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# RSV virology, strain variation, and surveillance measures

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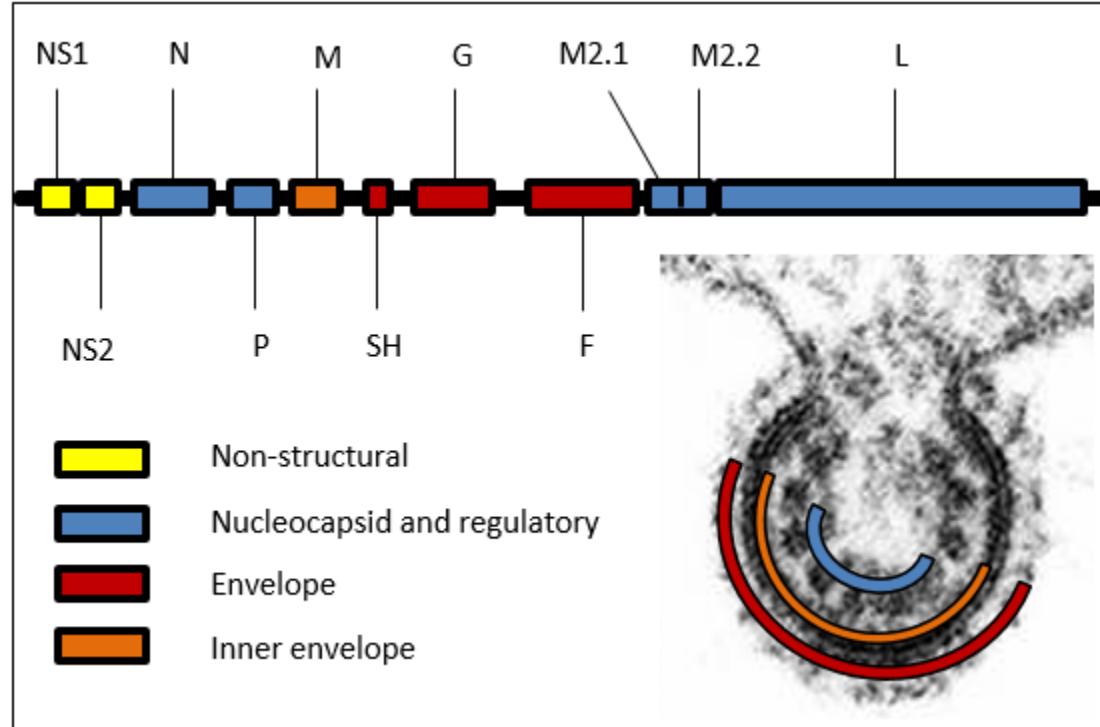
**Chief (acting) Laboratory Branch**

**Coronaviruses and Other Respiratory Viruses Division**

**Centers for Disease Control and Prevention**

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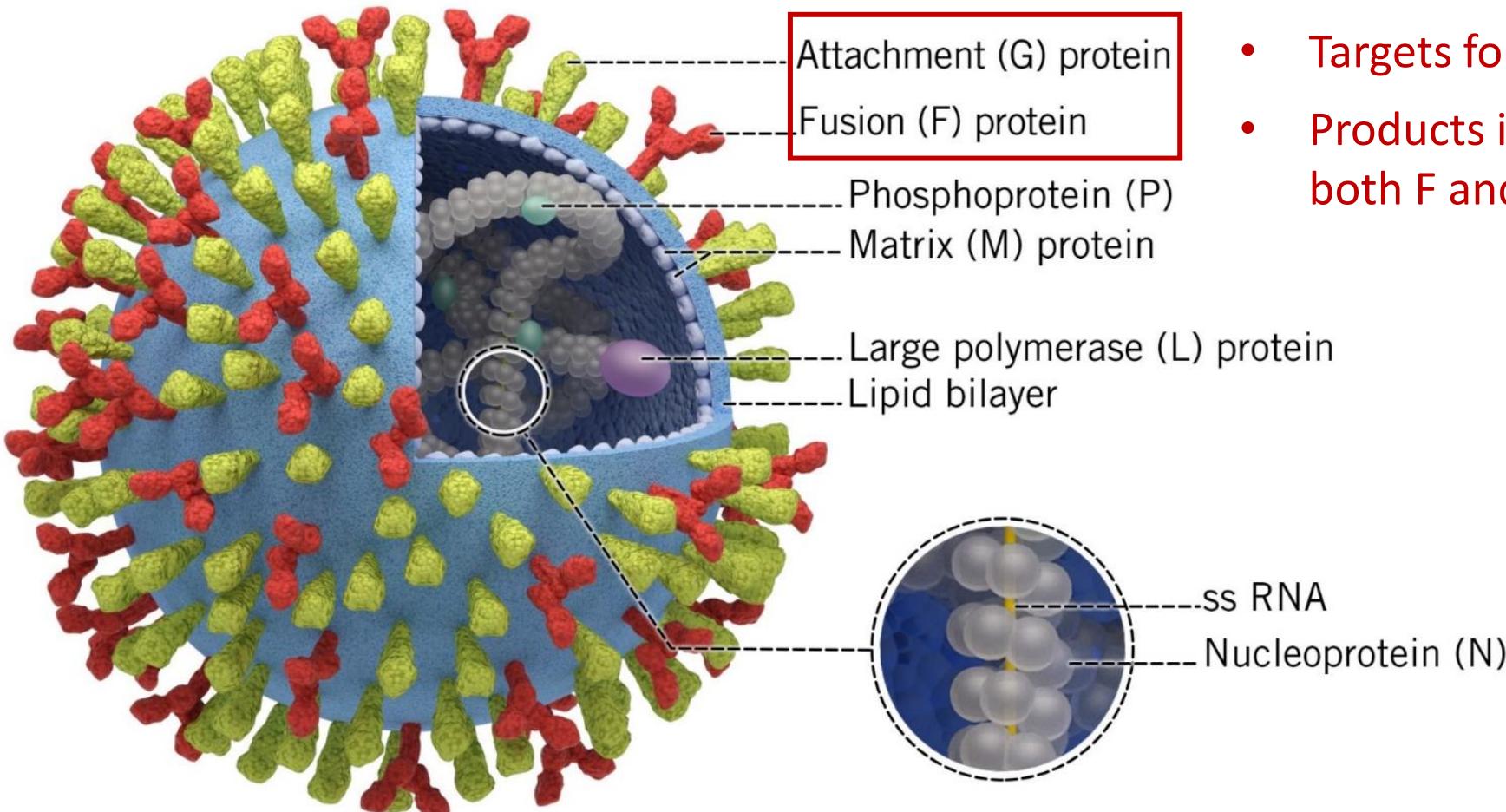
# RSV genome



[Respiratory Syncytial Virus \(RSV\) | British Society for Immunology](#)

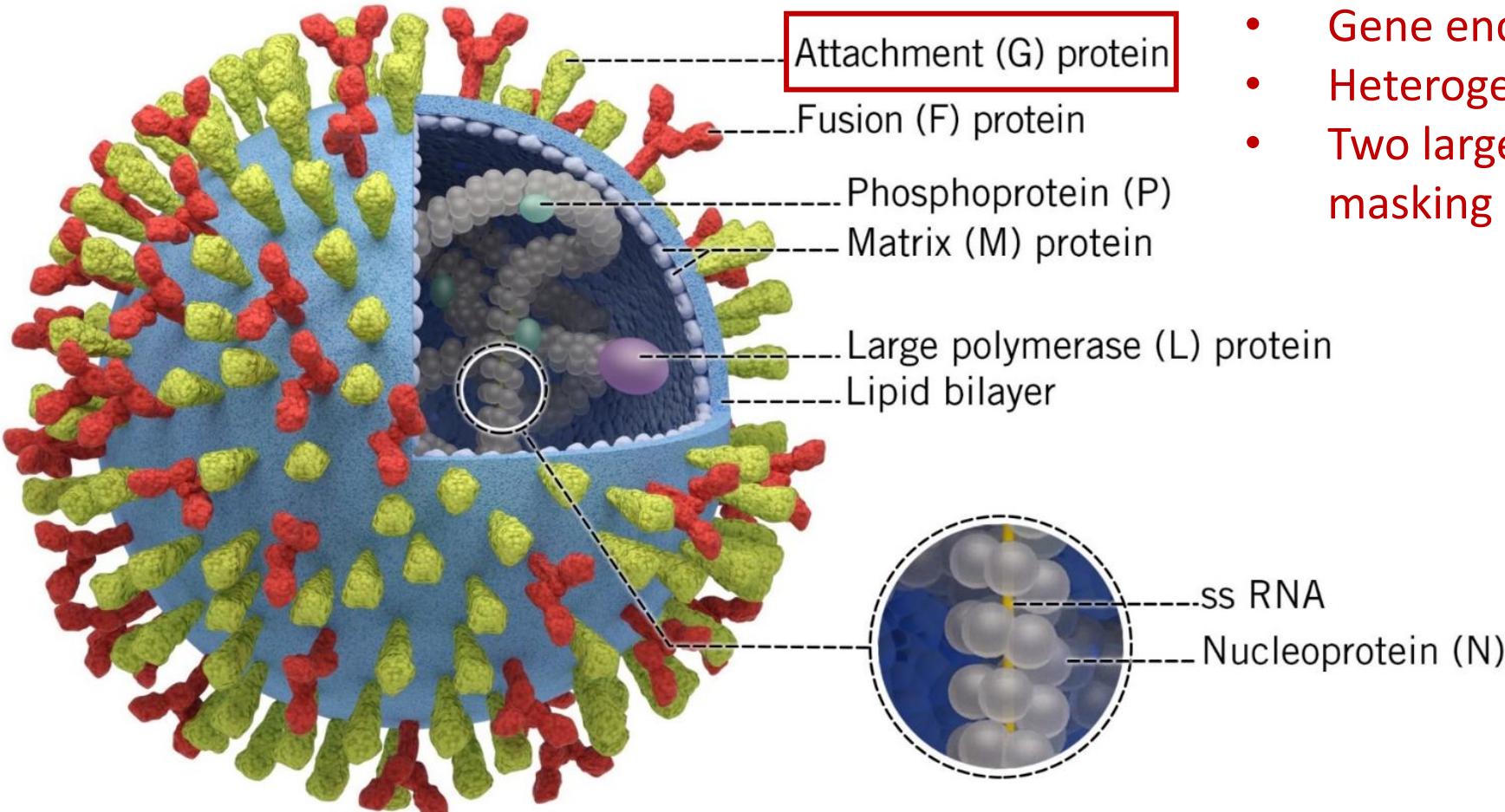
- Filamentous *Orthopneumovirus*
- 15.2 kbp genome
- Single stranded negative sense
- 11 viral proteins
- Divided into two subgroups / serotypes A and B
- RSV A and B co-circulate

# RSV – virion structure



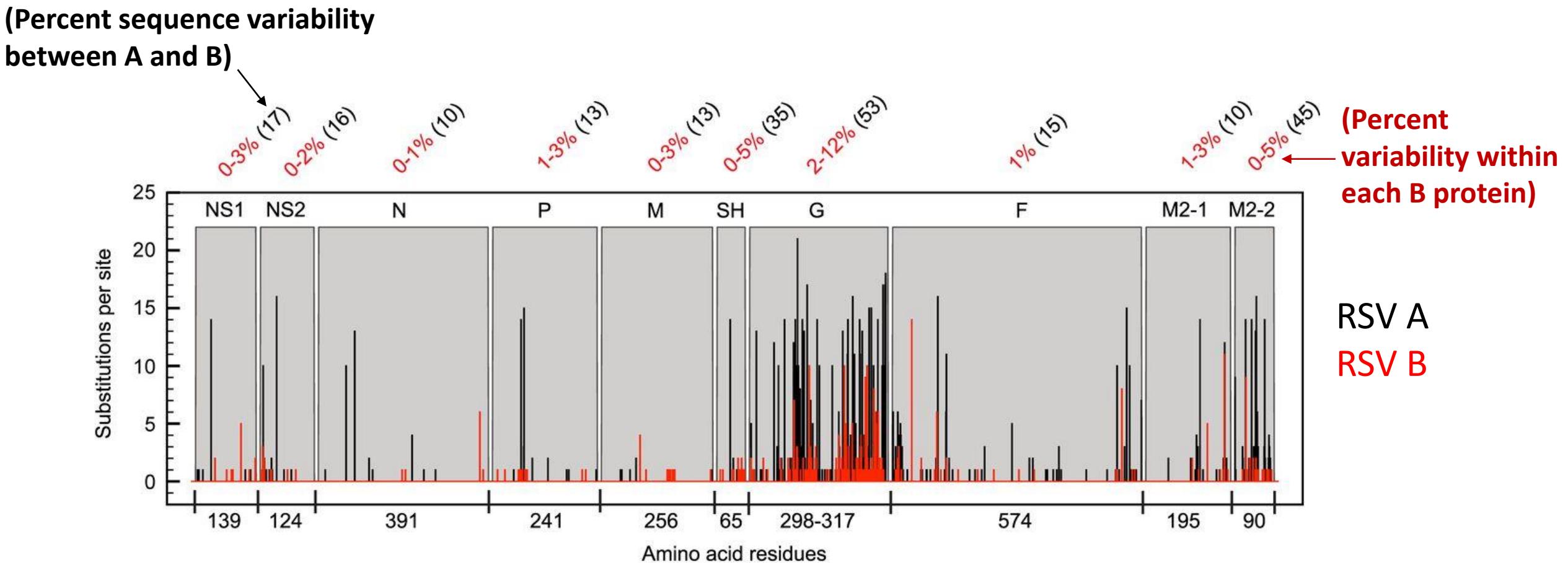
- Targets for neutralizing antibodies
- Products in target F alone or have both F and G

# RSV Glycoprotein (G)

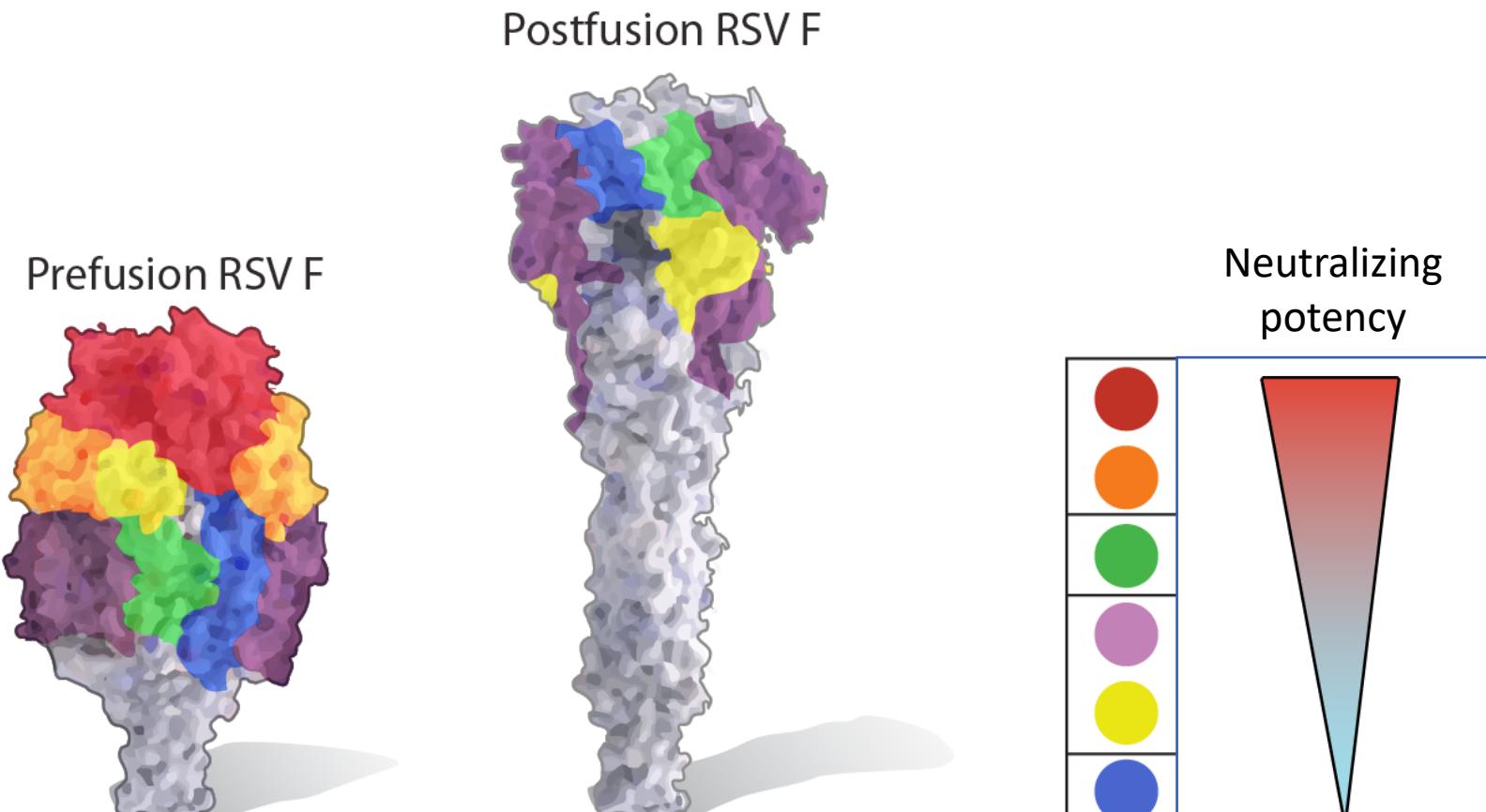


- Gene encoding G defines RSV A/B
- Heterogeneous sequence
- Two large mucin – like domains – antigen masking

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



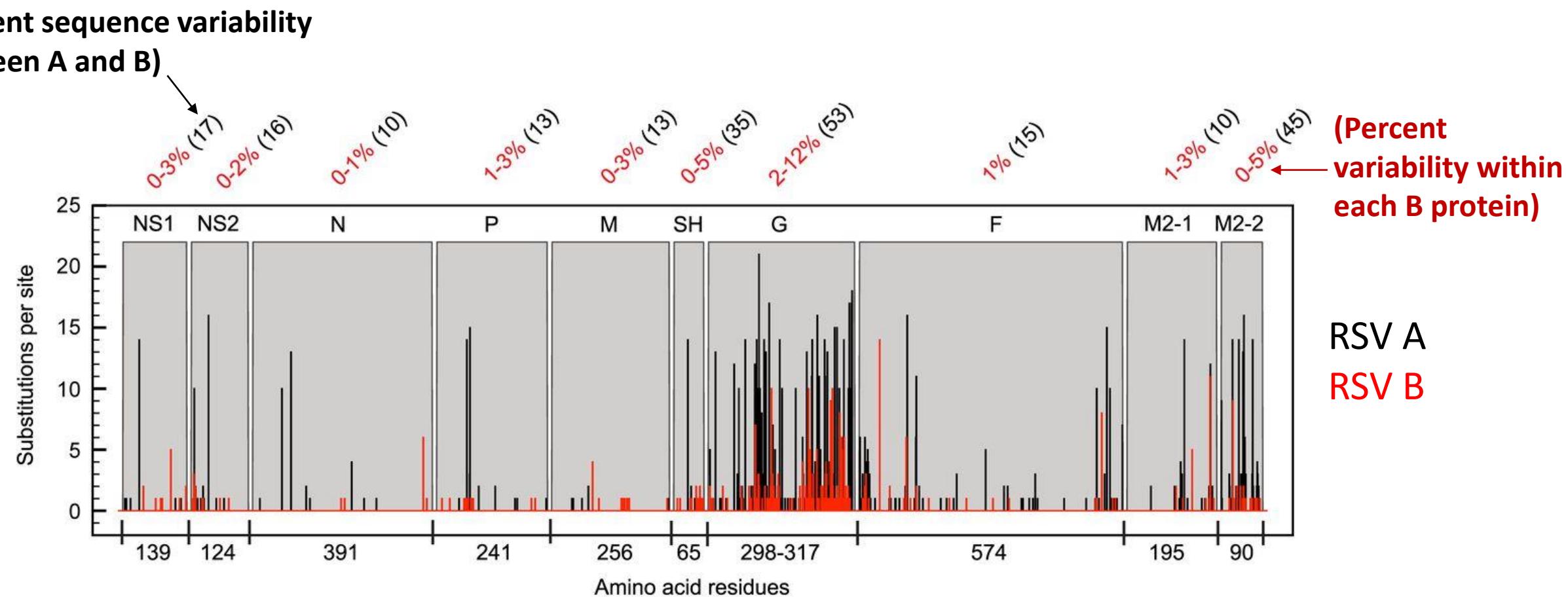
# The fusion (F) protein exists in two or more structural forms exposes different antigenic regions



SITE Ø SITE I SITE II SITE III SITE IV SITE V

Current Opinion in Virology

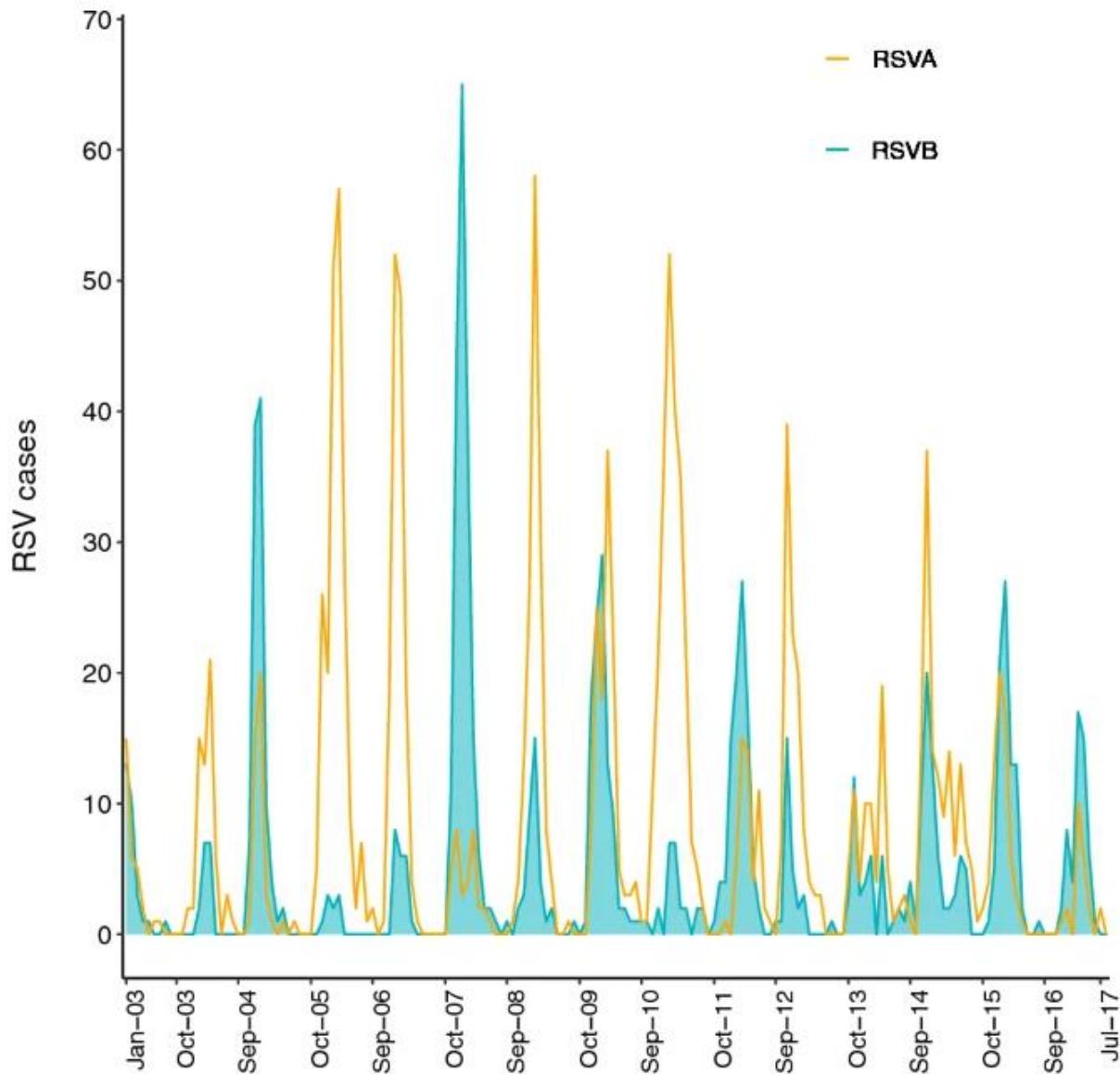
## RSV G gene is used to define RSV genotypes



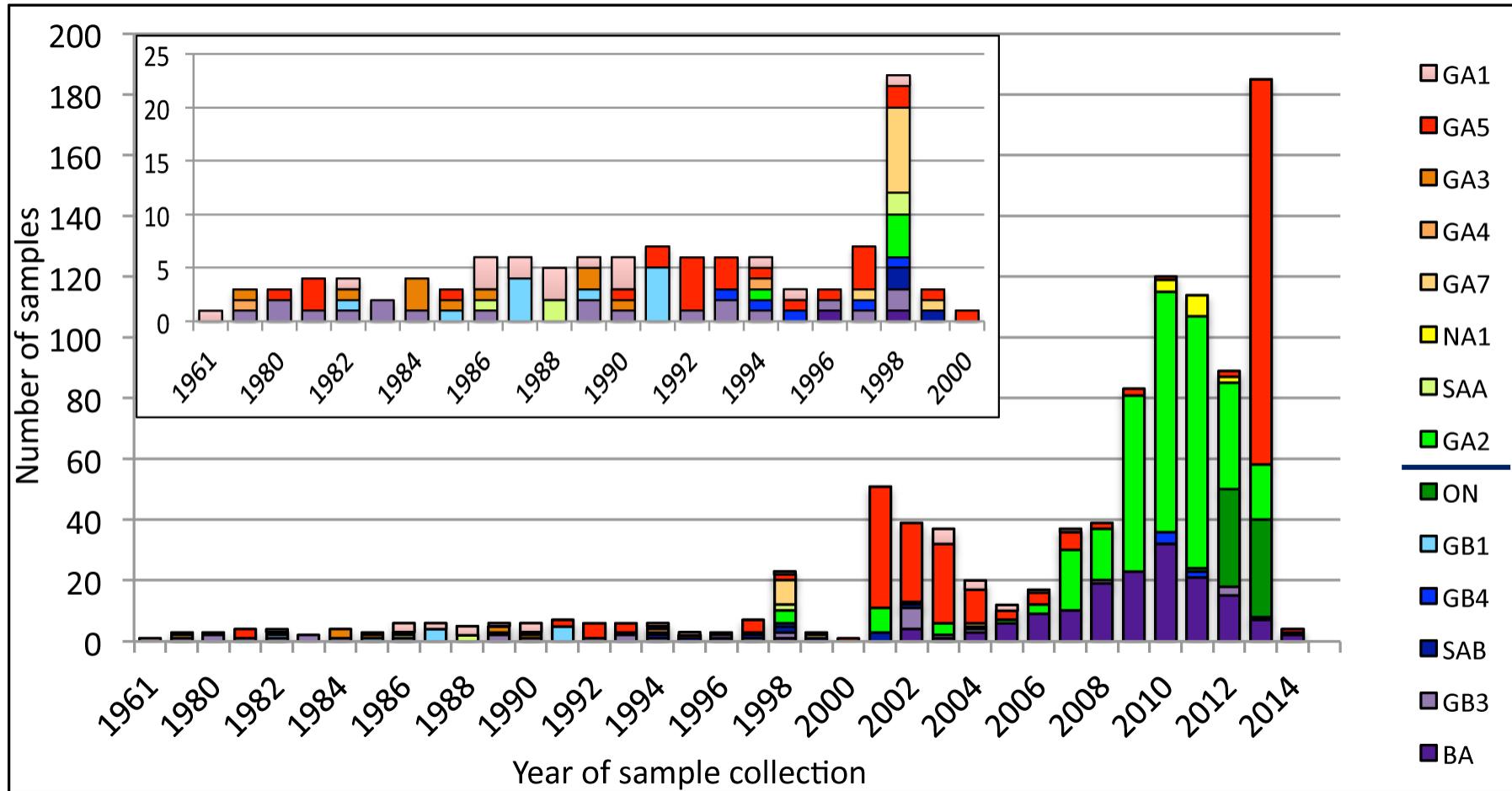
# Number of RSV sequences in Genbank by genotype as of 2017

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

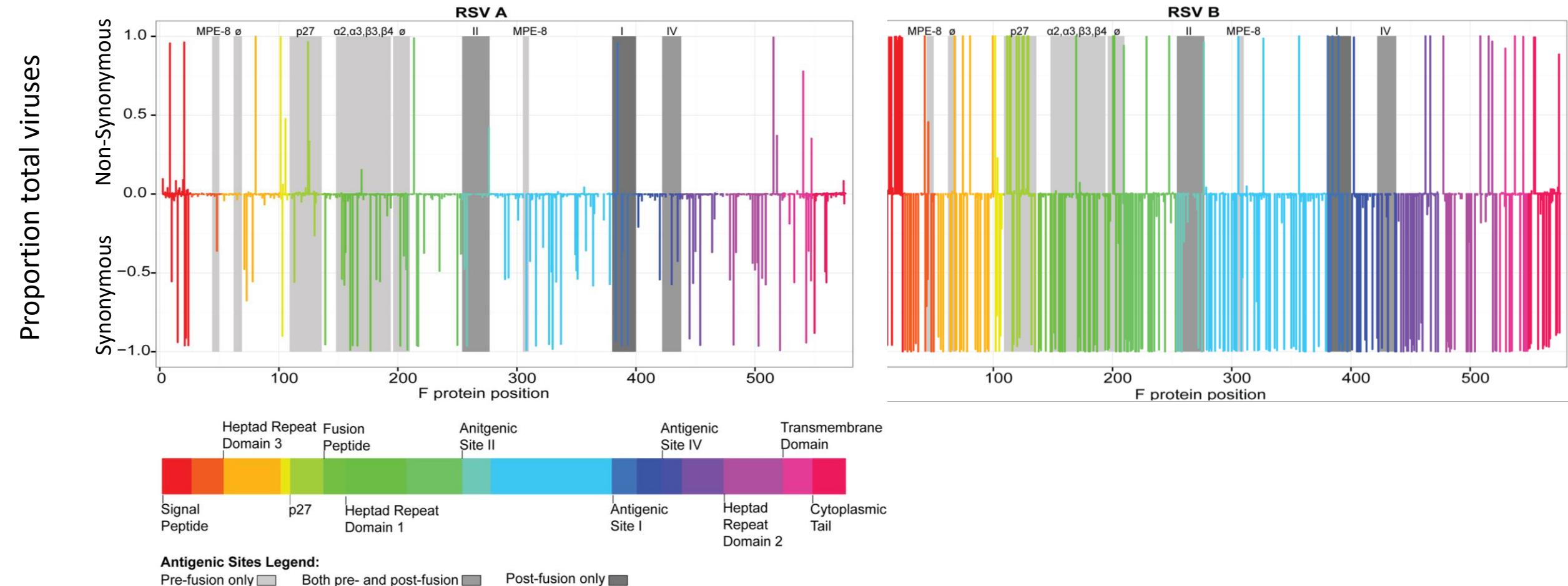
# RSV A and B viruses co-circulate



# RSV A and RSV B genotypes by year of sample collection



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

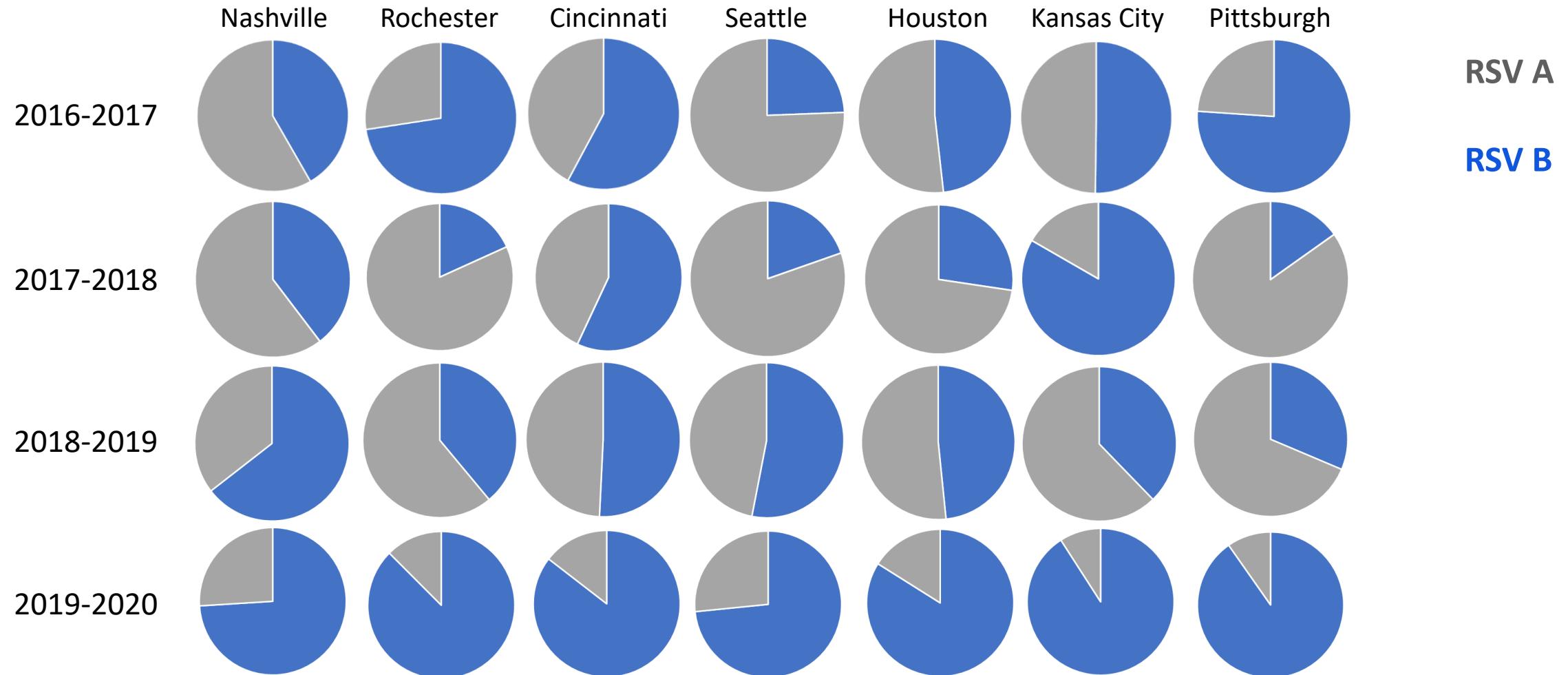


# RSV-associated disease burden estimates from the New Vaccine Surveillance Network (NVSN)

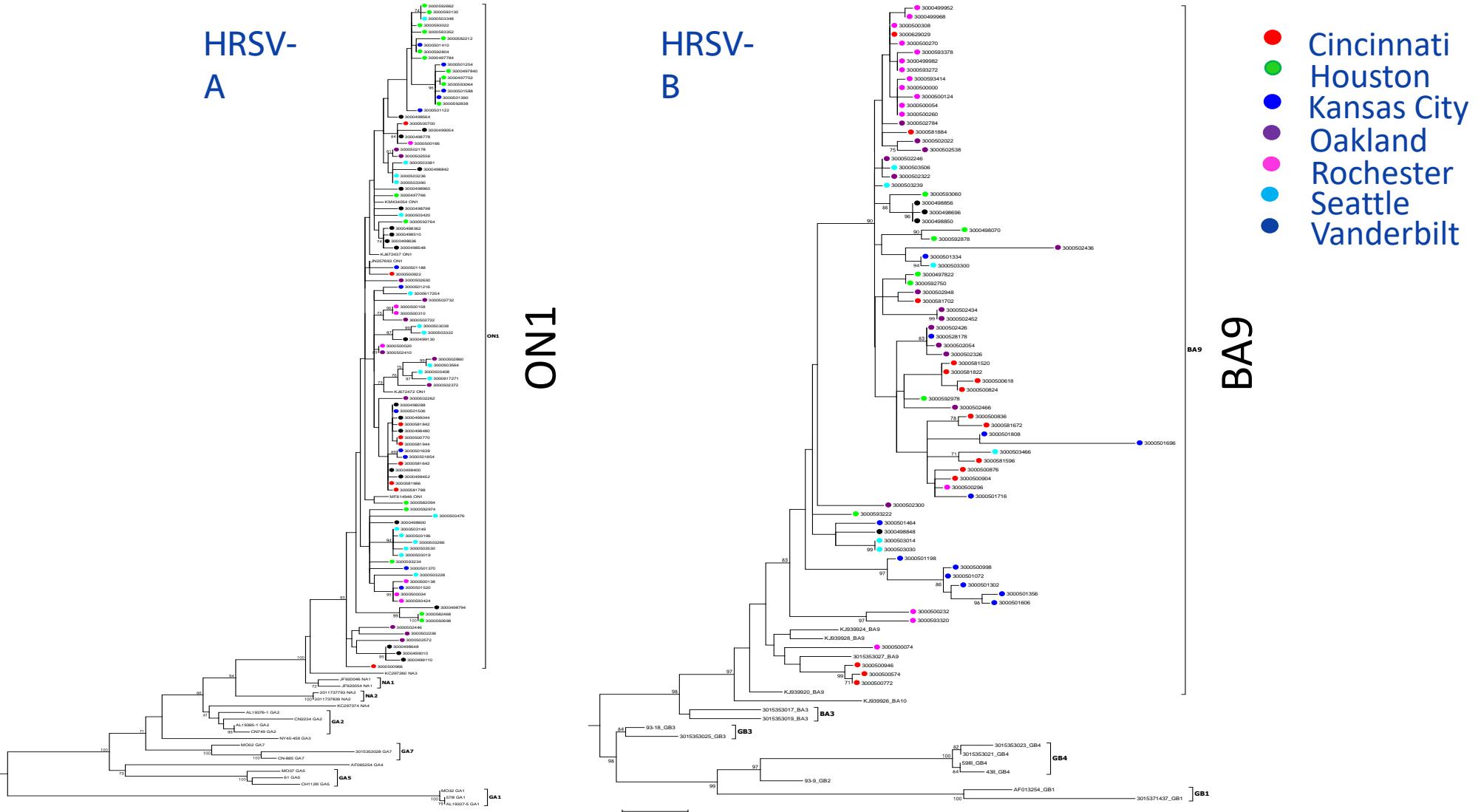


- Year-round acute respiratory illness (ARI) surveillance at 3 sites during 2000-2009
- Expanded to 7 sites during 2016-2021
- Prospective surveillance in inpatient, ED, outpatient clinics
- PCR testing for multiple respiratory viruses, including RSV
- Population denominators and market share used to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

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



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



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](http://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.

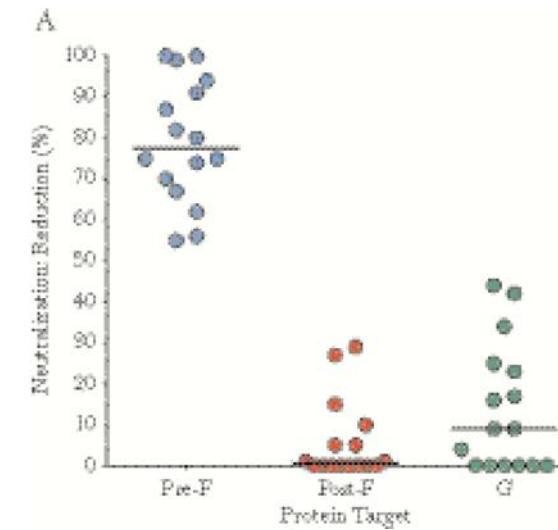
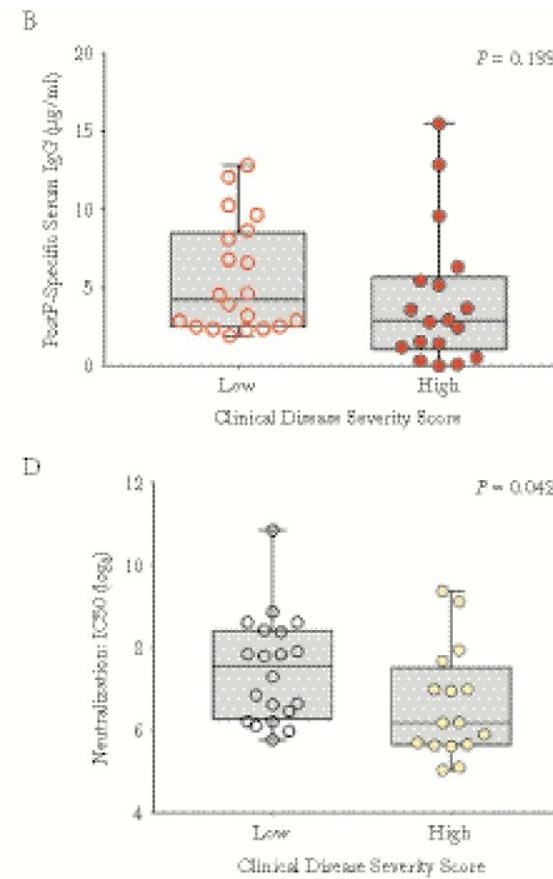
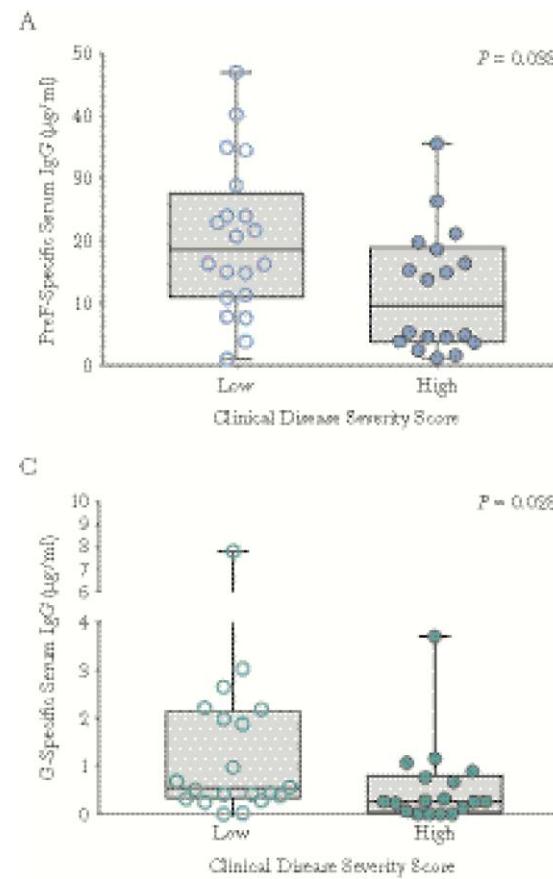
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# A-B subtypes co-circulated at differing percentages during U.S. 2015-2016 RSV season (NVSN)

| 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)                  |

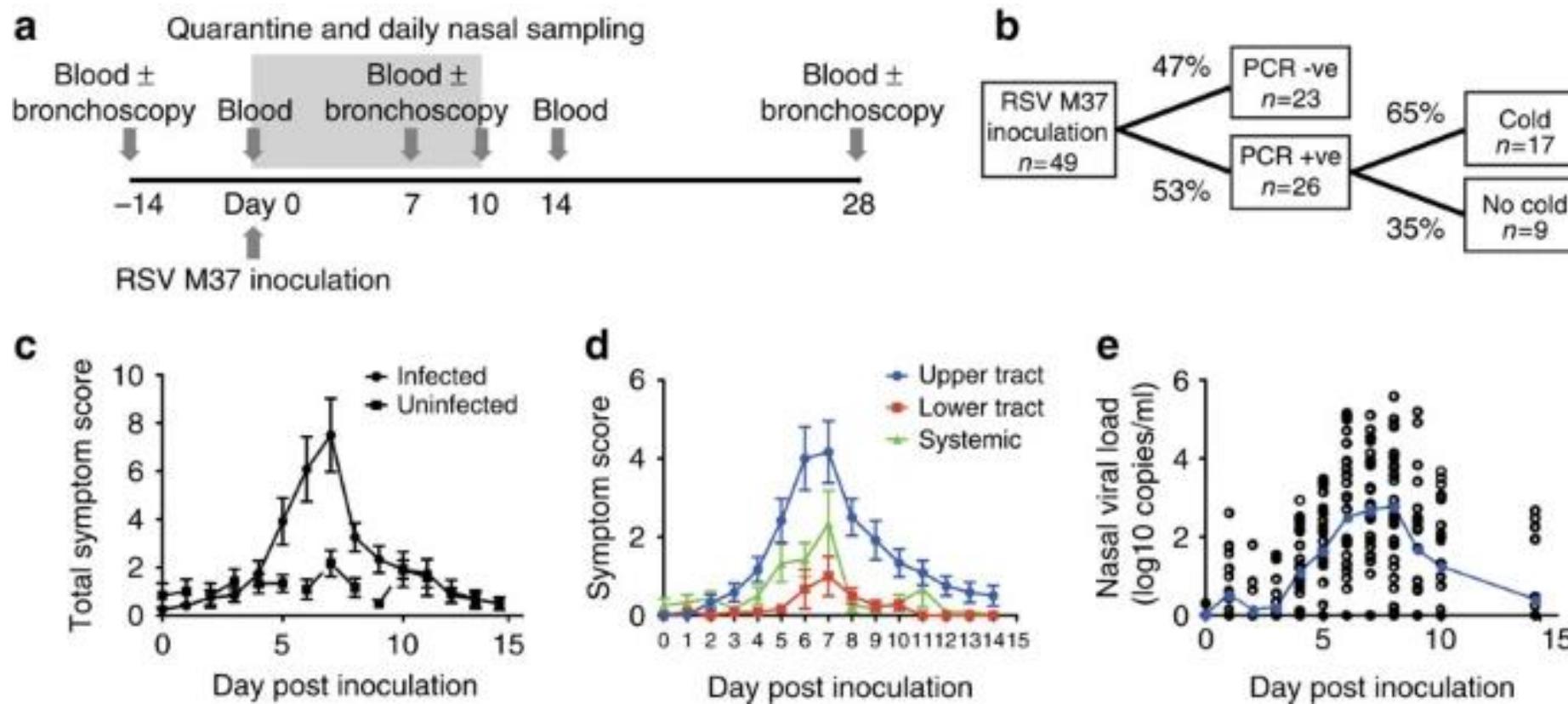
# Most neutralizing activity is directed against pre-fusion F in infants hospitalized with RSV



# 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-principle 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



# 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