FOURTEENTH INTERNATIONAL

ROTAVIRUS SYMPOSIUM

MARCH 14–16 **2023** BALI INDONESIA

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Characterising the diversity of unusual rotavirus strains in Australian children and adults

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14th International Rotavirus Symposium, Bali

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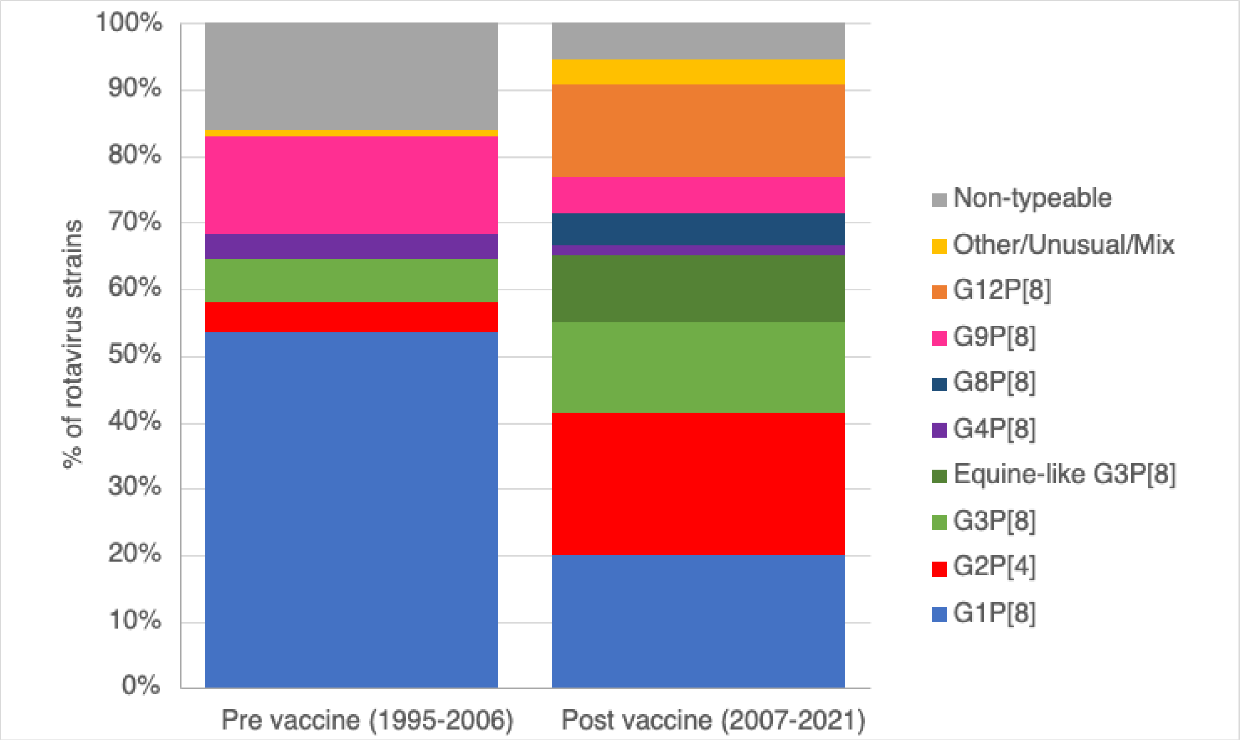
The vaccine era in Australia

- Australia Rotavirus Surveillance Program has monitored genotypes present in Australian children since 1989

- 19 collaborating laboratories nationwide collect rotavirus-positive specimens

- Vaccines were introduced in 2007
  - Rotarix used nationally since 2017

- Shift in genotype diversity
  - ↓ G1P[8]
  - ↑ G2P[4]
  - Emergence of equine-like G3P[8]
  - Emergence of G12P[8]
  - Emergence of G8P[8]
  - Emergence of G9P[4]
  - ↑ detection of unusual

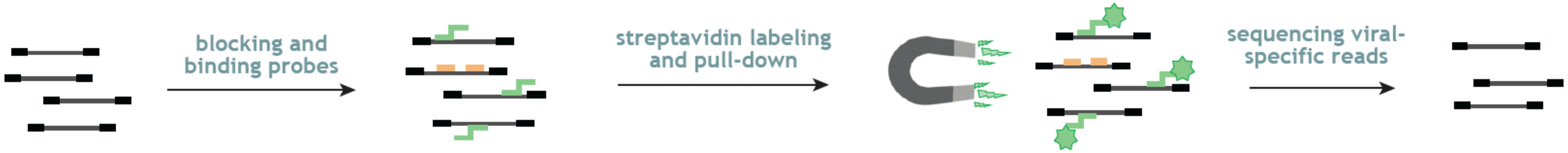


Genotype diversity in children <5 years

Methods

Poster 12

- Full genome sequencing (n=300)
  - Amplicon & random amplification
  - Twist Biosciences comprehensive viral panel



  - Nextera-XT Library preps & Illumina MiSeq/NextSeq

- Genome assembly
  - Custom Galaxy pipeline
  - Genome Detective

Genome Detective

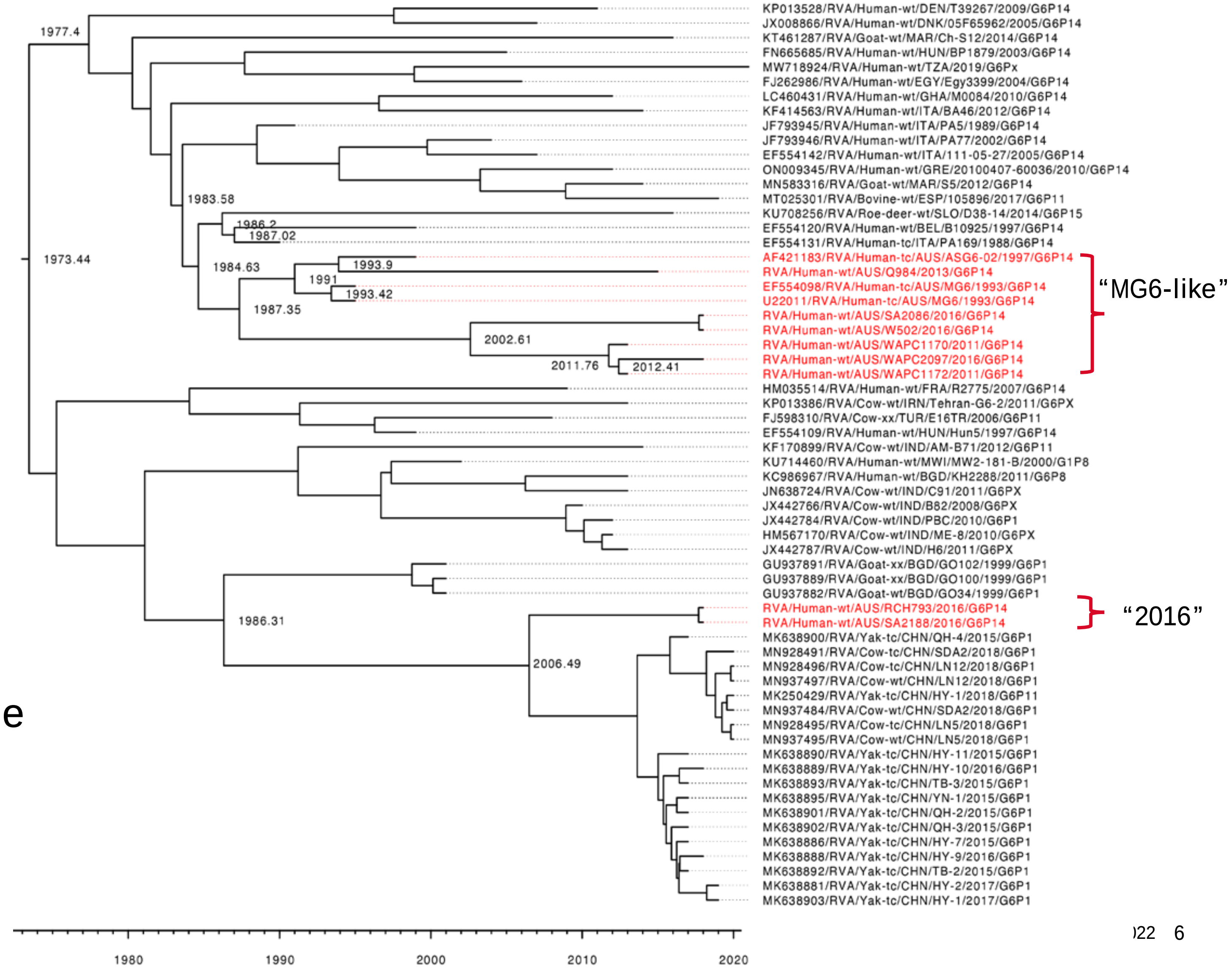
- Maximum Likelihood Phylogenetic analysis - RAxML-NGS
- Bayesian analysis - BEAST

Bovine-like strains

Genotype	VP7	VP4	VP6	VP1	VP2	VP3	NSP1	NSP2	NSP3	NSP4	NSP5
G6P[14] n=14	G6	P[14]	I2	R2	C2	M2	A11	N2	T6	E2	H3
G8P[14] n=27	G8	P[14]	I2	R2	C2	M2	A11	N2	T6	E2	H3
G10P[14] n=11	G10	P[14]	I2	R2	C2	M2	A11	N2	T6	E2	H3
G8P[1] n=1	G8	P[1]	I2	R2	C2	M2	A3	N2	T6	E2	H3
G8P[4] n=1	G8	P[4]	I2	R2	C2	M2	A2	N2	T2	E2	H2
G10P[25] n=1	G10	P[25]	I2	R2	C2	M2	A1	N1	T6	E2	H1

G6P[14] – VP7

- "MG6-like" cluster
  - Primarily in adults 16-84 yrs
  - Diverged from MG6-like ancestor in 1987
  - Unsampled diversity – long branch lengths
  - Repeated reintroduction?
  - Continued circulation at low frequency?
- "2016" cluster
  - Nov 2016 from 16.5 yrs and 21.6 yrs
  - shared a MRCA in 2006 with Chinese Cow/Yak strains
  - Poorly characterised endemic lineage of bovine origins
- Not closely related to previously characterised Australian bovine strains

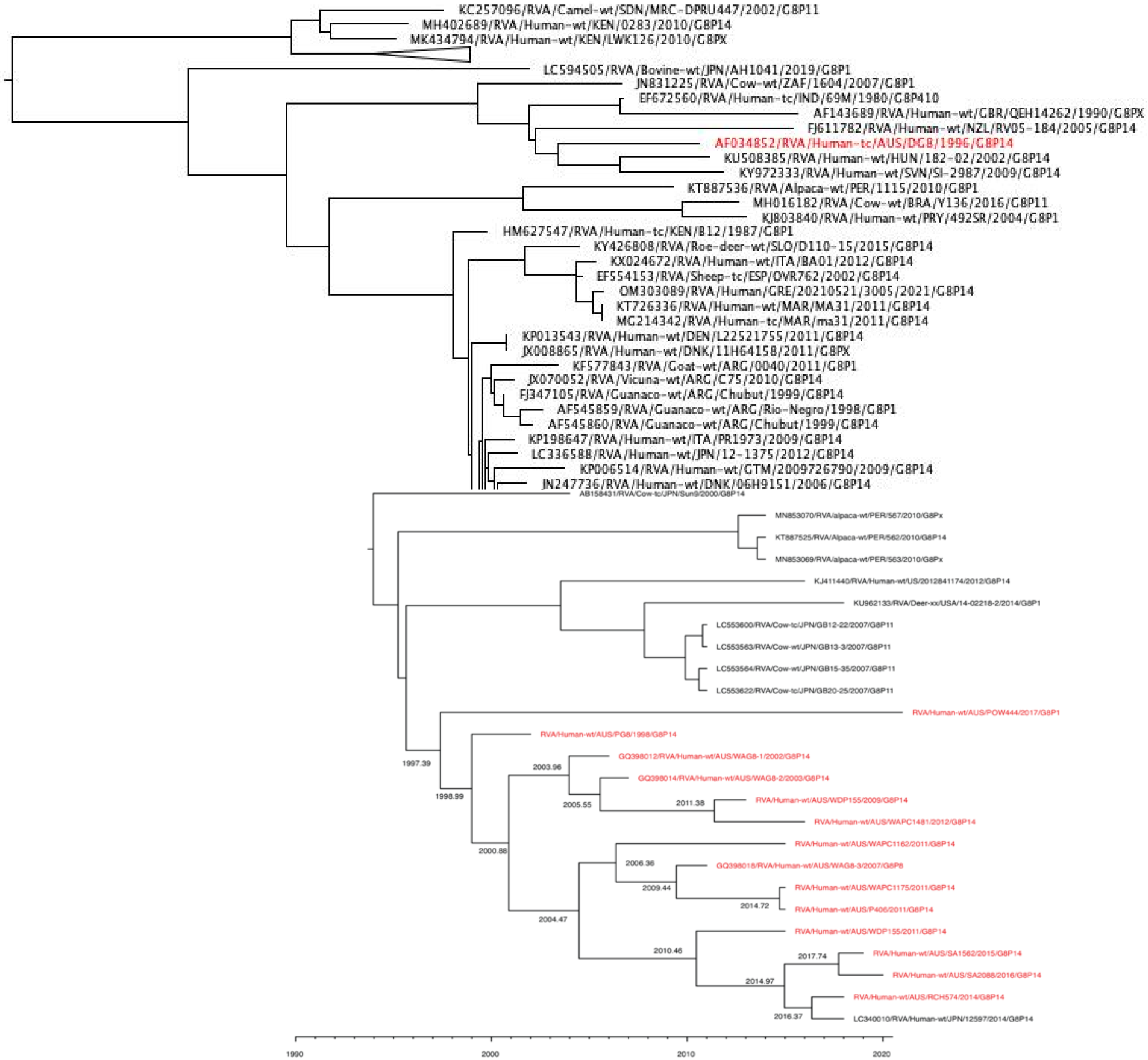


"MG6-like"

"2016"

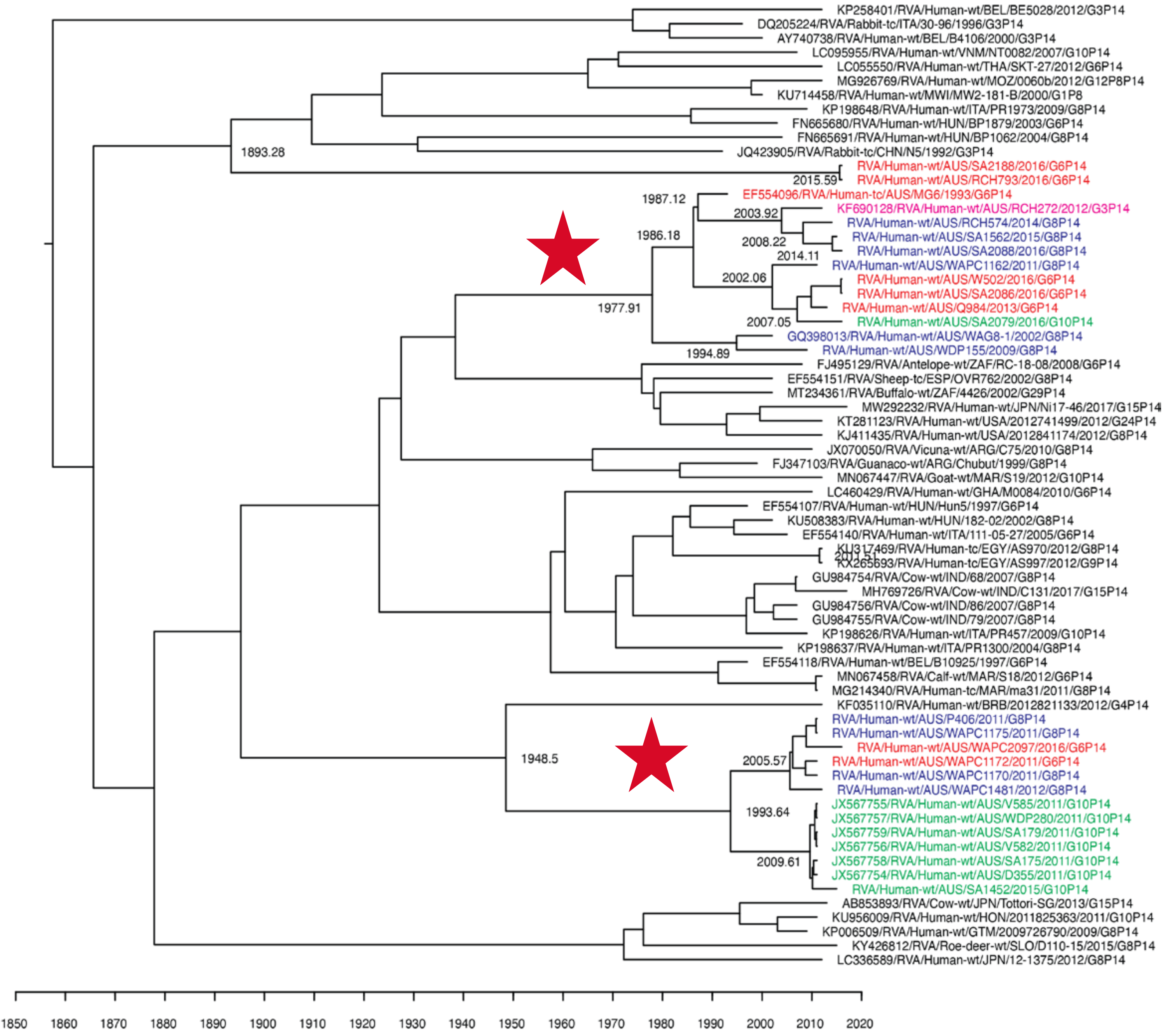
G8P[14] - VP7

- Predominant G8P[14] cluster
  - P[1]/P[8]
  - 1998 – 2017
  - Children <5
  - Within a bovine sub-lineage
  - MRCA 1997



P[14]

- 2 endemic P[14] variants - minor clustering based on G type
- “MG6-like” variant
  - G6 / G10 / G8 / G3
  - MRCA 1977
  - Diverged in 1930s
- “NT variant” variants shared a MRCA of 1993
  - Diverged in 1940s
- Historic divergence from global strains and prolonged endemic circulation and reassortment
- “2016” G6P[14]
  - Divergence from global strains in 1830s



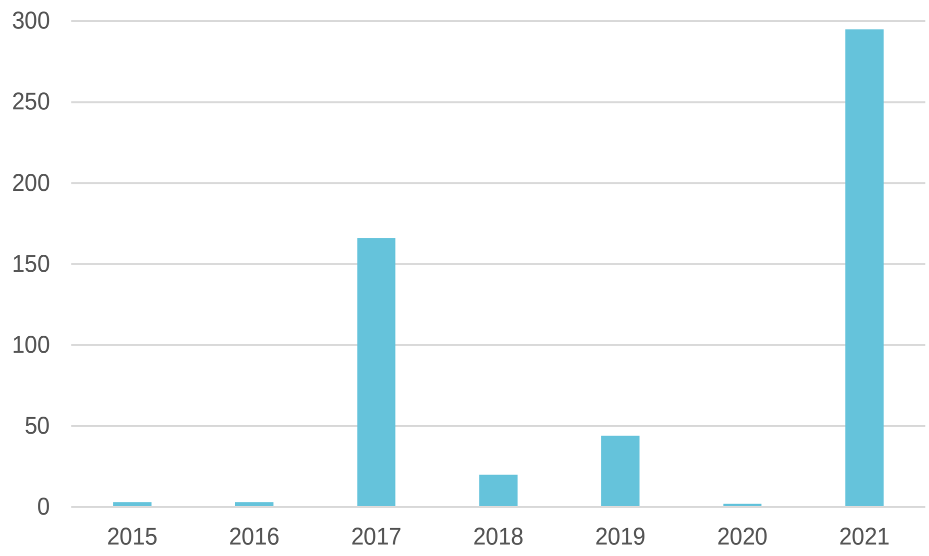
G8P[8]

- Pre-2017 - sporadic cases
  - G8-P8-I1-R1-C1-M1-A1-N1-T1-E1-H1

- 2017 outbreak in New South Wales
  - <5 years n=70
  - ≥ 5 years and adults n=96
  - Contemporary European G8P[8]
  - G8-P8-I2-R2-C2-M2-A2-N2-T2-E2-H2

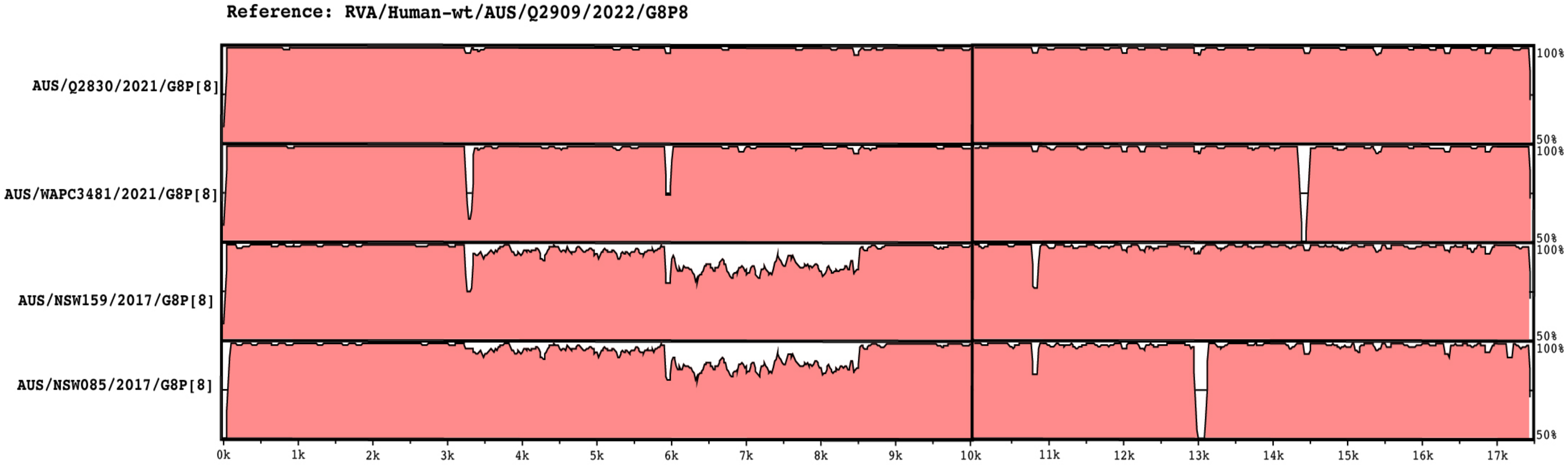
- 2021 outbreaks New South Wales and Victoria
  - <5 years n=147
  - ≥5 years and adults n=147
  - Reintroduction from global G8P[8]
  - G8-P8-I2-R2-C2-M2-A2-N2-T2-E2-H2

- 2022



G8P[8]

- 2021 and 2022 samples have a highly conserved genome
- 2017 outbreak strains vs. 2021/2022 outbreak
  - Highly conserved genome
  - Variant VP2 and VP3 genes

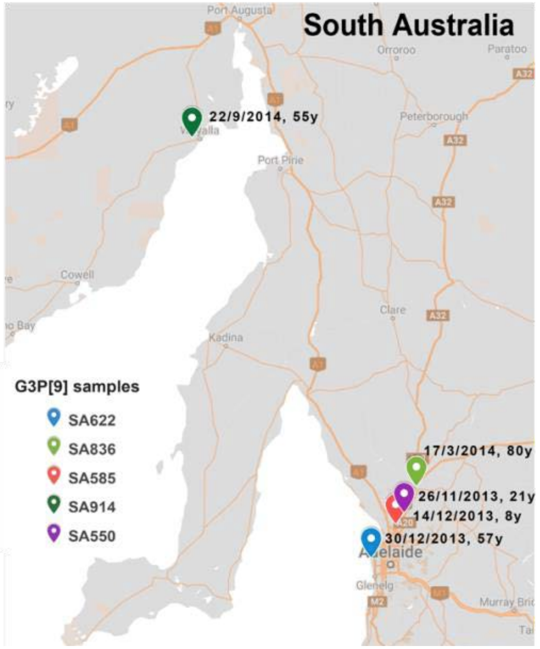


Canine/feline-like G3 strains

- G3P[9] (n=20)
  - Emerged in South Australia in 2013-2014

- G3P[3] (n=19)
  - Emerged in 2010 in Western Australia

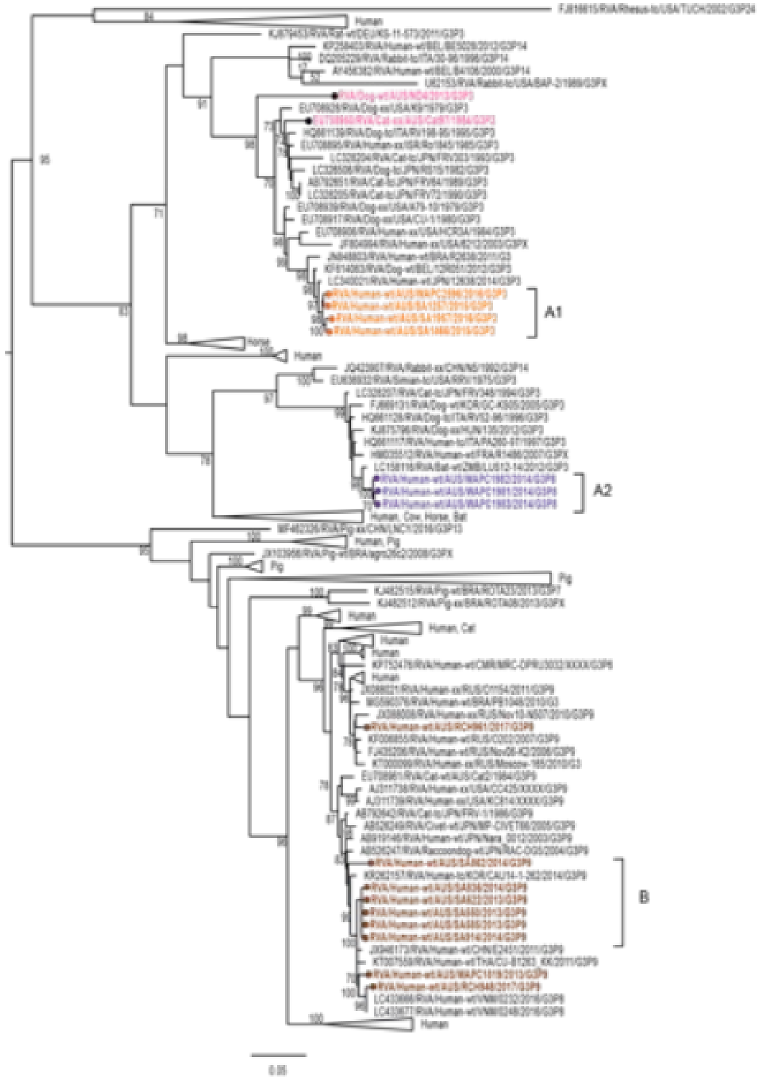
- Sporadic G3P[8] (n=3)
  - Backbone largely derived from G3P[3]



Genotype	VP7	VP4	VP6	VP1	VP2	VP3	NSP1	NSP2	NSP3	NSP4	NSP5
G3P[9]	G3	P[9]	I3	R3	C3	M3	A3	N3	T3	E3	H6
G3P[3]	G3	P[3]	I3	R3	C3	M3	A9	N2	T3	E3	H6
G3P[8]	G3	P[8]	I3	R3	C3	M3	A2	N2	T3	E3	H6

VP7 of canine/feline G3 strains

- G3P[3] cluster with canine & feline strains within the same clade as RVA/Dog-wt/AUS/ND4/2013/G3P[3]
- G3P[8] clustered in a different clade of canine and feline strains, shared high nucleotide similarity to RVA/Bat-wt/ZMB/LUS12-14/2012/G3P[3]
- G3P[9] cluster within a primarily human clade containing and the historic feline strain RVA/Cat-wt/AUS/Cat2/1984/G3P[9]
- More recent introductions into the human population



Conclusions

- Large diversity of rotavirus strains in Australia infecting adults and children
    - Zoonotic transmission and reassortment contributes to this diversity

- Emergence of DS-1 backbone strains e.g., G8P[8]

- Endemic circulation of variants that entered the human population decades ago via zoonotic transmission

- Recent emergence of some variants and direct zoonotic transmission events

- Diversity in animals is largely undescribed making it difficult to infer transmission events
    - One-Health Initiative

- Overall burden of rotavirus disease remains significantly reduced in the vaccine era but emerging variants can cause concern especially widespread outbreaks

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