Opportunities and benefits for inherited metabolic disease patients from an African rare disease biobank.

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Introduction

Conradie et al. 2021

Lack of support
- Government
- Financial

Limited clinical expertise

Lack of rare disease (RD) knowledge

Patients lost to follow up

Fear of exploitation

Fear of stigmatization

A call for global action for RD in Africa REQUIRED

The following issues need to be addressed

Baynam et al. 2020

Access to care and treatment

Genetic diseases

- Single gene disorders
- Chromosomal disorders
- Multifactorial disorders

Increasing awareness and documenting information

Ensuring patient unity

Ensuring the sustainability of patient organisations

Global policy developments

Program implementation and emphasis

Prevention

Ethics and good clinical and genetic practices

Congenital disorders prevention, diagnosis and treatment

Expanding the role of patient-advocacy groups

Improving quality of life

Avoiding health inequities
Opportunities and benefits for inherited metabolic disease patients from an African rare disease biobank.

Successful contributions from established inherited metabolic disease (IMD) biobanks (e.g. MetabERN)

Biomarker discoveries

New diagnostic assays

Drug development

Clinical Trials (with positive outcome)

Established the first rare disease “exclusive” biobank in South Africa and on the African continent.
## Opportunities and benefits for inherited metabolic disease patients from an African rare disease biobank.

**Table 1** Showcasing the research findings from a few studies on South African IMD cohorts

**Note:** Various mitochondrial disorders have been diagnosed in South Africa with myopathy as the primary clinical feature noted in the black cohort and encephalopathy or encephalomyopathy noted in the Caucasian cohort – mostly different mutations than the rest of the world with evidence of potential founder effects are evident (Smuts et al 2010 JIMD 33(S3) and Meldau et al 2020. J Clin Pathol. DOI: 10.1136/jclinpath-2020-207026)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Population specific Mutations</th>
<th>Time of diagnosis/phenotype</th>
<th>Population cohort</th>
<th>Literature reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gaucher disease</strong></td>
<td>GBA gene: c.1226A &gt; G (p.Asn409Ser) and c.1297G&gt;T (p.Val433Leu)</td>
<td>Subtype 1 (mostly hepatic features)</td>
<td>Ashkenazi Jewish population (Carrier frequency is 0.05 in South African Ashkenazi)</td>
<td>Morar et al., 1996. Clin Genet. 50: 78-84</td>
</tr>
<tr>
<td><strong>Gaucher disease</strong></td>
<td>GBA gene: c.222_224del (p.Thr75del) in combination with recNcil</td>
<td>Subtype 1 (limited neurological involvement)</td>
<td>Black population (carrier frequency for c.222_224del was found to be 1/66)</td>
<td>Arndt et al., 2009 Blood Cells Mol Dis. 43(1):129-33</td>
</tr>
<tr>
<td><strong>ALG6-Congenital disorder of glycosylation</strong></td>
<td>ALG6 gene: c.998C&gt;T (p.Ala333Val), c.1338dup (p.Val447fs) and c.257 + 5G&gt;A splice mutation, c.680G&gt;A(p.Gly227Glu)</td>
<td>Infancy – 2 phenotype 1) severe gastro-neurological 2) slower progression neurological</td>
<td>Caucasian population</td>
<td>Dercksen et al., 2013. JIMD-reports. 8:17-23</td>
</tr>
<tr>
<td><strong>Hepato-cerebral mitochondrial DNA depletion syndrome</strong></td>
<td>MPV17 gene: c.106C&gt;T(p.Gln36Ter)</td>
<td>Neonate-Infancy (All patients have hepatic and neuromuscular abnormalities)</td>
<td>Black population (Carrier frequency:1 in 68)</td>
<td>Meldau et al 2018Clinical Genetics 93(5)</td>
</tr>
</tbody>
</table>
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Concluding remarks

There is a great need for action towards prioritizing RD on the African continent. The need of RD patients often get overlooked when compared to providing basic needs (such as nutrition) and efforts aimed towards the prevention of communicable diseases. However, in order for SA to achieve the United Nations Sustainability Development Program Goal 3, namely “ensuring good health and well-being for all ages at all stages”, RD patients can no longer be left behind. It is therefore of the utmost importance to rethink standard practices in setting up RD infrastructure and networks in lower-middle income countries to overcome the barriers listed above.

Additional References:
Baynam et al. 2020; “A call for global action for rare diseases in Africa”; Nature Genetics; Vol 52; Jan 2020; pg 21-26
Conradie et al. 2021; “An Overview of Benefits and Challenges of Rare Disease Biobanking in Africa, Focusing on South Africa”; Biopreservation and Biobanking; 2021; Vol 19(2)

We invite you to contact us in terms of collaboration on this initiative (first of its type in Africa)

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