Meeting report series

Report of the 14th Diagnostics Scientific Committee Meeting

Vienna, Austria
May 14, 2018

Participants

Prof Kym Boycott, Ottawa, Canada – Chair
Assoc Prof Gareth Baynam, Perth, Australia – Vice Chair
Prof Xavier Estivill, Doha, Qatar
Prof Kenjiro Kosaki, Tokyo, Japan
Prof Jürgen Reichardt, Urcuquí, Ecuador
Prof François van der Westhuizen, Potchefstroom, South Africa
Dr Feng Zhang, Cambridge, MA, USA (by phone)

Dr Christopher Austin, Bethesda, MD, USA
Dr Lilian Lau, Paris, France
Dr Anne-Laure Pham Hung d’Alexandry d’Orengiani, Paris, France

Apologies

Prof Fowzan Sami Alkuraya, Riyadh, Kingdom of Saudi Arabia
Prof Anthony Brookes, Leicester, UK
Prof Gert Matthijs, Leuven, Belgium
Adj Prof Ann Nordgren, Stockholm, Sweden
Prof Yiming Wang, Shenzhen, China

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Agenda

1. Welcome and roundtable of members
2. DSC activities and areas of focus
3. Update re Task Forces and work plans
4. Upcoming Task Forces
5. Scientific publications and disseminations
6. DSC membership
1. Welcome and roundtable of members

The Chair of the Diagnostics Scientific Committee (DSC) welcomed its members to the meeting, and a roundtable took place for members to introduce themselves, as there are new members in attendance.

- **Prof Kym Boycott** is a clinical geneticist and senior scientist at the Children’s Hospital of Eastern Ontario and Professor of Pediatrics at the University of Ottawa. She has been the Chair of the DSC for six years.
- **Prof Gareth Baynam** is a clinical geneticist in Perth, Australia. He has been a member of the DSC for the past two years and is the Vice Chair of the DSC.
- **Prof Xavier Estivill** is a geneticist originally from Barcelona and is now senior investigator and Chair of the Genetics Program at the Sidra Medical and Research Centre in Qatar. He has been a member of the DSC for the last six years.
- **Prof Kenjiro Kosaki** is Professor of Medical Genetics and the Director of the Centre for Medical Genetics of Keio University School of Medicine in Tokyo. He has been a member of the DSC for over a year.
- **Prof Jürgen Reichardt (new member)** is a scientist by training and now the Vice Chancellor of the Research and Innovation Department of Yachay Tech University in Ecuador. He has just joined the DSC.
- **Prof Francois van der Westhuizen (new member)** is Professor of Biochemistry at the North-West University in South Africa and his work focuses on biochemical and genetic basis of mitochondrial diseases. He has just joined the DSC.

The DSC Chair also provided a brief overview of the following:

- Current membership of the DSC
- IRDiRC Vision and Goals 2017-2027
- Representation and member organizations of IRDiRC
  - Significant expansion of the patient advocacy members in 2017-2018
- IRDiRC Governance structure
- IRDiRC Policies and Guidelines
  - Should consider revising and updating while the last of the Scientific Committee (SC) members involved in the writing have not yet ended their mandate (which will be by February 2019)
- IRDiRC Recognized Resources
  - To discuss the process and impact of these resources during the joint SC meeting

2. DSC activities and areas of focus

With respect to IRDiRC’s goals, the DSC works towards:

- Initially, for 2011-2020:
  - Means to diagnose most rare diseases by 2020
New goals formulated for 2017-2027; those relevant to the DSC are:

- **Goal 1:** All patients coming to medical attention with a suspected rare disease will be diagnosed within one year if their disorder is known in the medical literature; all currently undiagnosable individuals will enter a globally coordinated diagnostic and research pipeline.

- **Goal 3:** Methodologies will be developed to assess the impact of diagnoses and therapies on rare disease patients.

**Discussion:** *How to measure success? What are the metrics?*

- **Challenge:** quantifying the number of rare genetic diseases and the causes of these diseases
  - Lack global standard on how to name a new rare disease
  - Lack global standard on how to establish a new gene-disease relationship
  - Lack methods to quantify the depth of rare disease (i.e., ceiling of number of rare diseases)
    - Predictive/speculative study estimated about 15,000 rare genetic diseases

- **Two databases currently keep track of the number of rare diseases and are used worldwide:***
  - Orphanet: classifies diseases by clinical presentation (e.g., hereditary spastic paraplegia (HSP) as the disease and is sub-classified by its many types)
  - OMIM: defines a disease by the causal gene (e.g., HSP 3, 4, etc)
  - Discovery discrepancies exist between the two databases because they use different standard operating procedures to count a novel gene vs a novel disease-gene relationship
  - These are labor and resource intensive efforts

- **Additionally, there are other resources counting rare diseases:**
  - Genetic Alliance: unsure of the status of the effort
  - ClinGen: based on gene-disease relationship
  - GARD: using a mix of sources
  - Global Genes: data primarily from the NIH (methodology unclear)

- **Suggested steps to a solution**
  - IRDiRC to engage curators of knowledge databases and other international stakeholders
    - Discuss elements to enable international interoperability of databases
    - Determine a standard operating procedure to coordinate updates
    - Propose actions and/or tools to reduce and/or improve process bottleneck
    - Include classifications such as Human Phenotype Ontology (HPO) terms and/or Orphacodes
  - **Issue global statement on metrics**
    - A holistic view of problem statement needed
    - Can be basis for funders to provide support and improve the metrics
    - Can state “current state of knowledge supports that xx of rare diseases exist, and xx have been identified to date” as a quantifying metric
  - Consider the possibility of a single, international unified list
    - Identify existing lists of rare diseases and the kind of information provided

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1. ME Samuels. Saturation of the Human Phenome; *Curr Genomics* 2010 Nov; 11(7):482-499. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3048311/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3048311/)
- Curation of a high-level list of recognized diseases following cross-mapping of diseases from both Orphanet and OMIM
- Additional cross-mapping to other datasets
  - Alternatively, keep track of a list of databases that maintain lists of rare diseases?

Funding and sustainability of resources
- Major and commonly-used resources at risk of disappearing when funding runs out
  - Funding by multiple stakeholders instead of relying on single funders
- Advantage of a unified knowledge database as key research infrastructure
  - Develop a curation tool to empower experts to participate, validate, aggregate knowledge and accelerate process (or can machine learning be used?)
  - Single authoritative source to facilitate coding in health databases

→ IRDiRC could host a meeting for Orphanet and OMIM representatives, as well as international stakeholders (GA4GH, EURORDIS ...) to share and collaborate on standards and protocols, and consider the possibility of a single, international unified list of rare diseases to be used as a global metric.

3. Update re Task Forces and work plans

3.1 IRDiRC Roadmap and DSC activity ideas

A list of activity ideas was generated last year from a combination of the following:
- Meetings and teleconferences of the Scientific and Constituent Committees
- Survey of the Consortium Assembly (CA)
- Discussion points of the 3rd IRDiRC Conference in Paris, France

These were compiled into an Excel, after which the Scientific Secretariat (Sci Sec) – together with the Operating Committee (OpComm) – assessed what can be realistically carried out by IRDiRC and what will require greater pool of manpower and budgetary resources.

From this list of actions, the following were also created and circulated as a meeting document:
- IRDiRC Roadmap 2018
  - Selected activities agreed in principle by the CA as key actions to commence in 2018
  - Full proposals of selected activities are to be developed by leading committee(s)
  - Sci Sec will support all activities as much as possible, under committee leadership
- Subset of DSC actions
  - Relevant to the DSC and should be prioritized for 2018-2019
  - Additional suggestions are welcomed

3.2 Matchmaker Exchange (MME) Task Force (completed)

MME is a federated network (www.matchmakerexchange.org) that connects databases of genotypic and phenotypic profiles to enable rare disease gene discovery through a common application programming interface (API). MME was the first task force led by the DSC.
There are currently about 50,000 use cases connected through MME API (developed by Global Alliance for Genomics and Health (GA4GH))

- System based on 2-sided matching (i.e., both databases connected if both contain a queried gene)
- Makes only 1-to-1 or point-to-point connections (i.e., cannot cross-query all databases in one go)
- Currently running and doing well, but problem with high false positive rate

Next steps
- Difficult to change the way current MME works and it is appropriate for its current use case of 2-sided hypothesis testing
- The DSC will ultimately focus on a different type of matchmaking, where 1-sided hypothesis testing can take place thereby enabling a deeper level of data interrogation (gene, variants, phase, HPO terms). The DSC will propose a task force in this area in the future.

3.3 Solving the Unsolved (STU) Task Force (active)

The Solving the Unsolved (STU) Task Force focuses on the patients who are likely to have a genetic mutation, but for which the whole-exome sequencing (WES) didn’t yield an attractive candidate gene.

The mandate of the STU Task Force is as follows:
- Develop a state-of-play document, including a comprehensive list of recognizable disorders that are currently unsolved with existing approaches
- Organize a workshop to present cutting edge research and innovative approaches in the areas of focus
- Develop an asset map, and identify gaps and missing tools
- Develop a set of recommendations to advance these approaches
- Publish a review paper on the scope of the problem and strategies to address the challenges
The STU Task Force met in Hinxton, UK in March 2018. Members were asked to consider different genetic mechanisms that could escape detection by WES and approaches to consider to identify them in patients. These are summarized in the following chart:

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Description</th>
<th>Approaches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genomic alterations</td>
<td></td>
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<tr>
<td>Small insertions/deletions</td>
<td>Small structural changes missed by WES</td>
<td>WGS</td>
</tr>
<tr>
<td>Large insertions/deletions</td>
<td>Larger structural changes missed by WES and microarray</td>
<td>WGS</td>
</tr>
<tr>
<td>Chromosomal rearrangements</td>
<td>Inversions/translocations; Multiple deletions/duplications</td>
<td>WGS</td>
</tr>
<tr>
<td>Repeat expansions</td>
<td>Triplet and other expansions</td>
<td>Long-read WGS</td>
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<tr>
<td>Gene regulation</td>
<td></td>
<td></td>
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<tr>
<td>Splicing mutations</td>
<td>Synonymous or splice site or intronic mutations</td>
<td>WGS, RNASeq</td>
</tr>
<tr>
<td>Other regulatory mutations</td>
<td>Promoter and enhancer mutations</td>
<td>WGS, RNASeq, High-C, Prediction Tools</td>
</tr>
<tr>
<td>Imprinting</td>
<td>Altered parent-of-origin specific expression pattern</td>
<td>Methylation arrays</td>
</tr>
<tr>
<td>Mosaicism</td>
<td></td>
<td></td>
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<tr>
<td>Tissue-specific mosaicism</td>
<td>Mosaic manifestations of Mendelian disorders; Disorders that manifest only as mosaicism</td>
<td>Deep sequencing of multiple tissues</td>
</tr>
<tr>
<td>Complex inheritance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unusual or less common</td>
<td>Sex-limited expression; necessary but not sufficient CNVs</td>
<td>Novel approaches to data analysis</td>
</tr>
<tr>
<td>inheritance patterns</td>
<td></td>
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</tr>
<tr>
<td>Digenic, oligogenic, polygenic</td>
<td>Interaction of two or more genes</td>
<td>Novel approaches to data analysis</td>
</tr>
<tr>
<td>Gene-environment interaction</td>
<td>Rare susceptibility allele combined with environmental trigger</td>
<td>Environmental exposure data capture; Validation in model organisms</td>
</tr>
<tr>
<td>Maternal effects</td>
<td>Mutation in the mother results in altered fetal environment</td>
<td>Environmental exposure data capture; Validation in model organisms</td>
</tr>
</tbody>
</table>

The outcome of this workshop is currently being written up as a manuscript, which will be submitted later this year.

4. Upcoming Task Forces

4.1 Clinical Data Sharing Task Force (future)

This is an approved Task Force. Its objective is to facilitate access to genome data from patients that were sequenced in the clinical environment for secondary use (variant interpretation, novel gene discovery, novel gene-disease relationships). In parallel, the DSC Chair was invited to participate in the Global Commission to End the Diagnostic Odyssey for Children with a Rare Disease and there is some overlap in interests with the proposed Task Force.

The Global Commission:
Is driven by EURORDIS-Rare Diseases Europe, in partnership with both Shire and Microsoft

Currently working in isolation

Aims to shorten the time for a patient to receive a clear diagnostic

Focuses on identifying barriers encountered by patients and healthcare providers who are trying to get a clear diagnosis and alleviate them

Consists of members from various backgrounds, from patient advocates, to geneticists, to other clinicians, to industry, from around the world which facilitates discussions with a wide set of opinions

Will develop a roadmap as a guide in the rare disease field, and may pilot some of the actions

For more detailed information, please see Annex 1 at the end of the report.

The above challenges have also been considered by DSC members:

- Telemedicine infrastructures can facilitate alleviation of some of the access issues
- Creation of frameworks can help define standard-of-care for an undiagnosed patient
- There are huge discrepancies from country to country regarding financial reimbursement of genetic testing
  - Even developed countries do not have uniform reimbursement policies

The Clinical Data Sharing Task Force could strategically benefit from the work of the Global Commission

- Global Commission is more clinically-focused while IRDiRC is research-focused
  - Actions from both entities would be complementary
- Wait for the recommendations of the Global Commission (roadmap) and planned pilots
  - Preferably start Task Force in early 2019, after the publication of the Global Commission recommendations
  - Consider leveraging activities that focus on aspects most relevant for IRDiRC

Concretely, the Clinical Data Sharing Task Force:

- Will retain the objective to facilitate access to clinical genome-wide sequencing for secondary use of data, focused on the discovery of disease mechanism
- Consider three potential dimensions but won’t be able to do all three:
  - Clinician-led: key focus will be on clinicians as stakeholder
  - Patient-led
  - Diagnostic lab-led
- Focus on secondary use of data and strategies for data sharing
  - Technical aspects of data sharing (e.g., core data elements, interface)
  - Justification on the importance of secondary use of data
  - Workflow challenges and strategies to enable such sharing
  - Collaborate with other IRDiRC Task Forces
    - Model Consent Clauses Task Force: clauses that facilitate secondary data sharing
    - Automatable Discovery and Access Task Force: discovery of data for research use
  - Additional aspects to address
    - Electronic consents
    - Databases: ideally IRDiRC Recognized Resources
    - Data ownership and cost for access
Workshop outcome can be a statement from the Task Force: why this aspect is important and what are the elements to facilitate clinical data sharing for secondary use, particularly for gene discovery to explain undiagnosed patients

→ Keep track of the Global Commission Roadmap publication and outcomes and inform full Committee

4.2 Next set of priorities: activities for 2019

4.2.1 Carrier screening

A group of DSC members participated in a scoping teleconference in February 2018

Carrying screening (CS) programs for recessive disorders exist in many countries

- Pre-natal: screening carried out prior to birth
- Pre-marital: mandatory for certain conditions in some countries, e.g. Saudi Arabia
- Newborn/neonatal: for serious treatable diseases
- Donor screening: screening of donated sperm or oocytes

Two main approaches for screening of disorders:

- Targeted carried screening (TCS): screening based on ethnicity or family history
- Expanded carrier screening (ECS): screening of many disorders without regard to race or ethnicity using a screening panel

- Both allow for informative reproductive choices for couples

Issues to consider

- Need an “easier”, affordable and more comprehensive test for different population (e.g. availability of chip for variants identified in the Middle East)
- Socio-economical aspects are largely unstudied
- Ethical aspects
- Education and genetic counselling

Potential Task Force focus

- Asset map of national activities (e.g. types of program, genetic set-ups, purposes)
- Guideline review
- Identify implementation knowledge gaps

A Task Force proposal will be refined and circulated among DSC members for feedback in 2019

→ Develop Carrier Screening Task Force proposal

4.2.2 Underrepresented populations

In order to meet IRDiRC’s Goal 1, special efforts are required for under-represented populations as well as populations in resource-poor areas, with a particular view to decrease health system access inequities in the field of rare diseases.

Three distinct populations to focus on (in order of priority):

- Indigenous populations in developed countries
  - e.g., Canada, USA, Australia
○ Technological infrastructure and experts already present
○ Ethical considerations may be very different between different indigenous populations

Emerging countries in diagnostics (or “Genomic-emerging countries”)
○ e.g., Japan, Lithuania
○ Technological infrastructure being put in place
○ Should engage these countries, such as packaging of toolkits and educational materials

Developing countries
○ e.g., South Africa, Ecuador
○ Encompass both a(n indigenous) population with limited access to healthcare facilities and a wealthier population
○ Technological breakthrough needed for full scale action

Will first start with indigenous populations in developed countries

Potential Task Force focus
○ Identify common points and differences between communities
○ How to develop toolbox to engage and enable partnership
○ Generate new knowledge that can be used to subsequently address global challenge in emerging countries
○ Language and culture will also be important aspects

A Task Force proposal will be refined and circulated among DSC members for feedback shortly

→ Develop Under-represented Population Task Force proposal

5. Scientific publication and dissemination

Efforts regarding IRDiRC publications have been fruitful and should be continued. Potential upcoming publishing opportunities to highlight IRDiRC activities and Task Forces include:

► *American Journal of Medical Genetics* Special Issue: late 2018; an overview of the currently well recognized but undiagnosed rare diseases
► *EMBO Reports*: late 2018; commentary on the need for transparency and collaboration to understand and develop diagnostics and therapies for rare diseases
► *Annual Review of Genomics and Human Genetics*: early 2019; the Chair has been invited to discuss new approaches for undiagnosed genetic disease

Additionally, IRDiRC and its Committees are invited to consider submitting articles to *Human Genomics*, among other journals that publish rare diseases research articles. DSC members are also encouraged to share information among members of any invitation(s) from other editors for articles that can be angled to promote IRDiRC and its activities, and inform the Sci Sec which may be able to assist.

6. DSC membership

The DSC is currently composed of 12 members; the mandate for three of them – including the Chair – will end in early 2019.
→ Approach potential new members of the DSC

**Action points**

- Encourage IRDiRC to begin a dialogue between Orphanet and OMIM regarding an international list of rare diseases
- Inform DSC of Global Commission outcomes
- Develop Carrier Screening Task Force proposal
- Develop Under-represented Population Task Force proposal
- Approach potential new members of the DSC
ANNEX 1

What are the barriers to diagnosis?

Our research found:

New interventions are needed to help physicians identify patients with a rare disease.
Primary care physicians are on the frontline of care and need to be knowledgeable about fundamental issues in medical genetics. However, interventions—beyond continuing medical education—are needed to help physicians identify patients with a rare disease.

There is opportunity to apply new technology to the rare disease field.
There have been many advancements in clinical technology, however these innovations have not been fully realized and applied to finding patients with a rare diseases.

We do not have to wait for more geneticists and other specialists.
The lack of geneticists and other specialists is a challenge for patients in accessing specialized care, but this challenge can be mitigated without waiting for a larger workforce.

Streamlining processes in a complicated healthcare system can improve time to diagnosis.
The ability for a patient to successfully navigate the diagnosis process is compounded by complexities in the healthcare system such as difficult referral processes and insurance coverage limitations.

Commission tracks

The Commission will focus on developing solutions in four areas that will lead to accelerating the time to diagnosis—and will organize its work accordingly

<table>
<thead>
<tr>
<th>Solution Track</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practice redesign</td>
<td>Develop innovative ways to enable geneticists and specialists to operate more efficiently so they can see more rare disease patients quicker—especially given the growing shortage of geneticists.</td>
</tr>
<tr>
<td>Primary care</td>
<td>Apply innovation and creative thinking to improve primary care physicians' ability to identify patients with a rare disease and refer to appropriate follow-up care.</td>
</tr>
<tr>
<td>engagement</td>
<td></td>
</tr>
<tr>
<td>Patient and caregiver</td>
<td>Create or identify new tools and approaches to empower patients and caregivers so they can navigate the health system more effectively.</td>
</tr>
<tr>
<td>empowerment</td>
<td></td>
</tr>
<tr>
<td>Global policy</td>
<td>Determine policy guidance at a global level that can be adapted to meet differentiated regional needs and work with national and local governments.</td>
</tr>
<tr>
<td>recommendations</td>
<td></td>
</tr>
</tbody>
</table>
Track 1 and Track 2 Barriers

**Barriers for Primary Care and Pediatrician Engagement:**
- Minimal / non-existent training or exposure to rare disease
- Lack of standard criteria to help diagnose many rare diseases
- Poor communication between PCPs and specialists
- Lack of awareness around which specialty to refer
- Access to diagnostic tools

**Barriers for Practice Redesign:**
- Shortage of geneticists
- High workload = inability to see more patients
- Fewer specialists in rural areas
- Inefficient practices that limit productivity (e.g., diagnosed patients making follow up visits, tests not ordered in advance of patient visit)

Track 3 and Track 4 Barriers

**Barriers for Patient and Caregiver Empowerment:**
- Difficulty navigating a complex, fragmented healthcare system
- Lack of vocabulary and sophistication to articulate siloes (i.e., knowing to tell a cardiologist about a liver problem)
- Parental lack of medical credibility (i.e., “crying wolf” scenario)
- Lack of patient-centered information

**Barriers for Global Policy Recommendations:**
- Inconsistent regulatory authority definitions of rare disease (i.e., rate vs. fixed number)
  - Relevance to diagnosis would be if there is universal rare disease diagnosis/testing policy
- Lack of globally accepted and/or regional differences in prevalence/statistics of patients living with a rare disease
- Absence of universally accepted screening and testing protocols to diagnose a rare disease
  - Lack of early diagnosis programs and adoption of existing technology (i.e., whole genome sequencing) in national health plans
  - Inconsistent reimbursement policy of rare disease testing
- Inadequate patient involvement in the policymaking process (i.e., raise the profile of patient voice during drug development)
Track 1: Primary Care and Pediatrician Engagement

Most feasible and highest impact solutions:

<table>
<thead>
<tr>
<th>Solution</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Launch multifactorial machine learning pilot projects (3 pilots)</td>
<td>Utilize machine learning to recognize symptom patterns that a PCP or pediatrician may not immediately associate with a rare disease. This machine learning would be piloted in three different areas: 1. Medical records data, 2. Patient reported data, 3. Facial and other recognition (e.g., voice, gait)</td>
</tr>
<tr>
<td>Expand access to next generation sequencing (NGS) / genetic test – using set criteria</td>
<td>Introduce a streamlined system whereby a physician completes a form explaining request for genetic testing and then experts review and recommend a diagnostic path forward. Priority should be patients who have been undiagnosed / been to x doctors over y period of time.</td>
</tr>
<tr>
<td>Strengthen and broaden patient resources for diagnosis</td>
<td>Expand /develop digital platforms that crowd source patient information; design searchable databases for self-screening / self-search</td>
</tr>
</tbody>
</table>

Track 2: Practice Redesign

Most feasible and highest impact solutions:

<table>
<thead>
<tr>
<th>Solution</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Establish triage center in genetics clinics</td>
<td>Create a triage function / department within genetics clinics to help ensure that patients are seen by the right physician, tests are ordered in advance, and all data on the patient is properly collected</td>
</tr>
<tr>
<td>Information capture for rural/remote patients</td>
<td>Gather all information (as much standardized as possible) needed in rural / remote setting prior to being seen by a geneticist (can help with triage), to avoid patient traveling long distances multiple times</td>
</tr>
<tr>
<td>Create standardized and easy-to-understand lab reports</td>
<td>Develop standardized genetic testing reports so PCPs, pediatricians, and other specialists can uniformly understand the results; enables geneticists to spend time where they are needed</td>
</tr>
</tbody>
</table>
Examples of Enabling Technologies

- **Artificial intelligence and machine learning everywhere**
  In combination to provide predictions and personalization around rare disease feature constellations

- **Patient and provider engagement**
  Around social computing; Create trust in the ecosystem through blockchain

- **Cognitive services**
  To add phenotypical recognition to genomic data to help overcome the difficulty of gene expression

- **Lowering cost**
  Of genome screening and analysis with cloud services and advance analytics

What’s Next

- **Meeting 1**
  In-Person
  Cambridge, MA
  April 5

- **Meeting 2**
  Virtual
  May 22

- **Meeting 3**
  In-Person
  Redmond, WA
  Sep. 4 & 5

- **Q4 2018**
  Review/Finalize Roadmap with Co-Chairs and Commission Members

- **Q1 2019**
  Externally Launch Roadmap

- Develop Roadmap Based on Meeting Output; Prepare to Launch Roadmap