................................................................. 29
Executive Summary

There is a revolution occurring in healthcare. New technologies are enabling molecular profiling of individuals to diagnose disease more precisely, to prescribe therapies that are better matched to the patient and their disease, and that enable more effective preventive medicine. This new form of medicine, which is termed personalized medicine, precision medicine, molecular medicine or precision health, offers the potential for improved patient outcomes, a more efficient healthcare system and a healthier population. Healthcare systems internationally are investing heavily to implement personalized medicine because there is a clear opportunity to develop more efficient and more effective healthcare delivery systems. Why not British Columbia?

Since the publication of the original “Roadmap to Bringing Personalized Medicine to British Columbians” in association with the first Personalized Medicine Summit meeting held in June 2015, the case for personalized medicine has been getting stronger, considerable technological advances have been made and many clinical successes have been achieved. However, personalized medicine in BC largely remains an uncoordinated effort of a certain clinical centres, not-for-profit organizations, start-up companies, and BC’s universities, with ad-hoc support from various government agencies. This situation is not changing fast enough. For BC to be a leader in patient-centric, molecularly-based personalized medicine, large-scale, province-wide action is required. We need to mobilize all stakeholders – public sector, private sector, academic centres and not-for-profit agencies – and establish a cohesive, well-funded program with the resources required to implement personalized medicine in BC at scale. There is no time to lose if we are to ensure that we deliver the best possible healthcare to our citizens, and that BC becomes a globally significant personalized medicine innovation hub with resulting economic benefits.

The Personalized Medicine Initiative (PMI), together with partners Genome BC (GBC), Life Sciences BC (LSBC), the Centre for Prevention of Organ Failure (PROOF), the Centre for Drug Research and Development (CDRD), and the Life Sciences Institute (LSI) at UBC have therefore organized the second Personalized Medicine Summit to be held at UBC, June 11-13, 2017. This document, “Roadmap 2.0: The Time is Now for Personalized Medicine in British Columbia” has been produced for the Summit in partnership with PricewaterhouseCoopers (PwC), and is a discussion document to help establish the path for BC to become an international leader in the practice of personalized medicine. It is noted that BC has remarkable resources and assets to build on, including a first-rate medical system, globally competitive expertise in molecular medicine technologies, and internationally recognized efforts in the implementation of personalized medicine approaches. BC also has significant advantages arising from its single-payer system. Taken together, these resources could lead to a globally competitive hub for advancing personalized medicine. However, if we do not act soon, the opportunity will be gone and we will be importing these advances from other countries rather than exporting our products and expertise.

Most personalized medicine programs worldwide have focused on genetic analyses such as whole genome sequencing to guide cancer treatment. However, aside from genetic diseases such as cancer and hereditary diseases, genomic analyses are not that informative about acquired diseases, such as infectious diseases and most chronic disorders. Additional analyses are required, such as measures of an individual’s proteome and metabolome (e.g. proteins and metabolites in blood), as well as their microbiome (e.g. bacteria in the gut). By combining genomic, proteomic, metabolomic and microbiomic data, “Omic” data clouds can be generated that can be used to diagnose most diseases and prescribe individualized ways to improve health.
BC has made significant progress in establishing resources to gather and interpret Omic data. Now we need to build on these resources to implement an approach to personalized medicine in BC that will put us in a competitive position globally. Priority objectives that need be achieved over the next three years in order to achieve global competitiveness are:

1. **The BC government should make a leadership commitment to personalized medicine.** The BC government, through the Ministries of Health, Finance, Innovation, and Advanced Education, should assume a leadership role to enable personalized medicine.

2. **BC should establish an umbrella organization to catalyse and implement personalized medicine.** BC should establish an umbrella organization (UMBO) representing healthcare stakeholders to implement personalized medicine. UMBO would provide governance for a provincial “Oomics” database and provide leadership on funding opportunities such as the Federal “supercluster” initiative.

3. **BC should build on established strengths in personalized medicine.** Efforts must be made to enhance world-leading personalized medicine initiatives already underway in BC that are introducing molecularly-based medicine into the population.

4. **BC should construct a unique 25,000 person Oomics database in high cost/morbidity/mortality diseases.** This database would contain Oomics (genomics, proteomics, metabolomics, microbiomics) molecular profiling of British Columbians suffering from high burden diseases to establish a globally unique database to enhance patient-centric healthcare, translational research, innovation and make BC a global leader in the personalized medicine revolution.

In summary, implementation of personalized medicine in BC will lead to improved health of our citizens through early detection of disease, better matching of treatment to disease and improved ways of maintaining health. Globally, personalized medicine will likely lead to the largest industries the world has ever known. Roadmap 2.0 points the way forward so that British Columbians can become the healthiest in the world and can also participate in the considerable economic benefits that will accrue to leaders in the introduction of personalized medicine.
Why Is Personalized Medicine Important?

Everyone is born with a highly individual genetic blueprint, their genome, half of which comes from their mother and half from their father. As a result, every person starts life as a highly unique individual. Further, as a person gets older, the ways their genes function and are influenced by their lifestyle choices, their diet, and the bacteria that live inside and on the individual as well as the external environment they live in. Thus, as a result of an individual’s genetic inheritance and their subsequent life experience, each persons’ molecular makeup is very different from anybody else’s, which is the reason personalized medicine is so important.

Medical progress to date has largely been the result of advances that benefit people in general, resulting in “one size fits all” therapies which work for most people but may not work for a person who is not “average”. Until now, such population wide advances were the most efficient ways of improving health, but new technologies are now transforming medicine by enabling a movement to healthcare that is tailored to each unique individual. These new technologies allow detailed molecular level analyses to be made on the individual, which in turn can be used to diagnose disease, to match therapy to the particular disease and person, to detect disease before it becomes life threatening, and to optimize individual health.

The first step for a personalized medicine approach consists of making comprehensive molecular analyses of the molecules that each person is made of. When transformed into digital form, the resulting “data clouds” characterize that person more precisely than anyone has ever been characterized before. By comparing that individual’s data cloud to databases containing the world’s medical literature, molecules (“biomarkers”) can be identified in each person whose composition or concentration are abnormal and that are associated with states of health or disease. These biomarkers can be used as diagnostics to ascertain risk of disease, the presence of disease and enable better matching of treatment to disease. They can also be used to detect trends towards disease, thus enabling more effective preventive healthcare.

Individualized data clouds also allow patients to access to the latest medical advances. Medical knowledge is doubling every 1.6 years, personalized medicine allows our citizens to benefit from these advances by comparing their data clouds to continually updated medical data bases. This means that new medical findings relevant to them will be known almost immediately. Currently it takes 15 years or more for new medical advances to reach the doctor’s office.

The importance of personalized medicine is being recognized globally. England, the United States, Germany, China, Australia and India are only a few of the many countries that have made the substantial investments necessary to move towards molecular-based, precision medicine. Interestingly, most of these initiatives are focusing on genomic analyses with particular emphasis on cancer treatment. The opportunity exists for BC to move forward in a differentiated manner by employing a multi-Omic approach to diagnosing and treating all diseases. This approach will also enable more effective preventive medicine to maintain health.

Regardless of the way in which personalized medicine is introduced in BC it is imperative that as a community we establish coherent strategies for implementation that are accompanied by an appropriate level of investment. These strategies must involve commitment by, and collaboration between, government, universities, clinicians, health authorities and the private sector. In turn, we believe this will require coordination by an umbrella organization representing relevant stakeholders if we are to move personalized medicine practices from concept to reality in BC.
Why is Personalized Medicine Happening Now?

As noted, the practice of personalized medicine requires comprehensive data-clouds describing individuals at the molecular level. The reason personalized medicine is possible now is that the cost of generating this data is dropping rapidly each year. For example, the cost of sequencing a human genome has decreased from more than $1 billion in 2000 to less than $1,000 today\(^1\) (see Figure 2), as a result over a million genomes have now been sequenced\(^2\).

Similarly, the costs of other “Omic” analyses are decreasing rapidly. Proteomic analyses of hundreds of proteins in the blood and metabolomic analyses of hundreds of metabolites can now cost less than $500 each. Detailed microbiomic analyses of a thousand bacteria in the gut cost less than that.

This rapid reduction in costs is making personalized medicine become much more accessible for the consumer. For $2,000 or less, a person can now generate a comprehensive individual genomic, proteomic, metabolomic and microbiomic profile. This is important because protein, metabolite and microbiome analyses can provide real-time diagnostics for the presence of diseases that a person may have right now, as opposed to genomic information that indicates their risk of disease over a lifetime. These Omic profiles can also show whether the treatments the patient is receiving are working and can indicate whether preventive medicine approaches or lifestyle changes are effective.

Omic profiling, rather than just genome sequencing, is therefore now becoming a practical way of practicing personalized medicine. It is this opportunity that BC must act upon to take a leadership position in bringing personalized medicine to the population that is both effective and practical across many high burden disease areas. Few other jurisdictions have taken on this challenge and we have the opportunity and skills to be first. The challenge is to gather Omic data across a variety of people - both well and ill - and use this data to understand how to better treat disease and maintain health. The value of comprehensive Omic profiling,

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\(^1\) (National Human Genome Research Institute, 2016)

\(^2\) (Regalado, 2014)

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*Figure 2 - Rapidly Falling Costs Drive Growth in Human Genome Sequencing*
as opposed to just genome sequencing, is straightforward to illustrate. Blood, for example, bathes every organ in the body. Many of the molecules in the blood are derived from these organs as well as disease sites such as tumors. Proteomic and metabolomic analyses of molecules in the blood therefore contain an enormous amount of diagnostic information in the form of proteins and metabolites that can be used to detect early stage disease as well as reflect response to therapy.

Box 1: Zuri Scrivens, Trish Keating and Personalized Genomics for Cancer Therapy

The Personalized Onco-Genomics (POG) program at the BC Cancer Agency develops highly personalized therapies for treating cancer patients. This involves sequencing the cancer genome, identifying genetic mutations that are driving cancer cell growth, and devising novel therapies based on these mutations.

Zuri Scrivens was 33 when she was diagnosed with breast cancer. When the cancer reappeared at 35, she was enrolled in POG. On the basis of a genome sequencing analysis, metformin, a drug normally used to treat diabetes, was prescribed, together with a standard chemotherapy drug. Her cancer is now in remission.

Trish Keating was diagnosed with colorectal cancer and underwent five years of chemotherapy, surgery, and radiation therapy. When her cancer returned yet again, she was enrolled in the POG program and her tumour was sequenced. On the basis of this information a drug normally used to treat high blood pressure was prescribed. Within weeks of treatment with the blood pressure drug, Ms. Keating’s tumour was rendered nearly undetectable.

Our health is also affected by environmental factors such as the enormous number of bacteria and other microbes that live in and on each of us. These organisms can influence immune function, neurological conditions and metabolic disorders. Thus microbiomic analyses of bacteria in the colon or other locations provides insights into causes of many important diseases.

In summary, truly personalized medicine is being enabled because comprehensive Omic profiles can now be performed at costs that are increasingly affordable. These personal “data-clouds” consisting of genomic, proteomic, metabolomic, and other Omic profiles to characterize each individual very precisely, have major potential for detecting disease, matching treatment to disease and monitoring response to therapy. Analysis of Omic profiles can potentially allow early stage detection of over 500 diseases, ranging from cancer to heart disease to diabetes to inflammatory bowel disease. The potential benefits of early detection of disease for preventive medicine are clear.

What Are Examples of Personalized Medicine?

There are already many examples of personalized medicine practices. The use of genomic analyses to personalize the treatment of cancer is a lead example. Cancer is increasingly being treated according to the genetic profile of the cancer itself rather than the tissue it originates from (e.g. breast, colon, prostate, etc.). BC has considerable strengths in this area as demonstrated by the POG program at the BC Cancer Agency (see Box 1). Other genetic tests for cancer are coming on line to limit patient exposure to potentially harmful side effects of cancer treatments.

Genomic analyses can also be used to diagnose genetic diseases other than cancer. In the US, The Food and Drug Administration recently approved 10 of the personal-genomics company 23andMe’s screening tests for genetic health risks, including one for Alzheimer’s and one for a rare blood disorder.

The pharmaceutical industry is increasingly developing biomarkers as “companion diagnostics” to determine whether a drug is safe and effective for an individual. Approximately one-third of drugs in clinical development, and two-thirds in pre-clinical development, use biomarkers to guide prescription and treatment decisions. These biomarker tests target therapeutics to the appropriate patients by

3 (Personalized Medicine Coalition, 2014)
identifying who may benefit and who may not. This matching process could reduce health system costs in addition to helping the patient.

Genetic tests are also becoming available to avoid adverse drug reactions to prescribed medications. Currently many drugs have FDA-approved genetic biomarkers to avoid adverse reactions in patients with particular genetic profiles. These biomarkers are not currently utilized as doctors do not have access to the genetic profile of their patients. This leads to risky “trial and error” medication choices.

Genetic analyses are also improving diagnosis and management of rare diseases. Such patients often undergo a “diagnostic odyssey” to determine the reason for their symptoms. This exacerbates patient suffering and places expensive demands on the healthcare system. Whole genome sequencing is proving effective for specific diagnosing of rare and inherited genetic disorders and, in some cases, is providing an improved treatment strategy.

A final point is that the introduction of molecular medicine will also address inequalities in healthcare arising from differences in gender, ethnicity or age. Medicine based on individual molecular-level profiles will take such differences into account in a natural manner.

**What Are the Barriers to Implementing Personalized Medicine?**

While personalized medicine is clearly the future of medicine, there are many barriers to be overcome. Issues include access to information, education, training, consistent methods of storing and analysing data, regulatory and privacy issues for Omic data to

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*Figure 3 - Canada and BC at a Glance*[^1] - [^15]

[^1]: (U.S. Food and Drug Administration, 2017)
name but a few. Personalized medicine also signifies a shift in power from the healthcare system to the healthcare consumer, who will soon have access to detailed molecular-level information about themselves to diagnose disease and monitor the effectiveness of therapy. This transition must be supported and encouraged.

**Data Storage Capability & Capacity** “Big data” databases where patient data can be securely stored, analysed and shared are essential to the practice of personalized medicine. Advanced artificial intelligence capabilities are also required to compare individual data-clouds to the world’s scientific and clinical literature to access the latest medical advances. Clinicians must have seamless access to clinical and healthcare data records in addition to Omic profile data, to be able to be able to provide the best advice to their patients. Currently, healthcare data resides in silos that do not necessarily communicate with one another. Rectifying this situation will require new government policies around data security and privacy.

**Regulatory** As noted, healthcare consumers will increasingly have access to Omic profiles on which they will base healthcare decisions. Appropriate regulation is required to ensure such analyses are accurate and the diagnostics derived from these analyses are validated. The US FDA has produced draft guidance documents in these areas\(^5,6\) and we need to do the same. In addition to improving patient outcomes, these diagnostics enable comparative effectiveness research\(^7,8,9,10\) to discover cost-effective ways of improving healthcare.

**Advanced Analytics Capability & Capacity** Systematic studies relevant to the BC healthcare system are required to evaluate the cost/benefit equation associated with the introduction of molecular diagnostics. Such analyses require understanding of costs beyond those of the molecular test, such as the cost implications of the choice of drug and the number of hospitalizations avoided.

BC must also generate healthcare data to improve care in complex, high-cost disease states, many of which are associated with elderly patients. On p. 18, we suggest a population-wide Omic study of 25,000 British Columbians suffering from high cost, high burden diseases. Molecular profiles of many patients will be required to ascertain biomarkers associated with disease, disease progression, and identification of those who would benefit from standard therapy and those who would not. Analysis of this data will require advanced data analytics capabilities.

**Informed Consent** There is currently no consistent provincial guidelines for informed consent to use genetic or Omic data for research. Informed consent of patients is necessary for their participation in research where benefits only accrue from analyses of data arising from large numbers of patients willing to securely share anonymized information. The BC government needs to develop policy and a clear governance framework that enables harmonized consent both for initial analysis and for re-contact. Related issues include patient engagement and ownership of data.

**Awareness, Education & Training** A wide range of healthcare professionals (physicians, genetic counsellors, pharmacists, lab technicians and nurses) will be involved in gathering, communicating, interpreting and using of molecular information. These healthcare professionals will need to be trained, resourced, and incentivized to participate fully in the integration of personalized medicine into mainstream clinical practice. Clinical practice guidelines and educational materials must be updated to include guidance regarding use of molecular analyses.

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5 (U.S. Food and Drug Administration, 2014)  
6 (U.S. Food and Drug Administration, 2014)  
7 (Naik & Petersen, 2009)  
8 (Lantos & Spertus, 2014)  
9 (Mushlin & Ghomrawi, 2010)  
10 (VanLare, Conway, & Sox, 2010)
How Can We Implement Personalized Medicine in BC?

Implementation of personalized medicine practices in BC is currently due to relatively uncoordinated efforts in academia, the healthcare system and private industry. Improved collaboration and coordination of resources and effort is required and shared strategic framework must be developed for personalized medicine. The benefits will be substantial, leading to the best healthcare possible for our citizens, a more efficient and effective healthcare system, and considerable economic benefits stemming from the creation of new personalized medicine based industries.

BC is well-placed to be a global contender in personalized medicine if we have the shared purpose and vision to take on the challenge. Our strengths include an advanced, comprehensive medical system, globally recognized scientists and clinicians skilled in the practice of molecular medicine (see Appendix ii), and a single payer universal healthcare system with an inherent interest in preventing disease and improving efficiencies in healthcare delivery. It is vital that we leverage these resources to become a leader in the personalized medicine revolution.

This Roadmap contains four recommendations that provide a pathway towards enabling personalized medicine in BC. These are that: (1) the BC government should make a leadership commitment to personalized medicine; (2) we should establish and fund an umbrella organization to provide leadership and governance to guide the implementation of personalized medicine; (3) we should build on our assets by increasing support for new and ongoing personalized medicine efforts in our community; and (4) we initiate a unique, population-wide Omic database that will establish BC as a leader in the practice of personalized medicine. These recommendations are summarized in Figure 4 and expanded upon in the sections that follow.

Figure 4 – Implementation Recommendations

- **Make a Provincial Government Leadership Commitment**
  The government to make a financial commitment and set priorities

- **Form a Collaborative Implementation Organization**
  Develop a formal umbrella organization representing stakeholders in healthcare

- **Build On Our Assets**
  Strengthen and leverage our globally competitive initiatives in personalized medicine

- **Construct Omic Data Clouds for 25,000 British Columbians**
  Build a unique database that establishes BC as a leader in the personalized medicine revolution
1. Make A Provincial Government Leadership Commitment

Make a Commitment for BC to be a Leader in Personalized Medicine

In order for BC to develop a leadership position in molecularly-based, personalized medicine, it must become a government priority. The ways in which this commitment could be expressed are summarized in Recommendations 2-4 that follow. A purposeful, well-defined commitment by the government to develop policies and a strategic framework to encourage molecular medicine development, leverage our assets and facilitate implementation of personalized medicine is required.

Benefits for the Population

The potential benefits of personalized molecularly-based medicine include more effective treatments for patients suffering from cancer and other critical diseases, reduced adverse reactions to prescription drugs, earlier disease detection and better matching of treatment to disease to name but a few. Particular benefits will arise from improved matching of treatments to individuals regardless of sex, ethnicity or age. Current “one size fits all” therapies are less sensitive to such differences, leading to ineffective or inappropriate treatments.

Personalized medicine will also improve the treatment of common chronic diseases that are currently not well managed. An example is type 2 diabetes, where molecular profiling is revealing multiple subtypes\(^{11}\), suggesting a need to better match therapy to the particular form of the disease. Similar issues exist for patients with kidney diseases, cardiovascular and immune disorders, and abnormal cholesterol levels\(^ {12}\). Personalized approaches will likely lead to improved outcomes and more efficient use of healthcare resources.

Benefits for Healthcare

The healthcare system is under increasing pressure to deliver high quality care effectively and efficiently. Currently 44% of the healthcare budget\(^ {13}\) ($228 billion) is spent on people over the age of 65, whom constitute 16.6% of the population\(^ {14}\). The proportion of Canadians over the age of 65 is projected to be 25.2%\(^ {15}\) by 2036. The cost of treating seniors will consume more than 50% of healthcare dollars by 2028 if current trends continue.

The situation is even more critical in BC. We are collectively aging faster than most of Canada\(^ {16}\) and BC seniors will comprise 26.5%\(^ {17}\) of the BC population by 2040 and will consume more than 50% of healthcare costs by 2022 (see Figure 5). Personalized medicine represents one way in which medical costs can potentially be managed better. For example, approximately 50% of prescribed drugs do not help the person they are prescribed for\(^ {18,19}\) partly due to genetic differences between patients. This is estimated to cost BC $1.5 billion annually. Adverse drug reactions to prescribed drugs cost BC approximately $0.5 billion annually in hospital care. Better matching of drug to the individual and the disease they are suffering from could be expected to significantly reduce these costs.

There is also considerable potential to reduce healthcare costs by using molecular profiling data for identifying trends towards disease, thus enabling preventive medicine. The most effective way to

\(^{11}\) (American Diabetes Association, 2014)
\(^{12}\) (Krol, 2014)
\(^{13}\) (Canadian Institute for Health Information (CIHI), 2016)
\(^{14}\) (Statistics Canada, 2016)
\(^{15}\) (Statistics Canada, 2016)
\(^{16}\) (Statistics Canada, 2016)
\(^{17}\) (BC Stats, 2016)
\(^{18}\) (Evans & Relling, 1999)
\(^{19}\) (Spear, 2001)
reduce healthcare costs is to avoid people getting ill in the first place.

**Benefits to the Economy**

Personalized medicine will drive innovation and increase the economic benefit to the life science and technology sectors in BC. This includes commercial development of biomarkers to diagnose disease, designing biomarkers that match drugs to the patient and building applications that use molecular-level information to guide individual behavior to improve health.

The increased availability of detailed molecular-level profiles of individuals, when integrated with their healthcare data, will create insights that accelerate the discovery of new drug targets, new diagnostics and the new therapeutics that are specifically targeted to treat the disease the patient is suffering from. The clinical trials process will be expedited by correlating drug efficacy with patient-specific molecular profiles. Further, the use of molecular information also enables new clinical indications for established drugs (see **Box 1**).

Personalized medicine will also accelerate the formation of new companies to benefit the BC economy. For example, local pharmaceutical companies have developed novel classes of drugs discovered through molecular analyses of large patient cohorts. Others are using Omic analyses to ensure cancer drugs will work on the particular form of cancer the patient has or to avoid adverse reactions to prescription drugs. BC has a growing number of life sciences companies exploiting the personalized medicine revolution as noted on p. 18–20.

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**Figure 5 - Senior Consumption of Healthcare $ in BC**

Inflection point in 2023 where senior consumption of healthcare $ overtakes consumption by non-seniors.

Senior consumption of healthcare $ increases 80% from $10B in 2015 to $18B in 2040.

Widening Gap: $4.4B

Seniors are estimated to comprise 26.5% of BC’s population by 2040 vs. 18% in 2016, an increase of 8.5%.

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20 (Milne, 2014)

21 (Artenstein & Opal, 2011)
2. Form A Collaborative Implementation Organization

Establish an Umbrella Organization to Implement Personalized Medicine in BC

In the global context, BC is a small community. We must collaborate and cooperate in order to compete nationally and internationally in the personalized medicine revolution. A motivating point is that this revolution in healthcare is coming whether we like it or not. We need to be in the vanguard of this revolution, and benefit from the economic and innovation benefits available to early adopters. A high degree of collaboration and coordination is required among stakeholders to make this happen.

We recommend that BC establish a non-profit Umbrella Organization (UMBO) representing a coalition of stakeholders in personalized medicine to implement personalized medicine in BC. UMBO would have representation from patient organizations, academia, government, Health Authorities, health practitioners and industry. The mandate of the organization would be to provide the necessary leadership and governance to drive the implementation of personalized medicine into the frontlines of healthcare, to educate stakeholders, to lead the associated system change required and to support the realization of economic benefits in the form of new companies. Further, this organization would be expected to play a lead role in establishing a national presence and enabling Canada to become an international leader.

A central role of the UMBO would be to establish and manage an Omics database that provides a secure repository for all molecular-level characterizations of BC residents in various states of disease and health. UMBO would facilitate data aggregation, data interpretation and data sharing. This “big data” database would be made available to BC clinicians and scientists to stratify disease and match treatments more precisely to disease, as well as identify new targets for treating disease. The UMBO would be responsible for all aspects of governance.

Figure 6 - Stakeholder Engagement Map

The UMBO would also have the mandate to encourage the system change in government, healthcare delivery, and society to support effectively implement personalized medicine.

UMBO would also develop new funding streams and commercialization opportunities. The “supercluster” initiative of the Canadian government, which requires a united effort of BC stakeholders, is an example. UMBO’s ambition would be to establish BC as a major driver of innovation and wealth creation in the application of personalized medicine and to benefit from the creation of high-quality employment opportunities in this knowledge-based industry.
3. Leverage Our Assets

Amplify Our Strengths

To implement personalized medicine in BC we must build on our strengths. BC is achieving significant global impact in many areas of personalized medicine. These efforts must be amplified and scaled to anchor personalized medicine as a lead priority and opportunity in healthcare, academia and industry in BC. Here we provide nine examples of ongoing efforts, there are many more.

A comprehensive program of treatment optimization coupled with outreach and supported by personalized medicine has allowed Julio Montaner and colleagues at the BC Centre of Excellence in HIV/AIDS to virtually control the HIV/AIDS epidemic. This work and other initiatives stemming from it (see Example 1) are world-leading efforts that must be expanded.

Example 1: Personalized Medicine for treatment of HIV/AIDS and Hepatitis C

By using the genetic information of both the patient and their HIV and/or Hepatitis C strains, clinicians are able to determine the most effective drug cocktail to use and minimize side effects that may lead to the patient discontinuing treatment. This project is helping to save time and money while also significantly decreasing the number of new HIV/AIDS cases. This has already led to reductions in morbidity and mortality of more than 90% in BC, as well as an estimated reduction of >3200 new cases of HIV infection.

BC is also globally competitive in the utilization of genetic analyses to guide the treatment of cancer. UBC Professor David Huntsman and his colleagues have developed cost effective tools to better match cancer patients with treatment options and a platform for empowering pathology laboratories around the world to deliver leading edge cancer tests (see Example 2). We have an opportunity to build on these successes to improve the effectiveness of cancer care in BC.

Example 2: Tailoring Chemotherapy to the Patient’s Cancer Genome to Enhance Anti-Cancer Potency

Approximately 75% of the drugs used for cancer chemotherapy do not work on the patient they are prescribed for\(^2\). Contextual Genomics has developed a genetic analysis that tests for 90 mutations in the tumour genome that can be targeted by currently available drugs. Testing was provided to 2,000 Canadian cancer patients through their “National Access Program”. The experience gained has led to multiple partnerships to provide this testing both within Canada and internationally. Contextual’s focus on cost effectiveness, quality and empowerment of local health systems has underpinned strong growth.

The Personalized Oncogenomics (POG) program at the BC Cancer Agency recognizes that cancer should be treated by matching therapy to the mutation driving the cancer. Currently we treat cancer using a one-size-fits all approach according to the location of the cancer (breast, colon, prostate, lung etc.), using therapies that may be inappropriate. As indicated in Box 1 and Example 3, these efforts are leading to new breakthroughs in the treatment of cancer that must be amplified.

Example 3: Tailoring Cancer Therapy to the Genetic Form of the Cancer

The POG program at the BCCA led by Dr. Marco Marra and Steven Jones, targets the root cause of the cancer. BCCA oncologists, pathologists and other clinicians along with the Genome Sciences Centre (GSC), decode the genome – the entire DNA – of each patient’s cancer, to understand what is enabling it to grow. This information assists clinical decision-making regarding treatment strategies to block its growth, identify clinical trials that the patient may benefit from, and potentially identify less toxic and more effective therapeutic options.

BC also has strengths in the development of genetic tests to avoid adverse drug reactions to commonly prescribed drugs used in family practice situations. Adverse Drug Reactions (ADRs) are currently the fourth leading cause of death in North America (>100,000 deaths per year)\(^2\). Predictive tests to determine who is at risk of an adverse reaction to a prescribed drug will be of considerable benefit to patients and could lower healthcare costs substantially. Dr. Martin Dawes (UBC Family Practice) is developing a genetic test (see Example 4) to guide prescription practices in the family practice setting, where 85% of drugs are prescribed. Remarkably, this represents the first time in the world that genetic data is being used to guide prescription of drugs in family practice.

Example 4: Pharmacogenomics (PGx) in Primary Care

The PGx in primary care initiative led by Martin Dawes (UBC Department of Family Practice) has developed and will be implementing through GenXys Healthcare Solutions a medication decision support system (MDSS) that incorporates genetic and clinical information to guide prescriptions for 40 common diseases. It is anticipated that implementation of this MDSS by family doctors and pharmacists will result in improved patient outcomes (i.e., fewer adverse drug reactions) and reduced costs (i.e., fewer hospital admissions). A primary care pharmacogenetics testing panel has been developed as part of this work, to report on 60 SNP’s that are related to drug metabolism.

In a related project, an initiative from UBC is utilizing community pharmacists to determine whether a patient is at risk for an adverse reaction to a prescribed drug using whole exome sequencing (see Example 5). It is clear that empowering pharmacists in this way is an important way forward in making sure that patients benefit from molecular level information.

Example 5: Genomics for Precision Drug Therapy in the Community Pharmacy

This project led by Corey Nislow (UBC Faculty of Pharmaceutical Sciences) is showing that...
residing in the gut or other locations in or on the body. Such characterizations are vital to understanding many common diseases (see Example 7).

### Example 7: Microbiome and human health

A human body contains more than 10 times as many bacteria as it does human cells and the composition of microbiome can strongly influence one’s health. Disorders that have been identified with a dysfunctional microbiome include allergies, obesity, premature birth, inflammatory bowel disease and neurological defects. Microbiome Insights, a UBC spin-out provides a vital service to characterize the human microbiome that may be expected to lead to more effective ways to control related diseases, and expects to introduce a gut health test to monitor the effectiveness of dietary and other changes to achieve a “healthier” microbiome.

The next example concerns the need to be able to generate the comprehensive Omic data clouds required to diagnose disease more precisely, to ascertain whether therapies are working, to detect the recurrence of disease and to enable the practice of more effective preventive medicine. The Molecular You Corporation has been set up by principals from UBC, the University of Alberta (U of A) and the University of Victoria (U Vic) to build such data clouds and interpret them (see Example 8). The MYCo profiling capabilities can also be used to characterize patients suffering from disease ranging from cancer to diabetes to neurological disorders among many others to stratify subtypes of disease and match therapy more appropriately to the individual suffering from the disease.

### Example 8: Omic data clouds for disease stratification and preventive medicine

As noted throughout this Roadmap comprehensive Omic data clouds are required to practice personalized medicine. The Molecular You Corporation (MYCo) was formed to generate and interpret comprehensive Omic data clouds. MYCo represents a fusion of world-leading expertise from three universities in Western Canada and includes Dr. David Wishart (U. of A), Dr. Christoph Borchers (U Vic) and Drs. Cullis, McManus, Russell and Huntsman from UBC. MYCo brings together world leading proteomics (Borchers) and metabolomics (Wishart) expertise, as well as extensive clinical and informatics expertise (McManus, Russell and Huntsman). MYCo takes person-specific data clouds (700,000 SNPs from the genome, ~400 proteins and metabolites in blood and >1,000 bacteria in fecal matter) and provides diagnostic and prognostic information for over 500 diseases. MYCo works through MDs to provide this information to clients, together with dietary, exercise, lifestyle, supplements and other information to maintain and improve health.

A final example concerns the value of gathering Omic information over populations, discovery of unusual phenotypes can lead to new ways to treat disease. Drs. Michael Hayden and Simon Pimstone have exploited such information to develop new drugs to treat neurological disorders, see Example 9.

### Example 9: Genomics for Drug Discovery

Knowledge of human genomics for people with rare genetic defects can lead to identification of new targets to treat previously untreatable conditions. Xenon Pharmaceuticals is a BC-based company developing therapeutics to treat neurological disorders. Mutations in a gene called KCNQ2 cause an extreme epilepsy disorder characterized by multiple, daily, treatment-resistant seizures in children. XEN1101 is a drug that targets the gene product of KCNQ2, and could be a new treatment for these children. Another Xenon drug, XEN901 is designed to treat children with mutations in a gene called SCN8A who also experience severe seizures. Both XEN901 and XEN1101 are personalized drugs that could enable a better match between the drug and a child suffering from epilepsy.

BC therefore has major strengths which can be leveraged to build a globally competitive and internationally recognized personalized medicine program. Prioritized resources must be applied to these successful programs to amplify their efforts and to accelerate adoption into the broader BC health sector and beyond.
4. Generate Omic Data-Clouds for 25,000 British Columbians

Construct a Globally Unique Omic Database

The medicine of the future will be data-driven, enabled by the generation and interpretation of molecular-level Omic data-clouds describing each individual with a precision never possible before. Other jurisdictions are realizing this as well, however most efforts are focused largely on genomic analyses (see Appendix iii). As emphasized here, genomic analyses inform on disease risks over a lifetime but give less information on diseases the individual actually has. Other Omic analyses are required, such as proteomic and metabolomic analyses of proteins and metabolites in the blood, as well as microbiomic analyses of bacteria in the stool. The resulting data-clouds can give much more precise diagnostics of current states of health and progression of disease.

We recommend that BC gather standardized, longitudinal (over 5 years), comprehensive molecular data clouds for 25,000 volunteers representing a cross-section of the patient communities that incur the highest costs, both in terms of mortality/morbidity as well as monetary costs to the healthcare system. These volunteers would be drawn from cohorts representing major disease states and will involve all socioeconomic, age, sex, and ethnic populations. The molecular analyses will include a genomic analysis as well as proteomic, metabolomic, microbiomic, and possibly other Omic analyses. Additional data, such as data from wearables to report on activity and vital signs, could be included.

This effort would use the database managed by the UMBO described under Recommendation 2. The areas of disease focus would include: cancer, autism, and chronic diseases of the aged such as dementia, Alzheimer’s, Parkinson’s, diabetes, heart failure, and COPD, among others. When combined with phenotypic and clinical data, these molecular data clouds will provide a remarkable discovery and innovation engine. Benefits could include identification of new biomarkers associated with disease and precursors to disease, the most appropriate ways to treat an individual’s disease, better ways to optimize performance and the most efficient use of healthcare resources.

The database will allow clinicians to stratify patients in any given disease cohort into those who respond to current therapy and those who may not. This will allow the development of more appropriate therapies for non-responders. Better matching of therapy to the individual will not only improve outcomes but make the healthcare system more efficient. There is room for improvement, more than 50% of prescribed drugs do not work on the patients they are prescribed to.

Figure 7 – UMBO Omic database containing data from 25,000 British Columbians

The comprehensive Omic database covering 20 or more high impact diseases would distinguish BC from most, if not all, other jurisdictions and would establish BC as a contender in the global...
race towards personalized, precision medicine. The database will catalyse considerable translational research, drive innovation, and commercialization. It will enable BC’s research community to use human data to inform basic research aimed at understanding the causes of disease and methods to treat disease. Further, establishing and utilizing the database will drive the necessary system changes required to enable personalized medicine to be effectively practiced in BC.

**Conclusion**

Personalized medicine is a reality that is happening now. We have a choice to participate now and develop personalized medicine practices here in BC that we can export, or we can procrastinate and purchase molecular medicine products and practices from other jurisdictions in a few years time. This Roadmap summarizes the need for introduction of personalized medicine practices, the advantages this will bring, the strengths that BC can build on, and the ways that personalized medicine could be enabled and implemented. We hope that the strategies and priorities suggested here will motivate the stakeholder actions necessary to scale personalized medicine efforts in BC. It is important that the benefits of the personalized medicine revolution be made available to BC’s population and that BC becomes a leading force in the movement towards individualized care based on Omic profiling. A potential implementation roadmap is summarized in Figure 8.

*Figure 8 - Implementation Roadmap for Personalized Medicine in BC*
Appendix

i. Glossary

**Adverse drug reactions** (ADRs): Detrimental effects of a medication that was correctly administered at the right dose for therapeutic or prevent use.

**Big data**: Large and complex sets of data that cannot be manipulated or analyzed using standard data processing applications and tools. In biology, it refers to the rapidly growing amount of digital data such sequence data, other molecular information (e.g., proteome), connectomics (the comprehensive mapping of every neuron in the brain with its neighbour), and other biological information. Advanced computing infrastructure and predictive analytics (i.e., modelling, machine learning, and data mining) are used to process and unlock the value contain within big data sets.

**Biobank**: A large collection of human biosamples for research purposes.

**Biomarker**: A molecular signature (e.g., DNA, RNA, protein, metabolite, microflora, or a combination of thereof) indicative of some biological state or condition (usually in reference to a particular diseased state).

**Biosamples**: Samples containing biological materials such as blood, urine, saliva, stool, tissue, etc.

**Companion diagnostic**: A medical device or laboratory test that provides information to guide for the safe and effective use of a corresponding treatment (i.e., drug or biological product such as an antibody therapy). The test helps determine whether a particular therapeutic product’s benefits are greater than any potential side effects or risks to the patient.

**Comparative Effectiveness Research** (CER): Research that directly compares existing health care interventions to determine which work best for which patients and which pose the greatest benefits and harms.

**Data cloud**: A “virtual” environment (i.e., remote computing infrastructure) where information of all types can be stored and accessed in real-time. When used in relationship to health, the data cloud encompasses the individual’s identification, medical history (i.e., electronic medical records), clinical information (e.g., blood work), molecular information (e.g., genome, proteome, metabolome, microbiome), and information measured by wearable technology.

**DNA** (deoxyribonucleic acid): Self-replicating polymer (sequence) of nucleic acids that is present in nearly all living organisms. It is the carrier of genetic information that encodes the instructions for the development and functioning of all known living organisms.

**Electronic medical records** (EMRs; or electronic health records [EHRs]): An electronic record of an individual’s health information that is theoretically capable of being shared across different healthcare settings.

**Epigenomics**: The study of the chemical compounds and the processes that modify (i.e., epigenetic marks) the genome and its associated proteins to regulate the expression of genes in a cell.
Gene: A sequence of DNA that codes for a particular protein with a specific function in a cell.

Genome: The complete set of genes or genetic material encoded in the DNA in a cell or organism.

Genomics: The study of the structure, function, evolution, and mapping of the genetic material (i.e., DNA, RNA) present in a cell or organism.

Metabolites: Small molecule intermediaries and products of metabolism (usually less than 1500 Daltons).

Metabolomics: The study of the complete set of metabolites within an organism, cell, or tissue and the chemical processes involved in their production and breakdown.

Microbiome: The study of the complete set of indigenous microbial organisms in a biological specimen or those associated with another organism, such as a human.

Omics: Refers to fields of biology that at aims at the collective characterization and quantification of pools of biological molecules (or measurements) that translate into the structure, function, and dynamics of an organism(s). These biological measurements include, but not limited to, DNA (genome), RNA (transcriptome), proteins (proteome), metabolites (metabolome), microflora (microbiome), and neural connections in the brain (connectome).

Personalized Medicine (precision medicine or stratified medicine): The use of molecular-based individual information to guide medical decisions, practices, and/or therapies.

Pharmacogenomics: The study of the individual’s genetic information and how it affects drug response.

Phenotype: An organism’s observable characteristics or traits (e.g., physical appearance, biochemical or physiological properties, behaviour).

Preventive healthcare (preventive medicine): Healthcare that focuses on proactive strategies to avoid disease development as opposed to disease treatment. Molecular understanding such as genetic sequencing of an individual can inform of disease risk, thus allowing the individual to take pre-emptive measures such lifestyle changes or preventive surgery (i.e., in the case of certain breast/ovarian cancers, the ‘Jolie effect’) to avoid development of disease.

Proteomics: The study of the complete set of proteins that is or can be expressed by a cell, tissue or organism.

RNA (ribonucleic acid): Like DNA, it is a polymer of nucleic acid present in all living cells and organisms, that act as a messenger carrying instructions from DNA for controlling the synthesis of proteins.

Sequencing (DNA sequencing, genetic sequencing, whole genome sequencing): The process of determining the order of nucleotides within a genetic sequence.

Transcriptomics: The study of all the messenger RNA molecules expressed from the genome of an organism.

Wearable technology (wearable devices): Wearable electronic devices that contain wireless sensors to remotely measure the body’s physiological parameters (e.g., blood pressure, beats per minute, blood oxygenation, brain activity) as well as physical activity (e.g., steps taken, flights of stairs climbed).
## ii. Personalized Medicine Resources in BC

<table>
<thead>
<tr>
<th>Academic Research Institutes</th>
<th>Spinal Cord Injury and Neurology</th>
</tr>
</thead>
<tbody>
<tr>
<td>• University of British Columbia</td>
<td>• NeuroDevNetNCE</td>
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<tr>
<td>• Simon Fraser University</td>
<td>• iCORD</td>
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<tr>
<td>• University of Victoria</td>
<td>• Djavad Mowafaghian Centre for Brain Health</td>
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<tr>
<th>Cancer</th>
<th>Infectious Diseases</th>
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<tr>
<td>• BC Cancer Agency</td>
<td>• BC Centre for Disease Control</td>
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<td>• Michael Smith Genomic Sciences Centre</td>
<td>• BC Centre for Excellence in HIV / AIDS</td>
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<td>• The Vancouver Prostate Centre</td>
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<tr>
<th>Cardiovascular Lung and Health</th>
<th>Drug Development</th>
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<tr>
<td>• PROOF Centre</td>
<td>• Centre for Drug Research &amp; Development (CDRD)</td>
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<td>• Centre for Heart Lung Innovation</td>
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<tr>
<td>• Canadian Arrhythmia Network (CANet) NCE</td>
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<tr>
<td>• Institute for Heart + Lung Health</td>
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<th>Pediatrics</th>
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<tr>
<td>• Child &amp; Family Research Institute</td>
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<td>• Centre for Molecular Medicine and Therapeutics</td>
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## iii. Details on Other Omic Initiatives

<table>
<thead>
<tr>
<th>Name of Initiative (Organization)</th>
<th>Public/ Private</th>
<th>Main Objective</th>
<th>Cohort Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precision Medicine Initiative <em>(United States Government)</em></td>
<td>Public</td>
<td>Establish a molecular (genomics) database of 1 million voluntary Americans to conduct research to improve diagnostics and treatments for disease, starting first with cancer.</td>
<td>1 million</td>
</tr>
<tr>
<td>100,000 Genomes Project <em>(Genomics England; NHS)</em></td>
<td>Public</td>
<td>Establish a database of 100,000 genomes to enable new scientific discoveries and insight to bring benefits to patients with rare diseases or cancer.</td>
<td>100,000</td>
</tr>
<tr>
<td>Million Veterans Project <em>(US Department of Veterans Affairs)</em></td>
<td>Public</td>
<td>Establish a database of genomic and medical data to understand how genes affect health and disease, such as diabetes, cancer, and post-traumatic stress, in order to improve healthcare for veterans.</td>
<td>1 million (&gt;345,000 volunteers registered)</td>
</tr>
<tr>
<td>Personal Genome Project <em>(Harvard Medical School)</em></td>
<td>Public</td>
<td>Establish an open-access database of non-anonymized whole genome and longitudinal clinical data to better understand human traits and health.</td>
<td>100,000</td>
</tr>
<tr>
<td>Million Omics Database Project <em>(Beijing Genome Institute)</em></td>
<td>Private</td>
<td>Establish a molecular medicine database for 1 million people that include: genomic, transcriptomics, epigenomics, metabolomic, and microbiomics data for health and commercial benefits.</td>
<td>1 million</td>
</tr>
<tr>
<td>23andMe</td>
<td>Private</td>
<td>Provide whole genome sequencing services to consumers and establish a database of genomic information for use in health research and development of new drugs.</td>
<td>&gt;1,000,000 clients</td>
</tr>
<tr>
<td>The Baseline Study <em>(Google X Life Sciences)</em></td>
<td>Private</td>
<td>Collect genetic and molecular data to analyze and uncover biomarkers for disease.</td>
<td>&gt;100,000</td>
</tr>
</tbody>
</table>
### Human Longevity Inc.  
**Private**  
Compile the most comprehensive database on human genotypes and phenotypes using the latest genomics, proteomics, microbiomics, informatics, computing, and cell therapy technologies to understand aging and associated diseases.  
100,000 per year

### Human Genetics Initiative  
**Private**  
Collect and analyze the genetic information of 100,000 individuals to develop new drug targets and pharmacogenomics markers.  
>100,000

### 100K Wellness Project  
**Private**  
“P4 Medicine” using the latest molecular profiling and wearable technologies to amass a database for understanding health at the molecular level and enabling preventive medicine.  
100,000
iv. References


illumina-says-228000-human-genomes-will-be-sequenced-this-year/


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