

Experimental human rhinovirus infection  
induces exaggerated  
anti-viral and B cell receptor gene expression  
in peripheral B cells from asthmatics

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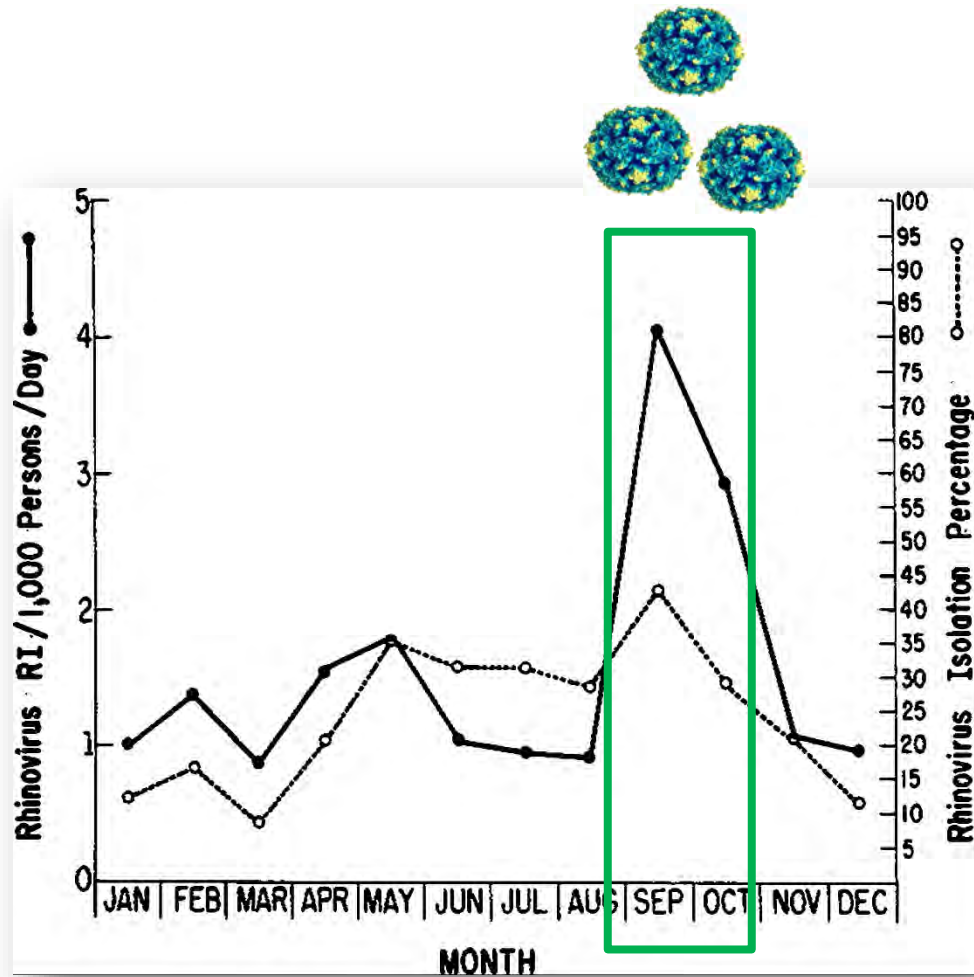
**HUNTING**  
*Season*



*is now*

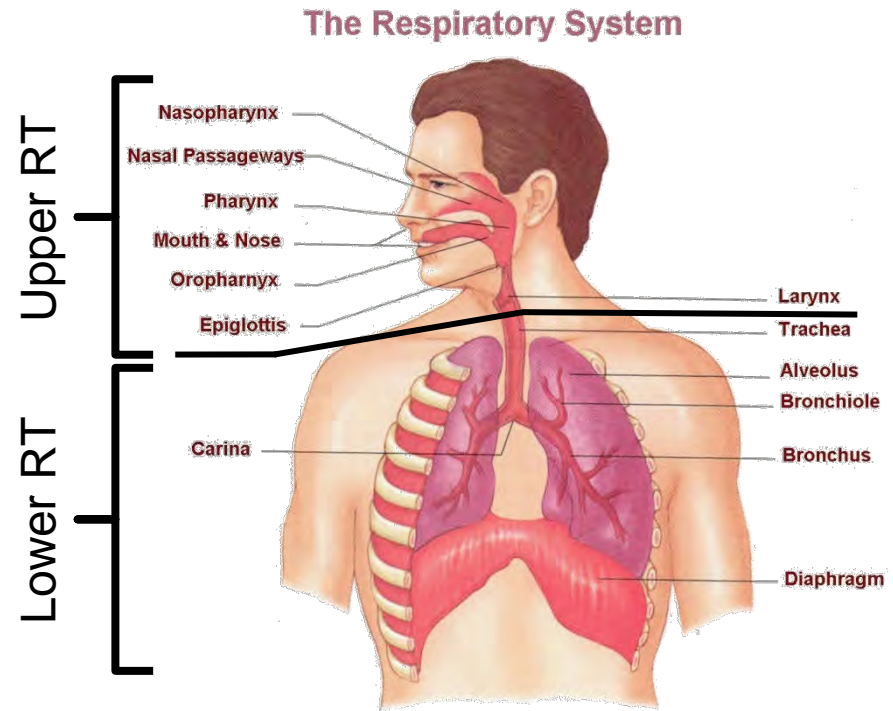
**OPEN**

# It is rhinovirus season!



# Clinical relevance of respiratory viruses

- **50% of all respiratory tract infections caused by rhinovirus**
- Billions of people infected each year
- Rhinovirus infects cells of upper and lower respiratory tract (RT)
- Symptoms: common cold, bronchiolitis, pneumonia, onset and exacerbation of asthma



# It is rhinovirus season!

Immune system



Respiratory viruses





# The immune system army



Close combat



T cell



Long-range combat



B cell



Strong man

Ready for the messy  
work



Macrophages

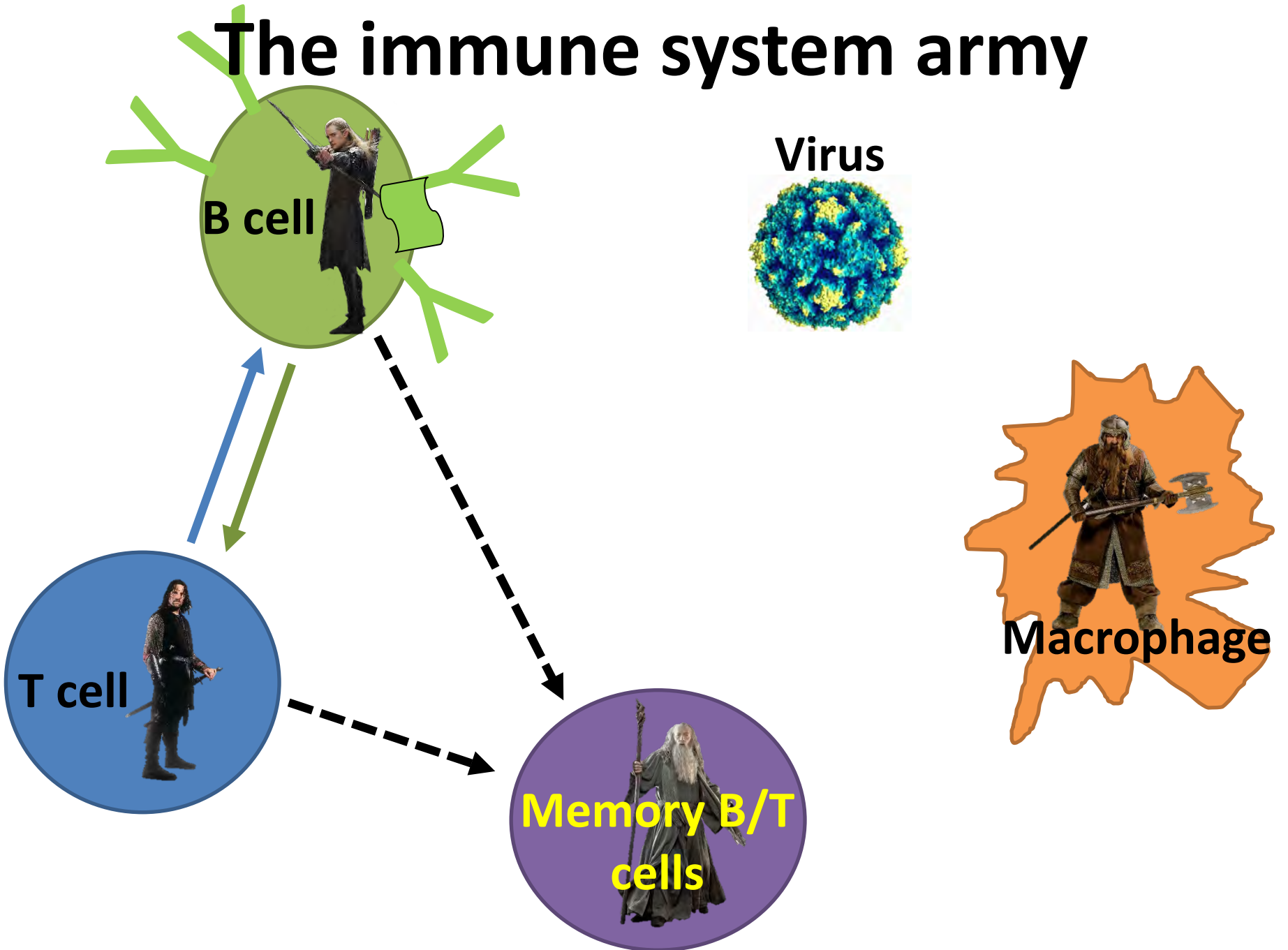


Remembers everything  
and gives advice



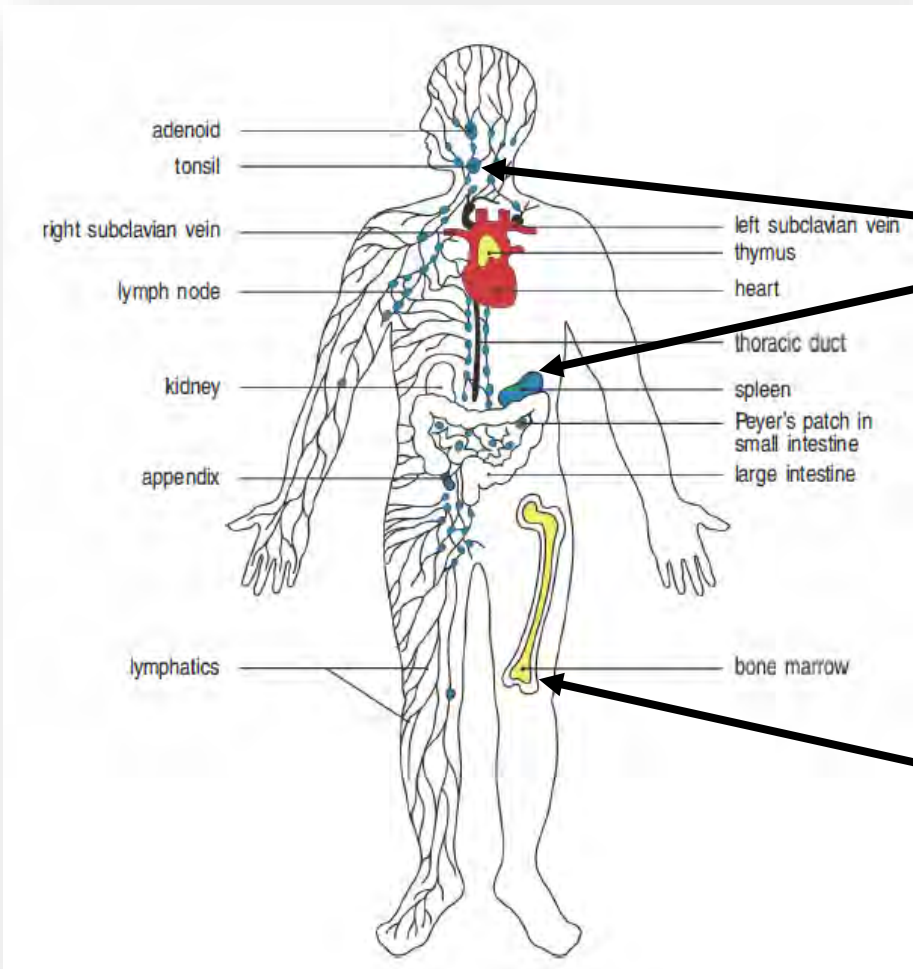
Memory B/T  
cells

# The immune system army



# The immune system army

## The human lymphoid system



**Where B cells come in contact with viruses**



**Early B cell development**



# Aim of this study



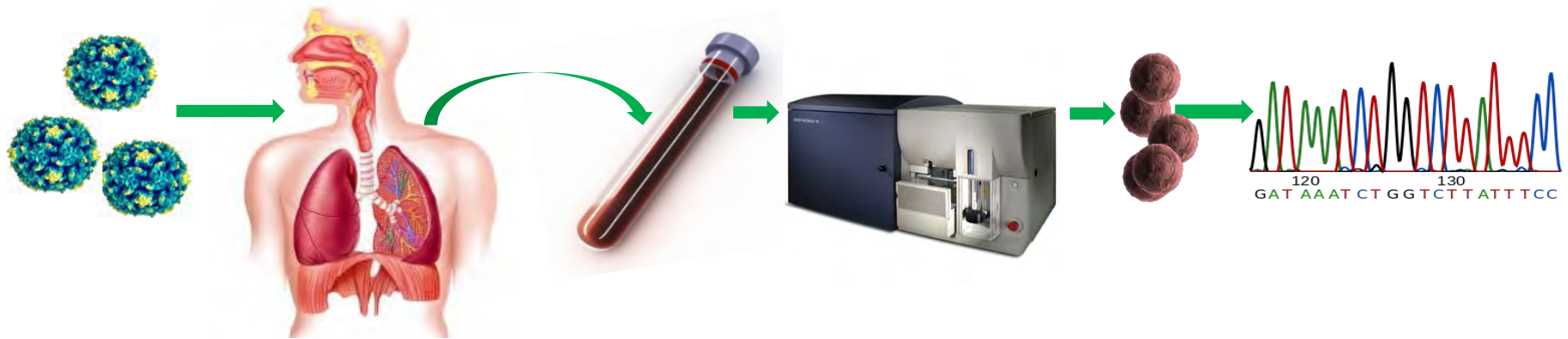
**This study**

**B cells  
functions**

**Rhinovirus  
infection**

- 1. Study the role of B cells in fighting rhinoviruses**
- 2. Assess whether asthmatics have a deficient response to rhinoviruses**

# Experimental design



Rhinovirus  
infection

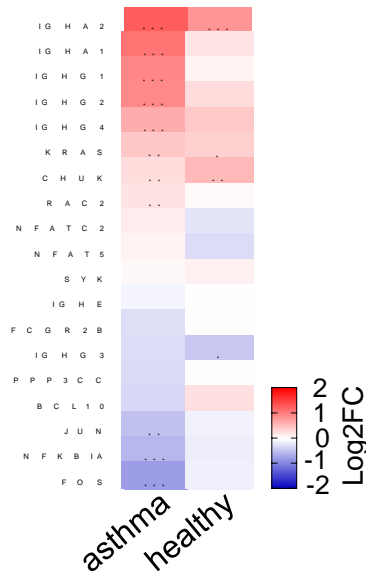
Blood drawn  
after infection

Purify B cells

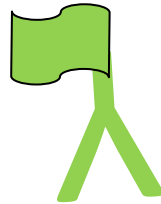
Gene expression

# Genes expressed upon infection

## BCR signalling



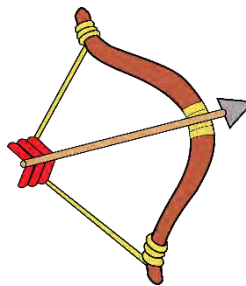
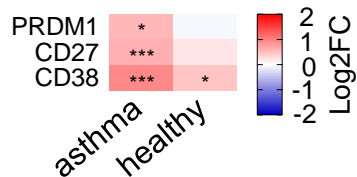
«Genes to built antibodies»



## Fighting «foreign intruders»

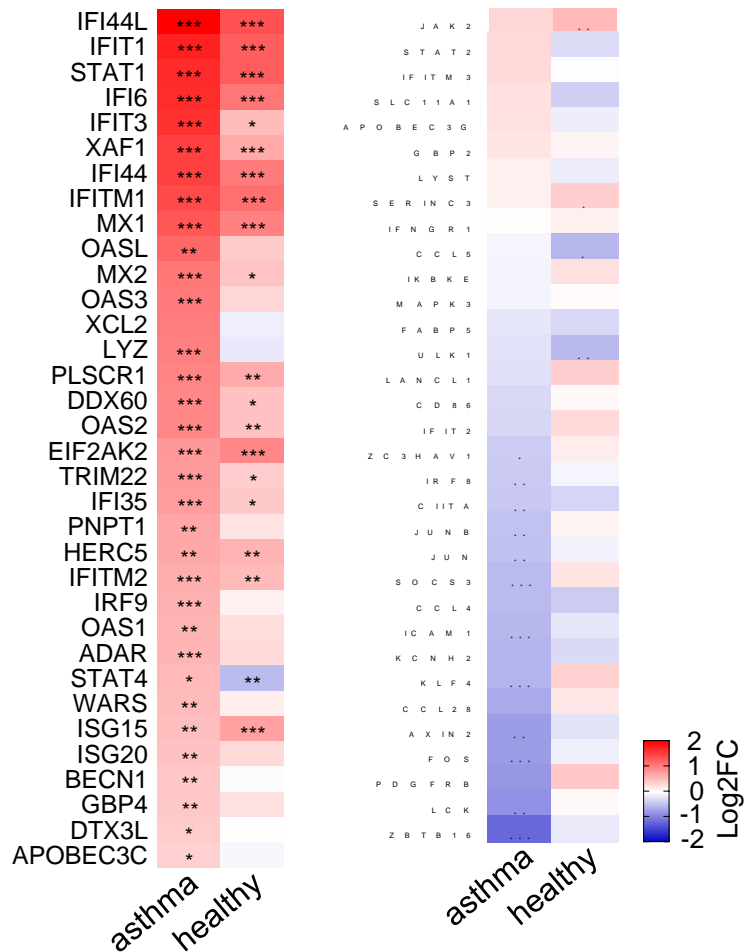


## Plasmablast related genes



# Genes expressed upon infection

## Antiviral response genes

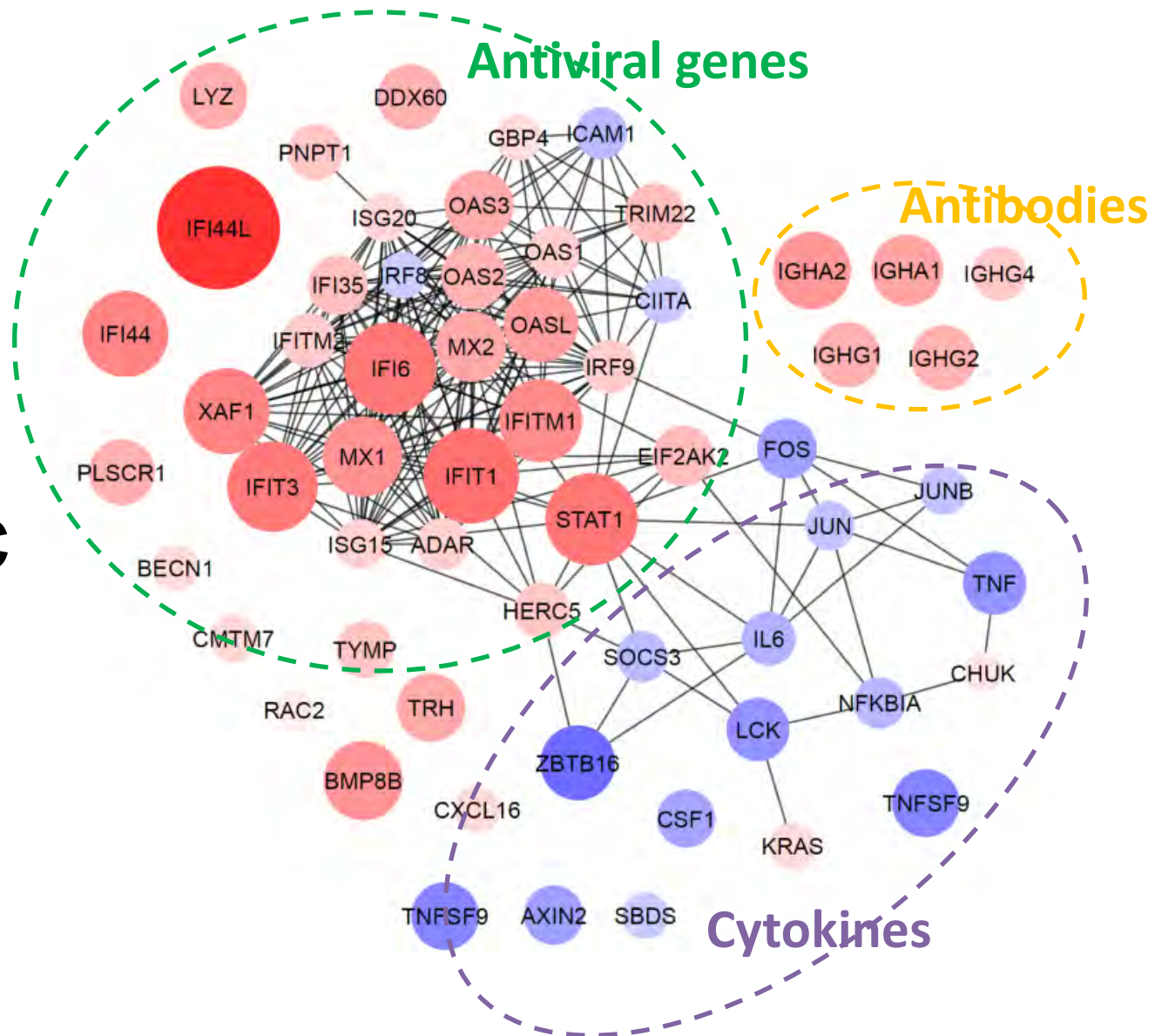


«Internal affairs» inside the cells



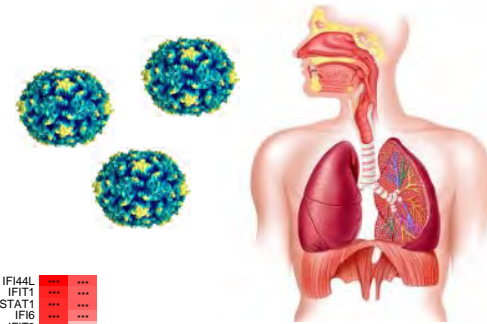
# Genes expressed upon infection

Gene  
expression  
in  
**asthmatic**  
subjects

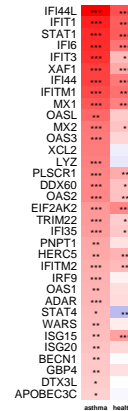


# Conclusions

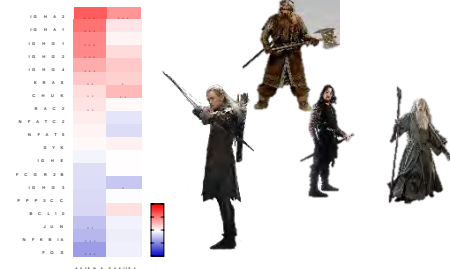
Experimental human  
rhinovirus infection



induces exaggerated  
anti-viral gene  
expression



and B cell receptor gene  
expression

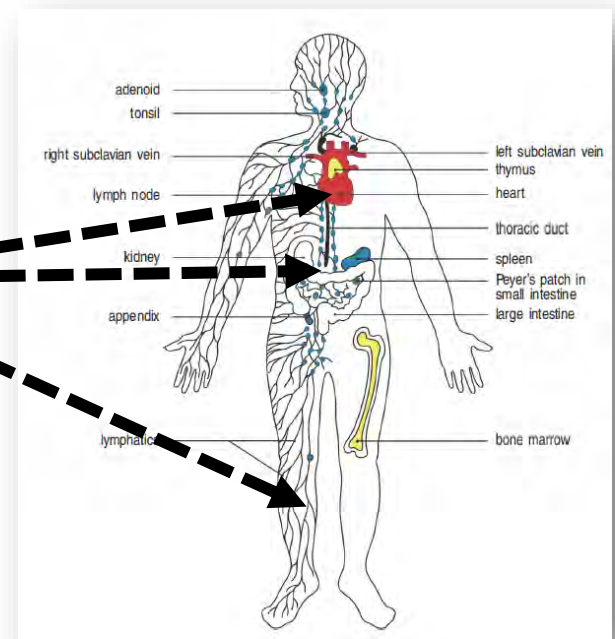
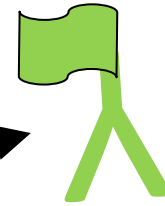
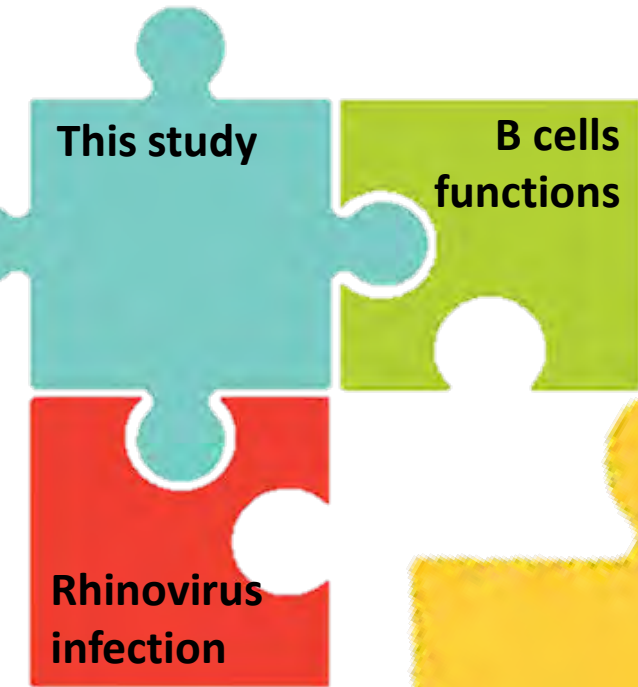


in peripheral B cells  
from asthmatics





# Outlook



# Acknowledgements



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**University of  
Zurich** <sup>UZH</sup>



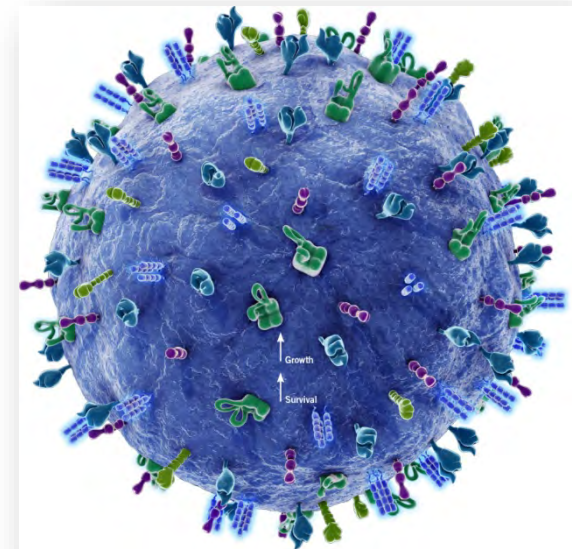
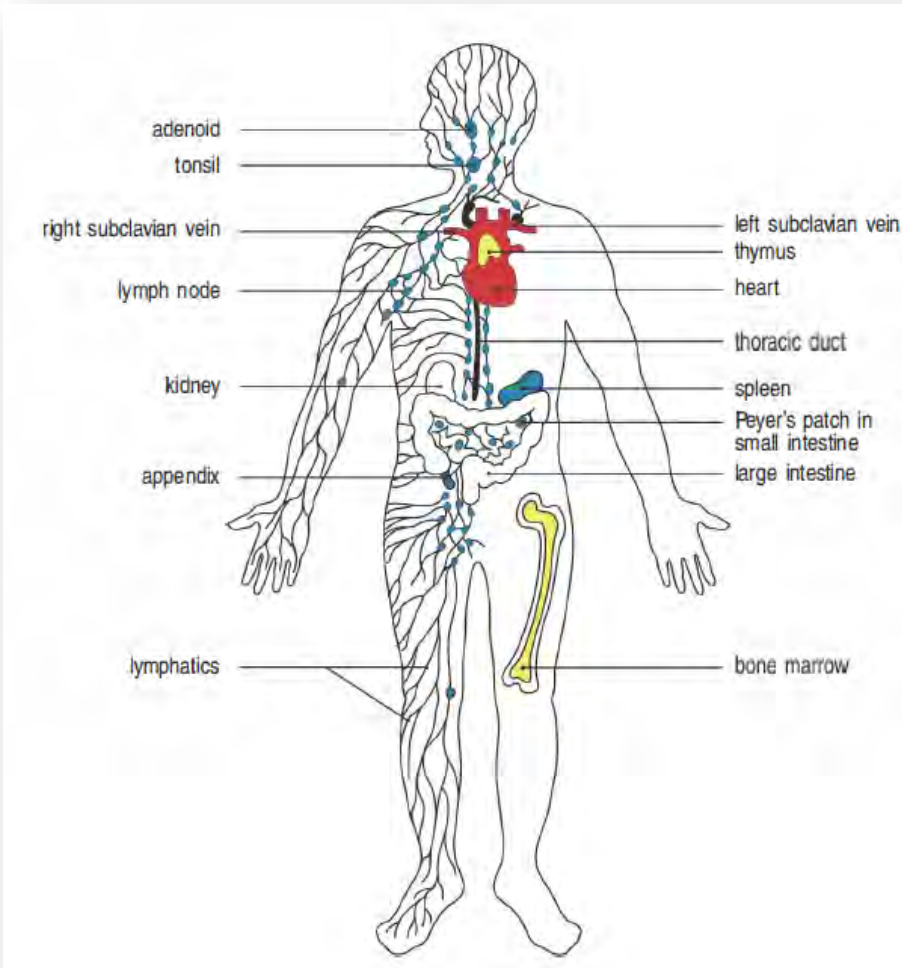
**MiM** Microbiology  
Immunology



**Thank you for your  
attention and  
questions!**

# The human lymphoid system: Where B cells come from...

## The human lymphoid system



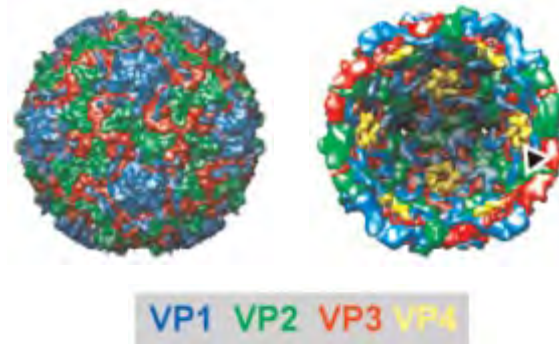
Receptors for:

- Cell-cell contact
- Cytokines (IFN- $\alpha$  and others)
- Pathogens (rhinovirus)

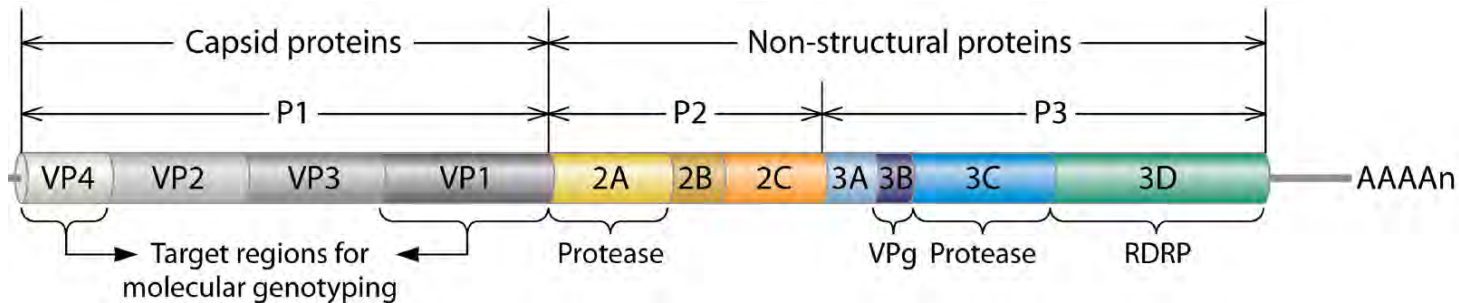
# Rhinovirus

## Structure:

- 30 nm diameter
- Icosahedral capsid

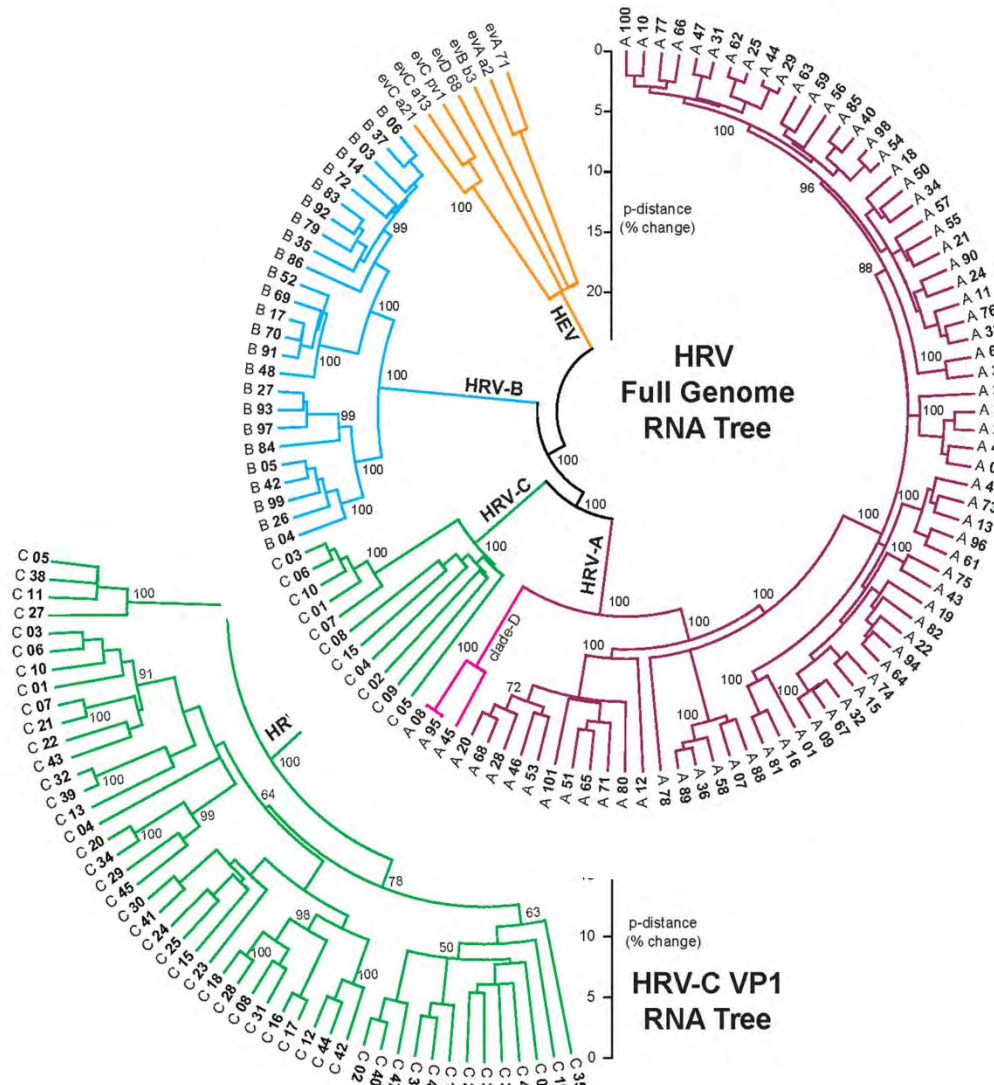


- RNA translated into polyprotein precursor

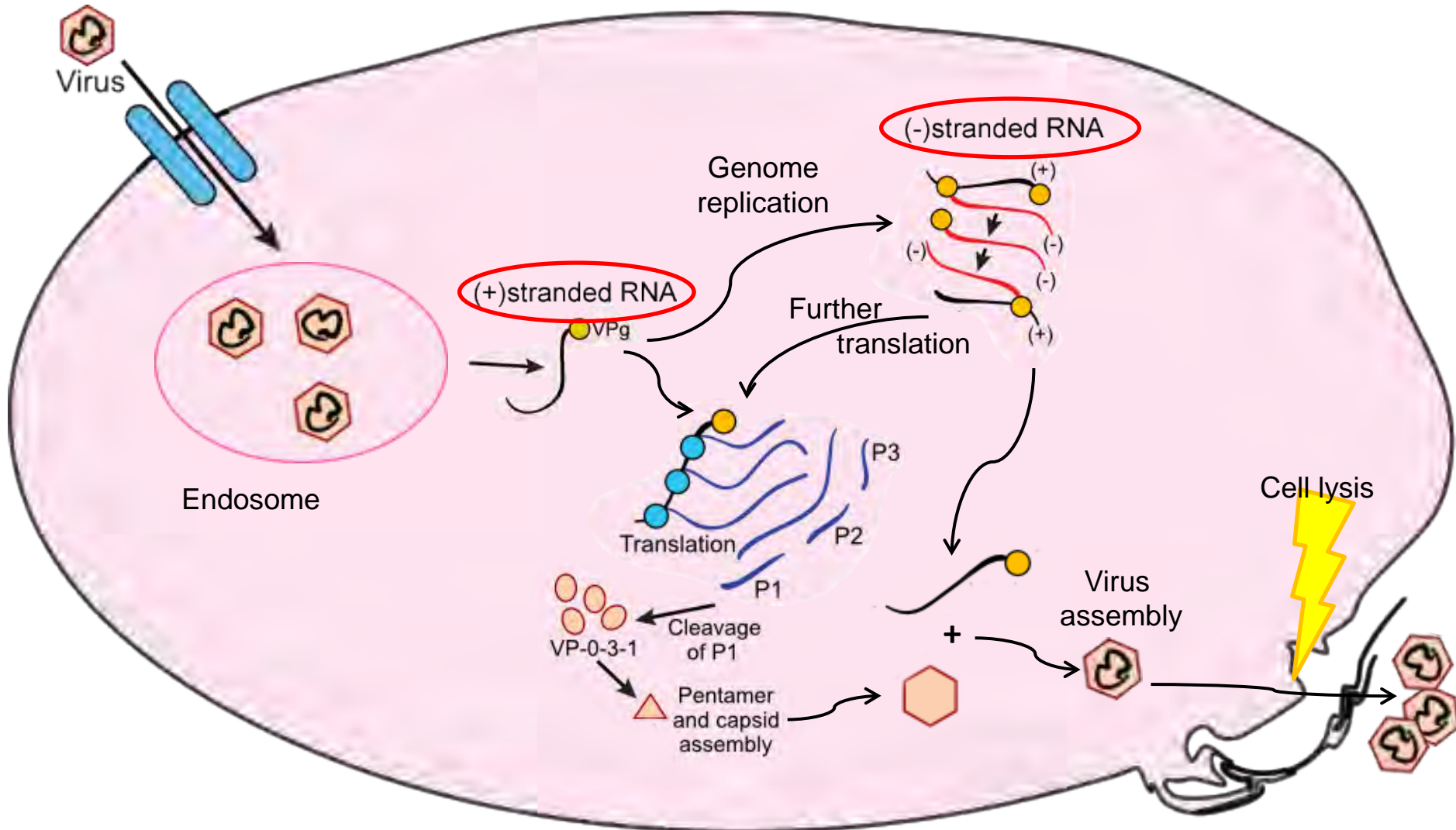




# Diversity of rhinoviruses



## Virus replication





## Human rhinovirus and asthma

- Nearly 90% of children with wheezing illness associated with HRV at year 3 develop asthma by year 6.

*Jackson, DJ et al. Am.J.Respir.Crit.Med. 2008.*

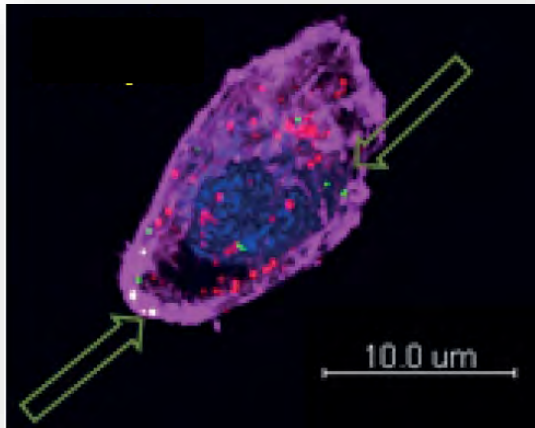
- Infants hospitalized with HRV associated viral bronchiolitis have 2-3 fold increased risk of asthma in later childhood.

*Gern, JE. J.Virol. 2010.*

- HRV is detected in 85% of children hospitalized with asthma exacerbations. HRV-C is highly associated with asthma exacerbations.

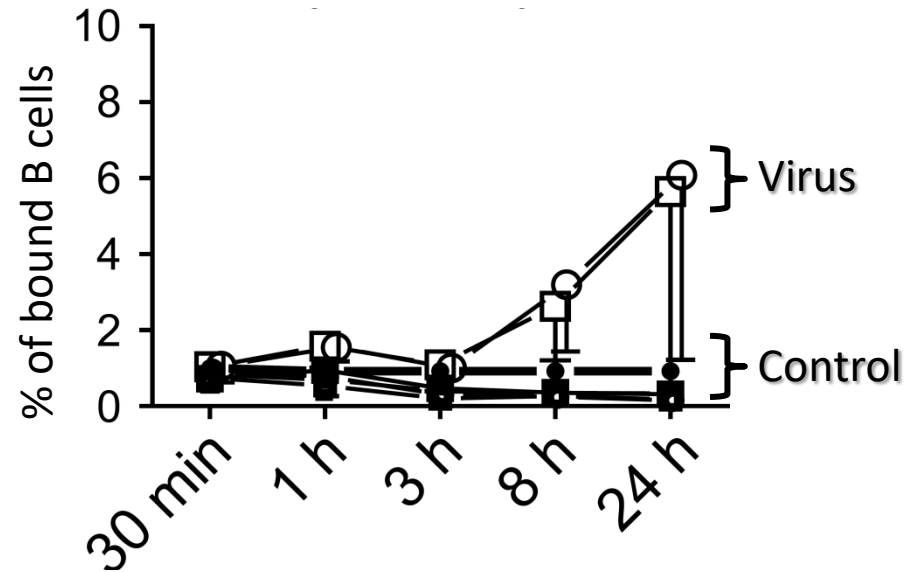
*Mak, RKY et al. Pediatr. Infect. Dis. 2011.*

## Rhinovirus binds to B cells!

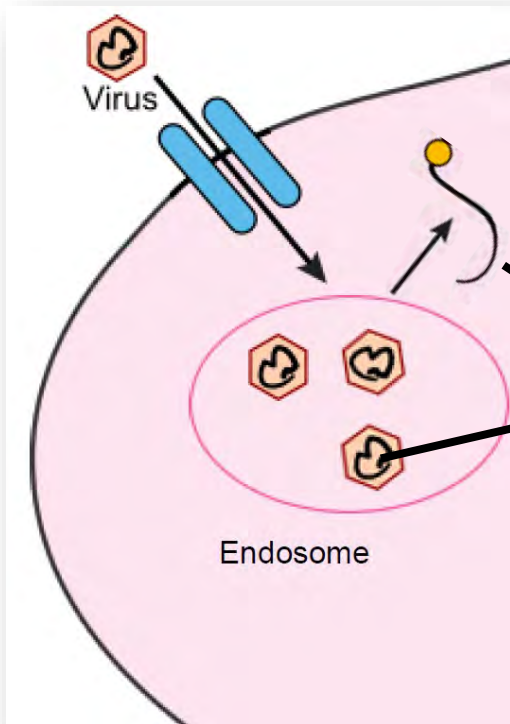


- Cell nuclei
- B cell marker on cell surface
- Rhinovirus

## Rhinovirus binding after 24h



# B cells can be Infected



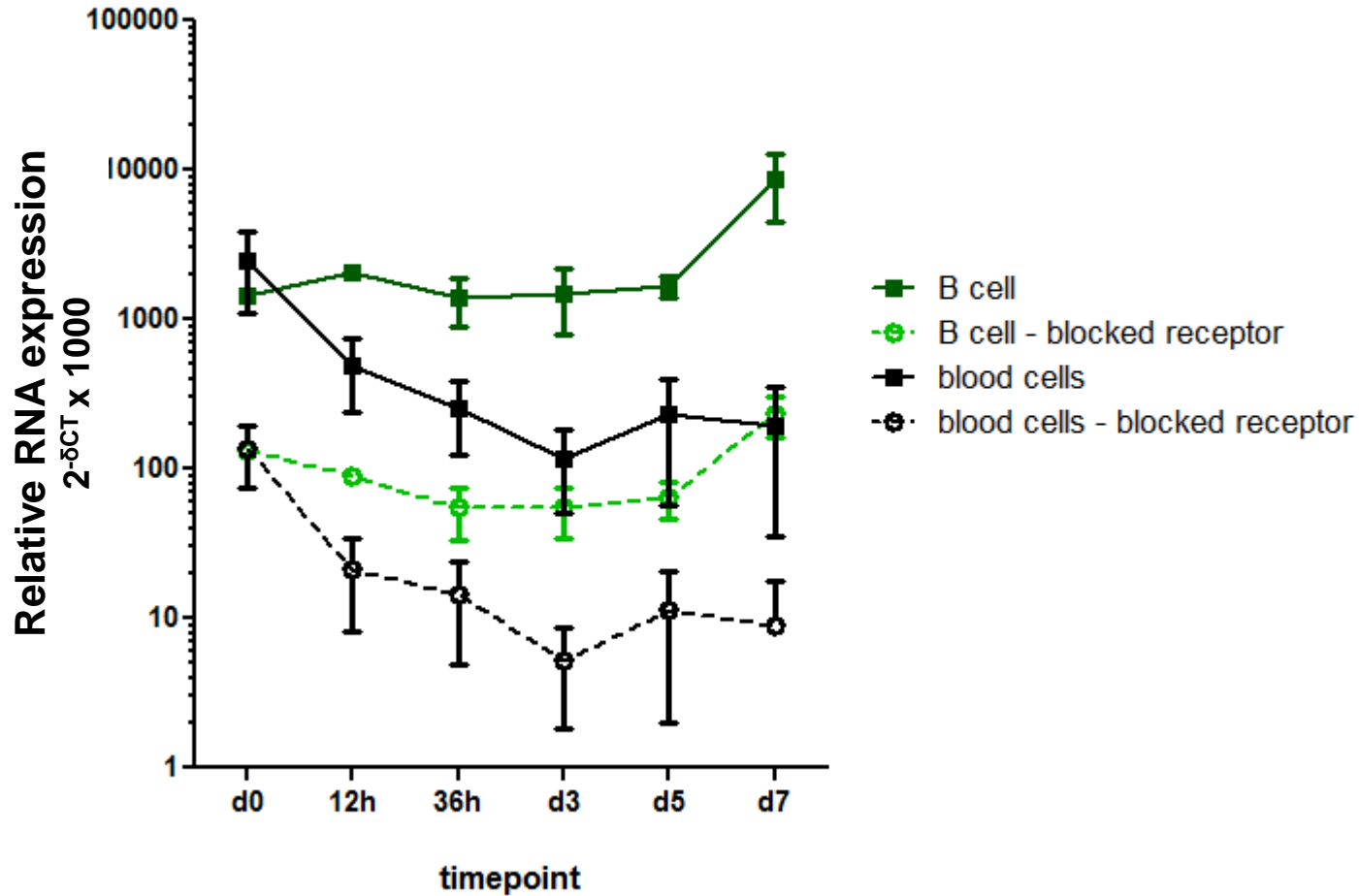
**Collect  
viral RNA**  
At different  
timepoints  
after infection

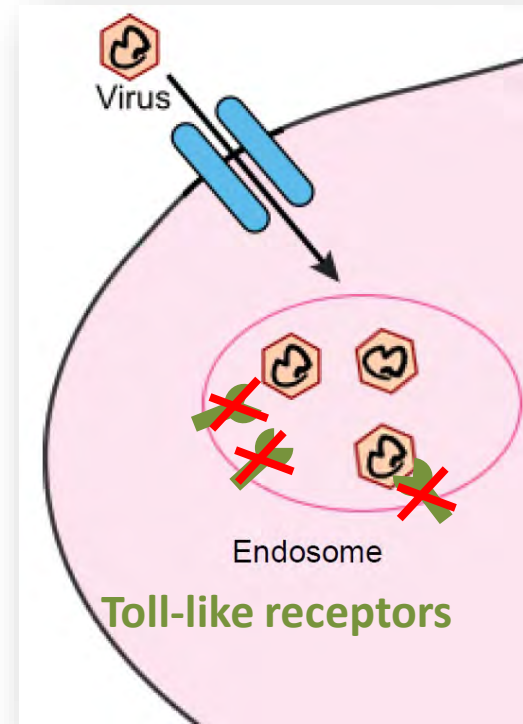
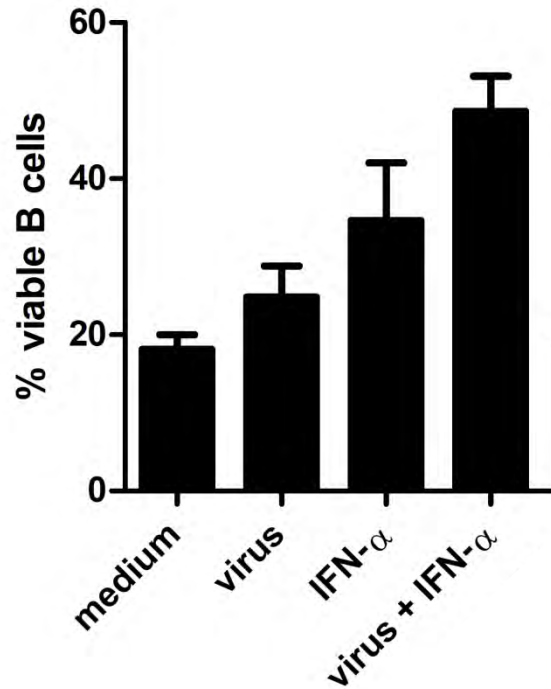


**Check how much virus is there:**  
Measure the amount of  
viral RNA

# B cells can be Infected

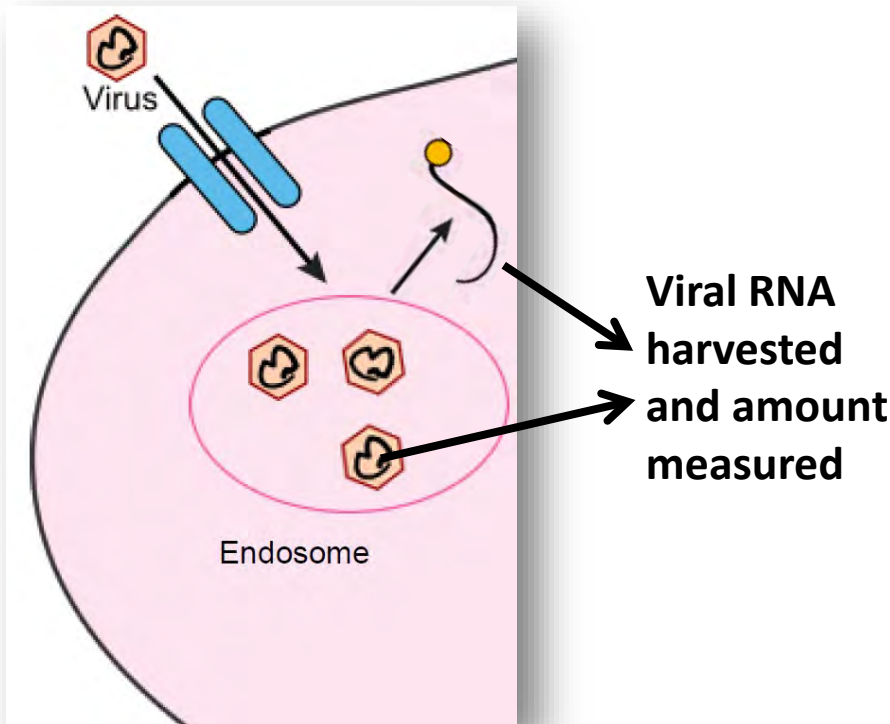
B cells and blood cells in comparison



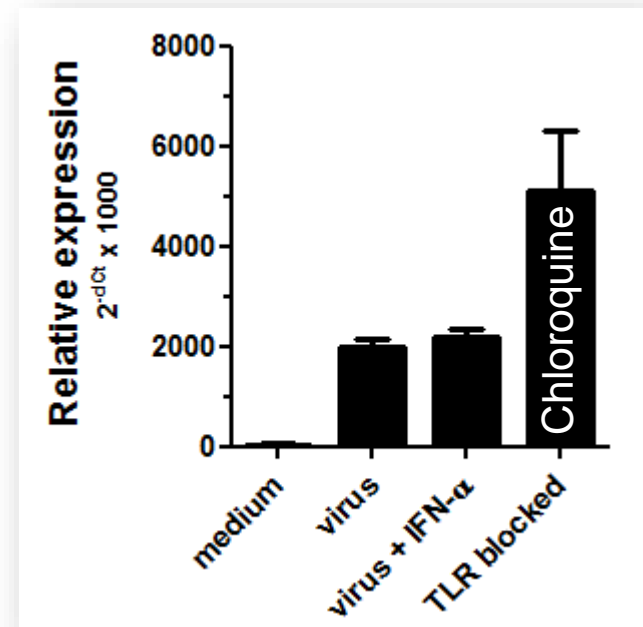


Because boosting cell survival

- ❖ IFN- $\alpha$  + Rhinovirus
- ❖ Toll-like receptor signalling



Viral load



Because extremely high virus load  
❖ Toll-like receptor blocking