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

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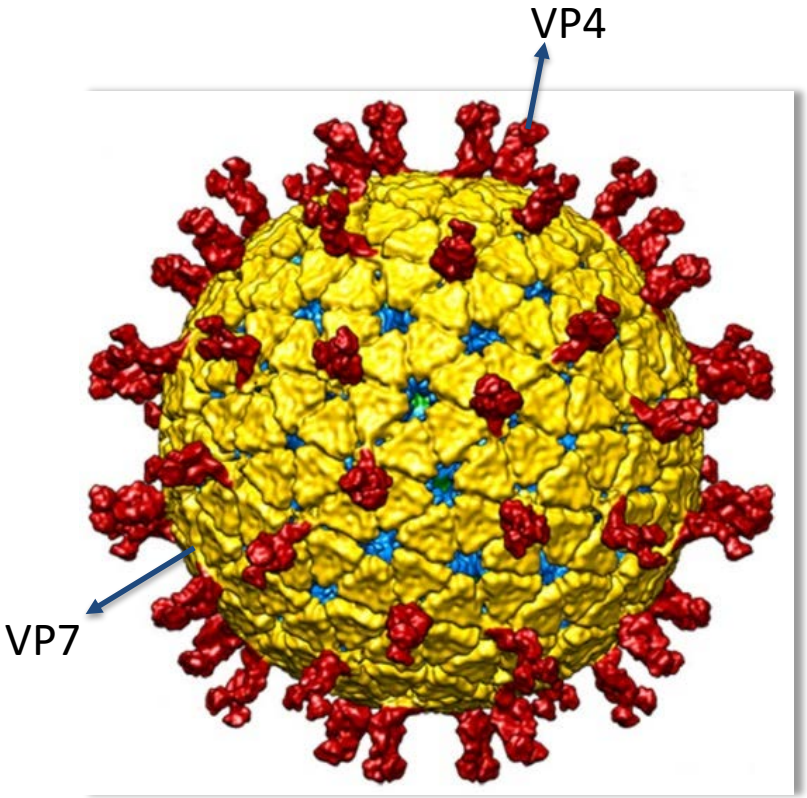
INTRODUCTION

BACKGROUND

- 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, drugstotal.com, Rodríguez *et al.*, 2014

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BACKGROUND

- The Rotavirus Classification Working Group (RCWG)
  - Gx-P[x]-Ix-Rx-Cx-Mx-Ax-Nx-Tx-Ex-Hx (x- genotype number)

Genotype	G	P	I	R	C	M	A	N	T	E	H
Protein	VP7	VP4	VP6	VP1	VP2	VP3	NSP1	NSP2	NSP3	NSP4	NSP5

- 36 G, 51 P, 26 I, 22 R, 20 C, 20 M, 31 A, 22 N, 22 T, 27 E and 22 H genotypes (as at 2018)

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

https://rega.kuleuven.be/cev/viralmetagenomics/virus-classification ; Matthijnssens *et al.*, 2011

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AIM AND OBJECTIVE

AIM

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

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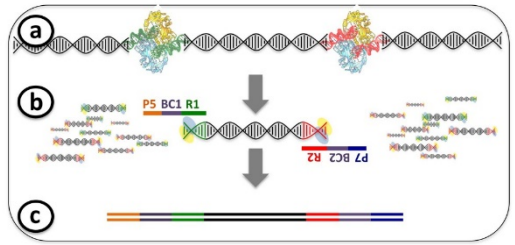
OBJECTIVE

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

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Bioinformatics tools

geneious prime

CLC Genomics Workbench Version 7.0.4 Loading Fonts

RotaC 2.0 automated genotyping tool for Group A rotaviruses. Read More

Nucleotide BLAST
nucleotide ▶ nucleotide

MEGA Molecular Evolutionary Genetics Analysis

SWISS-MODEL

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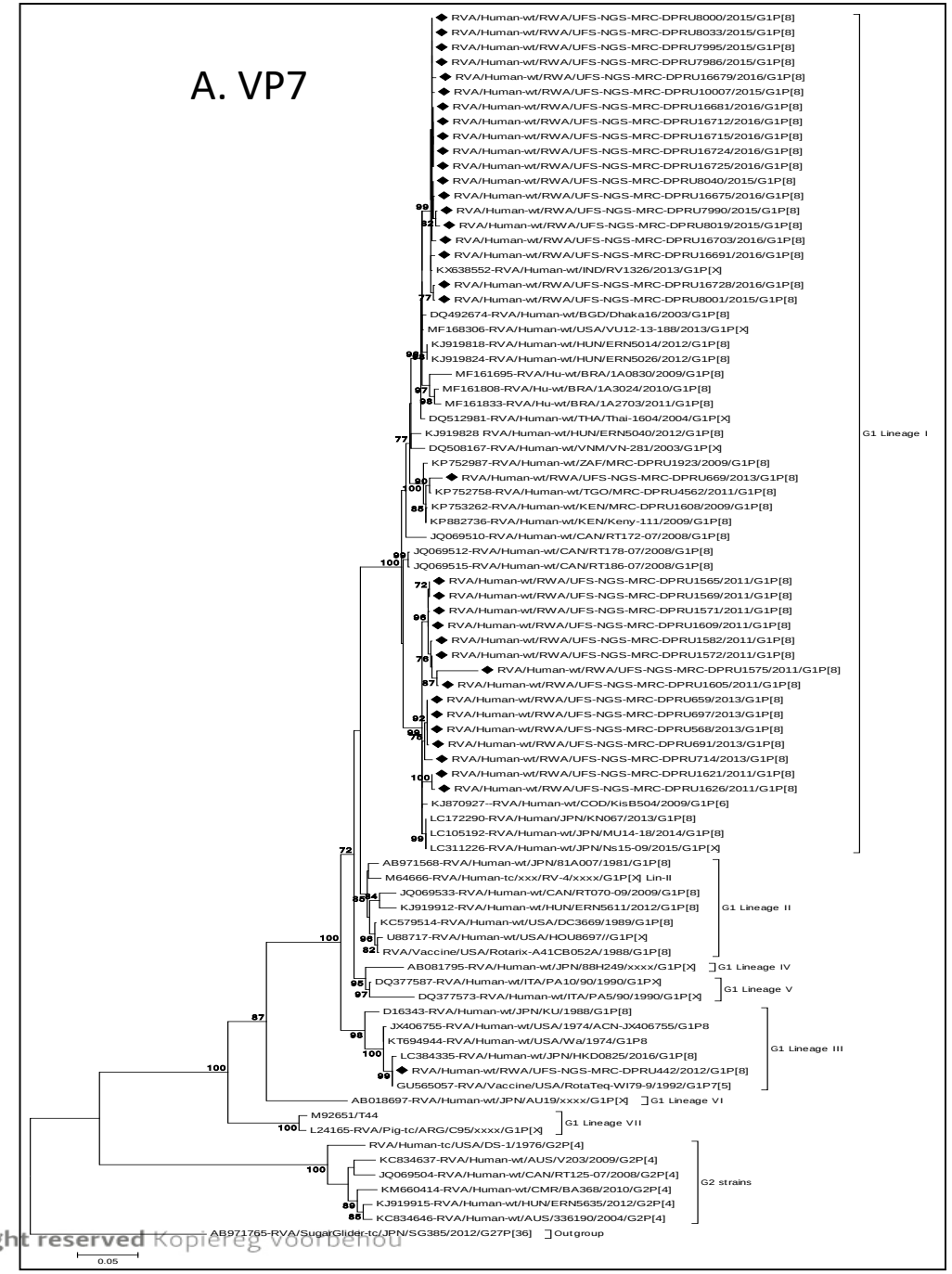
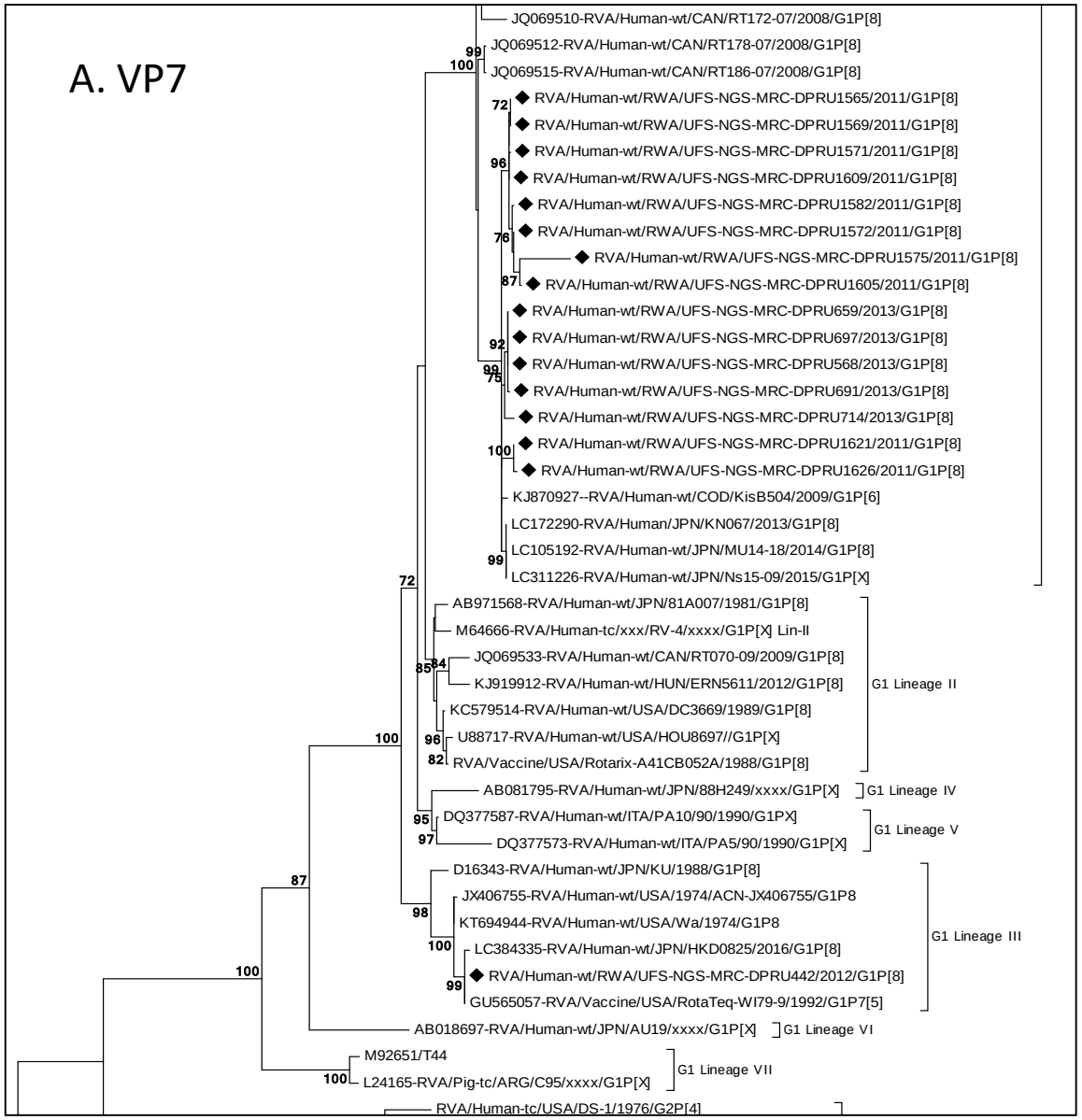
RESULTS AND DISCUSSION

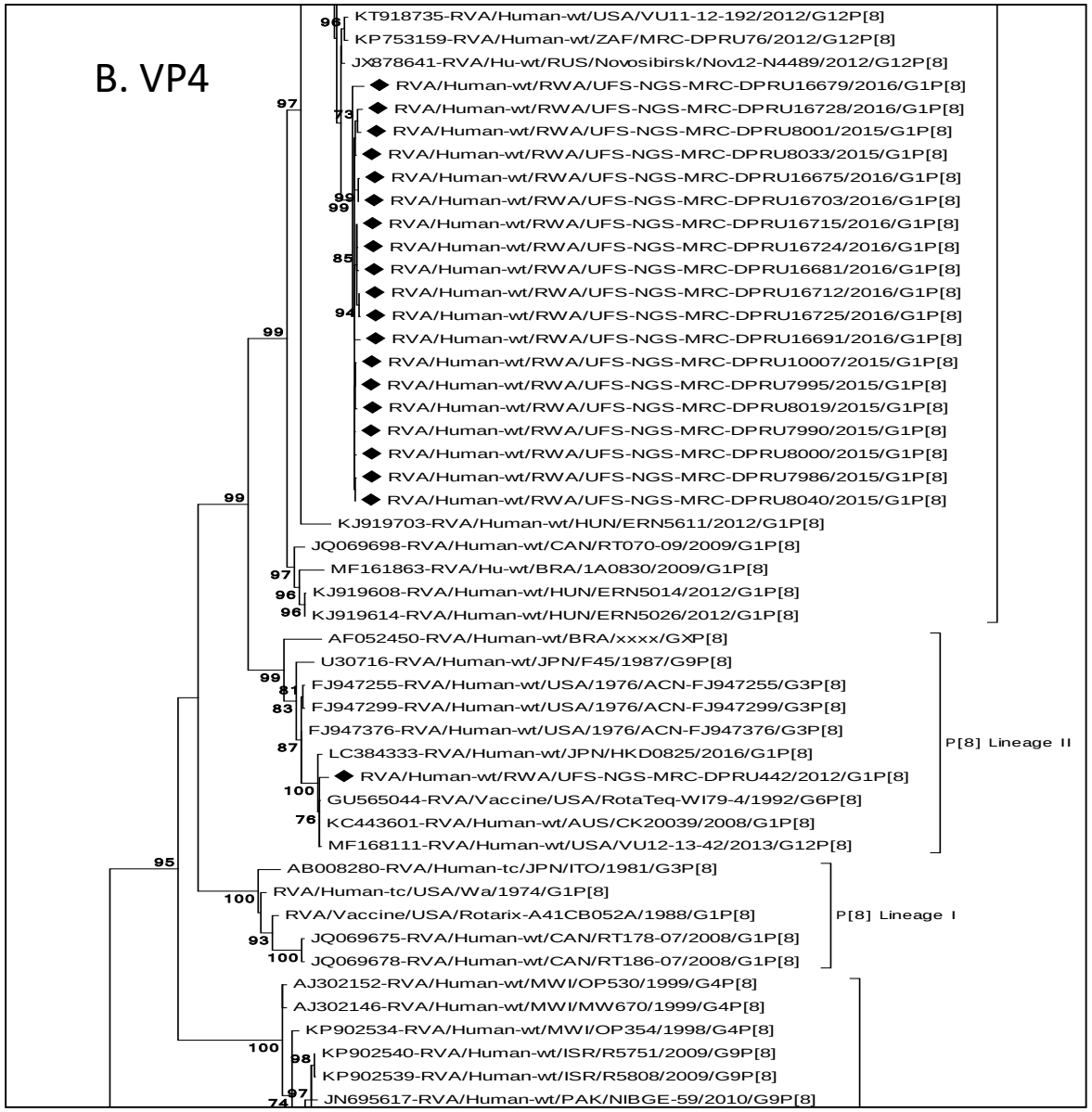
PHYLOGENETIC ANALYSIS

Genotype	VP7	VP4	VP6	VP1	VP2	VP3	NSP1	NSP2	NSP3	NSP4	NSP5
35 Wild-type Strains (10 pre- and 25 post vaccine)	G1	P[8]	I1	R1	C1	M1	A1	N1	T1	E1	H1
1 Reassortant strain (Post vaccine)	G1	P[8]	I2	R2	C2	M2	A3	N2	T6	E2	H3
RVA/Vaccine/USA/Rotateq-W179-4/1992/G6P[8]	G6	P[8]	I2	R2	C2	M2	A3	N2	T6	E2	H3
RVA/Vaccine/USA/Rotateq-W179-9/1992/G1P[5]	G1	P[5]	I2	R2	C2	M1	A3	N2	T6	E2	H3

VP7 (Glycoprotein [G-type])	VP4 (Protease sensitive [P-type])
Seven lineages	**Four lineages**
Lineage I Wild type nt (aa): 91.5% (89.4-100%)	**Lineage III** Wild type nt (aa): 95.8-100% (90.8-100%)
Lineage III Reassortant strain: • 100% with RotaTeq™ • 93.4% (91%) with Rotarix™	**Lineage II** Reassortant strain: • 99.4% (98.9%) with RotaTeq™ • 90% (78%) with Rotarix™







VP7 PROTEIN STRUCTURE

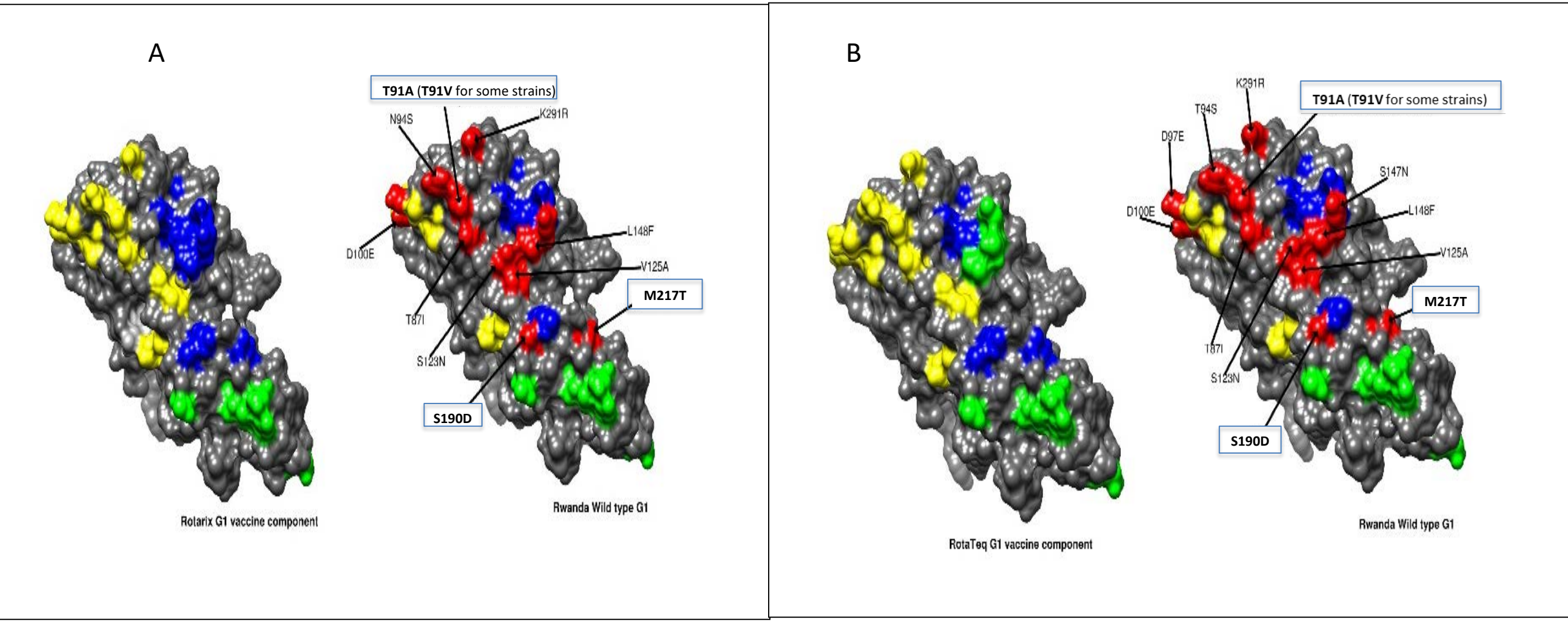


Figure: (A and B) Surface representation of the VP7 monomer. Antigenic epitopes are colored in yellow (7-1a), green (7-1b), and blue (7-2). Surface-exposed residues that differ between circulating strains in Rwanda and G1 strain contained in Rotarix® or RotaTeq® are shown in red.

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CYTOTOXIC T LYMPHOCYTES

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

	VP7 Wild-type strain
RotaTeq™	**T41F**/S, V42M and A46V
Rotarix™	**Y41F**/S, V42M, A46V

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VP4 PROTEIN STRUCTURE

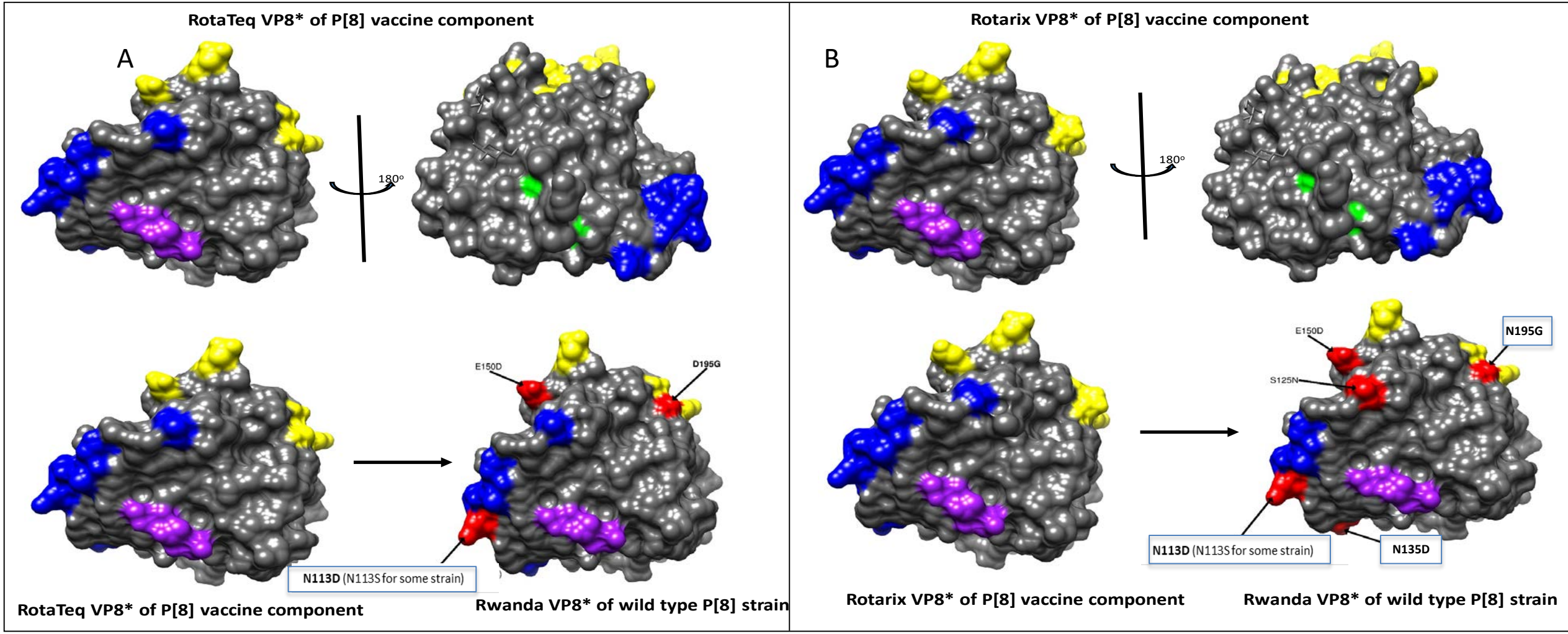

Figure: (A and B) Surface representation of the VP8* section of the VP4 monomer. Antigenic epitopes are colored in yellow (8-1), green (8-2), blue (8-3) and purple (8-4). Surface-exposed residues that differ between circulating strains in Rwanda and P[8] strain contained in Rotarix® or RotaTeq® are shown in red.

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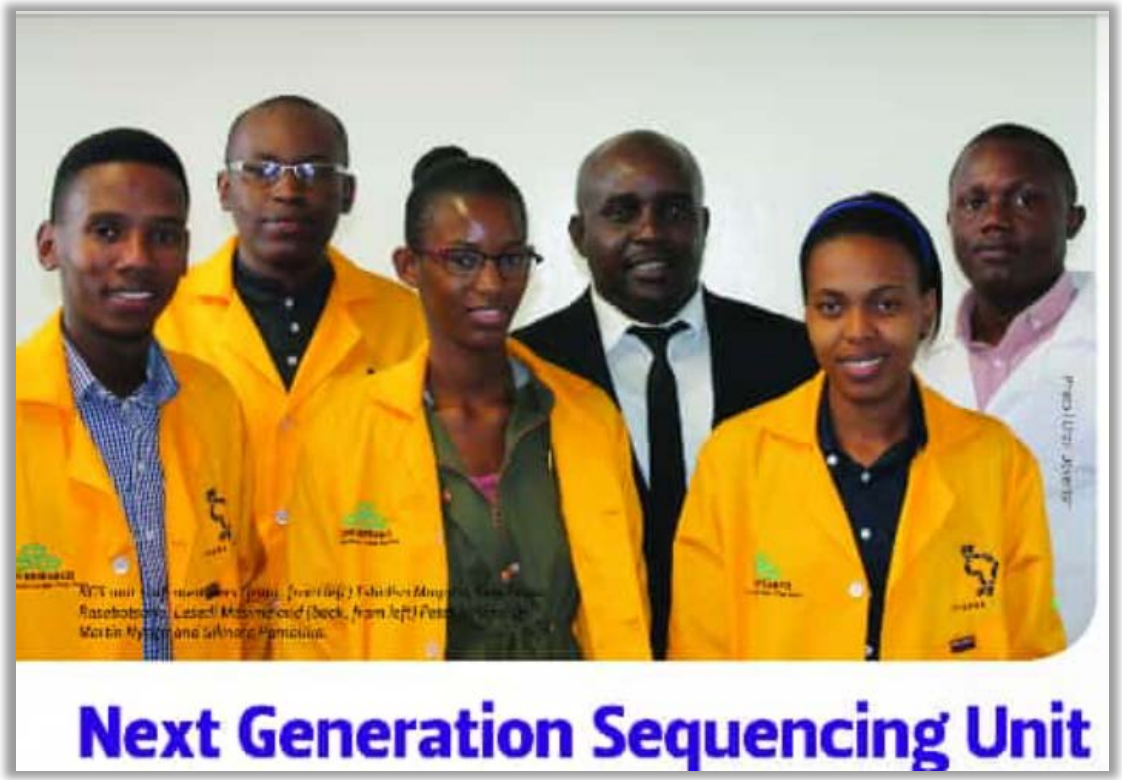
CONCLUSION

- **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

- Dr Martin (Lead Researcher)
- Dr Esona
- UFS-NGS Team
- MRC-DPRU Team
- Rwanda Team



THANK YOU
DANKIE

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