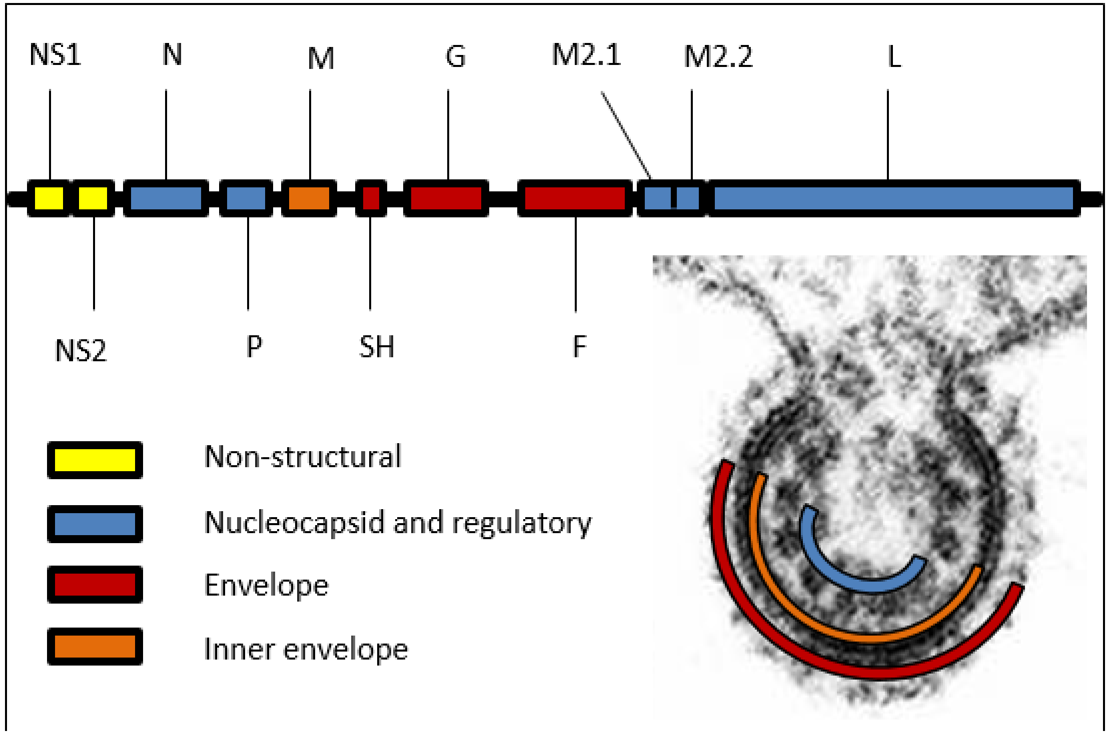
Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

RSV virology, strain variation, and surveillance measures

Natalie J. Thornburg, PhD
Chief (acting) Laboratory Branch
Coronaviruses and Other Respiratory Viruses Division
Centers for Disease Control and Prevention

May 18, 2023

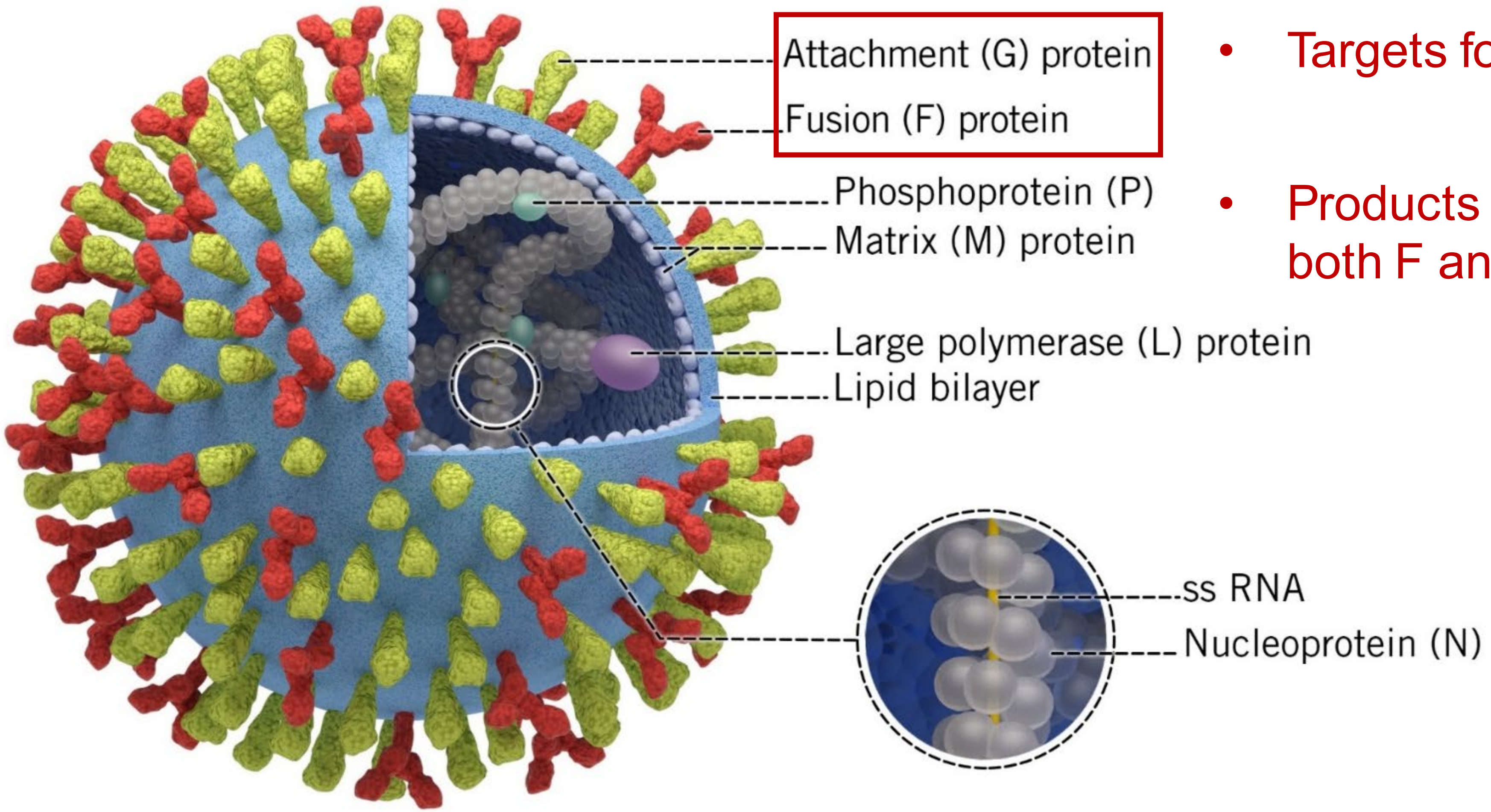
RSV genome



Respiratory Syncytial Virus (RSV) | British Society for Immunology

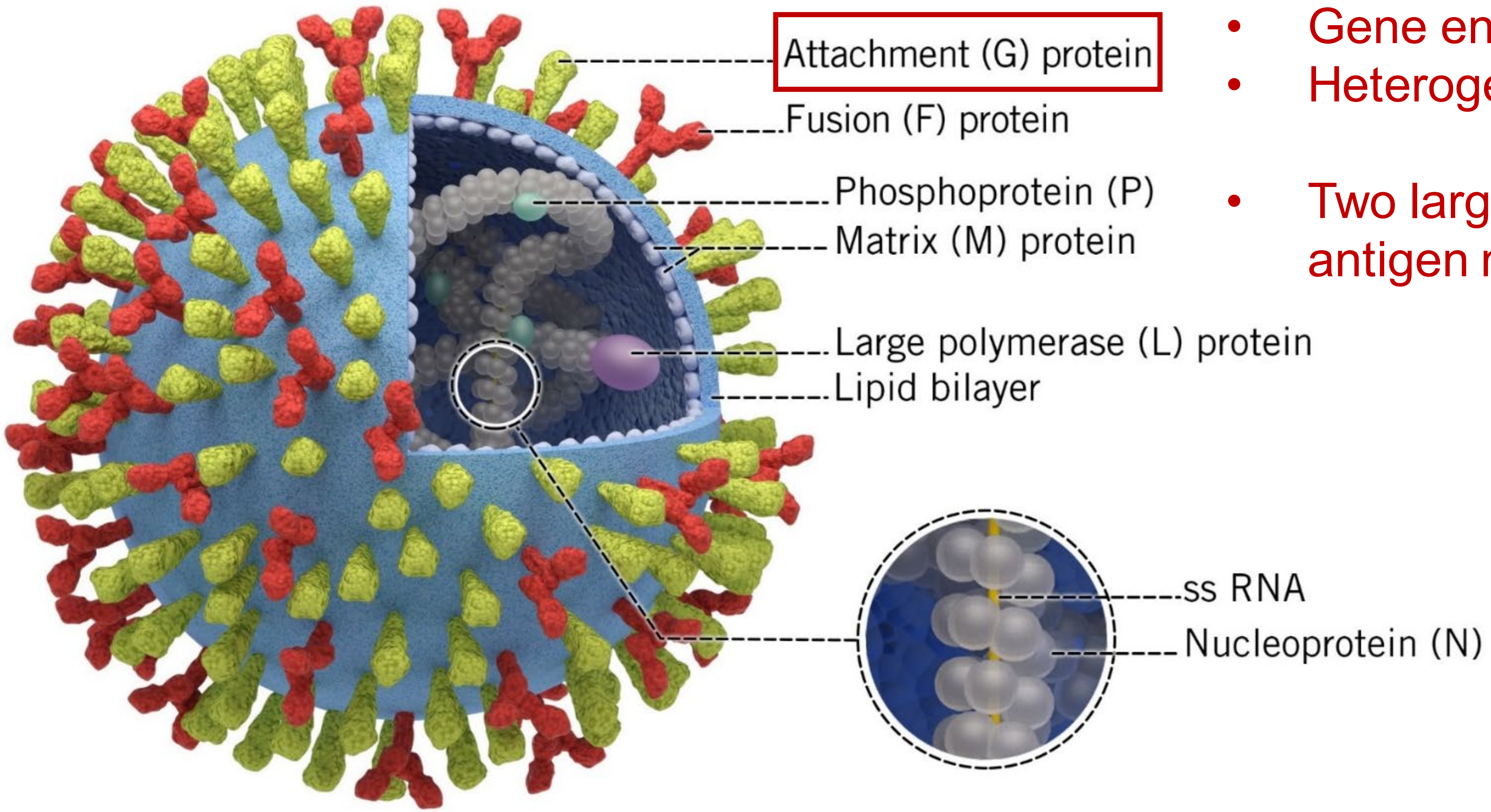
- Filamentous *Orthopneumovirus*
- 15.2 kbp genome
- Single stranded negative sense
- 11 viral proteins
- Divided into two subgroups / serotypes A and B
- RSV A and B co-circulate

RSV – virion structure



- Targets for neutralizing antibodies
- Products in target F alone or have both F and G

RSV Glycoprotein (G)

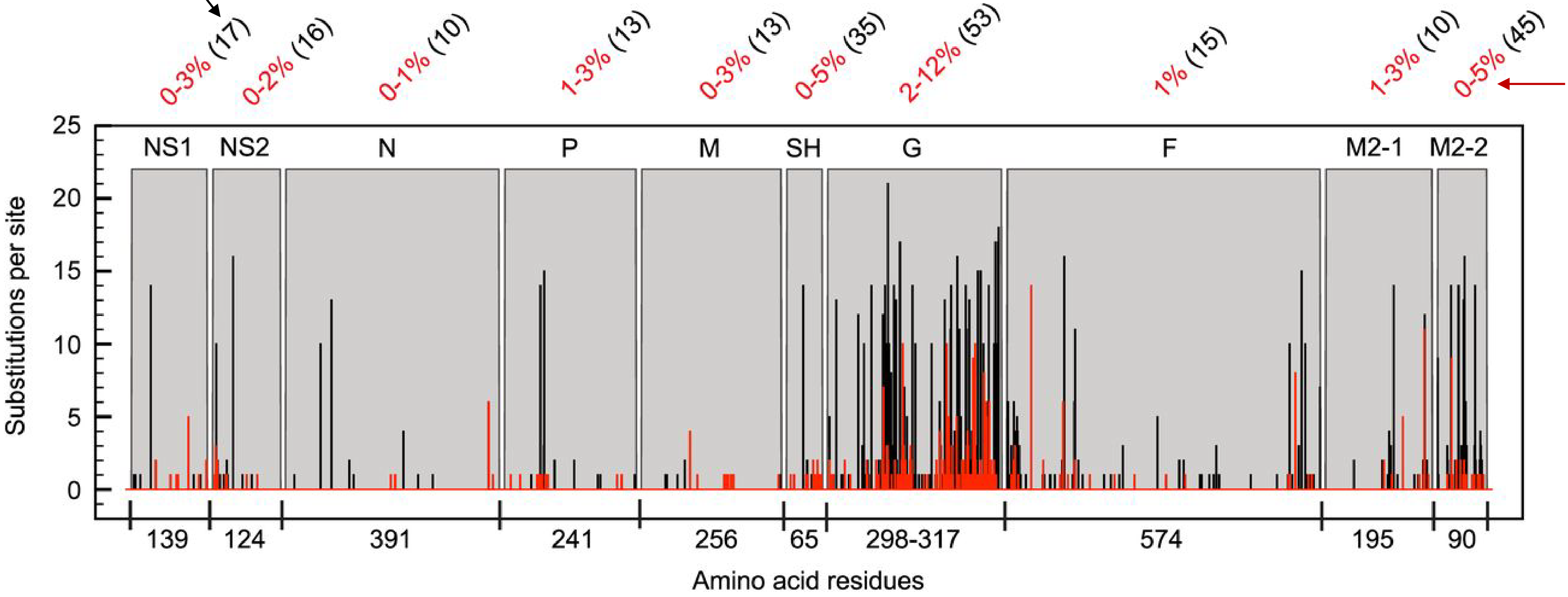


- Gene encoding G defines RSV A/B
- Heterogeneous sequence

- Two large mucin – like domains – antigen masking

RSV G gene is the most variable in the genome (F is more conserved)

(Percent sequence variability between A and B)



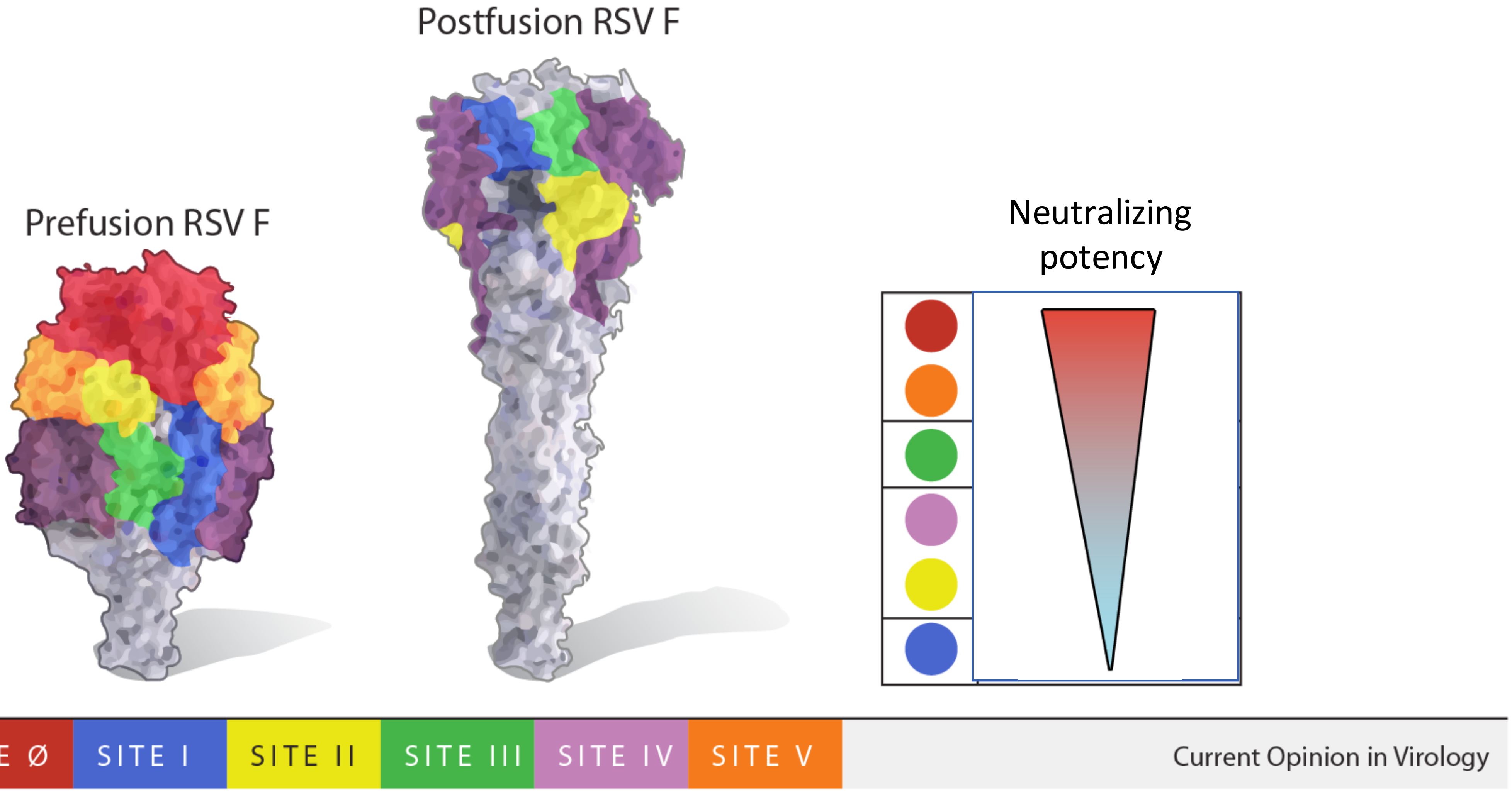
(Percent variability within each B protein)

RSV A

RSV B

Lydia Tan et al. J. Virol. 2013;87:8213-8226

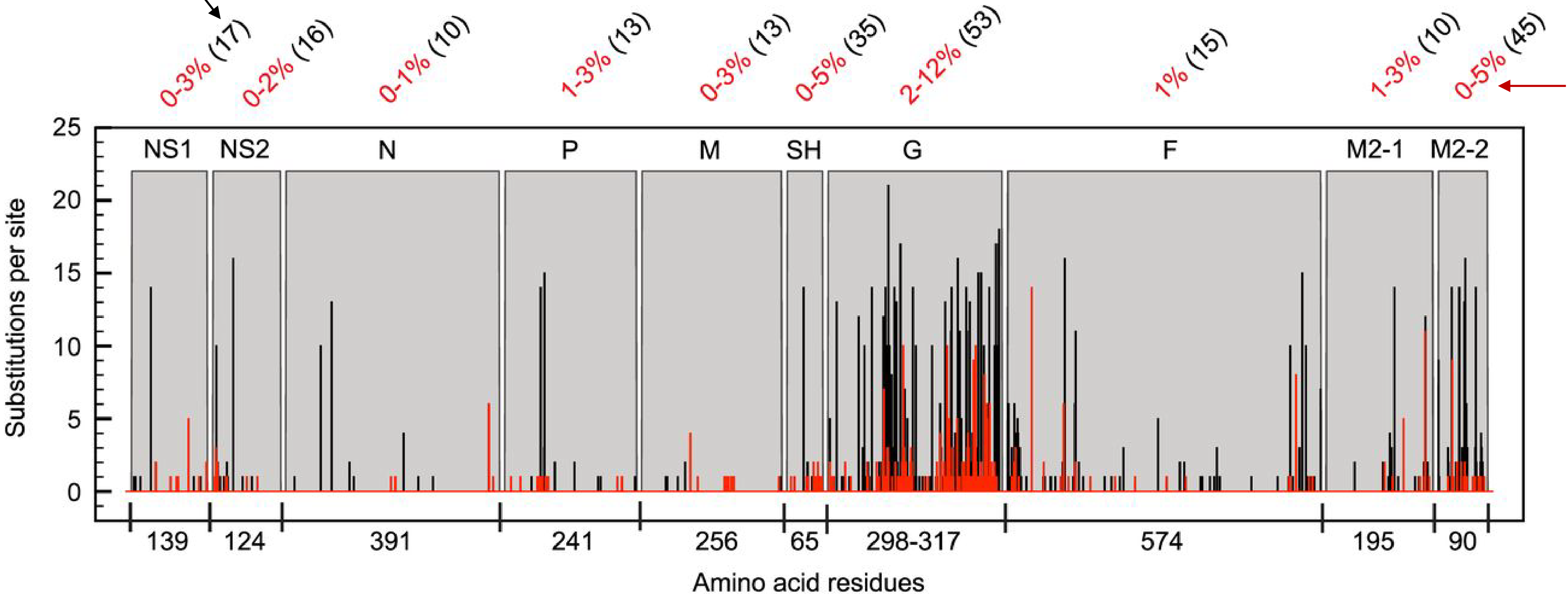
The fusion (F) protein exists in two or more structural forms exposes different antigenic regions



Graham B. Current Opinion in Virology. 23: 107-112. 2017.

RSV G gene is used to defined RSV genotypes

(Percent sequence variability between A and B)

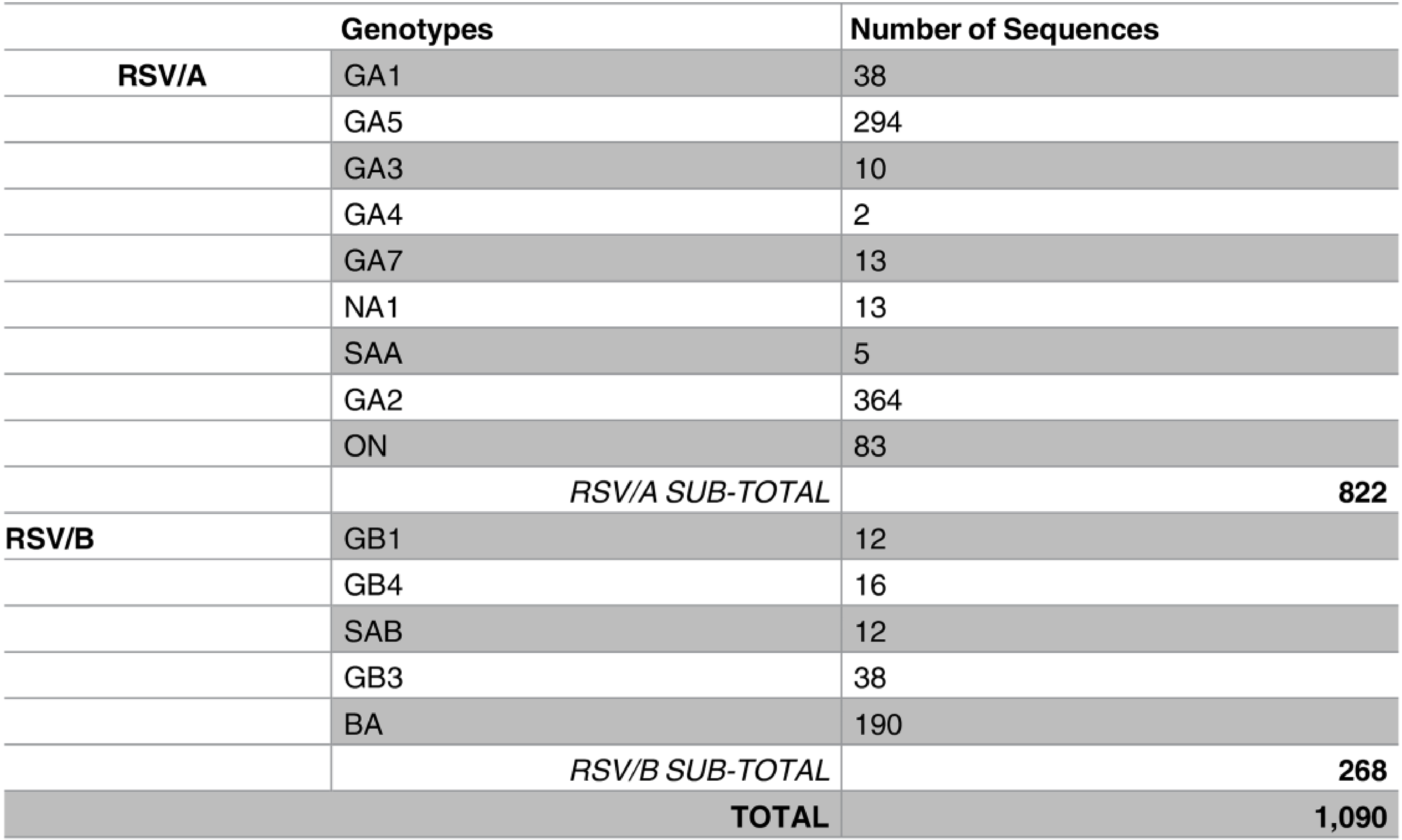


(Percent variability within each B protein)

RSV A
RSV B

Lydia Tan et al. J. Virol. 2013;87:8213-8226

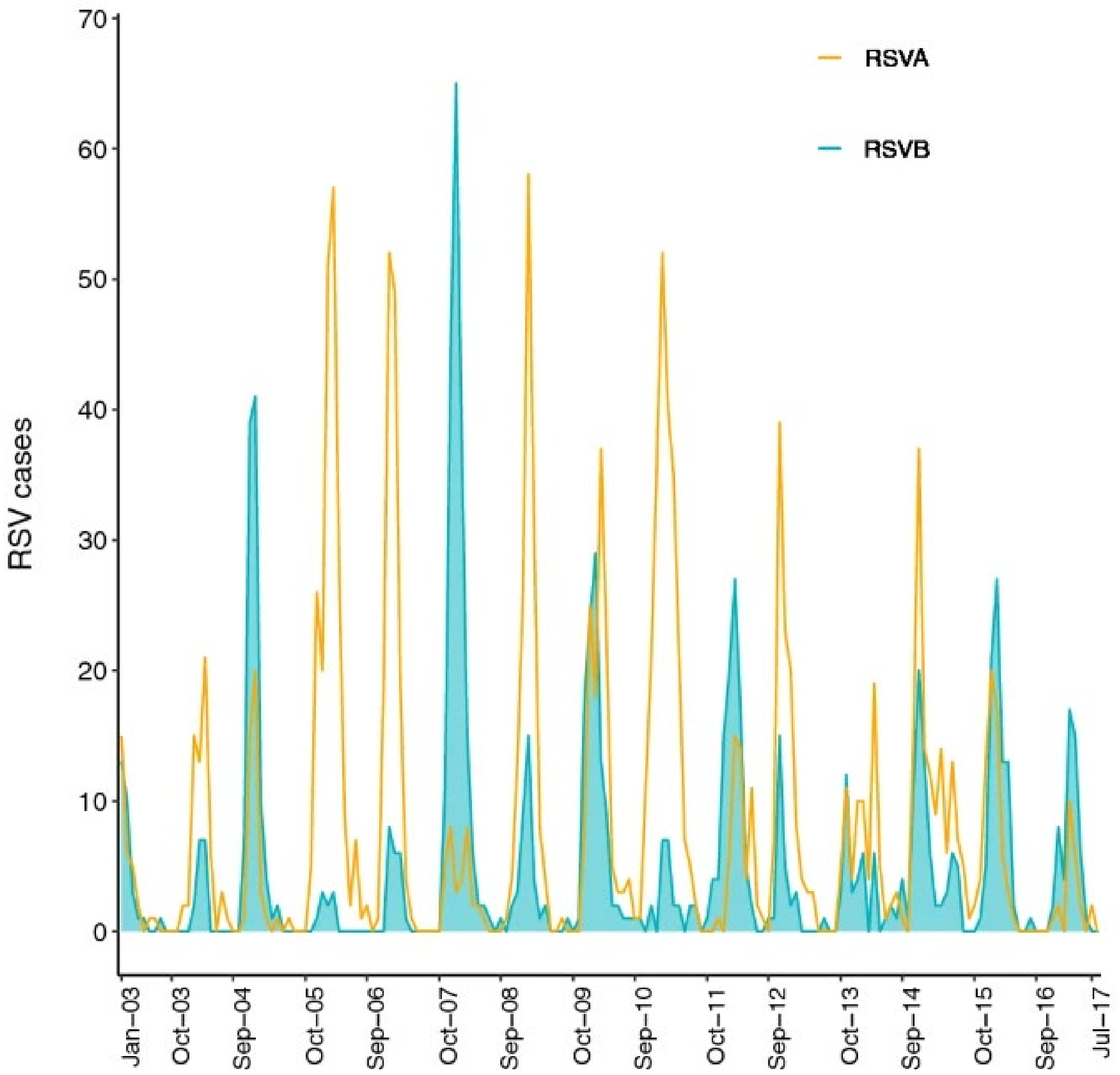
Number of RSV sequences in Genbank by genotype as of 2017



	Genotypes	**Number of Sequences**
RSV/A	GA1	38
	GA5	294
	GA3	10
	GA4	2
	GA7	13
	NA1	13
	SAA	5
	GA2	364
	ON	83
	RSV/A SUB-TOTAL	**822**
RSV/B	GB1	12
	GB4	16
	SAB	12
	GB3	38
	BA	190
	RSV/B SUB-TOTAL	**268**
	TOTAL	**1,090**

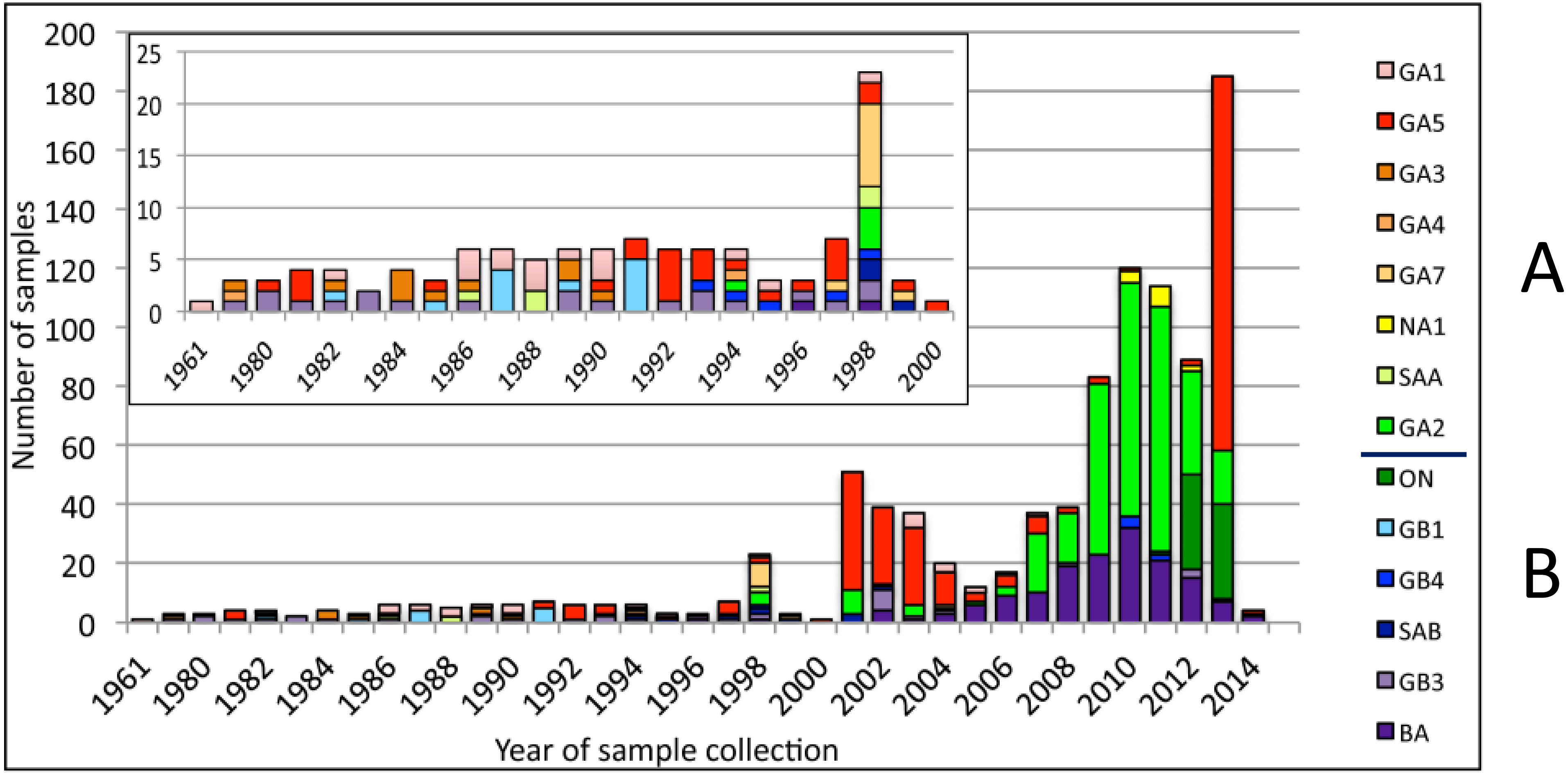
Hause et al. Plos One. 0175792. 2017

RSV A and B viruses co-circulate



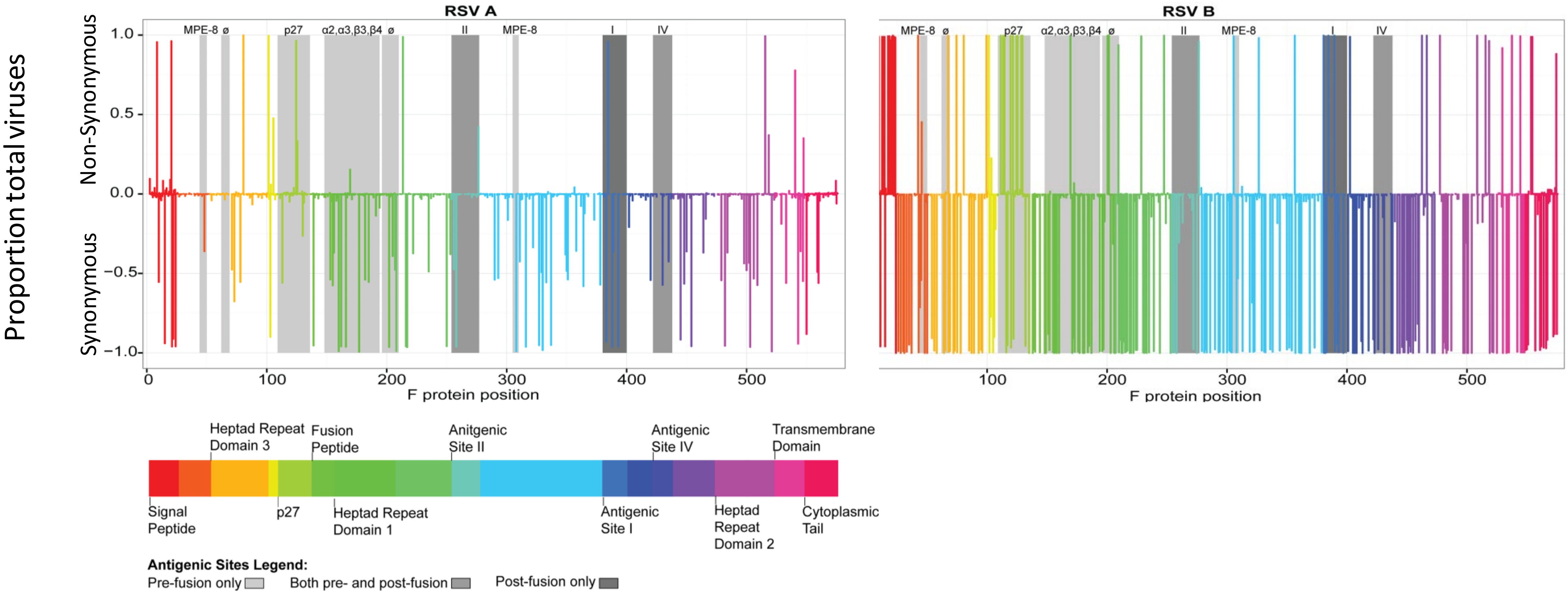
Kamau et al. *Scientific Reports*. 10: 21176 (202

RSV A and RSV B genotypes by year of sample collection



Hause et al. Plos One. 0175792. 2017

Some sequence variability is observed in RSV F, more observed in B viruses

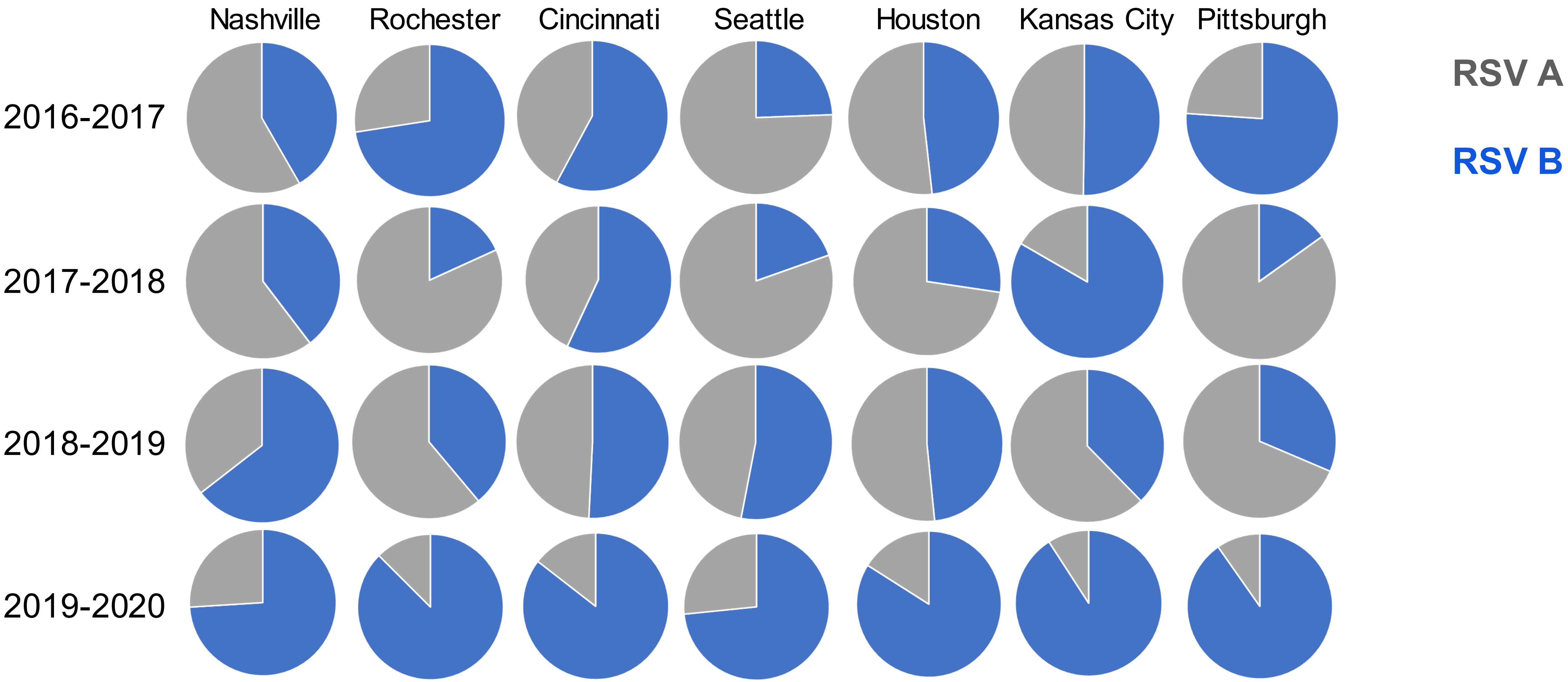


Hause et al. Plos One. 0175792. 2017

RSV-associated disease burden estimates from the New Vaccine Surveillance Network (NVSN)

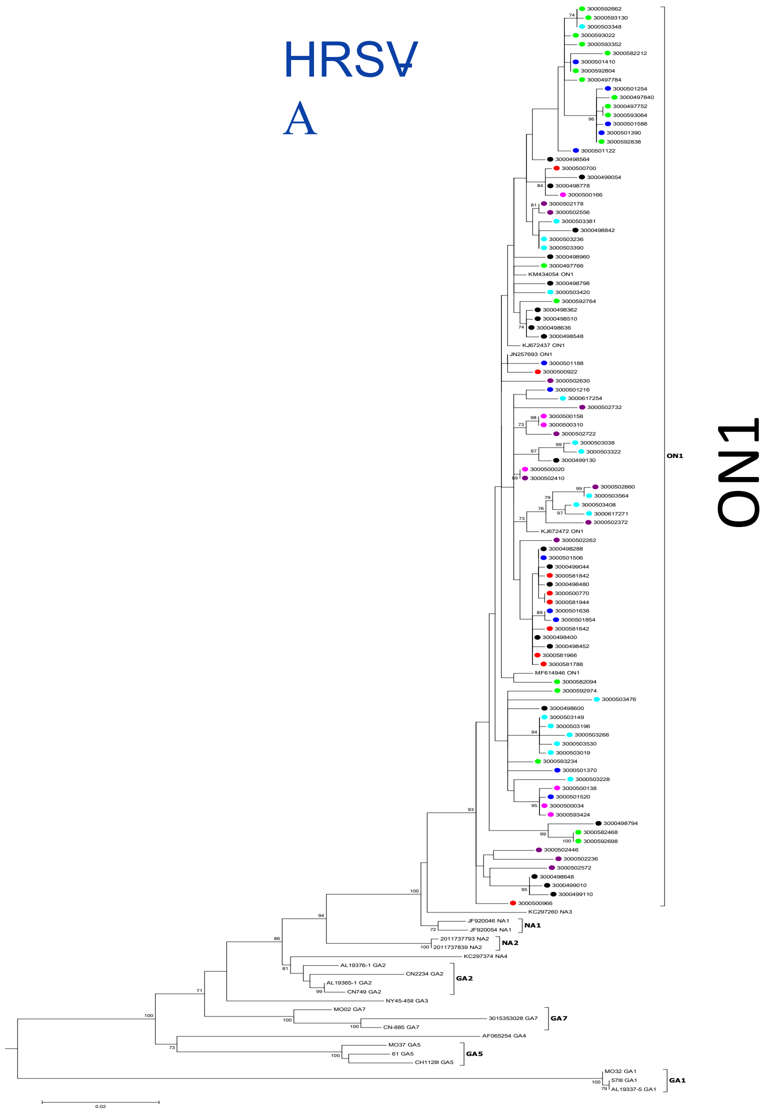
- Year-round acute respiratory illness (ARI) surveillance at 3 sites during 2000-2009
- Expanded to 7 sites during 2016-2021
- Prospective surveillance in inpatient, ED, outpatient clinics
- PCR testing for multiple respiratory viruses, including RSV
- Population denominators and market share used to estimate disease burden

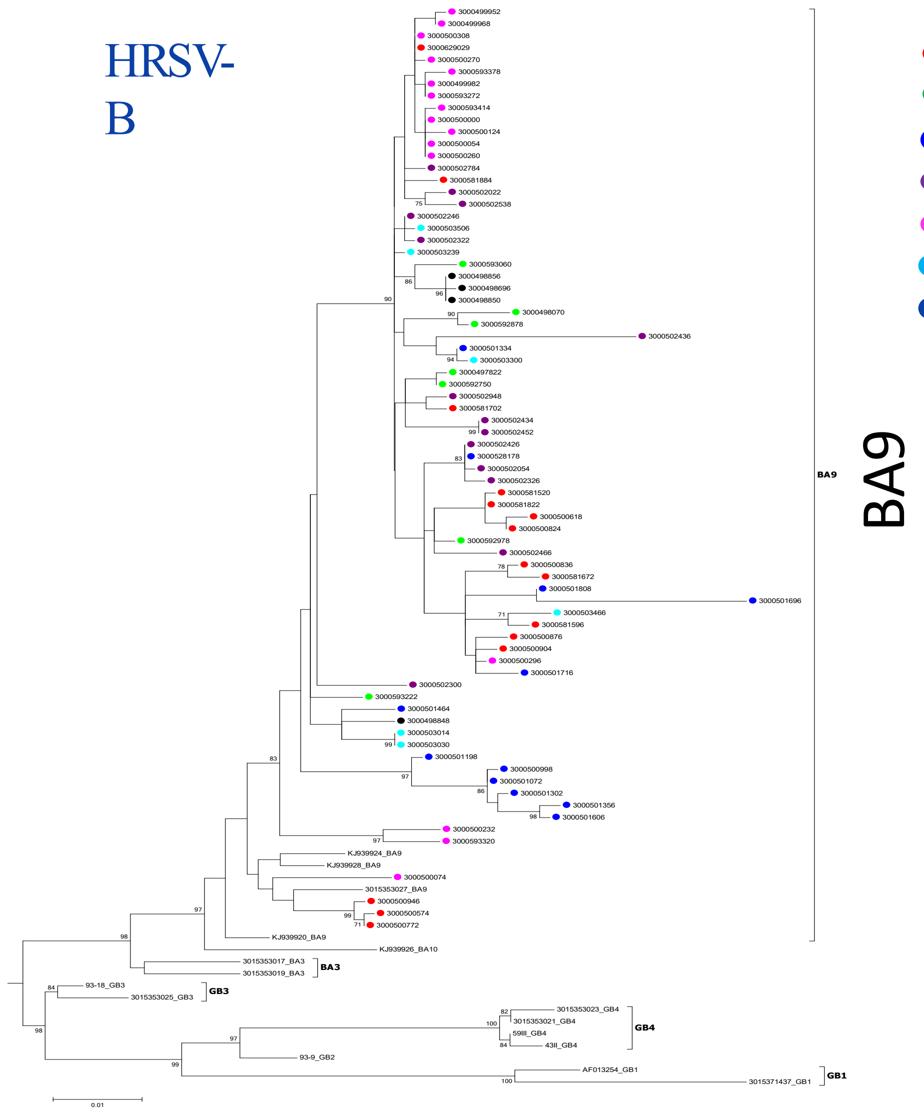
RSV A and B co-circulate, differ regionally, and from year-to-year



NVSN unpublished data

ON1 and BA9 genotypes dominated during the 15-16 season and did not differ between sites





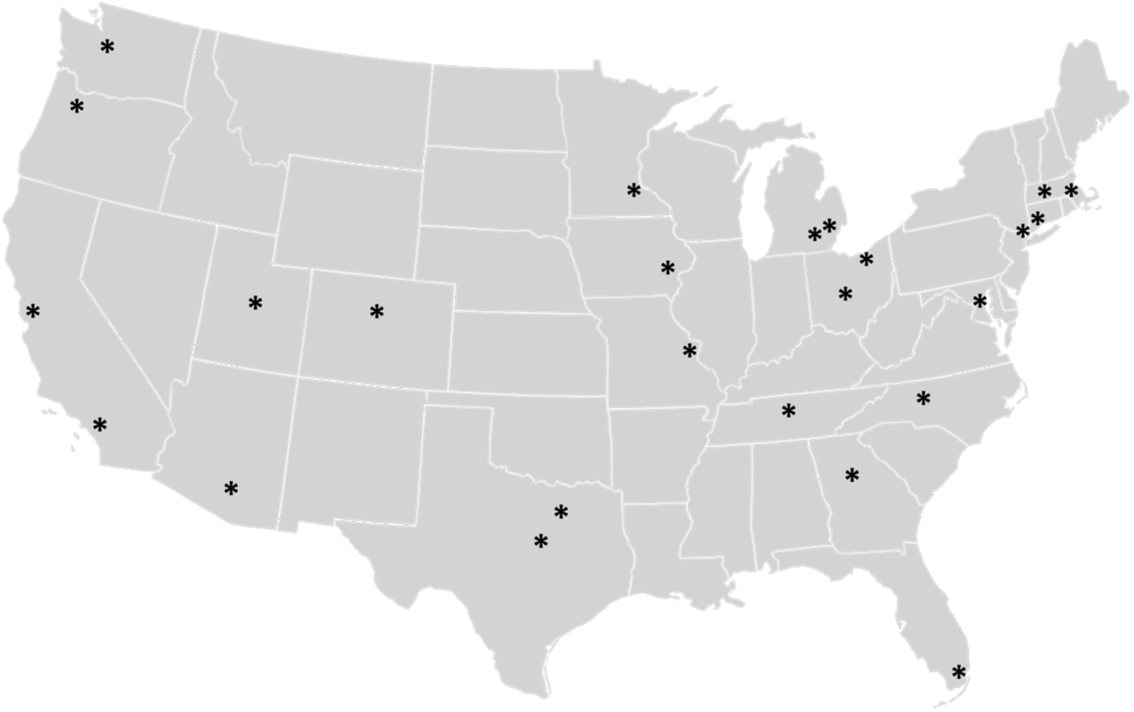
● Cincinnati
● Houston
● Kansas City
● Oakland
● Rochester
● Seattle
● Vanderbilt

CDC and NVSN unpublished data

IVY Network — 25 hospitals, 20 U.S. States

IVY

INVESTIGATING RESPIRATORY VIRUSES IN THE ACUTELY ILL



Summary

- F and G are targets of neutralizing antibodies with most potent antibodies directed against F
- RSV G is the most heterogenous gene and is used to define RSV genotypes
- There is less heterogeneity in RSV F, but more is observed in B viruses in comparison to A
- RSV A and B viruses co-circulate
- NVSN collects specimens that can be used for A/B surveillance as well as genomic and viral surveillance

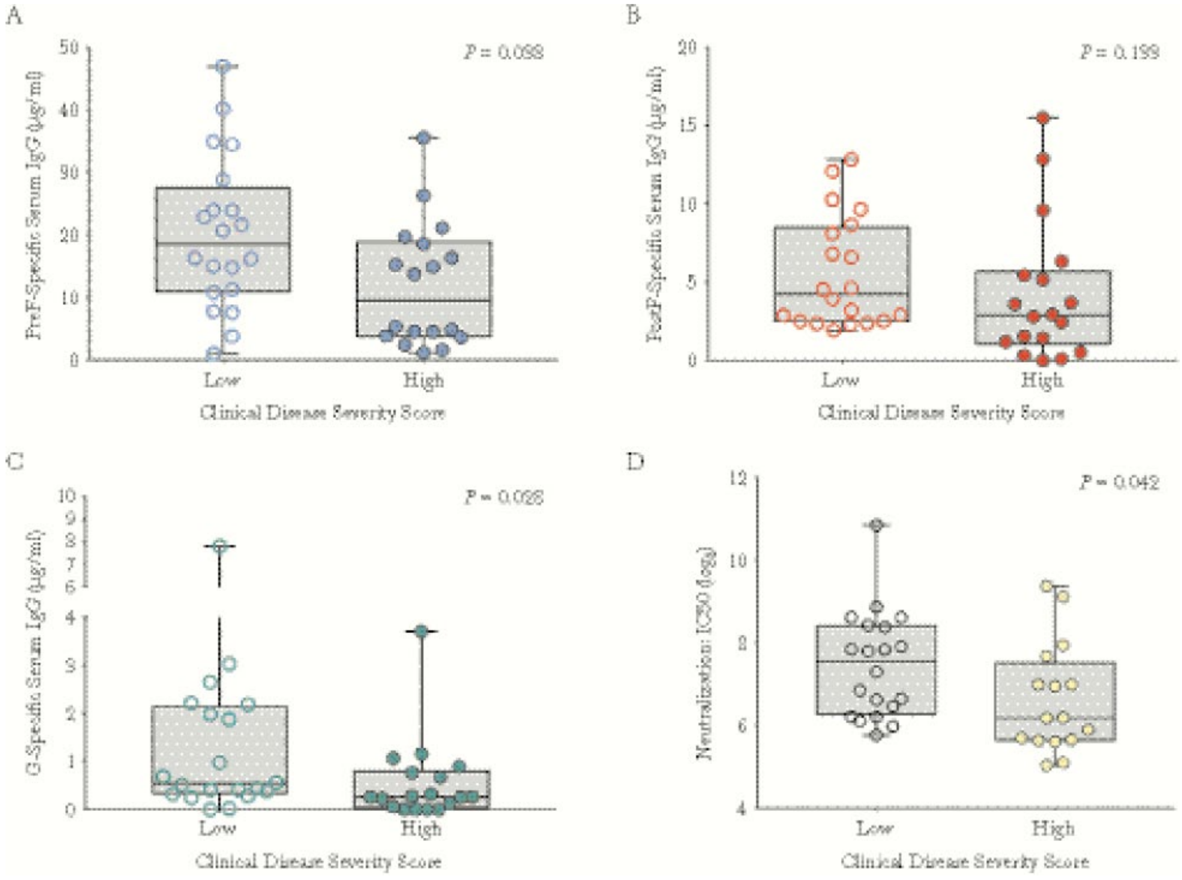
For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

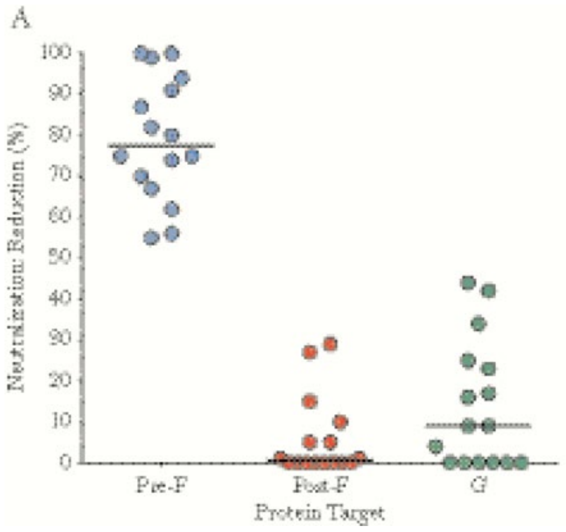
A-B subtypes co-circulated at differing percentages during U.S. 2015-2016 RSV season (NVSN)

Site	(RSV positive)	RSV-positive (%)	HRSV-A (%)	HRSV-B (%)	HRSV-A/B coinfection (%)
Cincinnati	162	64 (98.5)	24 (37.5)	40 (62.5)	0
Houston	280	83 (98.8)	61 (73.5)	20 (24.1)	2 (2.4)
Kansas City	137	50 (100.0)	25 (50)	25 (50)	0
Oakland	111	49 (98.0)	25 (51.0)	24 (49.0)	0
Rochester	108	50 (100.0)	9 (18.0)	41 (82.0)	0
Seattle	147	50 (100.0)	37 (74.0)	13 (26.0)	0
Vanderbilt	156	48 (96.0)	39 (81.3)	9 (18.8)	0
Total	1101	394 (98.7)	220 (55.8)	172 (43.7)	2 (0.5)

CDC and NVSN unpublished data

Most neutralizing activity is directed against pre-fusion F in infants hospitalized with RSV



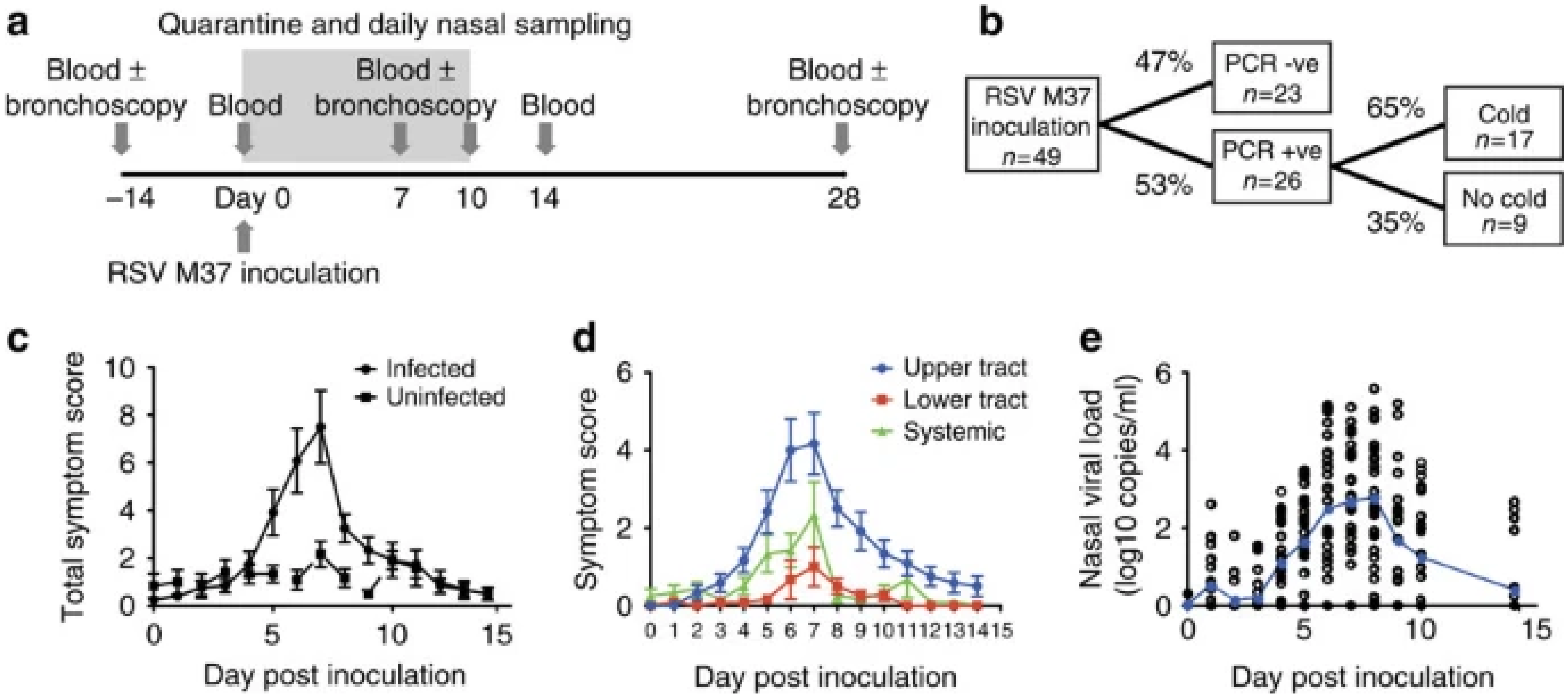


Capella et al. JID. 216: 1398-1406 (2017)

Contributors of anti-RSV G and RSV-F to immunity

- Neutralizing activity against both G and F in cell culture that is dependent on the cell culture model used
- Most potent antibodies are directed against F
- Use of prophylactic mAb in high-risk infants is proof-of-principal that high titers of anti-F antibody sufficient for protection against severe disease

Approximately half RSV A challenged adults became infected, and 65% of them had symptoms



Jozwik et al. Nature communications 6: 10224. (2015)

Conclusions from adult human challenge models

- Adults are susceptible to reinfection independent of antigenic change in virus
- Infection may be asymptomatic or symptomatic
- Protection against all infection (sterilizing) does not correlate with serum antibody titers, though limited by small numbers of participants
  - Protection did correlate with nasal IgA
  - Infection induced poor IgA memory B cell responses
- Protection against symptoms if participants became infected correlated with pre-existing virus-specific tissue resident memory CD8+ T cells