BRIDGING THE GAP IN TRANSLATIONAL GENOMICS - THE NEED FOR COLLABORATIVE STRATEGIES

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Outline

1. Translational genomics today
2. Implications for health service delivery
3. What does this mean for haemoglobinopathies?
4. Need for international collaborations/networks
5. Harmonising efforts within and between countries – practical tools and steps
The ‘omics’ era

Sequencing technologies: whole-genome, whole exome, transcriptome, epigenome generate considerable amounts of personal genome data for analysis

Large scale human genome projects: UK Biobank, International Human Epigenome Consortium, 100,000 Genomes, AZ 2M genomes, NIH All of US

= BIG DATA, cloud computing, brings data and analysis outside of the “personal” creates issues for privacy, ethics, ownership, security, machine learning
Declaration of interests

• GV aims to increase the amount of information about clinically validated and classified genomic variants available on the internet in open, curated databases by means of cooperation at the individual, organizational, national, regional and international levels so that all people can benefit from advances in genomic medicine.

• GV focusses on increasing the quality and quantity of genomic data that is collected, curated, interpreted and shared for clinical practice.

• GV is an international NGO working to build capacity in the practice of responsible genomics. To ensure that this contributes to improving global health outcomes, it focusses on increasing both the quality and quantity of genomic knowledge that is collected, curated, interpreted and shared for clinical practice.

• GV is an NGO with operational status with UNESCO and has an MOU with WHO.

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Why haemoglobinopathies? - situational analysis

According to WHO, current estimates are –

• About 7% of the global population carries an abnormal haemoglobin gene; in African region many countries have 10 – 40% of the population carrying the gene, giving an estimated SCD prevalence of 2%; In countries such as Cameroon, Republic of Congo, Gabon, Ghana and Nigeria the prevalence is between 20% to 30% while in some parts of Uganda it is as high as 45%
• Between 300,000 and 500,000 children are born with clinically identifiable and significant haemoglobin disorders each year
• Approximately 80% of affected children are born in countries classified as low income
• Of those affected children an estimated 70-80% will have SCD and the rest will have some form of thalassaemia; it is the most prevalent genetic disease in African region
• Between 50 and 80% of children with SCD dies each year in LMICs; about 50 - 80% of the 400 000 babies born with SCD each year in Africa will die before they are 5 yo
• Between 50, 000 and 100, 000 of children with thalassaemia major die each year in LMICs

By 2050, the number of people with SCD is expected to increase by ~30% globally.
The problem is increasing

Several factors are driving increased numbers in the foreseeable future –

1. population growth
2. lack of good management of cases and
3. migration of people across various regions of the world.
GG2020 Challenge explained

Project Goals:

1. To see growth in the quality and quantity of curated inputs from low and middle-income countries into internationally recognized genetic databases. Tackling haemoglobinopathies is an ideal entry point for these countries to develop the necessary infrastructure and expertise that can expand into other areas.

2. To harmonize the sharing of all relevant genetic data between countries in accordance with international best practice that includes all the relevant ethical and regulatory frameworks and policies required to serve and protect patients at the same time the biotechnical systems and procedures are developed.

3. To ensure that the storage, curation and sharing of the relevant DNA variation information is sustainable in the medium and longer term by expanding and strengthening the international network of professionals, including curators, researchers, clinicians, bioinformaticians, counsellors, patients groups and health bureaucrats – particularly those from low and middle-income countries.

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At the same time this will -

- Raise the profile of genomic medicine in low and middle income countries among health bureaucrats in national, regional and international health organizations.
- Develop the capability of health professionals required for diagnosing, treating and counseling carriers in low and middle income countries thus giving them a greater voice and profile among genomic researchers and clinicians globally so they can actively participate in regional and international partnerships related to
  - genomic medicine research and
  - innovative health service delivery in low resource settings
- Put greater emphasis on prevention and cost-effectiveness in Primary Health Care
## Establishing national baseline

### Complete Country Checklist

<table>
<thead>
<tr>
<th>Description</th>
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<tr>
<td>Describe the disease burden in their country, incidence/prevalence, screening services, registries, assess the quality of this information</td>
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<tr>
<td>Degree of central reporting or national co-ordination – who does it, who has access,</td>
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<tr>
<td>Document the nature and level of diagnostic services currently available, including DNA/mutation analysis, molecular diagnosis – generation of clinical information</td>
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<tr>
<td><strong>Determine to degree of national co-ordination and planning</strong> – What kind of clinical information is available; Is there a national database of some kind – genotype, phenotype; if not, is there interest in this; <strong>is there a MOH focal point?</strong></td>
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<td><strong>Determine bodies involved in dealing with ethical, social, legal issues – consent, privacy, incidental findings</strong></td>
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<td>What type of resources are available: funding from public/private health sectors; availability of infrastructure, skilled workforce, counsellors</td>
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<tr>
<td><strong>Level of professional education available in human genomics</strong> – for nurses, diagnosticians, doctors, diagnosticians, counsellors - level of interest?</td>
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<tr>
<td>Treatment and Prevention services</td>
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<tr>
<td>Future plans, affiliations, research agenda ( national priorities and involvement in international projects)</td>
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<tr>
<th><strong>A</strong></th>
<th>Countries where services are well established with a national system for prevention and control</th>
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| **B** | Countries where some elements of a national control program exist but it is not available to all; more efforts is needed in areas like  
  i) improving access to services  
  ii) raising awareness among families and patients, health professionals and community in general  
  iii) establishing national centres of excellence/expertise to provide advice, measure progress  
  iv) ensure that savings from disease prevention are returned back to expand and improve services |
| **C** | Countries where expertise in diagnosis, treatment, management and prevention exists but is not part of a sustainable national control program |
| **D** | Countries where services are limited or not available |

(CATEGORISING NATIONAL RESPONSES TO HAEMOGLOBIN DISORDERS (ref WHO 2008))
Mismatch between problem and solutions

The challenge is

- Views of these diseases need to be up-dated; much has been learned in recent years about their underlying morphology and how to successfully manage treatment
- While much is known, it needs to be more systematically applied
- Inequitable access to safe and appropriate genetic services in many parts of the world
- According to TIF and WHO there is great heterogeneity in approaches among different regions and countries of the world
- According to WHO (AFRO, 2008) laboratory facilities for accurate diagnosis are limited; there are too few adequately trained health professionals
- Despite high profile interventions in 2008 at UN and adoption of a resolution at UNGA, plus several resolutions of the WHA, investment in prevention and management remains inadequate
What needs to be done

1. Raise the profile of hereditary haemoglobin disorders on the agenda of Ministries of Health, particularly those in low and middle-income countries

2. Ensure that advances in human genomics, including simple molecular technologies for disease control, are integrated into new innovative models for PHC and service delivery

3. Apply these new techniques to strengthen prevention and cost-effective service delivery

4. Achieve this through inter-country co-operations and knowledge sharing – south-south and south-north

5. See approaches to addressing haemoglobinopathies as a means of addressing broader issues of integrating genomics into health care
## GG2020 – two levels of action

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<th>AT NATIONAL/COUNTRY LEVEL</th>
<th>AT INTERNATIONAL/REGIONAL LEVEL</th>
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<tbody>
<tr>
<td>Identify who is working in the field – researchers, diagnosticians, clinicians</td>
<td>Identify ‘safe havens’ for data = recognized curated databases</td>
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<td>Identify who is generating data on haemoglobinopathies - who keeps this data now?</td>
<td>Apply internationally agreed nomenclature, data standards, file formats etc</td>
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<td>Determine who has an interest in using the information, quality of data</td>
<td>Link between countries, clinicians researchers etc. to identify common issues</td>
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<td>Create a national group – formal or informal</td>
<td>Review data access models to determine suitability, international quality standards</td>
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<td>Ethics, conflict of interest – identify local regulations and requirements – privacy, consent – who are key players?</td>
<td>Harmonise with already agreed privacy, consent processes</td>
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<td>Identify other partners – national groups/societies, patient groups, counsellors, public health officials</td>
<td>Contribute to interpretation of pathogenicity; genotype/phenotype alignment</td>
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<td>Determine level of interest at local and national government level – Ministry of Health/ WHO</td>
<td>Contribute to global epidemiological surveys and other knowledge relevant to understanding complexity</td>
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<td>Future plans – how might this be changing in next 5 to 10 years</td>
<td>Identify patterns across countries: common challenges, problems</td>
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How we can help

- Ethics checklist
- Minimum requirements for database curators
- Use of LOVD 3
- LOVD User group – access to training support
- Ithanet database curators
- International Expert Panel
- Harmonise your national efforts with other countries
Minimum requirements for variant databases

These requirements are aimed at providing guidance to:

• **database administrators** about which fields they are expected use in when implementing in their database management systems;

• **curators** about which information they are expected to check and ask for; to

• **data submitters** about which information they are expected to collect and provide; and

• **database users** about what they should expect to find in the database.
Implications for precision medicine

Need to broaden the dialogue when we consider ‘precision medicine’ – a long term process

• Ethics to include the right to benefit from advances in science – refer http://genomicsandhealth.org/working-groups/regulatory-and-ethics-working-group
• Need to recognize problems of low-resource settings, equity, access
• Tackle challenge of diversity in populations, sub-populations

Participate in and improve your own knowledge
• Dig data discussions
• Development of frameworks for governance of health data sets
• Improve your own skills and knowledge in this area

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- Dr E Kelley, Dr M-C Bouesseau, WHO

- Board of Global Variome, UK

- March of Dimes, American College of MG&G

- Many GG2020 members in all countries
What is a Country Node? What do they do?

An HVP Country Node has three components:

1. A repository, or linked network of databases, that collect and store information on variation in the human genome that has been generated within each country to enable the sharing of that information both nationally and internationally;

2. A governance structure that ensures that the work of the Node is both sustainable in the long term and is consistent with all relevant national and international ethical, legal and social requirements; and

3. A set of policies and procedures that ensures that the repository is operated and maintained in a responsible and accountable manner that is consistent with both national and HVP standards.

The three components above enable HVP Country Nodes to carry out specific roles both within their country and internationally:

• Taking an active role in ensuring that data on variation is easily shared among research institutes, projects, diagnostic laboratories and clinics;

• Contributing to building the capacity for storing and sharing data responsibly within the field of medical genetics and genomics;

• Monitoring and reporting on activities that will contribute to better targeting of healthcare planning and policy development; and

• Sharing data between other HVP Country Nodes and international Gene/Disease Specific Databases in the Human Variome Project Consortium.

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