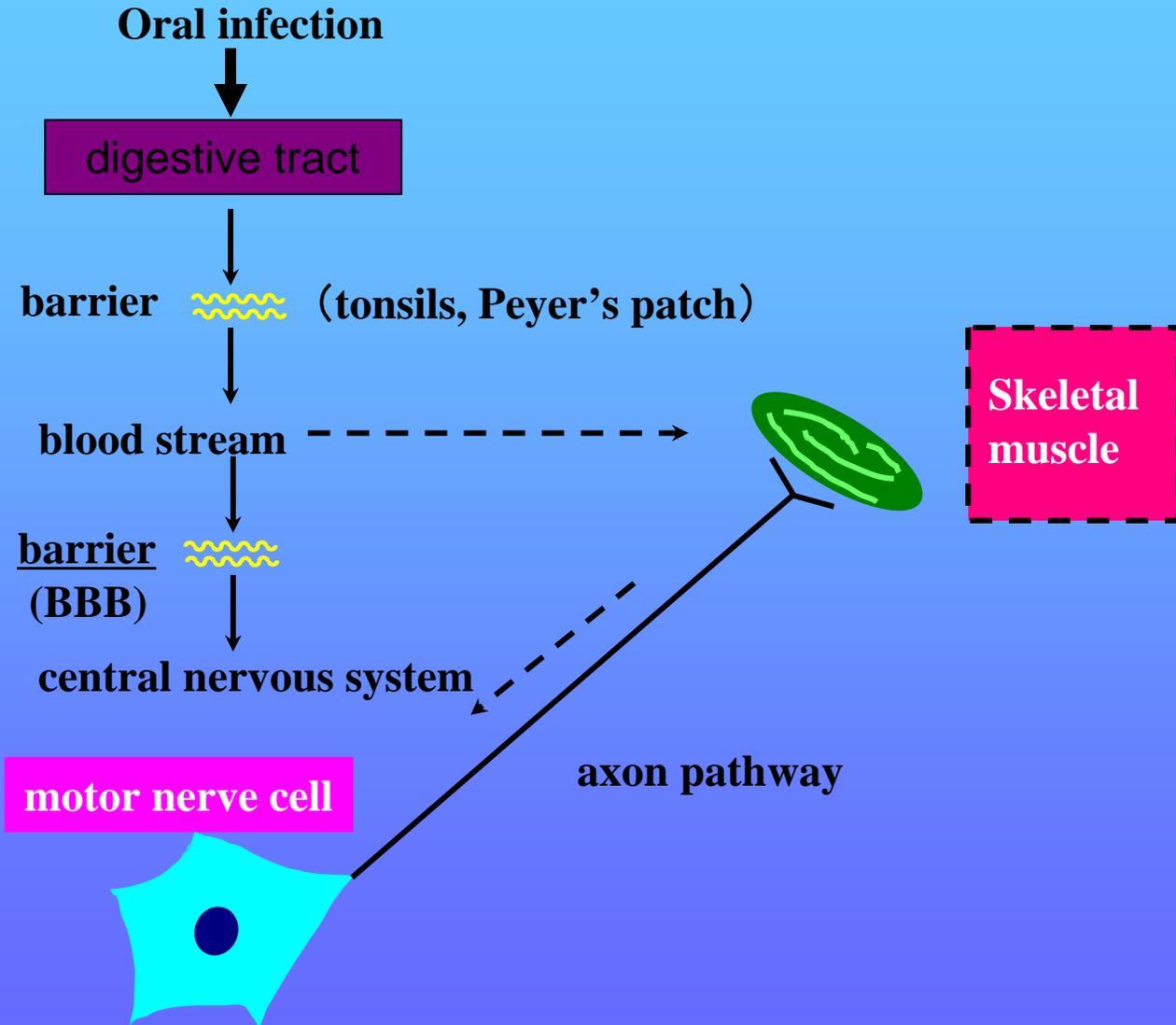


Replication of polio virus and dissemination



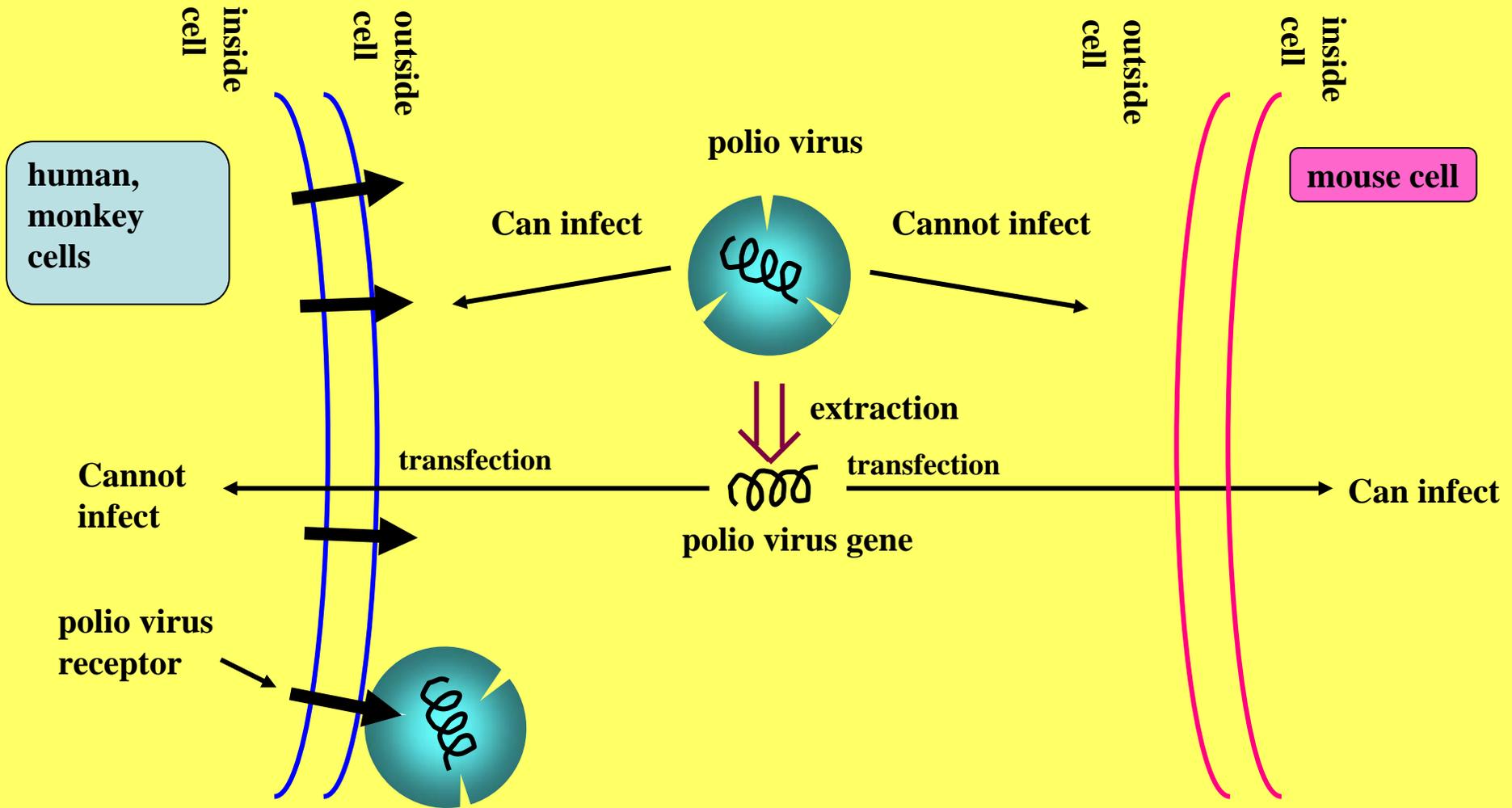
Research on pathogenicity

1. Mechanisms for determining species-specificity
2. Mechanisms of dissemination
3. Mechanisms for determining tissue-specificity
4. Ability to cause damage to the target cell

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Role of poliovirus receptor during polio virus infection



exon 1 2 3 4 5 6 7 8

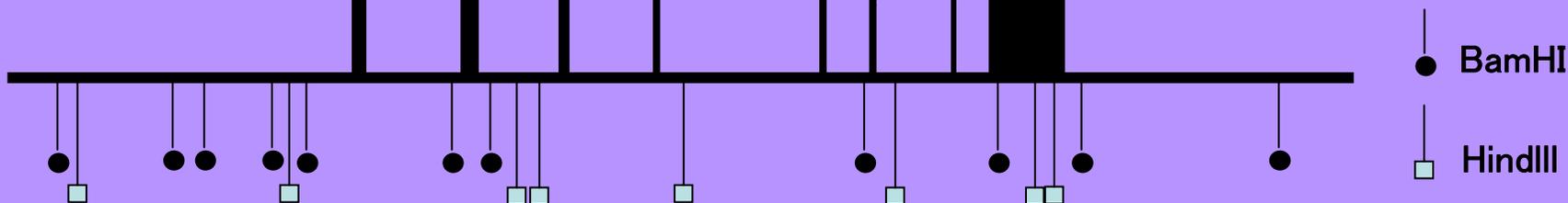
ATG

TGA

PVR α

PVR β

PVR γ



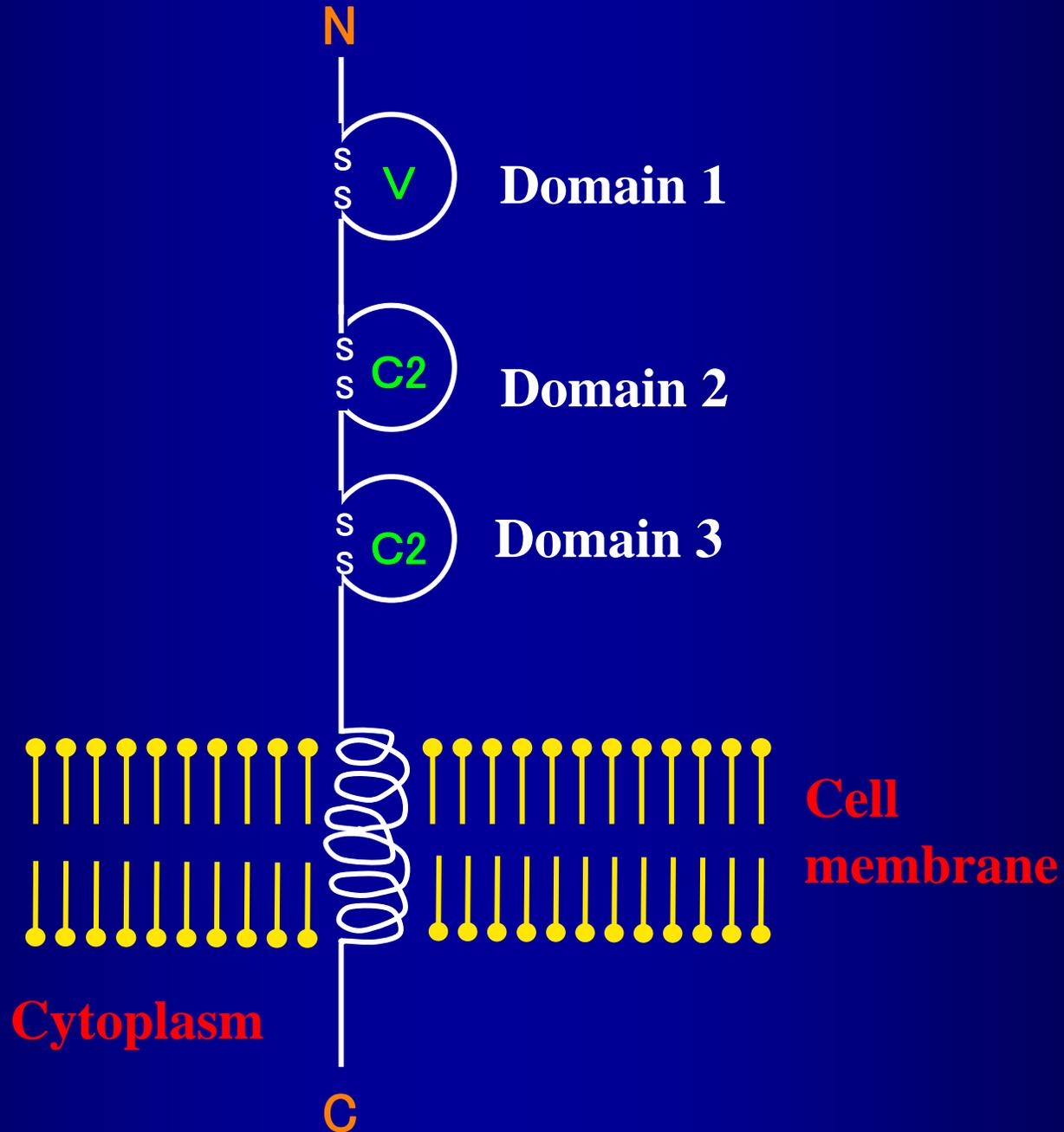
HC 3

HC 5

10 Kb



Structure of Poliovirus Receptor (PVR; CD155)





3 days after
i.c. injection of 7.5×10^7 pfu
Polio virus Sabin strain

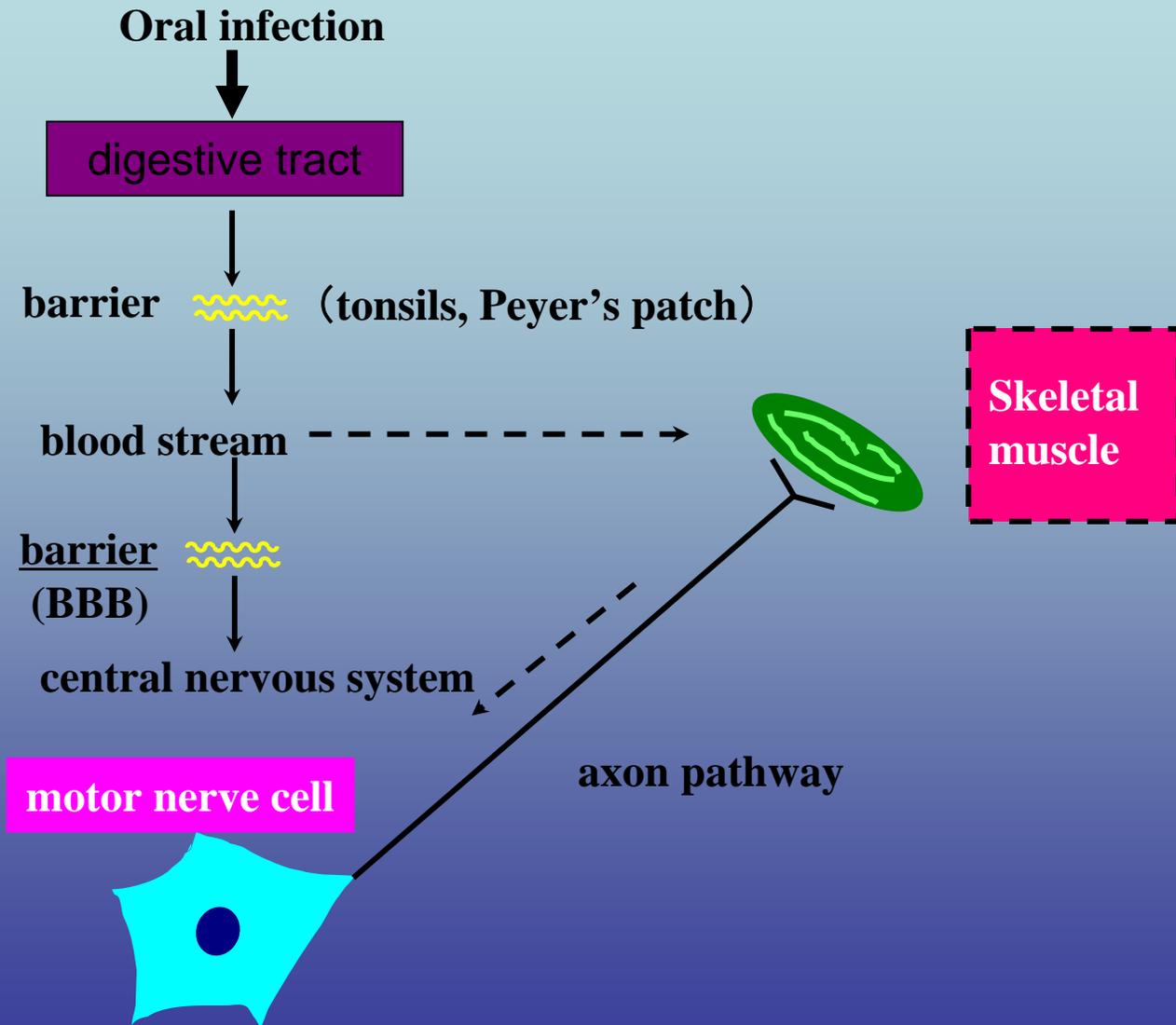
Principles of viral tropism

- 1. Receptor-dependent tropism**
- 2. Protease-dependent tropism**
- 3. IRES-dependent tropism**
- 4. Natural immunity-dependent tropism**
- 5. Others**

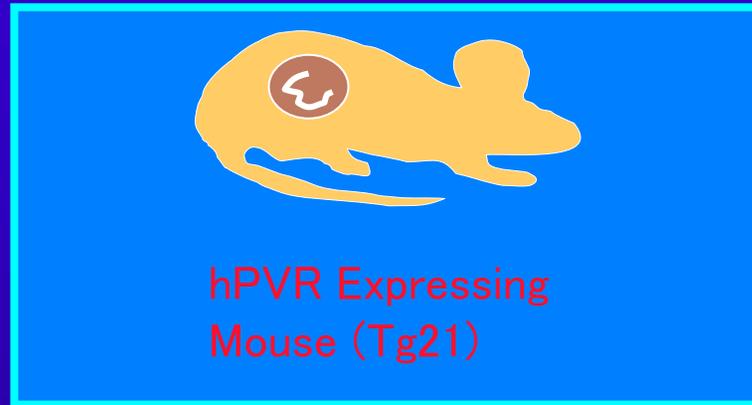
Research on pathogenicity

1. Mechanisms determining species-specificity
2. **Mechanisms of dissemination**
3. Mechanisms determining tissue-specificity
4. Ability to cause damage to the target cell

Replication of polio virus and transmission in the body



Neurotropic Polio virus Infection



	Tissue Distribution	BBB Permeation	CNS Toxicity
Mahoney	?	?	Strong
Sabin 1	?	?	Very Weak

Speed of PV accumulation in the blood of a mouse cerebrum

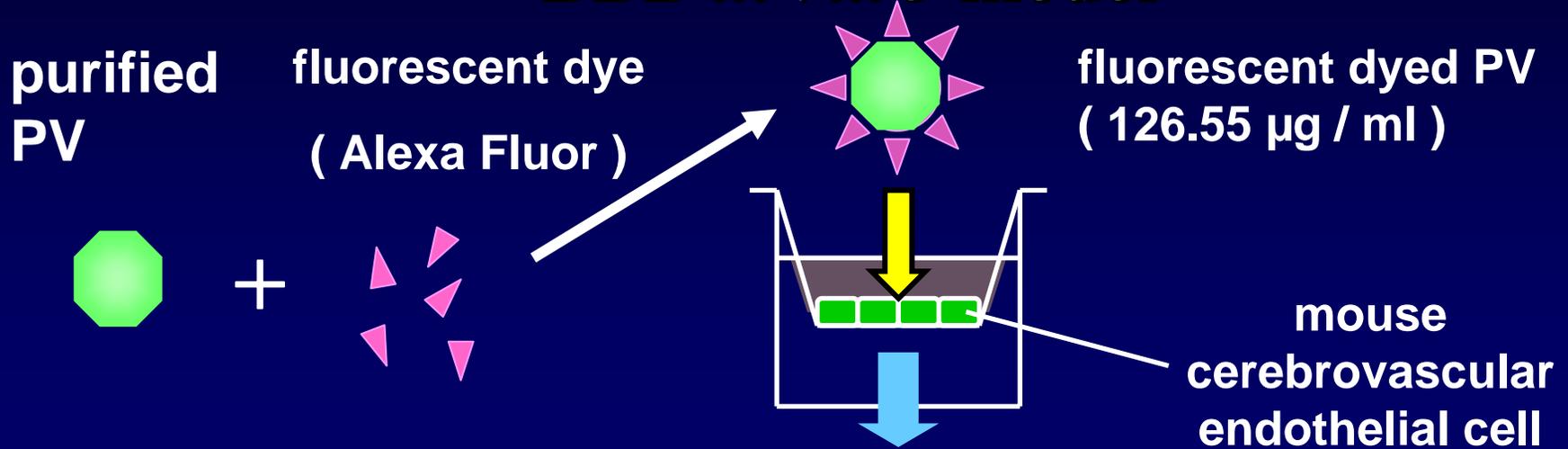
virus and control substances	speed of accumulation ($\mu\text{l} / \text{min} / \text{g tissue}$)	
	mouse with CD155 expression	mouse without CD155 expression
PV (Mahoney)	0.164	0.123
Negative control (Albumin)	—	0.001
Positive control (Cationized rat serum albumin)	0.123 (Rat)	

(Yang et al.,1997, Virology 229 , 421- 428)

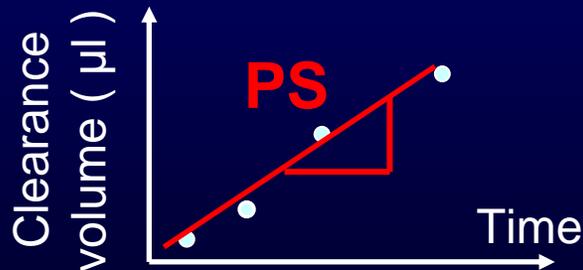


In BBB percolation of PV in the mouse, proactive import occurs in the brain independent of CD155.

Percolation examination using the BBB *in vitro* model



Periodic measurement of fluorescence after PV addition



$$\text{Clearance volume (} \mu\text{l) = } \frac{\text{amount of PV moved to basolateral surface (} \mu\text{g)}}{\text{Primary concentration of PV at the luminal surface (} \mu\text{g} / \mu\text{l)}}$$

(PS : Permeability-surface area product)

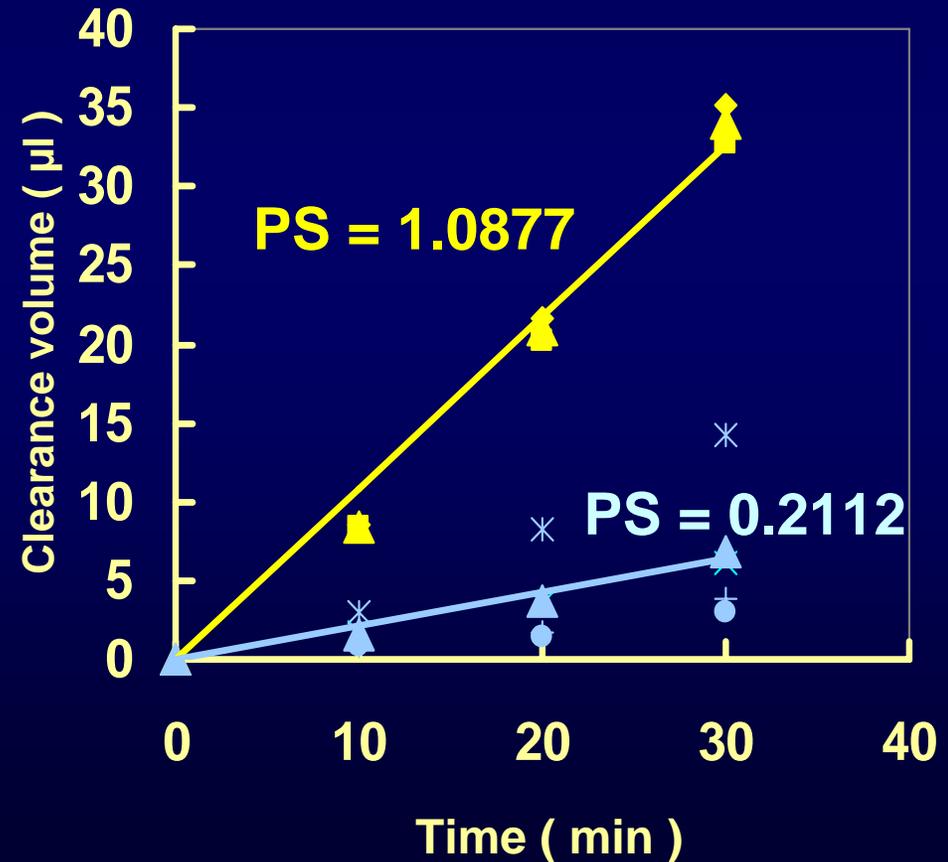
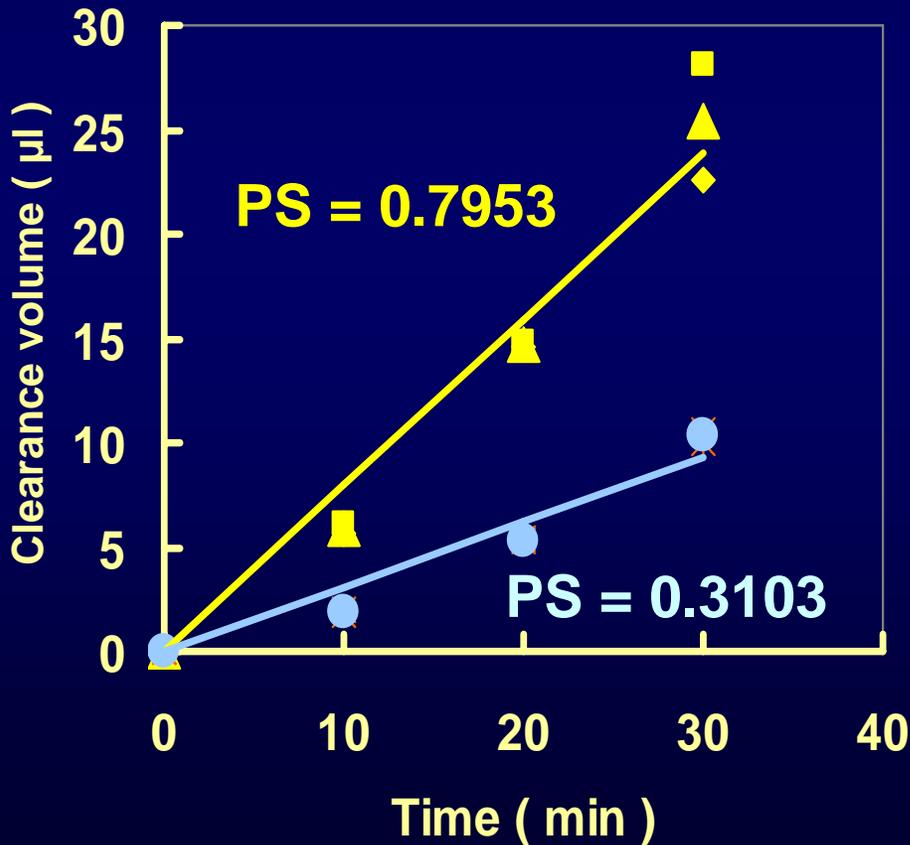
PV percolation in the BBB *in vitro* model is extremely high

Transferrin (mw 80K)

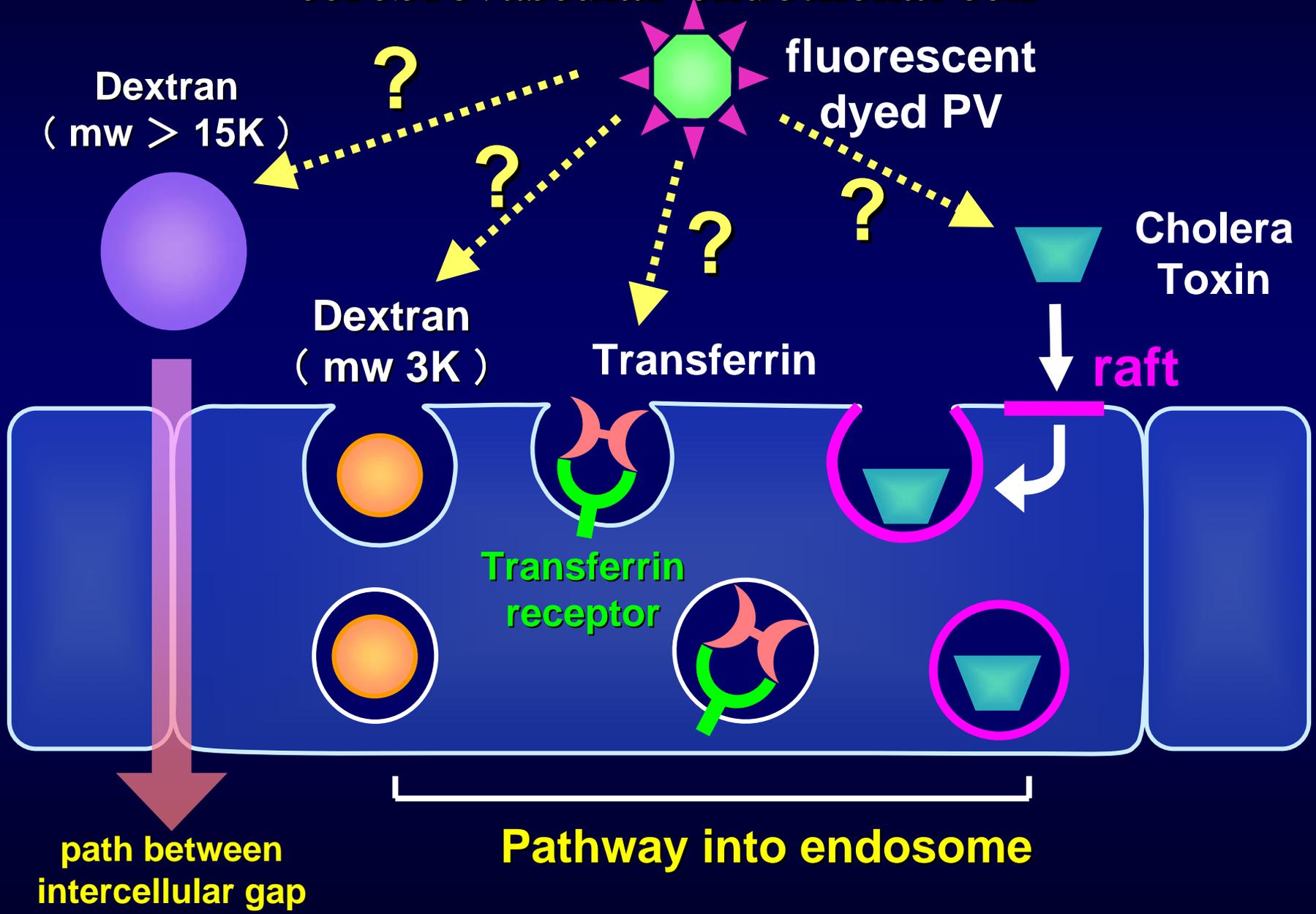
Dextran (mw 70K)

PV (mw 9800K)

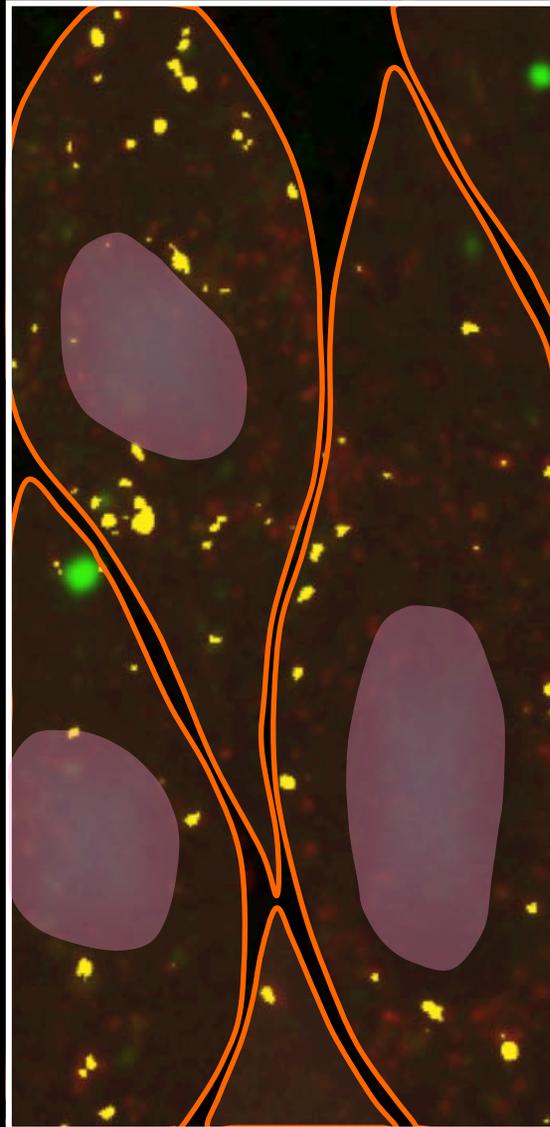
Dextran (mw 2000K)



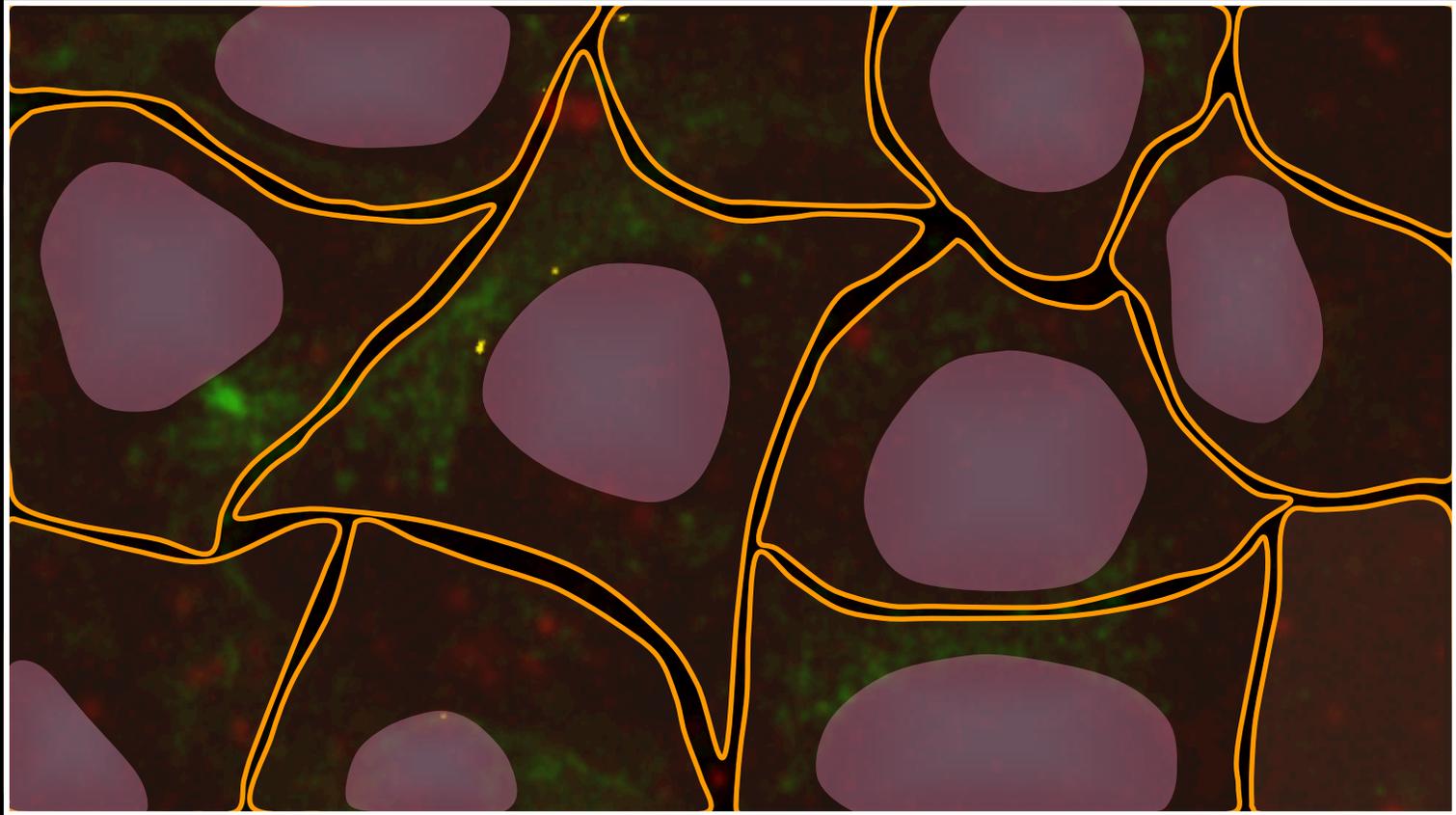
Examination of PV intake into a mouse cerebrovascular-endothelial cell



PV + Dextran (mw. 3K)

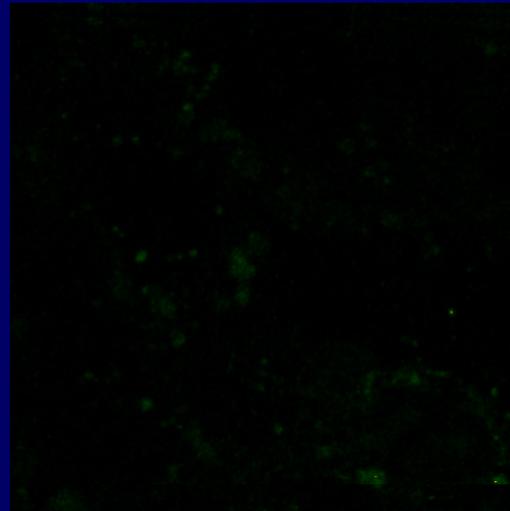
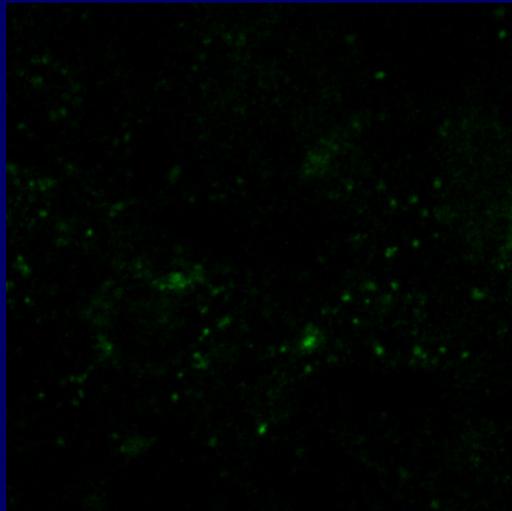


PV + Cholera Toxin



10

Endocytosis of transferrin (Tf) is inhibited by PV



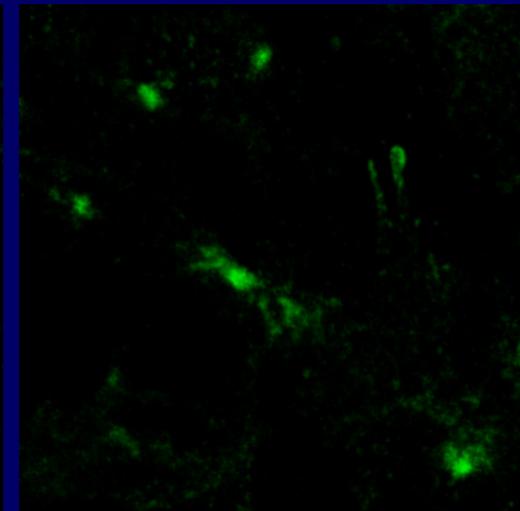
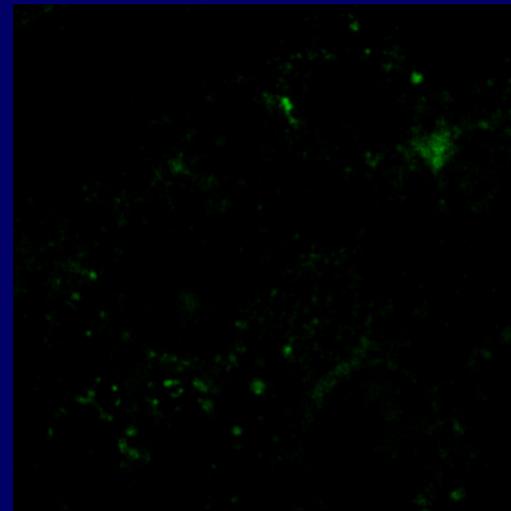
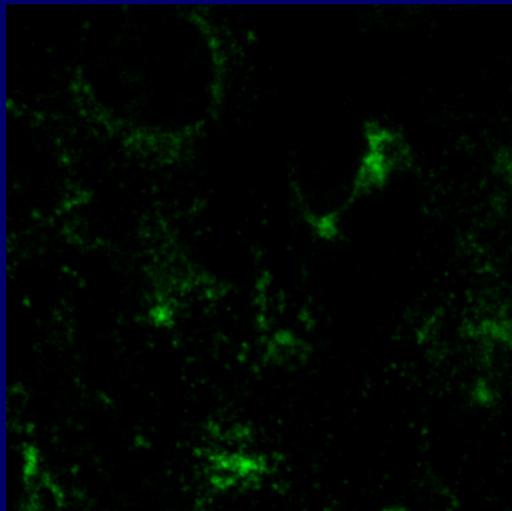
Alexa 488 - Tf
10 μ g / ml
(MBEC4 cell)

— 20 μ m

Purified PV

—

m.o.i. 5000



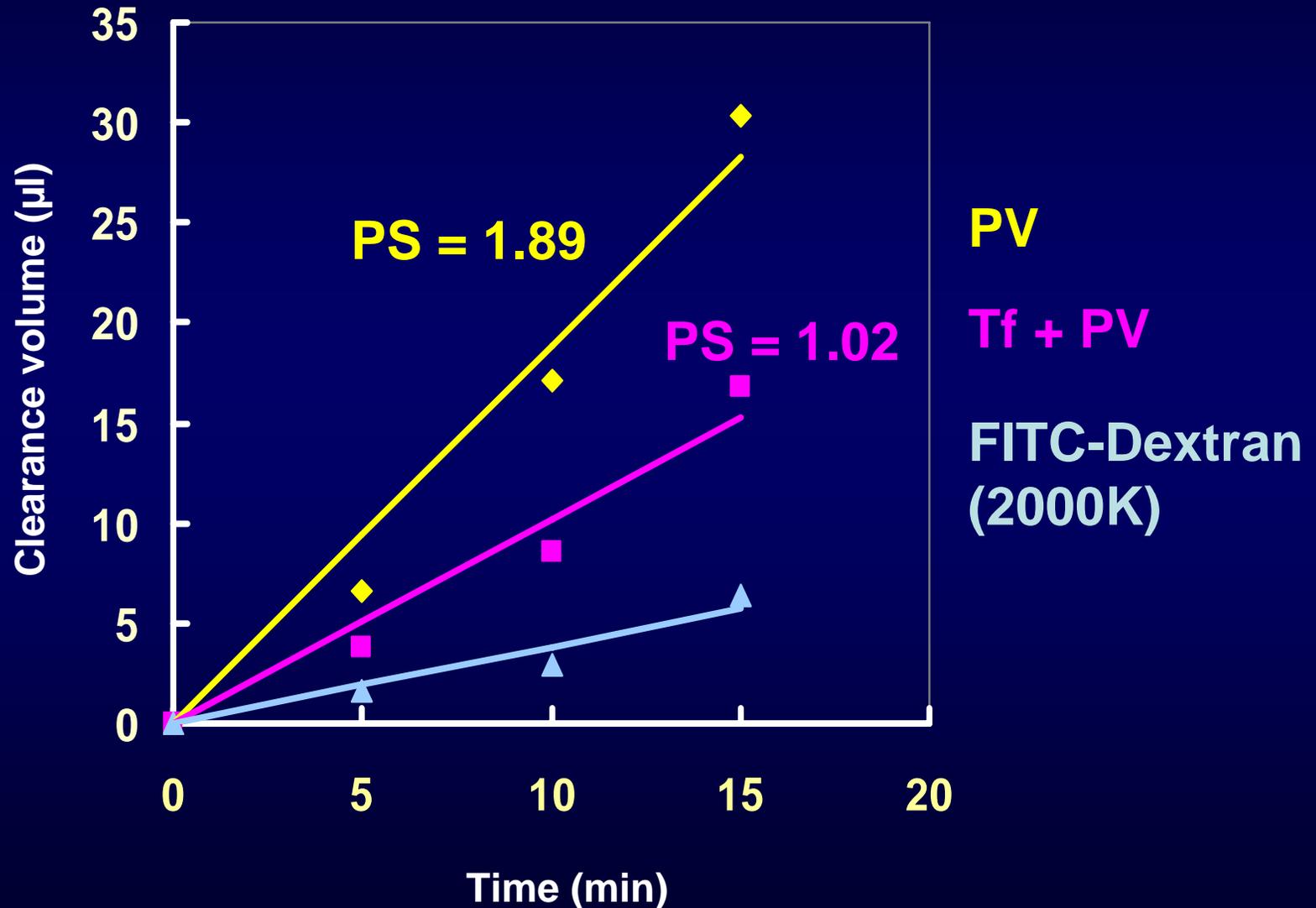
Dextran
(mw
15K - 20K)

—

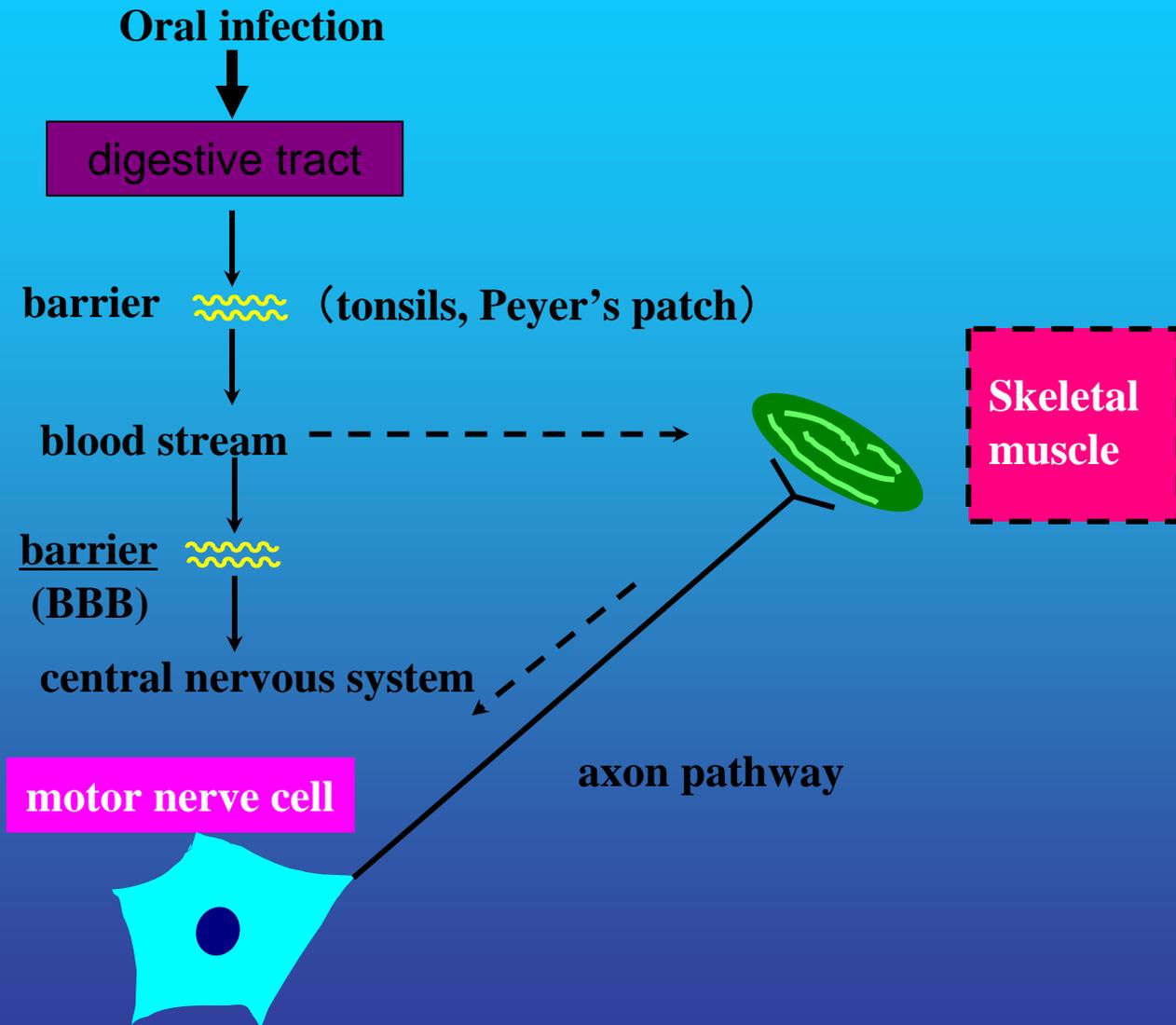
667 μ g / ml

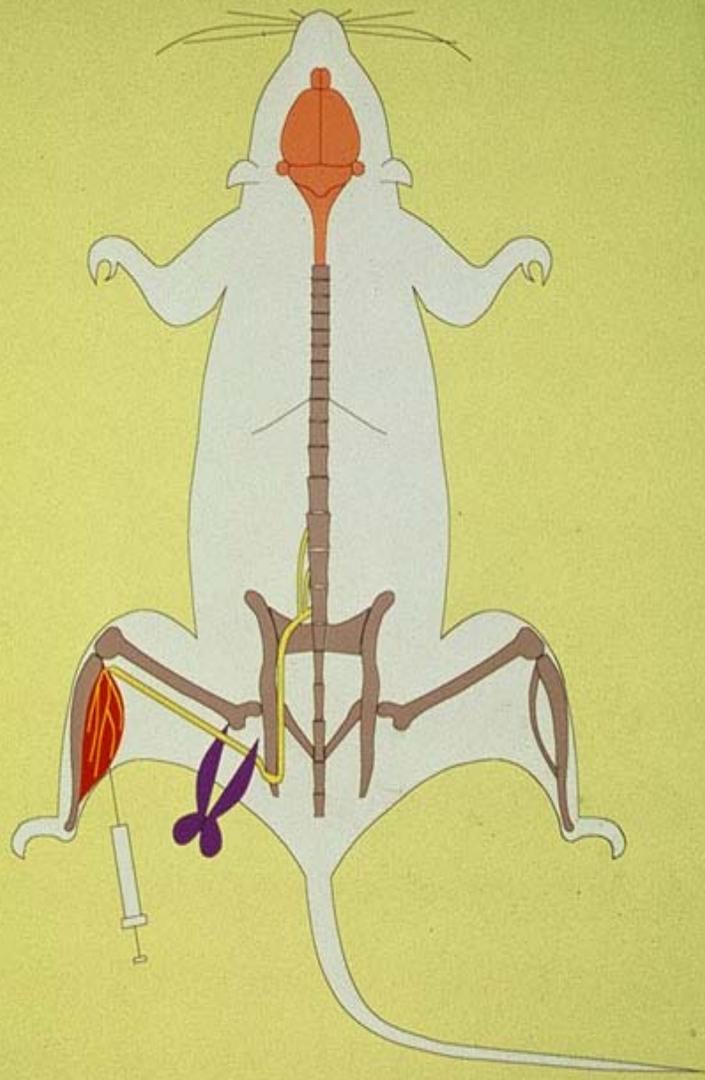
1mg / ml

PV percolation in BBB *in vitro* model is lowered by Tf



Replication of polio virus and transmission in the body





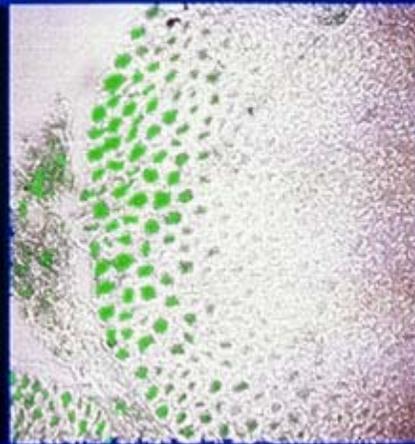
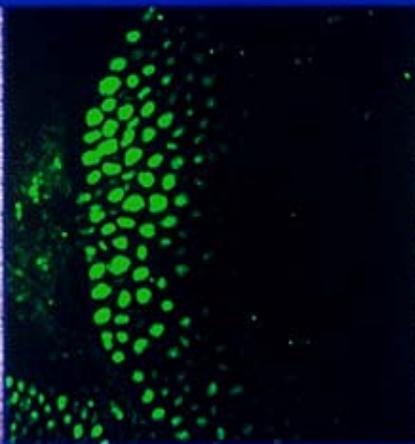
**Intramuscular Injection
and Transection**

PV i.m.

Transmission

Anti-PV

Transmission
+Anti-PV

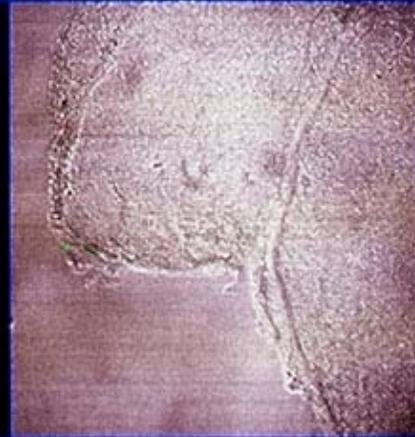
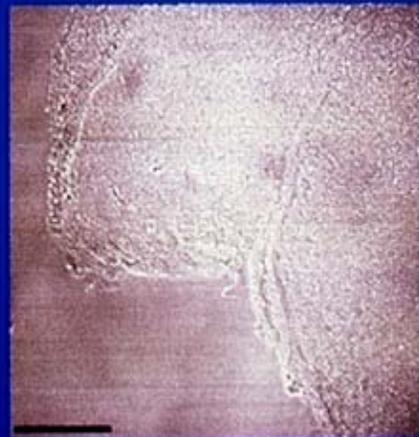


Mock i.m.

Transmission

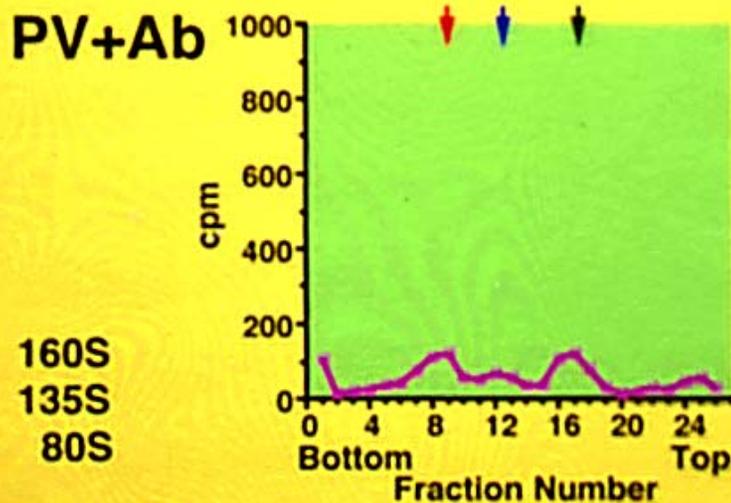
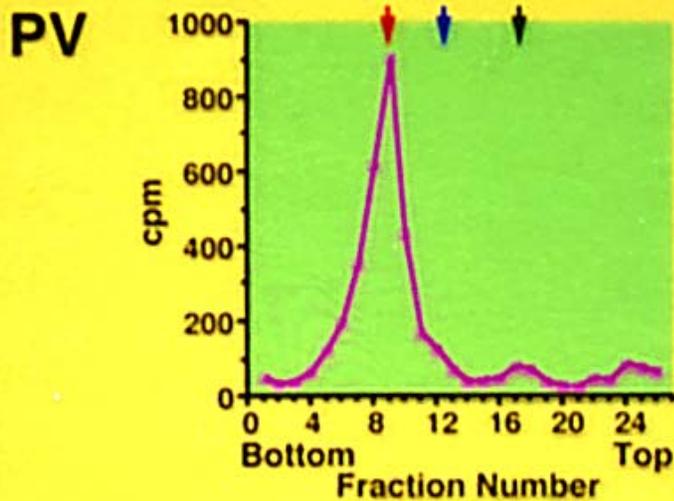
Anti-PV

Transmission
+Anti-PV



— 50 μ m

Sucrose Density Gradient Analysis of ^{35}S -labeled PV in Sciatic Nerve (1.5 h.a.i.)



160S
135S
80S

Mouse: Tg21

Virus: 5×10^7 PFU/20 μ l (6.9×10^5 cpm)

Antibody: Anti-PVR mAb (p286) 42 μ g/20 μ l

Polio virus antigen inside an ischiadic nerve axon 2cm away from administration

Sampling time	PV antigen
1.5h	— — +
3h	+ + +
6h	+ + +
12h	— ± ±

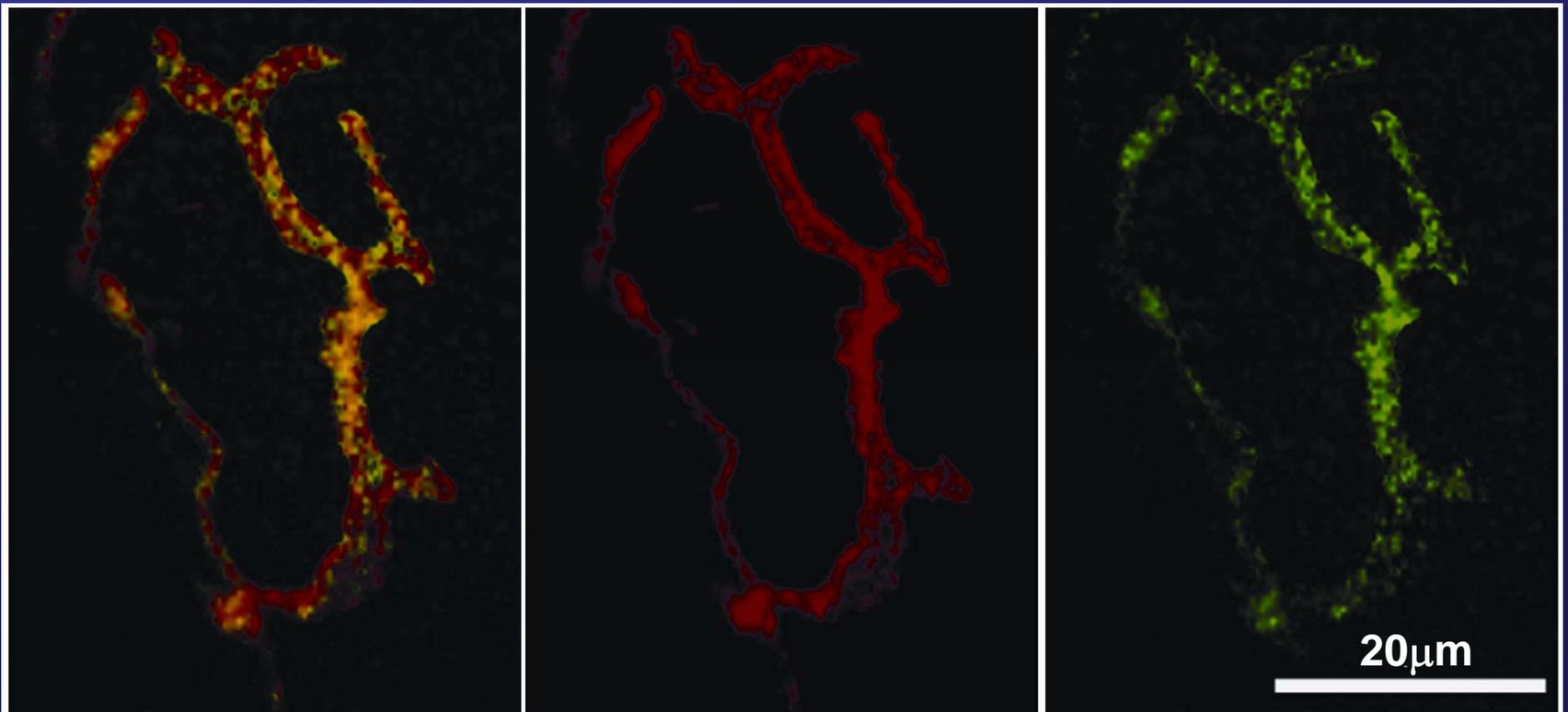
PV localized at neuromuscular junctions in Tg mice

Tg +PV

Merge

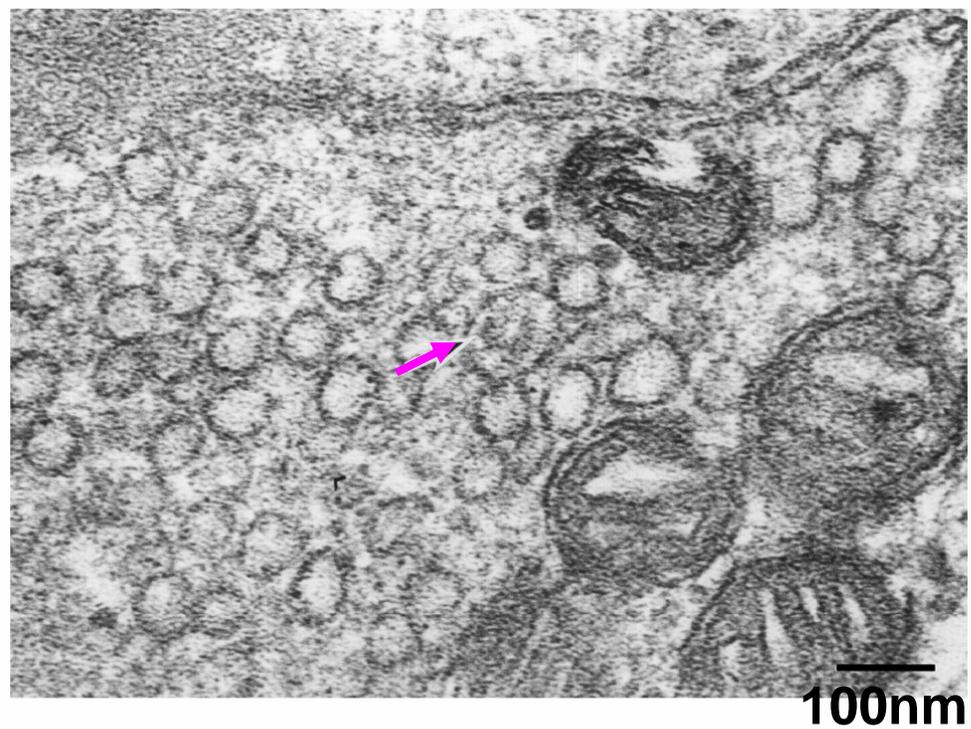
α -bungarotoxin

PV

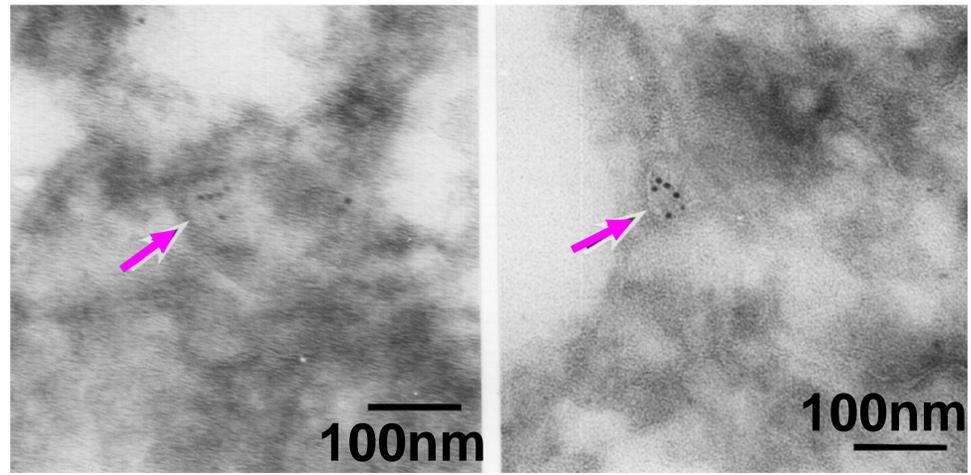


Neuromuscular junction of a Tg mouse 1.5 hrs after PV injection

Transmission
electron
microscope



Immunity
electron
microscope
(detects PV)



Dynein Motor Protein Associates with PVR Cytoplasmic Domain

