Towards precision medicine for type 1 diabetes in Australia

A PLATFORM FOR CONVERSATION & COLLABORATION

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JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

Australian Type 1 Diabetes Clinical Research Network

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EXECUTIVE SUMMARY

JDRF Australia envisions a future where precision medicine is at the heart of the prevention, diagnosis, treatment and prognostication of type 1 diabetes (T1D), paving the way towards a world without T1D. This White Paper is an invitation to work with JDRF Australia to create that future.

There is clear and mounting evidence for the potential impact of genomic medicine to transform T1D care. Australia's strong and rapidly evolving ecosystem of genomic expertise, technology and infrastructure provides a powerful motivation to lead the way in embedding genomic medicine in T1D.

JDRF Australia sought to elucidate the path towards this vision by mining the collective wisdom of an Expert Panel, which brought together deep expertise from a wide range of fields relevant to genomics. Through an iterative consultation series, research directions were developed that will expand the accumulated genomic research knowledge, embedding genomic medicine in future care models.

This consultation series comprised four phases:

Phase I: A landscape analysis allowed us to collate the knowledge base around existing genomic workforce and infrastructure, and the state of science in T1D genomics in Australia. We established a comprehensive stakeholder map, Expert Panel and consultation plan.

Phase II: An exploratory workshop was facilitated with members of the Expert Panel to elucidate current T1D research efforts and aspirations, with a view to developing a fit-for-purpose approach to bringing precision medicine to T1D patients in Australia.

Phase III: Research directions towards precision medicine were established through hosting a series of individual and collective discussions with members of the Expert Panel, allowing them to further explore the opinions and aspirations voiced in the Exploratory Workshop.

Phase IV: A vision towards precision medicine in T1D was outlined and is summarised in this White Paper, representing the culmination of efforts to collate and distil the findings of this process, and to outline the path towards genomic medicine in T1D in Australia and JDRF Australia's vision of precision medicine in T1D.

Through this process, it was agreed that the focus of T1D discovery in this field needs to shift from Genome Wide Association Studies (GWAS) to functional genomics with the aim of determining gene function and establishing cellular connectivity. This shift recognises the successful integration of genomic discovery into T1D to date, the impressive infrastructure in the field here in Australia, and the strength of JDRF Australia's commitment to pushing the field forward.

Priority Areas for functional genomic research directions were identified as follows:

PRIORITY AREA 1 – *Prevention of disease onset and progression across all stages of T1D* by leveraging and developing local expertise to address critical and clinically relevant research questions such

JDRF Australia is proud to have led such a collaborative process and is deeply appreciative of the thoughtful and passionate input from Australia's leading T1D experts.

JDRF Australia will work with the research community and its partners to deliver a research ecosystem that supports these priority areas.

as connecting risk-associated gene variants to their function in cells, addressing heterogeneity of progression and conducting research that enables preservation of the beta cell health.

PRIORITY AREA 2 – *Strengthening existing biobanks, datasets, and purpose-built cohorts to advance genomic research in Australia* by improving researcher access to existing datasets, thereby facilitating adequately powered studies that can accelerate the understanding of T1D pathogenesis.

PRIORITY AREA 3 – *Targeting genomic research interventions* by focusing on research that will accelerate the translation of genomic research in earlier access to benefits by all patients, including addressing disparities in genomic and non-genomic findings bringing together intersecting, cutting-edge technologies and supporting capacity building, accelerating genomics-driven drug discovery and the development of novel therapeutics, conducting clinical trials and seeking national and international collaborations.

With an emphasis on outcomes for patients, JDRF Australia will establish a T1D Genomics Consortium enabling scientists to elucidate the critical research questions and lead to the embedding of genomic medicine in T1D in Australia. The T1D Genomics Consortium will be truly collaborative and expert team that crosses disciplines and spans multiple institutions, connecting the best-of-field in Australia with leading global efforts.

We envisage that the work conducted by the T1D Genomics Consortium will form the foundations of T1D precision medicine in Australia, and that one-size-fits-all clinical management of T1D will be replaced with customised approaches for all people living with T1D, bringing the right treatments, to the right patients at the right time.

For this vision to become reality, JDRF Australia will work with the researchers towards establishing strong foundations and clear alignment of the program. It is anticipated that the T1D Genomics Consortium will:

1. Tap into existing expertise, leading technology and advanced infrastructure and strengthen connections between existing successful initiatives; and

2. Align and connect with key global research efforts to deliver a paradigm shift in T1D research.

Discovery scientists and clinician-researchers, implementers and educators, their clinical datasets and study cohorts, together with the world class facilities and infrastructure built over the last decade, have created a momentum that brings with it unprecedented opportunity and hope. Functional genomics and new methodologies have the power to fill in the gaps of knowledge. We all have a responsibility to take the next step towards precision medicine for T1D in Australia.

JDRF Australia believes that the T1D Genomics Consortium, through collaboration, integration and expansion across the current and future efforts, could bring precision medicine to Australians living with, or at-risk of developing, T1D.

CONTENTS

INTRODUCTION

Type 1 diabetes (T1D) is a chronic autoimmune condition in which destruction of the beta cells in the islets of Langerhans in the pancreas results in insulin deficiency and hyperglycaemia. This pancreatic beta cell destruction is secondary to autoimmune events[1,2].

T1D develops in genetically susceptible individuals following an environmental trigger or triggers. After the discovery of insulin in 1921, exogenous insulin was, for over one hundred years, the only approved treatment for T1D and the only way to maintain blood glucose levels in the blood within the normal range. However, on 17 November 2022, with the approval of Teplizumab[3] by the United States Food and Drug Administration (FDA), people living with early T1D (Stage 2) will have access to a new therapy to prevent progression to clinical T1D (Stage 3). Several other potentially impactful therapies are in the advanced stages of clinical testing. However, these therapies appear to provide benefits in some groups of patients with T1D but not in others, an indication of heterogeneity of T1D[4].

In the last decade, research has highlighted the importance of the interplay between our genes, the microbiome and the immune system as some of the critically contributing factors in disease pathogenesis[5]. Approaches towards disease prediction, prevention and cures require novel paradigms to provide a better understanding of what appears to be a highly individualised gene-environment interplay leading to development of a variety of diseases including T1D.

Genomics-led discoveries have laid the path towards further definition of such interactions[6]. Supporting these discoveries could, in the future, enable clinicians to meet each patient's needs based on their unique set of genetic and physiological traits as well as environmental influences. This is the promise of precision medicine, also known as "personalised medicine", as an innovative approach to tailoring disease prevention and treatment by taking into account differences in people's genes, environment, and lifestyle.

The goal of precision medicine is to target the right treatments to the right patients and at the right time. To understand the pathway towards precision medicine for T1D, JDRF Australia embarked upon a four-phased approach that included a detailed landscape analysis and an iterative stakeholder consultation process centred around an Expert Panel concluding in the release of this White Paper.

This White Paper describes the burden of T1D, the contribution of genetic and genomic discovery to advances in T1D care, the impressive genomic expertise and infrastructure right here in Australia, including the existing foundations of genomic medicine in T1D. It then begins to look forward, defining research directions that will pave the way towards precision medicine for T1D, including the specific research direction recommendations and priorities that emerged from the consultation process, and outlining JDRF Australia's vision for precision medicine in T1D in Australia, including the immediate next steps: the establishment of a T1D Genomics Consortium.

JDRF Australia thanks the Expert Panel for their generosity in sharing not only their wisdom but also their hopes for a future of precision medicine in T1D. We are excited to work together to achieve this shared vision.

ABOUT JDRF

JDRF is dedicated to creating a world without T1D. Throughout the world, we lead the fight against T1D by funding research to find cures and improve lives for those living with the condition.

At the time of publication of this White Paper, JDRF has invested $3.3 billion in T1D research worldwide, across all disease stages and research disciplines. JDRF has been part of every major breakthrough in T1D care in the last 50 years, contributing to major shifts in our understanding of T1D development, treatment, and prevention.

Locally, JDRF has been investing in the best ideas and researchers for more than 40 years. In the last decade alone, JDRF Australia has invested $162.1 million into T1D research. By working collaboratively with other leading diabetes organisation in Australia, we advocate and secure affordable and equitable access to new therapies for all Australians living with T1D[7].

We collaborate with academic institutions, policy makers, and corporate and industry partners to develop and deliver innovative therapies to people living with T1D. Our efforts have created a cohesive ecosystem of research programs and infrastructure, driving research from bench to bedside. Central to this ecosystem is the Type 1 Diabetes Clinical Research Network (T1DCRN), through which, since 2011, JDRF Australia has invested $72 million from the Federal Government in to Australian T1D research, including $5.9 million through key funding schemes and programs in 2022 alone.

Led by JDRF Australia, the T1DCRN is a national framework underpinning the most promising T1D clinical research and clinical trials. Focused on patient benefit, it provides a platform to accelerate therapies and amplify research impact. Initiatives under the T1DCRN have supported more than 300 researchers across 70 institutes, connecting approximately 2,500 Australians living with T1D with the latest research, treatments, and technologies.

Through the T1DCRN and other key programs, JDRF Australia has built a track record of successful implementation of initiatives focused on disease prevention, new therapies and building research capacity in T1D in Australia (Figure 1). For example, one strategic research goal for JDRF is to identify children at risk of T1D, and thus prevent the onset of clinical diabetes, capture data, provide clinical trial platforms, and accelerate the pace of translation by embedding outcomes into clinical care. To achieve this goal, JDRF supports the following major programs and centres:

- The Environmental Determinants of Islet Autoimmunity Study (**ENDIA**) - an Australian prospective pregnancy cohort study investigating the environmental triggers responsible for the autoimmune process that leads to T1D.
- Type1Screen (**T1S**) - a program offering antibody testing to children and young adults to determine if they are at risk of developing T1D.
- Type 1 Diabetes National Screening Program, a General Population Screening pilot (**GPS**) - an Australia-wide autoantibody screening program. Its objective is to identify those in the population who are in the early, preclinical stage of T1D, who will benefit most from taking part in clinical trials of therapies that aim to slow or prevent the onset of the disease.
- Australasian Type 1 Diabetes Immunotherapy Collaborative (**ATIC**) - a highly interconnected consortium run by leading Australian immunologists and endocrinologists and a platform that has the capacity to facilitate the conduct of clinical trials according to international standards, thereby strengthening Australia's reputation as a preferred site.
- The Rio Tinto Children's Diabetes Centre, a JDRF Global Centre of Excellence(**CoE**) - focused on implementation science and building Australia's infrastructure and human capital.

In addition, JDRF Australia established the Australasian Diabetes Data Network (**ADDN**), an Australia and New Zealand Type 1 registry capturing patient data across clinical networks, which was important to securing reimbursement

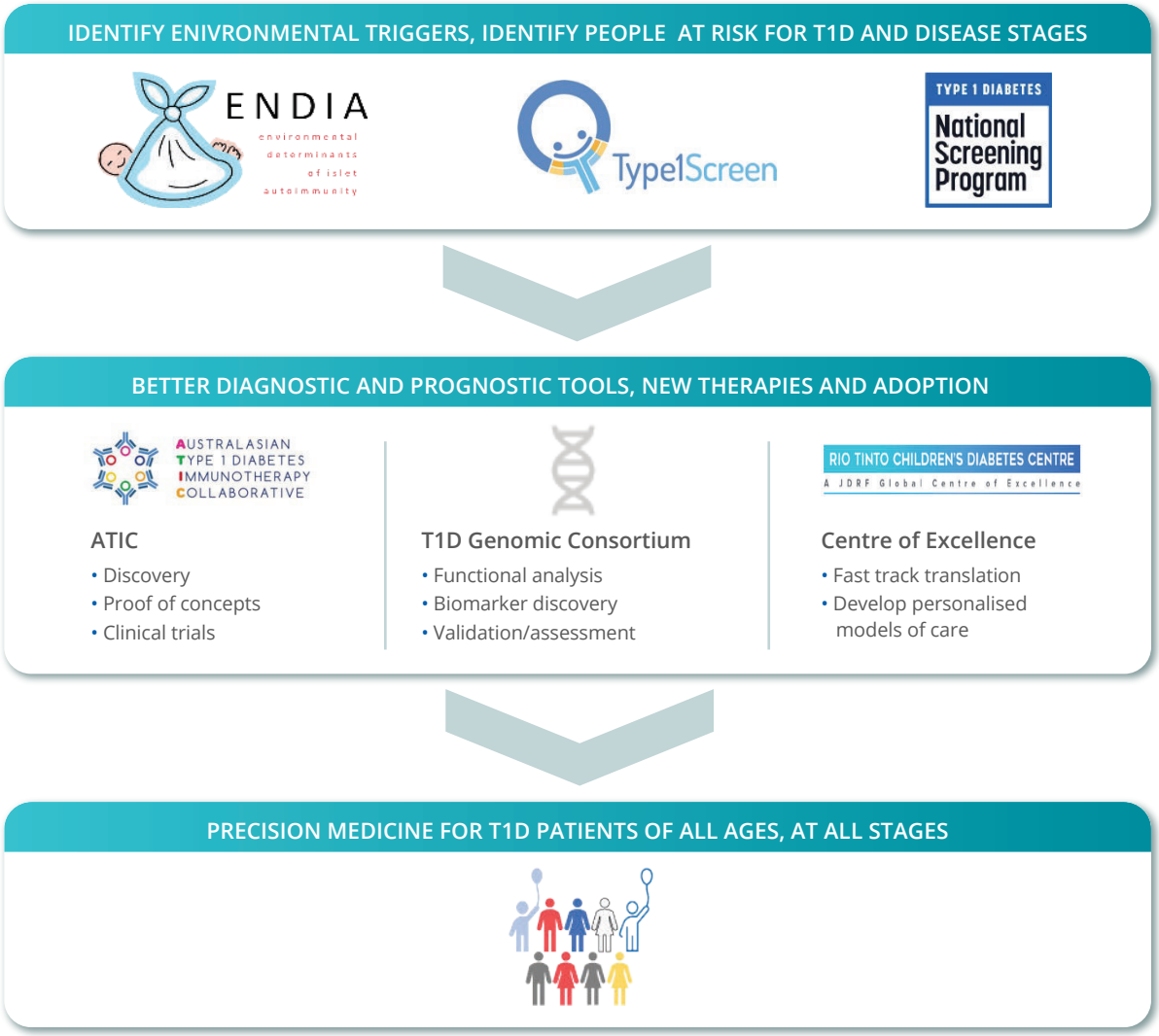

Figure 1. Established T1DCRN programs focused on identifying environmental triggers, identifying people at risk for T1D and disease stages such as the GPS, T1S and ENDIA, have been strategically implemented to interconnect with ATIC and the CoE and deepen our knowledge around how T1D develops and ensure optimal translation and faster outcomes. A T1D Genomic Consortium will be an extension of ongoing programs, enabling synergies across the board.

for Continuous Glucose Monitoring (CGM) for T1D patients in Australia.

Within the next three years, JDRF Australia and T1DCRN will continue to build on these prior achievements and increase the impact of T1D research via expansion of its scientific foci. Updated research directions will bring new talent, knowledge and cross-disciplinary collaborations relevant to the field addressing T1D pathogenesis related research questions with an emphasis on heterogeneity.

It is envisaged that data stemming from this research will inform precision medicine approaches. Accordingly, the T1D Genomics Consortium described later in this Paper will form a natural extension and integral part of JDRF Australia funded centres and consortia (Figure 1B) and will connect advanced genomic infrastructure present in Australia with both ready and maturing T1D-specific research outcomes.

TYPE 1 DIABETES IS A GLOBAL CONDITION WITH A SUBSTANTIAL DISEASE BURDEN

T1D is a chronic autoimmune disease that develops from an interaction of genetic and environmental factors. Together, these factors trigger the autoimmune destruction of pancreatic beta cells, characterised by immune cell infiltration of the pancreatic islets, inflammation, and progressive beta cell loss, leading to loss of insulin production[1,8].

Throughout the world, T1D incidence has risen over the past three decades, with an average annual increase of 3-4%[9].

The 2021 modelling of the global incidence, prevalence, and mortality of T1D with projection to 2040, conducted by JDRF for the **T1D Index**, found that there were about 8.4 million individuals worldwide with T1D: of these 1.5 million (18%) were younger than 20 years and 5.4 million (64%) were aged 20–59 years. In that year there were about 35,000 non-diagnosed individuals who died within 12 months of symptomatic onset. The missing prevalent cases were 3.7 million for that year[10].

In Australia, nearly 130,000 individuals are living with clinically diagnosed T1D. It is estimated that an additional 25,000 individuals are in the early stages of the disease, although undiagnosed. The 2021 **T1D Health Economics Report** commissioned by JDRF Australia revealed that Australia has one of the highest incidence rates of T1D in children, ranking 16th out of 123 countries globally.

One in two people with T1D are hospitalised every year in Australia. As many as 39% of new cases of T1D every year in Australia (over 900 individuals) are diagnosed when individuals suffer diabetic ketoacidosis (DKA), requiring emergency care. Of these, 53% are children aged 0-19 years old. At least 40% of individuals living with T1D have developed complications, with more than a quarter experiencing more than two complications, the most common of which is neuropathy. People with T1D are five times more likely to suffer from depression, and nearly twice as likely to suffer from anxiety compared to people without T1D.

In addition to the burden on individuals and families, the report states that the annual cost of T1D to the Australian economy is conservatively estimated at $2.9 billion, with an average lifetime cost for each patient of approximately $400,000.

Due to its complex aetiopathology, T1D remains a lifelong illness without a cure. Patients rely on delivery of exogenous insulin to correct glucose levels in the blood and are burdened with frequent monitoring of blood glucose levels, persistent concerns regarding food choices and, in many cases, suffer from major complications of the disease.

TYPE 1 DIABETES IS A COMPLEX CONDITION DRIVEN BY GENETIC AND ENVIRONMENTAL FACTORS

Following the discovery of the link between T1D and the Human Leukocyte Antigen (HLA) gene in 1974[6,11,12], a combination of HLA haplotypes and non-HLA genes are used to predict risk of developing T1D. HLA is a cell surface molecule and a key component of the immune system, specialised in presenting antigenic peptides to the T-cell receptor (TCR). This function, known as cell-mediated immunity, when working correctly, protects us from disease. Impairment of its function is associated with susceptibility to viral infections and autoimmune diseases[13]. The autoimmune reaction triggered by specific HLA molecules leads to the destruction of pancreatic beta cells, the loss of which precipitates into unstable and eventually unregulated glucose levels in the blood[1,14].

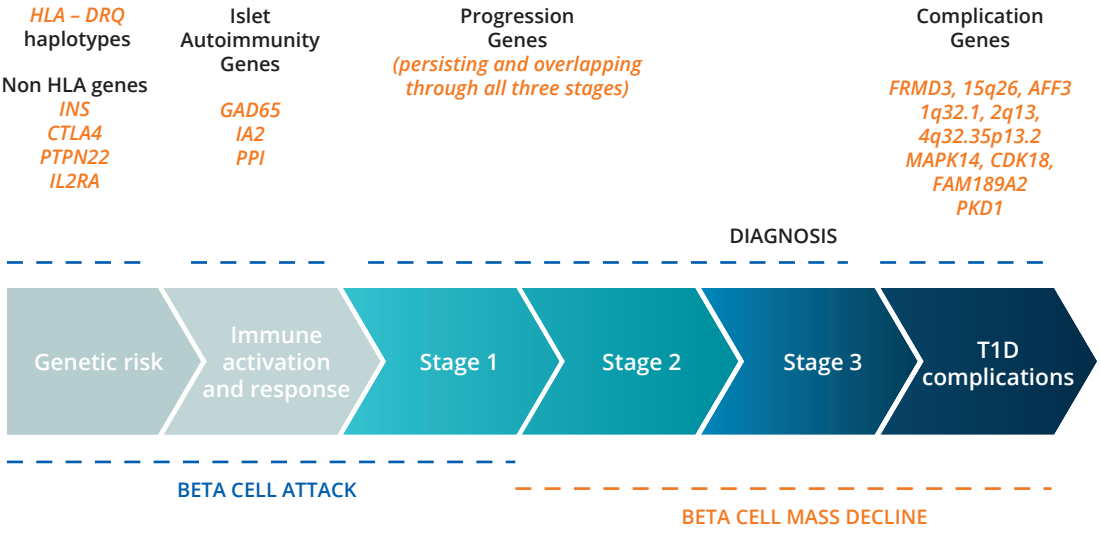

Figure 2. T1D is driven by HLA and non-HLA genetic factors strongly associated with the occurrence of autoimmunity and complications. GWAS has made a significant contribution in the discovery of genomic regions associated with T1D risk and progression.

Studies of the genome have revealed that the HLA locus on chromosome 6p21 contributes as much as 50% of the genetic susceptibility to T1D[15]. The Environmental Determinants of Diabetes in the Young (TEDDY) study revealed that familial risk in T1D is supported by an identical twin concordance rate of nearly 70% and a sibling concordance rate of 8-10%[16].

Genome wide association studies (GWAS) have shed light on other genomic regions[17,18] associated with T1D progression and complications, enabling better understanding of risk prediction, progression and T1D complications (Figure 2). In 2009, GWAS identified over 40 loci associated with T1D risk[19].

Currently, the number of genetic variants conferring susceptibility to T1D across the human genome stands at 60, with some falling outside the coding regions of biologically relevant genes. Identified variants located in non-coding regions can potentially confer T1D genetic risk. These long non-coding RNAs, enhancers and promoters affect gene expression in specific cell types, including T cells[20-23]. To date, research has uncovered the function of only a few non-HLA genes identified by GWAS. More specifically, *PTPN22* has been shown to participate in TCR signalling pathways; *IL-2RA* is reported to negatively impact *IL-2* sensitivity, which is critical to regulatory T cell (Treg) function, and; *CTLA4* controls peripheral Treg proliferation, thus playing a significant role in regulating the autoimmunity of the pancreas, recently reviewed by Zayec *et al*[8] (Figure 2). All four, *INS, CTLA4, PTPN22*, and *IL-2RA* are involved in determining risk, making these genes targets for development of new therapies[8]. A number of other genes are also found to be associated with T1D complications, but their function remains unknown[24].

GWAS does not explain all genetically inheritable disease, as it is predicated on common alleles. Genetic susceptibility does not fully explain, nor is it enough to trigger, the onset of T1D. Owing to research in large population cohorts, it is now known that progression of many diseases[27]

It is not yet understood how various environmental triggers, either alone or together, conspire to give rise to the onset of the disease, hence this area remains one of intense focus of research.

including T1D[25,28] has multifaceted contributors – a combination of genetic risk and environmental factors[19,29]. Environmental triggers can affect gene expression, introducing epigenetic modifications such as DNA methylation, histone modification, and non-coding RNA. In T1D, these triggers have been identified by prospective birth cohorts and include geographic location[25], viral infections[26,27], receiving childhood vaccinations[28], exposure to toxins[29,30], vitamin D levels[31] and changes in composition of gut microbiota[32]. It is envisaged that the combination of genetic susceptibility with one or more environmental triggers and epigenetic changes leads to autoimmunity, ultimately causing beta cell destruction and the onset of T1D.

GENETIC AND GENOMIC DISCOVERIES HOLD THE POTENTIAL TO TRANSFORM T1D PREVENTION AND CARE

Accumulation of genetic and genomic data has enabled important research that may, in the future, inform strategies for better T1D prevention. One example of this research is the refining of the Diabetes Genetic Risk Score 1 (GRS1) to GRS2[33]. GRS2 uses 67 single nucleotide polymorphisms (SNPs) and accounts for interactions between 18 HLA DR-DQ haplotype combinations to better predict T1D risk (Figure 3) (recently reviewed by Carr *et al*[34]). GRS2 is more predictive in early life, additionally to its role in T1D-risk stratification, it improves discrimination between T1D and Type 2 Diabetes (T2D) and it differentiates between non-autoimmune forms of rare diabetes types such as monogenic diabetes.

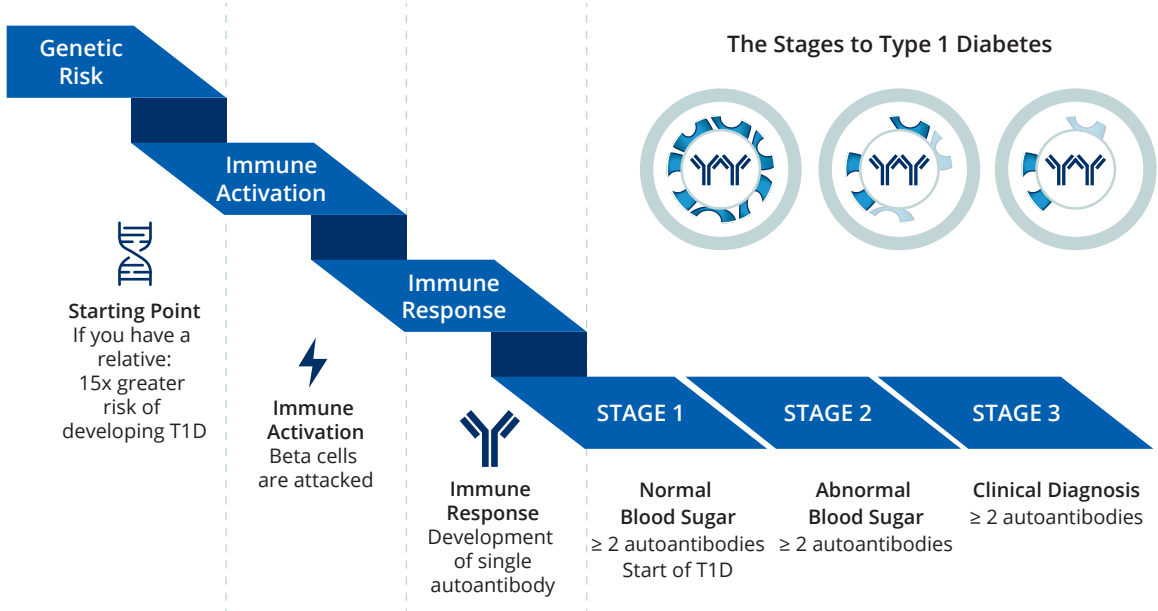

Figure 3. As per the scientific statement of JDRF, The Endocrine Society and The American Diabetes Association, T1D is a continuum that progresses sequentially at variable but predictable rates through distinct identifiable stages prior to the onset of symptoms[36].

A scientific statement of JDRF, The Endocrine Society and The American Diabetes Association, proposes that the development of T1D should be viewed as the progression through a continuum of three distinct stages. The first two stages are pre-symptomatic. Stage 1 of T1D is defined as the presence of beta cell autoimmunity characterised by the presence of two or more islet autoantibodies with normoglycemia; Stage 2 of T1D is defined by the presence of beta cell autoimmunity with impaired glucose tolerance; and Stage 3 of T1D is defined as the onset of symptomatic disease. Persistent presence of two or more islet autoantibodies is a validated approach to identify individuals that are at high risk of developing T1D at some stage in their lifetime[35]. However, the time of appearance of autoantibodies and what triggers progression through T1D stages, remains unknown.

Duration of asymptomatic preclinical disease (Stage 1 and 2) between individuals varies widely[37]: the shortest reported time from autoantibody seroconversion to clinical symptom manifestation is two months and the longest interval is reported to be 21 years (from 11 to 32 years old)[38]. While the condition is commonly diagnosed in childhood, age-related endotypes of T1D with different underlying aetiopathological mechanisms in children aged less than seven years, compared with those diagnosed at age 13 or older have been reported[39]. This suggests that there might be heterogeneity in mechanisms that drive progression from presymptomatic to clinical disease.

Better understanding of the triggers of progression from the asymptomatic, Stage 1 to Stage 2 and then to symptomatic Stage 3 of T1D is key to developing individual or group-patient-centred approaches to prevent and treat T1D. The task is to characterise each phase of T1D development starting with genetic variants relevant to specific stages, understanding environmental factors triggering the onset of T1D.

As the condition progresses to the clinical or metabolic stage of T1D (Stage 3), beta cell population declines further leading to insulin deficiency and hyperglycaemia. Patients rely on the precise adjustment of exogenous insulin to attempt to maintain glucose levels in the blood within normal ranges. Advances in technology,

> **“What if all diabetes clinics were about prevention of type 1 diabetes?”**
>
> **Prof Thomas Kay**
> Director of St Vincent’s Institute of Medical Research, Victoria

including continuous glucose monitoring systems (CGMs) and novel insulin delivery technologies connected through sophisticated algorithms into automated hybrid-close loops, have enabled patients to optimise their glucose levels, reduce the risk of severe hypoglycaemia and improve quality of life[40]. However, despite these advances, the commitment of clinical care teams and the dedication to self-management of people living with T1D, meeting glycaemic targets remains a daily challenge to many patients.

A range of potentially impactful therapies is currently in the pipeline and at different stages of testing in the laboratory and clinical trials around the world[2,41,42]. Antigen specific therapies such as Remygen, YMCY-0098, BCG and Diamyd, B-cell therapies such as Verapamil and Temelibab, immune modulators such as Baricitinib, Iscalimab, Ladarixin and Anti Thymocyte Globulin (ATG), Interleukin-2 (IL-2)/anti-Tumour Necrosis Factor (TNF)/Glucagon-like Peptide-1 (GLP-1) and T cell immune modulators such as ATG/Granulocyte-Colony Stimulating Factor (G-CSF), Abatacept, T-Regulatory Cell (TREG) vaccine, Alefacept, TREGs/Il-2 and others. Considering the heterogeneity aspects of T1D aetiology discussed earlier, it is unlikely that these drug candidates would work equally well for all designated groups of T1D patients. For some, the benefit to side effects ratio may not be acceptable. It is imperative that the future choice of disease modifying therapies can be tailored to the needs of subgroups of patients for the most impact and benefit at the right time.

Long-term research efforts in developing new therapies that can arrest the disease in Stage 2 led to the FDA approval of Teplizumab, an anti-CD3 monoclonal antibody designed to interfere with the immune attack, thus delaying beta cell destruction. Teplizumab is the only therapy approved by the U.S. Food and Drug Administration (FDA)[43] for a subset of patients who currently have Stage 2 T1D[3,44]. Teplizumab, known as

Tzield, can delay the onset of Stage 3 T1D in adults and paediatric patients 8 years and older by up to three years, providing further evidence towards the viability of immunotherapy in the context of autoimmune diseases. However, data show that 53% of Teplizumab treated patients present with a significantly greater C-peptide response compared to the placebo treated group and the non-responders. Such differential response to treatment is yet to be investigated and further underscores heterogeneity and the importance of investment into genomic medicine.

UTILISING FUNCTIONAL GENOMICS TO DISSECT CRITICAL STEPS OF T1D PATHOGENESIS

There are currently significant research gaps around the presentation diversity of T1D, limiting our understanding of disease aetiopathogenesis and hindering the application of personalised medicine approaches in T1D care (Figure 4). As mentioned in this paper, discordant progression in identical twins at high risk of developing T1D, variability in time taken to progress from asymptomatic

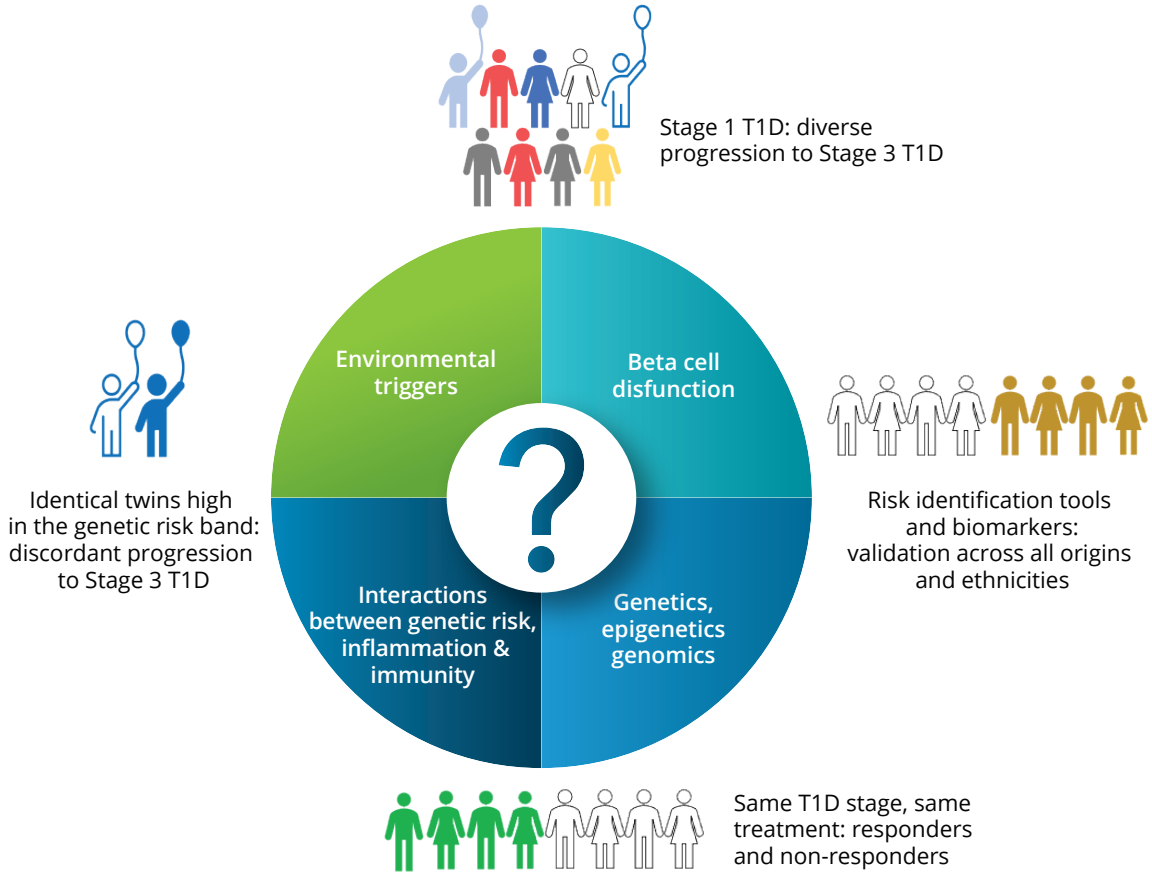

Figure 4. The quest to change the model of care for T1D patients relies on the provision of answers to the many remaining critical questions about the disease onset and development, and particularly the as-yet unexplained differences in disease presentation.

to the symptomatic or clinical stage of the disease (progression from Stage 1 to Stage 3), differences in responding to treatment targeting patients at various disease stages and the role of environmental triggers in initiating autoimmunity and beta cell decline are some of the most significant areas of investigation in the field.

Clarifying the potential impact of possible environmental triggers that drive T1D heterogeneity to achieve better T1D care[4,42,45] will require a global research effort, inclusive of advanced technologies, infrastructure, diverse expertise, time and major investments.

Connecting genetic risk with the environment involves connecting any genetic risk for T1D directly to the genes that are disrupted, and to achieve this, it is necessary to map the connections in the immune cells involved in T1D pathogenesis. Identification of transcriptomic signatures of gene expression that denote different stages of progression to T1D is possible. Further transcriptomics research on chromosomal landscaping to dissect the 3D chromosomal map in specific cells implicated on the onset of autoimmunity are needed.

Platforms dedicated to collection of data across all stages of the disease that integrate genetic and genomic testing would help determine whether distinct genomic signatures exist, improving our knowledge around gene and cellular processes that confer progression. Conducting research in cohorts of patients with T1D who do not have family history for T1D, would enable group comparison and add an important dimension to this work.

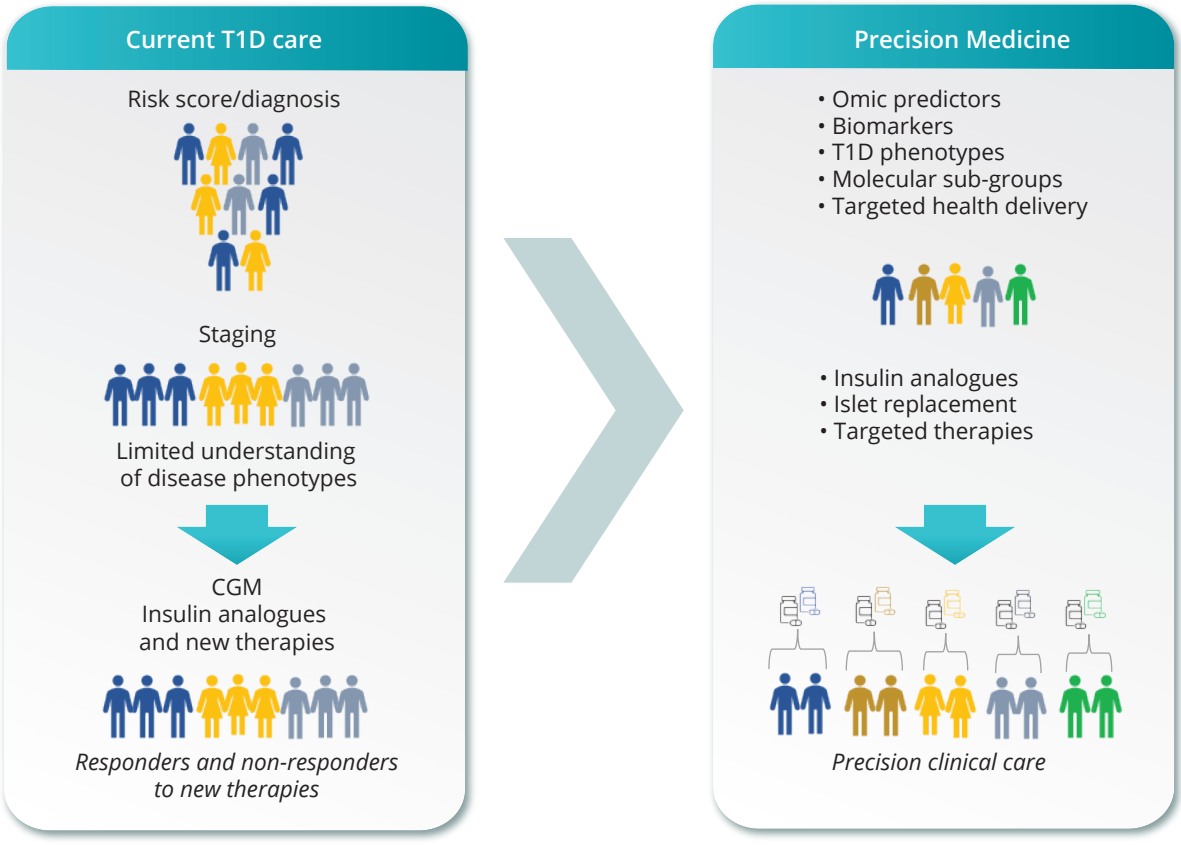

Figure 5. Our improved understanding of the pathogenesis of T1D will lead to better risk stratification, better understanding of phenotypes and endotypes of T1D, transforming current T1D care to precision driven prediction, prevention and treatments.

Functional genomics would also be a significant tool to dissect differences between responders versus non-responders at the genetic and cellular level and potentially uncover new pathogenesis mechanisms that bring together endogenous and environmental drivers of disease. Mechanistic, functional genomic studies on samples collected from randomised immunotherapy clinical trials, would determine differences between these groups, potentially uncovering endotypes of the condition that mostly benefit from specific therapies.

In Australia, JDRF Australia would like to see a research effort spanning functional genomics to clinical translation, with the goal of forming a full understanding of the genomic landscape of T1D from nucleotide level to the 3D architecture of the genomes and using the outcomes of this research to improve the accuracy of preclinical diagnosis and response to therapy.

Central to the formulation of specific research questions and the continuation and success of this research is the harmonisation, linkage and sharing of datasets and registries, ensuring adequate and ethical platforms that enable consent for genomic research are in place. A not-to-be missed opportunity for addressing the diversity of presentation of the condition in Australia is to tap into international and national, established, and unique cohorts that follow participants from birth such as ENDIA, T1S and virtual non-T1D biorepositories such as Generation Victoria. Building data interpretation skills and capacity to bring the results of this research to fruition is also needed.

> **“Studies of the genome have generated a wealth of data. Now we need a giant functional attack that will enable us to understand diabetes at a molecular level.”**
>
> **Prof Shane Grey**
> Head, Transplantation Immunology Group
> Garvan Institute of Medical Research

Combined with advances in gene therapy and islet replacement, a functional genomics research approach can lead to discovery that will inform more personalised or group-centred prevention and treatment in T1D care.

BROAD AUSTRALIAN GENOMIC EXPERTISE AND INFRASTRUCTURE

Integration of genomic expertise and technology into clinical practice requires substantial support of research across all stages of the translational pipeline so that the clinical use of genomics is safe, cost-effective, and equitable. Genomics linked to precision medicine will also require working across a complex ecosystem of allied expertise to underpin the clinical care with a just, and progressive framework of ethical, legal, and social issues associated with using genomic information in healthcare.

In Australia, both State and Commonwealth health departments recognise the power of precision medicine in addressing clinical management challenges associated with chronic conditions. In the last decade, the Australian precision medicine ecosystem was enriched by first establishing the National Health Genomics Policy Framework, followed by substantial Federal Government funding and implementation of a clinical genomic medicine approach facilitated by state-based services (summarised in Figure 6).

Figure 6. Australia is home to numerous state-of-the-art genomic facilities and world leaders conducting genomic and non-genomic research across various disease fields, including T1D.

Under the Medical Research Future Fund (MRFF), the Australian Government supports the *Genomic Health Futures Mission* (GHFM), a $500 million investment over 10 years that is aimed at integrating genomic knowledge into clinical practice. Intended outcomes include improving diagnosis of many diseases, advancing genomic technologies, and enabling precision medicine – all of which have positioned Australia as one of the global leaders in genomic research.

In May 2021, the GHFM awarded over $104 million to genomic research nationally, funding genomic research in 11 universities and two major medical research institutes, with nearly $35 million going towards research support. The focus areas of the initiative include research into infantile epilepsy and sepsis, rapid diagnosis of critically ill children, as well as a major reproductive carrier screening project. Combined with the Centre for Ethics of Paediatric Genomics, these initiatives are aimed at improving paediatric care.

The largest national initiative in genomic medicine is **Australian Genomics**. Established in 2015, Australian Genomics is a partnership of 100

organisations. It brings together 440 collaborators from a national network of organisations including diagnostic laboratories, clinical genetic services, research, and academic institutions. This collaborative is building the evidence base to support the appropriate implementation of genomic technologies into the Australian healthcare system.

Between 2021 and 2023, the focus of Australian Genomics is to support the efficiency, effectiveness, and impact of genomic research, distilling research outcomes to inform government policy and practice, and working with clinical and research communities to translate genomic advances into healthcare. It represents Australia globally and is actively working with the Global Alliance for Genomics and Health (GA4GH). Australian Genomics has recently developed recommendations to the government to inform the implementation of a **National Approach to Genomic Information Management for Australia**.

The infrastructure and collaborative power established by Australian Genomics continues to successfully support research in many diseases.

In Australia, the impressive genomic expertise and infrastructure, paired with the availability of electronic health data pertaining to large populations, have the potential to be leveraged, bringing together a powerful collaboration, expanding genomic and non-genomic research networks in T1D.

TOWARDS EMBEDDING PRECISION MEDICINE IN T1D IN AUSTRALIA

Genetic and genomic discoveries have to date provided several clues that have the potential to improve our understanding of how the condition develops. JDRF Australia will help build on this momentum to establish the foundations of precision medicine in T1D in Australia, recognising the opportunity that this presents for other conditions with high disease burden and no cure.

The following points give us great confidence that, through combining international knowledge with local expertise and infrastructure, embedding genomics into JDRF Australia's strategic research portfolio with a vision towards precision medicine in T1D in Australia is the way forward:

- Functional genomics is a powerful concept to connect clinicians and researchers for the common goal of investigating the functional impact of identified and yet to be discovered genetic variants involved in the development of T1D. It will contribute to advances in knowledge required to eventually prevent and cure the condition, such as a better understanding of the aetiology and pathogenesis of T1D, as well as integration of all knowledge to achieve individual diagnosis and disease treatment.
- Genomic research is increasingly becoming more cost-effective, given the wider use of genetic and genomic testing.
- Existing T1D registries and cohorts focused on T1D or/and focusing more broadly either in diabetes or other disease, uniquely contribute to global research and discovery into the disease journey, establishing links between risk factors and health outcomes that can be used to support the genomic research agenda. These include:

  — Environmental Determinants of Islet Autoimmunity - **ENDIA**, 1,500 babies who have a first-degree relative with T1D investigating gene-

environment interactions that may contribute to the development of islet autoimmunity and T1D. The strength of ENDIA is the prospective, comprehensive and frequent systems-wide profiling from early pregnancy through to early childhood, to capture dynamic environmental exposures that may shape the development of islet autoimmunity[46-48].

— Pregnancy and Neonatal Diabetes Outcomes in Remote Australia - **PANDORA** at Menzies School of Health Research a mixed T1D and T2D longitudinal birth cohort study of mothers and their children (baseline of 1,100) primarily designed to assess outcomes of diabetes in pregnancy in the Northern Territory (NT), Australia, including high-risk Aboriginal women and their children, now referred to as Wave 2 T1D[49].

— Generation Victoria (**GenV**), a high-capacity virtual biobank open to all babies born in Victoria, Australia, and their parents, designed to answer multiple questions about preterm birth, mental health and illness, obesity, learning, allergies and more.

- Australia has an established, skilled genetic and genomic workforce already contributing to the global research efforts of determining how T1D develops and how it can be prevented and cured. Australian researchers are at the forefront of functional genomics, having established niches of much-needed expertise, state-of-the-art facilities, and a trained bioinformatics workforce embedded within ongoing genomic initiatives nationally. This wealth of expertise is spread across all states and several research institutes. A few examples of this work are listed below:

— Prof Simon C. Barry at **The University of Adelaide** is using cell type-specific multi-omics datasets to determine disease mechanisms[50]. Recently they have developed a variant filtering workflow to link genetic variants to target genes in a cell-specific manner. This will allow them to identify candidate SNPs and target genes associated with the loss of immune tolerance in Treg cells in T1D.

— Extensive expertise in transcriptomics coupled with innovative technology and methodology, led by Prof Leonard C. Harrison at the **Walter and Eliza Hall for Medical Research** continues to fill in the knowledge gaps around which genes at what time during T1D development are important and using this as a foundation to look at gene function and immune cell changes. Notably, they have recently demonstrated that even small sample numbers identify transcriptomic signatures of gene expression that denote different stages of progression to T1D[31].

— Dr Ki Wook Kim at **The University of New South Wales** is set to investigate changes in the transcriptome and virome of human pancreatic islets prior to or following the development of T1D using Next-Generation Sequencing (NGS) technologies, especially those involving the dysregulation of microRNAs.

— Currently, Australian researchers are working to build a world-first map of the connections between genetic risk regions for T1D and the immune system genes that they are associated with. This expertise is not only unique and complementary to international genomic research efforts, but it is also fundamental and necessary to the field, with the potential to accelerate discovery and position T1D genomic medicine as a national priority.

— Prof Grant Morahan at **Harry Perkins Institute of Medical Research** and Prof Leonard C. Harrison have a long history of contribution to genomics and prevention of T1D.

> **“To succeed you don’t necessarily have to be a hub. Innovation can stem from a small group of people or even a single brilliant mind.”**
>
> **Prof Simon C. Barry**
> Head, Molecular Immunology Group
> Robinson Research Institute
> Co-Director Functional Genomics, South Australia

— Prof Peter Colman and Assoc Prof John Wentworth at **Walter and Eliza Hall Institute of Medical Research** and **Royal Melbourne Hospital** lead the TrialNet team focusing on T1D prevention with the aim of delaying progression before and after diagnosis. Assoc Prof John Wentworth and Dr Michelle So at **St Vincent's Institute of Medical Research**, have a particular interest in addressing what drives the difference in rate of progression between adults and children.

— Dr Kristine Bell from the **Charles Perkins Centre**, University of Sydney is working on identifying children at risk of developing T1D early through general population screening.

- In 2021 JDRF Australia established ATIC, an immunotherapy collaborative that brings together a national multidisciplinary team. The team has successfully built a clinical trial platform dedicated to testing of disease modifying therapies. Australian-based clinical trials of novel immunotherapies are currently underway, and strategies of how to preserve the pancreatic beta cell population in T1D and others are being investigated. For example:

  — In a world-first, in 2021, Prof Thomas Kay and Assoc Prof John Wentworth and their team at **St Vincent's Institute of Medical Research** began testing of Baricitinib, a JAK/STAT inhibitor, which has been shown to stop the immune system from attacking the beta cells of the pancreas. Baricitinib is being used to treat newly diagnosed T1D patients[51]. The team are in the process of clinical trial data analysis. Functional genomics studies are also complementary to such trials, enabling monitoring of the patient's response to treatment.

  — Based at the **Garvan Institute of Medical Research**, Prof Shane Grey, a leading expert in functional genomics and T1D complications, is currently leading a world-first human safety study testing a novel islet gene therapy in an islet transplant program.

> "To be able to drive a national effort in genomics for type 1 diabetes we need revolutionary action."
>
> **Dr Tiffany Boughtwood**
> Managing Director
> Australian Genomics, Victoria

- Outcomes of a genomic medicine-focused program can be readily taken up for translation by **The Rio Tinto Children's Diabetes Centre, a JDRF Global Centre of Excellence**. Led by Prof Elizabeth Davis and Prof Tim Jones, the team works in collaboration with global experts to better understand and change the way we treat T1D by developing personalised models of care that are tailored to individuals.

Importantly, genomics offer an extremely unique opportunity to determine diabetes phenotypes in Aboriginal and Torres Strait Islander, remote and very remote populations, to deliver better diagnostic and treatment options, essential in Closing the Gap in Australia and a strategic goal of JDRF Australia (i.e. less than 1% of all genetic association studies in Australia have specifically involved Aboriginal and Torres Strait Islander and other ethnically diverse populations).

Australia also represents a distinct geographic location. Discoveries will allow for comparative studies amongst its multi-ethnic groups as well as between other geographic locations in the world, thus adding a unique dimension to this research and deepening our understanding of the aetiology of T1D.

PAVING THE WAY TOWARDS PRECISION MEDICINE FOR T1D IN AUSTRALIA

To build on the above points and to begin to pave the way towards precision medicine in T1D in Australia, JDRF Australia embarked upon a four-phased approach, summarised in Figure 7 and detailed below.

Phase I: Landscape analysis

In 2020, JDRF Australia commenced the approach by undertaking a comprehensive landscape analysis. This allowed us to collate the knowledge base around existing genomic workforce and infrastructure, and the state of science in T1D genomics in Australia. This formed the basis of subsequent discussions that explored options for harnessing this existing infrastructure and expertise to embed genomic medicine and, ultimately, move towards precision medicine in T1D in Australia.

We also established a comprehensive stakeholder map, which was used to establish an Expert Panel and inform a consultation plan, leading into Phase II. Members of the Expert Panel, listed on page 1, include experts in functional genomics, clinicians, bioinformaticians, data custodians, implementers, and drivers of genomic and biobanking initiatives in other fields.

Phase II: Exploratory Workshop

This Workshop with members of the Expert Panel was designed to facilitate an exploratory

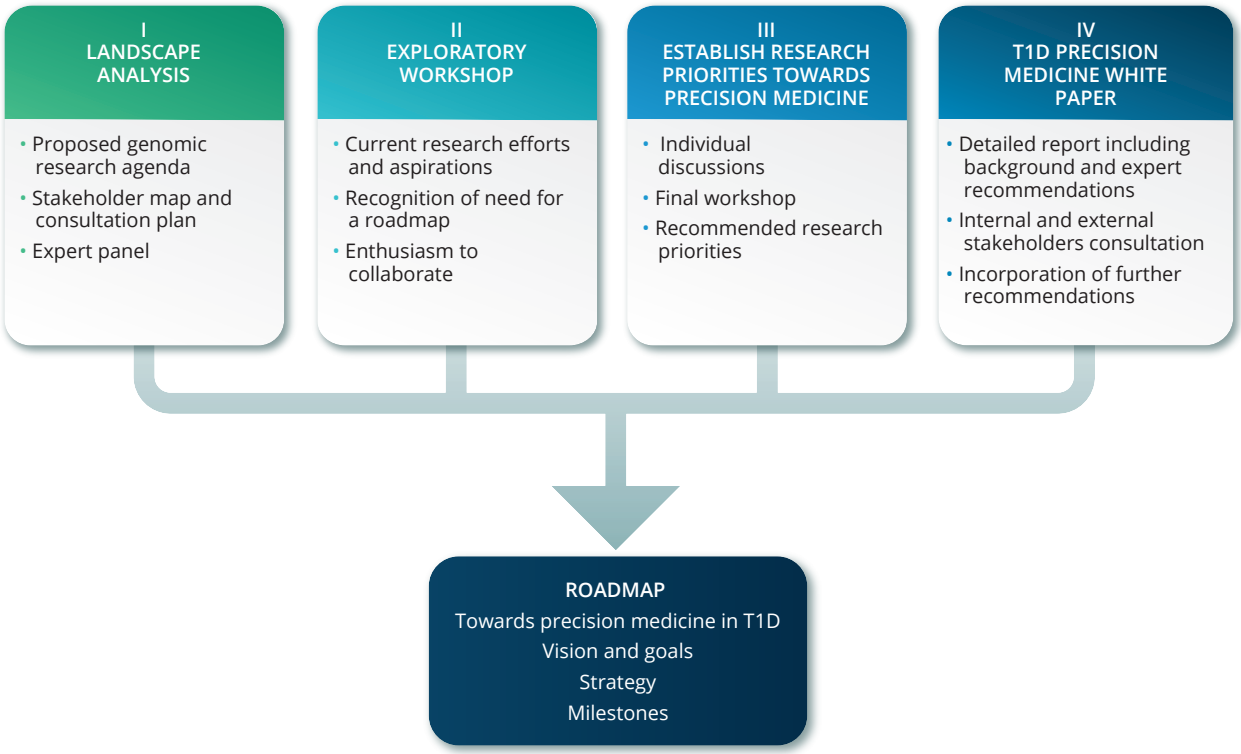

Figure 7. JDRF Australia progressed from a landscape analysis to the roadmap presented in this White Paper via a series of consultations with 16 members of an Expert Panel, brought together to represent the gamut of expertise required to inform a specific agenda towards precision medicine for T1D in Australia.

conversation to elucidate current T1D research efforts and aspirations, with a view to developing a fit-for-purpose approach to bringing precision medicine to T1D patients in Australia.

Discussion of the group was wide-ranging, including:

1. The importance of genomics to the whole pipeline of T1D, from basic research, risk stratification, genomic resolution of atypical cases and capability building through linkage of datasets and optimisation of biorepositories.

   The Expert Panel noted that, as indicated by the landscape analysis findings (Figure 8), lack of accessibility of various project-driven population registries and biobanks currently in use, which are often established as biological tools for specific projects, is an ongoing issue. Currently, only the Australasian Diabetes Data Network (**ADDN**), an Australia and New Zealand T1D registry capturing patient data across clinical networks, established by JDRF, is managed by a platform (BioGrid) that links and shares these tools making the entries readily accessible.

   The Expert Panel acknowledged that T1D clinical researchers both understand the value of sharing databases and agree that access to more data enhances their research. Persistent barriers to greater accessibility to patient databases include: the lack of adequate informed consent for genetic and genomic research; lengthy ethics approval processes and delays introduced by de-identification of data prior to sharing; data integrity issues of external databases; data consistency affected by the variety of data platforms used from different institutions, which makes data extraction and comparison difficult, and lack of funding to secure adequate resources and overall infrastructure.

2. The need to avoid predominance of one genomic research area in T1D, but rather to employ active and strategic planning to take the best elements of different approaches and apply them to various stages of the T1D pipeline.

3. Consideration of strategic evaluation of the strengths and weaknesses of translational research in T1D in Australia. The small population of Australia was noted as a challenge, while the possibility of developing small but well curated datasets and biorepositories was identified as an opportunity.

4. The importance of selecting a niche for Australian research to excel in, given the gamut of global T1D activity.

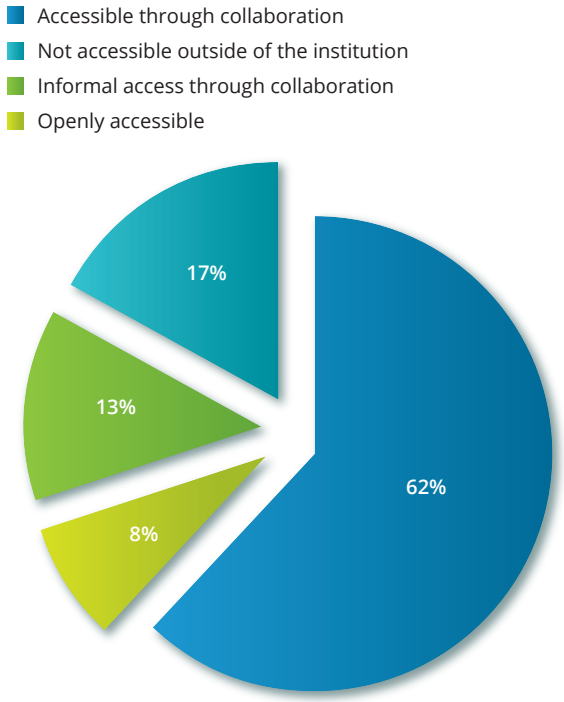

Figure 8. Most biobanks and registries are accessible upon approval of an application (62%), another 13% are accessible through collaboration, and 8% are publicly accessible (Figure 9). The remaining 17% are not accessible outside of the host institution.

The primary outcome of the discussion and collaboration was recognition of the need to elucidate the pathway towards embedding functional genomics in T1D, which would then enable precision medicine to be brought to T1D patients in Australia. There was great enthusiasm and willingness from participants to be a part of this journey.

Phase III: Establish research directions towards precision medicine

JDRF Australia then hosted a series of individual discussions with Members of the Expert Panel, allowing them to further unpack the opinions and aspirations voiced in the Exploratory Workshop.

Through the process of collating and thematically analysing the input obtained through the Exploratory Workshop and these individual discussions, JDRF Australia identified the following Priority Areas for functional genomic research directions:

- Prevention of disease development and progression, across all stages of T1D
- The need to strengthen existing biobanks, datasets, and purpose-built cohorts
- Strategic 'interventions' that could accelerate advancement in genomic research

These Priority Areas informed the agenda of the Final Workshop, the focus of which was to identify specific T1D research directions that would pave the way towards precision medicine.

In the Final Workshop, Expert Panel discussions highlighted existing capacity in functional genomics, including transcriptomics, phenomics and proteomics within and outside the T1D field in Australia. Participants identified Australia's unique strengths in the space of functional genomic research and corresponding clinical outcome aspirations, both in the short- and in the long-term.

An overarching theme to emerge from the Final Workshop was that the focus of T1D discovery in the field needs to shift toward causality and connectivity research employing functional genomics, inclusive of genomics and epigenomics research, transcriptomics, proteomics, phenomics and metabolomics to elucidate T1D aetiopathogenesis of the disease leading to disease model driven prediction, prevention and treatments (Figure 9).

Phase IV: Draft a White Paper outlining the path towards precision medicine in T1D in Australia

Emerging from Phases I to III, JDRF Australia collated and distilled the findings of this process, seeking to clearly articulate what needs to be done and what can be done in the Australian context, to move towards precision medicine for T1D in Australia.

JDRF Australia then considered what the implementation process would look like, and the mechanism required to pursue these research directions, recognising the need for this mechanism to be both bold *and* realistic; forward-thinking *and* built on strong foundations.

This White Paper presents the outcome of these considerations: our vision for T1D to be embedded in precision medicine agenda in Australia via an incremental JDRF Australia-led strategic approach centred around a national T1D Genomics Consortium.

Figure 9. Functional genomics will help generate interdependent and interconnected knowledge by studying genetic risk at the chromosome level of the cells that play a significant role in T1D pathogenesis, develop biomarkers that will inform better stratification and drug discovery, enabling precision medicine approaches for T1D prevention and treatment.

RESEARCH PRIORITY AREAS FOR PRECISION MEDICINE IN AUSTRALIA

The Priority Areas outlined in this section clearly emerged from the approach outlined above, involving extensive consultations with the Expert Panel. Presented below, these priority areas are organised according to the research gap to which they best respond.

PRIORITY AREA 1 – Prevention of disease onset and progression across all stages of T1D

To progress Priority Area 1 the most urgent focus research areas are:

1.1 Conduct functional genomics research to determine causality. Methods that can be readily employed include:

—using a cellular genomics approach to connect risk associated T1D SNPs to their function/s in specific cells to elucidate processes associated with altered immune function and in T1D disease pathogenesis.

—associating identified SNPs within other regions of the chromosomes and identifying new SNPs involved in immune response regulation.

1.2 Focus on research aimed at understanding T1D heterogeneity. Methods that can be readily employed include:

—narrowing the genomic research question based on clinical observations and establishing cohorts of patients who do not have a relative with T1D, leveraging existing screening programs and population registries.

—using a combination of GWAS and cellular genomics approaches to determine diabetes phenotypes in Aboriginal and Torres Strait Islander youth, particularly in remote and very remote populations, presenting with mixed clinical features of both T1D and T2D.

1.3 Conduct research that deepens our understanding on how to preserve the healthy function of beta cells.

1.4 Link and share longitudinal datasets to track disease progression for each patient over time and uncover the genomic, clinical, social, and environmental determinants of T1D risk and complication development.

PRIORITY AREA 2 – Strengthening existing biobanks, datasets, and purpose-built cohorts to advance genomic research in Australia

The research directions under Priority Area 2 focus on improving access to existing datasets, thereby supporting adequately powered studies that can accelerate the understanding of T1D pathogenesis:

2.1 Encourage and support a national strategy in biobanking and population registries as critical genomic research tools can be utilised to advance critical questions on genomics of T1D.

2.2 Take advantage of national healthcare databases and investigate all relevant cohorts with the aim of cleaning, optimising, harmonising, and linking patient data.

2.3 Move towards a centralised approach to data sharing, as well as linkage based on best practice biobanking models (e.g., Generation Victoria) that will enable data gathering large enough to make scientifically and clinically meaningful comparisons.

2.4 Combine and mine existing data using artificial intelligence (AI) to predict the risk of disease outcomes (e.g., complications) while simultaneously supporting AI expertise in Australia to serve the needs of the T1D community.

2.5 Address identified barriers to clinical trial participation and obtain general consent from patients for all new data collections starting from 2023, thereby minimising lost opportunities for genomic research in relevant clinical cohorts.

2.6 Determine a pathway for access to whole genome sequencing for T1D, which is currently an exceedingly arduous process and a strategic problem due to ethical considerations, by identifying, analysing, prioritising, sharing, and linking accumulated data.

PRIORITY AREA 3 – Targeting genomic research interventions

The research directions under Priority Area 3 focus on strategic 'interventions' that, when implemented, will accelerate the advancement of genomic research in T1D, resulting in earlier access to benefits by all patients:

3.1 Seek and establish national and international collaborations to avoid duplication and accelerate genomics-driven drug discovery and the development of novel therapeutics.

3.2 Bring together intersecting, cutting-edge technologies to advance genomic research, including machine learning and AI computing, and support this with recruitment of, and career development support for, geneticists and bioinformaticians to enable capacity building in T1D genomics.

3.3 Support studies focused on validation of genomic research outcomes and clinical trial secondary analysis to determine underlying mechanisms of the observed varied responses to disease modifying therapies.

> "I am interested in genes that, in combination with the environment influences, are required for the development of islet autoimmunity, and genes that then drive progression to clinical diabetes."
>
> **Prof Leonard C. Harrison**
> Population Health and Immunity Division
> Walter and Eliza Hall Institute of Medical Research, Victoria

3.4 Conduct research into understanding the burden of T1D among Aboriginal and/or Torres Strait Islander people and communities; determine ethical and social implications of genomics; identify barriers and establish strategies to overcome these barriers and work jointly with health professionals, researchers, and members of the community to facilitate trust and public engagement.

3.5 Develop a knowledge exchange plan aimed at disseminating and promoting the uptake of the outcomes of genomic research in clinical care and empowering T1D communities.

JDRF AUSTRALIA'S 10-YEAR VISION FOR T1D PRECISION MEDICINE IN AUSTRALIA

This White Paper has thus far explored the advances in genomics medicine, including available technologies and analytical tools; the momentum created in genomic medicine in Australia through government funding initiatives, and the readiness and capacity of the Australian T1D research workforce to significantly contribute to embedding genomics in T1D in Australia.

In alignment with the Precision Medicine T1D Consensus Report of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)[36], JDRF Australia aspires to work collaboratively with T1D stakeholders across the nation to transform T1D care for Australian patients by progressing precision prevention, diagnosis, treatment, and prognosis of the disease.

To achieve this transformation in T1D care, JDRF Australia's vision is to drive the establishment of a virtual T1D Genomics Consortium, a truly collaborative and expert team that crosses disciplines and spans multiple institutions, connecting the best-of-field in Australia with leading global efforts. T1D Genomics Consortium research investigators will be connected with global efforts to enhance their ability to pursue the research directions outlined above. Importantly, the Consortium will be founded on:

- Patient-centredness, collaboration and transparency, which should underpin the research conducted under the Genomic Consortium's umbrella every step of the way.
- The engagement of JDRF Australia with implementers, educators, and policymakers to

optimise research translation and adoption into T1D care for all Australians at risk of developing and living with the condition.

An important objective of the T1D Genomics Consortium will be to harness the power of genomic medicine to address population disparities, with a particular focus on closing the gap and ensuring that Aboriginal and Torres Strait Islander young people have access to, and receive, equitable standards of care throughout the T1D journey.

Within the coming decade, our shared vision for functional genomics research is to transform T1D care by delivering the following:

In precision prevention:

- An early childhood diagnosis for all at-risk Australian children via general population screening.
- A substantial improvement of our understanding of safe primary prevention approaches which, when implemented, would lead to incremental reduction of the number of individuals progressing to metabolic disease.
- Significant advancement towards individualised or/and group prevention strategies for all Australians.

In precision diagnosis:

- Utilise genomic information to predict progression through all the stages of T1D.
- Link to phenotype-specific biomarkers to enable patient sub-group classification.

In precision treatment:

- Every person across different stages of T1D has the opportunity to be enrolled in a clinical trial to enable unique genetic/genomic profiling and personalised treatment regimes.
- Use functional genomic research outcomes to shorten the adoption timeline of new therapies into personalised care.

In precision prognosis:

- Develop and test predictive algorithms of progression based on a patient's unique environment characteristics.
- Work with multiple stakeholders to drive development of guidelines that ensure that patients across all T1D stages are eligible to access treatments and advanced technologies.

WHAT WILL IT TAKE TO ACHIEVE THIS SHARED VISION?

Underpinned by JDRF Australia's commitment, translation and delivery of this vision will rely upon agility, strong engagement and collaborative action of the Genomic Consortium and other key stakeholders.

Presently, we are at the beginning of the journey in precision medicine in T1D. To enable the growth and maturity of the Consortium, in collaboration with its stakeholders, JDRF Australia will:

- Advocate for the inclusion of T1D on the national genomics agenda.
- Identify and engage with critical health sector leaders who will support JDRF Australia to achieve this vision, such as: clinicians and non-clinicians, researchers, pharmaceutical companies, policymakers, strategic partners, and patients across the nation to boost recruitment, facilitate innovation, and encourage translation and adoption of safe and effective genomic interventions.
- Develop stakeholder communication strategies to disseminate knowledge and increase awareness amongst all stakeholders.
- Work with T1D partners, national and international funders, including the Federal Government, and the community to ensure sustainability and progress of genomic innovation and translation in T1D.

CONCLUSION

This White Paper presents a shared vision of experts and JDRF Australia for bringing precision medicine to T1D in Australia. It provides a snapshot of the burden of T1D, the impact of genetic and genomic discovery on T1D care, and existing genomic infrastructure and expertise in Australia. It also outlines how, with the invaluable input of the Expert Panel via a series of targeted consultations, JDRF Australia has realised a clear view of the research that can be done and must be done to embed genomic medicine in T1D in Australia.

The establishment of the T1D Genomics Consortium will be a step towards assembling the brightest T1D team in country. The research conducted by this team will contribute to the formation of a clear picture of T1D aetiology.

In taking these first steps, JDRF Australia sets in motion its vision for bringing precision prevention, precision treatment and precision prognosis to T1D care in the coming decade.

This important work starts now. JDRF Australia invites all stakeholders to join the conversation in support of an endeavour that has the potential to transform the way T1D is prevented, treated, and eventually cured.

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