ANALYSIS OF G1P[8] WHOLE GENOME CONSTELLATIONS IDENTIFIED A VACCINE-DERIVED STRAIN IN RWANDA


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Department of Virology, Next Generation Sequencing Unit
INTRODUCTION
• Vaccination coverage was 98-99% by 2016
  – Significant reduction in RV-associated morbidity and mortality

• Binary classification
  – The outer capsid proteins
    • VP4 (Protease sensitive [P-type])
    • VP7 (Glycoprotein [G-type])

Ngabo et al., 2016; Estes and Kapikian, 2007

Adapted from: farmapana.com, drugtotal.com, Rodriguez et al., 2014
The Rotavirus Classification Working Group (RCWG)
- Gx-P[x]-Rx-Cx-Mx-Ax-Nx-Tx-Ex-Hx (x- genotype number)


In partnership with WHO/AFRO, the UFS-NGS Unit
- Rotavirus surveillance study on a whole genome level
- Focusing on Rwanda as a pilot study
AIM AND OBJECTIVE
AIM

To determine the changes in the whole genome composition of circulating human G1P[8] strains in Rwanda
OBJECTIVE

To explore the probable evidence of rotavirus vaccine pressure on G1P[8] strains from Rwanda between 2011 and 2016
METHODOLOGY
dsRNA extraction and cDNA synthesis

Library Preparation

Sequencing

Clean-up and Pooling
RESULTS AND DISCUSSION
## PHYLOGENETIC ANALYSIS

<table>
<thead>
<tr>
<th>Genotype</th>
<th>VP7</th>
<th>VP4</th>
<th>VP6</th>
<th>VP1</th>
<th>VP2</th>
<th>VP3</th>
<th>NSP1</th>
<th>NSP2</th>
<th>NSP3</th>
<th>NSP4</th>
<th>NSP5</th>
</tr>
</thead>
<tbody>
<tr>
<td>35 Wild-type Strains (10 pre- and 25 post vaccine)</td>
<td>G1</td>
<td>P[8]</td>
<td>I1</td>
<td>R1</td>
<td>C1</td>
<td>M1</td>
<td>A1</td>
<td>N1</td>
<td>T1</td>
<td>E1</td>
<td>H1</td>
</tr>
<tr>
<td>1 Reassortant strain (Post vaccine)</td>
<td>G1</td>
<td>P[8]</td>
<td>I2</td>
<td>R2</td>
<td>C2</td>
<td>M2</td>
<td>A3</td>
<td>N2</td>
<td>T6</td>
<td>E2</td>
<td>H3</td>
</tr>
</tbody>
</table>

### VP7 (Glycoprotein [G-type])

<table>
<thead>
<tr>
<th>Seven lineages</th>
<th>VP4 (Protease sensitive [P-type])</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lineage I</strong></td>
<td><strong>Four lineages</strong></td>
</tr>
<tr>
<td>Wild type nt (aa): 91.5% (89.4-100%)</td>
<td><strong>Lineage III</strong></td>
</tr>
<tr>
<td>Wild type nt (aa): 95.8-100% (90.8-100%)</td>
<td><strong>Lineage II</strong></td>
</tr>
<tr>
<td><strong>Lineage III</strong></td>
<td><strong>Lineage I</strong></td>
</tr>
<tr>
<td>Reassortant strain:</td>
<td><strong>Reassortant strain:</strong></td>
</tr>
<tr>
<td>• 100% with RotaTeq™</td>
<td>• 99.4% (98.9%) with RotaTeq™</td>
</tr>
<tr>
<td>• 93.4% (91%) with Rotarix™</td>
<td>• 90% (78%) with Rotarix™</td>
</tr>
</tbody>
</table>
Figure: (A and B) Surface representation of the VP7 monomer. Antigenic epitopes are colored in yellow (7-1a), green (7-1b), and blue (7-2). Surface-exposed residues that differ between circulating strains in Rwanda and G1 strain contained in Rotarix® or RotaTeq® are shown in red.
## CYTOTOXIC T LYMPHOCYTES

- Linked to clearing rotavirus infection resulting in protection against re-infection
  - Amino acid position 16-28 and 40-52

<table>
<thead>
<tr>
<th></th>
<th>VP7 Wild-type strain</th>
</tr>
</thead>
<tbody>
<tr>
<td>RotaTeq™</td>
<td>T41F/S, V42M and A46V</td>
</tr>
<tr>
<td>Rotarix™</td>
<td>Y41F/S, V42M, A46V</td>
</tr>
</tbody>
</table>
Figure: (A and B) Surface representation of the VP8* section of the VP4 monomer. Antigenic epitopes are colored in yellow (8-1), green (8-2), blue (8-3) and purple (8-4). Surface-exposed residues that differ between circulating strains in Rwanda and P[8] strain contained in Rotarix® or RotaTeq® are shown in red.

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CONCLUSION
• The first WHO surveillance study to report on the G1P[8] circulating strains pre and post vaccine introduction on a whole genome level in Rwanda
  – There is diversity among the Wild type strains
  – Reassortant strain showed close relationship with a RotaTeq™ vaccine
  – Changes in the neutralization epitopes
    • might play a role in generating vaccine-escape mutants

• Surveillance on a whole genome level
  – to monitor this changes
ACKNOWLEDGEMENTS

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- Dr Esona
- UFS-NGS Team
- MRC-DPRU Team
- Rwanda Team
THANK YOU
DANKIE

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