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RSV virology, strain variation, and surveillance measures

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Centers for Disease Control and Prevention

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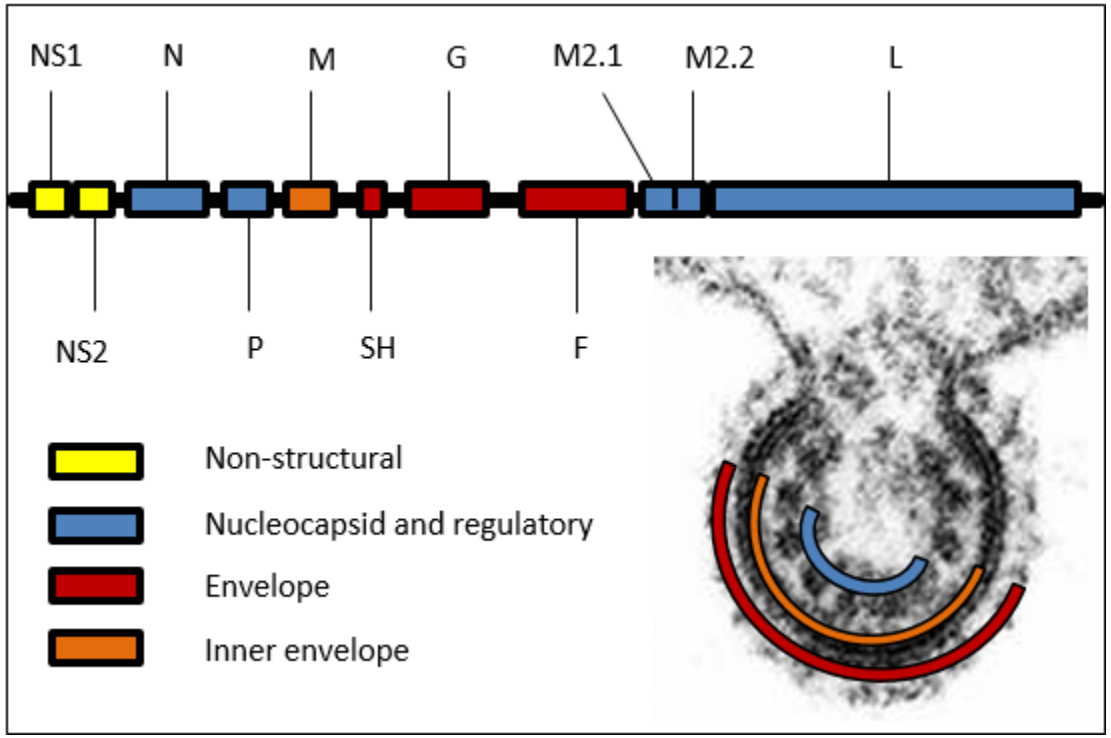
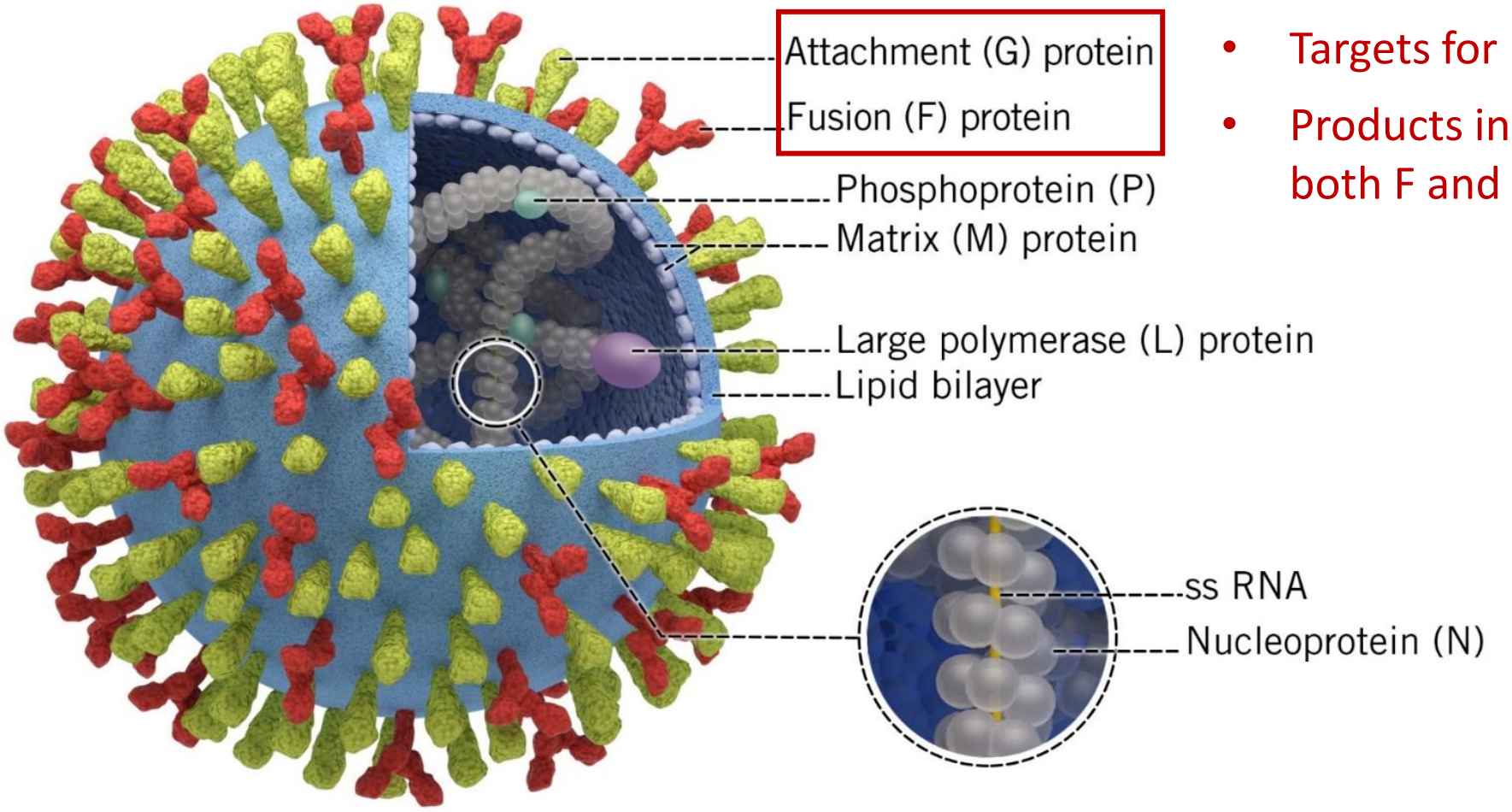
RSV genome



Respiratory Syncytial Virus (RSV) | British Society for Immunology

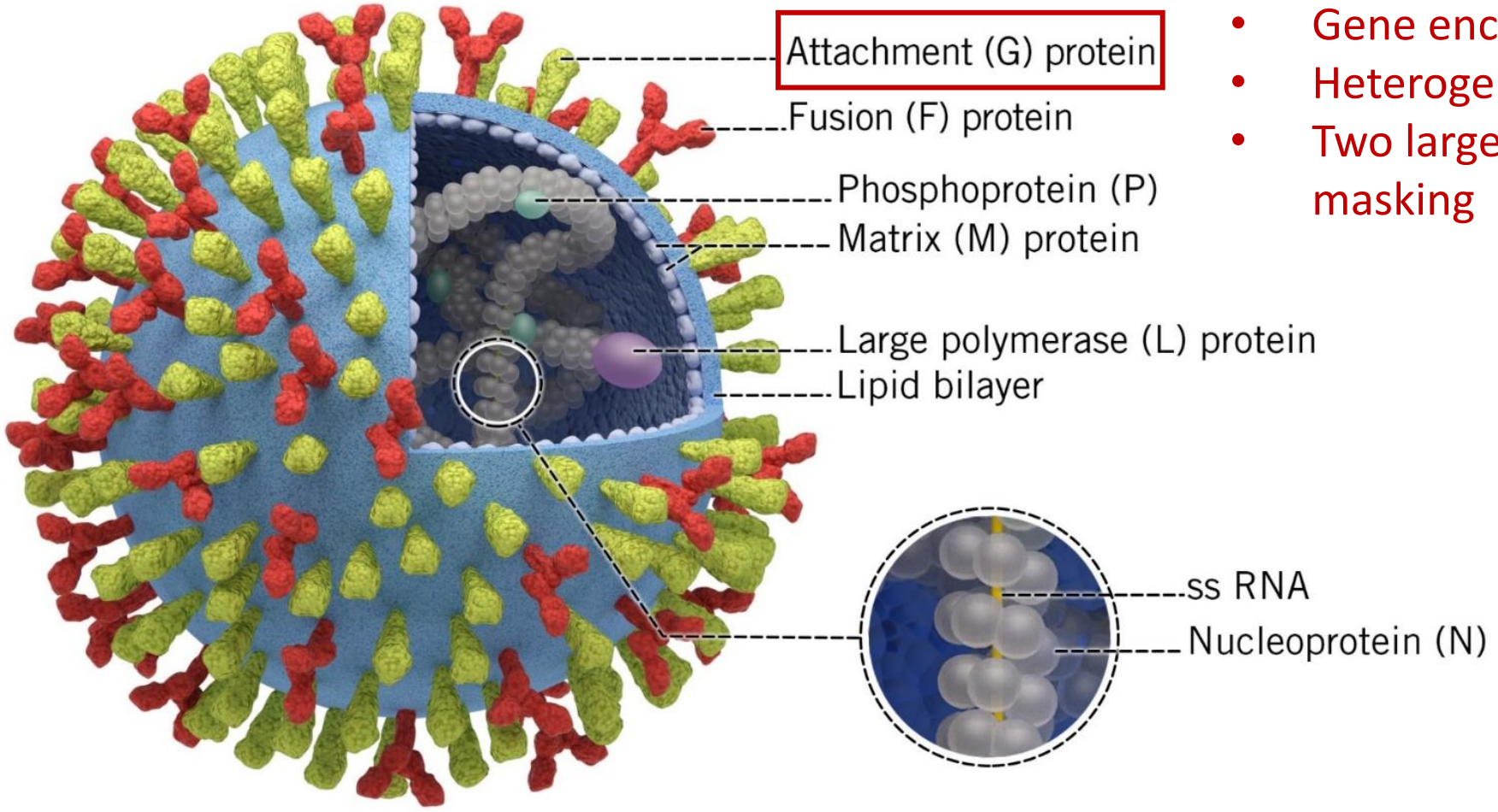
- Filamentous *Orthopneumovirus*
- 15.2 kbp genome
- Single stranded negative sense
- 11 viral proteins
- Divided into two subgroups / serotypes A and B
- RSV A and B co-circulate

RSV – virion structure



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

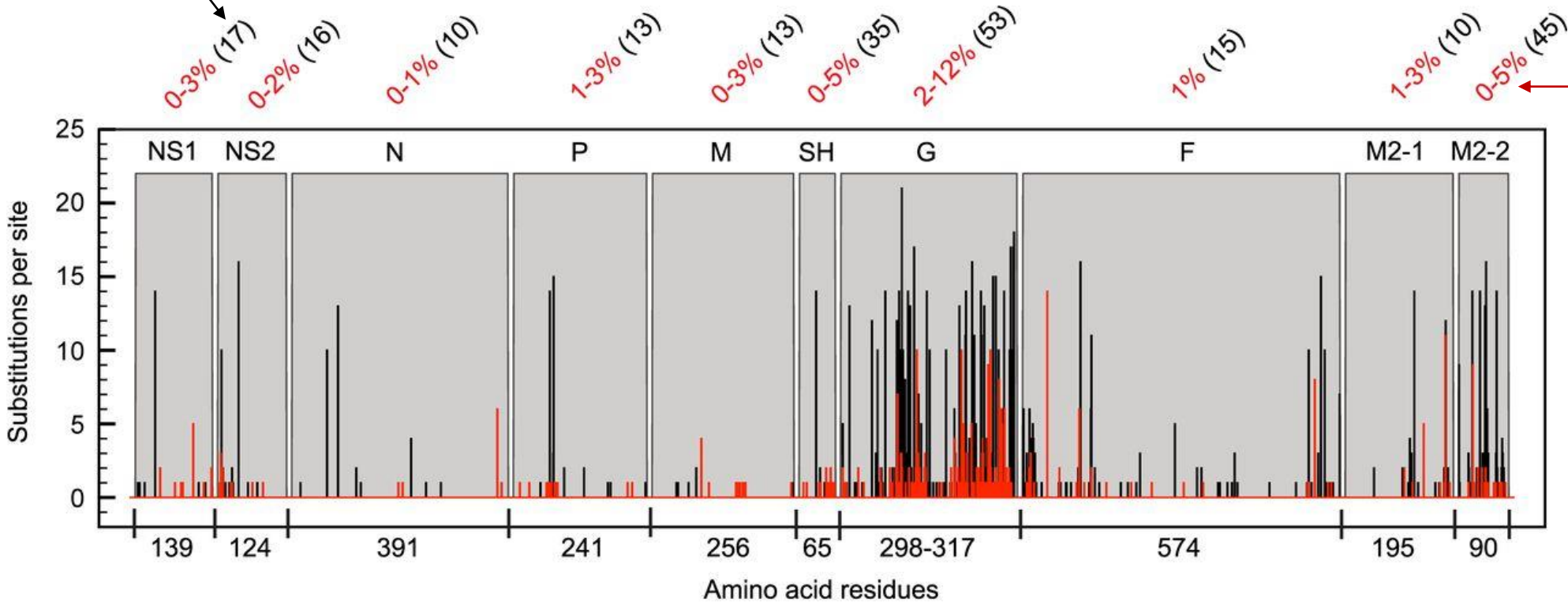
RSV Glycoprotein (G)



- 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)



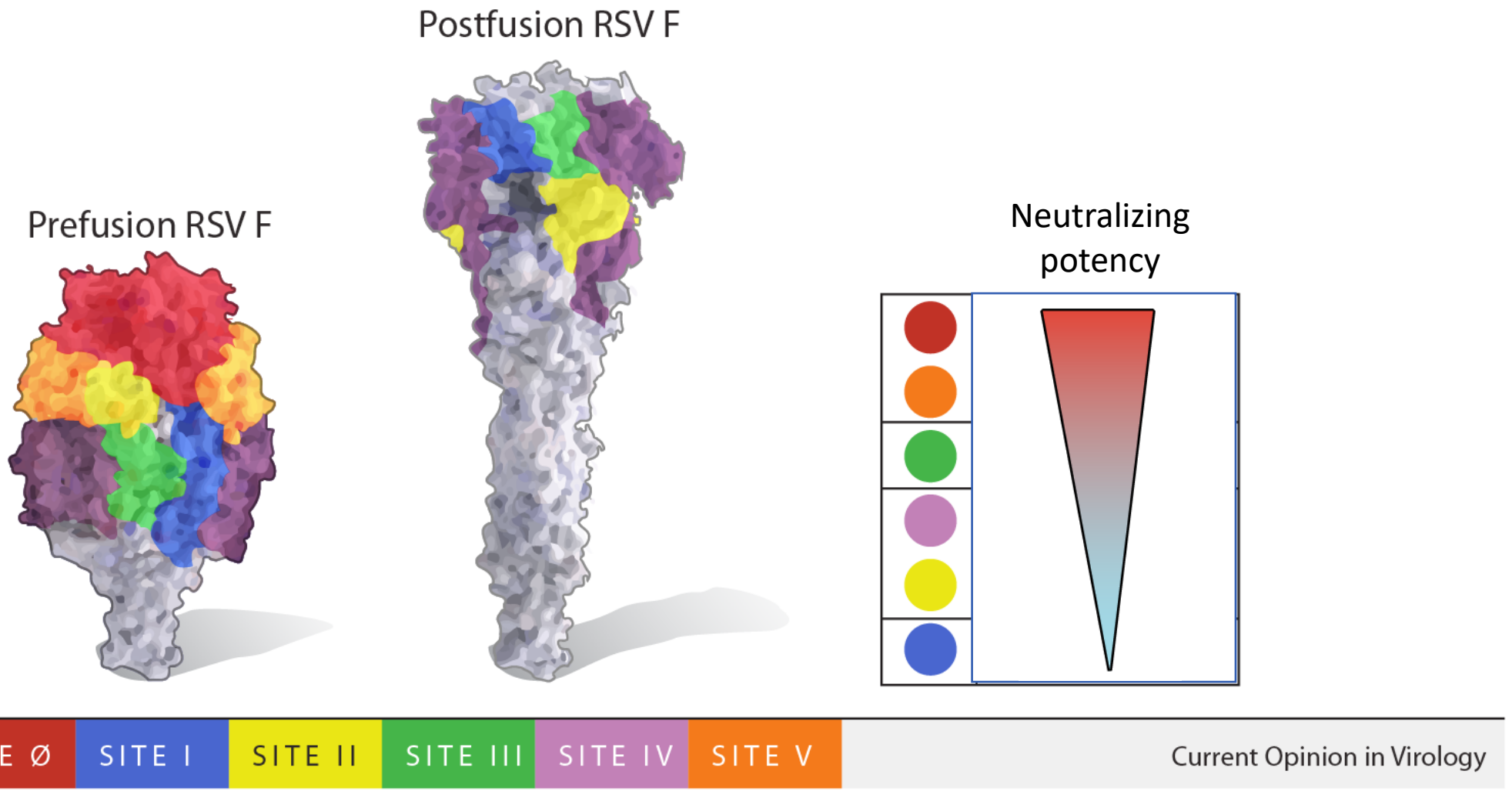
(Percent variability within each B protein)

RSV A

RSV B

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

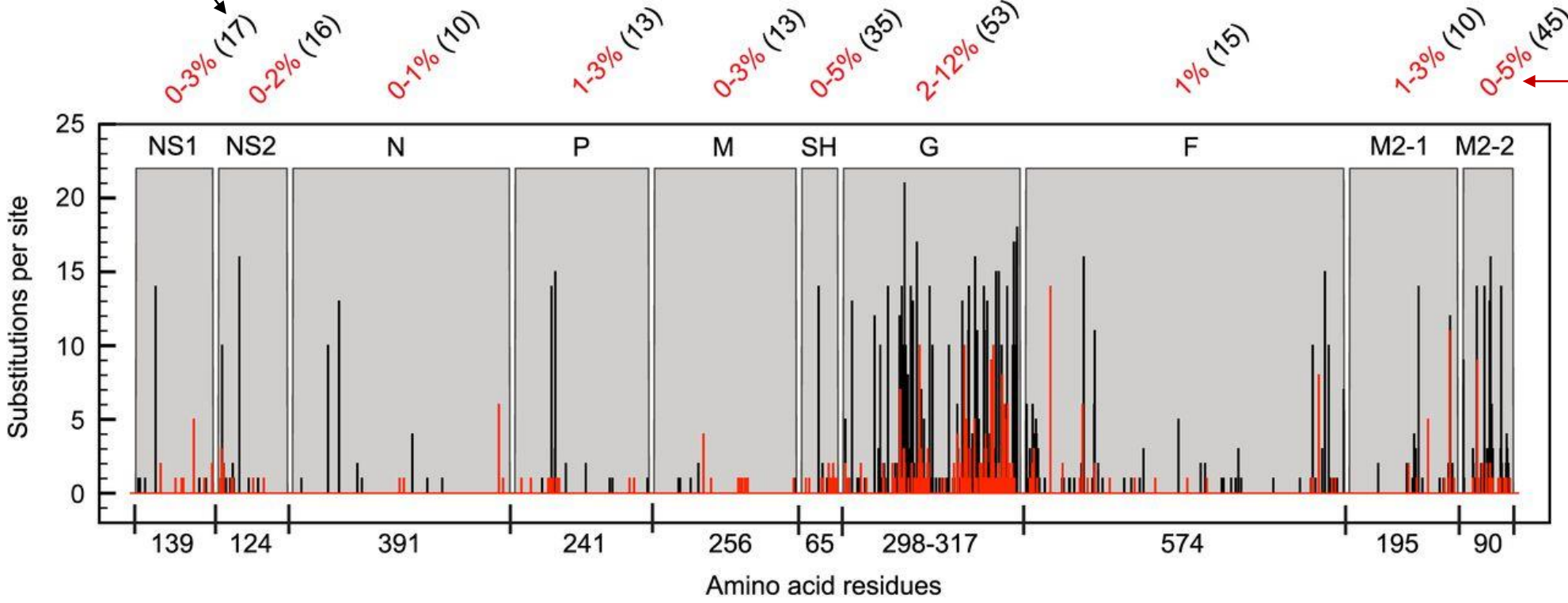
The fusion (F) protein exists in two or more structural forms exposes different antigenic regions



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

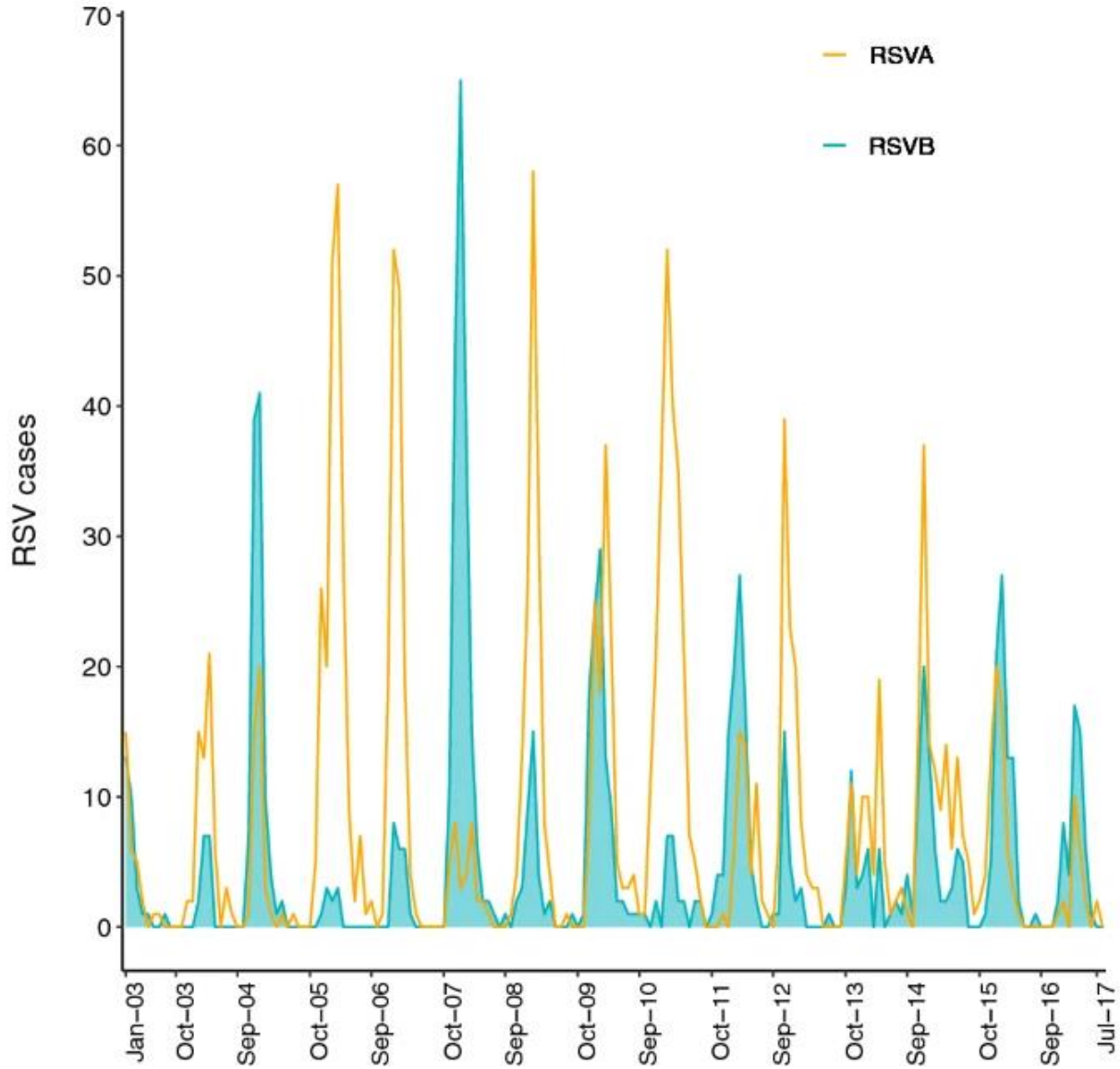
Lydia Tan et al. J. Virol. 2013;87:8213-8226

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**

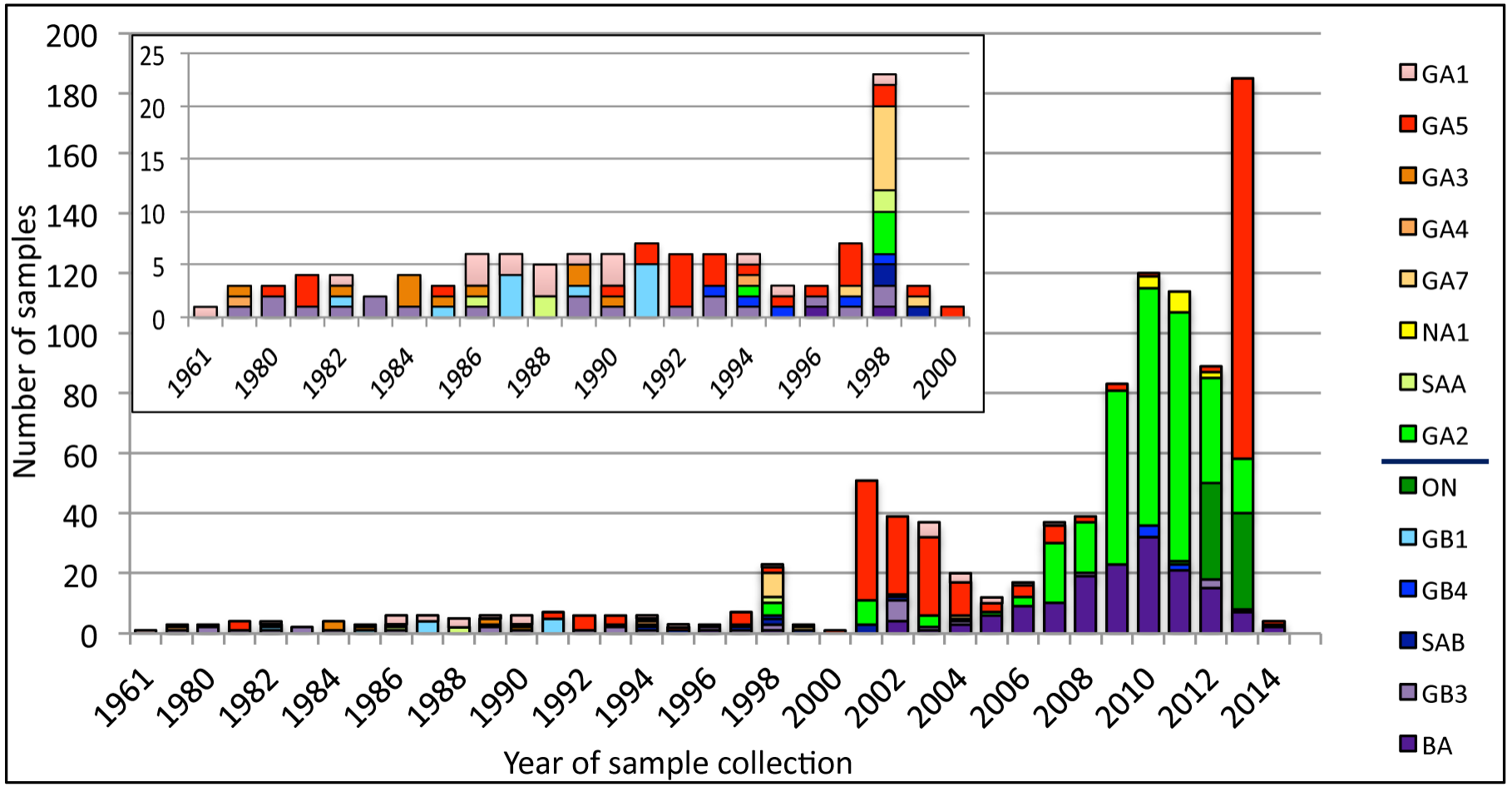
Hause et al. Plos One. 0175792. 2017

RSV A and B viruses co-circulate



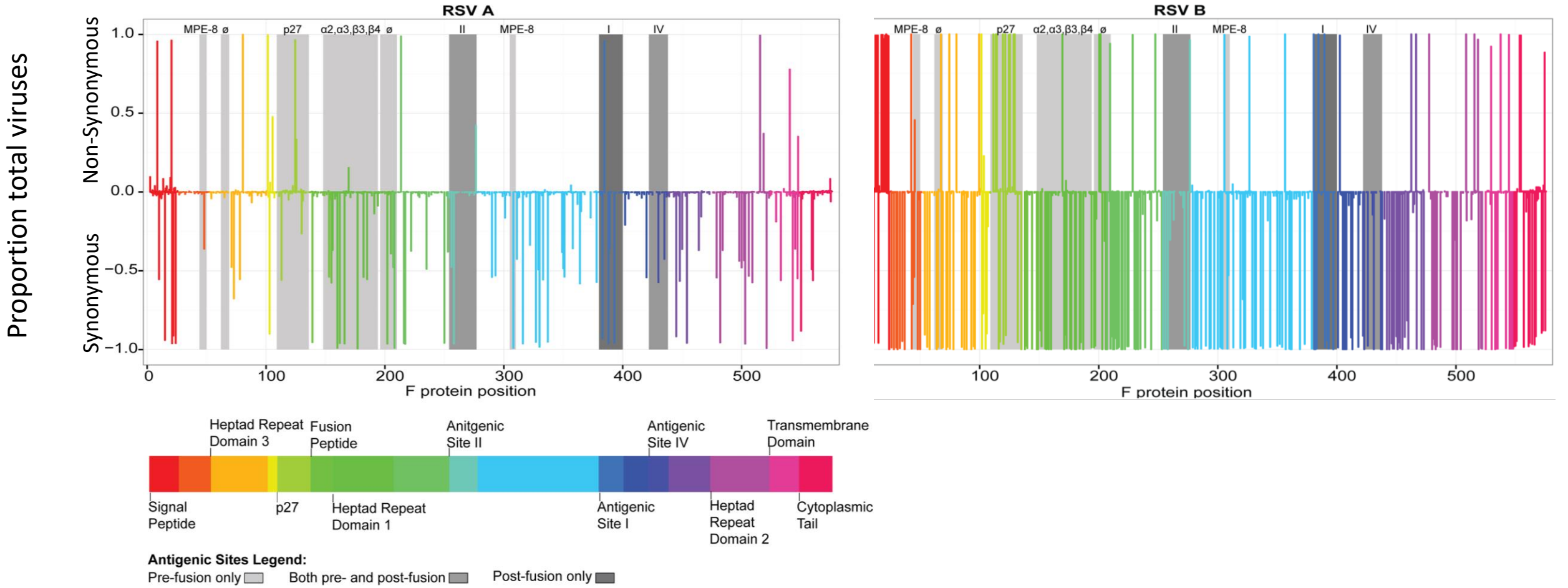
Kamau et al. *Scientific Reports*. 10: 21176 (2020)

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

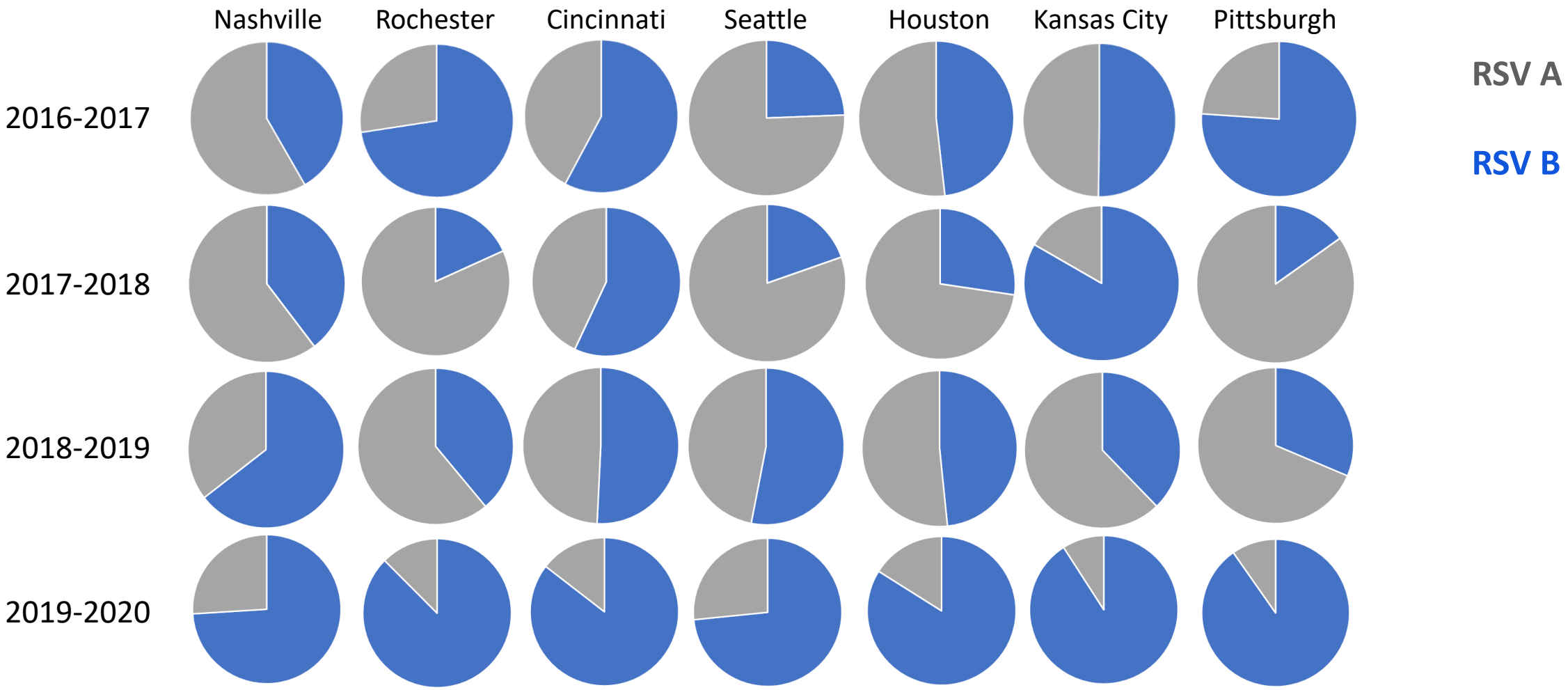


Hause et al. Plos One. 0175792. 2017

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

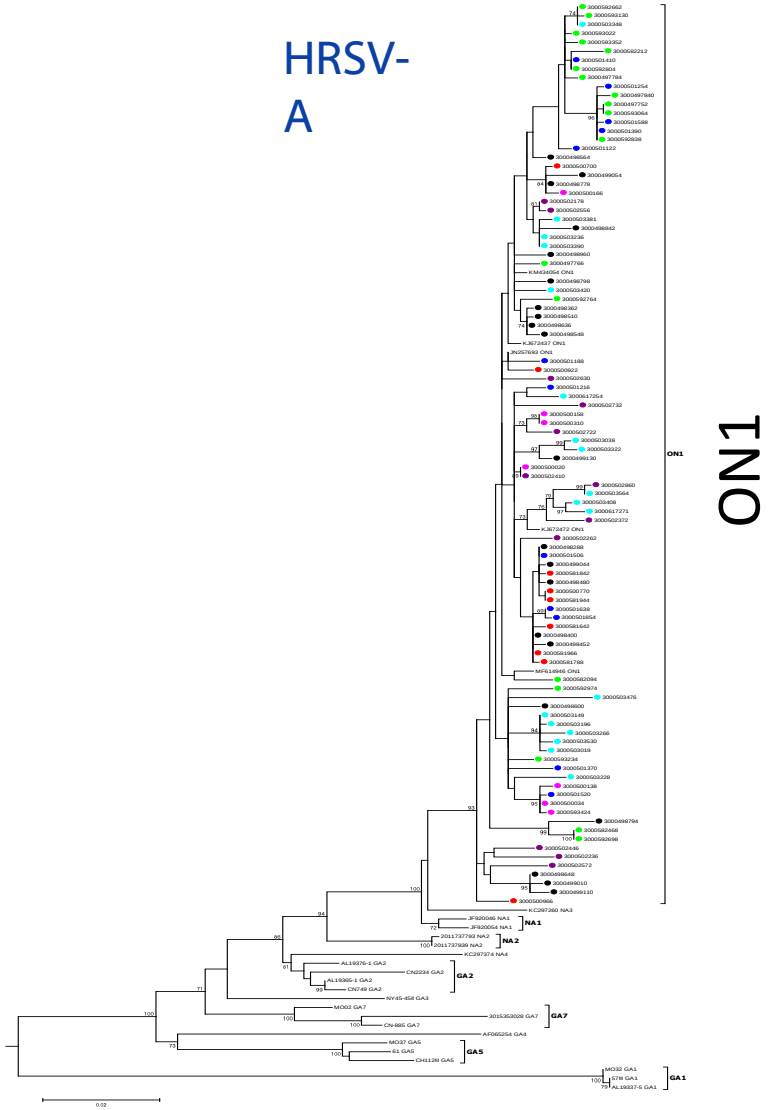
RSV A and B co-circulate, differ regionally, and from year-to-year



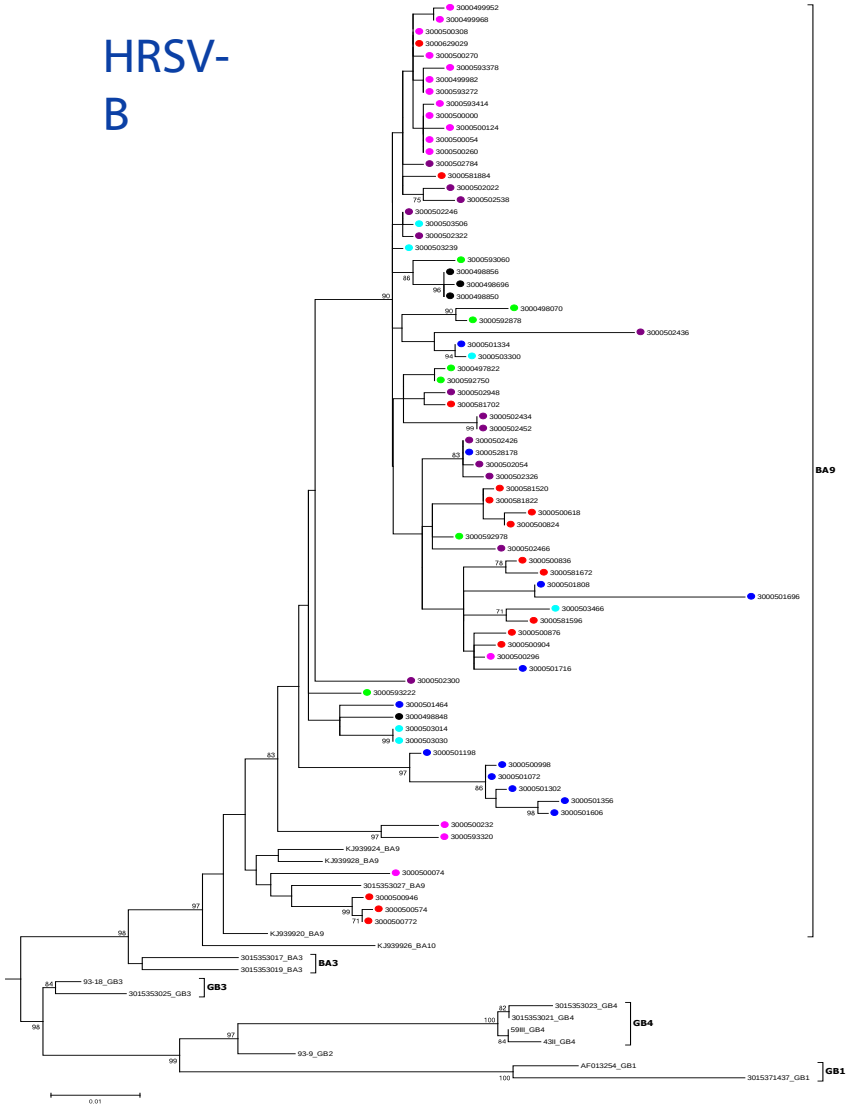
NVSN unpublished data

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

HRSV-A



HRSV-B



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

CDC and NVSN unpublished data

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

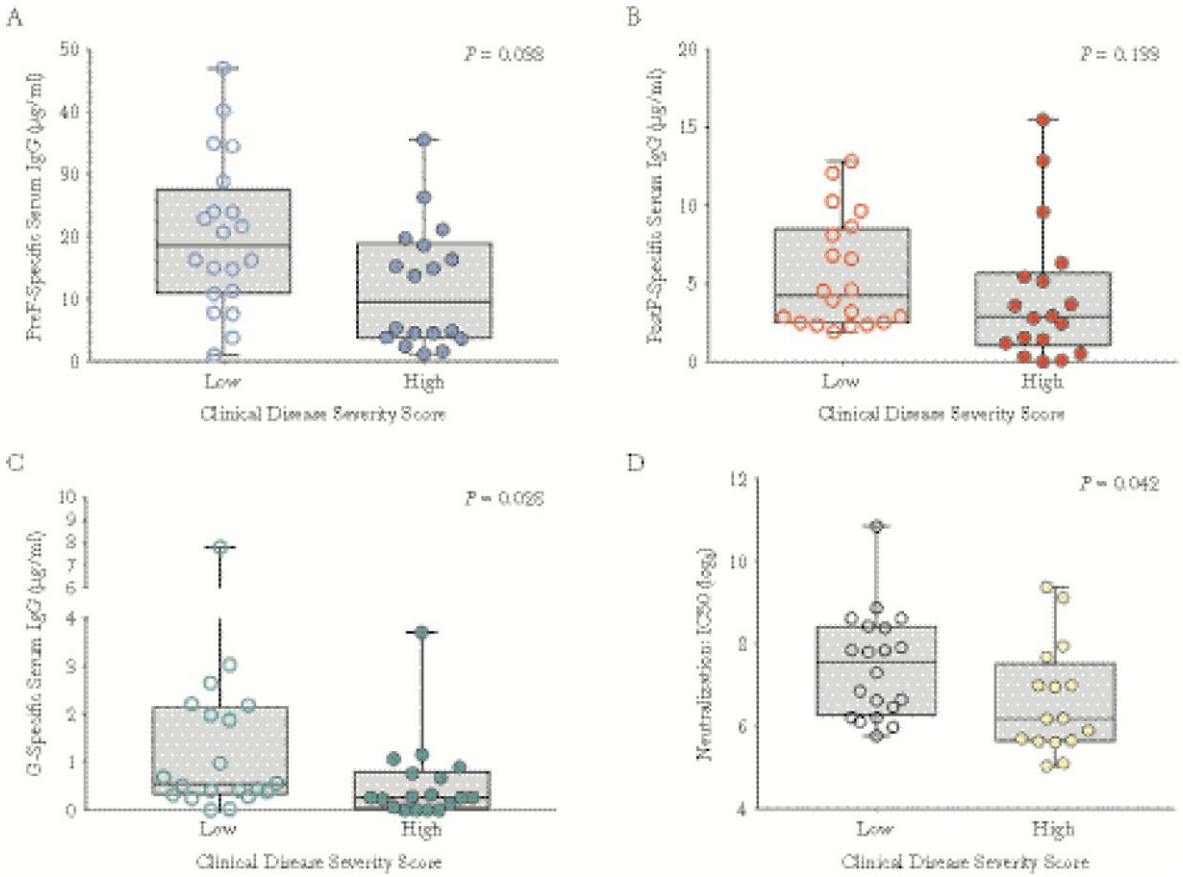
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

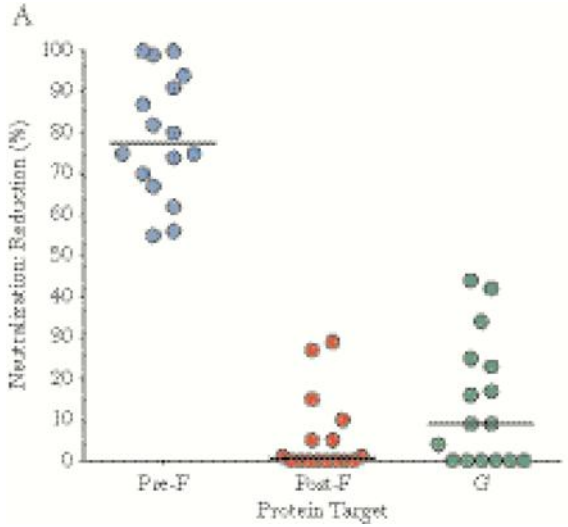
A-B subtypes co-circulated at differing percentages during U.S. 2015-2016 RSV season (NVSN)

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



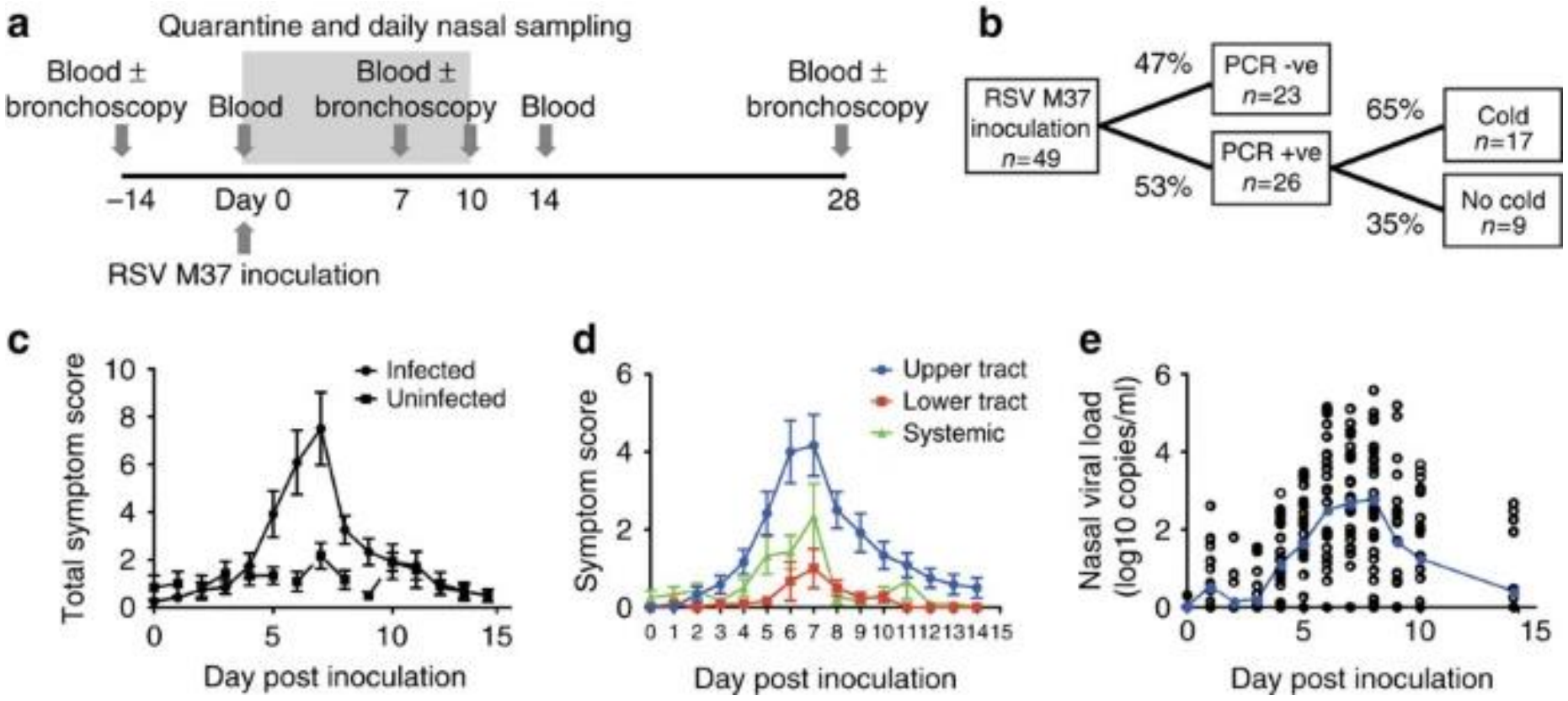


Capella et al. JID. 216: 1398-1406 (2017)

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