Strategic Plan

2019 – 2024

Contents

Executive Summary

1. Metabolomics

Metabolomics is the study of the metabolome—the complete set of small-molecule metabolites found within a biological sample. These metabolites arise from biochemical processes in cells within the organism itself, but also from processes occurring in the wide variety of other organisms living within it, such as bacteria on the skin and other organs, or within the gut (the "microbiome"), as well as from parasites, viruses, fungi, phages, etc.

Analysis of the metabolome provides a near real-time, unique "snapshot" of an organism's biochemistry. Sophisticated technologies can identify and quantify these metabolites, allowing them to be clearly linked to other technologies and assays such as genomics, transcriptomics, and proteomics (when integrated, termed "multi-omics"). In essence, metabolomics is a next generation "translator" that allows us to understand and predict what is happening within living cells, as mediated by all the other omics processes. Since changes to the metabolome reflect changes in the health and disease status of all living organisms, this opens enormous opportunities for precision diagnoses, individually targeted interventions, and a sensitive tool for a wide range of life-system monitoring.

2. The Metabolomics Innovation Centre (TMIC)

TMIC was formed in 2011 with the vision of becoming one of the world's premier metabolomics facilities, offering the widest possible range of cutting-edge, comprehensive, quantitative metabolomic research capabilities and services. It operates as a "distributed network Platform" through an administrative support team and 7 "Nodes" or laboratories distributed among the University of Alberta (UofA), (including the core lab plus three other labs), the University of Victoria (UVic), McMaster University, and McGill University, with an agreement to integrate a Node at the University of Calgary in the coming months. This model affords additional power, flexibility, and customization compared to a single-site model.

TMIC's **vision** is

> *To improve life through the power of metabolomics.*

The **mission** of TMIC is:

> *To catalyze innovation and translate metabolomics from the laboratory to real-world use by creating novel technologies, providing cutting-edge analytic services, sharing foundational data resources, and equipping the next generation of scientists and users. The ultimate goal is to enable the creation of a strong metabolomics industry in Canada and generate social and economic benefits for Canadians.*

TMIC maintains a comprehensive suite of state-of-the-art instrumentation and highly skilled personnel to provide innovative metabolomic services, resources, databases and bioinformatics, plus training, and technology development and knowledge transfer for a wide range of users in three "tiers":

- First tier – External (Canadian and international academic researchers);
- Second tier – Industrial firms commercializing novel metabolomics-enabled technologies;
- Third tier – People and organizations (e.g., in healthcare, government, non-governmental organizations (NGOs)) using these technologies to improve life.

Since its inception in 2011 through to December 2019, TMIC has received $9.43 million in platform funding from Genome Canada and $3.1 million from the Canada Foundation for Innovation's Major Science Initiatives program (CFI-MSI). An additional $2.6 million in funding to TMIC has been requested from Genome Canada for the period of April 2020 to March 2022, and $4.4 million from for the period of April 2020 to March 2023. Co-funding from other agencies (including Alberta Innovates, Canada Research Chairs, Western Economic Diversification, Genome Alberta, Genome BC, the Canadian Institutes of Health Research, the UofA, UVic and McGill) has provided another $5.5 million to TMIC until 2022.

3. The Opportunities for TMIC

TMIC has the potential to catalyze Canadian leadership in metabolomics technology development, and to provide the resource underpinnings to allow its users and partners to pursue and drive transformative socioeconomic benefits (SEBs). This potential rests upon its expertise in technology innovation, its function as a cutting-edge research platform, and is supported by a massive and internationally recognized data resource.

On the technologies side, metabolomics is experiencing near exponential growth: research activities are growing at a rate of about 15%/yr., while the global metabolomics market was valued at $1.64 billion in 2018 and is expected to reach $3.6 billion by 2024 [1]. TMIC is already demonstrating global leadership in the development of advanced instrumentation, innovative metabolomics kits, cutting-edge software, and comprehensive software and databases. These have tremendous commercial potential, especially when strengthened through a multi-omics approach. While it is likely outside the scope of this 5-year plan, a stretch objective for TMIC is to assist in Canada becoming a leading centre for innovative metabolomics enterprises, eventually helping Canadian industry capture a significant portion of this world market.

On the SEB side, there is an enormous potential to use metabolomics and in a wide range of sectors, although these are still largely at the research stage. A small sample includes human precision medicine (e.g., cancer, diabetes, autism, Alzheimer's, and heart disease); food animal production and welfare (e.g., improving production, reducing feedstock and antibiotic use, increasing animal health and welfare); agriculture and agri-food production (e.g., identifying biotic and abiotic stressors and interventions, reducing chemical use and environmental harm; fewer trade sanctions); and improving natural resource use and sustainability (e.g., identifying pollutants, pests, and pathogens; improved efficiencies and lower effluents; more timely interventions; better mine site reclamation outcomes). TMIC intends to foster development and practical use of such applications by first targeting exposome[1] studies to identify harmful natural and manmade chemical exposures, then partnering with industry and healthcare organizations to identify their effects, and eventually expanding more broadly through proactive relationships with other users and sectors, and for other uses.

In both technology development and SEBs, TMIC intends to be a thought leader, using cutting-edge technology development and training, and fostering a multi-omics approach to drive this vision for our partners in academic, public, and private user organizations.

4. TMIC Guiding Principles

- ***Innovative –*** State-of-the-art in all aspects.
- ***Collaborative*** – Proactively foster collaboration within the Platform, and with our users

[1] The exposome measures all of an individual's lifetime environmental exposures and how these relate to health.

- ***Accountable –*** Manage with integrity, transparency, and accountability.
- ***Confidential*** – Ensure the privacy of data, findings, and intellectual property (IP) as appropriate.
- ***Inclusive*** – Maintain and promote inclusivity, diversity, and equity in TMIC.
- ***Sustainable*** – Sustain and attract the human and financial resources required to succeed.
- ***Enabling benefits for Canadians*** – Maximize the relevance and practical application of TMIC research and technology development for our community of external users.
- ***Excellence –*** Attract and retain highly skilled people, offer high-quality cost-effective services, and pursue projects where metabolomics science and applications are of the most benefit.

5. Five-Year Strategic Objectives

(1) Platform – Make TMIC a World-class "Go To" Source for Metabolomics services. The *Target communities* are both the research community, and industry wishing to develop and utilize novel metabolomic technologies.

(2) Science – Strengthen the Canadian Metabolomics Scientific Community. The *Target communities* are both in-house TMIC staff, and the broader external Canadian scientific community – the "first tier" of external users – that either conducts metabolomics analyses themselves or rely upon TMIC to move this external research forwards.

(3) Commercial – Strengthen the Canadian Metabolomics-Enabled Industry. The *Target community* is Industry, as the "second tier" of external users, to support commercialization of novel technologies and devices either employing metabolomics directly, or developed using metabolomics data and analyses.

(4) Societal – Develop Workflows and Services to Integrate Metabolomics Data and Devices into Practical End-user Applications. The *Target community* is the "third tier" of users, who will use those commercial devices for SEBs in clinical diagnoses, regulatory decisions, environmental monitoring, etc.

6. Governance and Management

Governance - The Board of Directors (the "Board" or "BoD") advises all Member Institutions which reporting to the UofA (as host institution) and monitors TMIC activities in accordance with its Constitution, and subject to endorsement by the UofA. The Board structure consists of no less than 11 highly qualified senior individuals from the academic, not-for-profit and private sectors, including the Vice Presidents of Research from the two Founding Partners (UVic and UofA), one members from each of TMIC's major funders, two ex officio members from the TMIC Management Committee (both non-voting) and at least six independent or at-large members. The revised governing structure is designed to strengthen the "external face" of TMIC, ensuring that it has balanced demographic and jurisdictional representation, it's decisions and directions truly reflect the needs of the larger community, and it keeps a strategic focus on delivering scientific, societal and economic benefits for Canadians.

Management. TMIC is managed by a Management Committee (MC) consisting of the scientific co-directors and an Operations Manager (appointed by the Dean of Science at the UofA). The MC is supported by a number of Node-based, non-academic support staff. The MC has the overall responsibility for guiding and ensuring TMIC's operational, financial and scientific goals, as well as its vision for the future are met, in accordance with the strategies, policies, programs and performance requirements recommended by the Board. A Nodes Committee (NC) comprising all Node Leaders is TMIC's general management body and is chaired by a member of the MC (chosen on an annual rotating basis). An International Scientific Advisory

Committee (ISAC) reports to the TMIC Management Committee and Board, evaluating TMIC's scientific progress and providing scientific advice and guidance.

1. Introduction

1.1 Metabolomics

Metabolomics is the study of the metabolome—the complete set of small-molecule metabolites found within a biological sample. These metabolites represent the end-products derived from thousands of interacting genes, proteins and physiological processes, many of which respond to the environment. These metabolites arise from biochemical processes in cells within the organism itself, but also from processes in the wide variety of other organisms living within it, such as bacteria on the skin and other organs, or within the gut (the "microbiome"), as well as from parasites, viruses, fungi, phages, etc.

Analysis of the metabolome provides a near real-time "snapshot" of the biochemistry occurring within any given living organism. A number of sophisticated technologies originally developed for analytical chemistry now exist that can both identify and quantify tiny amounts of these metabolites, for the first time allowing them to be clearly linked to other 'omics technologies and assays such as genomics, transcriptomics, proteomics, epigenomics, and metagenomics, plus related disciplines such as bioinformatics and synthetic biology (together termed "multi-omics").

Metabolomics thus provides a unique window on gene-environment interactions and permits robust, quantitative phenotyping of difficult-to-characterize organisms. Interest in metabolomics is growing exponentially as more scientists, in many disciplines, realize its potential to accurately measure phenotypic traits, probe system-wide interactions, integrate multiple omics measurements and discover novel biomarkers. Just as biochemistry for many years has been the "translator" that allowed scientists to understand the relationship between the chemistry and biology of living organisms, metabolomics is the "next generation translator". It allows us to fully understand and predict the chemistry happening within living cells, as mediated by all the other omics processes that regulate gene activity, protein building and use, and the responses of these processes to the environment, with artificial intelligence (AI) and machine learning (ML) approaches used to correlate the massive data sets generated by each type of assay.

Since the metabolome changes as the biochemistry and health of the overall organism changes, these measurements can be used to identify ongoing changes in the organism's overall health and disease status. These concepts apply to all living organisms (including humans, food animals, and agricultural crops) and the environment in which they live (e.g., water quality as affected by pathogens living in it).

1.2 The Promise of Metabolomics – *"What if?"*

What if? TMIC intends to be a thought leader in the *"What if?"* of metabolomics. What if, through advanced computational techniques and models, metabolomics can be positioned as one component of an integrated "multi-omics" approach to the life sciences (also called "cross-omics, or "poly-omics")? What if this integrated approach can be operationalized through highly innovative commercial metabolomics products and services, led by Canadian researchers and industry, and supported by TMIC resources? What if these products and services in turn can be brought to bear on some of the most

pressing problems facing Canada and the world, including healthcare, food animal production, agriculture and agri-food, the environment, and quality of life, generating important socioeconomic benefits (SEBs) for society?

User sectors are eager – even desperate – for effective solutions to many problems that are nearly-intractable through conventional means, and these will be a source of enormous market pull if Canada can develop an effective, explicit, and concrete strategy to solve them through metabolomics. TMIC intends to catalyze these efforts – it will provide the underlying Platform resources to enable researchers, industry, and user organizations to conduct strategic and applied projects, but also proactively help identify important practical SEB opportunities for these users to pursue separately.

Canada can then be positioned to be a global player in two important fields: (1) developing commercial metabolomics-enabled technologies; and (2) fostering and catalyzing the development of solutions for practical social, economic, and environmental applications. In the current Strategic Plan, TMIC has initiated a very ambitious strategy and operations plan intended to make it a thought leader in these areas, helping drive the efforts of users and developers of practical SEB applications to realize these impacts over the coming years.

2. The Metabolomics Innovation Centre (TMIC)

2.1 Vision and Mission

TMIC's **vision** is

> *To improve life through the power of metabolomics.*

The **mission** of TMIC is:

> *To catalyze innovation and translate metabolomics from the laboratory to real-world use by creating novel technologies, providing cutting-edge analytic services, sharing foundational data resources, and equipping the next generation of scientists and users.*[2] *The ultimate goal is to enable the creation of a strong metabolomics industry in Canada and generate social and economic benefits for Canadians.*

2.2 TMIC History and Structure

TMIC is a national distributed network that provides metabolomics services for academia, and public and private sector clients throughout Canada and internationally. The Nodes (see below) that make up the TMIC Network are also leaders in developing the enabling technologies behind these cutting-edge services and are enabling applications in all aspects of life sciences.

Over the past decade, Canada has emerged as a world leader in metabolomics research by pioneering the development of innovative hardware, software, databases, chemical libraries and methodologies to perform comprehensive metabolomic analyses of biological samples. To consolidate and exploit this expertise, TMIC was formed in 2011 with the vision of becoming one of the world's premier metabolomics facilities, offering the widest possible range of cutting-edge, comprehensive, quantitative metabolomic

[2] See section 2.3 for a discussion of the user communities.

research capabilities and services. Now operating as a distributed network of Nodes, TMIC maintains a comprehensive suite of state-of-the-art instrumentation (valued at > $26 million) and highly skilled personnel to provide innovative metabolomic services and resources, training, and technology development and transfer. Moving forward, increased use of artificial intelligence (AI) and machine learning (ML) will open up even more opportunities to exploit metabolomics data for insights on biological systems.

Since its inception in 2011 through to December 2019, TMIC has received $9.43 million in platform funding from Genome Canada and $2.87 million from the Canada Foundation for Innovation's Major Science Initiatives program (CFI-MSI). An additional $2.8 million from Genome Canada and $2.9 million from CFI in funding to TMIC has been requested for the period April 2020 to March 2022. Co-funding from other agencies (including Alberta Innovates, Canada Research Chairs, Western Economic Diversification, Genome Alberta, Genome British Columbia, the Canadian Institutes of Health Research, the UofA, UVic and McGill) has provided another $5.5 million in co-funding.

TMIC operates through an administrative core and 7 "Nodes" or laboratories distributed among the UofA (four labs), the University of Victoria (UVic), McMaster University, and McGill University, with agreement to integrate a Node at the University of Calgary beginning in April 2020 as shown in Figure 1. TMIC is in the process of transferring portions of the activities in the UVic node to the McGill node as a result of Dr. Christoph Borchers move to McGill on July 1, 2019. After March 31, 2020, UVic and McGIll will divide their service and technology development activities with UVic handling service requests from Ontario west and McGill handling service requests from Quebec east.

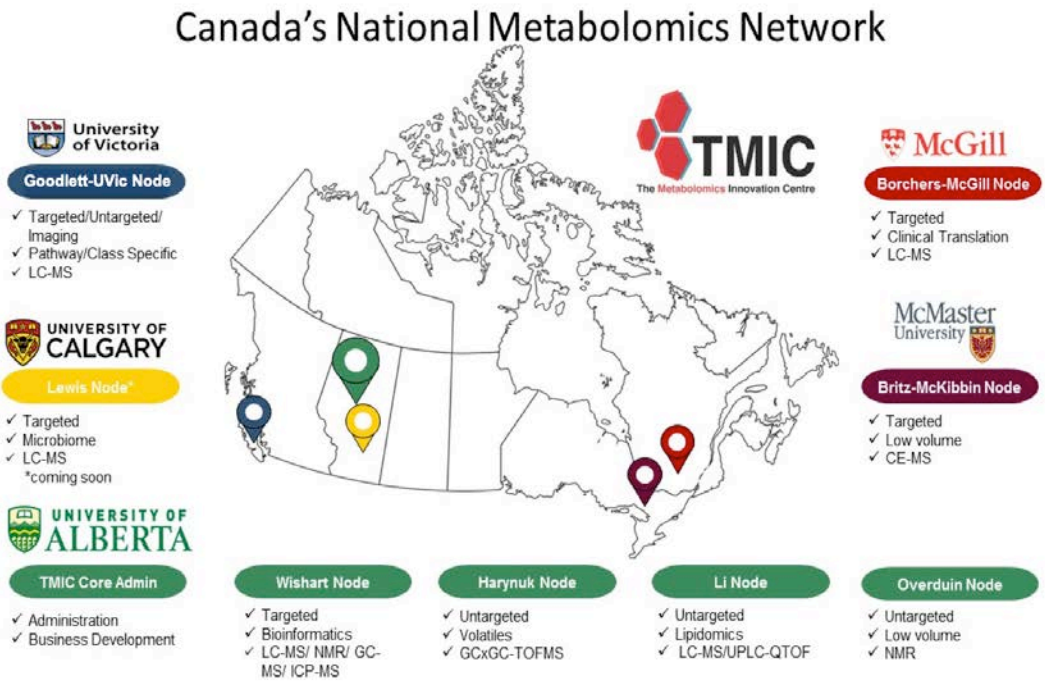

Figure 1 The TMIC platform network

2.3 Achieving the TMIC Mission

TMIC achieves its Mission through a portfolio of activities that support the platform, research and training, outreach, and good governance and management as follows:

The Platform

- Maintaining state-of-the-art (SOA) and internationally recognized metabolomics infrastructure capability: equipment, software, analytics, databases, bioinformatics, and technical capacity within the distributed TMIC Platform for service provision to the 'omics community.
- Jointly, with our academic partners, conducting highly innovative technology development to develop novel services for cutting-edge needs arising for our users.
- Renewing and upgrading SOA in-house infrastructure, housed in dedicated lab spaces and facilities.

Research and Training

- Providing metabolomics leadership, support, services, databases, and bioinformatics to the broad Canadian and international academic research communities.
- Enabling excellence in Canadian metabolomic research.
- Fostering capacity development through workshops, international conferences, and hosting visiting scientists, post-doctoral fellows, and students in TMIC's Research Hotel.
- Training highly qualified personnel (HQP), including researchers and technicians, who go on to prestigious and important positions in academia, industry, government, and non-governmental organizations (NGOs).

Outreach, Technology Transfer, and Knowledge Translation

- Providing metabolomics services to private and public sector users (both technology development and/or use of metabolomics for developing other novel technologies).
- Mainstreaming the deployment of metabolomics in the larger life sciences and 'omics research ecosystem.
- Partnering with user organizations to pursue key strategic opportunities in human health, other life sciences, and non-life-sciences applications (e.g., resource extraction).
- Proactively enhancing TMIC's profile through a two-way interface with the broader metabolomics community – Canadian and international.
- Supporting technology transfer and knowledge translation (TT/KT) through robust validation and published specifications for all novel technologies (e.g., kits and devices).
- Effectively managing intellectual property (IP), with a focus on generating socioeconomic benefits for Canadians.

Governance and management

- Enhancing the efficiency and effectiveness of TMIC as a Platform comprising a distributed network of Nodes to maximize the capabilities and opportunities of the distributed model.
- Implementing high quality governance, management, and operations systems, including service and TT/KT pipelines to deliver accessible, accurate, reproducible, and highest quality services at the lowest possible cost.

- Ensuring sustainable funding to maintain our infrastructure as SOA, provide outstanding services, and conduct outreach, KT/TT, and training, including through partnerships or service contracts with large-scale end-users on a case-by-case basis.
- Updating and monitoring key performance indicators (KPIs) that align with TMIC's Strategic and Operational Objectives, and with the goals and requirements of the major funders.

2.4 Three Tiers of Users

Within our overall strategy, we recognize three tiers of external users[3]:

- *First tier*: External Canadian and international academic researchers who use TMIC services in a variety of ways, including conducting discovery research specifically on metabolomics processes, biomarkers, etc.; using metabolomics results as part of other kinds of research studies (e.g., related to epigenetics); using metabolomics to investigate practical applications (e.g., point-of-care [POC] medical diagnostics, precision medicine); and/or developing novel metabolomics equipment, assays, software, databases, etc. Benefits to researchers include increased ability to do novel research, faster and more efficiently, on more organisms and taking into account more environmental factors, coupled with more partnering opportunities.
- *Second tier*: Industry is another tier of external users, as they attempt to commercialize novel technologies and devices either employing metabolomics directly (including novel metabolomics equipment), or that are developed using metabolomics analyses, data, software, etc. They may or may not do so collaboratively with TMIC, depending on the needs of the individual project, IP concerns, internal R&D capability, resources, etc. Benefits to industry include increased sales revenues, internal cost savings, improved reputation, and greater market share of transformative technologies.
- *Third tier*: The next tier of users are the people and organizations who attempt to fulfill TMIC's Vision: to use the power of metabolomics to improve life. This third tier uses data and/or technologies developed either directly by TMIC, or by its first and second tier users, to solve practical problems. They reside in organizations such as healthcare (including both service providers and health authorities), government and regulatory organizations (e.g., those monitoring environmental quality, or food animal welfare, or the safety of industrial effluents and tailings, etc.), NGOs (e.g., environmental watchdogs), and the general public. Benefits to these groups will include more timely interventions, higher quality of life, higher efficiencies, lower costs, better national security, more resilient environment, and more resource sustainability.

While TMIC is mostly focused on the first tier of users at this stage of its development, our strategic objectives and operational goals take note of the needs of all three user tiers. It is anticipated that over the term of this Strategic Plan TMIC will strengthen its activities and outputs directed at second and third tier users as it continues to validate assays, as metabolomics continues to be accepted as a

[3] Whether a given user might be considered an "*end*"-user depends on where they stand in the value chain. Typically, companies would normally be considered the end-users, but the company's customers are the next users along the chain, and for health applications there are "middle people" – the healthcare providers and health authorities, with patients and their families being the true "end" users. To avoid ambiguity, we refer to the three tiers of users instead of referring to any of them as "end" users.

mainstream 'omics tool, and as further partnerships, collaborations, and practical technology development initiatives with these users are constructed.

2.5 TMIC Guiding Principles

TMIC will be guided in all activities, both those in-house and those involving external parties, by a comprehensive set of core values summarized below:

Innovative. We will be state-of-the-art in all aspects: being at the cutting edge of metabolomics science and technology development, offering the best services, attracting and retaining the best people, and focusing our energies on strategic choices to support the most important research and innovation initiatives.

Collaborative. We will be proactive in fostering collaboration within the TMIC Platform, and between the Platform and the community of TMIC users and partners[4] (e.g., with external partners for joint projects, TT/KT, training, etc.)

Accountable. We will manage Platform operations with integrity, transparency, and accountability, including maintaining effective stewardship of TMIC resources.

Confidential. At all times we will ensure the privacy of data, findings, and IP as appropriate.

Inclusive. We maintain and promote these values, including seeking people with a diversity of perspectives and experiences in TMIC and its governing bodies, and ensuring our policies, practices, and procedures provide equitable access to opportunities and resources.

Sustainable. TMIC is committed to sustaining and attracting the human and financial resources required to deliver on our vision and mission.

Enabling benefits for Canadians. TMIC does not exist for its own benefit, nor is research done using the Platform done only for pure research purposes. We recognize that our ultimate goals are to maximize the relevance and practical application of metabolomics research and technology development for users within industry, government, healthcare systems, and the general public.

Excellence. We will attract and (when appropriate) retain highly skilled HQP, offer high-quality cost-effective services, pursue projects where novel metabolomics science and applications are of the most benefit, and always stay at the cutting edge of metabolomics science.

2.6 The Opportunities for TMIC

2.6.1 Introduction and Environmental Scan

Metabolomics has experienced near exponential growth over the past 16 years. In 1999, only 2 papers were published on this subject; in 2018, more than 5000 papers were published. Based on studies reported by several consulting agencies, the global metabolomics market was valued at $1.64 billion in 2018 and is expected to reach $3.6 billion by 2024.[2] The market is divided into metabolomic instruments

[4] The community of users and partners involves the researchers and technical personnel associated with each TMIC Node, research trainees, external researchers who collaborate with TMIC personnel on joint projects and industry and public sector partners.

and reagents (80%) and metabolomic services and software (20%). Analysis of the numbers of metabolomics publications indicates that metabolomics research activities are growing at a rate of about 15%/yr.

The explosive growth of metabolomics, combined with high impact metabolomic discoveries in diseases such as cancer, has led to significant investments in metabolomics facilities around the world. In particular the US has invested more than $65 million in its Regional Comprehensive Metabolomics Resource Cores while US universities are believed to have invested an equal amount into establishing metabolomics core facilities across the US. Canada has invested >$30 million in its metabolomics activities and infrastructure. These investments have helped catalyze the appearance of more than 80 university-based metabolomics facilities across North America over the past 8 years. In addition, Australia has invested more than $49 million in its Metabolomics Australia platform, the Netherlands has invested >$69 million into the Netherlands Metabolomics Centre and the UK has invested >$45 million in establishing the Phenome Centre[5] in Imperial College London. Additional Phenome Centres in Singapore ($9 million), Birmingham, UK ($12 million) and Perth, Australia, a component of Metabolomics Australia ($10 million) have also emerged. Growth has also occurred through the establishment of metabolomics service companies such as Metabolon in the USA ($128 million raised, and >$180 million valuation after 6 rounds of investment), Nightingale in Finland (>$6 million) and Biocrates (>$20 million) in Austria.

Different countries have adopted different models for their metabolomics enterprises. The USA has chosen a regionally competitive model with different centres with complementary strengths competing with each other for grants and business. On the other hand, Canada, the Netherlands and Australia have adopted a network model where regional centres work together under a single umbrella organization (TMIC in Canada, Metabolomics Australia in Australia, and the Netherlands Metabolomics Centre in Holland) to provide comprehensive and somewhat uniform metabolomic services. Similarly, the Phenome Centre concept which originated in Imperial College in the UK has allowed the creation of a common set of protocols that can be shared across countries or cities (London, Birmingham, Singapore, Western Australia).

The Netherlands Metabolomics Center (NMC), which is led by Dr. Thomas Hanekmeier, has been actively developing targeted metabolomic technologies for higher throughput and lower cost metabolomic analyses. Their goals are to increase the number of analytes measured to >2000 molecules. The NMC is also developing technologies to perform single cell or low volume metabolomics with cell cultures and organoid systems. It is primarily focused on health applications and the translation of metabolomics towards the clinic and has evolved to work more closely with genomics and proteomics facilities as part of a multi-omics (cross-disciplinary) initiative.

Metabolomics Australia (MA), now directed by Malcolm McConville, focuses most of its activities towards food, agriculture and non-health applications of metabolomics. It offers a wide variety of metabolomics

[5] Whereas metabolomics deals with the chemical processes involving metabolites, phenomics is a larger domain of scientific study dealing with the physical and biochemical traits produced by an organism over the course of development and in response to genetic mutation and environmental influences. In other words, phenomics studies the physical properties of an organism at both large and small scales. A simple example from the livestock production sector is studying phenotype traits such as animal weight at the large scale and gut nutrient absorption mechanisms at the small scale. Both may be linked to genomic and environmental factors, and metabolomics can help assess the small-scale factors more quickly and easily than traditional invasive measures.

platforms including NMR, LC-MS, GC-MS and metabolite imaging. MA has supported a modest effort in software development over the past 10 years and like the Phenome Centers, it has worked closely with instrument vendors to enhance or drive its technology development. Metabolomics Australia offers a mix of targeted and untargeted metabolomics, although its major focus has turned to targeted metabolomics assays. Some of the major challenges facing MA include coordinating activities across many Nodes, geographic isolation, and not emphasizing health applications of metabolomics.

Several major metabolomics centres exist in the USA. Two predominant ones are the West Coast Metabolomics Centre (WCMC) and the Broad Institute:

- The WCMC is led by Oliver Fiehn and operated by UC Davis. It has evolved to be one of the largest and more successful metabolomics core facilities in the USA and has recently branched out to Sacramento where it has established a clinical metabolomics facility. The UC-Davis facility focuses primarily on food/agricultural or natural science applications of metabolomics. The WCMC is very active in technology development and metabolomics software development and tends to perform untargeted metabolomics more than targeted metabolomics.
- The Broad Institute is led by Clay Clish, operates out of Boston, and has established a very successful core facility for human health applications in metabolomics. It has adopted many of the same technologies as Metabolon and offers very extensive (600+ molecules) metabolite profiling platform. The Broad Institute is so heavily used that it rarely accepts studies that have less than 1000 samples.

For both organizations, sustainable funding and having too many requests for their capacity, have been major challenges.

2.6.2 TMIC's competitive advantages

In this larger international context, TMIC is well positioned as an effective player on the world metabolomics stage with its recognized scientific leadership[6], distributed delivery system and a stable funding base. Particular opportunities involve continued development of advanced technologies (e.g., light-based detection/quantification of colorimetric assays or impedance-based detection/quantification of molecular recognition assays), innovative metabolomics kits, cutting-edge software, and comprehensive databases to allow metabolomics research to be conducted much more easily and more robustly by many more researchers. One of TMIC's Nodes (led by Dr. Wishart, UofA) leads the world in metabolomics software and database development. It is responsible for creating and maintaining most of the world's major metabolomic databases, including the Human Metabolome Database (HMDB), the DrugBank Database, the Yeast Metabolome Database (YMDB), the food composition database (FooDB), the Small Molecule Pathway Database (SMPDB) and the Toxin Target database (the "toxic exposome database"; T3DB).

TMIC is also responsible for creating and maintaining many of the world's most widely used metabolomics software tools, including MetaboAnalyst (for data interpretation), CFM-ID (for MS spectral prediction and

[6] TMIC's co-director, Dr. David Wishart, is an internationally recognized researcher who leads the Human Metabolome Project (2006-present), a multi-university, multi-investigator project that is cataloguing the known metabolites in human tissues and biofluids. The outcomes are being archived on a freely accessible web-resource called the Human Metabolome Database (HMDB).

compound ID), Bayesil (for NMR-based metabolomics), ClassyFire (for automated compound classification) and BioTransformer (for comprehensive metabolism prediction). Just as Bethesda, MD is known as the home of GenBank and the world's genomic data resources and Cambridge, UK is known as the home of UniProt and the world's proteomic data resources, Edmonton, Canada, is known as the home of HMDB and the world's metabolomic data resources. TMIC's data resources receive >46.4 million web hits, handle >11.9 million data users and are cited >2000 times each year. More than 50% of all published papers in the field of metabolomics cite these resources. Likewise, all of the national metabolomic centres mentioned in the Environmental Scan depend on TMIC's software tools and databases to perform their activities.

TMIC has also been very effective in developing a culture to encourage and facilitate translation, including establishing spin-offs. To date, TMIC's node leaders have spun out or helped create nearly 30% of the world's metabolomics service companies including Chenomx (started in 2000), Metabolomics Technologies Inc. (started in 2010), MRM Proteomics (started in 2010), OMx Health Analytics Inc. (started in 2012), Molecular You (started in 2014), MetaSci (started in 2017), NovaMedicalTesting Inc. (started in 2017) and MetabolomiX (started in 2019). These companies, which collectively employ >50 people, offer a range of metabolomic-based services, software, reagents and applications.

Other than the WCMC (in California) and MA (in Australia), most national metabolomics centres around the world are heavily focused on human health. TMIC handles a much more diverse research and service portfolio and has taken a leadership role in livestock metabolomics, food and agricultural metabolomics, and water/exposure science. TMIC is also well positioned to apply metabolomics technologies to the oil and gas sector, especially given the abundance of these activities and resources in Alberta. No other metabolomics centre in the world has any research activities in the area of oil and gas.

TMIC Node Leaders are also working hard in a "pathfinding" role to demonstrate access to the metabolomics market in China. Unlike what transpired with the commercialization of genomics in China, where the state invested over $1B into BGI, as of yet there is no real major competitor in the metabolomics space that can "control and influence" the Chinese market. There is a particular opportunity for TMIC to establish itself as a provider of metabolomics kits, in regions such as China, where human samples do not leave the country, The TMIC strategy of developing kits that can be sold into China, is synergistic with China's need and TMIC's translation vision.

Overall, TMIC has a strong track record of being a catalyst for demonstrating the utility of metabolomics. The opportunity for the next five years is to capitalize on these opportunities and demonstrate real value to industry and investors.

2.7 The Strategy

2.7.1 Overview

TMIC will contribute to the further development of metabolomics research and take advantage of both its strong competitive position and this growth in the external market by pursuing innovation in metabolomics services and building the capacity to meet anticipated demands. TMIC will pursue these goals through pursuit of four strategic objectives that are described in more detail in Section 3:

(1) Enhancing the Platform – making TMIC a world-class "Go To Source" for Metabolomics services;

(2) Supporting science – strengthening the Canadian metabolomics scientific community;
(3) Focusing on commercial benefits – strengthening the Canadian metabolomics-enabled industry; and
(4) Delivering societal benefits– developing workflows and services to "mainstream" metabolomics data and devices into practical end-user applications.

We anticipate that these approaches have the potential to significantly increase TMIC's user base, advance both basic and applied metabolomics science, facilitate TT/KT to industry, and encourage take-up by second and third tier users (see section 2.3).

2.7.2 The Network

The TMIC Platform is organized as a distributed network. Four TMIC Nodes (laboratories) are located at the UofA, three other TMIC Nodes (laboratories) are located at UVic, McMaster, and McGill, and an agreement (pending CFI's approval) has been reached to integrate a Node at the University of Calgary in April 2020. This model affords considerable additional power, flexibility, and customization compared to a single-site model, taking advantage of:

- The existing strong scientific and technology capabilities of Node Leaders and their teams at each site. Where these capabilities are complementary, this avoids the need to recreate them from scratch at other Nodes. Where these capabilities are similar, it provides the ability to much more quickly and easily provide equivalent services to users across the whole of Canada;
- The ability to target service, technology development, and user applications to specific sectors at individual Nodes, as appropriate to regional needs and the expertise and user linkages of the Nodes;
- Increased efficiencies in resource allocation across projects – the right team(s) is selected as appropriate to individual projects;
- The ability to bring larger and more cross-disciplinary and/or cross-sectoral teams to bear on complex problems, especially those benefitting from a multi-omics approach;
- The requirement to standardize procedures across Nodes, which will be of tremendous benefit when rolled out to metabolomics providers and users more broadly; and
- Significantly increased "branding" opportunities for TMIC to promote its capabilities both within Canada and especially on the world stage – more investigators will be working on more high-profile studies and applications under the "TMIC brand".

In recognition of this power of a distributed metabolomics capacity, and to make metabolomics more accessible and mainstream, TMIC has grown its network to include sites in Ontario (McMaster University) and Quebec (McGill University). This has added new technological capabilities and has strengthened TMIC's capacity in low-volume sample analysis, in pharmaco-metabolomics and clinical metabolomics. Capabilities at each site reflect a balance of local access to some metabolomics services, and the value of access to complementary technologies (e.g. targeted and untargeted metabolomics) across the network, while minimizing undue overlap.

Overview of Network Capacity and Activity

All Nodes are also involved in technology development

Borchers (U Victoria to July 1, 2019 and McGill) & Goodlett (U Victoria)

- Targeted metabolomics: Many targeted assays for either class specific metabolites (e.g. bile acids, sugars, nucleotides, nucleosides/nucleobases, fatty acids, amino acids, cardiolipins, lysophosphatidic acids, steroid hormones, phytohormones, aldehydes, etc.) or pathway specific assays (e.g., central carbon metabolism, amino acid metabolism, fatty acid metabolism, one-carbon metabolism, bile acid synthesis/metabolism, the MVA pathway, purine/pyrimidine synthesis, metabolism and salvage, sphingolipid synthesis/metabolism, and vitamin host-gut co-metabolism, etc.)
- Untargeted metabolomics: using UPLC-FT-MS - metabolites with positive-ion and negative-ion detection, as well as with metabolites from both extremely polar and non-polar compounds.
- Sectors: health, agriculture, environment among others.
- Types of metabolites: all metabolite classes and volatile metabolites including aldehydes and short-chain fatty acids.
- Main platforms: LC-MS (UPLC-MRM for targeted experiments on different triple quadrupole MS instruments or untargeted UPLC-HRMS on LTQ-oribitrap instruments). For MS imaging, 12-Tesla FTICR.

Britz-McKibbon (McMaster)

- Targeted, small volume.
- Sector: Health.
- Main platform: CE-MS.

Harynuk (University of Alberta)

- Untargeted, generally untargeted discovery type work.
- Some quantitative assays in urine and other matrices.
- Sectors: health (urine, fecal samples), agriculture (canola volatiles, swine), emerging - food (kefir)
- Types of metabolites: random volatiles (sweat and body odour on textiles). Emerging - supporting studies into breath volatiles.
- Main platforms: Comprehensive two-dimensional gas chromatography - time-of-flight mass spectrometry (GCxGC-TOFMS). A variety of automated sample injection options (liquid samples, thermal desorption, SPME, headspace).

Lewis (University of Calgary)

- Microbiome-related service work
- Sectors: health
- Main platforms: HF coupled to UHPLC, MS/UHPLC, QqQ/UHPLC

Li (University of Alberta)

- Untargeted metabolomics using chemical isotope labeling (CIL) LC-MS with high coverage and high quantification accuracy; untargeted lipidomics using UPLC-QTOF-MS with high coverage.
- Sectors: All sectors.
- Types of metabolites: all types of metabolites and lipids except volatiles.
- Main platform: LC-MS.

Overduin (University of Alberta)
- Untargeted metabolomics.
- Sectors: health, cell culture, lipids.
- Main Platform: NMR.

Wishart (University of Alberta)
- Targeted - quantitative (absolute quantification); bioinformatics, high-throughput and wide-coverage of metabolites in one assay.
- Databases (such as HMDB, FooDB, SMPDB, Exposome-Explorer).
- Software Tools: MetaboAnalyst, BioTransformer, CFM-ID.
- Sectors: Health, livestock, agriculture (plants), food & nutrition.
- Types of metabolites: polar & non-polar metabolites, uremic toxins, lipids, metals, vitamins, bio and exposure markers.
- Main platforms: DI/LC-MS/MS, NMR, GC-MS, ICP-MS, HPLC/UHPLC coupled with UV, FD-detectors.

The network has been particularly valuable in providing a forum for exchange on technology development projects. The development of easy-to-use metabolomics kits has been undertaken by three of the Nodes, each drawing on a specific area of interest and strength. Once beta tested, the kits are intended to provide the capacity for automated or semi-automated assays that are largely technology-agnostic, hence opening more opportunities for standardization, harmonization and commutability across TMIC Nodes and across metabolomics centres around the world. The kits are also a source of revenue, contributing to financial sustainability. There is now an extraordinary opportunity for TMIC to build out its network further across Canada to foster greater awareness and mainstreaming of metabolomics, and to lead the world in establishing best practices and much needed standardization.

DRUGBANK
- A comprehensive database of drugs, drug actions and drug targets developed by TMIC
- Launched in 2006, with major updates in 2008, 2011, 2015 and 2018
- Widely used to "repurpose" drugs based on data from 'omic studies
  - 10 million unique users each year
- 9335 small molecule drugs and 5030 experimental drugs
- Detailed ADMET, MOA and pharmacokinetic data
- 3969 drugs with metabolizing enzyme data and 1360 drug metabolites
- 6000 MS+NMR spectra
- 4493 unique drug targets
- 215 data fields for every drug

2.7.3 Key Accomplishments to Date

Support for discovery. Through TMIC and its collaborators, many important discoveries have been made relating to the composition of the human metabolome [3-7], how metabolomics relates to human [8-11] and animal health [12-13], livestock and crop productivity [14], natural product biosynthesis [15-16], drug interactions [17], microbial metabolism [18-19] and environmental monitoring [20]. These discoveries have been described in >330 papers (published over the past eight years) that have been authored by various TMIC scientists, users and collaborators. This output represents more than 70% of all metabolomics papers published by Canadian scientists since 2011. These papers have already been cited almost 18,000 times, providing a clear indication of their enormous impact in the scientific community. In addition, many of the discoveries enabled by TMIC have been presented at numerous international conferences (>170 abstracts and poster presentations and >280 invited oral presentations in the past eight years).

Service provision. Since 2011, TMIC has performed over 100,000 metabolomic analyses for more than 650 different users involved in nearly 1,200 projects. These service projects have generated more than $5 million in service revenue, with each of the last two years averaging >$1.3 million/year in service revenue.

Technology and database development. TMIC has made significant contributions to technology development, training and data analysis. Since 2011, TMIC has developed and made available 58 different metabolomic assays. These assays include specialized assays for vitamins, bile acids, urinary organic acids, sterols and oxysterols, nucleotides and cyclic dinucleotides, volatile compounds, catecholamines, polyphenols, carotenoids, acyl-CoAs, exposure and diet biomarkers, fatty acids, lipids and cardiolipins, central energy metabolites, one-carbon metabolism compounds, central carbon metabolism compounds, urea cycle compounds, sphingolipids, mevalonate pathway compounds, uremic toxins, phytohormones and phytosterols.

Further, TMIC has developed, upgraded or maintained 20+ different metabolomic databases (with different levels of completeness and verification) including the Human Metabolome Database (HMDB), DrugBank, the Toxic Exposome Database (T3DB), the *E. coli* Metabolome Database (ECMDB), the Yeast Metabolome Database (YMDB), MyCompoundID as well as analytical web-servers such as Bayesil, CFM-ID, GC-AutoFit, MetaboAnalyst, and many other tools. These resources have become a key component of many metabolomic activities around the world. Indeed, more than 25% of all published metabolomics papers cite the HMDB and nearly 35% cite MetaboAnalyst. Appendix A shows additional examples and further details about TMIC's "success stories."

Colon Polyp Detection and Colon Cancer Prevention

In 2013 Metabolomics Technologies Inc. (MTI) discovered a set of 12 metabolite biomarkers in urine that could be used to non-invasively detect intestinal polyps via NMR spectroscopy – PolypDx. But NMRs are not common in clinics.

TMIC took a 12 metabolite NMR-based assay and translated to a 3 metabolite MS based assay with identical performance, thereby making the test accessible to more institutions. MTI is providing the PolypDx test as a MS-based kit. PolypDx is now offered in dozens of labs in the US as a LDT (laboratory developed test) for polyp screening.

Training. Additionally, TMIC has trained more than 150 undergraduate students, graduate students, technicians and PDFs at its facilities. Since 2011 TMIC has presented at eight metabolomics training workshops: in Toronto (four times), Edmonton, Montreal (twice) and Vancouver using TMIC data resources as tools. These workshops have trained an additional 185 students. Since 2011, TMIC has hosted 60 researchers, PDFs and students from 19 countries in its Research Hotel Program.

Outreach. Since 2011, TMIC has produced MetaboNews, a monthly electronic newsletter that provides the latest information on publications, conferences, training, software, jobs, and products related to metabolomics. Now published in partnership with the Metabolomics Society, MetaboNews has become the official voice of the Metabolomics Society. Its circulation is larger than that of most metabolomics journals. It reaches more than 3,100 subscribers and is visited online by 2,800 users annually in more than 80 countries including almost 200 Canadian scientists

Technology transfer. Since its inception, TMIC has encouraged a culture of technology transfer amongst its staff and senior investigators. Relative to most other metabolomic centres around the world TMIC has an outstanding record of creating spin-offs, filing patents or generating licenses. Among the more notable spin-offs are OMx Health Analytics, a drug informatics company with 20+ employees and revenues >$1.5

million/year. OMx markets an enhanced version of DrugBank (developed in TMIC) that is now used by most major and mid-sized pharma companies around the world. Molecular You Corporation (MYCo), Canada's first precision health company is another TMIC spin-off. MYCo (www.molecularyou.com) uses multiomics measurements (including metabolomics) and advanced bioinformatics to provide comprehensive health and wellness guidance and coaching. MYCo has 15+ employees with offices and labs in Vancouver and Edmonton. Other spin-offs at early stages of conception are Tricca Technologies Inc., an Edmonton-based company aiming to produce a point-of-care (POC) metabolomics devices using technologies developed in TMIC; MetaSci Inc. a vendor of metabolite standards which is based in both Edmonton and Toronto as well as Nova Medical Testing Inc., an Edmonton-based metabolomics service company with seven employees that specializes in large-scale (>10,000 features) metabolome characterization using selective isotopic labeling techniques.

In addition to creating successful spin-off companies TMIC has also been patenting some of its key technologies and inventions. These include a patent (CPA, Serial No. 2,943,103) filed in 2016 for the production of gold nanoparticle conjugates, which are needed for the POC devices that TMIC scientists have been developing. They also include a patent (Provisional Patent: 105872-0), filed in 2019 for the measurement of metabolites (ascorbic acid) using paper-based colorimetric assays.

Licensing deals have also been struck with third parties, including OMx Health Analytics that generates greater than $300,000 in cash and in-kind support to TMIC.

Technology transfer at a glance – data for FY 2015-19	
Number of patents	2
Reports of invention	8
Number of licenses	5
Number of spin offs	3
Number of copyrights	4

Funding. In addition to its scientific, training and outreach accomplishments, TMIC has greatly facilitated the funding of metabolomics research in Canada. Since 2011, TMIC staff have helped TMIC's principal users and collaborators prepare >90 funding proposals (for CIHR, Genome Canada, NIH, CFI, Alberta Innovates - Health Solutions, Alberta Innovates Bio Solutions, NSERC, and others). These proposals led to >$40 million of funding being awarded to the applicants, with a significant portion (>10%) being directed towards TMIC services or activities.

3. Five-Year Strategic Objectives

3.1 Overview

Several strategic opportunities have been identified that would lever TMIC's experience and metabolomics expertise to benefit its three tiers of users. Work has already begun and meaningful outcomes could be realized in the shorter term (within the next 2-3 years). Others are in earlier stages of development and would likely reach fruition in the longer term (3-5 years), although TMIC recognizes that full success will almost certainly take even longer, with the current strategy serving as a springboard for further initiatives in the future.

All strategic initiatives will be agreed upon and developed further over time by TMIC's Nodes Committee for consideration and eventual review by the Board, and approval by the partner universities as per internal agreements with TMIC. Note that some initiatives will require significant additional funding by sources within Canada and internationally, especially those related to TT/KT.

TMIC's four strategic objectives[7] for 2019 – 2024 can be summarized as:

1. ***Platform*** – Make TMIC a World-class "Go To" Source for Metabolomics services
    a. *Target communities* – first tier users in the research community, second tier industry users wishing to develop and utilize novel metabolomic devices and technologies, and eventually third tier users of these devices and technologies for practical application.
2. ***Science*** – Strengthen the Canadian Metabolomics Scientific Community
    a. *Target communities* – both "in-house" TMIC staff, and the broader external Canadian scientific community (the "first tier" of external users) that either conducts metabolomics analyses themselves or relies upon TMIC to do so to move this external research forwards.
3. ***Commercial*** – Strengthen the Canadian Metabolomics-Enabled Industry
    a. *Target community* – Industry, as the "second tier" of external users, to support their commercialization of novel technologies, devices, and services either employing metabolomics directly, or developed using metabolomics analyses, data, etc.
4. ***Societal*** – Develop Workflows and Services to "Mainstream" Metabolomics Data and Devices into Practical End-user Applications
    a. *Target community* – The "third tier" of users: those using those commercial products and services for clinical diagnoses, regulatory decisions, environmental monitoring, etc.

The **Logic Chart** in Figure 2 outlines how TMIC has structured its Activities and Outputs to support the Outcomes and Impacts necessary to realize its Mission and ultimate Vision.

Note that each Strategic Objective will benefit from a variety of Activities undertaken by TMIC. While difficult to represent in a Logic Chart, the Activities, Outputs, Outcomes, and Impacts are not generally siloed. For example, Strategic Objective #1, making TMIC a world-class "go to" source for metabolomics services, is only achieved through a combination of Activities directed towards providing outstanding services, fostering TT/KT, obtaining sufficient funding to maintain effective services, outreach to users so they know about TMIC, and strong governance, management, and operational systems to keep TMIC running on track.

[7] Note also the TMIC 2019 SWOT analysis (Appendix B) that has informed this set of strategic objectives.

Figure 2 - TMIC Logic Chart (*Legend: "Platform" = Internal TMIC platform actions & effects; "Cluster" = Broad R&D cluster end-users)*

1 & 2. Vision & Mission

1. VISION: *Improving life through the power of metabolomics*

2. MISSION: *Catalyzing innovation and translating metabolomics from the laboratory to the real-world use by creating novel technologies, providing cutting-edge analytic services, sharing foundational data resources, and equipping the next generation of scientists and end-users*

3. Ultimate Impacts *(Long-term effects; the underlying rationale for TMIC)*

3.1 Platform impacts
Core of a world-class metabolomics cluster – best infrastructure, best services, best people, best traceability to international standards
Financial and HQP sustainability

3.2 Scientific impacts
Canadian critical mass in world-class metabolomics research
Canadian critical mass in metabolomics-enabled measurement equipment, devices
Canadian critical mass of HQP

3.3 Commercial Impacts
World-class Canadian critical mass in metabolomics-enabled industrial products & services – measurement equipment, POC devices, software, analytics, databases, etc.
Canadian industrial cluster with strong IP & value chain through partnerships, patent positions, service agreements (w/ each other; w/ multinationals), supplier-customer links, etc.

3.4 Societal impacts
Better healthcare, agriculture, livestock production, water quality, environmental protection & sustainability, sustainable resource extraction, aquaculture, etc.
Increased regulatory / legal capabilities through evidence-based analysis & decision-making

4. Intermediate Impacts *(Mid-term effects arising from Outcomes – but NOT linearly tied to individual Outcomes; i.e., NOT siloed)*

4.1 Platform – *World-class* "go to" source for metabolomics services in Canada & International
Ramped-up SOA capabilities in metabolomics infrastructure, service provision, software, databases.

4.2 Science – Stronger Canadian Metabolomics Scientific Community:
Strong presence in metabolomics-based papers, publications, conference presentations, etc.
Strong HQP going on to academic positions

NEED – more explicit scientific HQP training

4.3 Commercial – *Stronger* Canadian Metabolomics-enabled industry:
Strong Canadian metabolomics-enabled industrial products & services – measurement equipment, POC devices, software, analytics, databases, etc.
New / strong firms and linkages, with strong HQP

NEED – more explicit industry HQP training

4.4 Societal – *Workflows and Services to integrate* metabolomics into practical end-user applications
Much stronger / easier access to metabolomic & related data, people, etc.

NEED - To identify barriers & opportunities for take-up, end-user needs, etc.

TMIC
The Metabolomics Innovation Center

5. Outcomes *(Near-term, from use of the Outputs)*

6. Outputs *(What is produced)*

7. Activities *(What is done)*

5.1 Services
Platform: More services & users; More fee-for-service revenues; Increased effectiveness & efficiency, reduced costs; Increased national presence

Cluster: Better, faster research, shorter turn-around; Increased access to external resources

5.2 KT/TT
Platform: More & more diversified users; More fee-for-service revenues

Cluster: Access to greater range of metabolites and/or sensitivity; Improved research capabilities; involvement in KT / TT, tech dev (some collaboratively with TMIC), patents, licenses, etc.

5.3 Funding
Platform: More competitiveness for funding of Platform operations

Cluster: More competitiveness for external funding for Platform users

5.4 Outreach
Platform: Better "fit" to needs of research & application communities

Cluster: More awareness of TMIC services, products, data, etc.; More links to potential partners, collaborators, networks, etc.

5.5 Gov'nce, Mgmt. & ops
Platform: More sustainability, flexibility, nat'l and int'l presence; Renewal by funding partners; Sustainable HQP

Cluster More input into, and transparency re., decisions on Platform infrastructure, resources, projects, funding, etc.

6.1 Services provision & expansion
Platform: Metabolomic analyses, reports, databases, etc.; More & better SOA infrastructure; New Nodes, partnerships; Access to more computational tools and resources; QMS System

Cluster: N/A

6.2 Products
Platform: New kits, POC devices, assays, platforms, etc.; Patents, licenses, etc., Start-ups and spin-offs, etc.; RHP grants

Cluster: Promote use of new services & products

6.3 Funding
Platform: Research & service proposals; Partnership agreements; License & royalty agreements; Revenues to TMIC

Cluster: R&D agreements re. Joint projects, partnerships, etc.

6.4 Outreach
MetaboNews, flyers, brochures, conference & workshop proceedings, etc.

Cluster: Input to, & feedback on, the above

6.5 Gov'nce mgmt. & ops
Platform: Strat & Mgmt. / Ops Plans; Strong BoD, Int'l SAB; Affiliation Agreements with host institutions (incl. Constitution, roles & responsibilities, etc.); KPIs; LIMS & chemical inventory mgmt., system ops & development; New hires

Cluster: Participate in above

7.1 Build & maintain capacity
Platform: Maintain quality Platform lab, equipment, database, and service / operations; Maintain / update equipment, lab space & databases; expand production capabilities; ISO certification, etc.

NEED – Improved, transparent, accountable Service pipeline; Formal Node agreements

Cluster: Use of services, participate in any expansions

7.2 KT/TT
Platform: Tech dev internal to TMIC; Project collaborations, IP mgmt. etc.; Research Hotel.
NEED – Formalized TT/KT pipeline, & IP guidelines, linked to UofA

Cluster: Participate in TT/KT (e.g., joint projects, collaborations)

7.3 Ensure sustainable funding
Platform: Find funding from: Grants; Industry & int'l partnerships; Licensing & royalties from tech dev, spin-offs, etc.; Fee-for-service revenues; Other gov't sources
NEED: Clear strategy, priorities, reporting, etc.

Cluster: Collaborate in funding bids

7.4 Outreach
All: Engage with research and user communities to develop Strategic Plan, service priorities, etc.; Website, annual conferences, workshops, etc.

NEED – More knowledge of TMIC by users, and of users by TMIC
Cluster:

7.5 Gov'nce, mgmt. & ops
Platform: Strategic & op'l planning, Node Leader, Node& staff meetings, etc.; Strengthen gov'ce & mgmt. in line with MSI & GC requirements; establish explicit strategic research objectives; Daily ops; Attract & retain best people

Cluster:

3.1 Strategic Objective #1 – Platform: Make TMIC a world class "Go To Place" for Metabolomics Services

3.1.1 Overview

This strategic objective builds on TMIC's already strong track record in advancing technology development, supported particularly by Genome Canada's funding. TMIC's three technology development goals for the next five years are:

- Goal #1 – *Advance and expand TMIC's analytical services*. TMIC will continue to actively develop new core capabilities and methods for enhanced services, improving the coverage and throughput of existing assays, developing new assays (including compound class-specific, pathway-specific and substrate-specific assays), and adding new core capabilities building on the actions of the last two years that focused on CE-based metabolomics, clinical (ISO17025) compliant metabolomics, and comprehensive lipidomics analysis.
- Goal #2 – *Increase accessibility and standardization*. TMIC will continue its initiatives to mainstream metabolomics through developing and publishing peer-reviewed metabolomic assays, further developing its novel metabolomic databases for increased completeness and verification, and deploying different metabolomics kits that convert high-demand assays into kits that are reproducible and readily used at most TMIC Nodes. These kits could be readily transferred to other public and for-profit service providers with the necessary equipment.
- Goal #3 – *Enrich TMIC's informatics resources*. TMIC will focus on updating or upgrading the existing databases, bioinformatics tools and web servers and to include additional 'omics data or capabilities. An additional thrust is developing new software resources to complement recent developments. This will include a multi-omics biomarker database (MarkerDB), a multi-omics data-mining tool (DataWrangler), a multi-omics pathway visualization tool (PathWhiz), a genome-to-metabolome conversion tool (G2M), and a comprehensive multi-omics pathway database (PathBank). TMIC is also continuing to expand its chemical libraries (now over 1,000 compounds), spectral libraries (>34,300 experimental spectra and >880,000 predicted spectra), and expanded (rationally predicted) chemical databases (>2 million compounds) using innovative biochemical and computational techniques.

3.1.2 Current status

Core analytical facilities. TMIC already houses more than $26 million in state-of-the-art metabolomics equipment, including multiple NMR, HPLC-UV, LC-MS/MS, DI-MS/MS, GC-MS/MS, GCxGC-TOF-MS, FT-MS, MALDI TOF-MS, ICP-MS, UPLC-MS. New services in CE-UV and CE-MS were offered to clients starting in 2017. During 2018 TMIC acquired 14 additional pieces of equipment and instrumentation, thereby significantly increasing service offerings and relevance to users in academia and industry. Appendix C provides a list of all major equipment in TMIC, including funding sources, date placed into operation, life expectancy and capacity assessments.

The new infrastructure allows TMIC to phase out older and less reliable equipment and increase TMIC's efficiencies and capacity to accommodate anticipated increases in user demand. The specialized CE-MS instrumentation has enabled five new TMIC services to be offered to users (see the TMIC website at www.metabolomicscentre.ca/). Some of the equipment (e.g. the Orbitrap MS, CE-MS) allows for greater

sensitivity or higher resolution, thus providing wider access to users with limited sample volumes and/or those users wanting more comprehensive coverage. Compared to other core facilities in Canada and around the world, TMIC has perhaps the greatest diversity of equipment or metabolomics platforms in any core facility (See Figure 3). However, maintaining such a suite of equipment as SOA is demanding and cost intensive, requiring an ongoing investment in high quality support personnel and service agreements where possible.

Our strategic objective is ambitious: to extend this infrastructure platform even further to make TMIC the world class "go to" metabolomics centre in Canada and internationally for access to assays based on technology innovation, assays that aren't yet mainstream elsewhere, and that are disseminated to other service providers through kits or other mechanisms.

3.1.3 Going forward

Key aspects of Strategic Objective #1 going forward include the following:

Platform

- *Develop and maintain a full suite of SOA equipment, services, analytics, and software*. New items of infrastructure will be sourced as appropriate, including development of infrastructure in-house, leasing of instruments through industry partners, purchase of research- or commercial-grade items, and collaborative development with first and second tier users and/or other industry partners.
- *Develop and maintain a rich and constantly enhanced set of metabolomic databases.* These will include comprehensive metadata so that they are interoperable at regional, national, and international levels. Already in TMIC's "DNA", but requiring extended partnerships, TMIC's strategy is to develop the tools to pull useful insights from large amounts of data required for valid biological interpretation, and aggregate different sources of relevant data in a meaningful way.
- *Provide: (1) routine, (2) customized, and (3) innovative metabolomics tools and tool development capacity in-house.* This includes having the scientific, technical, and design skills to accomplish theses, plus having sufficient resources to integrate highly innovative technology development into normal operations (e.g., through identification of potential gaps and opportunities, targeted project planning and resourcing, etc.).
- Allocate infrastructure rationally across Centre and Nodes, so that users can access the right infrastructure and expertise, for their specific research projects, in a timely manner.

Facility	Location	NMR	GC-MS	LC-MS	MS Imaging	Lipidomics	Fluxomics	ICP-MS	CE-MS	Metabolomics Kits	Chemical Libraries	Data Analysis/Software	Tech. Development
The Metabolomics Innovation Centre (Edmonton, Victoria, Montreal, Hamilton)		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Metabolomics Australia (Melbourne)		✓	✓	✓	✓		✓					✓	✓
West Coast Metabolomics Center (Davis CA)			✓	✓		✓	✓			✓	✓	✓	✓
Southeast Center for Integrated Metabolomics (Gainesville FL)		✓	✓	✓	✓		✓	✓			✓	✓	
RTI Eastern Regional Comprehensive Metabolomics Resource Core (Durham NC)		✓	✓	✓	✓			✓					
Netherlands Metabolomics Centre (Utrecht)		✓	✓	✓	✓	✓	✓	✓	✓			✓	✓
Resource Center for Stable Isotope-Resolved Metabolomics (Lexington, KY)		✓	✓	✓				✓			✓	✓	
MRC-NIHR Phenome Centre (London)		✓		✓	✓		✓					✓	
Goodman Cancer Research Centre Metabolomics Core Facility (Montreal)		✓	✓	✓			✓					✓	
Michigan Regional Comprehensive Metabolomics Resource Core (Ann Arbor MI)		✓	✓	✓		✓	✓					✓	✓
Metabolomics Core at Mayo Clinic (Rochester MN)		✓	✓	✓								✓	
BioNMR Centre (Calgary)		✓	✓										
Analytical Facility for Bioactive Molecules at the Hospital for Sick Children (Toronto)			✓	✓	✓	✓							

Figure 3. A comparison of TMIC core facilities and capabilities with other metabolomic core facilities.

Outreach and collaborations

- *Strengthen TMIC's national and international "brand visibility" and relevance to users through increased outreach so that:*
    - All user communities know TMIC well, including the services it offers, its competitive advantages over attempting metabolomics "in-house" within the user organizations or obtaining them from other service providers, collaboration and partnering opportunities, and key TT/KT opportunities;
    - TMIC understands its user communities and their needs; e.g., through participation and presentations in major user forums such as the Plant and Animal Genome Conference (PAG), ensuring that scientific and TT/KT application opportunities are well known to TMIC; and
    - Other 'omics researchers not currently employing metabolomics will be aware of its potential.
- *Strengthen branding also through other means,* e.g., outstanding publications; high-profile presentations; important alliances, partnerships, and collaborations with other leading metabolomics scientists; outstanding and heavily-used databases; and (eventually) critical participation in highly important practical applications for end-users.

Systems

Our goals are to provide easy, efficient, and timely access to metabolomics services for users, with the highest possible reproducibility and quality results at the lowest cost. This will include:

- A simple and transparent project intake, review, and approval process.
- High throughput, fast turnaround times, and cost-effective services for users (i.e., sufficiently high value for the cost).
- High cost-efficiency of operations vs. TMIC's overhead costs.
- Reliability, repeatability, accuracy, and precision of analytics, results, and reports to users. This is to include robust validation of these elements across Nodes:
    - Through continuing development of new standard operating procedures (SOPs) for all TMIC operators and technologies; and
    - Through the use of artificial intelligence (AI) and machine learning (ML) to account for unavoidable variability in individual equipment, sample preparation, operations, etc.

People (internal to TMIC)

- We currently have 36 staff dedicated to core service operations and management and 22 research and technology staff, plus 112 staff working on projects that are not directly part of TMIC but reside in affiliated groups and projects that benefit from TMICs expertise.
- TMIC will continue to develop and maintain state-of-the-art capabilities in TMIC scientists, technicians, and operations staff. These will be ensured both through appropriate hiring and retention of key staff, and by in-house and external training and upgrading as required.

3.2 Strategic Objective #2 – Science: Strengthen the Canadian Metabolomics Scientific Community

3.1.1 Overview

TMIC's success in achieving its ultimate Vision to "improve life through metabolomics" requires a deeper connection to its target communities: the first tier Canadian scientific community, the second tier industry community, and the third tier user communities, in order to demonstrate the power and value of metabolomics. This is an essential precursor to mainstreaming metabolomics into practical technologies, devices, analytics, and other uses. In this regard, the first step to take, and the one most feasible for TMIC at this time, is to strengthen the first tier of Canadian scientific users/partners associated with TMIC. While international users are of course welcomed and encouraged, TMIC must focus first on Canadian users in accordance with the significant Canadian funding that supports it.

There are two overlapping categories of people who will be targeted: (1) those most actively engaged with TMIC and its research leaders; and (2) the general scientific community, some of whom may have only limited engagement with TMIC (e.g., through one-off projects). Both categories, but particularly the former, can be proactively assisted by TMIC through various means such as joint planning, identification, and targeting of specific opportunities. These activities, in turn, may lead to collaborative research and technology development projects, partnerships focused on practical applications (e.g., marrying suppliers and customers), and so on. TMIC will act in a proactive manner to foster such outreach and collaborative opportunities across Canada and, where appropriate, around the world.

3.2.2 Current status

TMIC already has several initiatives in place that align with this strategic objective:

- Hosting training and informational workshops. As an example, the Canadian Bioinformatics Workshop (CBW) held in Montreal in 2018 https://bioinformatics.ca/workshops/informatics-and-statistics-for-metabolomics/ provided training for 30 participants on the use of TMIC bioinformatics resources.
- Participation in disciplinary conferences which feature speakers and poster presentations on metabolomics from TMIC Node members and their students/staff.
- An annual Canadian Metabolomics conference in Canmore, AB that provides engagement between TMIC Nodes and potential collaborators across Canada, as well as the opportunity for TMIC to showcase its research progress and services to sponsors and stakeholders (over 90 participants in May 2019).
- The Research Hotel Program - a no-cost, or low cost, to the user, hands-on training program hosted within TMIC facilities (already over-subscribed). Users of the Research Hotel Program visit TMIC facilities on site for anywhere from one day to one year and are provided with office/lab space, training by expert TMIC staff and the opportunity to apply their training to their own metabolomics project.

3.2.3 Going forward

Additional investment in outreach and knowledge mobilization will support this strategic objective. Key targets will be:

People (external to TMIC)

- *Foster and develop a strong number and quality of external scientists and technicians, assisted by the TMIC Platform*. There are two types of such "first tier" users:
    - Those focused upon *developing* novel metabolomics science (potentially in partnership with TMIC); and
    - Those *using* metabolomics to conduct their research (across any of a large number of research domains), and thus needing strong grounding in, and understanding of, metabolomics (but not necessarily focused upon the metabolomics itself).
- *Demonstrate international metabolomics leadership by Canadian scientists*, with recognition as evidenced by a strong record in publications, presentations, awards, etc.
- *Support Canadian scientists' participation in major international collaborative research initiatives*
    - Ideally in a leadership capacity for individual components, and/or for the initiative as a whole; and
    - Drawing on TMIC capacities.
- *Help develop and foster a strong cohort of HQP linked to TMIC*, e.g., through in-house training, use of TMIC resources, involvement in conferences, participation in the Research Hotel Program, etc. Within this strategic objective, it is intended that these HQP go on to prestigious positions in academia. (For Strategic Objectives #3 and #4, they will go on to important industry, government, or other end-user positions, respectively.)

Network (TMIC and others)

The intent is to encourage, foster, and as possible support the development of a broad and strong network of scientists centered upon TMIC. This will include:

- *Develop scientific linkages and collaborations across the community and internationally.*
- *Develop more linkages and integration amongst the various 'omics communities* – multi-omics for end-to-end linkage of metabolomics to, e.g., genomics, proteomics and microbiomics, supported by the pathway resources developed at TMIC.
- *Develop mechanisms to catalyze and support multidisciplinary and multisectoral collaborations (as appropriate) to identify, plan, and implement projects* – most technology development aimed at practical real-world applications will require participation from multiple partners in the scientific, industrial, healthcare, NGO and regulatory communities.

3.3 Strategic Objective #3 – Commercial: Strengthen the Canadian Metabolomics-Enabled Industry

3.3.1 Overview

The second tier of users – Canadian industry – has the potential to be an international force in the development of commercial metabolomics-enabled technologies, devices, and products and services. Known commercial targets include:

- advanced instrumentation;
- innovative metabolomics kits (e.g., for rapid metabolite identification);
- integrated devices (e.g., for point of care);
- cutting-edge software;
- comprehensive software; and
- integrated, user-friendly databases

3.3.2 Current status

See Appendix A for a number of examples related to the commercialization of TMIC-enabled technologies, including several successful spin-offs.

3.3.3 Going forward

TMIC intends to proactively support development of industry capabilities through a variety of means discussed below.

TMIC Platform

- *Connect researchers (in-house, and external) to these "second tier" industry users*. In addition to working with existing partners, TMIC sees itself as a central point of contact to foster additional connections; e.g.:
    - Publish online listings of projects, users, potential applications, and commercial opportunities that will support new connections without need of active TMIC involvement; e.g., through on-line searches by users; and
    - Conduct more proactive "matchmaking" by TMIC; e.g., through regular planning processes (identifying linkages among the three user tiers) and through dedicated workshops and working groups targeting high profile opportunities. (A number of models are used world-wide which provide foundational ideas; TMIC will investigate these.)
- *Provide new technologies, IP, knowledge, and know-how to help transform Canadian industry capabilities.* This is an essential feature of TMIC's in-house technology development processes and includes active KT/TT to industry, such as:
    - Provide early-stage technologies for development and commercialization by industry; e.g., kits, hand-held & POC devices, assays, databases, software, and platforms;
    - Within this, carefully monitor IP management to ensure the "Canadian" part of "Canadian social and economic benefits" is achieved;

  - Where appropriate, develop open source IP; e.g., in situations where the Canadian public or the environment would most benefit, again bearing in mind the ultimate goals of TMIC. On this point there is precedent because this was done with OMx Analytics through the negotiation of a license to maintain an open access version of DrugBank. This allows the academic community to continue to benefit from free access to DrugBank while commercial entities who use or distribute DrugBank content for profit can generate revenue.
- *Target opportunities as appropriate either in-house, or in collaborations, partnerships, patents, through licensing etc.*
  - TMIC will engage commercialization specialists either as in-house staff or contracted as needed on a case-by-case basis. This may include leveraging the capabilities of external organizations skilled in commercialization, spin-offs, and start-ups (e.g., Discovery Lab, TEC-Edmonton);
  - Patent lawyers will review technology development papers before publications.

Industry Cluster – "Second Tier" Users

TMIC will help strengthen the Canadian metabolomics-enabled industry capability. There is a chain of events that must occur for this to be achieved, including:

- *Ensure industry is highly knowledgeable and engaged with opportunities afforded by metabolomics* – TMIC outreach will be crucial here,
- *Foster enhanced metabolomics scientific and technical capability (receptor capacity) within Canadian industry*, including enhanced capability for *accepting* technology transfer and/or knowledge translation. In this case, TMIC's "on the job" training through its Research Hotel Program are crucial.
- *Actively engage industry on developing novel metabolomics-enabled products and services.* This will include both: (1) initiatives developed with TMIC through joint opportunities, collaborations, licensing, etc., and/or (2) through industry's in-house R&D (in which case industry knowledge and capabilities must be sufficient).
- *Pursue strong commercial development activities*. These require at a minimum:
  - Strong IP & patent positions through which TMIC and its university partners (and their industry Liaison offices or research service offices) provide expert advice;
  - A strong value chain (suppliers, customers, contracts, partnerships, etc.); and
  - Sufficient investments, capitalization, valuations – TMIC "matchmaking" activities can assist here.

3.4 Strategic Objective #4 – Societal: Develop Workflows and Services to "Mainstream" Metabolomics Data and Devices into Practical End-User Applications

3.4.1 Overview

Based on the most important practical user opportunities that TMIC identifies, TMIC will facilitate "Mainstreaming Metabolomics" for third tier users. There is an enormous potential to use metabolomics – ideally integrated with other 'omics through advanced computational methods – for a wide range of sectors and uses.

This will take advantage of TMIC's strengths in research and technology development and build on emerging opportunities in metabolomics, as well as TMIC's explicit focus on helping "first tier" scientists and "second tier" firms who are actively developing practical metabolomics applications. This will include making metabolomic measurements far faster, more portable and much more comprehensive. This, in turn, will make metabolomics technology more appealing to a wider range of "third tier" users.

3.4.2 Current status

In TMIC's implementation phase, this opportunity was not yet targeted, but the next five years will see the Centre initiate activities directed towards it.

3.4.3 Going forward

Specific elements of this "mainstreaming" objective include:

TMIC Platform

- *Support both second tier industry and tertiary users in developing and using metabolomics tools to realize their enormous scientific and commercial opportunities*. This will include having TMIC:
    - Investigate the most significant social and economic benefits that may be realized through such mainstreaming;
    - Pursue explicit opportunities through proactive outreach and collaborations with appropriate partners in second and third tier user communities in Canada and abroad;
    - Become a preferred beta test resource for equipment suppliers and, as such, access reduced prices to capital expenditures;
    - Ensure that the power of metabolomics (technologies and databases), and the capabilities of TMIC, are widely known throughout the 'omics research and user communities, both in Canada and abroad.
- *Investigate ways to leverage TMIC's extensive databases (and database development activities)*; e.g.:
    - Investigate novel applications of the TMIC store of data on environmental, phenotypic and clinical issues, etc., (derived from a huge variety of investigations), which offer the potential to support a very wide range of studies that may be completely different from the original targets; and

  - Investigate whether there are opportunities to not only develop databases from published literature as we are doing now, but to use suitably anonymized data from fee-for-service projects, given appropriate agreements and releases in place with users;
  - These can be used for targeted, proactive practical applications.
- *Develop TT/KT pipelines that are explicitly focused on practical applications of most benefit to users.* A small sample of these include those below, although in our next five years we will target only a small, doable number of them, identified jointly with our user communities:

  - *Human precision medicine* – Excluding violent deaths, >90% of all deaths are caused by small molecules or microbes versus just 8% from genetic causes. These are the molecules directly investigated by metabolomics. For example, cancer, diabetes, autism, Alzheimer's, and heart disease already have significant metabolomics research discoveries. In the near future they will benefit from linking these to genomics, proteomics, transcriptomics, etc., as well as to better knowledge of the microbiome and the exposome, for a full picture of the individual's state of health, nature of disease, chemical exposure, environmental factors, and identification of precision medicine therapeutic options, as well as potential adverse drug effects, prognostics, etc.

  - *Food animal production.* There is great need for simple and accurate testing within food animal production for both animal and human health and welfare, especially disease/pathogen diagnostics, but also related to issues such as exposure to toxins, climate change (e.g., heat tolerance) and productivity (higher weight gain, greater feed efficiency). This includes use throughout the value chain: primary producers, processors, shippers, retailers, consumers, and regulators such as the Canadian Food Inspection Agency (CFIA) and provincial ministries. Ultimately, this will lead to greater food animal health and welfare, greater production yield at lower costs, increased trade opportunities (especially avoiding major international sanctions related to diseases such as "mad cow"), greater consumer acceptance, and reduced human health issues.

  - *Agricultural crop production*. Similar issues pertain in this sector: a need to accurately and speedily assess crop phenotypes and identify plant chemo-responses to biotic and abiotic stressors (including pollutants, pests, and pathogens), ideally at the farm level. This again applies across the value chain (from producers to regulators) and at all stages: crop production, monitoring, application of pesticides and fungicides, trade, regulation and oversight, and consumer safety. And similar benefits will arise: greater crop production, of higher quality crops, at lower production costs, with fewer chemical applications to the environment, improved human health, and fewer trade sanctions.

  - *Improved natural resource use and sustainability, and environmental monitoring.* A very wide range of applications is eventually possible here, essentially mirroring applications in the agriculture/agri-food sectors, and based on TMIC's planned future exposome work (see below) in that metabolomics can help identify the presence and quantity of a wide variety of chemicals and organisms of interest, both beneficial and harmful. This can be

used to monitor, e.g., water and watershed quality (e.g., assessing contaminating chemicals or toxic compounds), the nature of the microbial community in mine site tailings (e.g., how can a mine site be successfully reclaimed following closure?), aquaculture (e.g., fin/shellfish health, presence of chemical toxins and pollutants), certifying forest products for world trade (as pest-free), monitoring the health of wild animals (e.g., fecal metabolite tests for chronic wasting disease in wild deer, elk, buffalo, which can transfer to commercial herds), and improving natural resource extraction efficiency (e.g., successful mine site reclamation through real time monitoring, and improved efficiencies and lower effluents for oil and gas extraction and refining (especially Canadian tar sands).

The commercial pipeline must integrate these tertiary user needs into product development, validation, training, etc. Therefore, TMIC will develop appropriate TT/KT pipelines that will help foster such integration:

- *Conduct pipeline development collaboratively with all tiers of users*, so that appropriate activities, outputs, roles, and responsibilities are identified, with TMIC supplying appropriate services and databases, technology development support, and fostering linkages among users.

- *As metabolomics technologies mature and become more integrated into these tertiary end-uses, multiple pipelines may be required*, as different user communities have very different needs, development and approval processes, etc.

"Third tier" User Cluster

The users need to be sufficiently knowledgeable and engaged with opportunities afforded by metabolomics that take-up is likely, widespread across the appropriate sector, and timely. This will entail various aspects for TMIC to address proactively and collaboratively with users, such as:

- *Help users develop enhanced internal capability for understanding, adopting, and using metabolomics-related TT/KT.* Some of this will happen through TMIC and other partners' outreach activities, but some will occur through explicit collaborations, training, in-field testing and piloting, etc.
- *Consider potential barriers to ultimate acceptance and take-up of the metabolomics-enabled technologies. This includes* scientific, technology, validation, regulatory, economic, consumer acceptance, environmental, and ethical barriers, as well as ways to overcome these.
- *In general, use a portfolio approach to project selection*, with a deliberate design to have projects spanning the spectrum from discovery to application, across sectors, and across low risk/low reward and high risk/high reward.

Initial targets. The SEB benefits discussed above are obviously plentiful and diverse, and far beyond what TMIC can address over the next five years. We are also well aware that, as a Platform, we can only provide the cutting-edge infrastructure and technology development to enable our users to conduct the necessary research, and to catalyze the development of practical outcomes by our users (including through IP protection, licensing, and spin-offs).

As a result, we have identified a small number of application-related targets against which we will measure progress over the course of this Strategic Plan. Key amongst those targets are:

(1) The exposome – improved methods for measuring chemical exposures in air, water, food and drugs;
(2) Database development, including a resource on chemical contaminants (ContaminantDB) and completion of PathBank and MarkerDB;
(3) Offering near complete mammalian metabolome coverage; and
(4) Multi-omics – integrating metabolomics with other omics into systems-wide life science studies.

Achievement of these targets will require partnerships with academe and industry, as well as pursuit of additional project funding. See more details in "Some Early Targets" in Appendix E.

4. TMIC Governance and Management

4.1 Overview

TMIC operates as an unincorporated entity under an Inter-Institutional Affiliation Agreement between the University of Alberta and the University of Victoria as founding partners. A TMIC Constitution sets out a structure for the governance of TMIC. While the Member Institutions retain ultimate legal authority with respect to the operation of TMIC, it is their stated intent, where it is reasonable to do so, to act in accordance with the directions of the updated TMIC governance and management structure.

4.2 Governance

Under the TMIC structure implemented in 2018-19, the Board of Directors (the "Board") is advisory to all Member Institutions and reports to the UofA as host institution. It is mandated to monitor the activities of TMIC in accordance with the roles and responsibilities defined in the Constitution, and subject to endorsement by member institutions, including formulating policies relating to TMIC, recommending strategic and management plans, oversight of operations, recommending approval of the budget, and monitoring performance. The Board is comprised of at least 11, but no more than 15 individuals from the academic, not-for-profit and private sectors, including the Vice Presidents of Research from the UofA (who temporarily serves as the Chair while the expanded Board is being appointed and a new Chair is elected) and UVic, one representative from each of Genome Alberta and Genome BC, two ex officio non-voting members from TMIC's Management Committee (representing its Node Leaders) and six independent or at large members.[8]

The constitution of the revised governing structure is designed to strengthen the "external face" of TMIC, ensuring that decisions and directions of TMIC truly reflect the needs of the larger community, and keep a strategic focus on delivering scientific, societal and economic benefits for Canadians.

The Board has four standing committees – Executive, Finance & Audit, Operations, and a Nominating Committee whose terms of reference are detailed in the Constitution.

[8] The Board will continue to include a significant number of independent directors.

4.3 Management

TMIC is managed by the TMIC Management Committee (MC) consisting of the scientific Co-Directors and an Operations Manager. The MC is supported by a number of non-academic support staff. The MC has the overall responsibility for guiding and ensuring TMIC's operational, financial and scientific goals, as well as its vision for the future are met, in accordance with the strategies, policies, programs and performance requirements recommended by the Board. A Nodes Committee (NC) comprising all Node Leaders is TMIC's general management body and is chaired by a member of the MC (chosen on an annual rotating basis). The Nodes Committee, the Management Committee and the Administrative Support Team (AST) work in tandem to develop new and innovative ways of enabling scientific research and translation. Within each Node, the leader for each operational team is responsible for daily management, with an emphasis on maintaining existing user relationships, developing new partnerships, effectively managing facilities and finances, and delivering high-quality services to support TMIC's strategic plans for growth, collaboration, and cutting-edge science. An International Scientific Advisory Committee (ISAC) reports to the Management Committee, and also to the Board. The ISAC evaluates TMIC's scientific progress and also provides advice and guidance to the TMIC Management Committee (MC), as well as the TMIC Board, to help ensure that TMIC achieves its stated objectives and milestones.

Figure 4 provides an overview of TMIC's governance and management structure. More details are provided in the Management Plan in Appendix D.

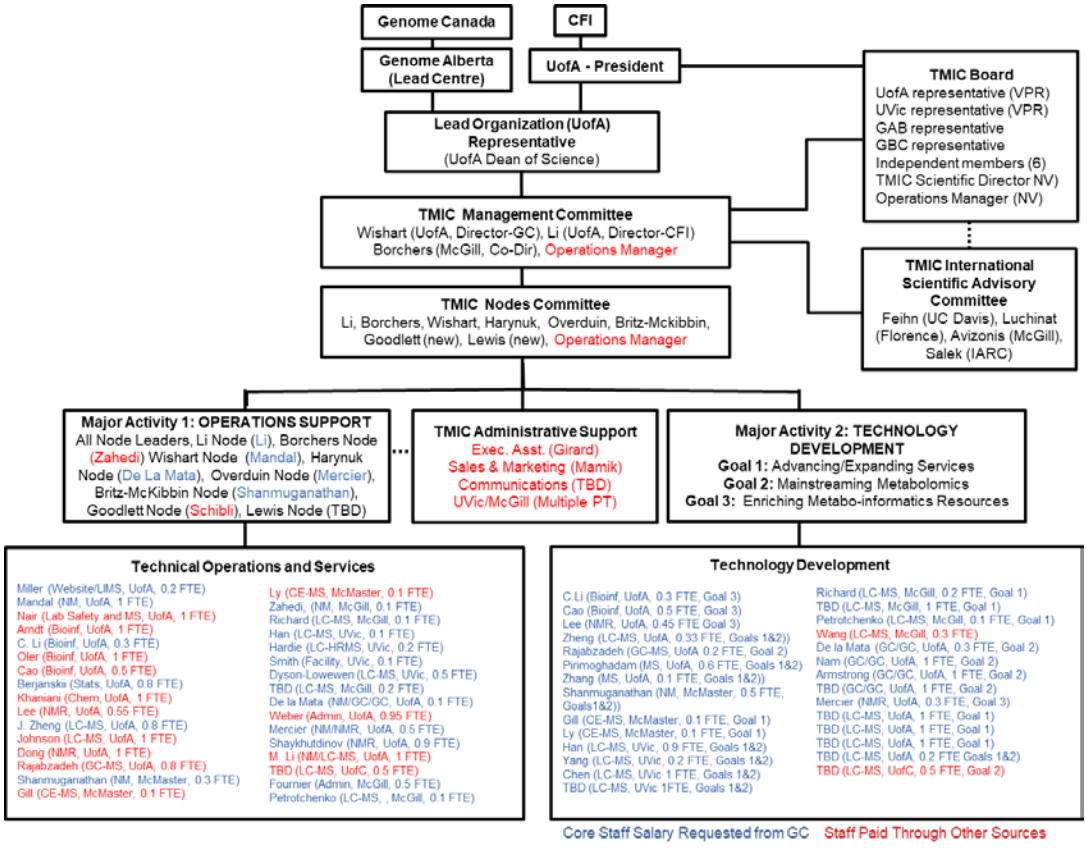

Figure 4. The TMIC Governance & Management Structure

5. Delivering the Plan

5.1 Implementing the Plan

In order to deliver on the vision in this Strategic Plan four key operational objectives have been identified and are outlined in more detail in the Implementation Plan (Appendix E):

- Build governance and management and operational capacity
- Maintain and build scientific and technical capacity
- Translate knowledge and technologies
- Ensure sustainable, diversified funding

Specific actions are identified for each operational objective. Annual Operating Plans will guide TMIC's priorities within this framework and serve as the benchmarking reference for the Board overview of Operations.

The other key element required to deliver on the plan is funding. Delivery on TMIC's vision requires highly skilled personnel and a diversified suite of state-of-the-art equipment that is professionally maintained and frequently updated, as well as resources for technology development and maintaining relationships with external users and partners. With operational funding now coming from CFI, Genome Canada, Western Economic Diversification, and service revenues, TMIC is moving towards a reasonable operational level of support for these core elements, although funding for the expanded governance model and the planned appointment and activities in translation has yet to be fully sourced. Such operational funding does not, however, provide for the necessary occasional major equipment upgrades (e.g. to replace the now inoperable 800 MHz NMR) that will need to be sought elsewhere. Financial and operational sustainability are constant challenges.

To appreciate the complexity of TMIC, a financial projection table has been prepared:

- TMIC operating and maintenance (O&M) costs (**Table 1**). These include expenses related to the support for technical and administrative personnel, equipment operations and maintenance, and general laboratory operations.
- TMIC revenues from all sources:

	Actual		Forecast			
	2017-18	**2018-19**	**2019-20**	**2020-21**	**2021-22**	**2022-23**
Revenue						
Grants/Industry	3,103,930	2,774,650	3,375,431	2,831,049	2,962,173	1,881,190
User Fees	472,431	504,045	1,757,379	1,900,000	2,100,000	2,400,000
Institution	15,000	61,290	386,717	70,000	70,000	820,000
Total Revenue	**3,591,361**	**3,339,985**	**5,519,527**	**4,801,049**	**5,132,173**	**5,101,190**
Expenses						
Personnel	(1,930,248)	(2,197,200)	(2,885,550)	(2,800,000)	(2,884,000)	(2,970,520)
Consumables	(1,023,079)	(1,117,435)	(2,103,319)	(1,812,860)	(2,060,500)	(1,942,761)
General Admin	(75,746)	(140,168)	(258,793)	(148,189)	(147,673)	(147,909)
Capital Costs	(24,900)	(62,182)	(632,253)	(40,000)	(40,000)	(40,000)
Total Expenses	**(3,053,973)**	**(3,516,985)**	**(5,879,915)**	**(4,801,049)**	**(5,132,173)**	**(5,101,190)**
Surplus (Deficit)	**537,388**	**(177,000)**	**360,388**	---	---	---
Balance Forward	---	**537,388**	**360,388**	---	---	---
Surplus (Deficit)	**537,388**	**360,388**	---	---	---	---

TABLE 1. Summary of Actual and Forecast Total TMIC Revenue and Expenses

5.2 Evaluating Progress

TMIC has established processes for tracking and measuring success, monitoring each of the KPIs outlined in Appendix E on an ongoing basis, administering annual user surveys and tracking newspaper/radio/TV stories about TMIC. A priority action is to revisit and expand the existing platform-specific KPIs to identify indicators that will reflect progress towards the downstream strategic objectives 3 and 4.

TMIC reports every four months to the Board, quarterly to Genome Canada and annually to CFI. As a platform that is still evolving in an enormously active scientific/technological domain, TMIC will conduct frequent monitoring activities to capture the fast-developing metabolomics and 'omics ecosystems, as well as frequent retrospective assessments of its deliverables.

5.3 Conclusion

TMIC is poised to deliver on its vision "To improve life through the power of metabolomics" through aggressive pursuit of its Vision and Mission:

> "To catalyze innovation and translate metabolomics from the laboratory to real-world use by creating novel technologies, providing cutting-edge analytic services, sharing foundational data resources, and equipping the next generation of scientists and users. The ultimate goal is to enable the creation of a strong metabolomics industry in Canada and generate social and economic benefits for Canadians."

TMIC's opportunity is to monitor the chemicals of life – the metabolome - and to put those metabolomic insights into the context of data from other 'omics technologies, interlace that with phenome/environment data in order to generate information about why living things and systems exist as they do and respond to stimuli as they do. Metabolomics is the "business-end" of monitoring living systems. If you understand these data, it allows more actionable responses than other 'omics measures alone.

Past investments in TMIC have provided Canada with state-of-the-art metabolomics infrastructure, world-class metabolomic assays, cutting-edge analytical software, comprehensive databases and chemical libraries, as well as highly skilled technical personnel in both targeted and untargeted metabolomics. Most importantly, those investments have built a capacity for technological innovation in novel methods to prepare and analyze samples, interpret data, and add value thorough combining metabolomic insights with other data, especially those from other omics sciences. Through consolidation and growth of its network of Nodes over the next five years, TMIC will be an even more central part of Canadian and indeed international research infrastructure while also growing its capability for dissemination, translation and commercialization.

A continued investment in TMIC, along with revenues brought in through its fee-for-service business model, will ensure the maintenance of resources that are essential to the metabolomics industry both in Canada and around the world. Looking to the future, strengthening TMIC support will pave the way for a larger, national metabolomics enterprise that fully harnesses the potential for metabolomics discovery and commercialization, for the benefit of all Canadians.

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7. List of Appendices

Appendix A – Recent Success Stories
Appendix B – SWOT Analysis of TMIC 2019
Appendix C – TMIC's Equipment Resources
Appendix D – The Implementation Plan

- Operational Objective #1 – Build Governance, Management, and Operational Capacity
- Operational Objective #2 – Maintain & Build Scientific & Technical Capacity
- Operational Objective #3 – Translate Knowledge and Technologies
- Operational Objective #4 – Ensure Sustainable, Diversified Funding
- Some Early Targets

Appendix E – TMIC's Key Performance Indicators as of May 2019