1 Respiratory Syncytial Virus

Family: *Pneumoviridae*

'Pneumon': Greek for lung

Single-stranded, negative-sense RNA genome

Genus: *Orthopneumovirus*

Example Species: Human Respiratory Syncytial Virus (RSV)

1.1 Characteristics of Orthopneumoviruses

Lipid membrane + negative-sense RNA genome

Genome: 15 kb in size, encoding 11 proteins (Fairly large for RNA viruses)

Hosts: Humans, cattle, rodents (RSV only in humans and chimpanzees)

Transmission: Respiratory

Surface glycoproteins [F(usion) and G(lycoprotein)] are targets of host antibody responses

1.2 RSV Pathogenesis and Transmission

RSV infects upper (and sometimes lower) respiratory tract

Re-infection is common

Young children: Lower respiratory tract infection (pneumonia, respiratory failure)

Everyone is infected by age 2

1.2.1 Seasonality

Due to both environmental factors and human behavior

Drastically decreased infections in 2020-21

1.2.2 Severity

RSV infections are most severe in babies ∼1 year

Most susceptible to severe RSV illness

Vertically transmitted antibodies wane over time

'Immunopathogenesis' likely plays a role

Low income, babies 0-4, and elderly 65+ are the most at risk

1.3 Source of RSV

First isolated from chimpanzees in 1955

Closely-related viruses in cows and more distantly-related in bats

1.4 Challenges for Vaccine Development

1. Early age of infection
2. Evasion of innate immunity
3. Natural immunity does not prevent reinfection
4. Vaccine-enhanced illness occurred with original RSV vaccine

1.4.1 Case Study: RSV Vaccine Candidate

1960s: Formalin-inactivated vaccine

Vaccine enhanced disease with subsequent infection in clinical trials

Non-neutralizing antibodies resulted in immunocomplexes forming 'inflammatory deposits' in lung tissue

1.5 Replication Cycle

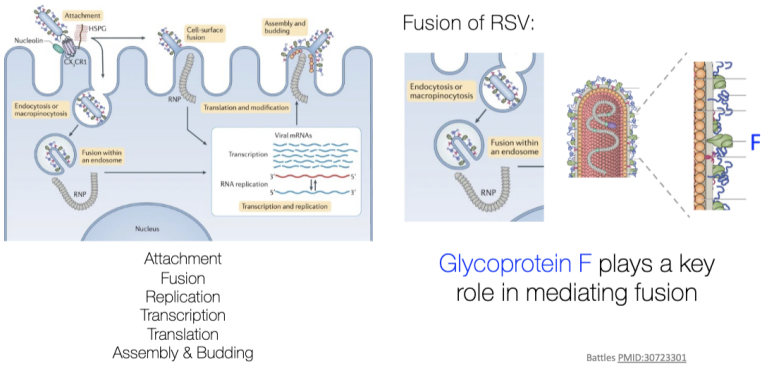

Figure 1: RSV Replication

The viral glycoprotein (envelope) changes shape (conformation) quite dramatically during fusion with the cell membrane

Good anti-RSV antibodies bind to specific places on the RSV F glycoprotein

The F protein exists in multiple shapes

1.5.1 Highly Effective RSV Vaccine

Some key antibody binding sites are not found in the postfusion F protein

Making antibodies to the postfusion protein is not helpful and can be harmful

New RSV vaccine only immunizes against prefusion F protein

Mutation introduced which 'locks' the protein in the prefusion conformation

Moderna mRNA RSV vaccine: 83.7% effective at preventing lower-respiratory disease

Vaccinating pregnant women protects babies through passive immunization (mother to baby)

1.5.2 Therapeutics

Monoclonal antibody therapy: Antibodies similar to those elicited by vaccine

Given to very high-risk infants