

The PRRSV fairytale

How a gentle virus turned into a monster



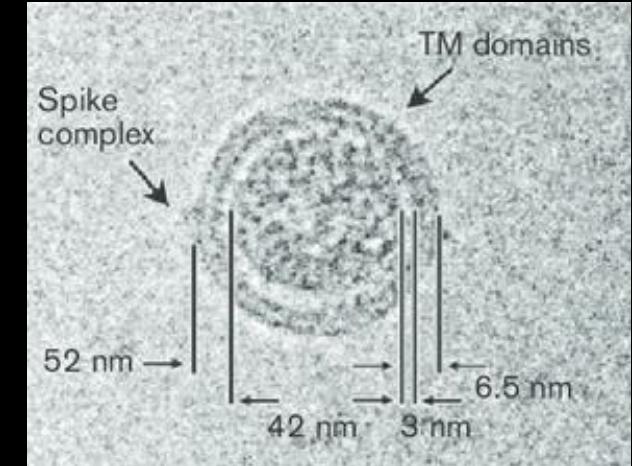
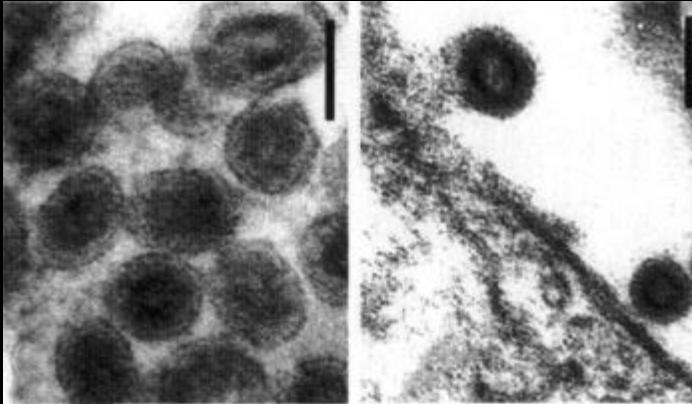
Hans
Nauwynck

Ghent University
Belgium

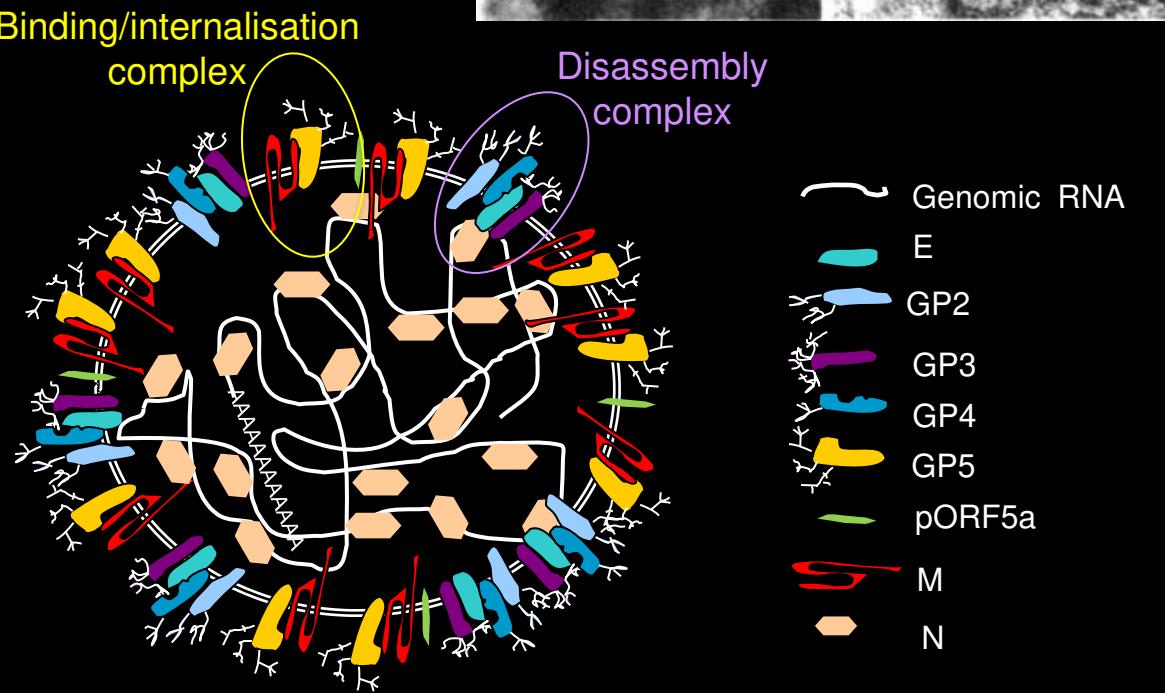
Laboratory of Virology
Faculty Veterinary Medicine

Porcine Reproductive & Respiratory Syndrome Virus - PRRSV

- Classification Order *Nidovirales*
 Family *Arteriviridae*

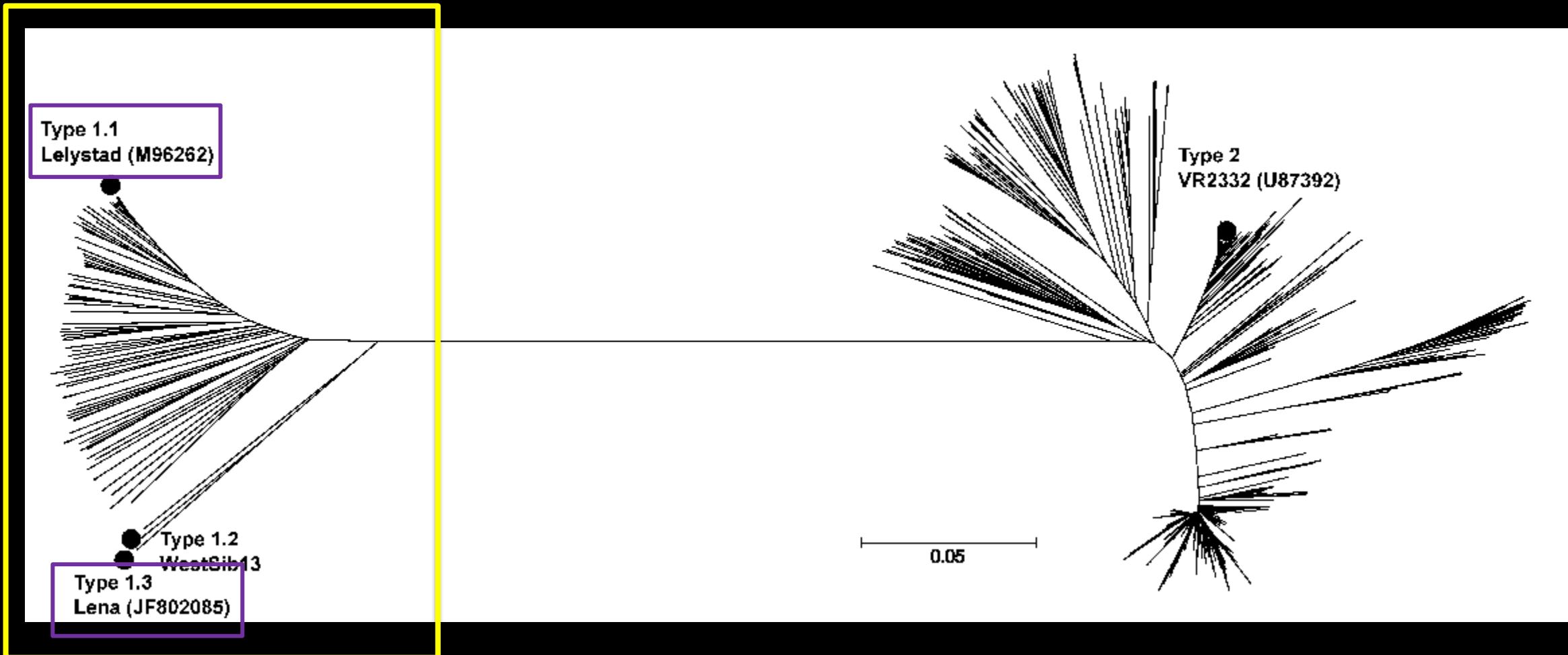


- Virion structure



Porcine Reproductive & Respiratory Syndrome Virus - PRRSV

- Huge genetic variation



PRRSV - mØ



Xiaobo
Duan



Nathalie
Vanderheijden



Gerald
Misinzo



Peter
Delputte



Hanne
Van Gorp



Wander
Van Breedam



Jiekong
Xie

Siglec⁺CD163⁺macrophages

nasal mucosa

lungs

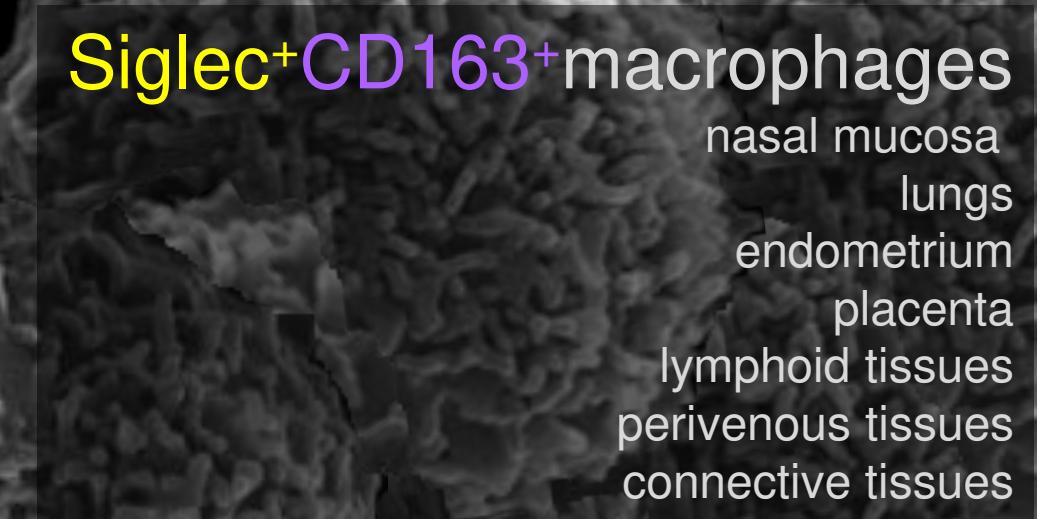
endometrium

placenta

lymphoid tissues

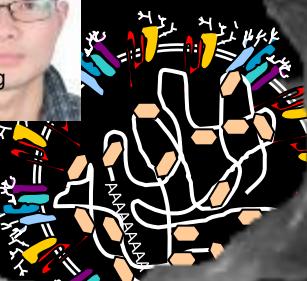
perivenous tissues

connective tissues



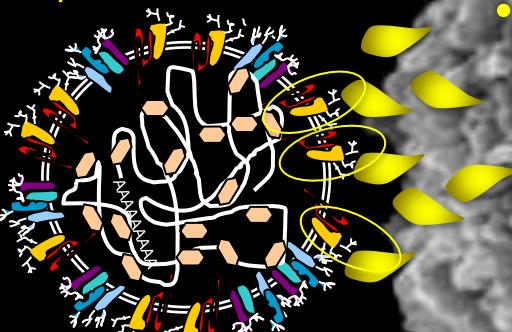
b. internalisation

- via siglec (clathrin/dynein)
-> **MGP5** (sugar tree-sialic acids)



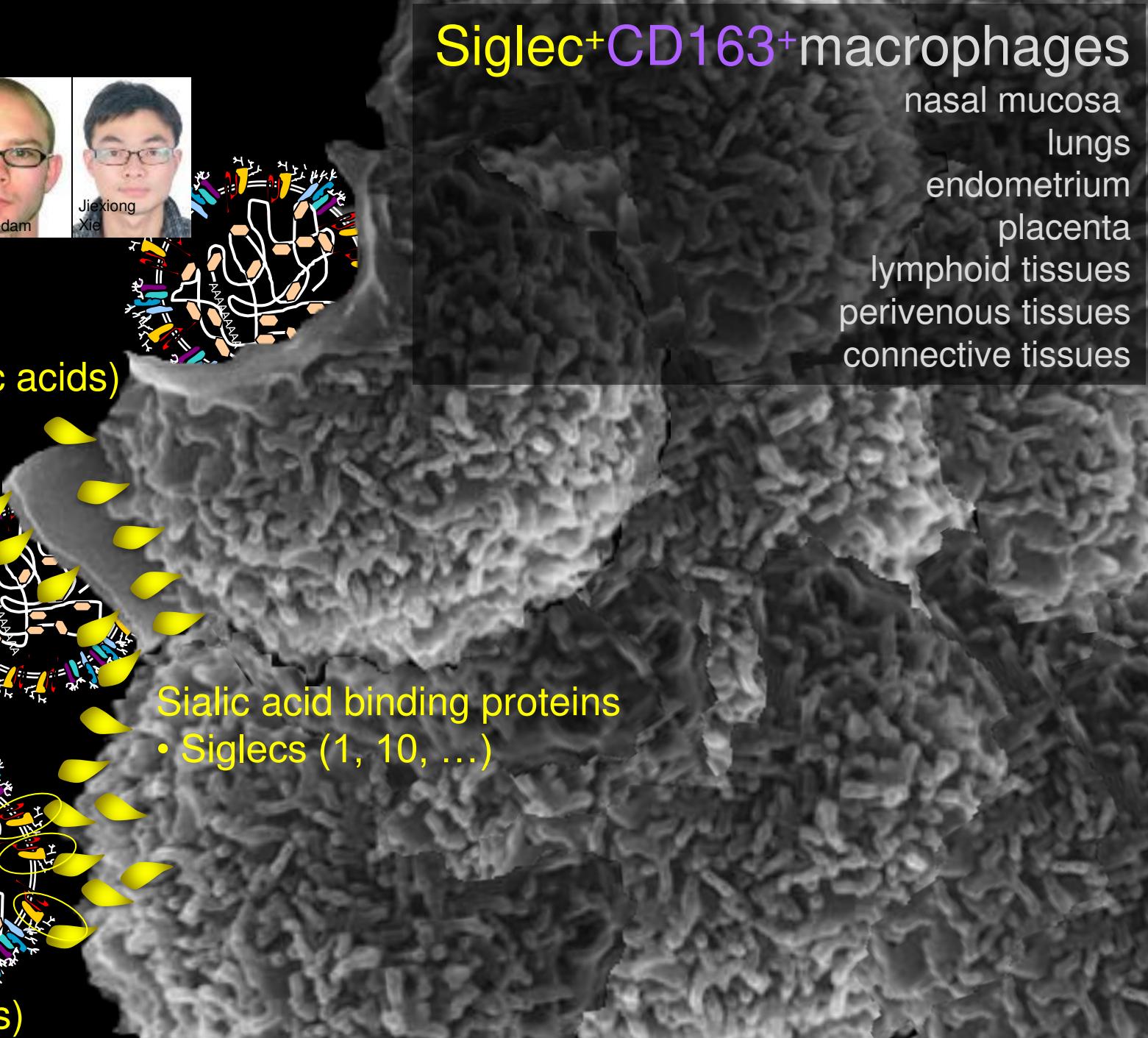
Binding/internalisation
complex

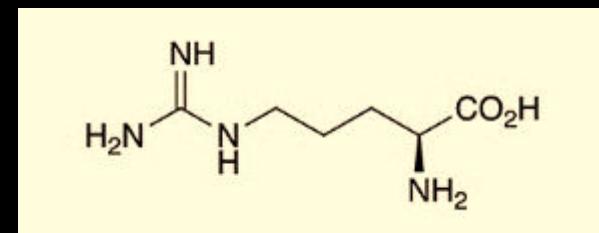
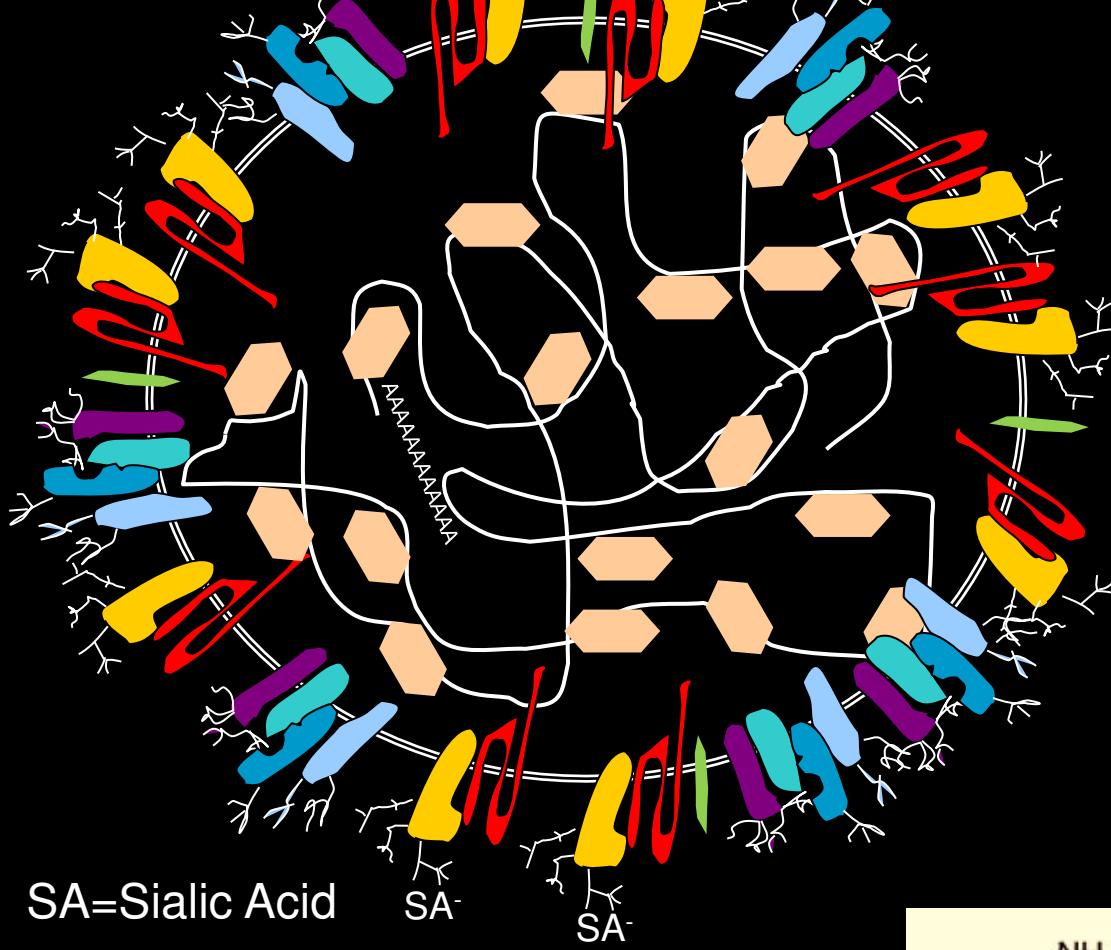
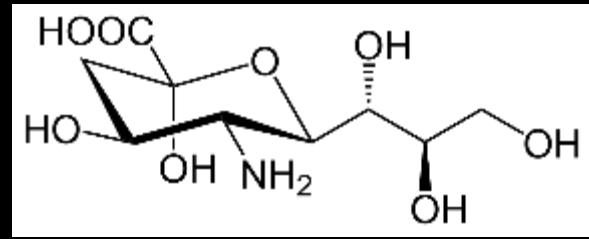
Sialic acid binding proteins
• Siglecs (1, 10, ...)



a. binding

- to heparan sulphate
-> **MGP5**
- to siglec
-> **MGP5** (sugar tree-sialic acids)

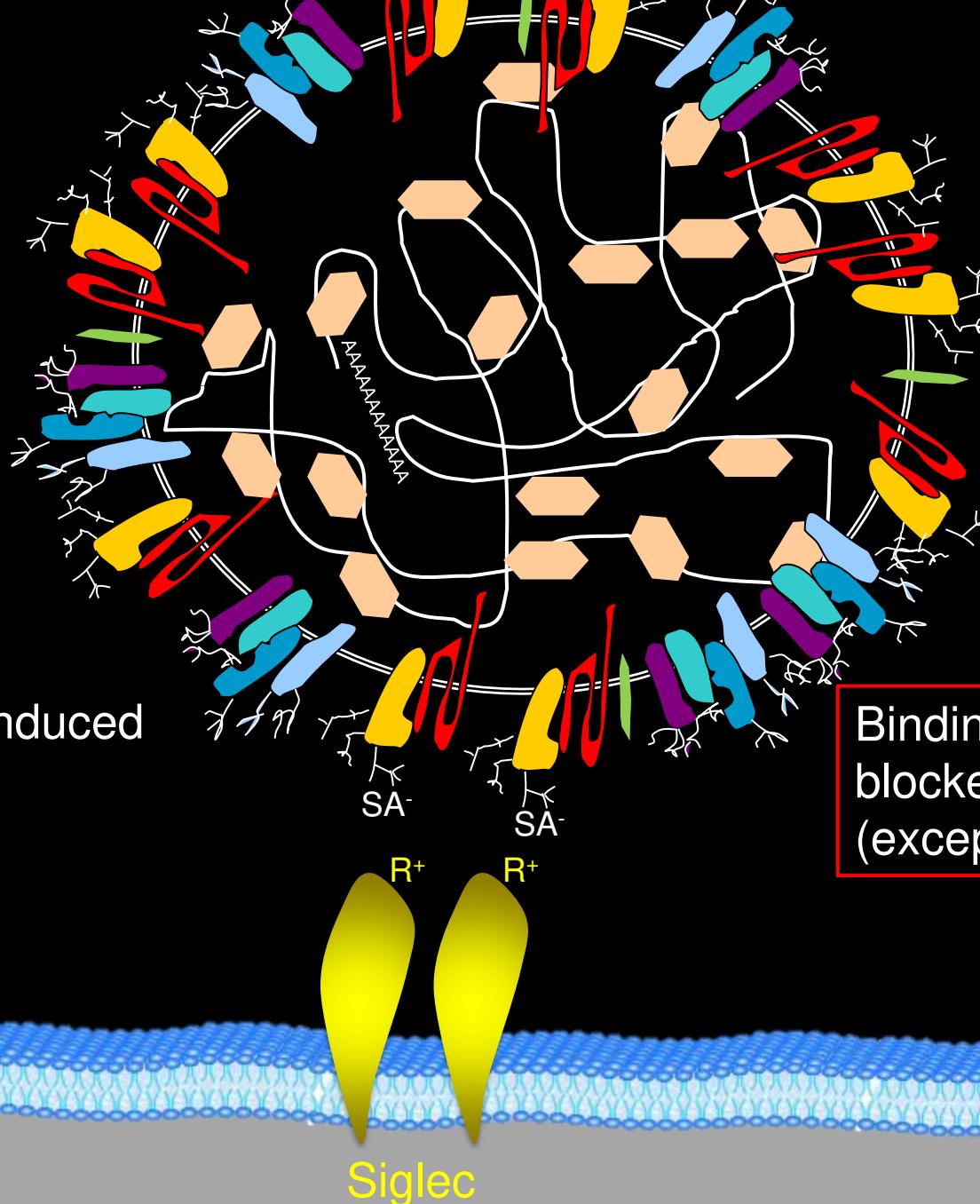




Macrophage

Macrophage

Antibodies are not induced by sugar trees



Binding cannot be directly
blocked by antibodies
(except by steric hindrance)

PRRSV - mØ



Siglec⁺CD163⁺macrophages

nasal mucosa

lungs

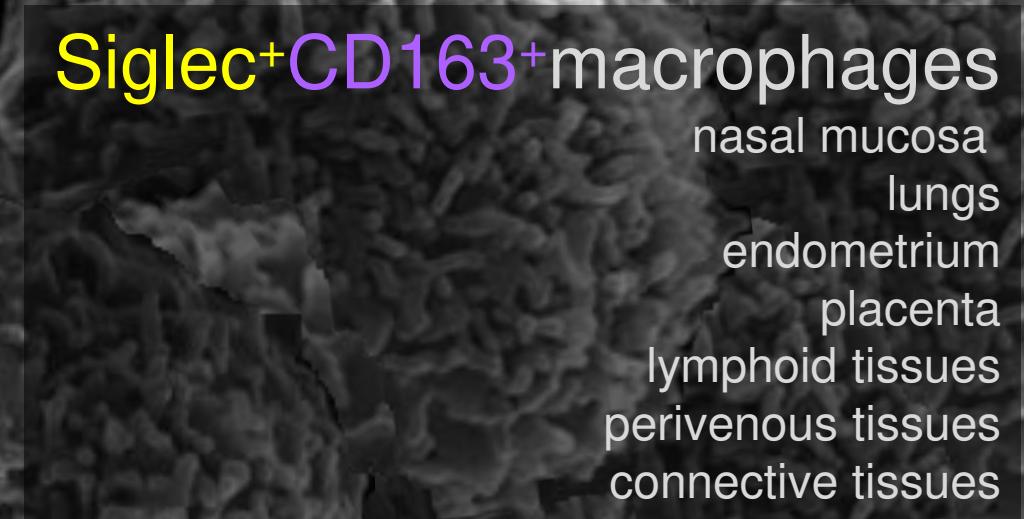
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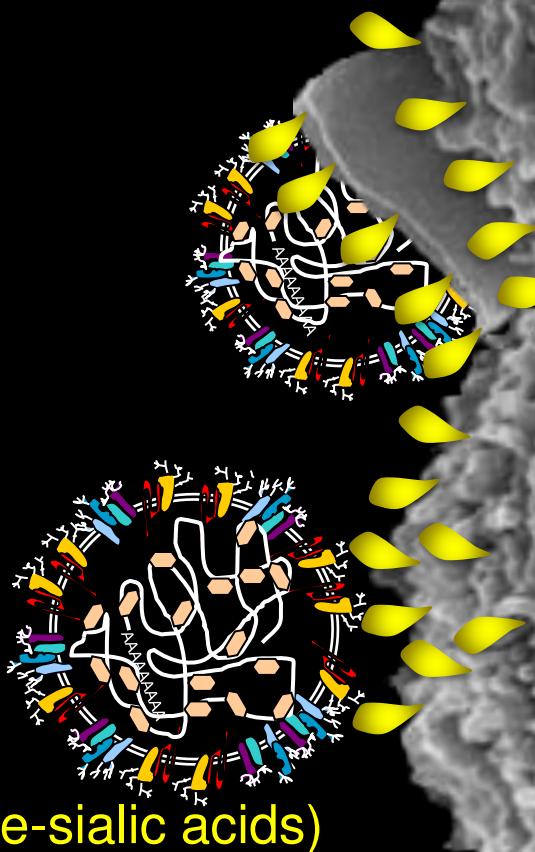
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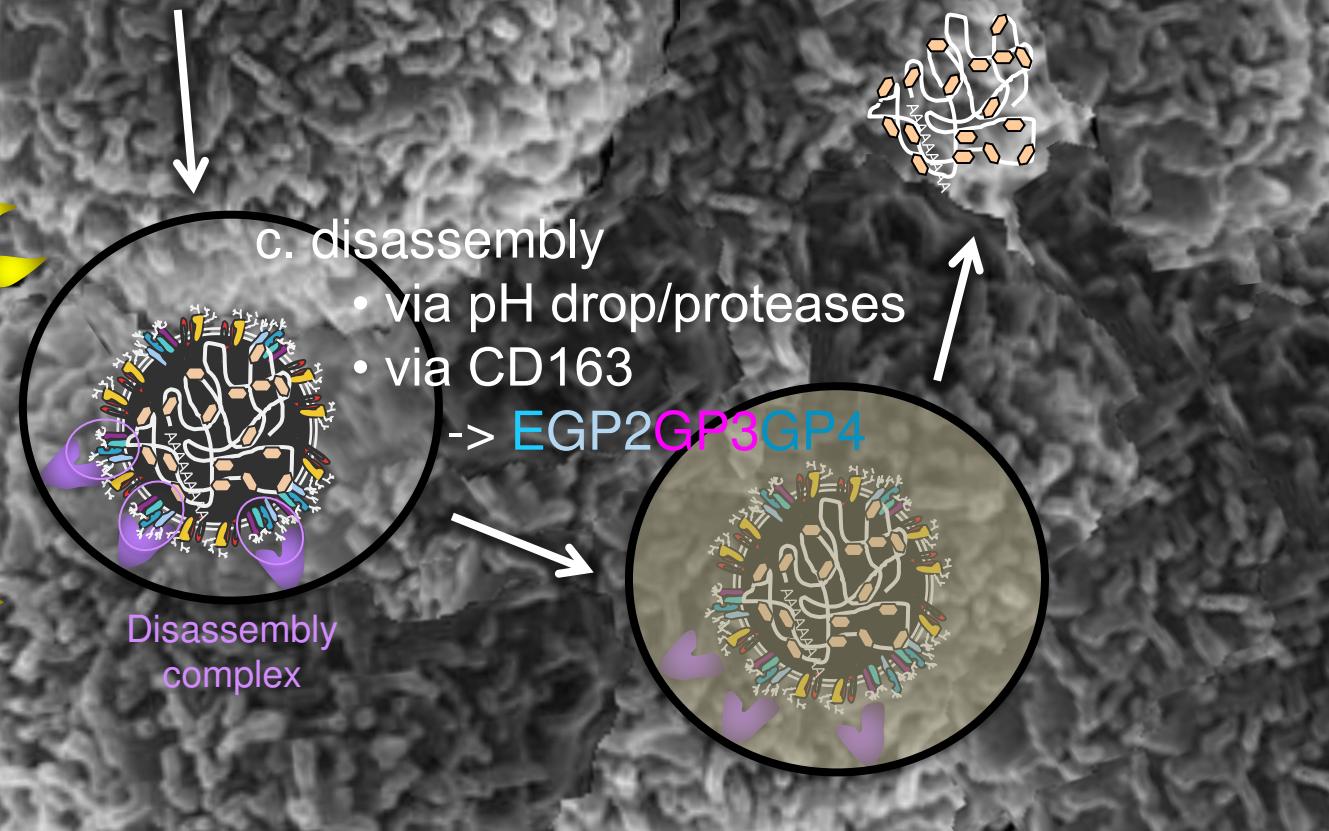
- to heparan sulphate
-> **MGP5**
- to siglec
-> **MGP5** (sugar tree-sialic acids)



c. disassembly

- via pH drop/proteases
- via CD163
-> **EGP2****GP3****GP4**

Disassembly complex



PRRSV - mØ



Siglec⁺CD163⁺macrophages

nasal mucosa

lungs

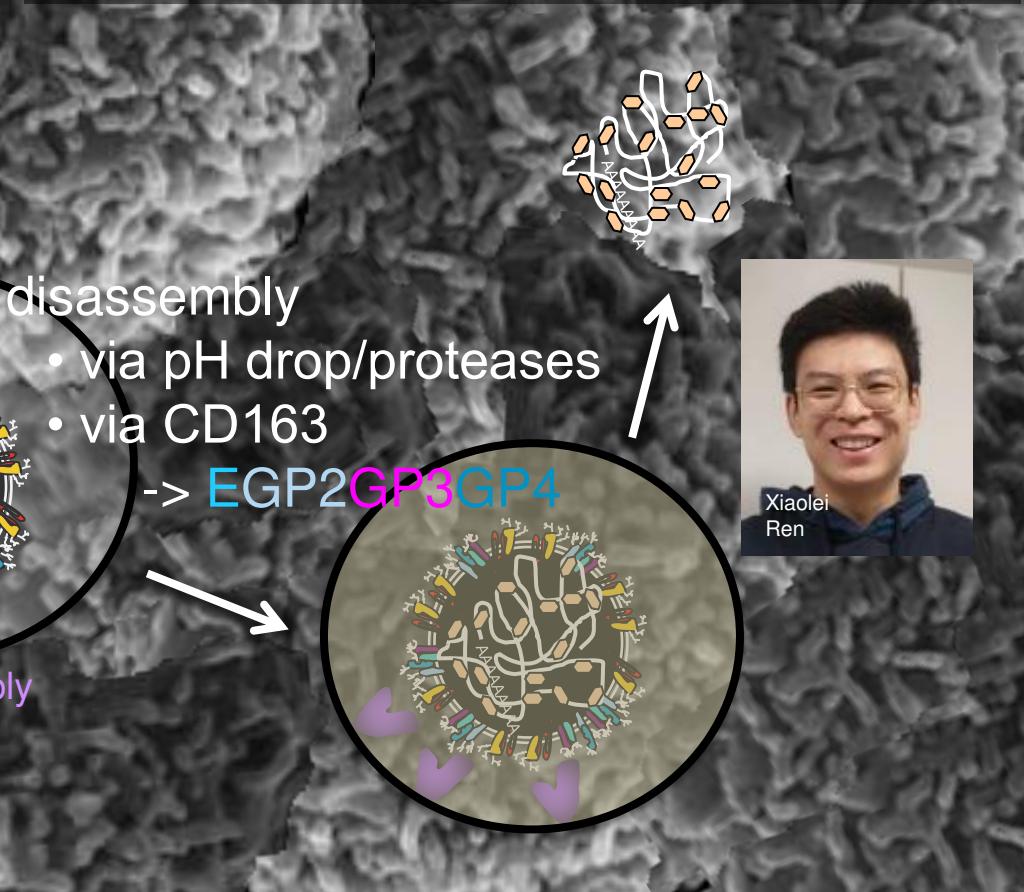
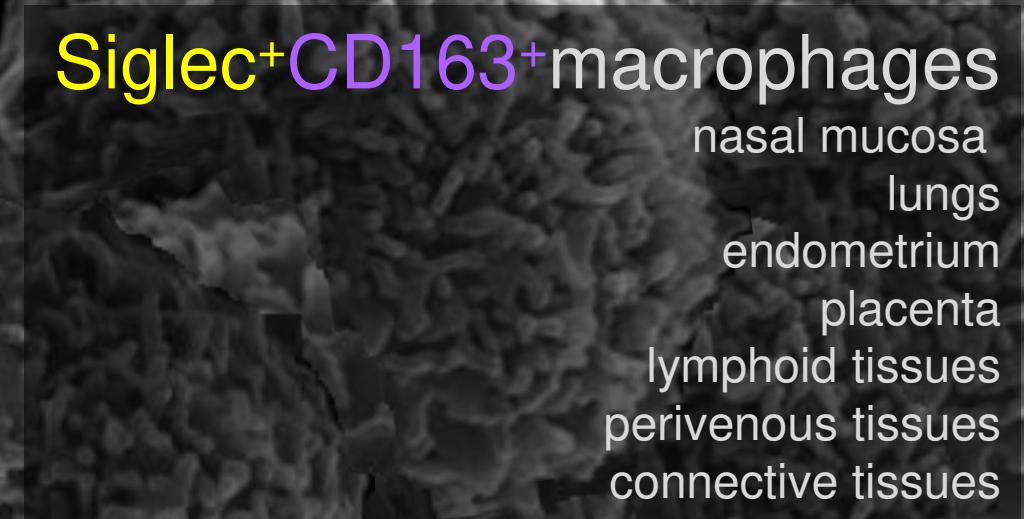
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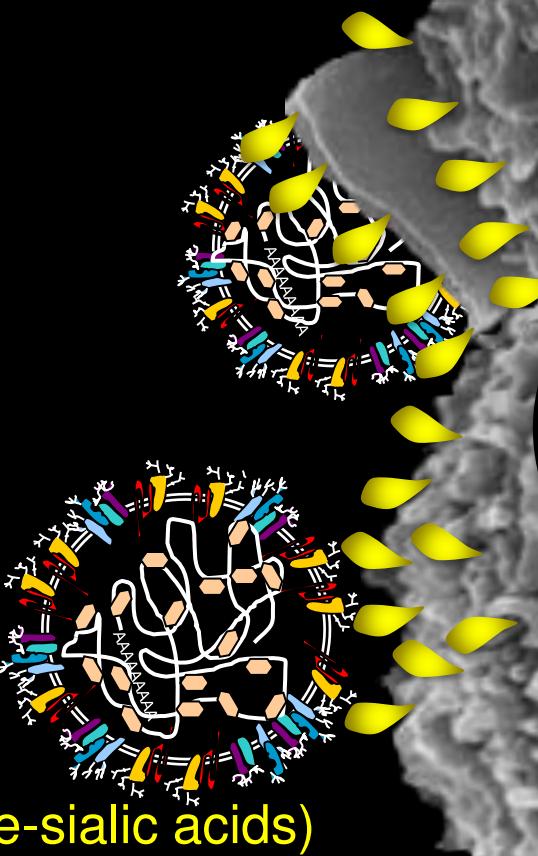
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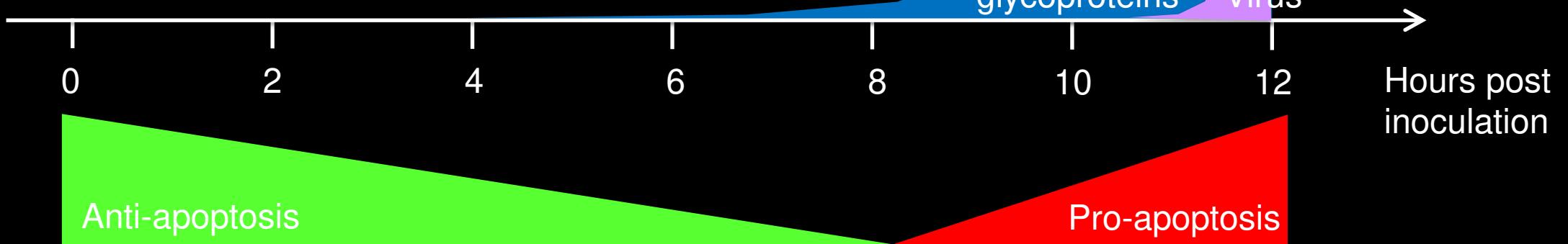
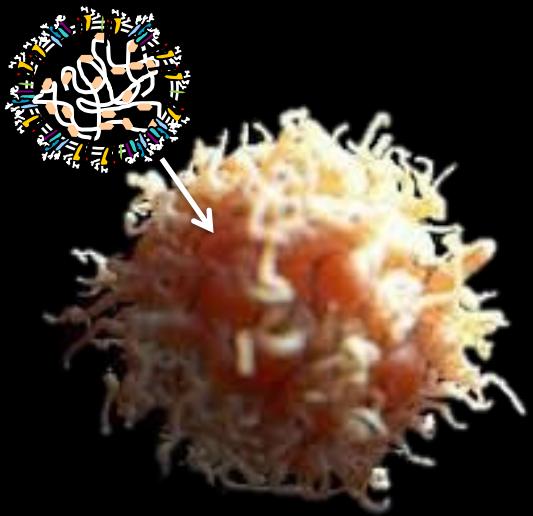
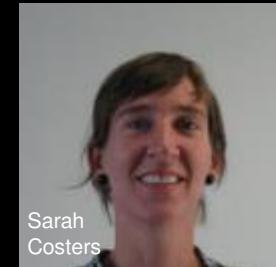
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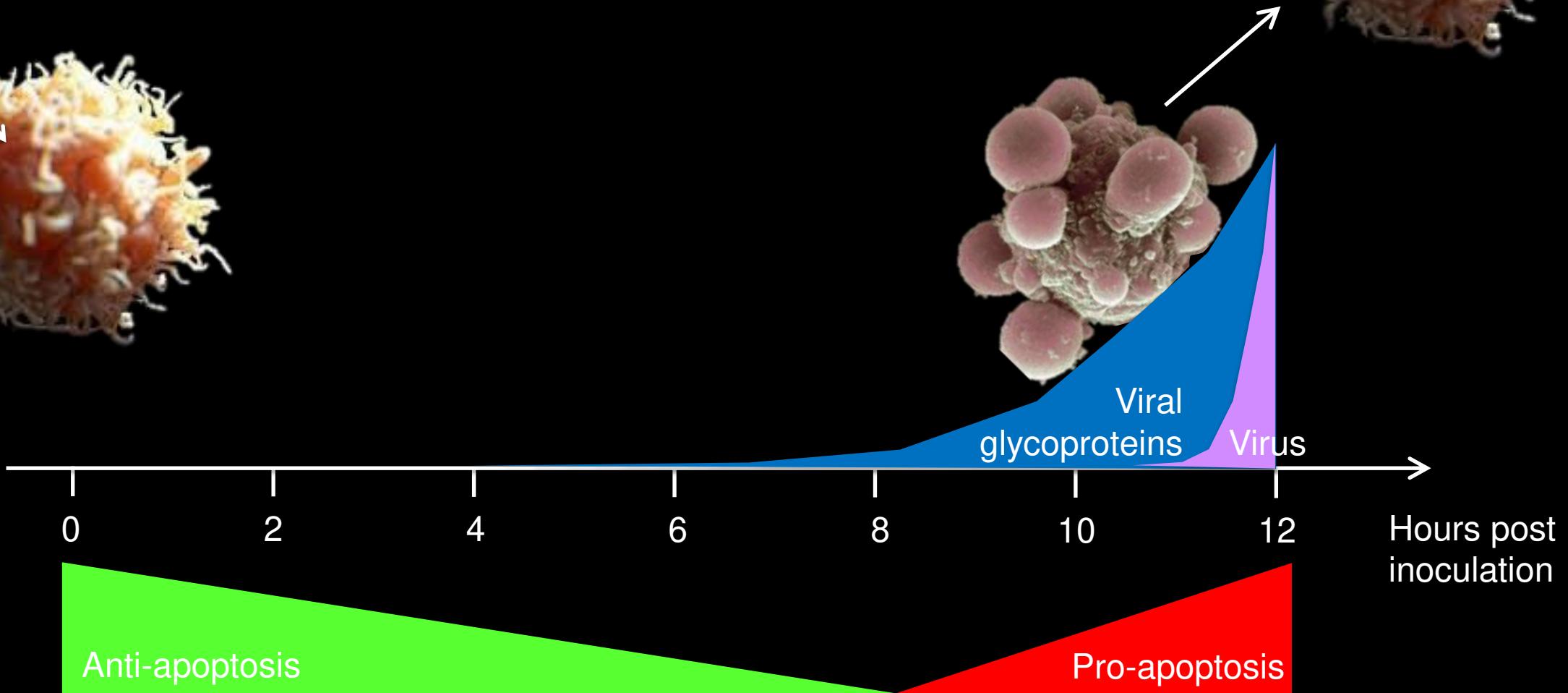
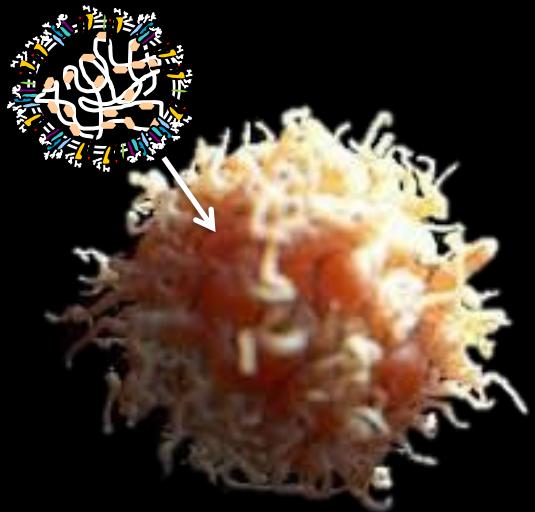
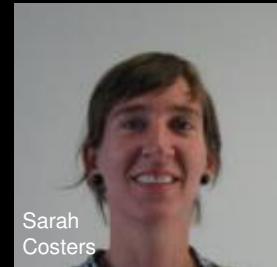
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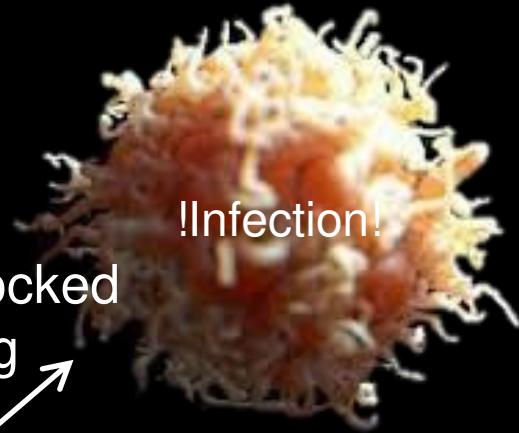
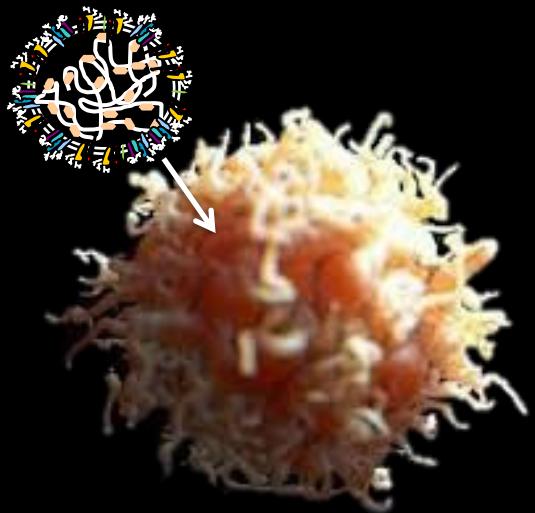
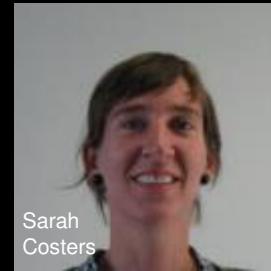
PRRSV - mØ replication cycle ~ apoptosis



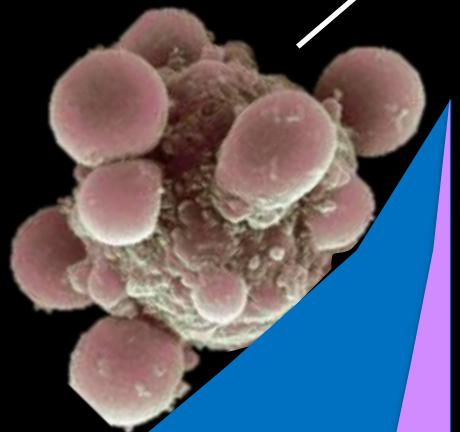
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PRRSV - mØ replication cycle ~ apoptosis

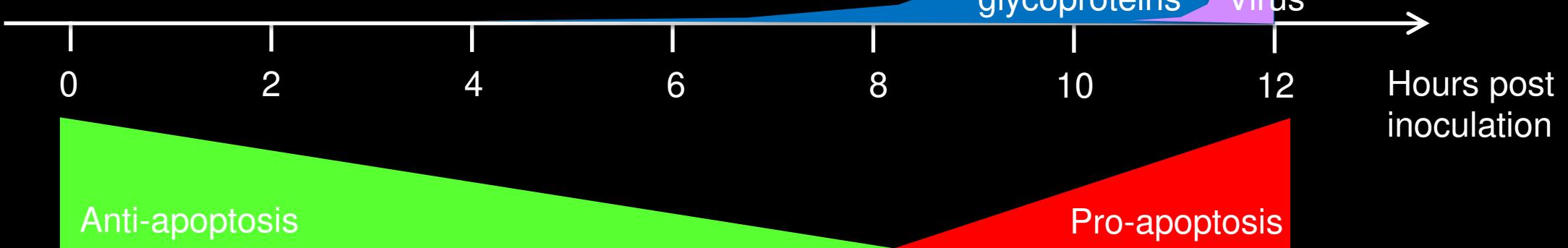


Cannot be blocked
by neutralizing
antibodies

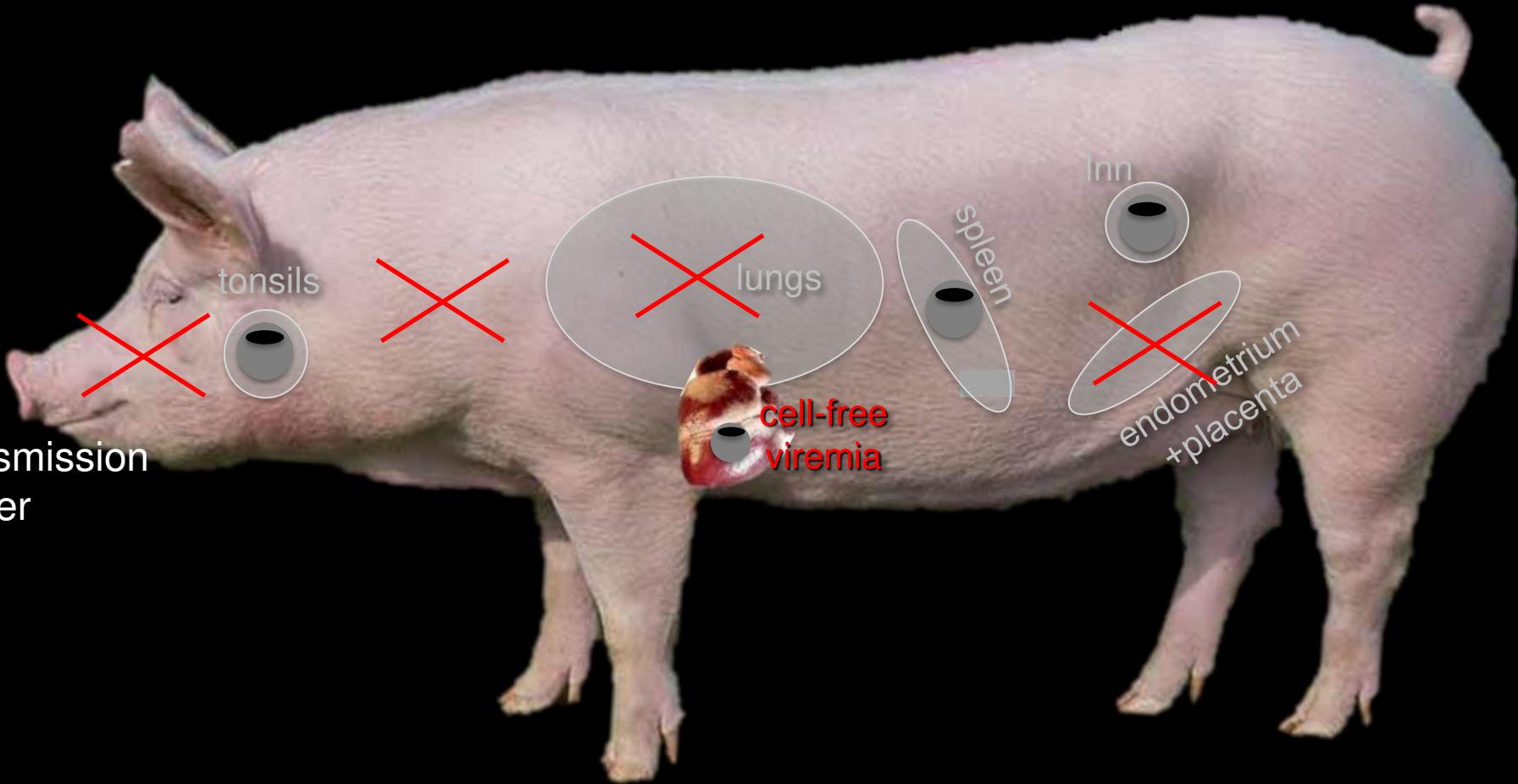
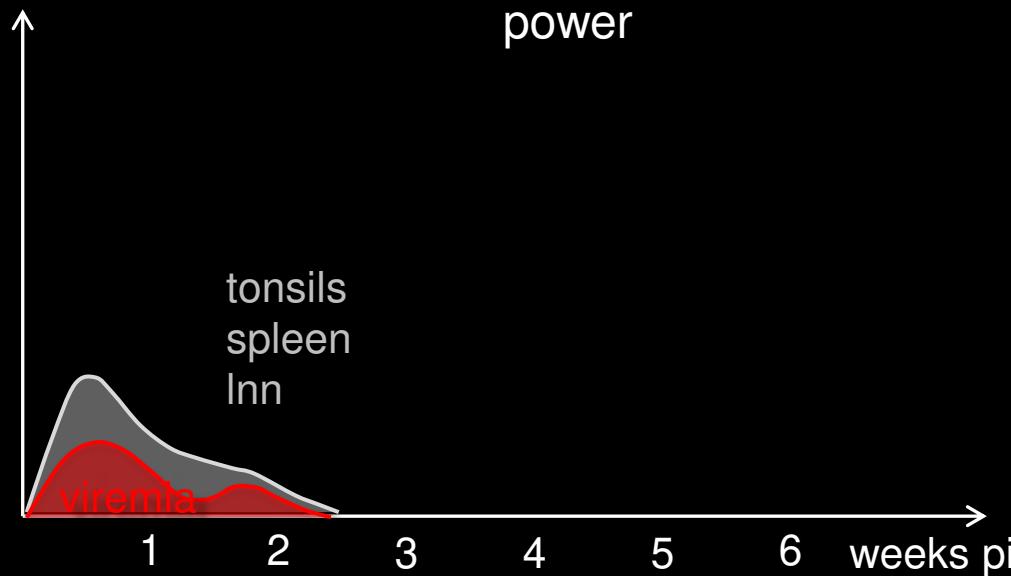


Viral
glycoproteins

Virus

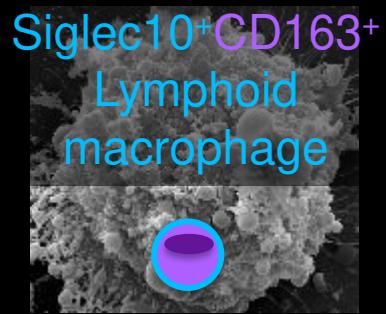


<1990 - Archetype PRRSV - hypothesis?

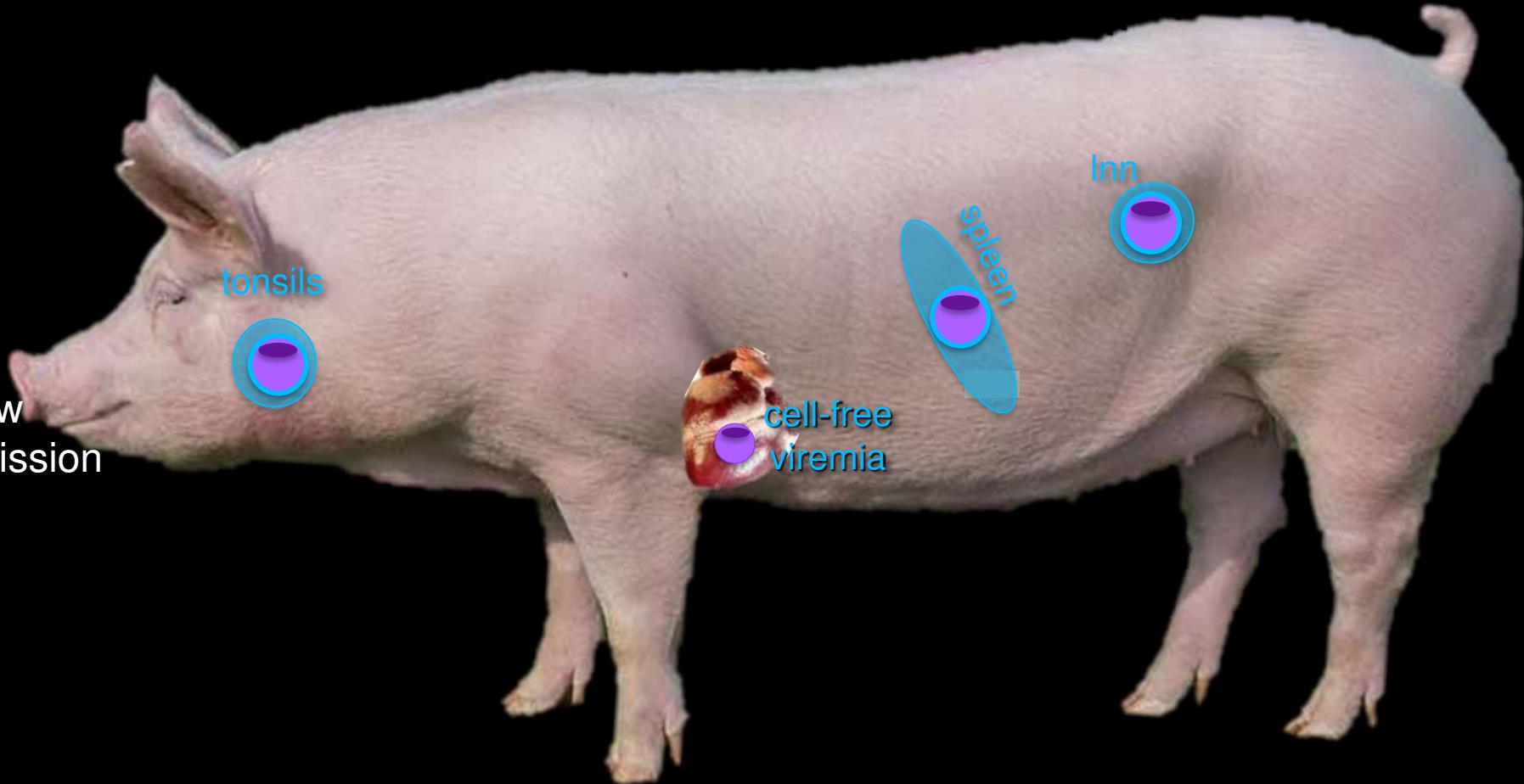


- low virulence/apathogenic

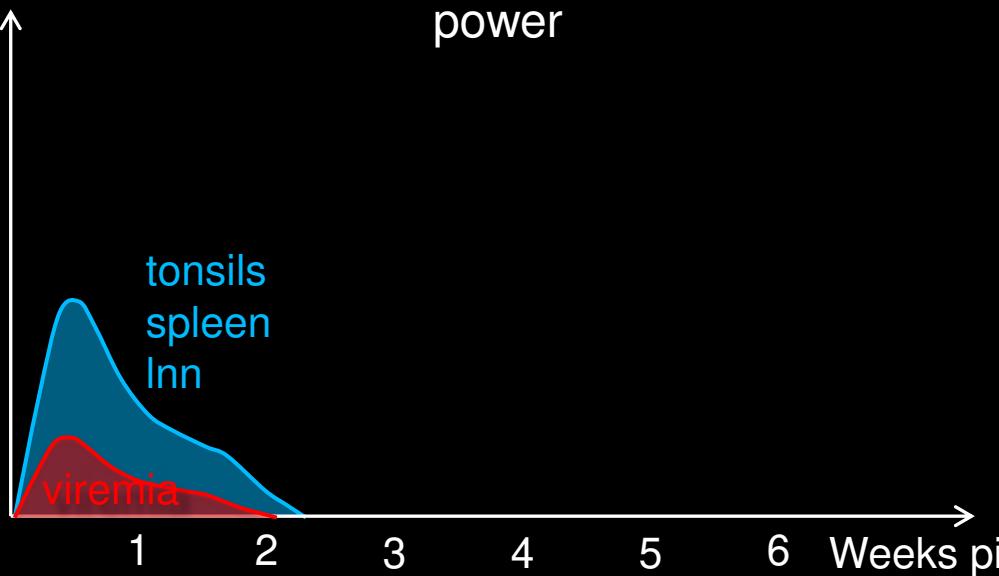
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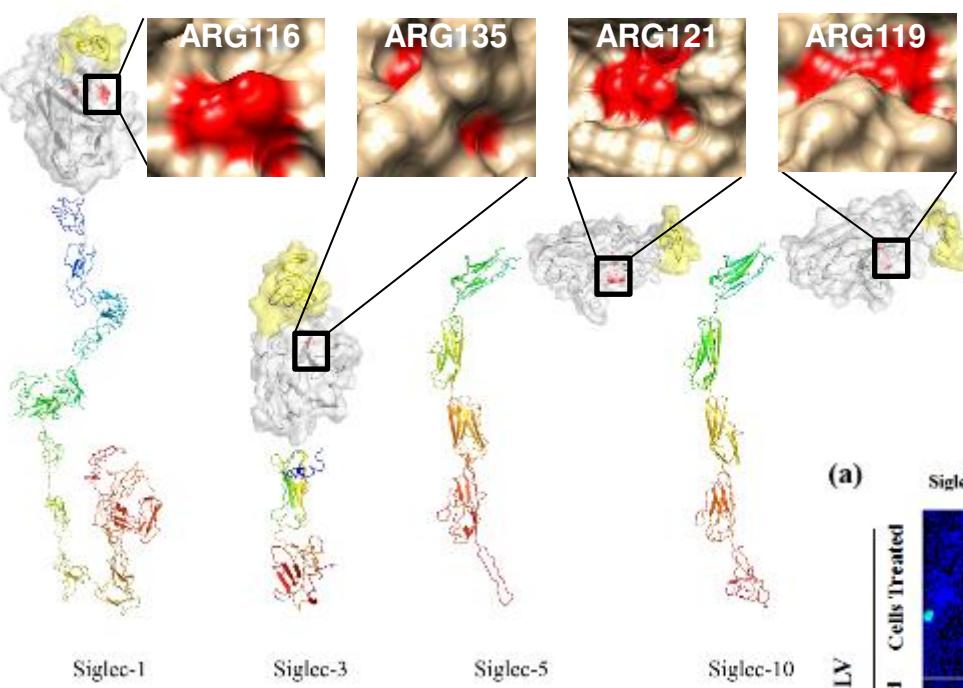


Infection



very low
transmission
power

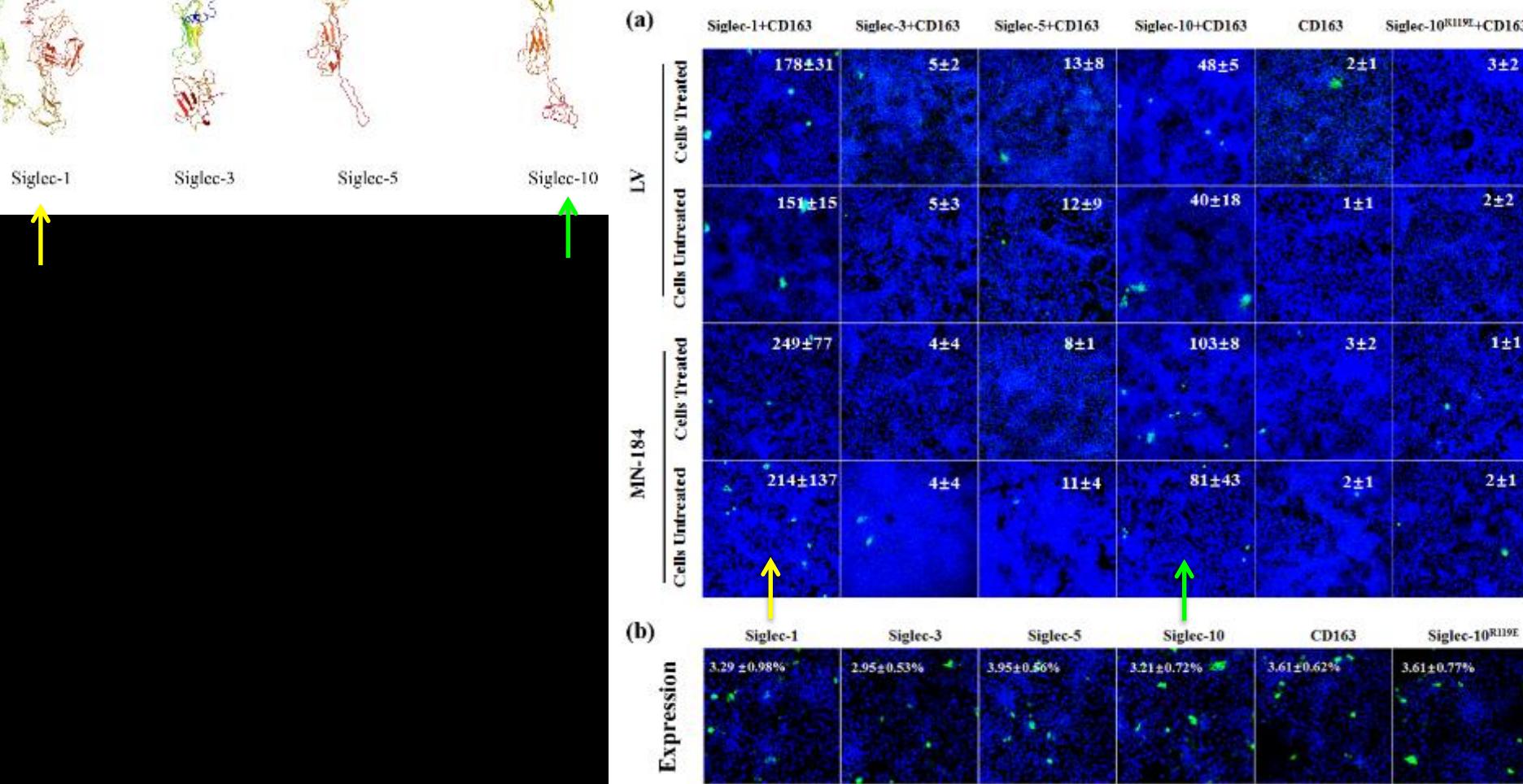




Siglec10 is a candidate archereceptor for PRRSV



Jiexiong Xie



Siglec1/Siglec10 preference ~ PRRSV strain

PK15S1-CD163
PK15S10-CD163

G1s1
LV
(Netherlands, 1991)

G1s3
Lena
(Belarus, 2007)

G2
VR2332
(USA, 1990)

G2
MN-184
(USA, 2001)

S1

S10

S1

S10

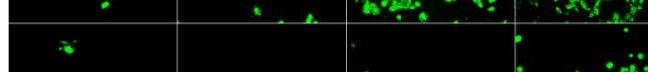
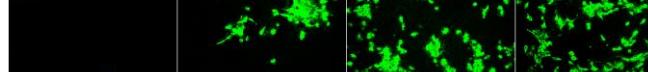
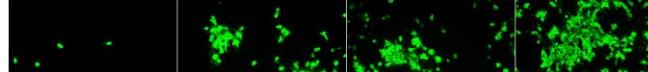
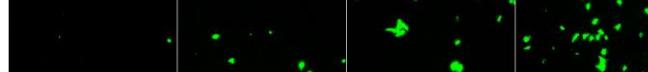
S1

S10

S1

S10

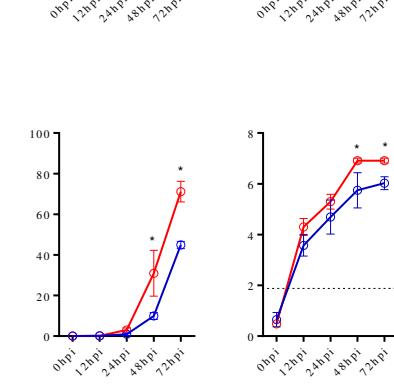
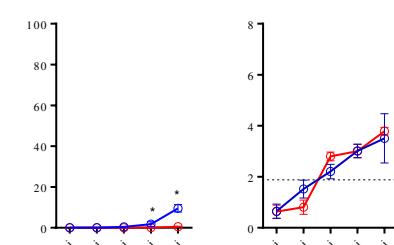
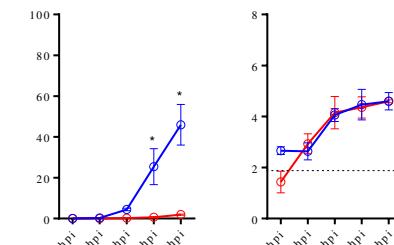
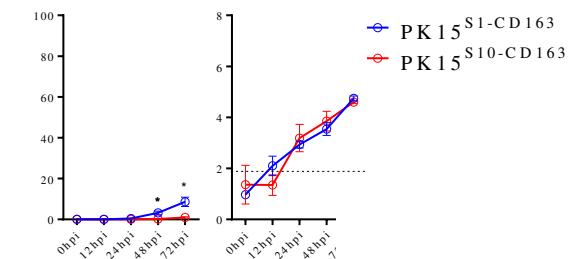
12hpi 24hpi 48hpi 72hpi



Infection rate (%)

(%)

Virus titer (\log_{10} TCID₅₀/ml)

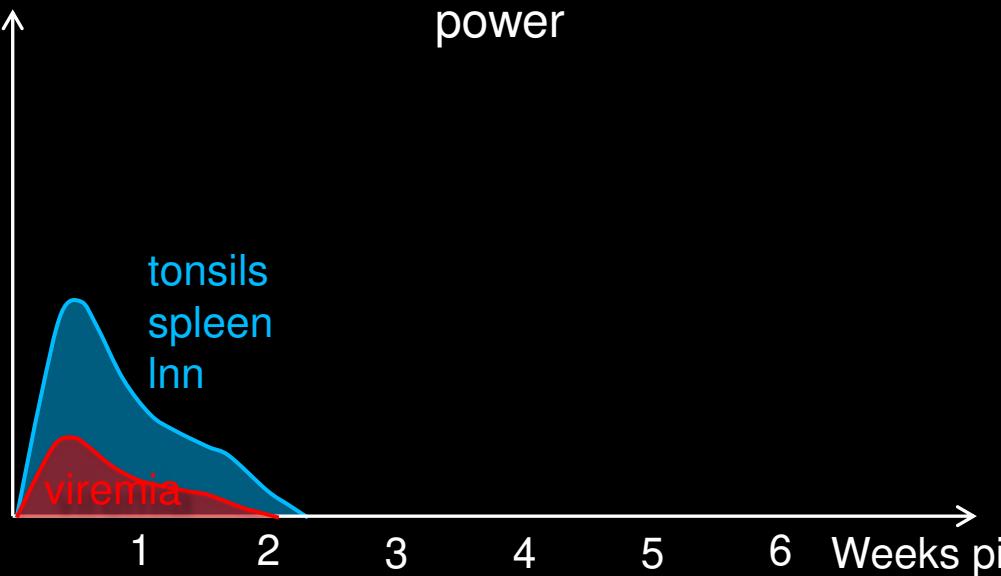
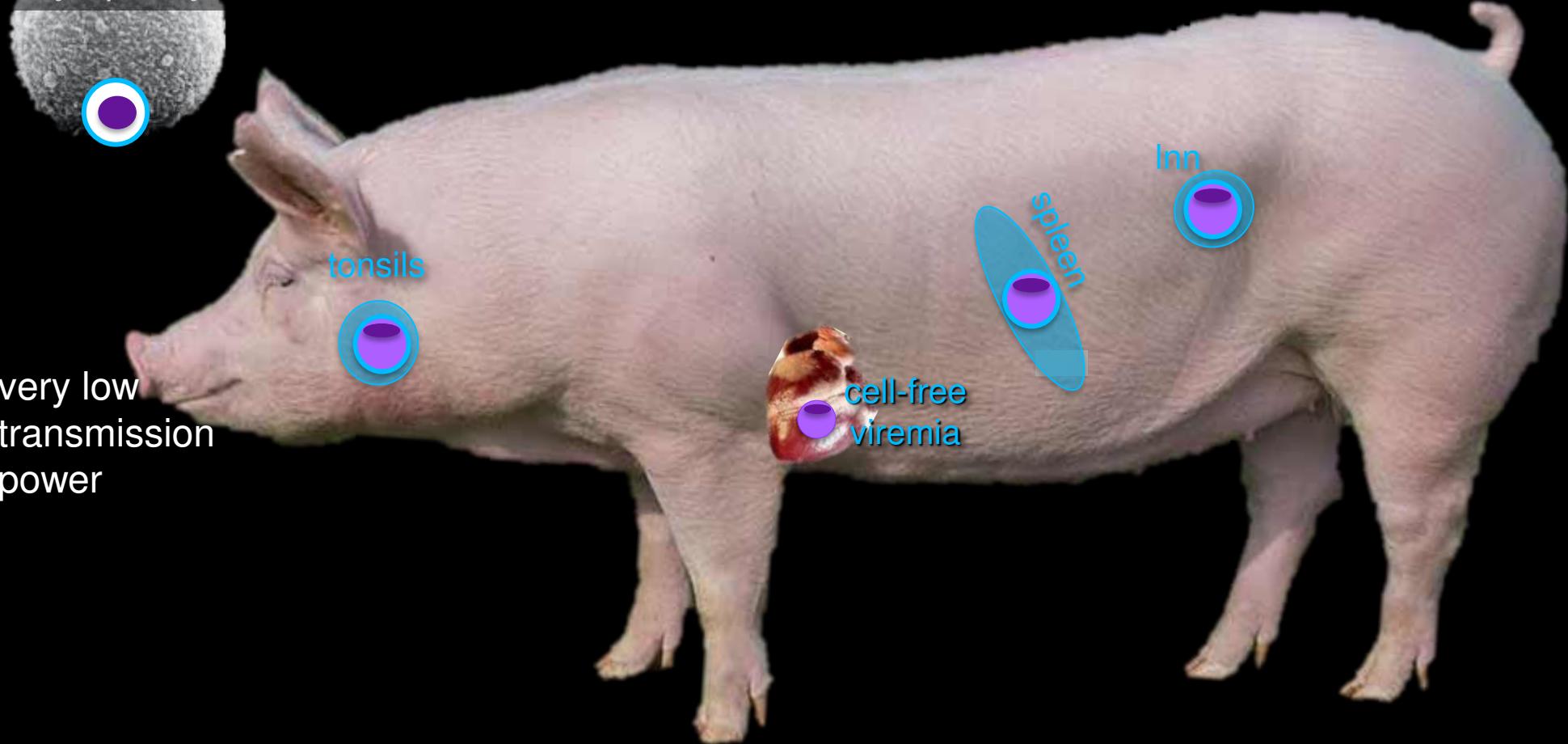


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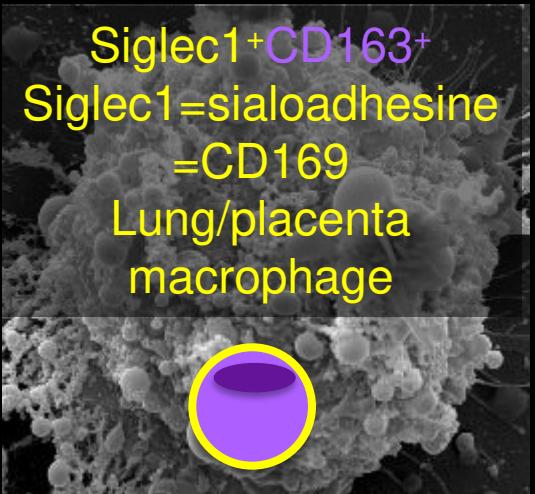


Infection

Siglec10⁺ Virus uptake but no disintegration
B-lymphocyte Persistence!

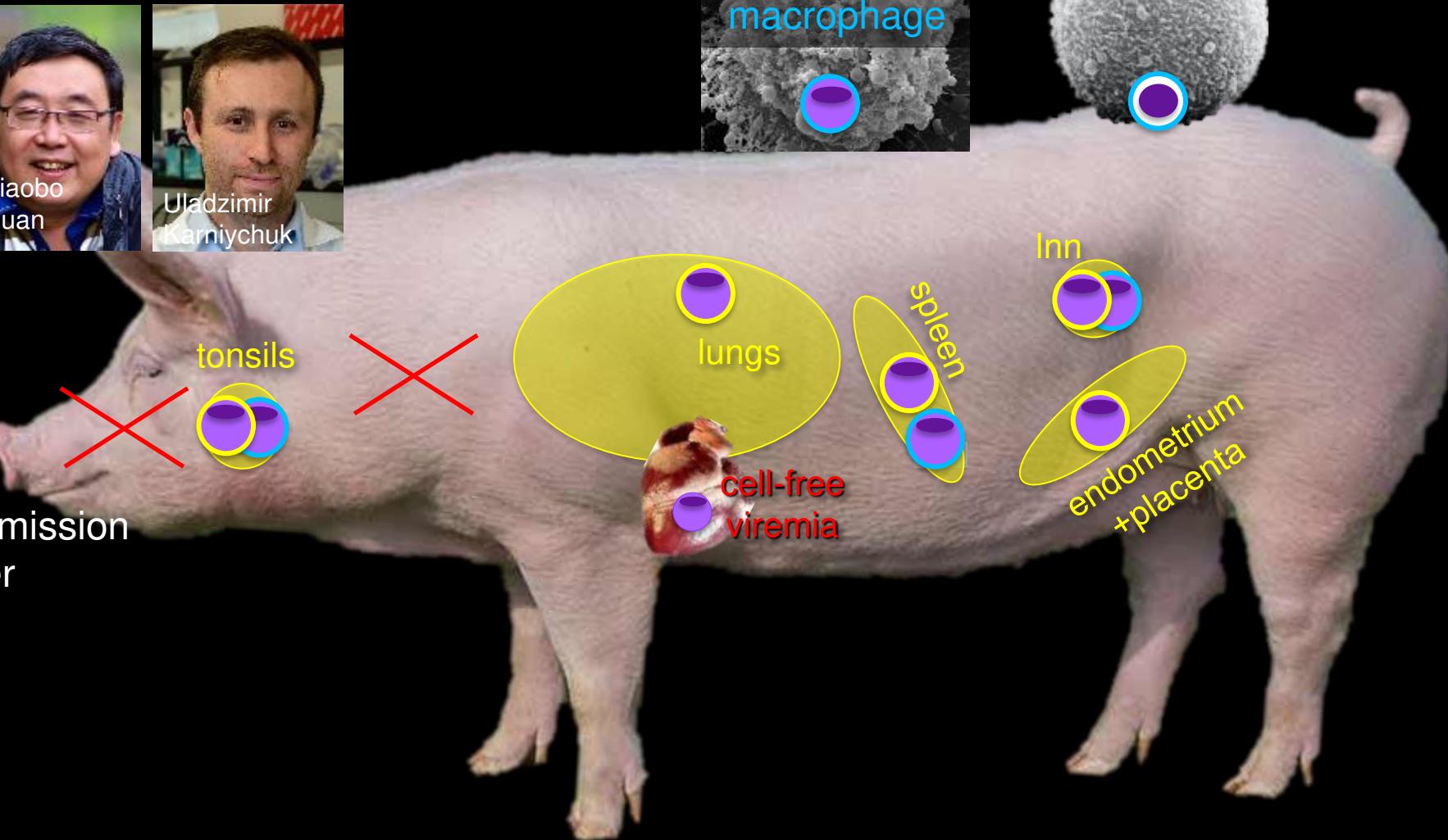
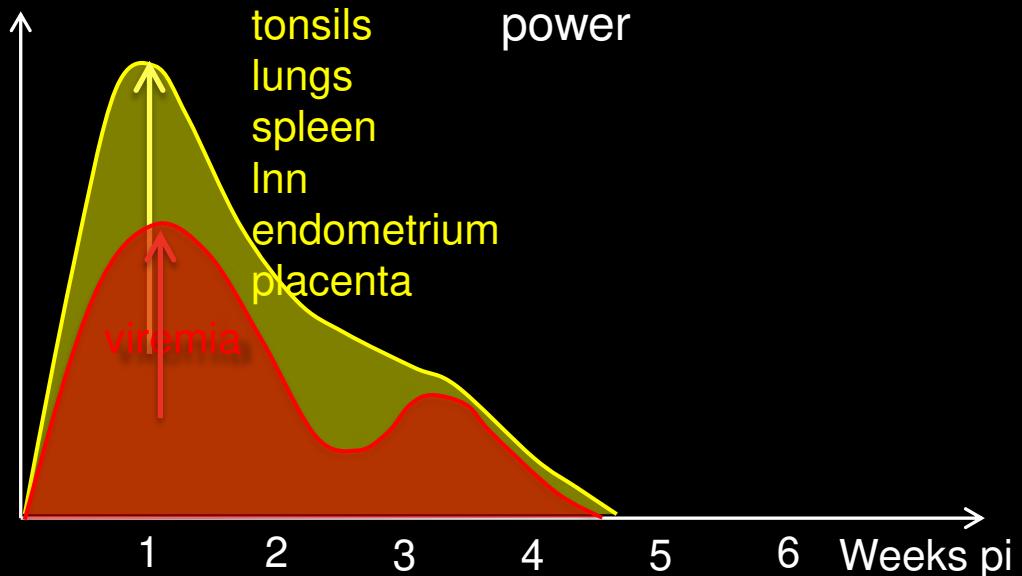


1990 - Low virulent PRRSV (G1s1;LV)



Infection

low
transmission
power

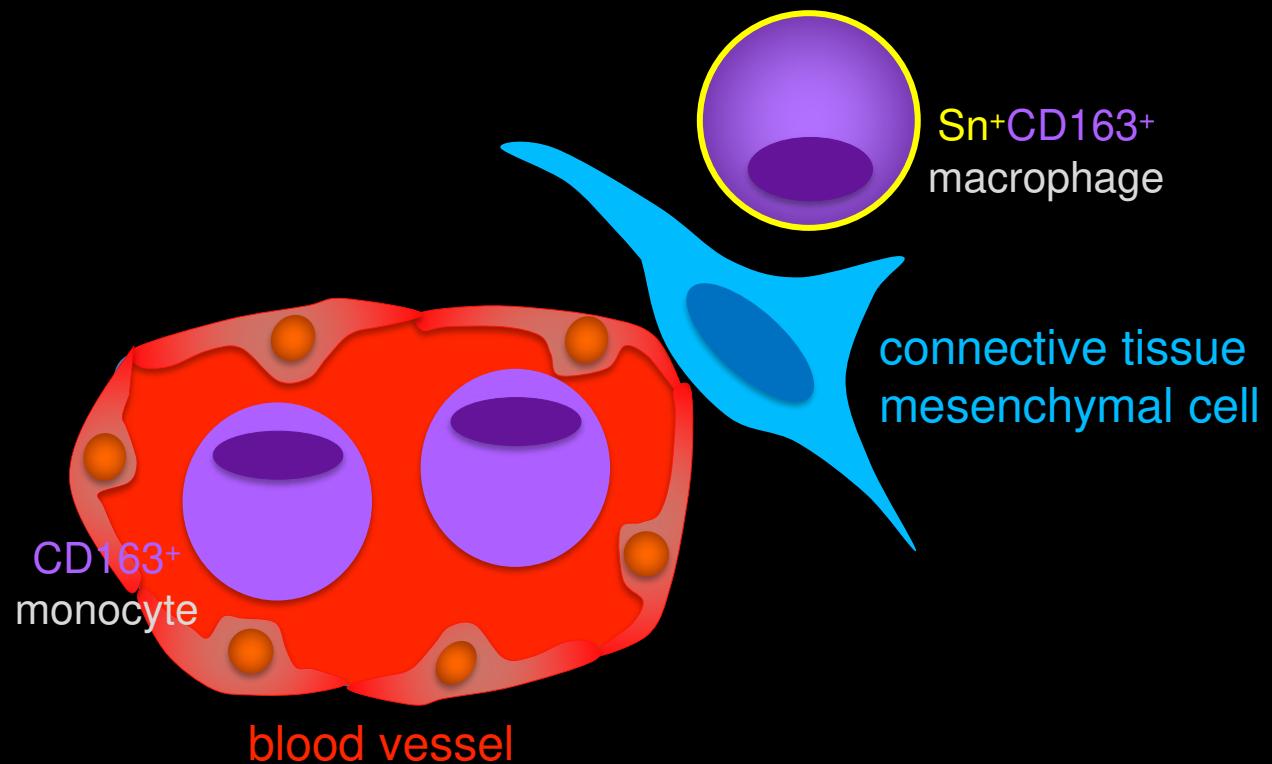


- no general/respiratory problems,
except during co-infections
- reproductive problems

Siglec1 induction in monocytes? → contact with mesenchymal cells



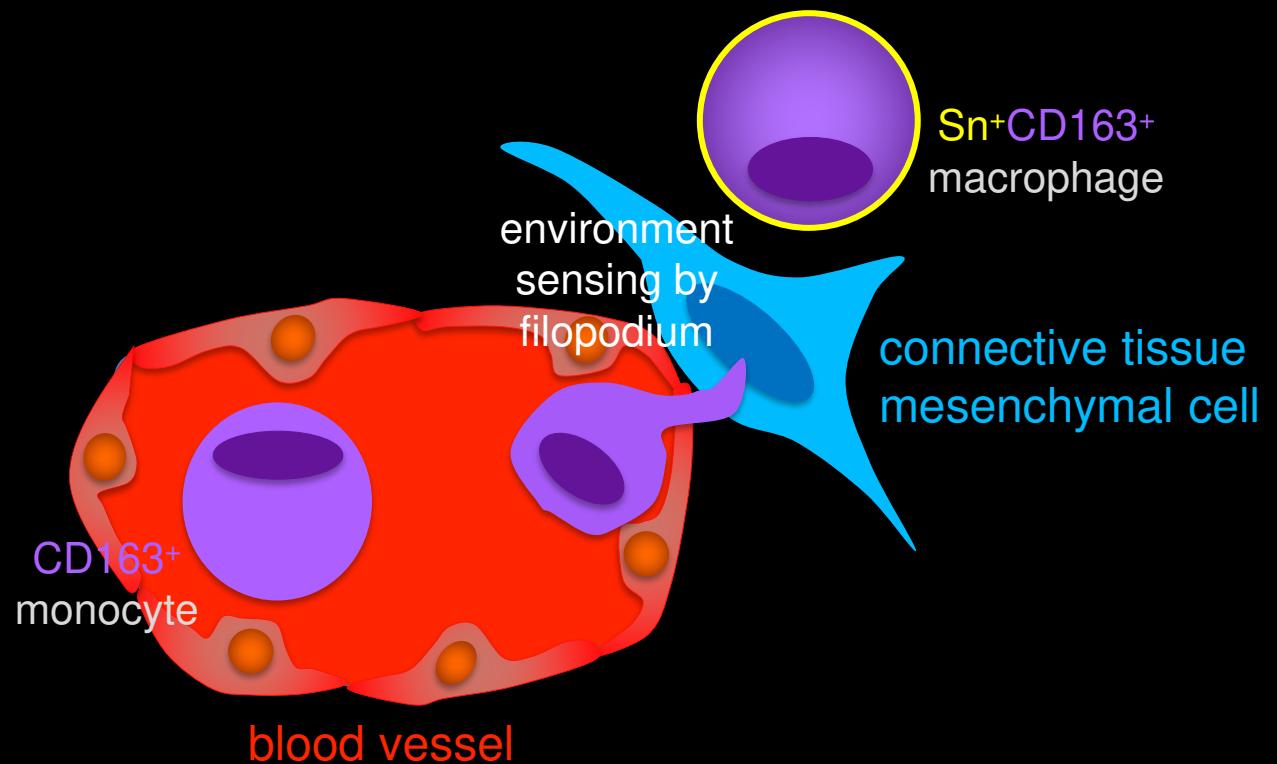
Abubakar Garba



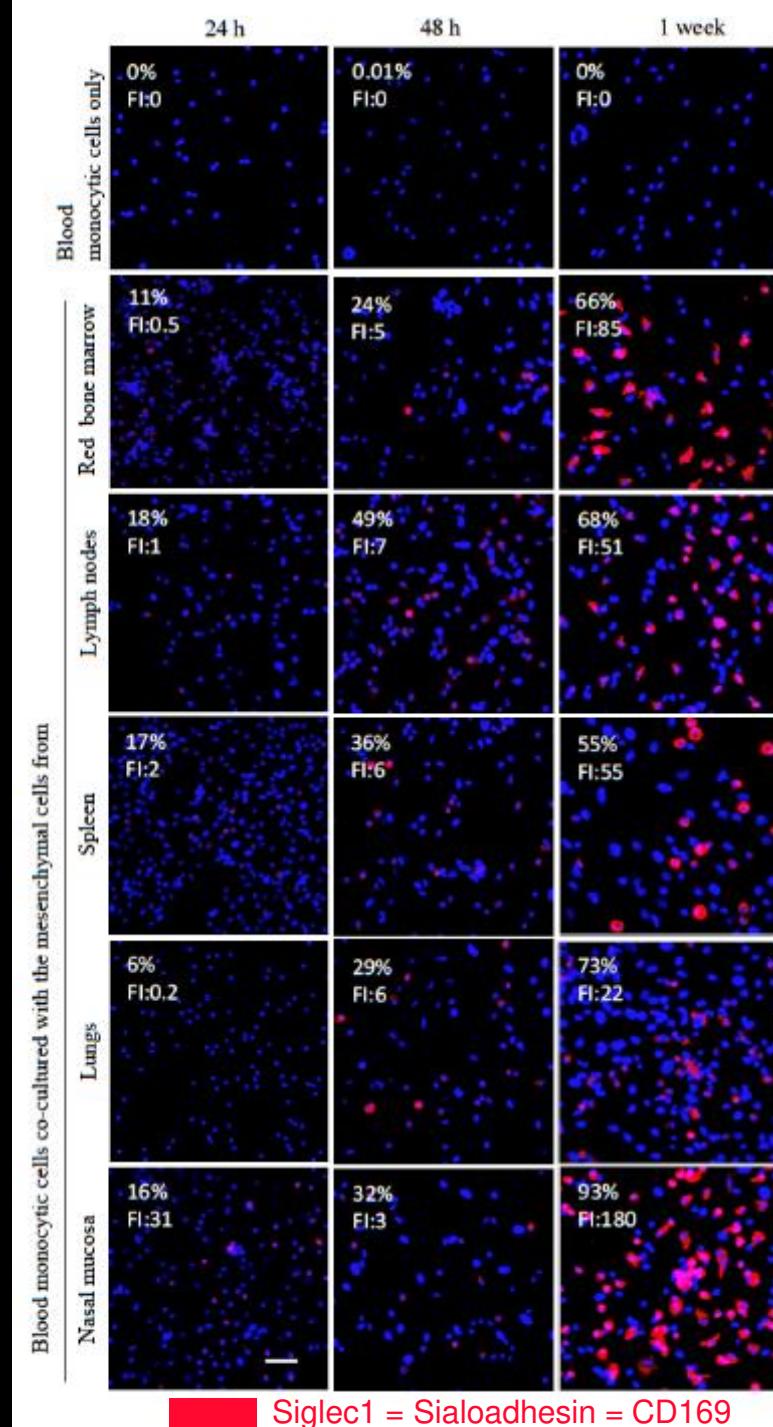
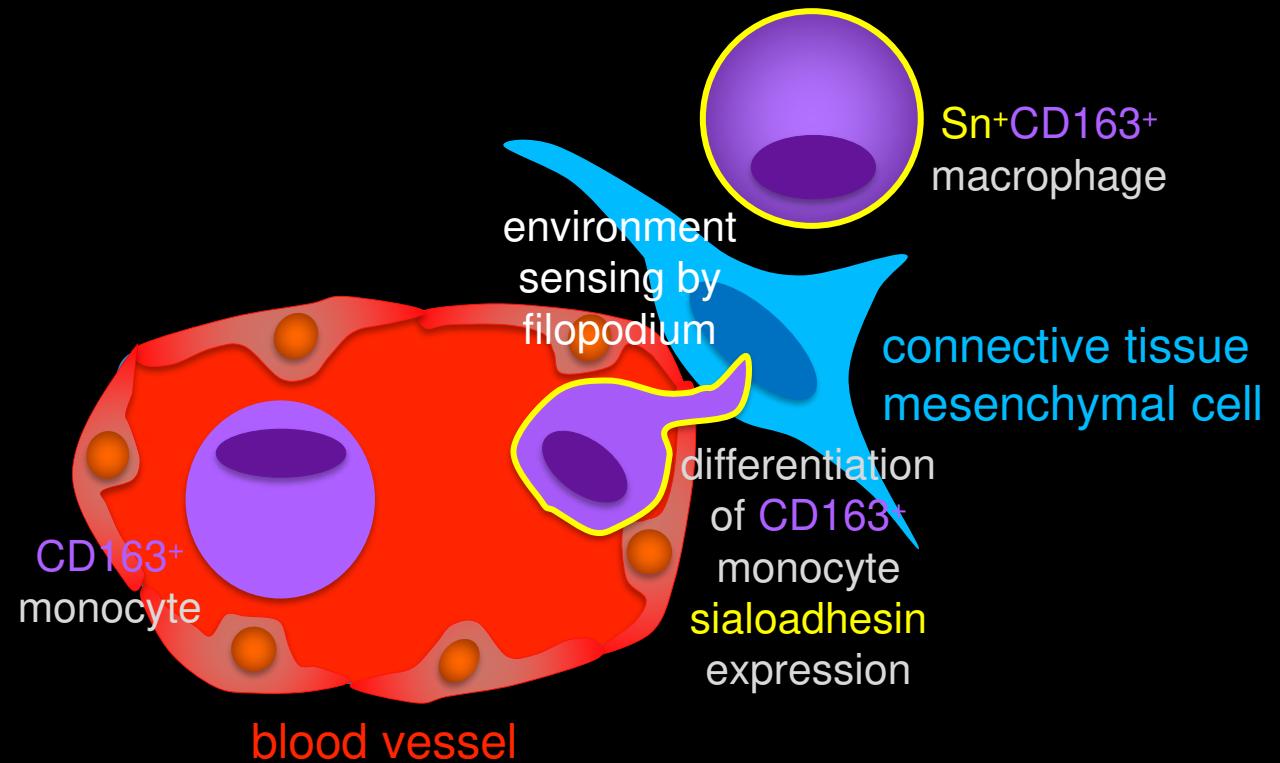
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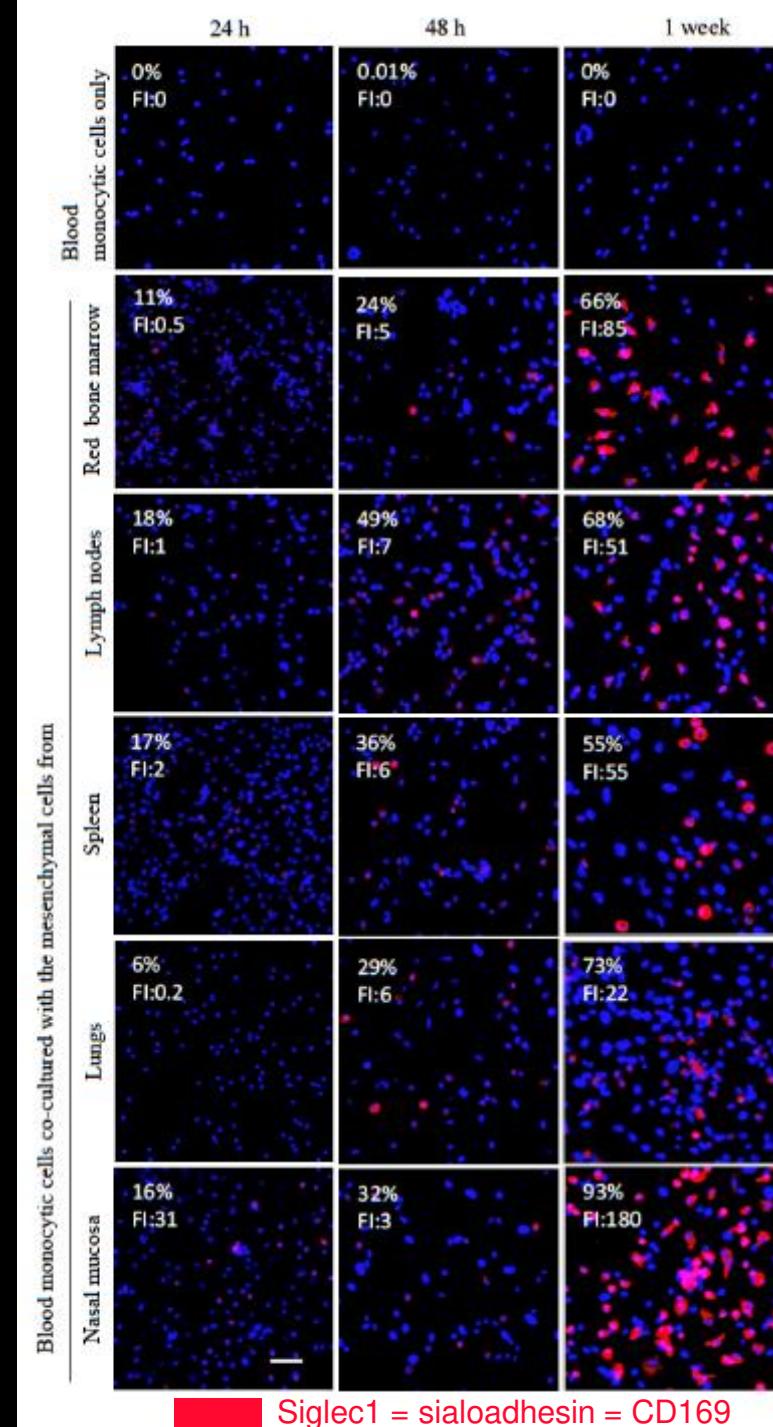
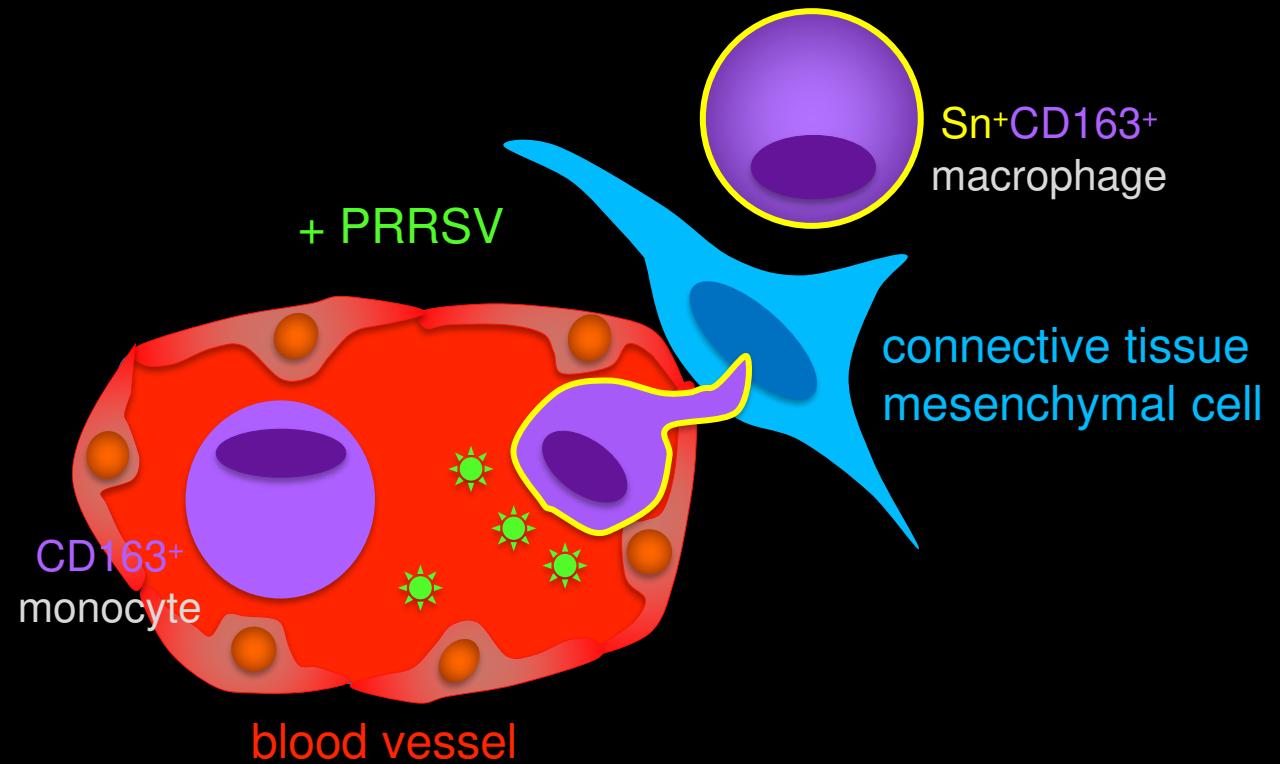


Siglec1 induction in monocytes? → contact with mesenchymal cells

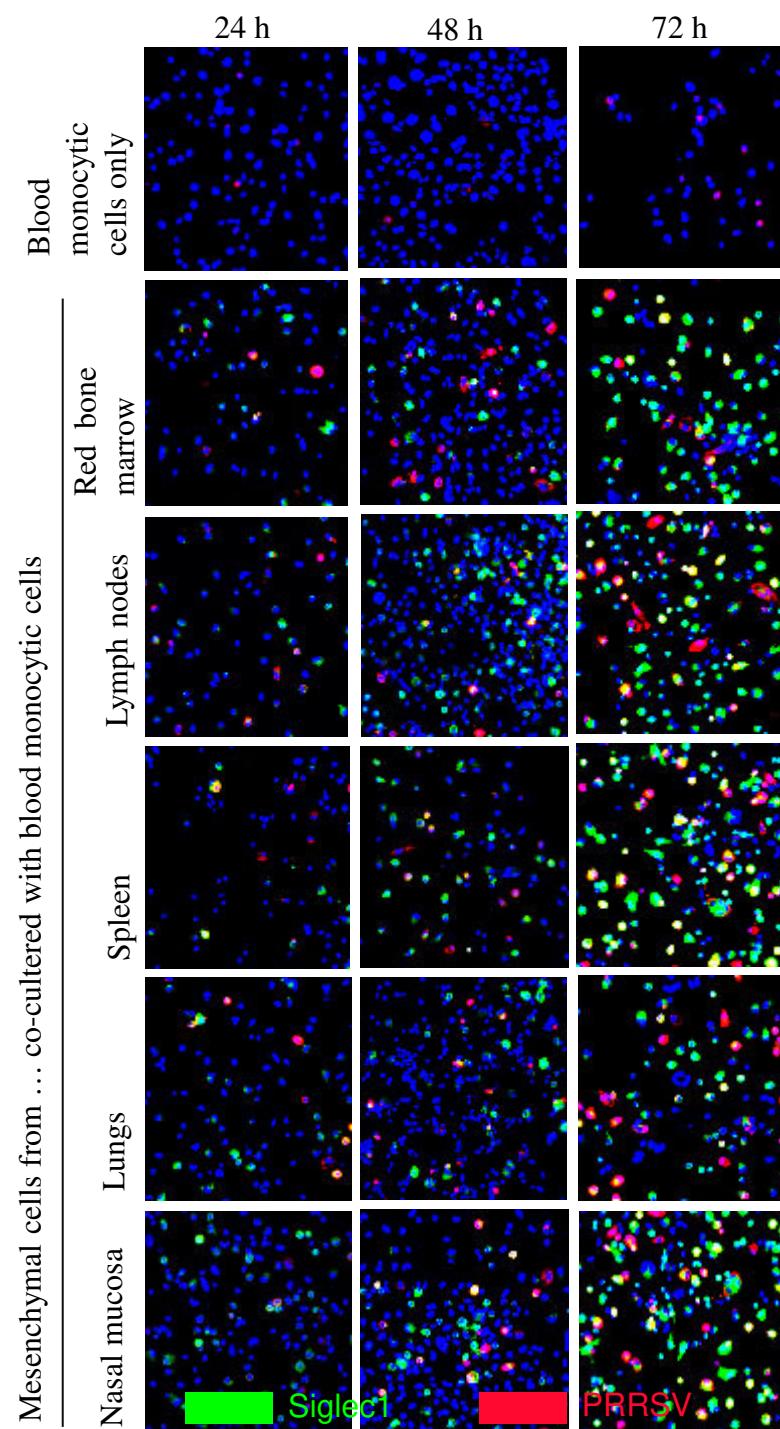
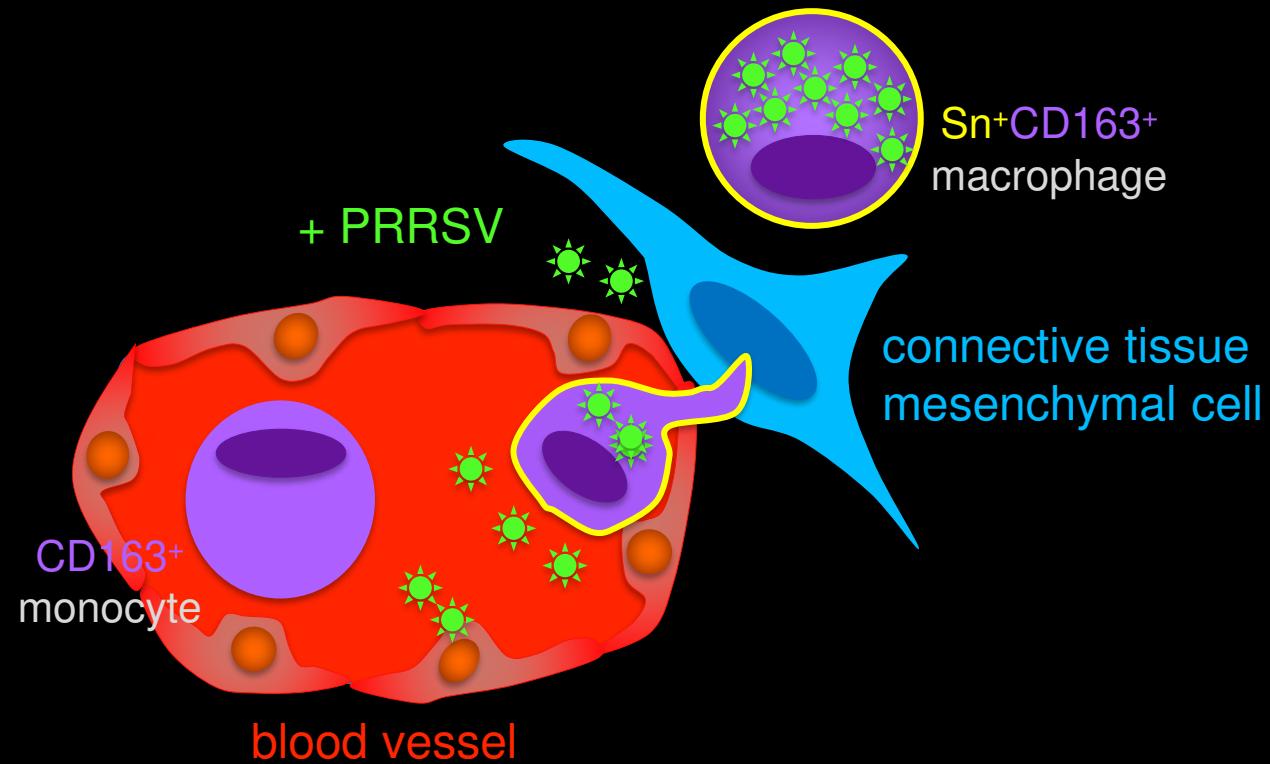


Siglec1 = Sialoadhesin = CD169

Siglec1 induction in monocytes? → contact with mesenchymal cells

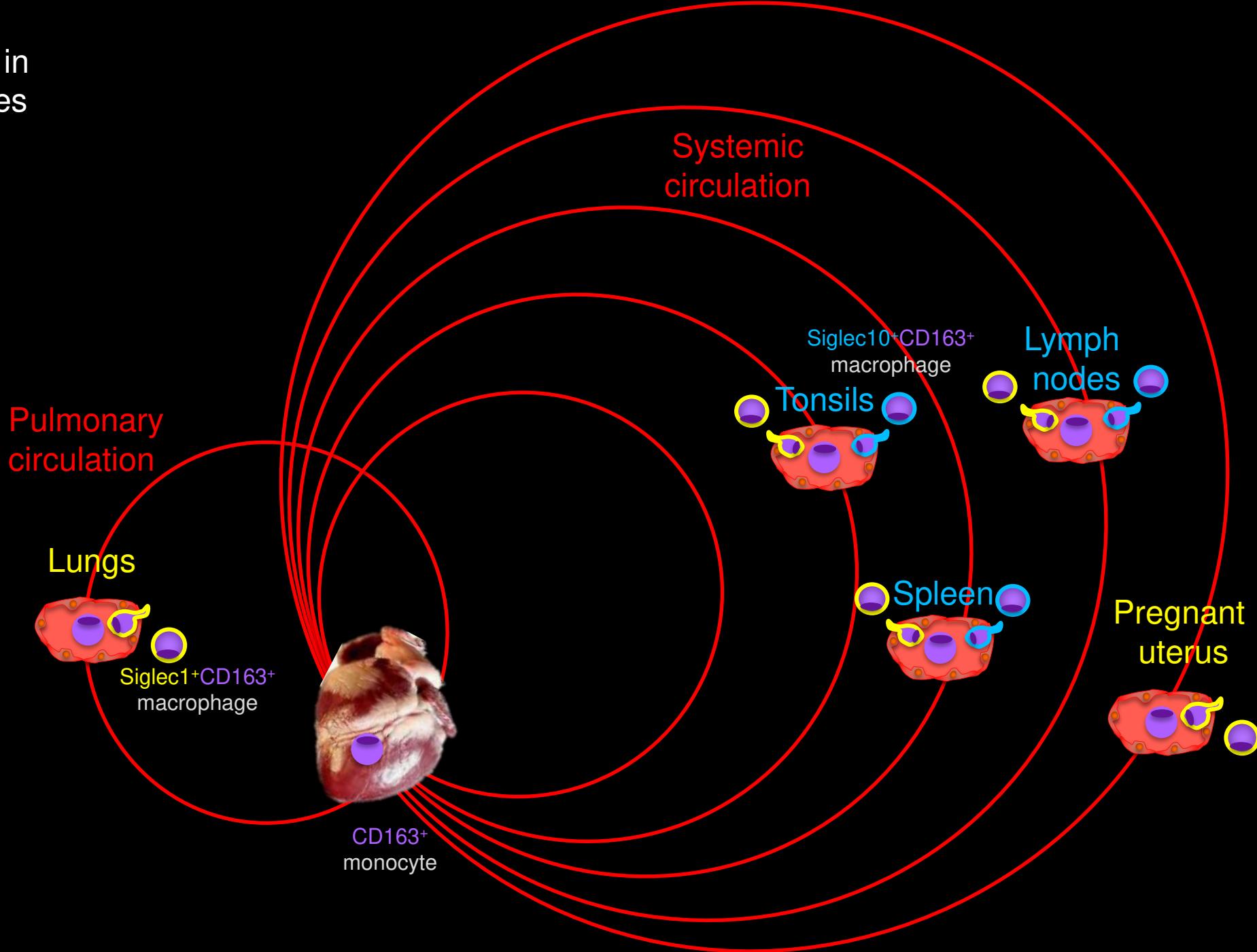


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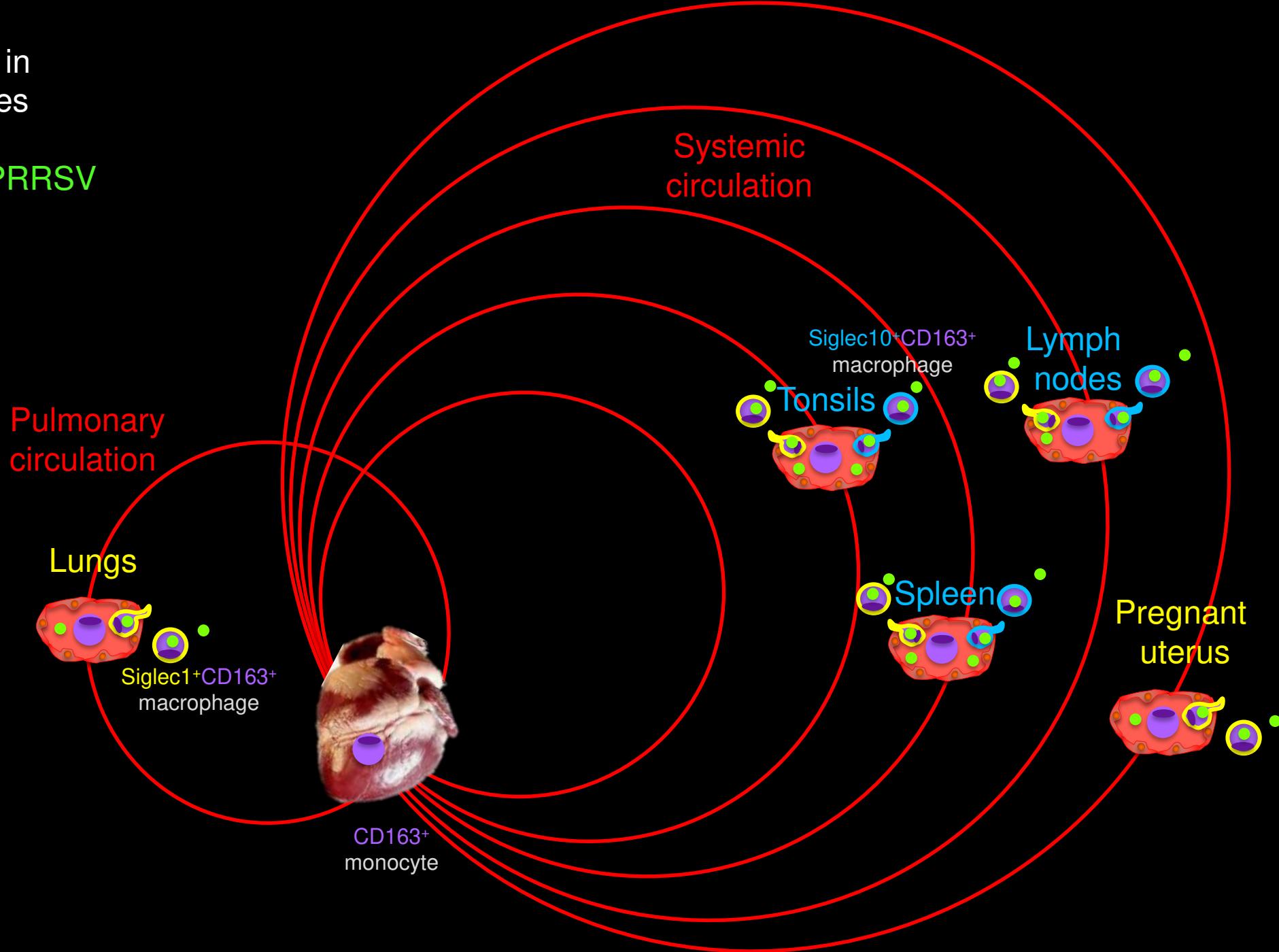
Macrophage differentiation in different tissues

Non-infected animals

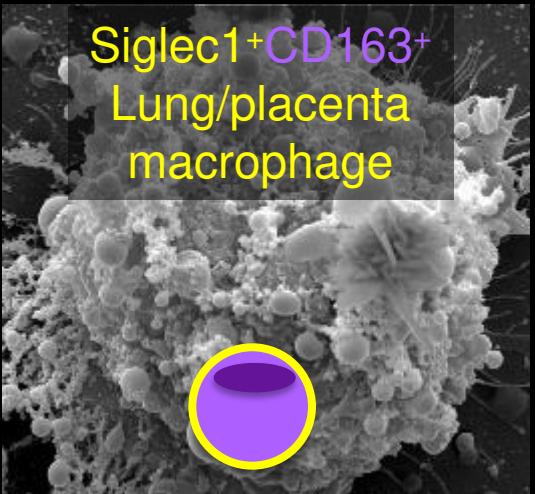


Macrophage differentiation in different tissues

Low virulent PRRSV
G1s1; LV-like

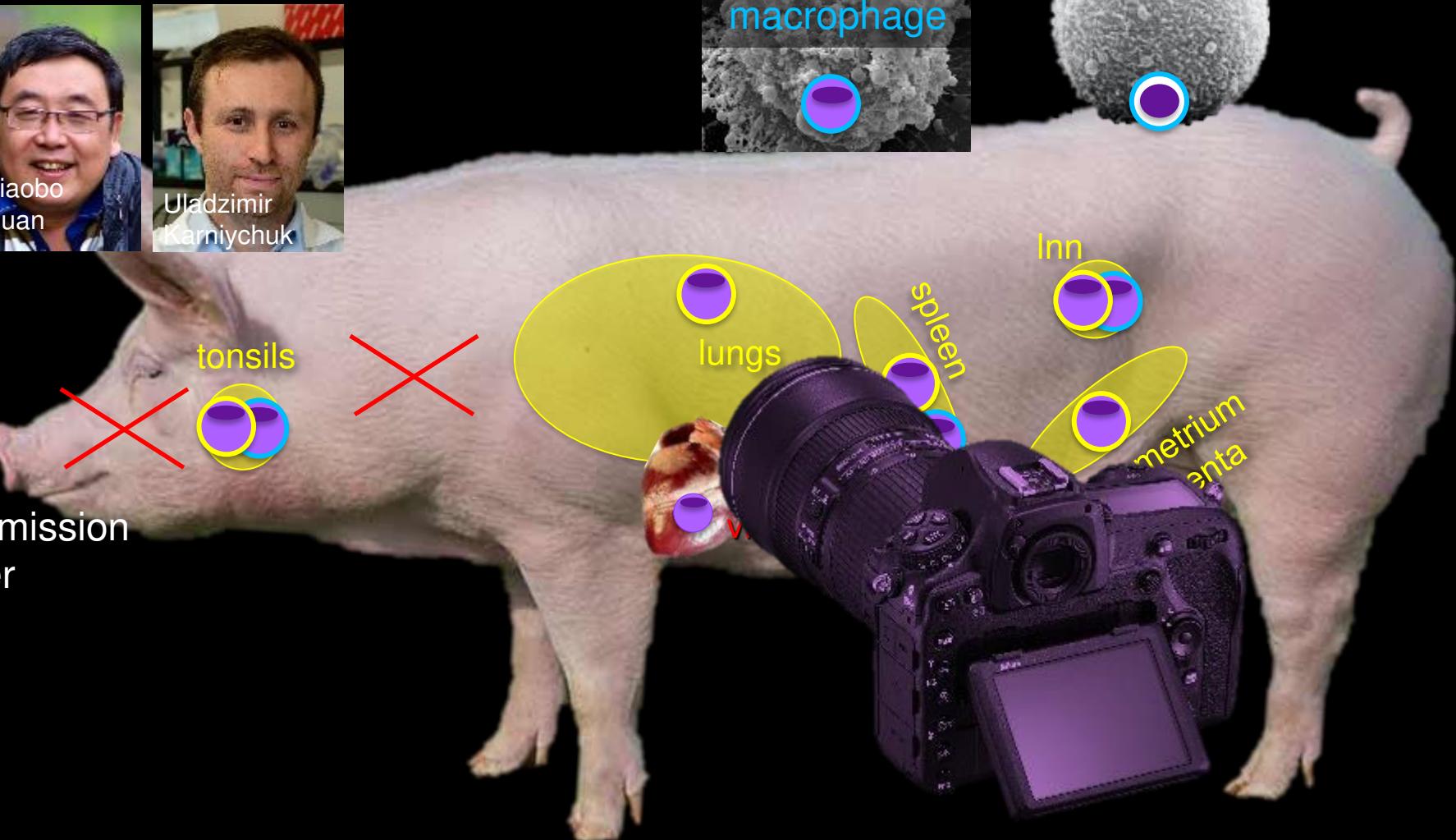
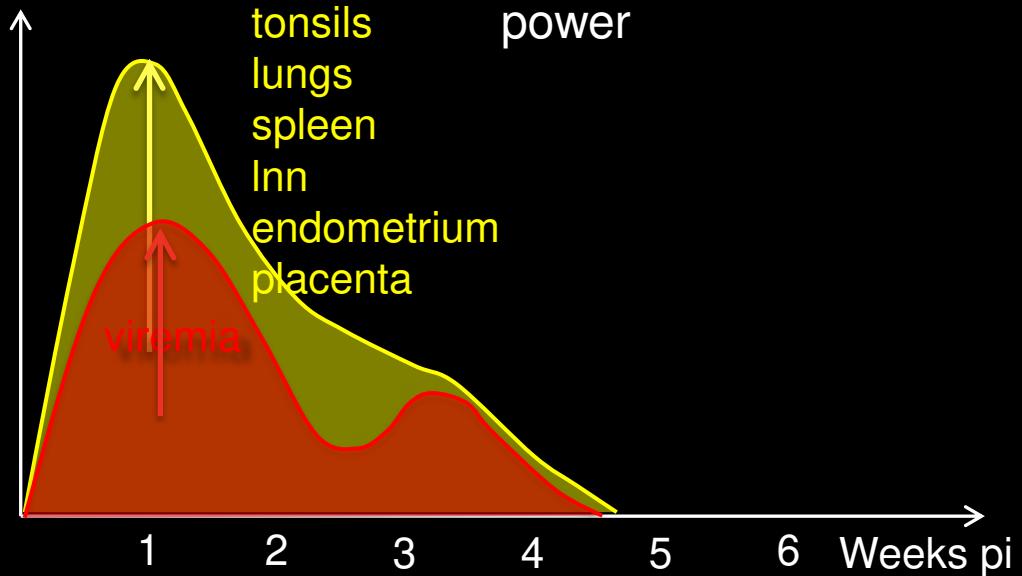


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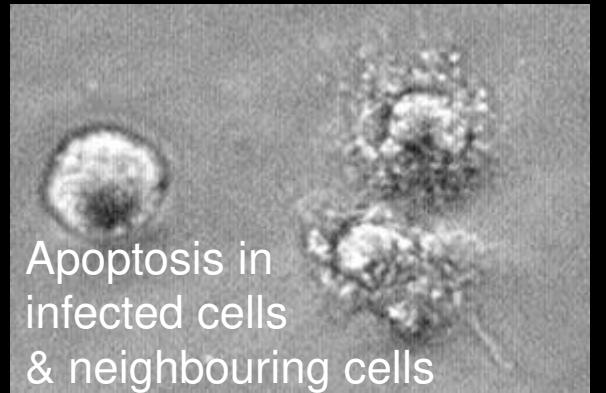
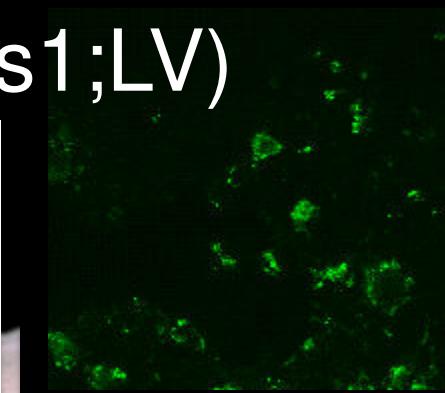
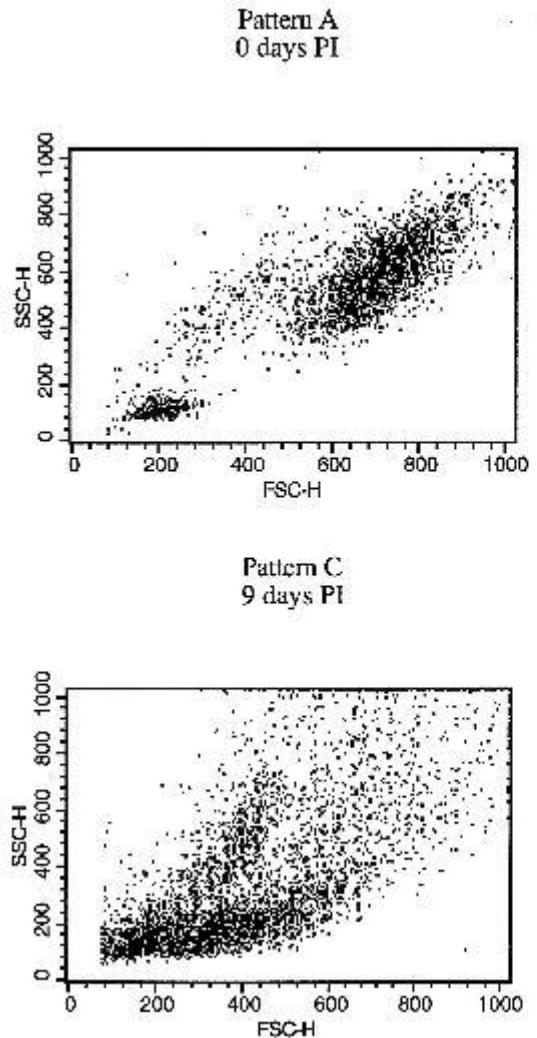
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low
transmission
power



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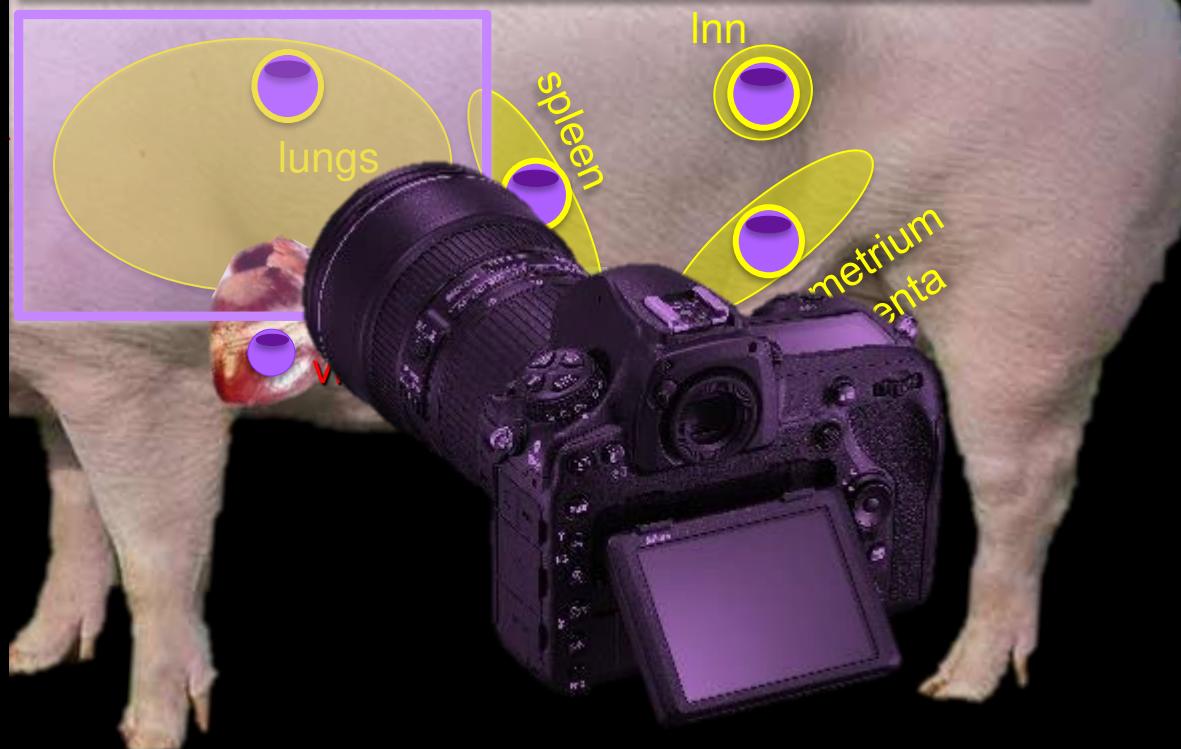
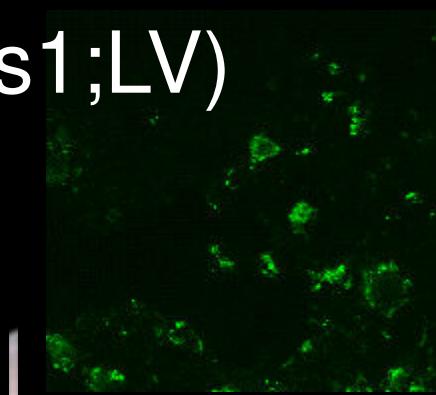
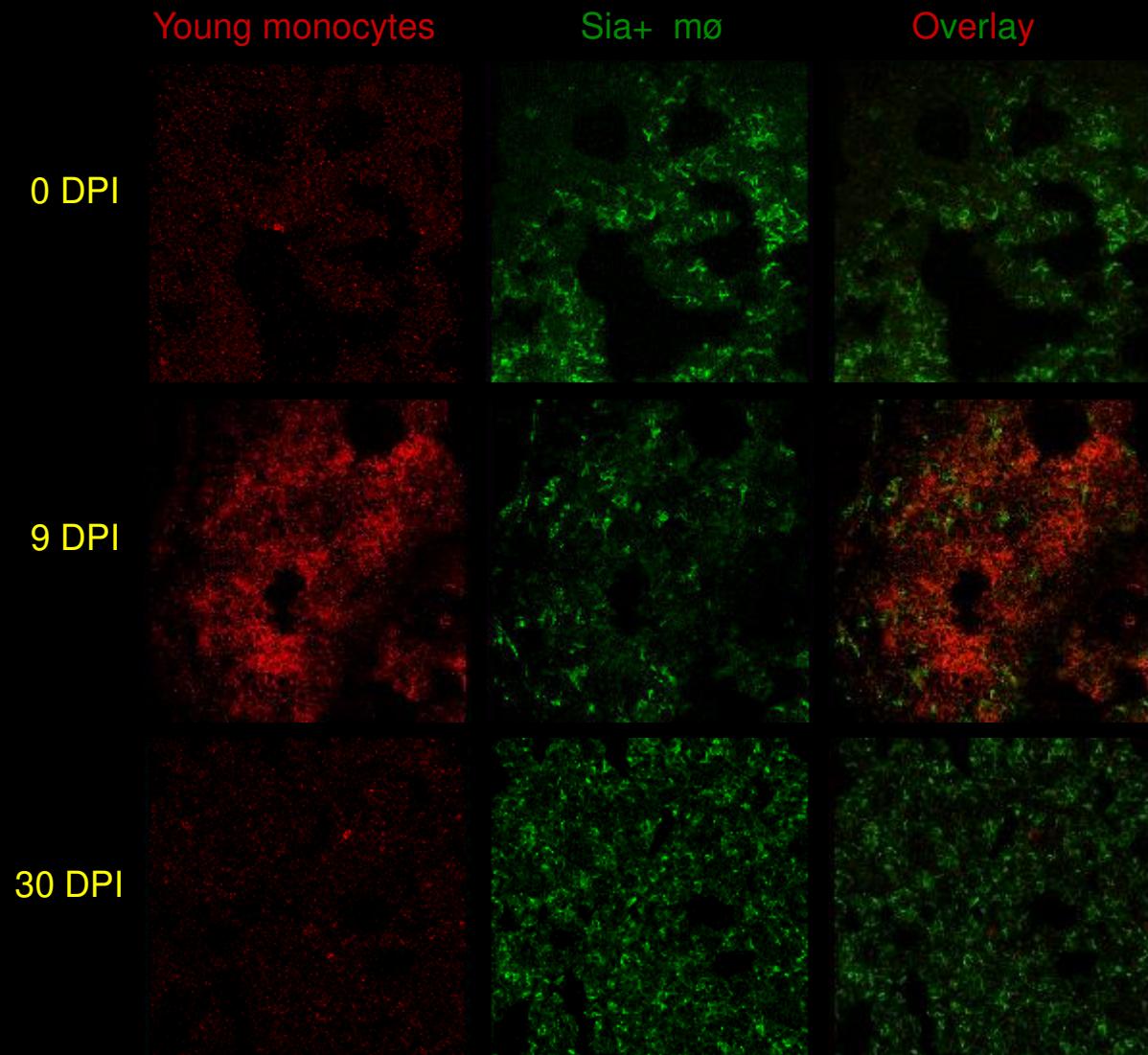


Apoptosis in
infected cells
& neighbouring cells



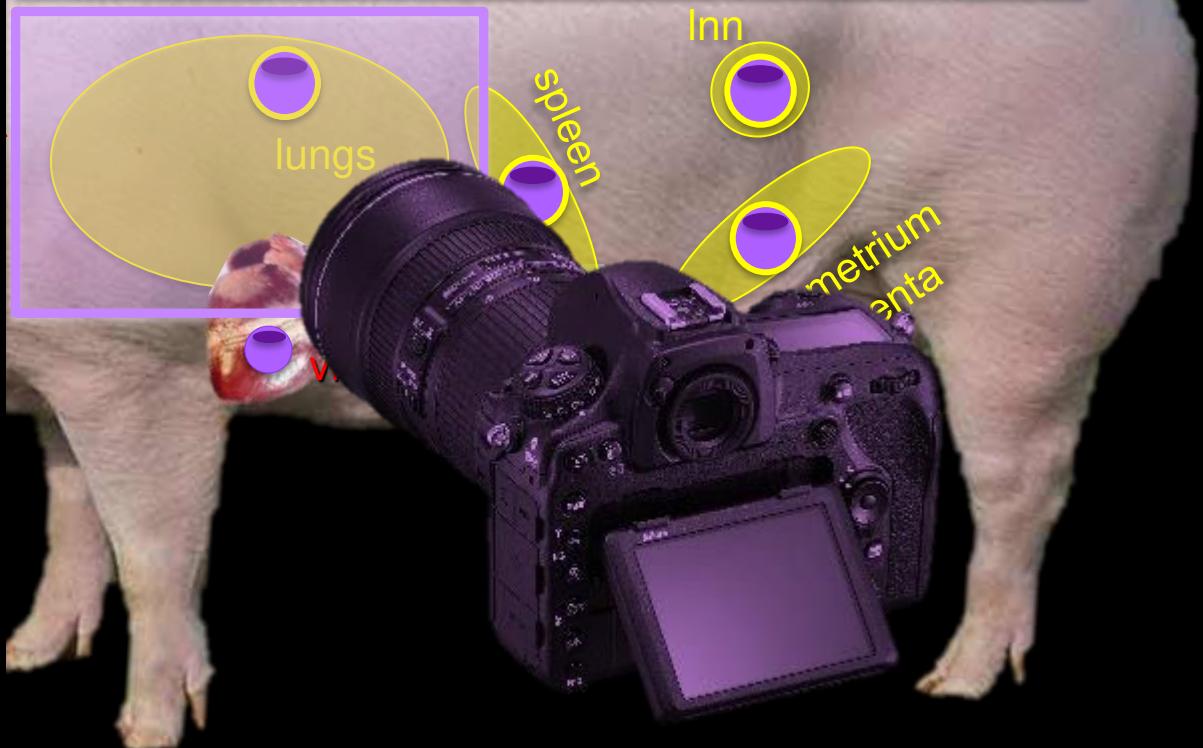
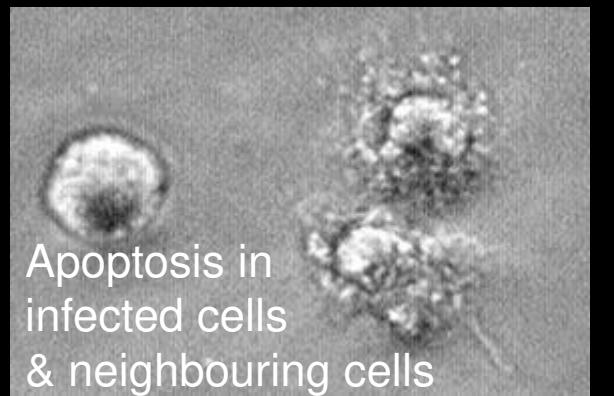
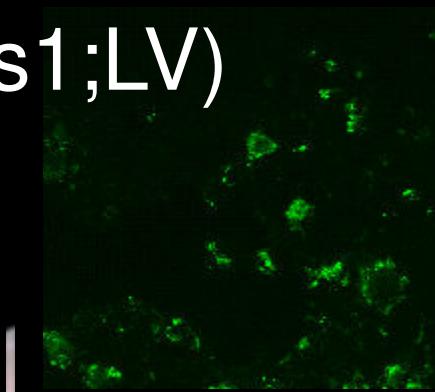
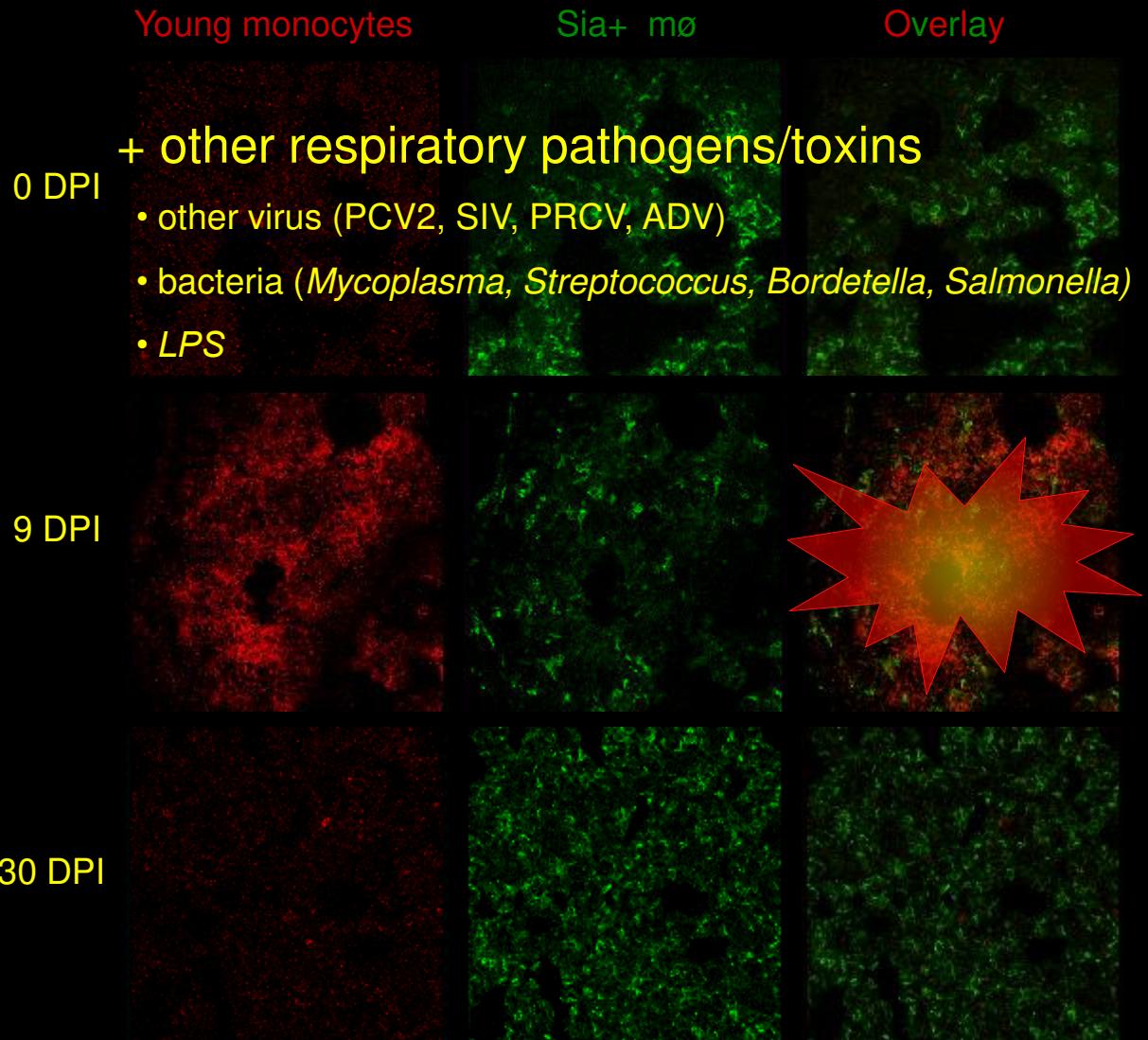
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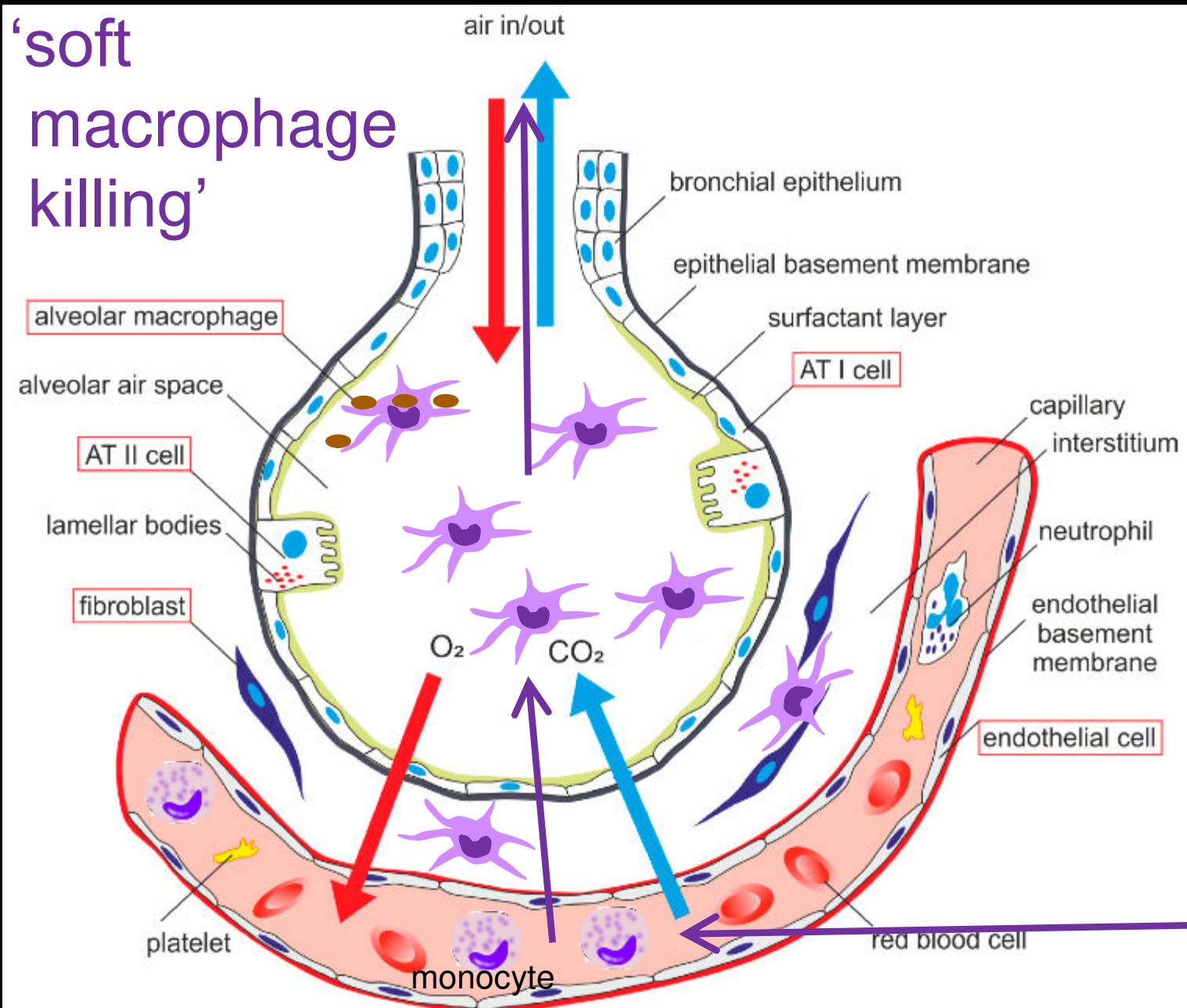
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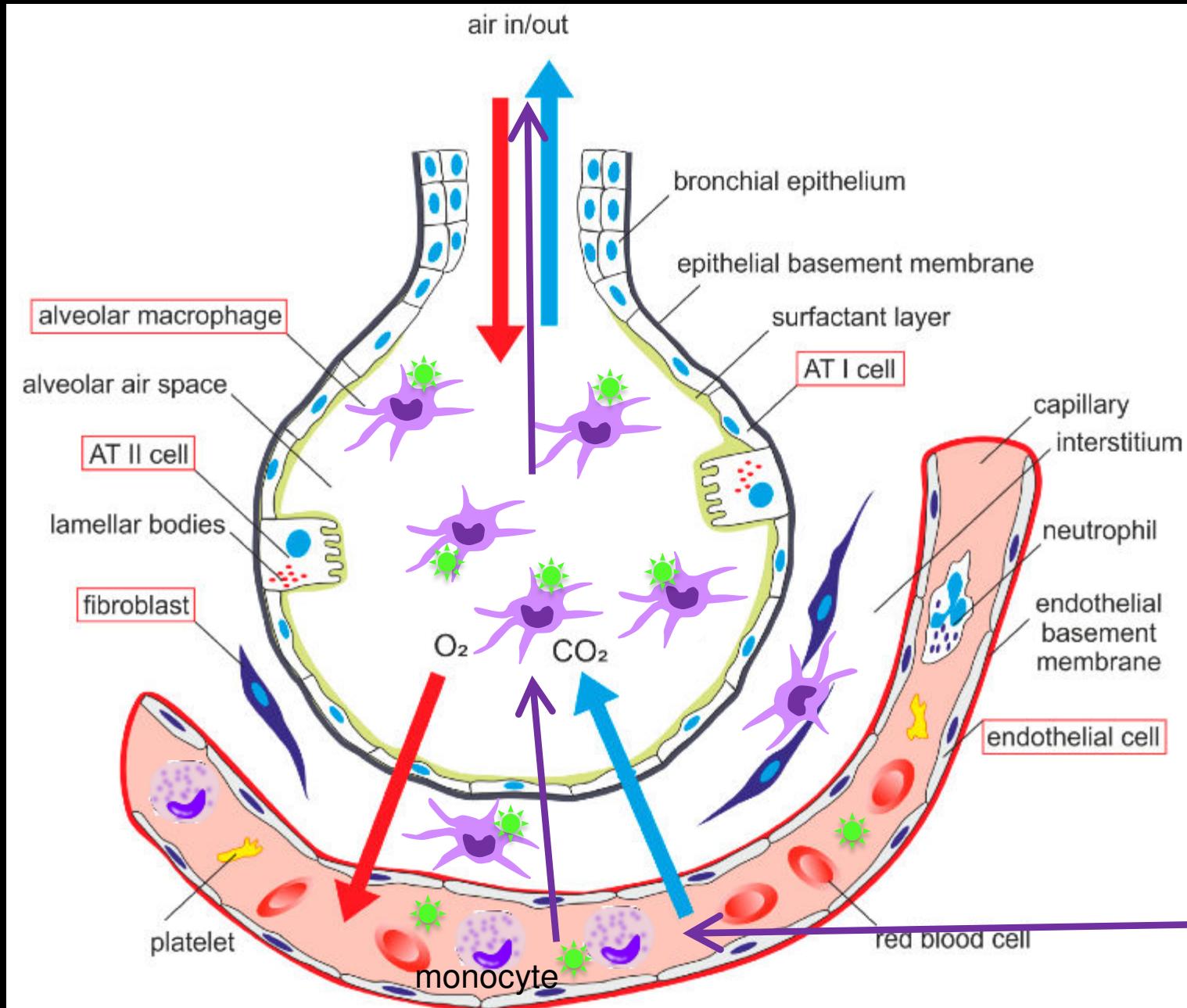


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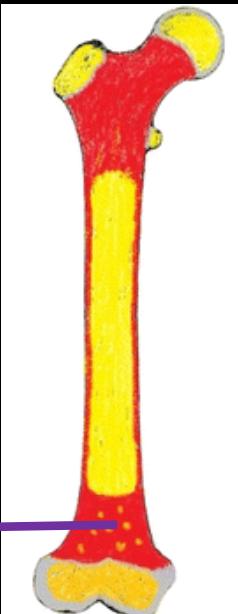
Alveolar space - homeostasis - 'soft killing'



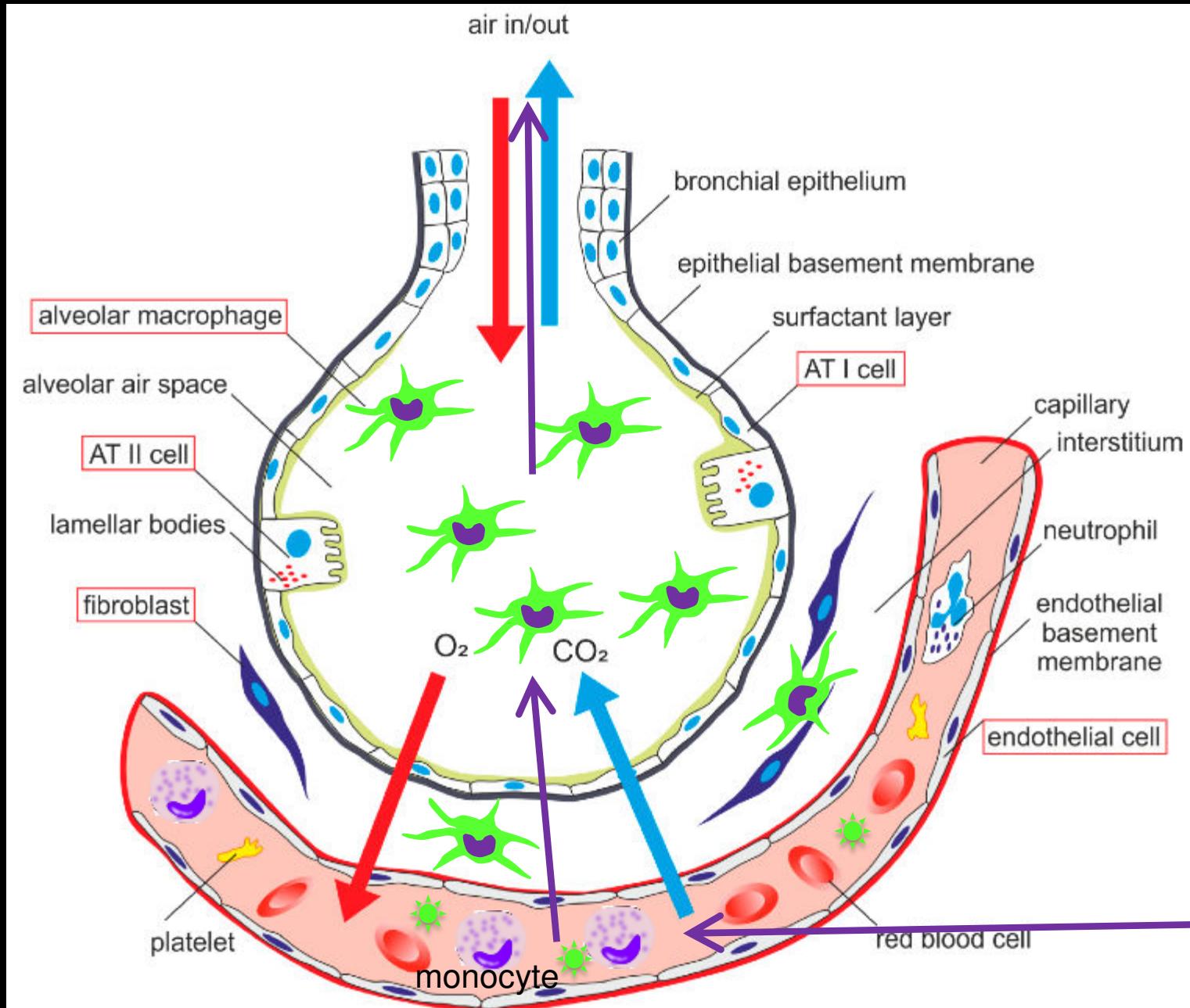
1990 - Low virulent PRRSV (G1s1;LV) *



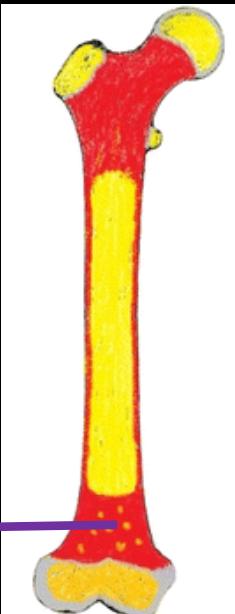
Red bone marrow



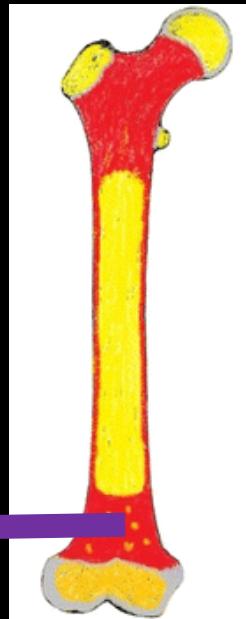
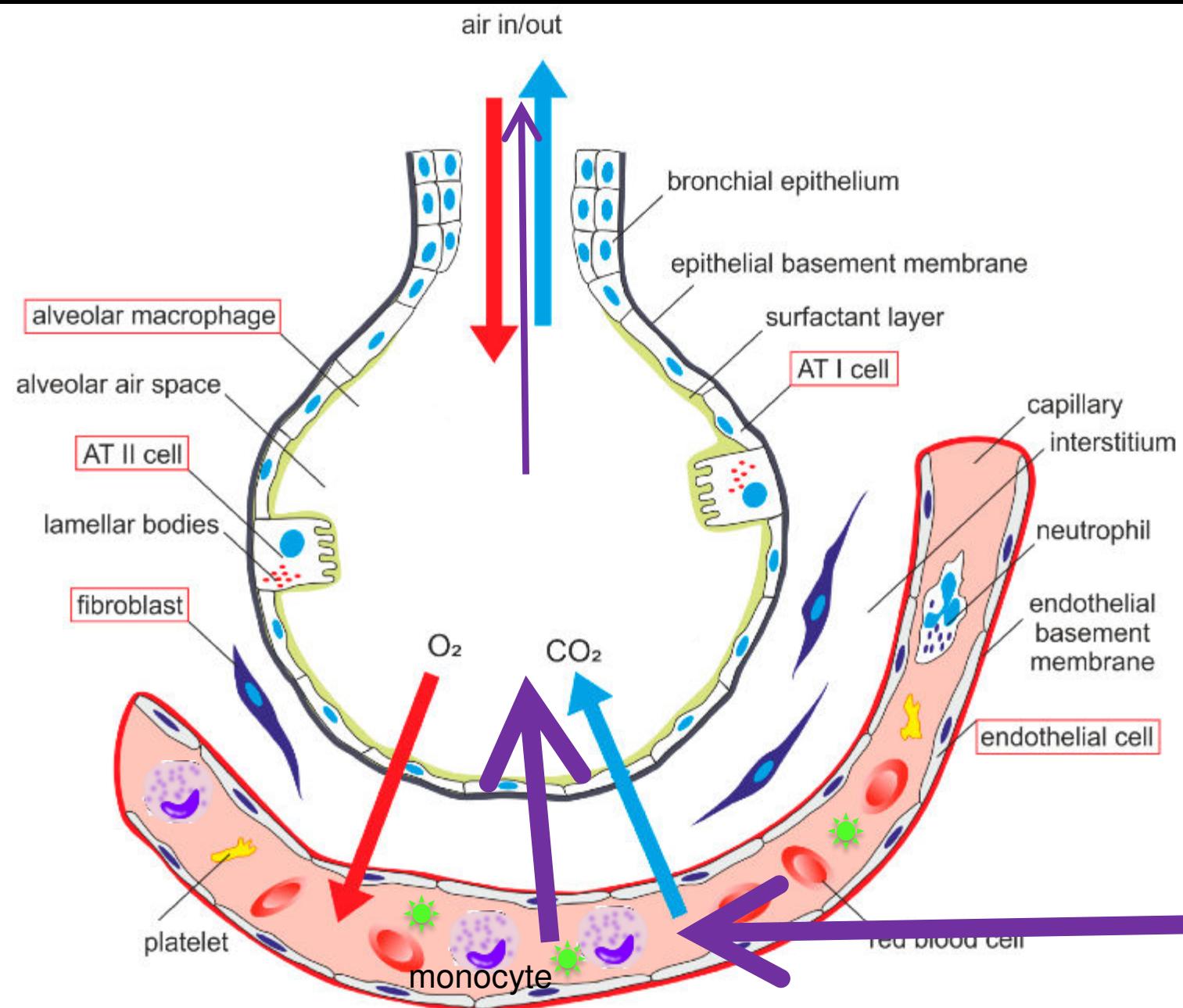
1990 - Low virulent PRRSV (G1s1;LV) *



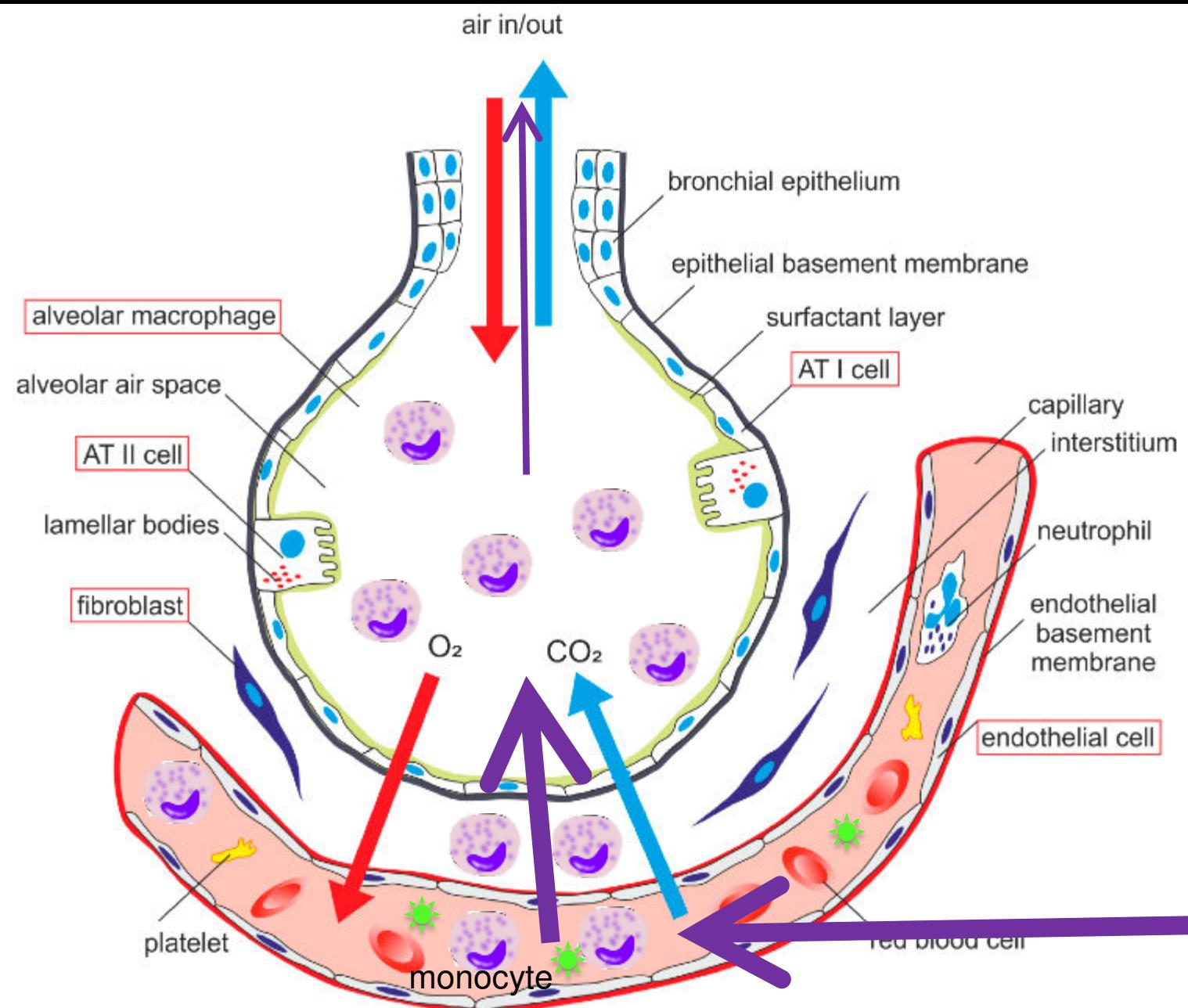
Red bone marrow



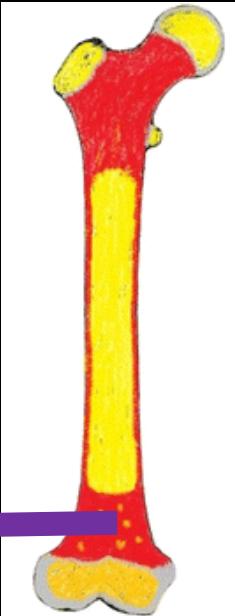
1990 - Low virulent PRRSV (G1s1;LV) *



1990 - Low virulent PRRSV (G1s1;LV) *

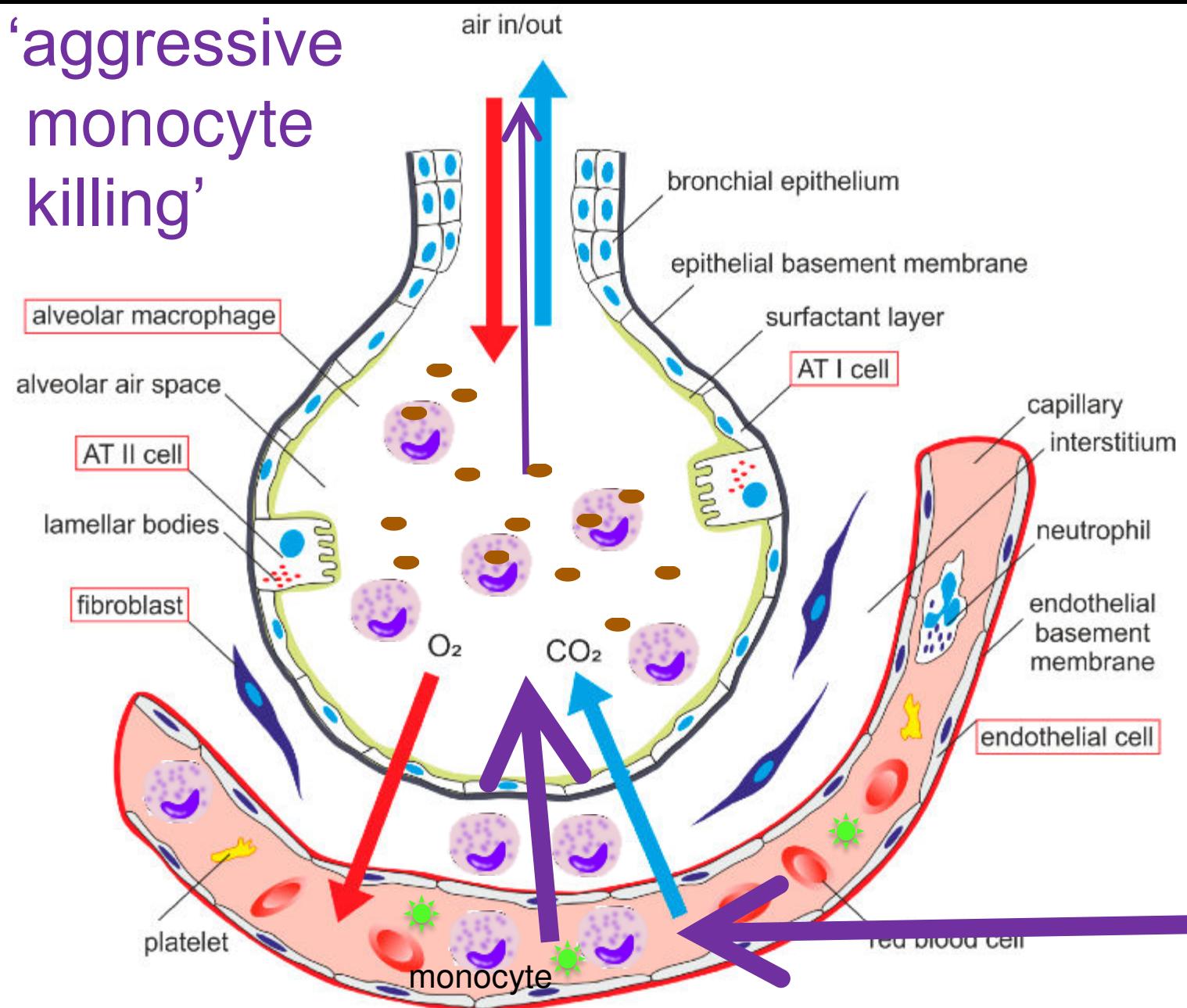


Red bone marrow

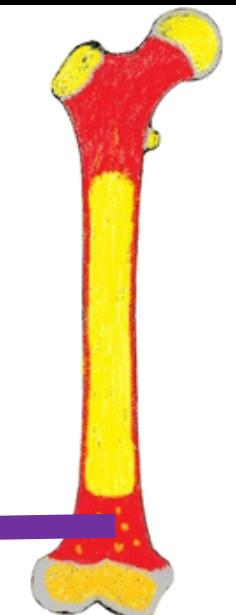


1990 - Low virulent PRRSV (G1s1;LV) *

'aggressive
monocyte
killing'

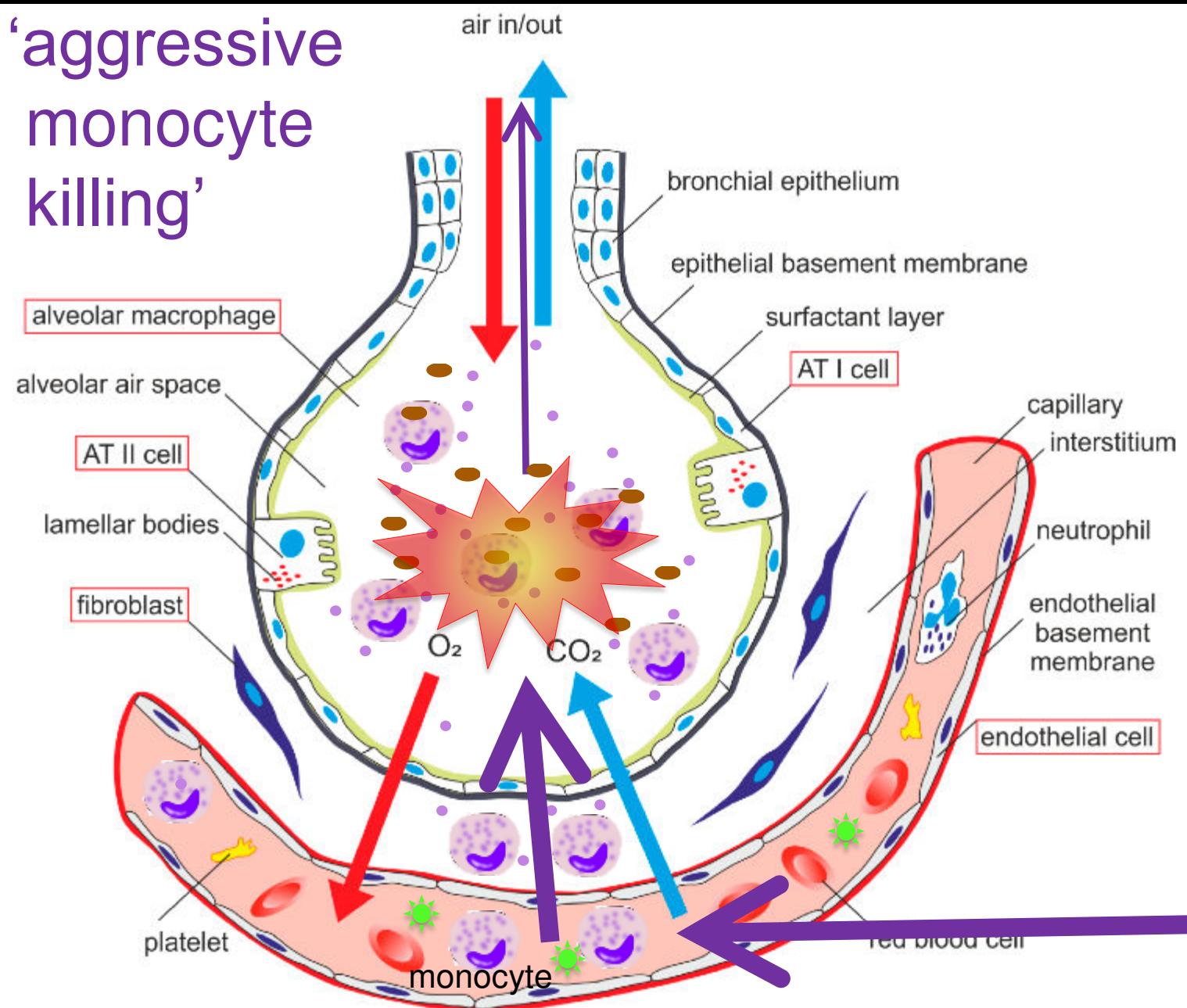


Red bone
marrow

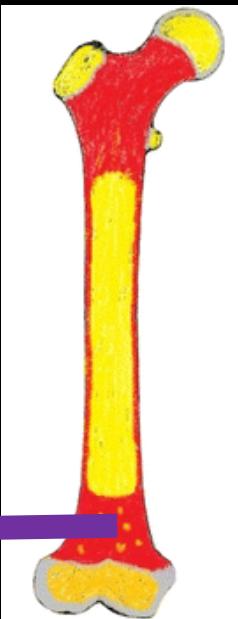


1990 - Low virulent PRRSV (G1s1;LV) *

'aggressive
monocyte
killing'



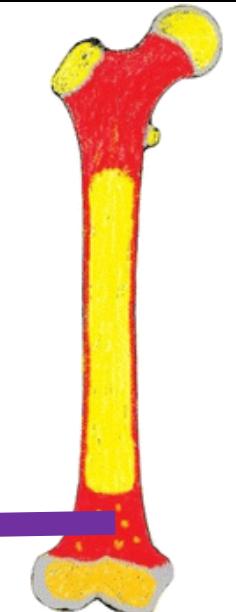
Red bone marrow



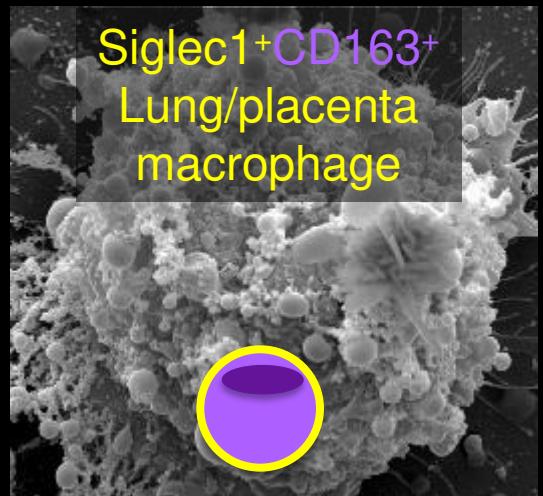
'aggressive
monocyte
killing'



Red bone marrow

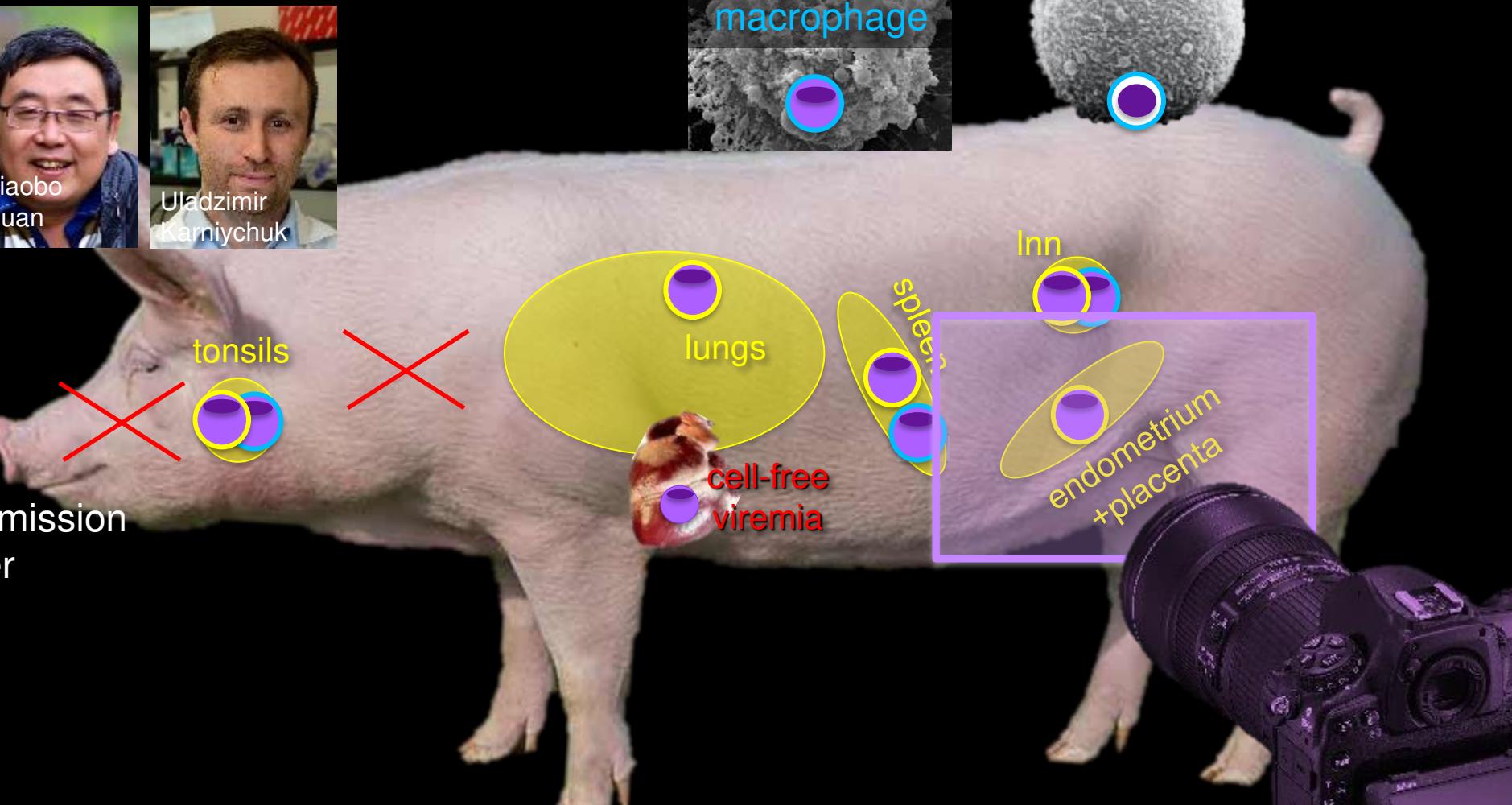
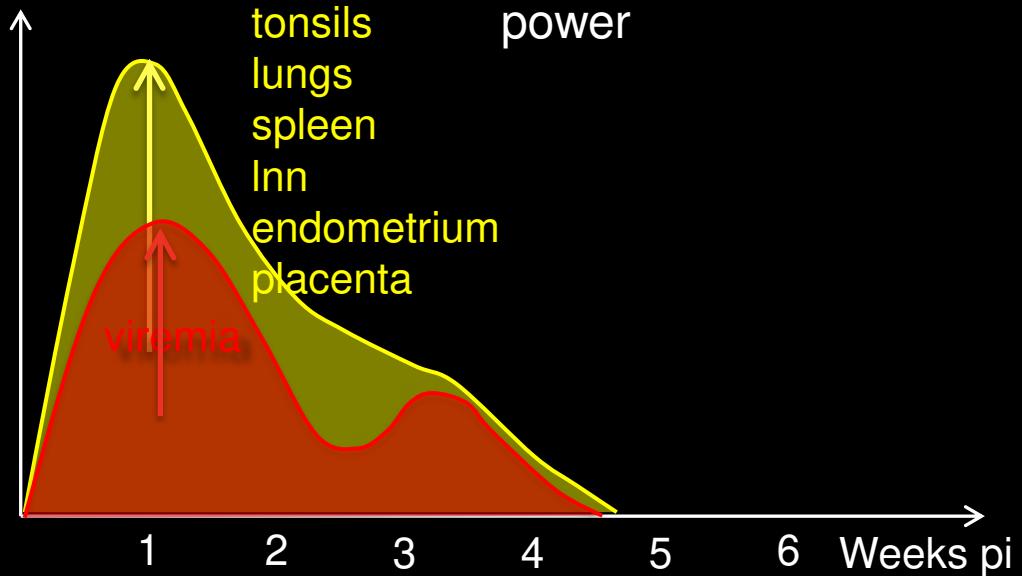


1990 - Low virulent PRRSV (G1s1;LV)



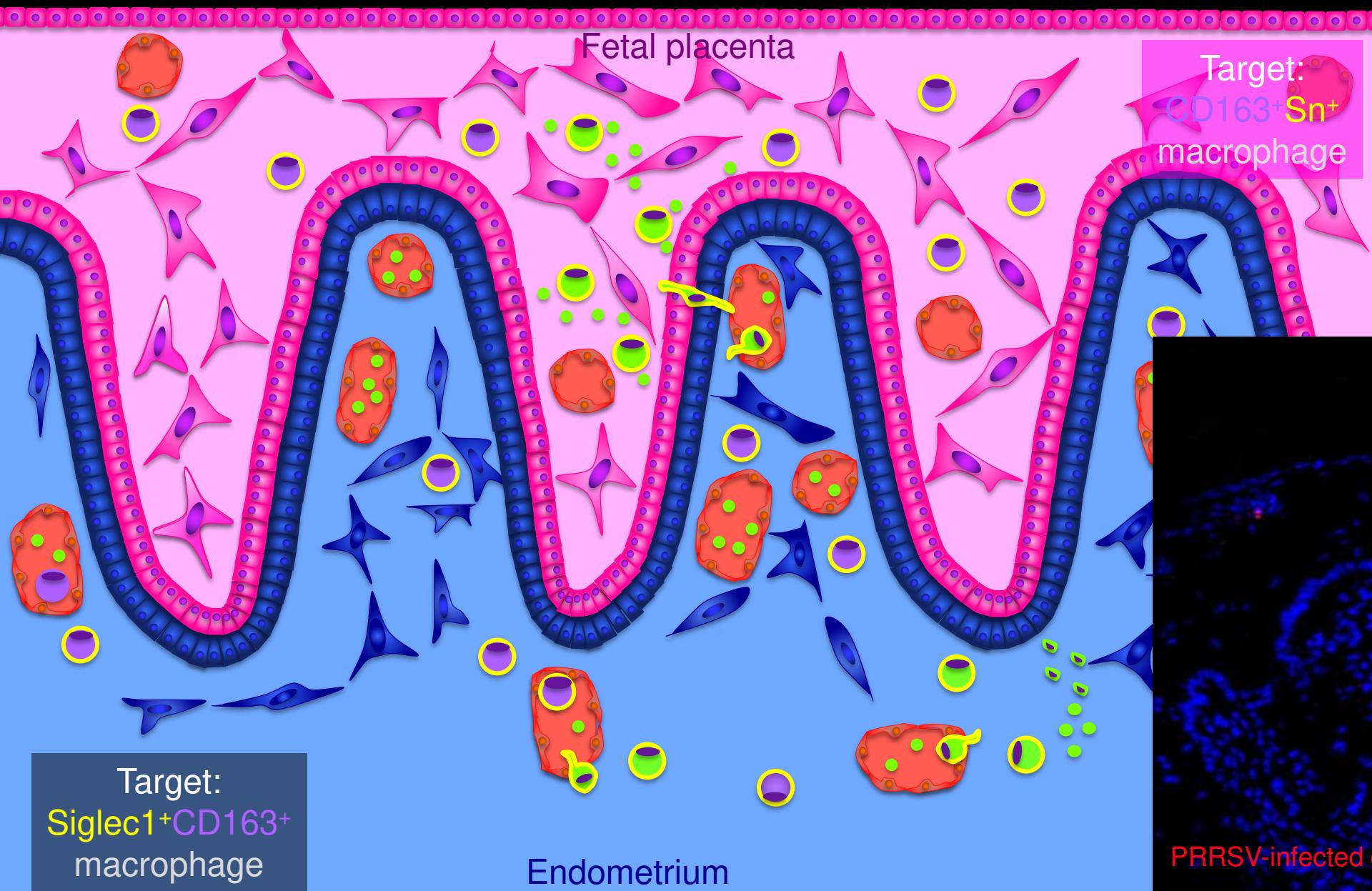
Infection

low
transmission
power

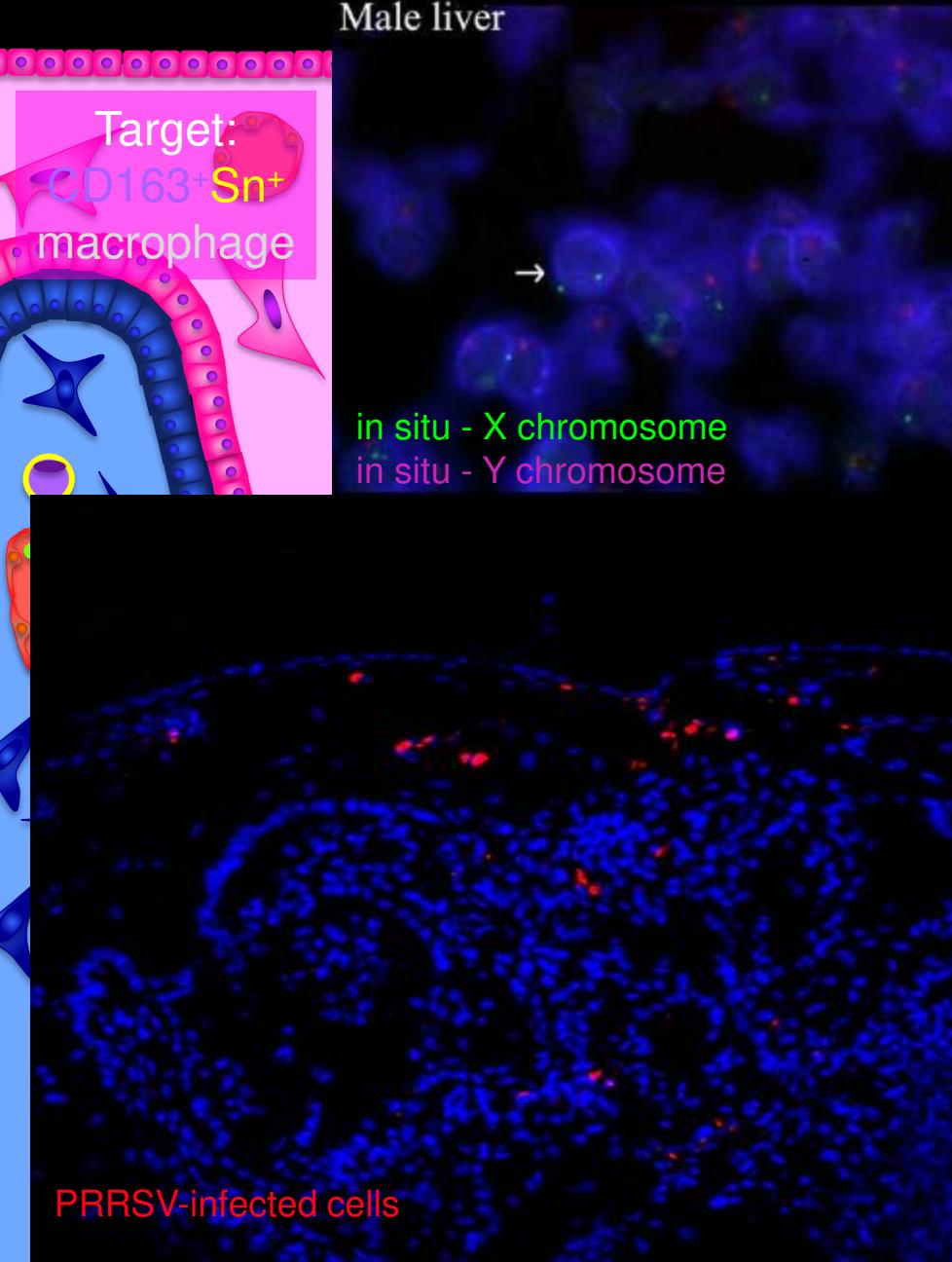


- no general/respiratory problems,
except during co-infections
- reproductive problems

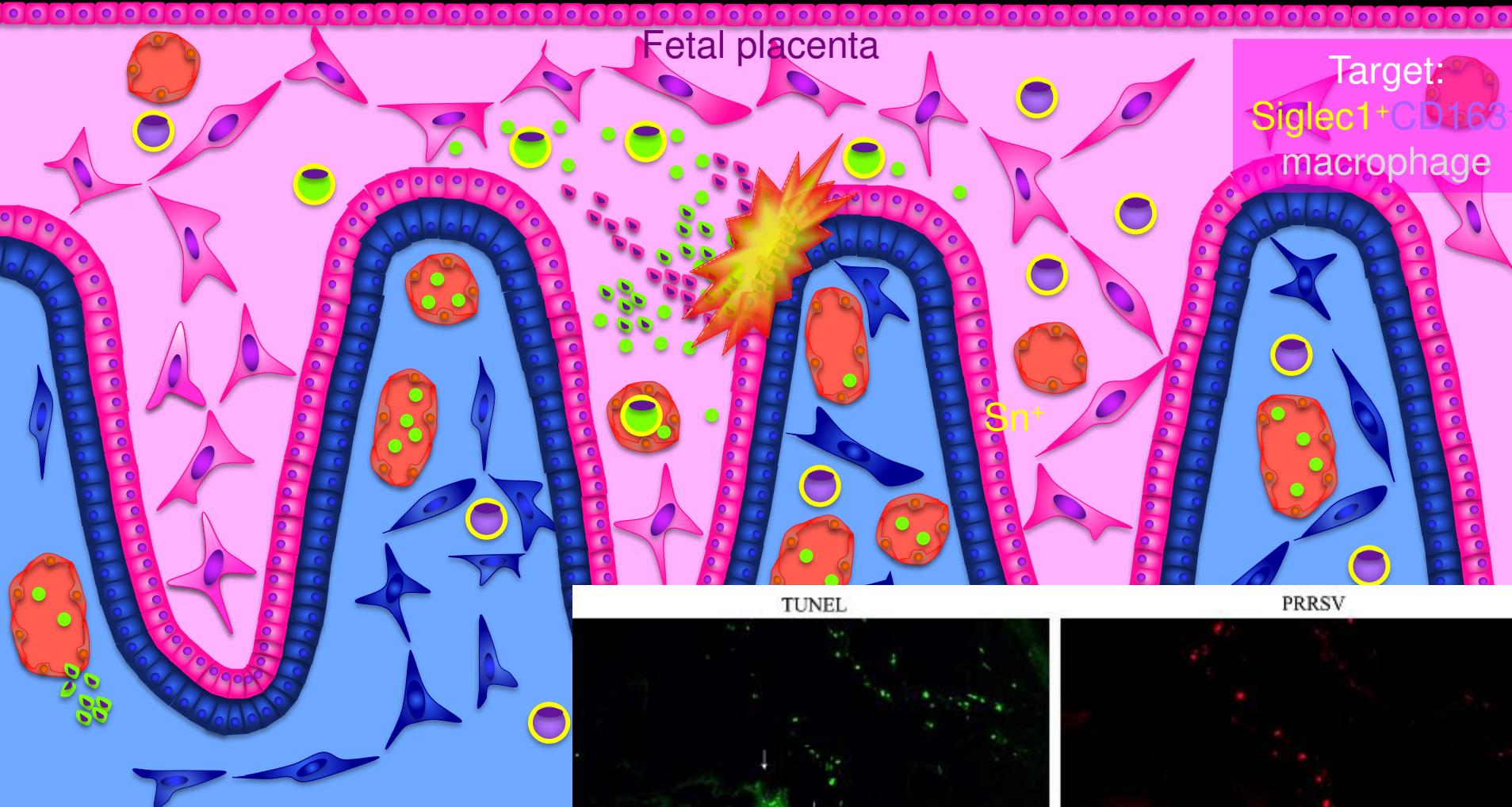
1990 - Low virulent PRRSV (G1s1;LV)



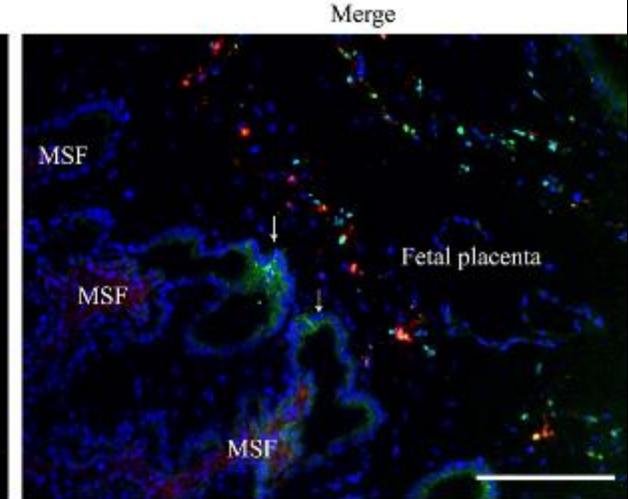
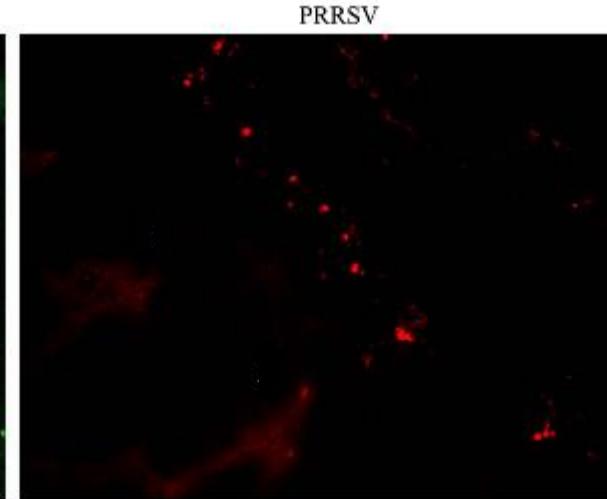
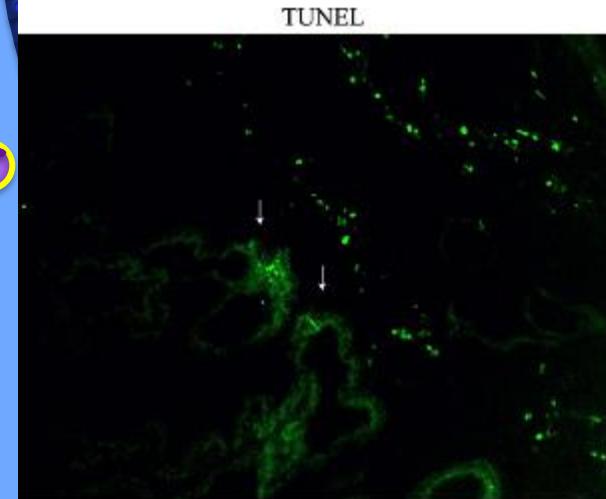
Male liver



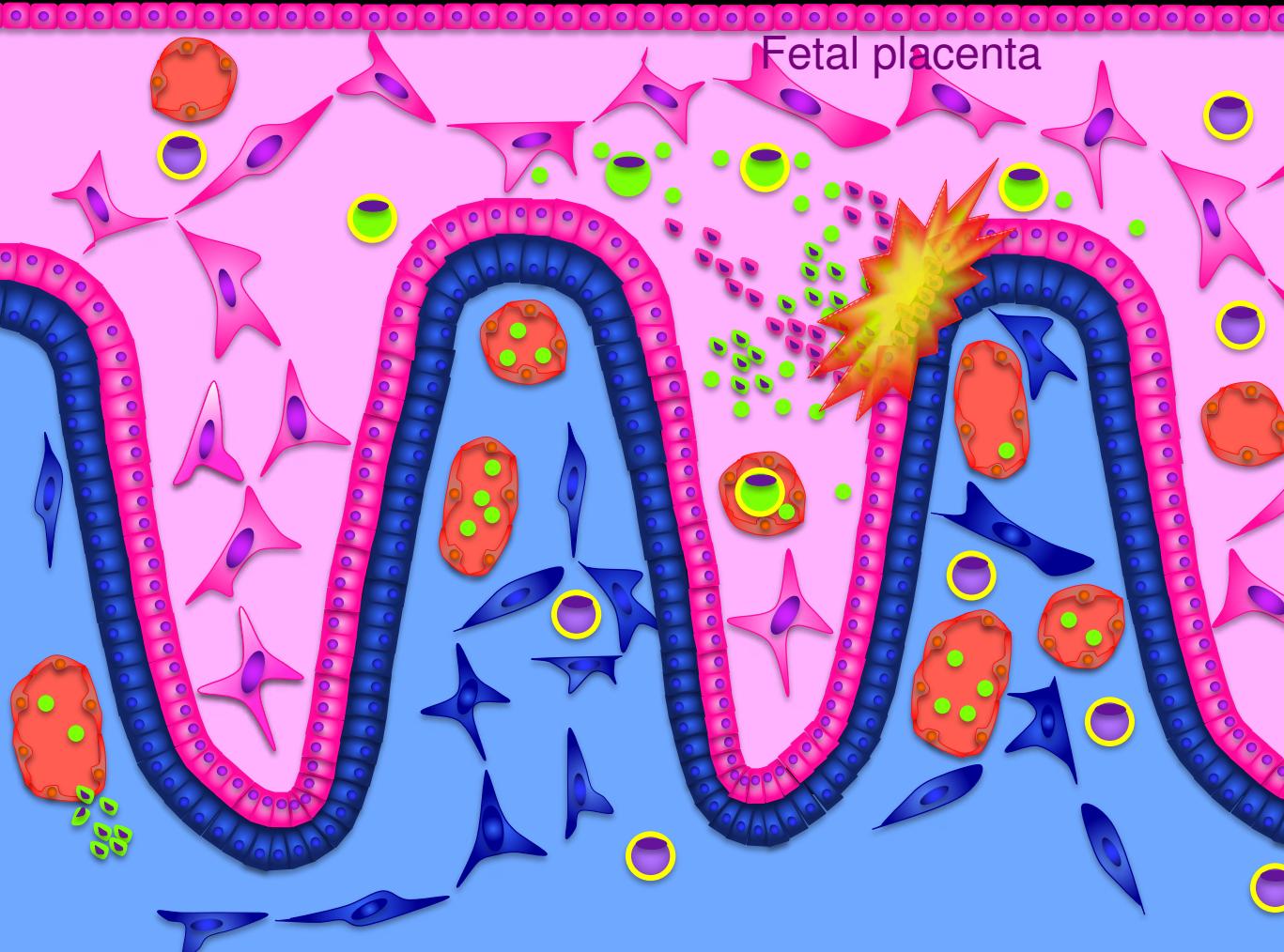
1990 - Low virulent PRRSV (G1s1;LV)



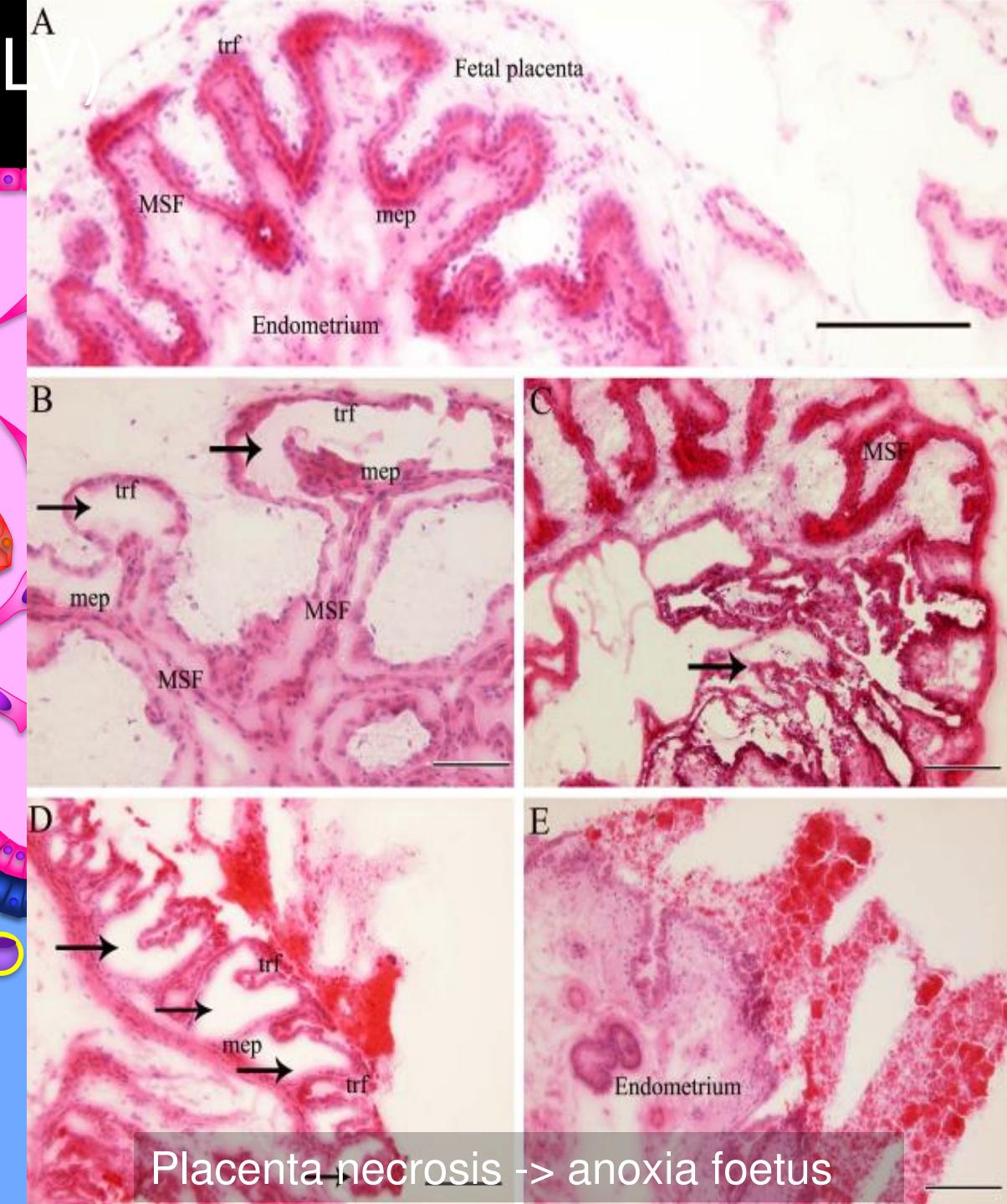
Target:
Siglec1⁺CD163⁺
macrophage



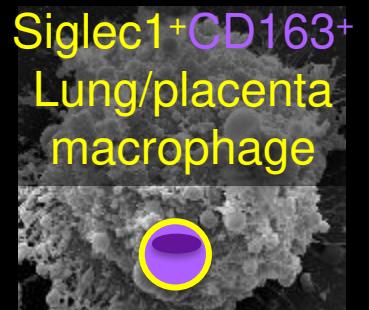
1990 - Low virulent PRRSV (G1s1;L)



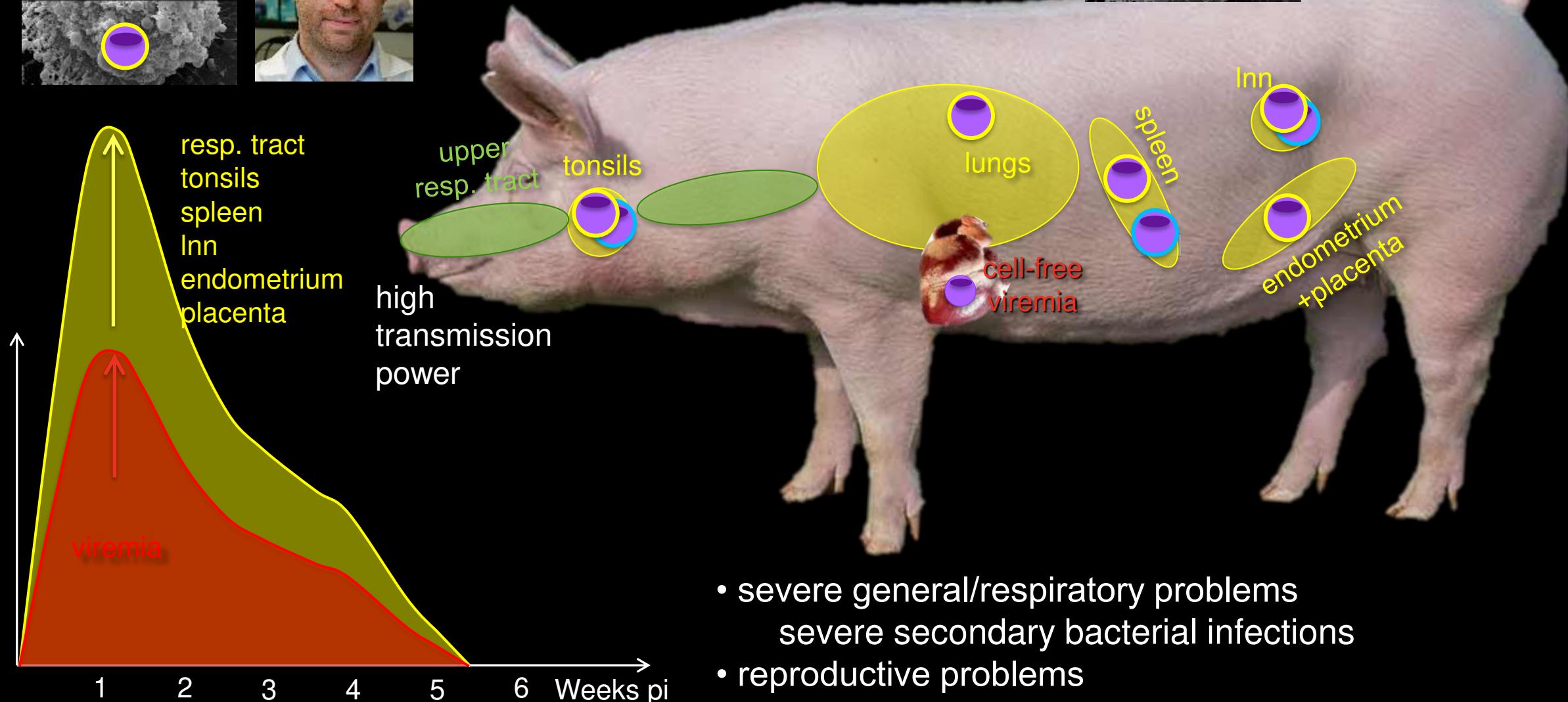
Target:
Siglec1⁺CD163⁺
macrophage



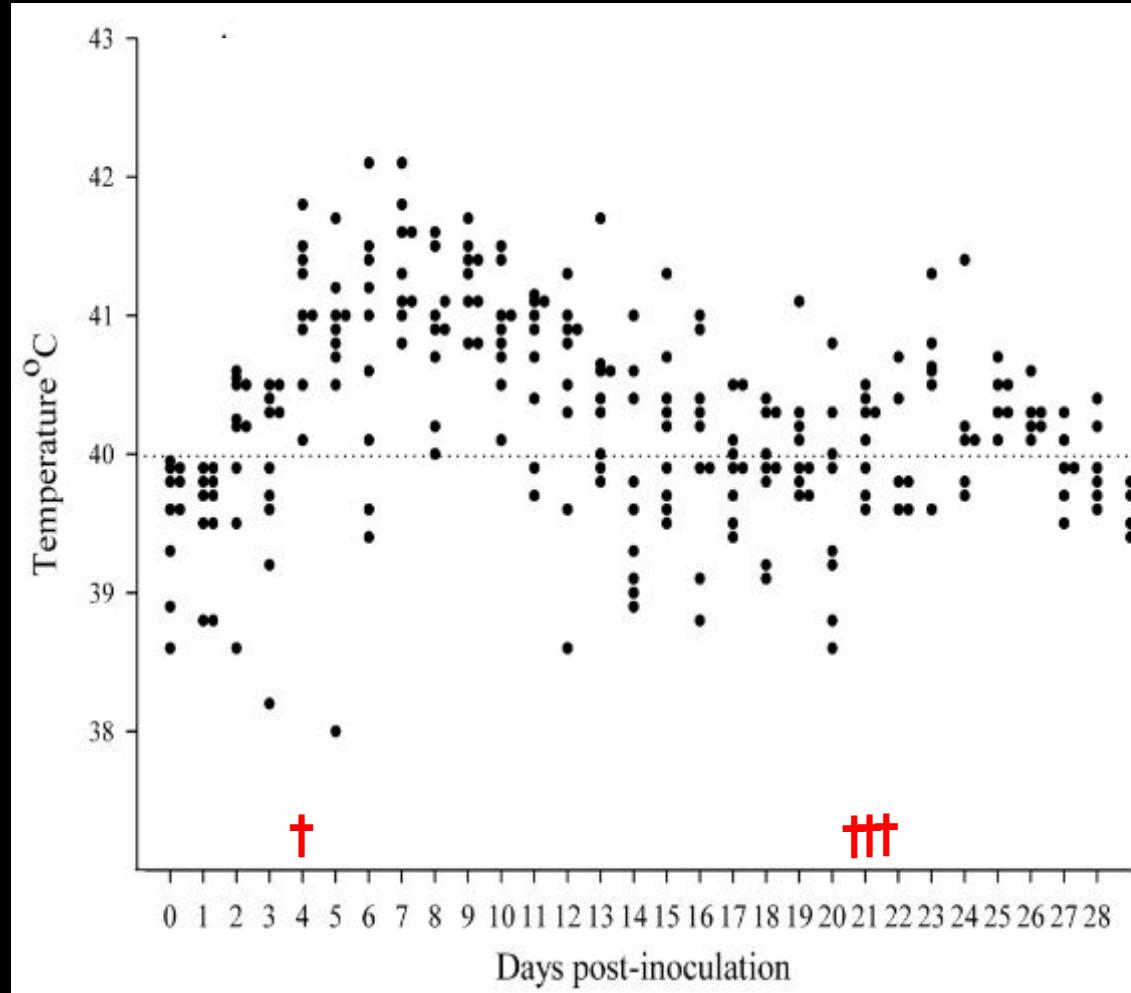
2006 - Highly virulent PRRSV (G1s3;Lena)



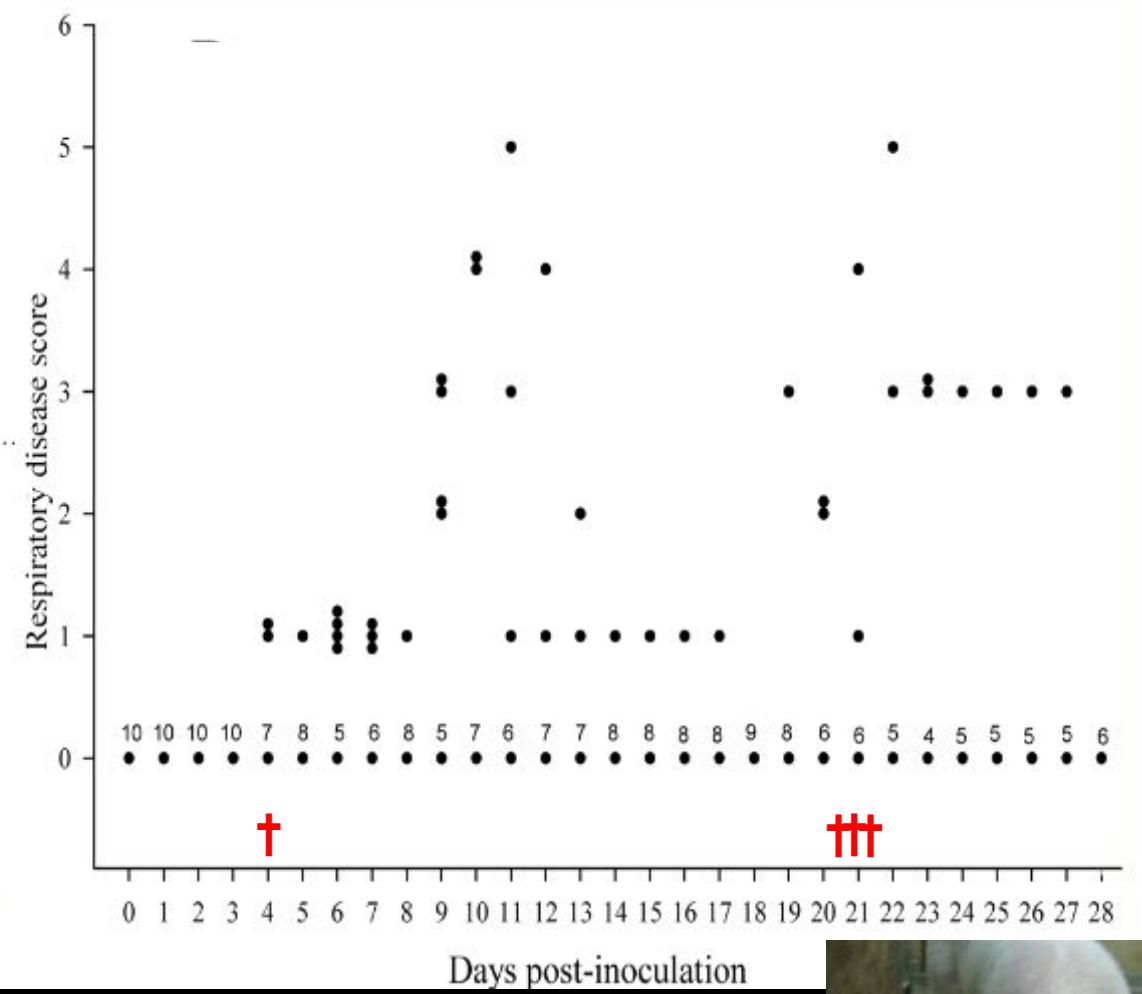
Uladzimir
Karniychuk



Body temperature



Respiratory score

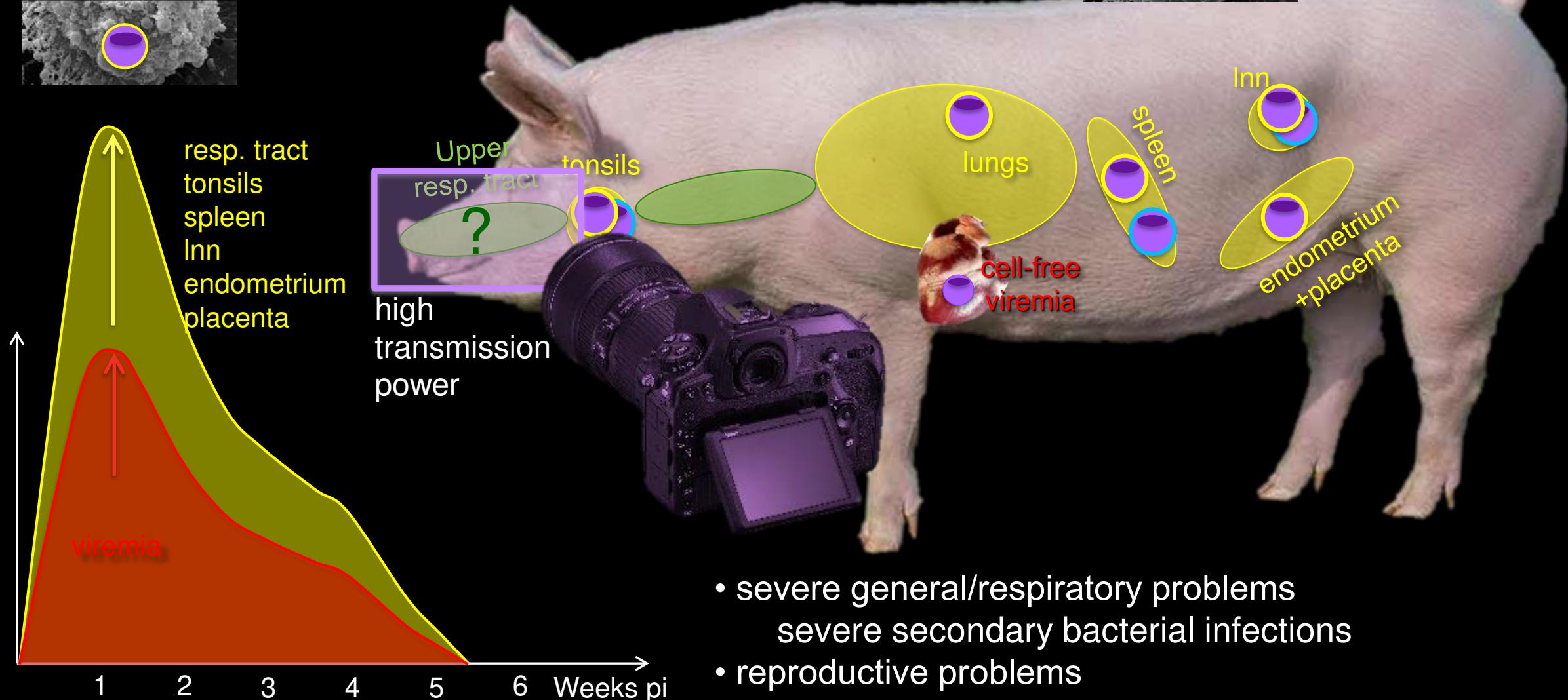
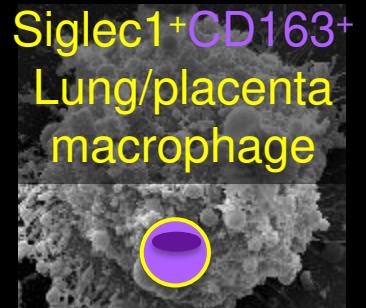


= high fever disease

= highly virulent Asian strains



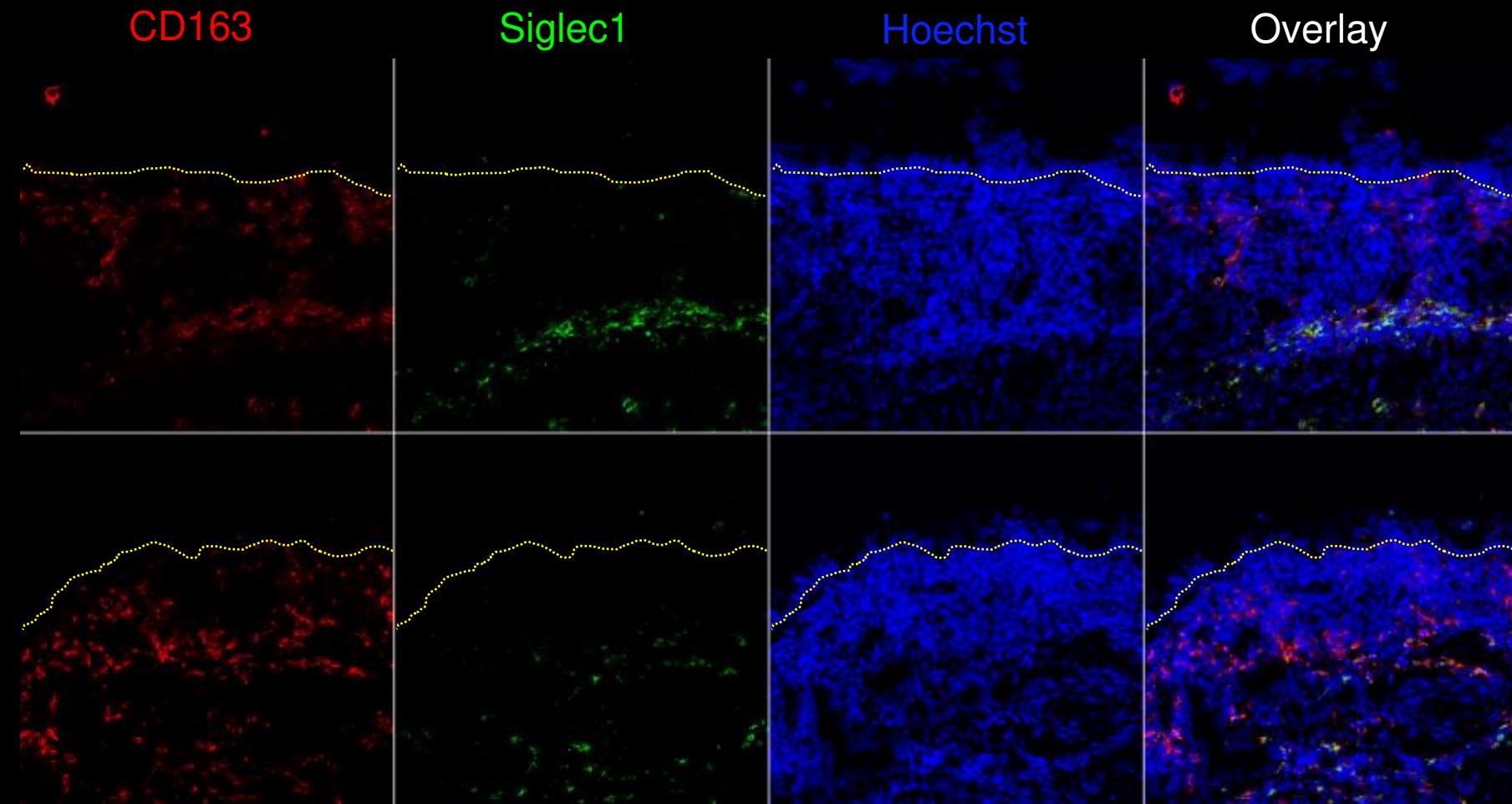
2006 - Highly virulent PRRSV (G1s3;Lena)



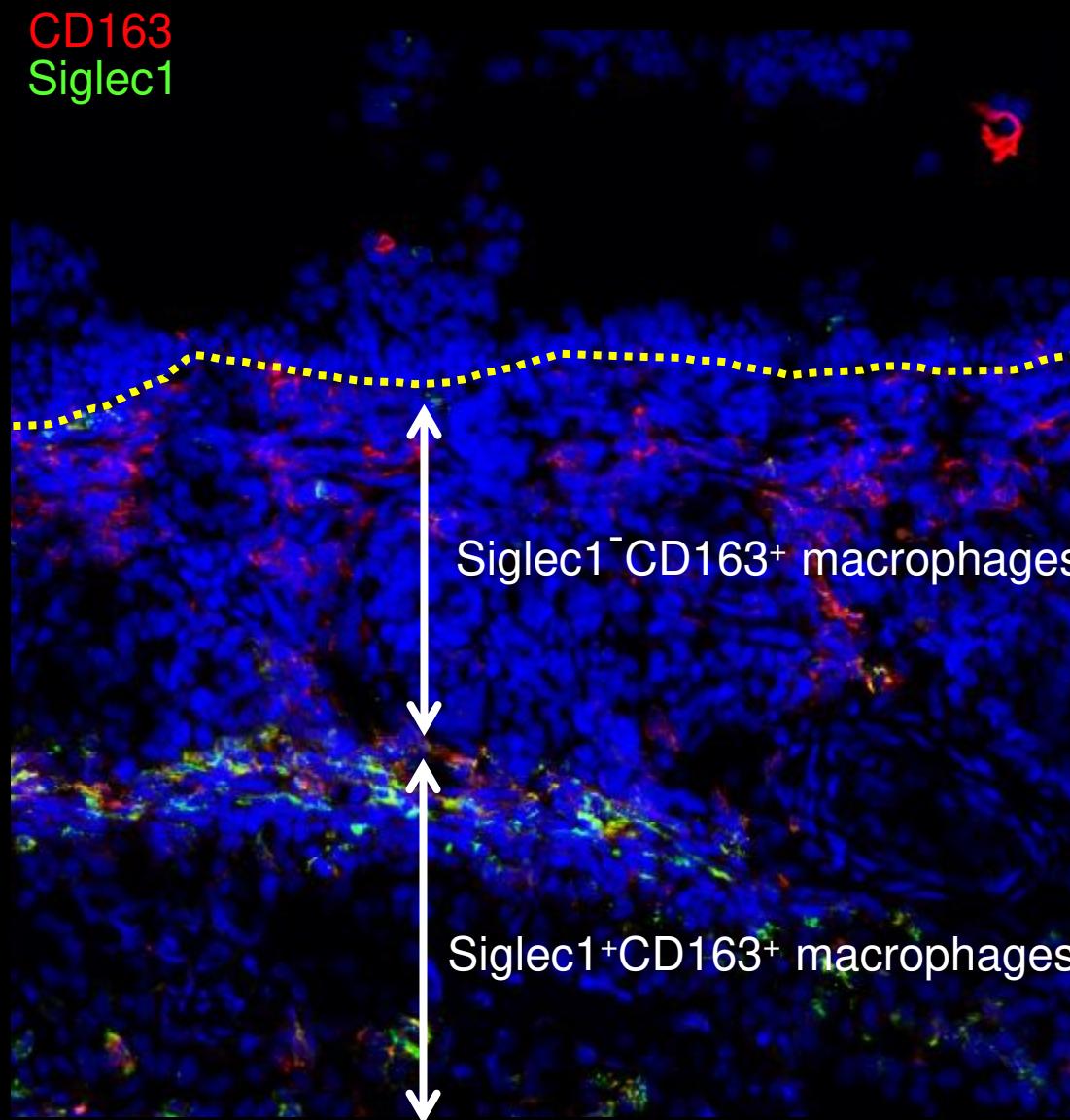
Siglec1 expression on CD163⁺ macrophages in the nasal mucosa



Dayoung Oh

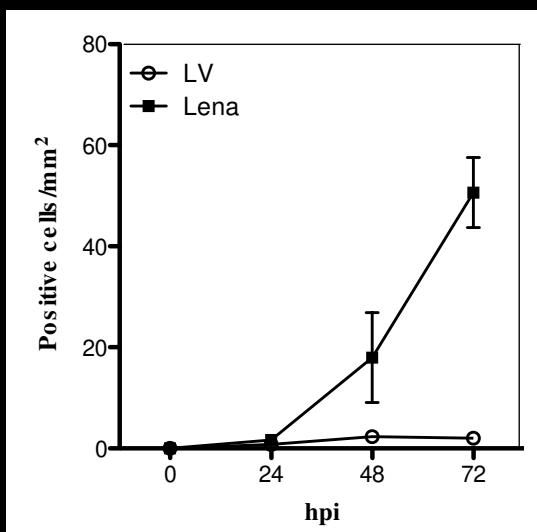
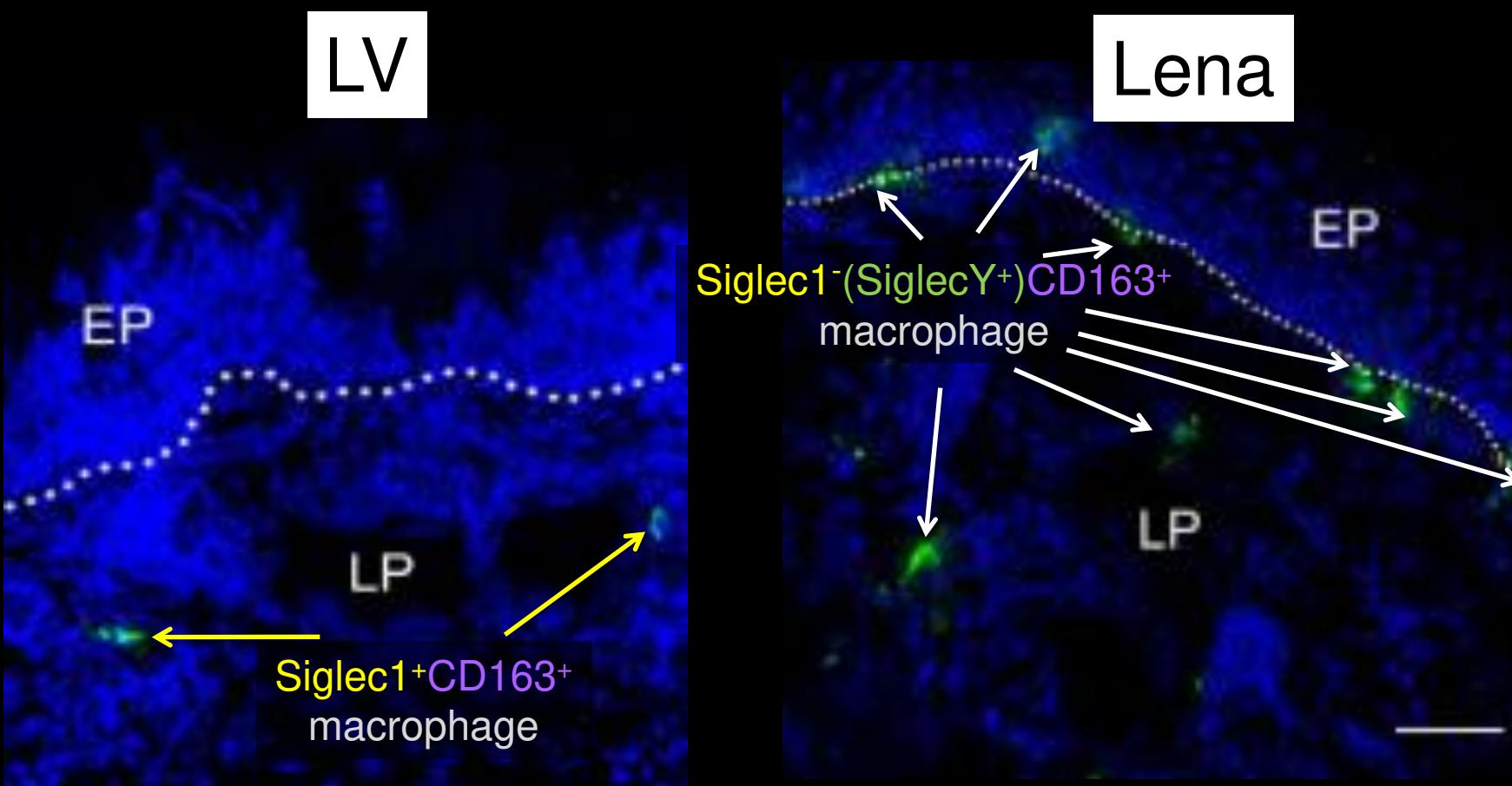


Nasal mucosa: 2 different populations of macrophages

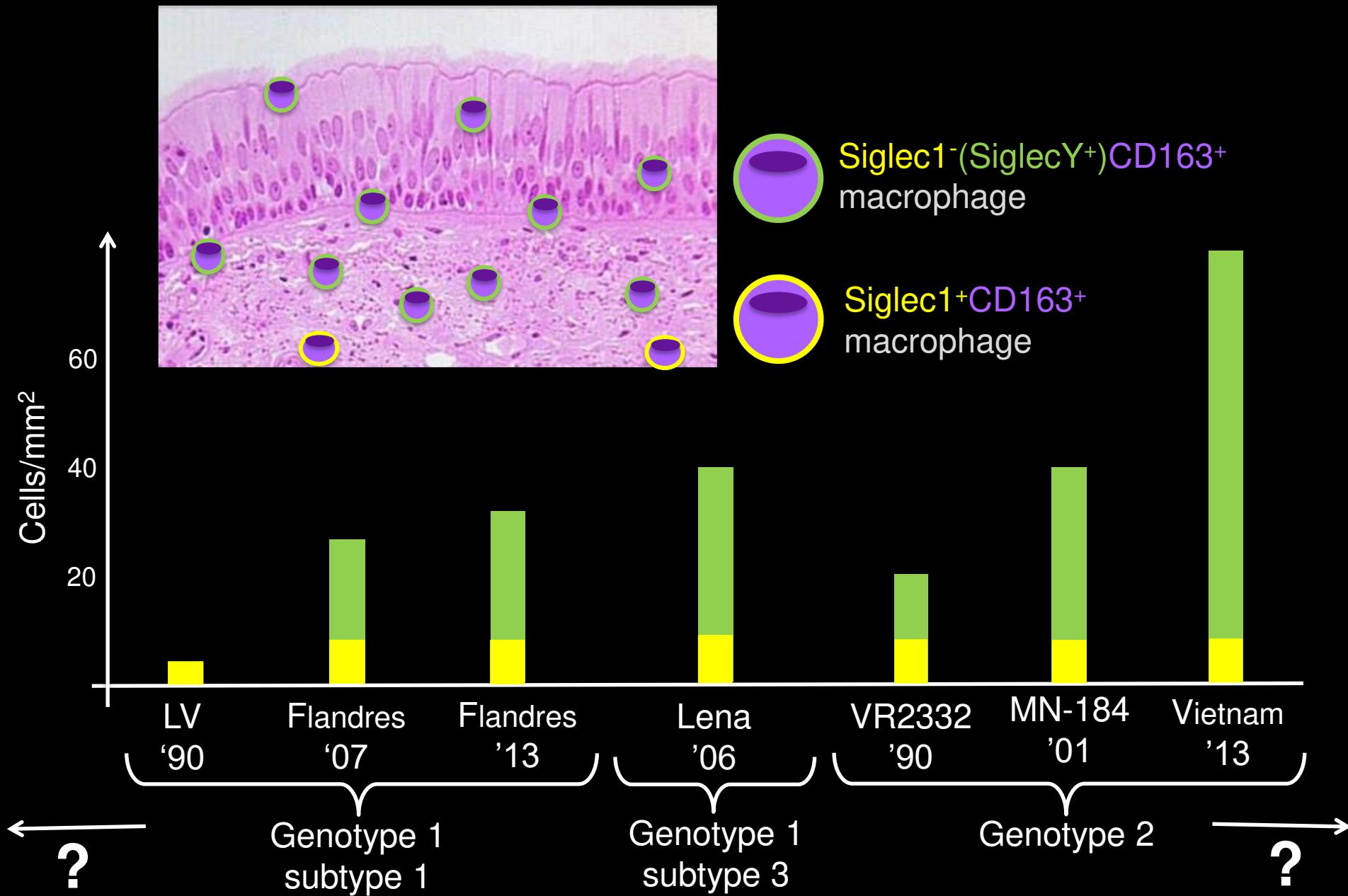




Ilias Frydas

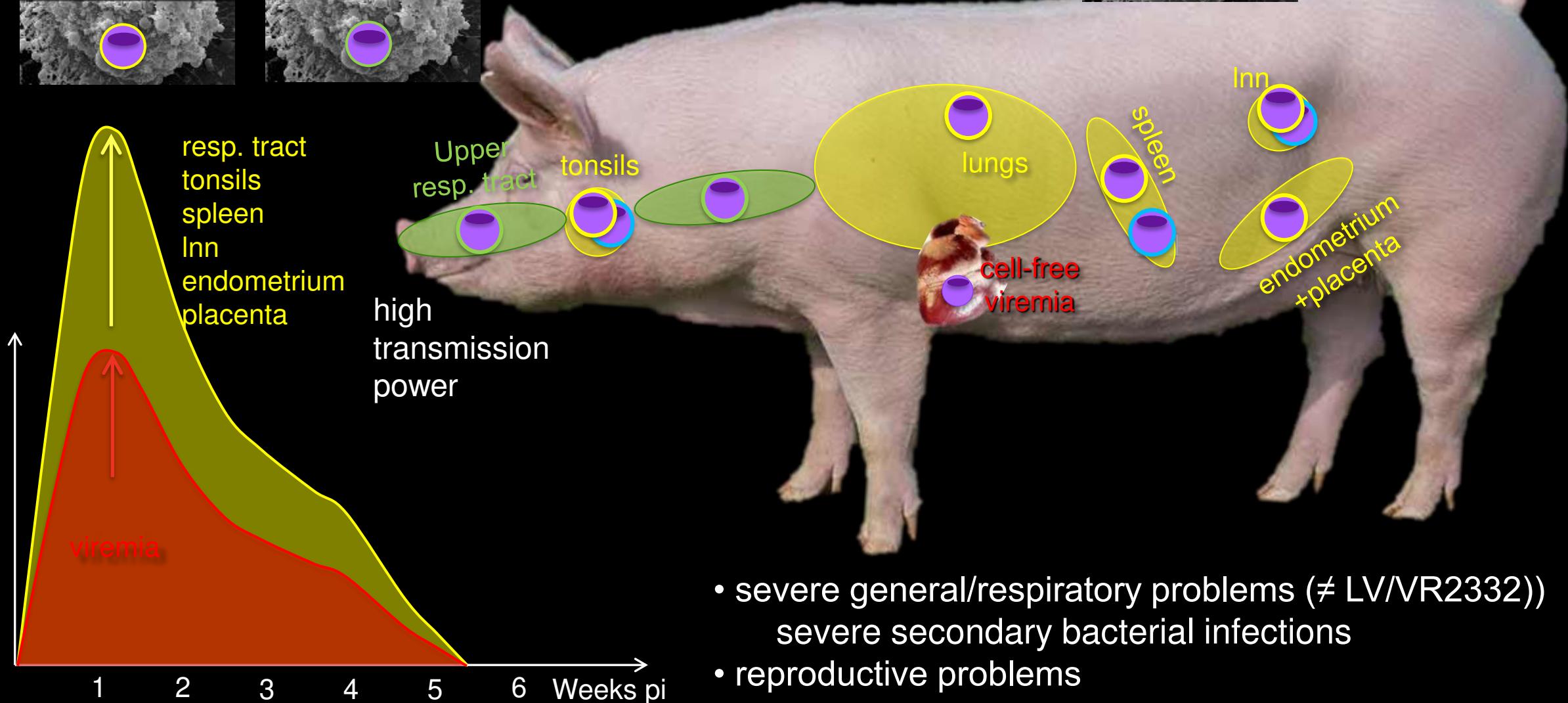
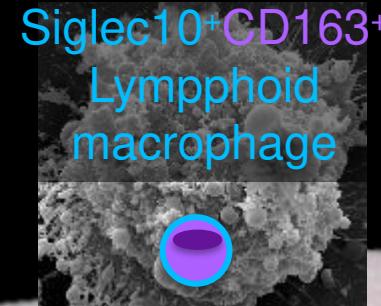


Replication in nasal mØ



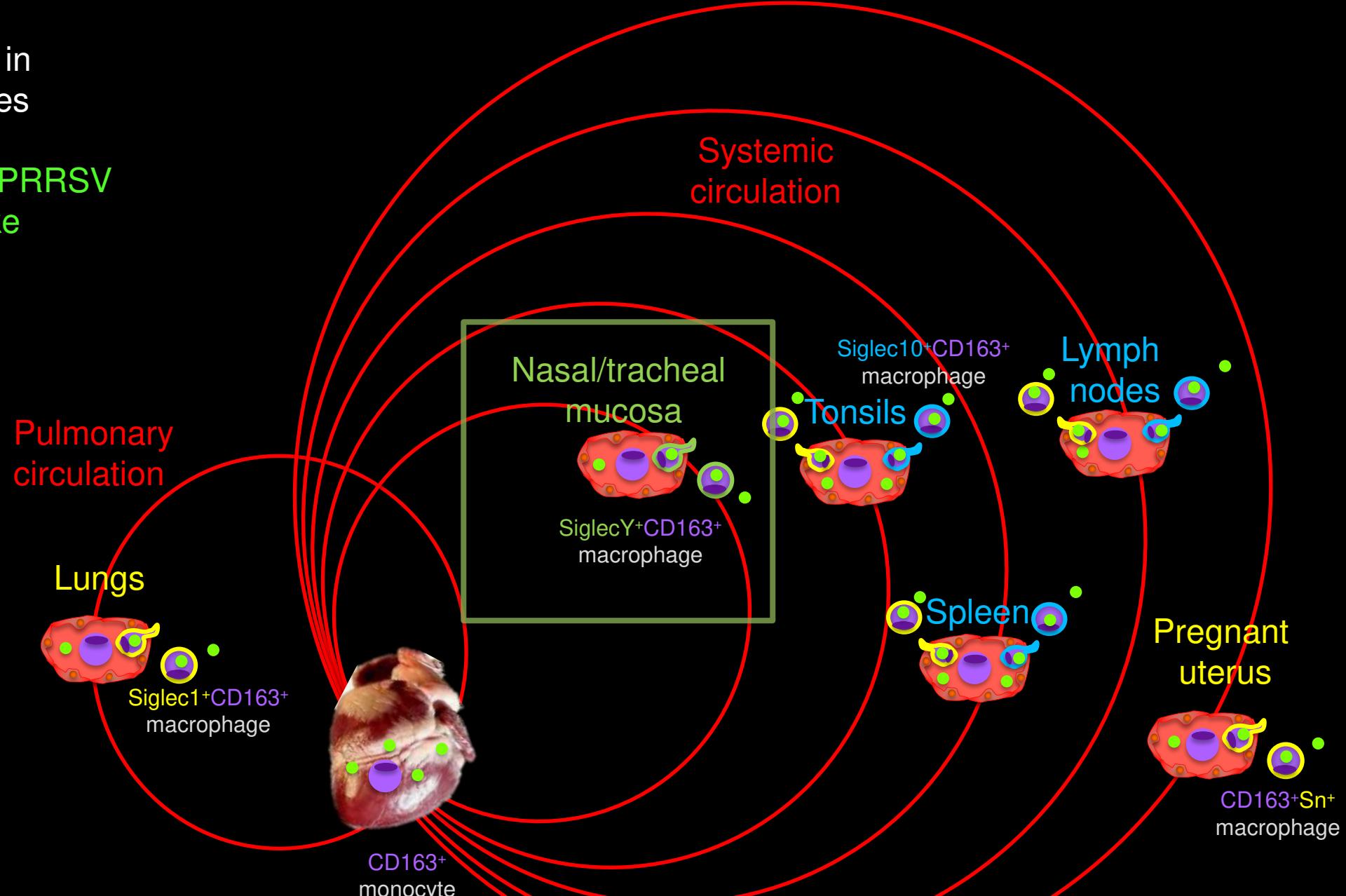
2006 - Highly virulent PRRSV (G1s3;Lena)

1

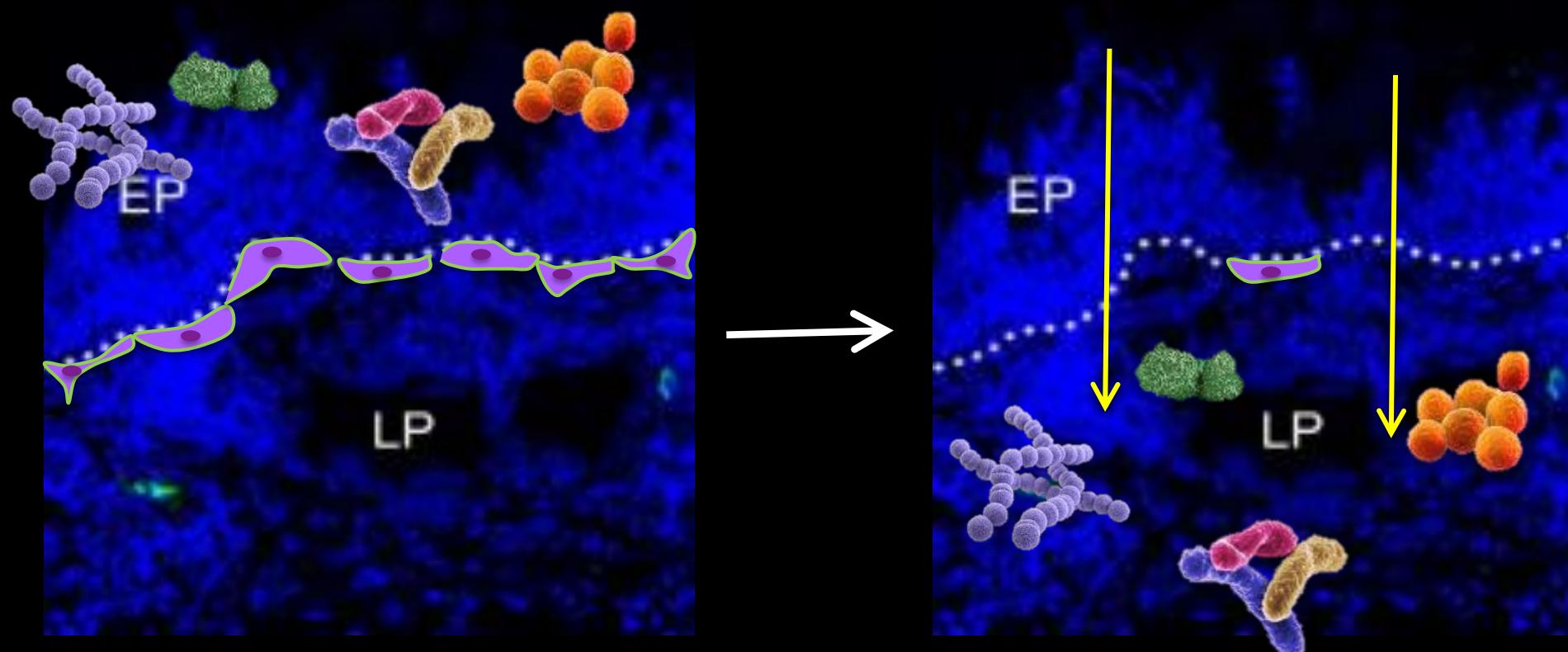


Macrophage differentiation in different tissues

Highly virulent PRRSV
G1s3;Lena-like



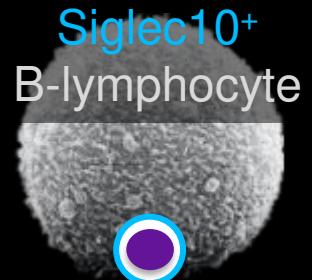
G1s3(Lena), recent G1s1, G2
Destruction of the superficial nasal mØ
~ STRONG invasion of bacteria
bacterial invasion/sepsis (e.g. *Streptococcus suis*)



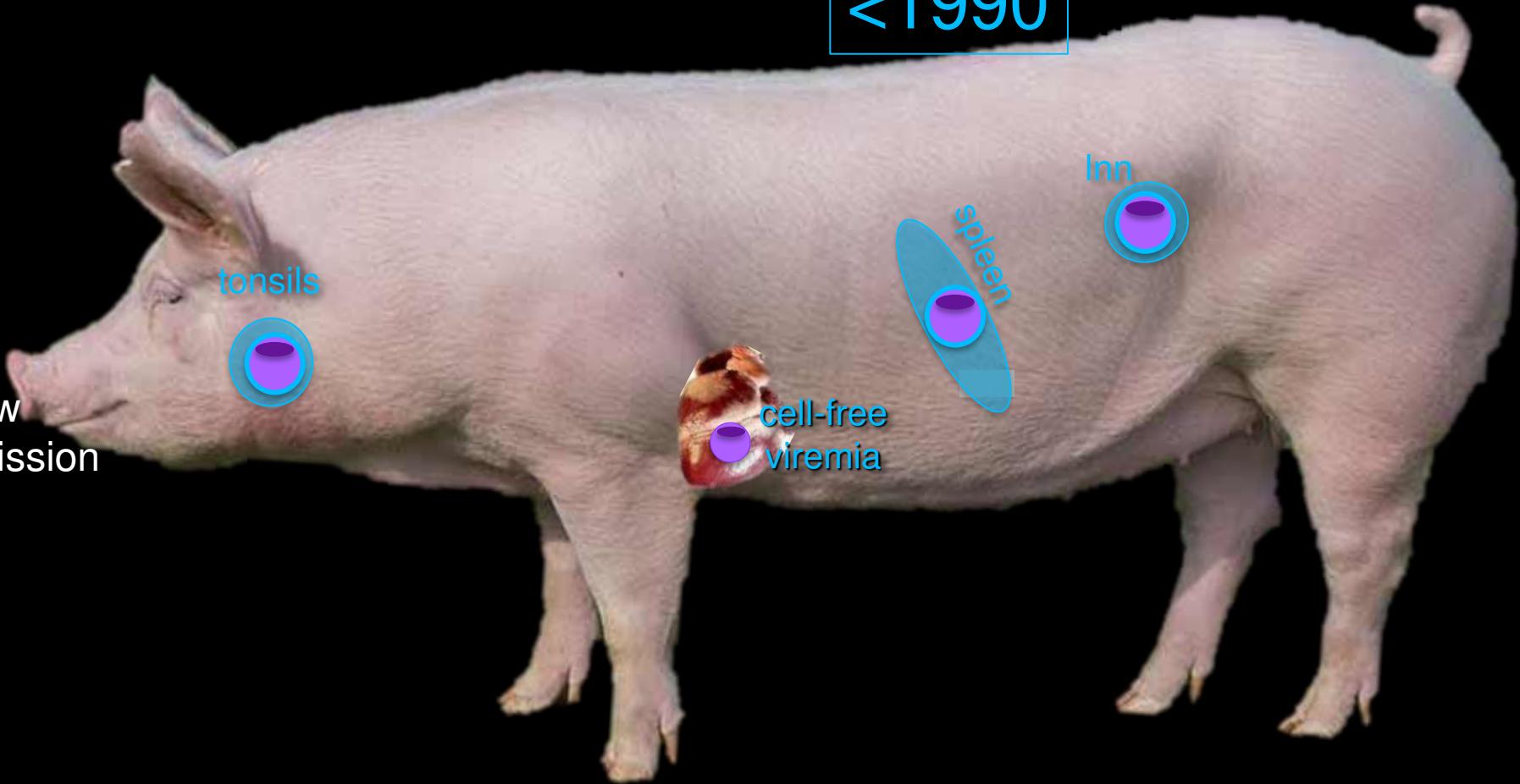
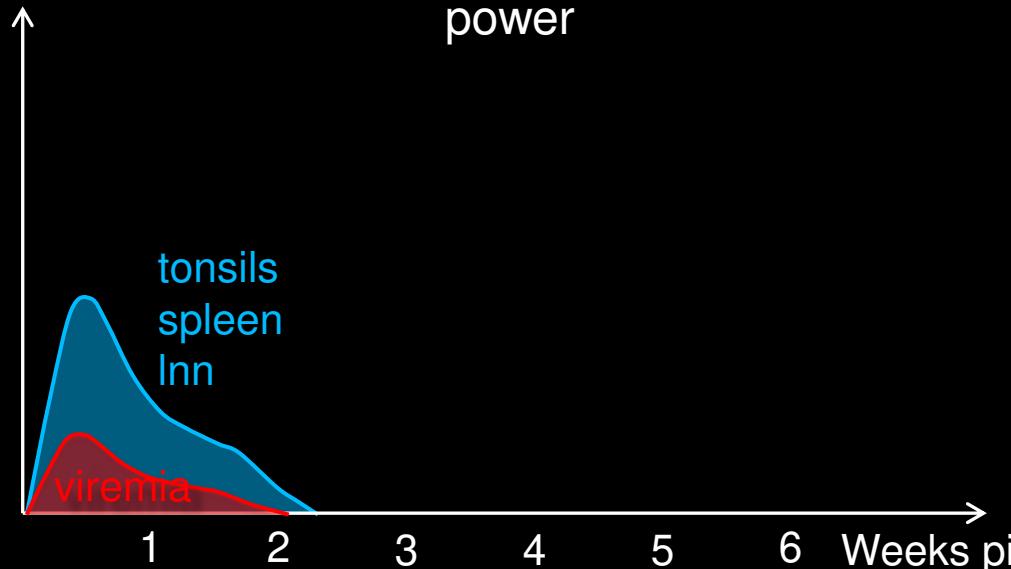
Hypothesis on the evolution of PRRSV-receptor interactions

SIGLEC HOPPING

<1990



very low
transmission
power

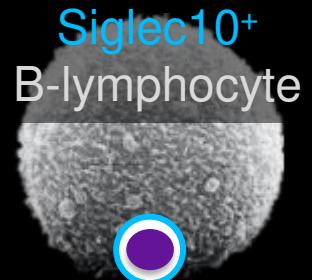


• subclinical

Hypothesis on the evolution of PRRSV-receptor interactions

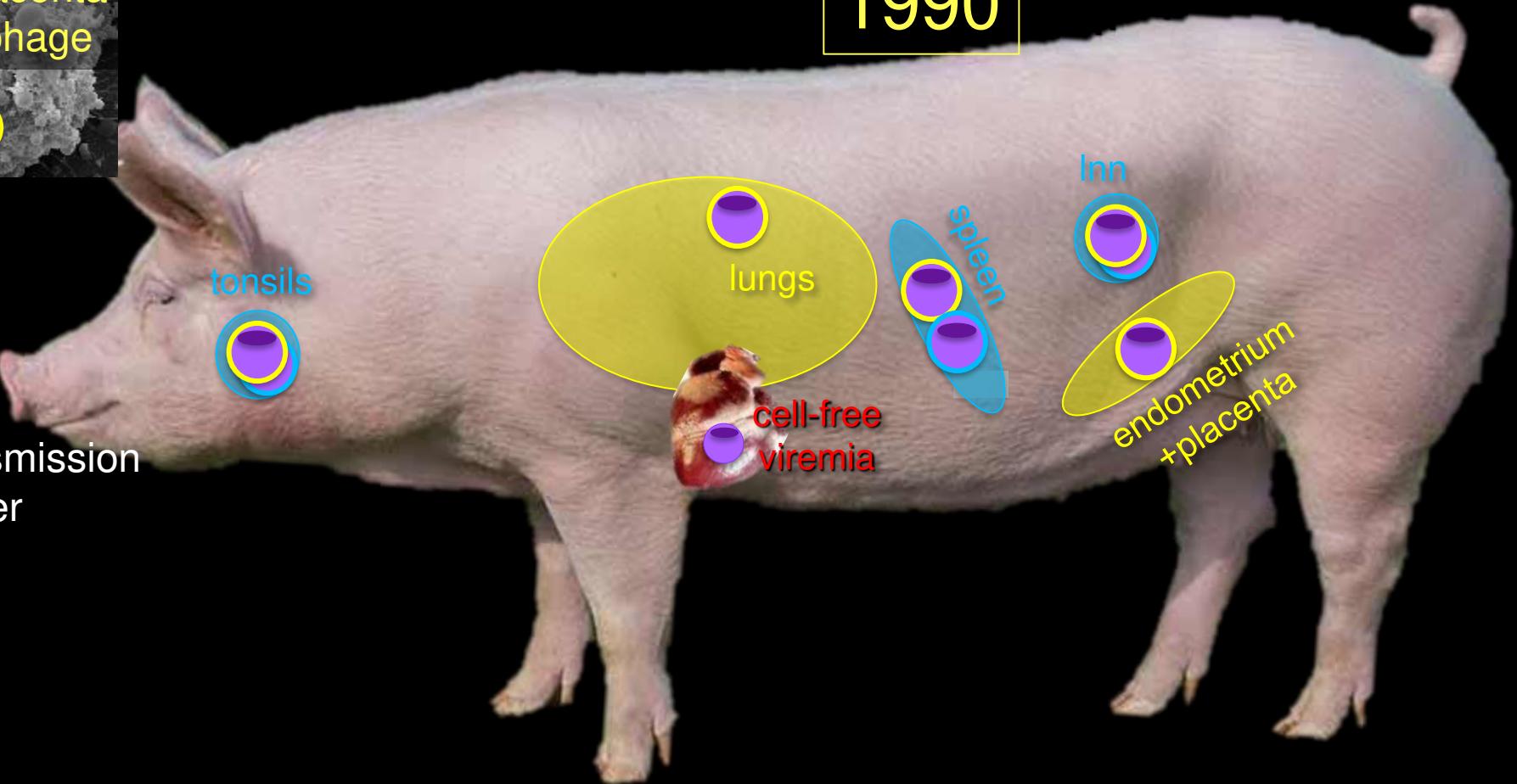
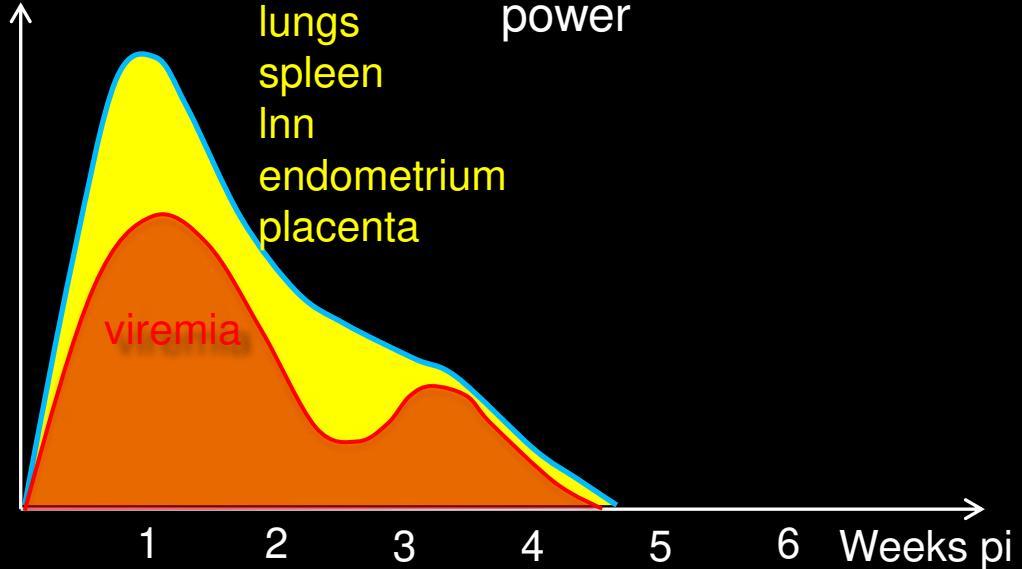
SIGLEC HOPPING

1990



tonsils
lungs
spleen
Inn
endometrium
placenta

low transmission power

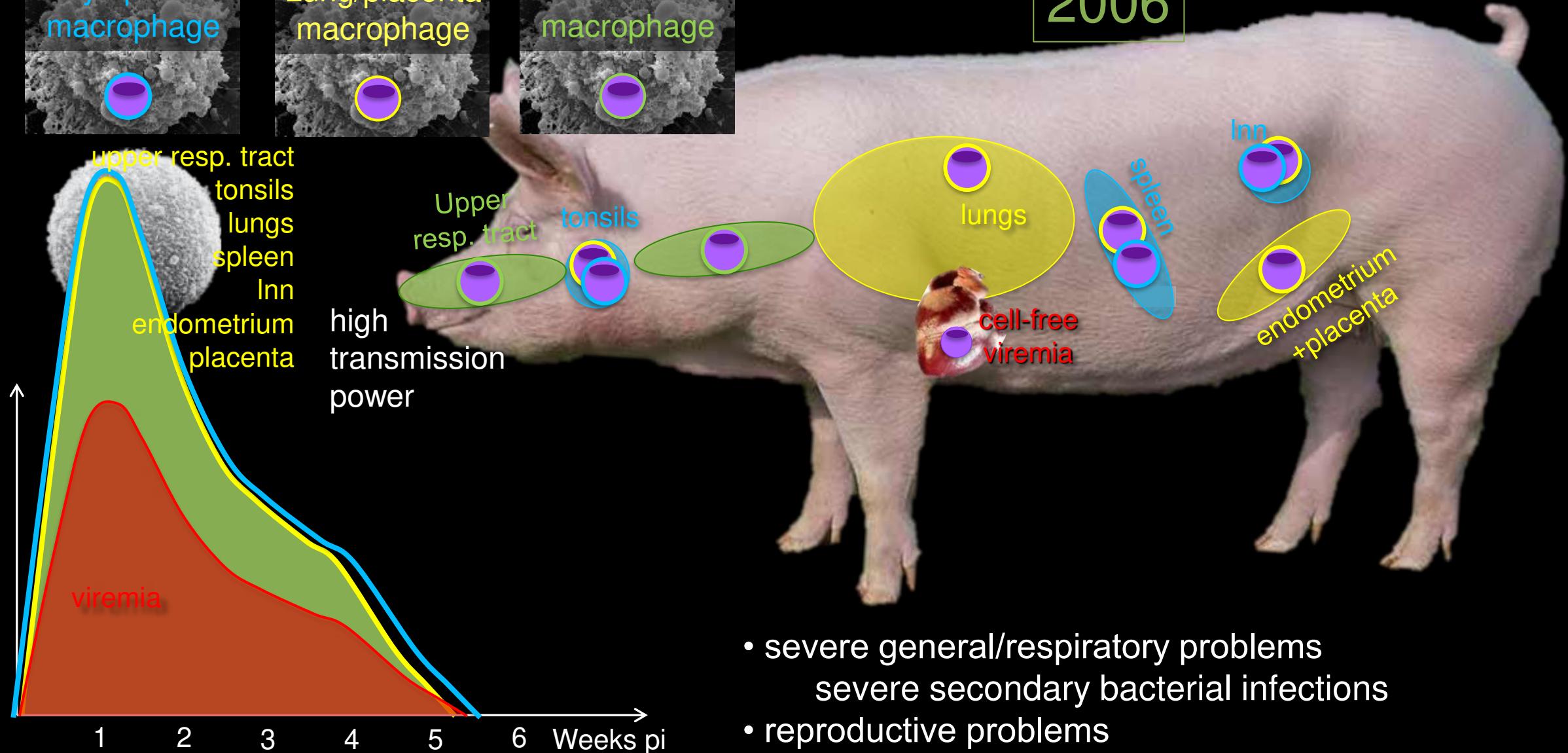


- no general/respiratory problems,
except during co-infections
- reproductive problems

Hypothesis on the evolution of PRRSV-receptor interactions

SIGLEC HOPPING

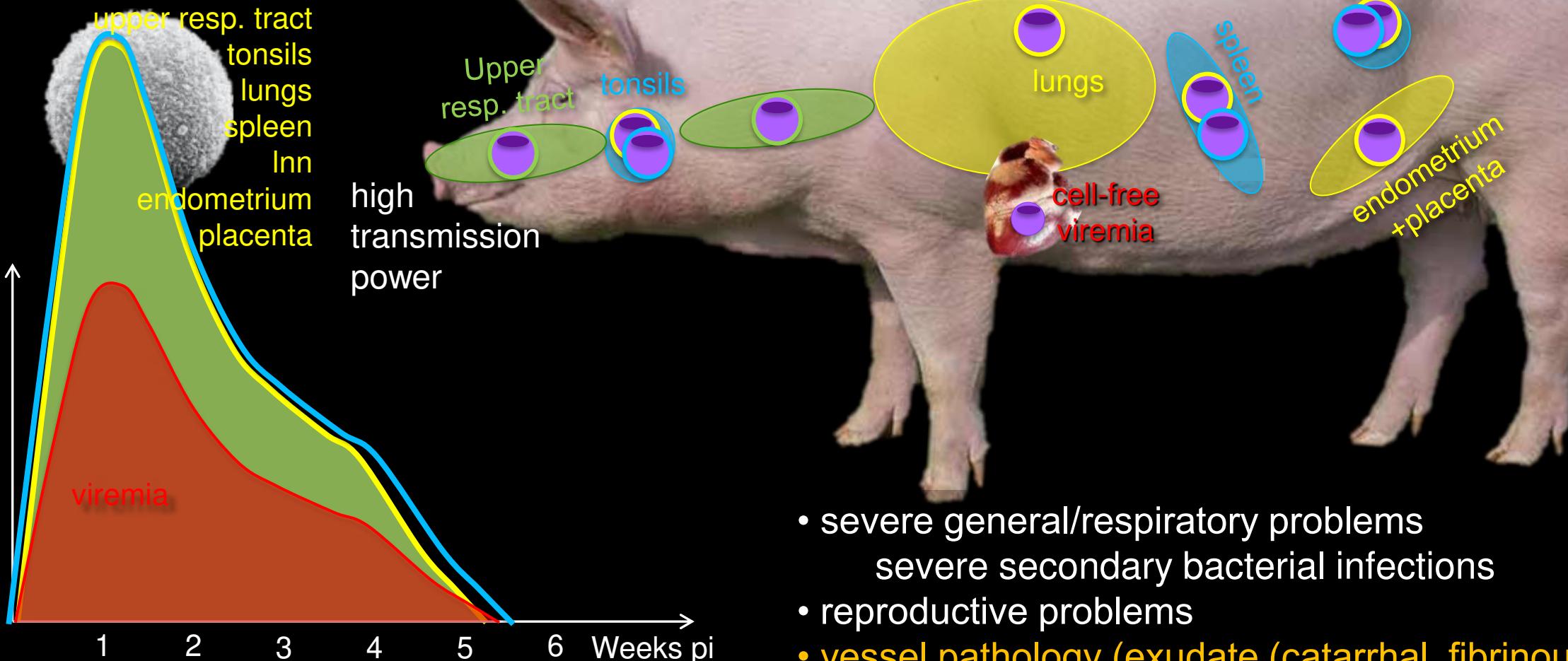
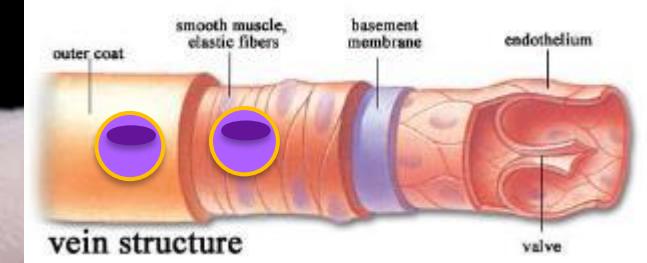
2006



Hypothesis on the evolution of PRRSV-receptor interactions

SIGLEC HOPPING

2006



- severe general/respiratory problems
severe secondary bacterial infections
- reproductive problems
- vessel pathology (exudate (catarrhal, fibrinous))





Questions?