The Chinese University of Hong Kong
Department of Microbiology
Joint Graduate Seminar 2011

Human Rhinovirus: An Ancient Enemy or a Wise Old Tutor

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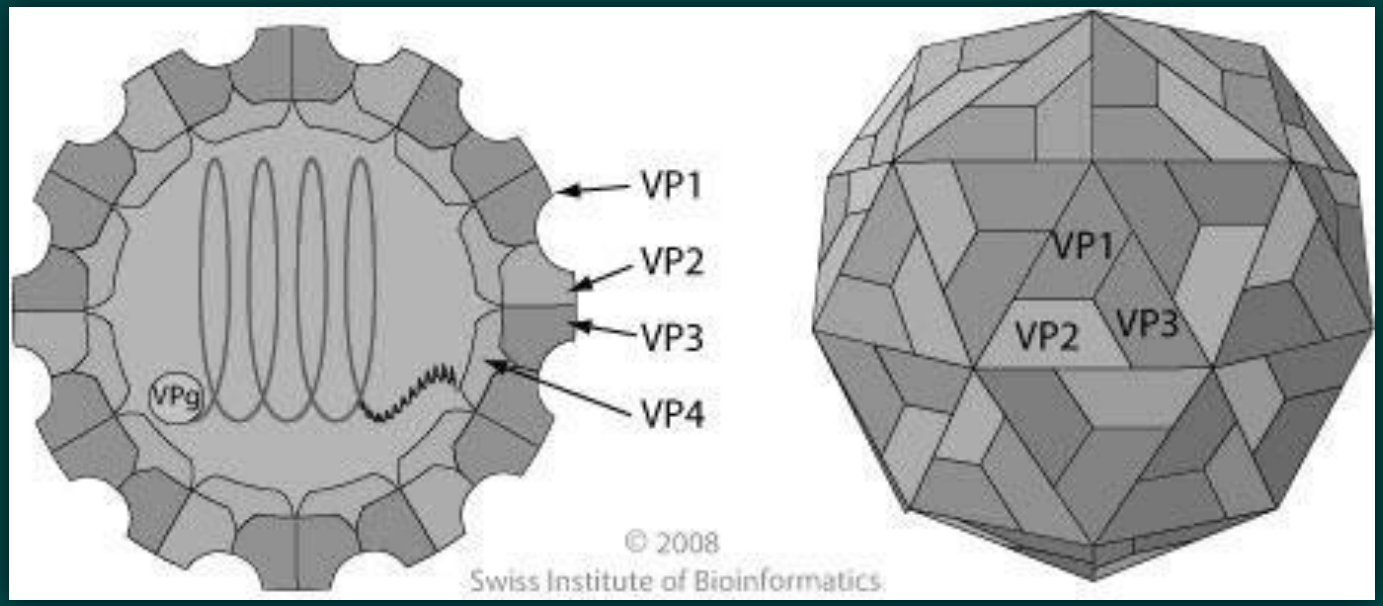
Introduction

Rhinovirion



- Small size (30nm)
- Non-enveloped
- 4 Capsid proteins (VP1, VP2, VP3, VP4)
- Linear, ssRNA (+), 7.1-8.9kb
- Icosahedral arrangement of 60 capsid subunits

Picornaviridae Family

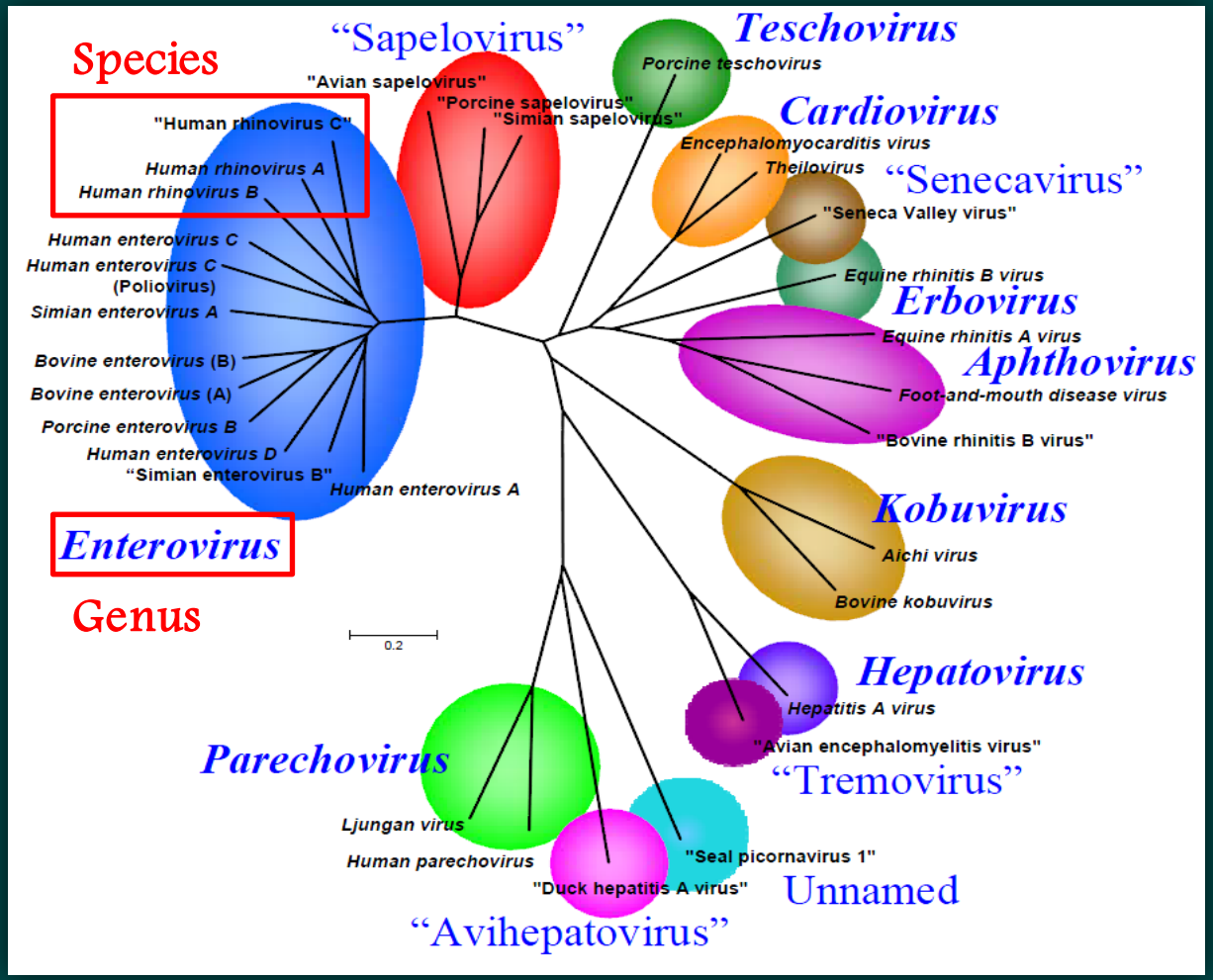


Figure 2. Unrooted Neighbor-joining tree of the *Picornaviridae* based on a comparison of the P1 capsid region. Adapted from http:// www. picornastudygroup.com/ posters/europic_2008.pdf

Genome Map

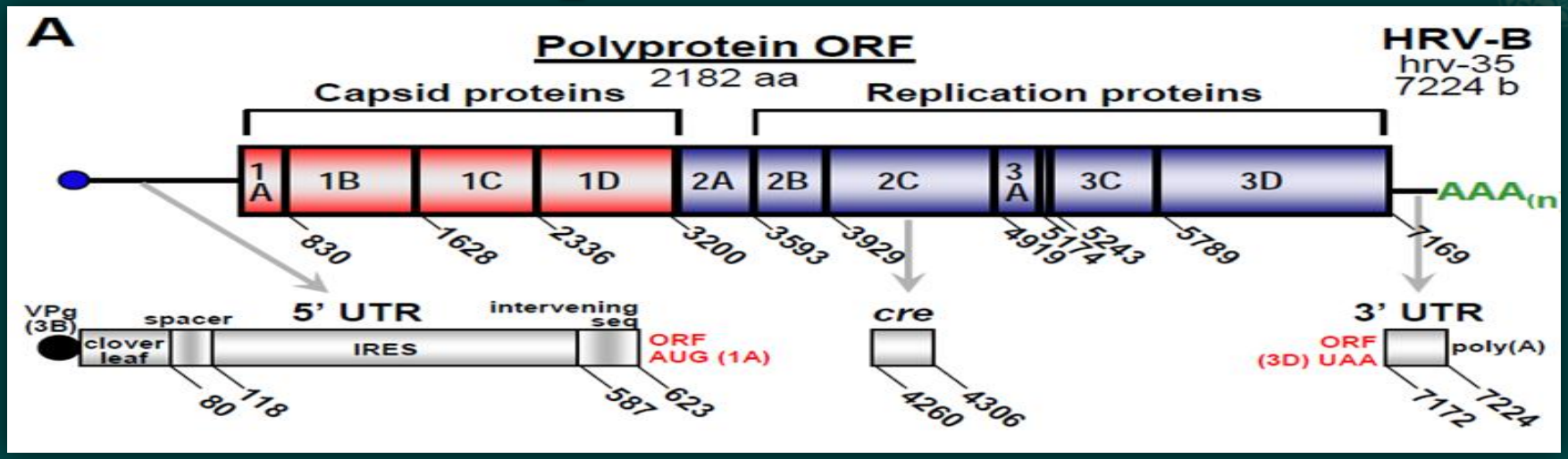


Figure 3. An HRV genome map. Adapted from Science, 2009, 324, p.55-59

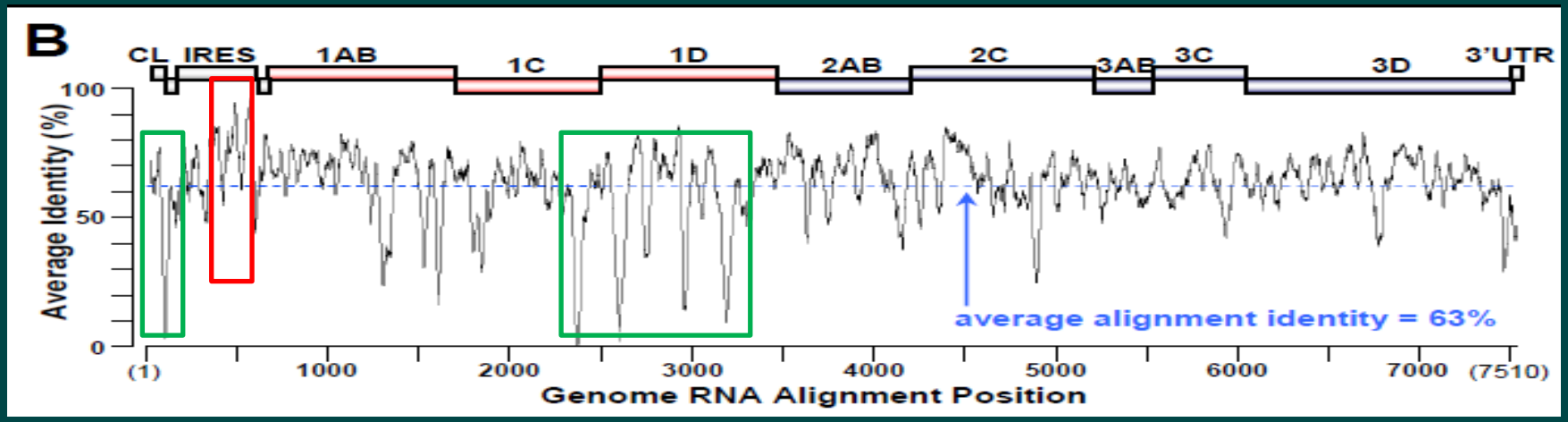


Figure 4. An average identity of RNA sequences . Adapted from Science, 2009, 324, p.55-59

HRV-Related Diseases

- Common cold
  - Upper respiratory tract illnesses (URTI)
  - Two-thirds caused by HRV
- Acute otitis media
  - Associated with 40% of HRV infection
- Lower respiratory tract illnesses (LRTI)
  - Bronchiolitis
  - Pneumonia
  - Acute exacerbations of chronic respiratory diseases

HRV-Associated Medical Burden

- Chief reason for unnecessary antibiotic prescription
  - Increased hospitalization of children with wheezing
  - Accelerated development of antibiotics-resistant bacteria
- Related Public Cost exceed USD10 billion each year

HRV Major Milestones

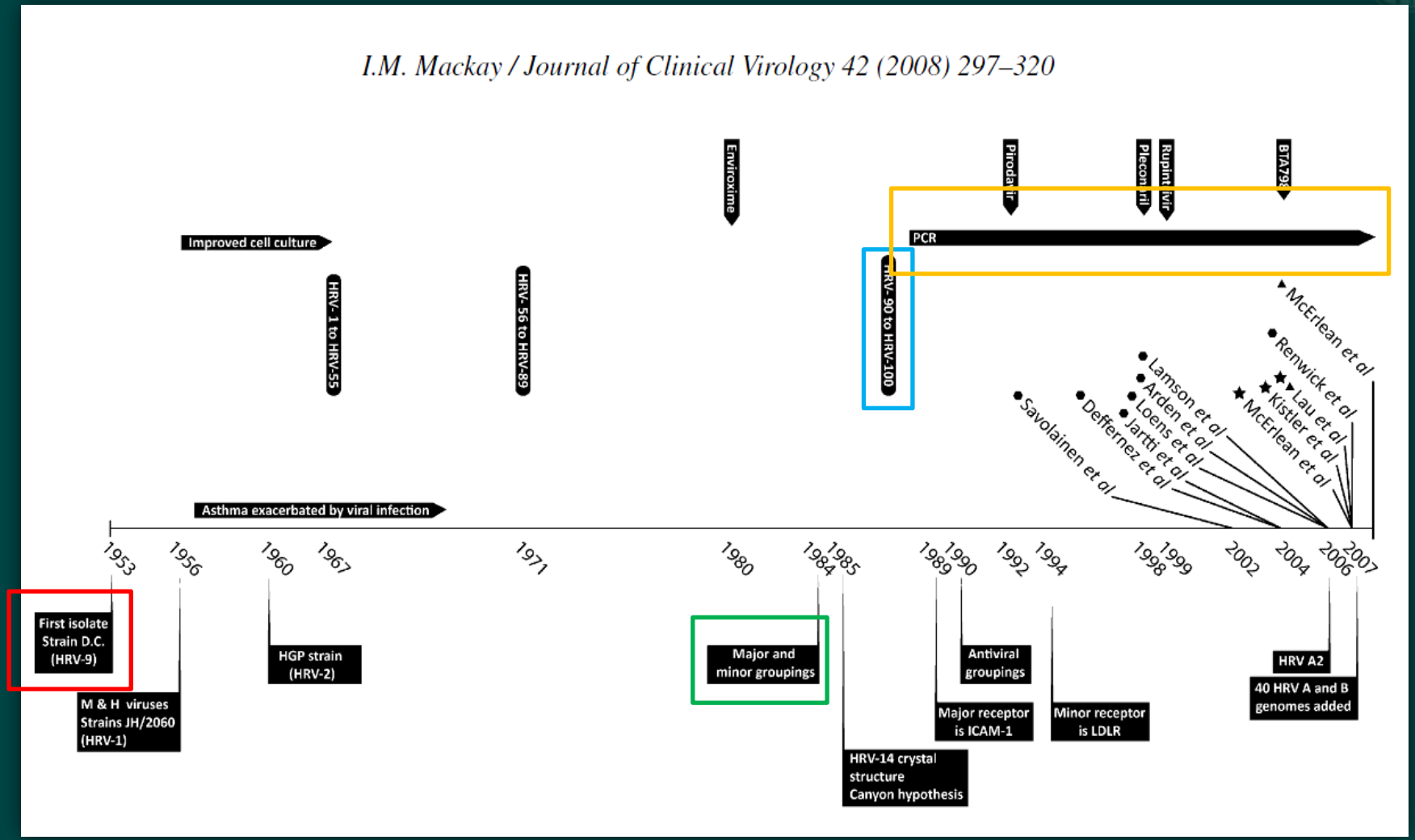


Figure 5. A distillation of some significant events in the history of HRV research.

HRV Detection in Ancient & Modern Era

Traditional Detection Method

- Tissue cell culture in multiple cell lines (33˚C) followed by acid lability test (pH 3)
  - Labor-intensive
  - Three to seven days for results
  - Properly handling to keep virus alive
  - Failure in detection of HRV-C species
  - Misclassification of enterovirus species as HRV

Traditional Detection Method

- Serological testing
- Antigen detection assays
  - Fluorescent antibody (FA) methods

Not practical: high antigenic variability of HRV strains

Molecular Detection Methods

- Nucleic acid amplification tests (NAAT)
  - Reverse transcription-polymerase chain reaction (RT-PCR)
  - Realtime RT-PCR
- 5' non-coding region
- Quick, Sensitive
- Primer-targeting region is also highly conserved among the enteroviruses
  - Additional steps to confirm HRVs e.g. probe, sequencing

HRV-A: 77 serotypes

HRV-B: 25 serotypes

HRV-C: 49 genotypes

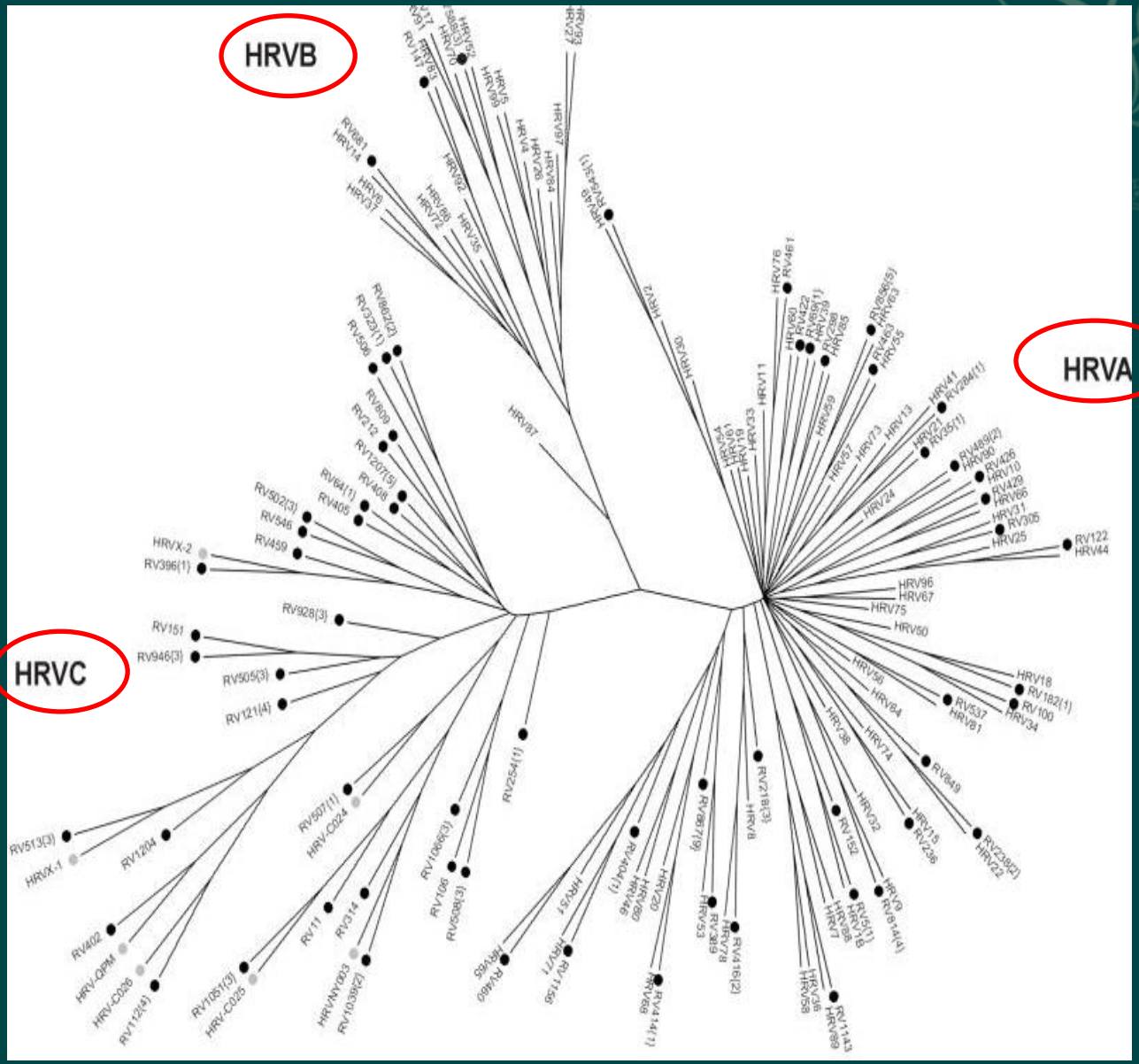


Figure 6. Phylogenetic tree depicting relationships between known HRV serotypes and novel HRV. East, J Clin Virol. 2009 September; 46(1): 85–89.

Relationship of Host & HRV

Symbiotic Relationship

- Proposed a mutualistic relationship of human with specific HRV species
  - Some HRV infection is harmless to host
    - up to 40% of asymptomatically HRV infection
  - Study proposed the benefit of HRV's immunomodulatory properties
    - set the threshold of immune system for URTI & LRTI

Upper Respiratory Tract illness

- Adult and children
- Respiratory viruses
  - Influenza virus (5%-15%)
  - Human coronavirus (8%)
- Up to 20 unique HRV strains circulate each season
  - Causing Two-thirds of common cold
- Direct effects of virus and proinflammatory responses

Acute Otitis Media (AOM)

- Children
- Bacterial aetiology
  - *Streptococcus pneumonia*
- Accompany with HRV infection
  - AOM-prone infants and children
    - 30% of HRV in nasopharyngeal swabs
  - Recurrent AOM's children
    - Large quantities of HRV DNA in adenoid tissues

Lower respiratory illnesses

- Bronchiolitis in infancy
- Childhood pneumonia
- Acute exacerbations of chronic respiratory diseases e.g. 1)Asthma 2) Chronic Obstructive Lung Disease 3) Cystic Fibrosis

Exacerbation of Asthma

- Children & Adults
- Respiratory picornaviruses
  - Up to 57% in children; up to 40% in adults linked to HRV infection
- Proposed synergistic effect of viral infection and stimuli in allergy individual

Proposed Mechanism~Exacerbation of Asthma

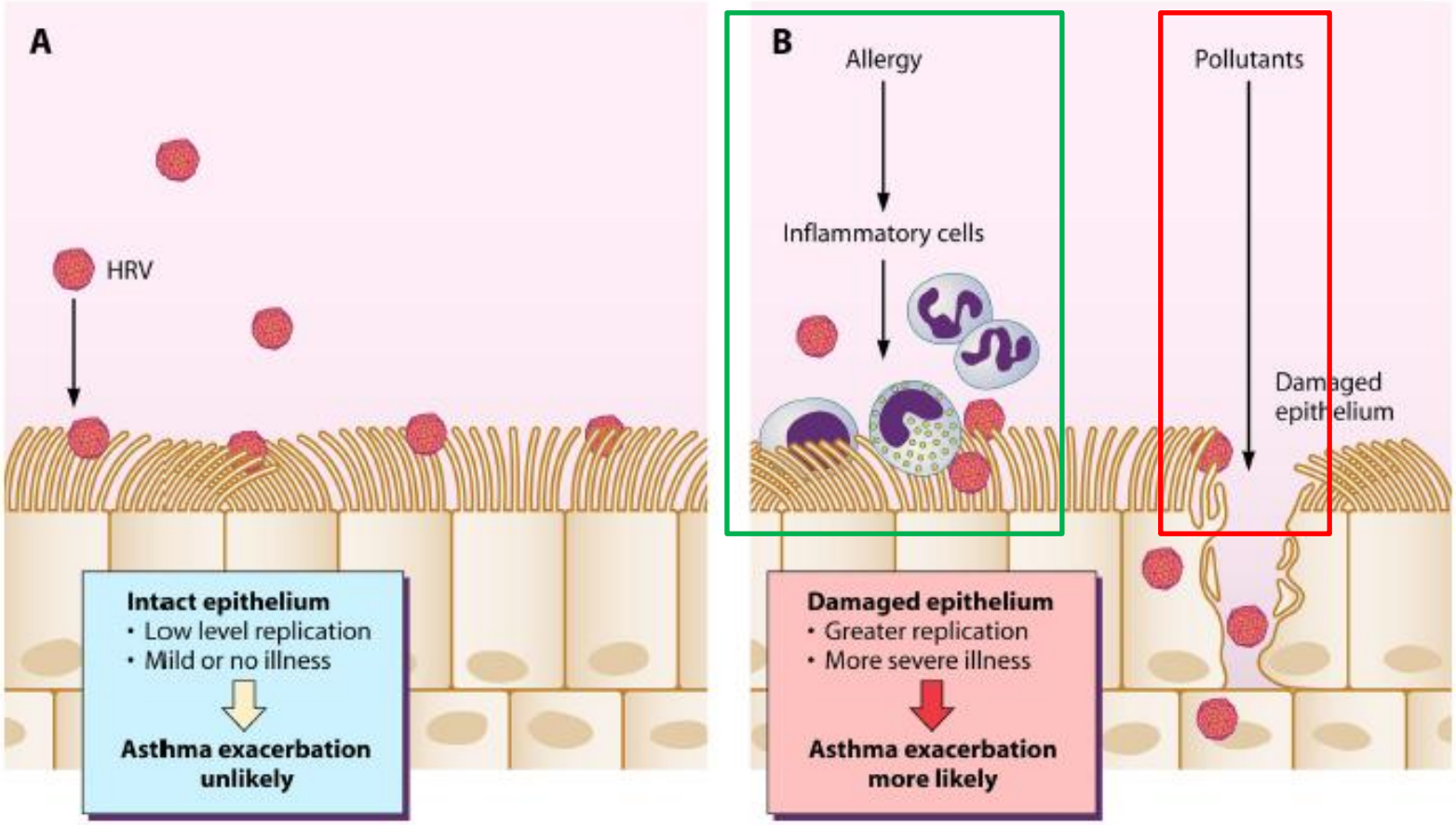


Figure 7. Proposed effects of epithelial integrity on severity of HRV infections and exacerbations of asthma Adapted from, Journal of Virology, Aug. 2010, p. 7418–7426

Conclusions

- HRVs have known for decades, but often considered as a mild disease-causing virus.
- Molecular diagnostics allow the discovery of new species (HRV-C), 49 strains and is related to more severe illnesses.
- Immunological studies proposed the symbiotic relationship between host and HRV, which may be species-specific.
- Characterization of traditional and novel HRVs must be continue to explode HRV phylogeny, biology, clinical impact and development of antiviral agents.

The End

Thank you