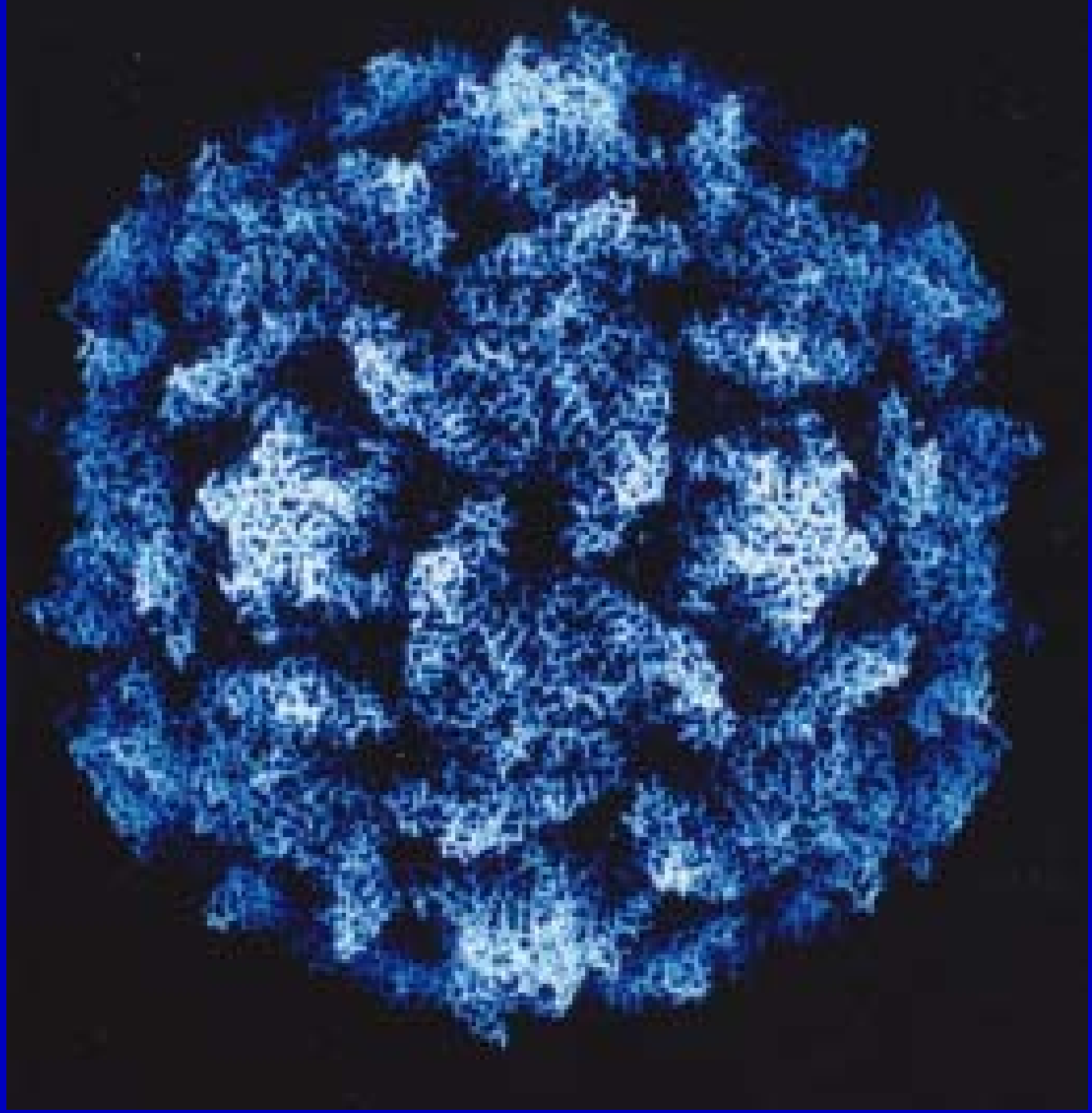
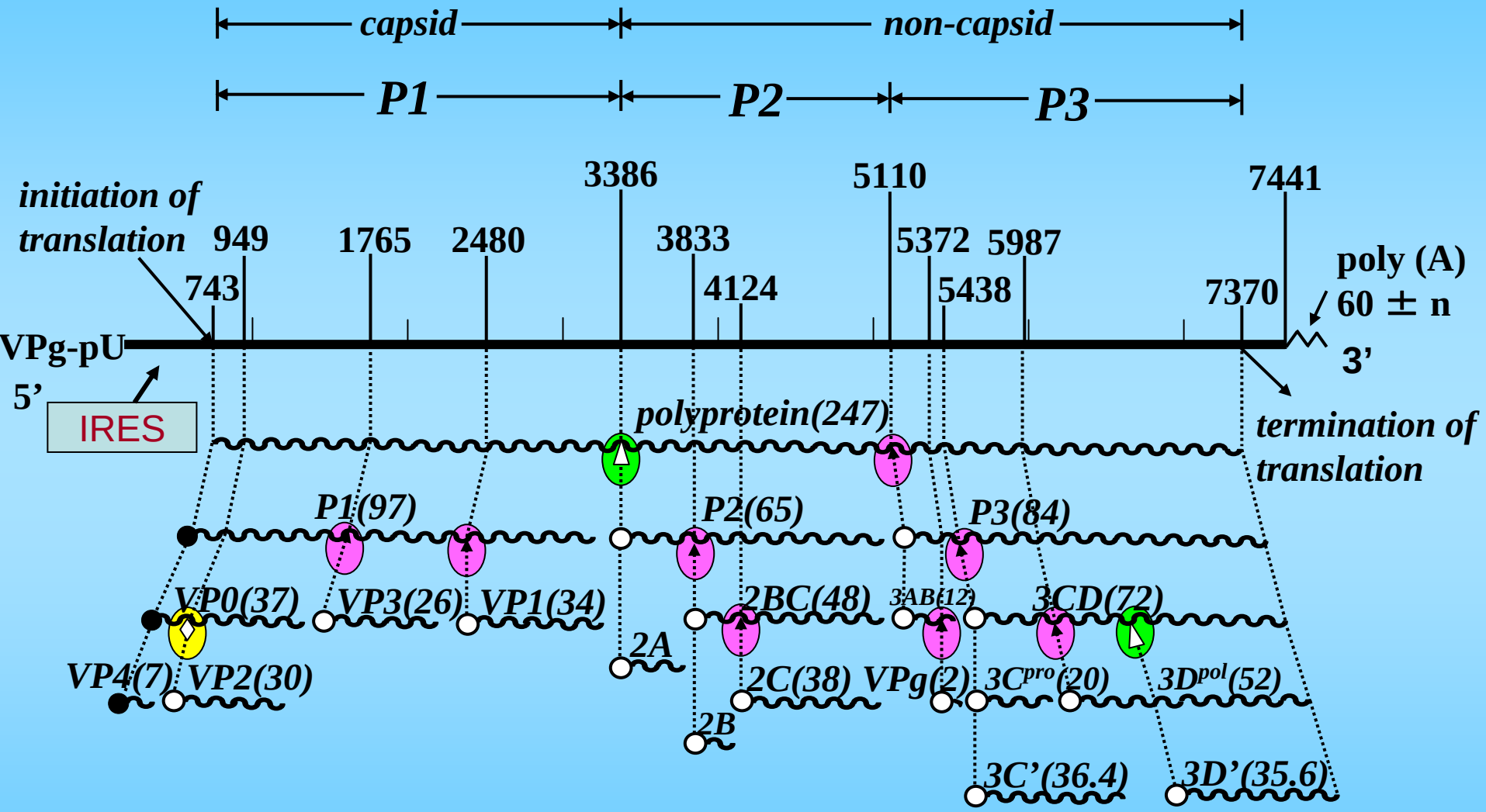
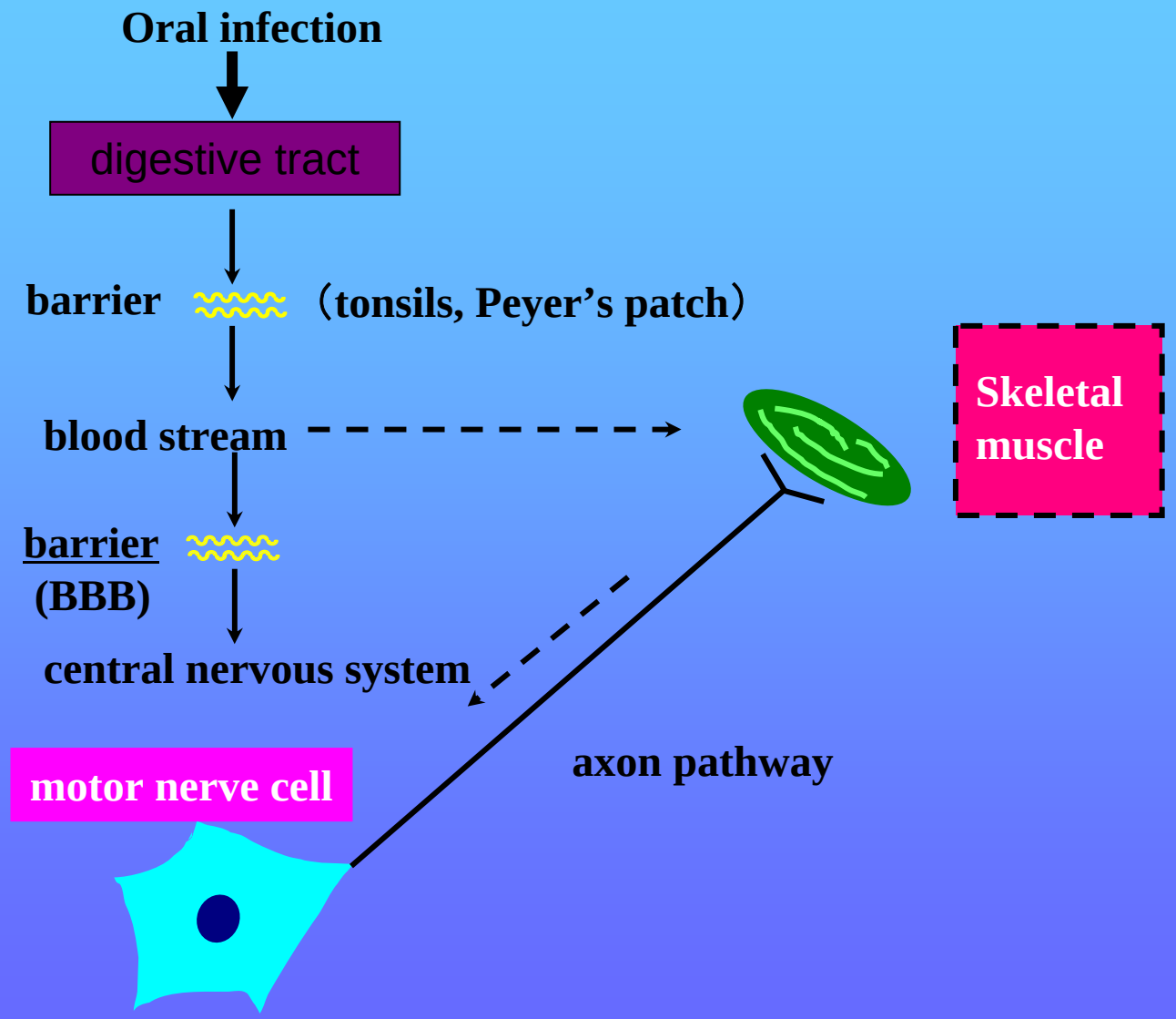



capsid
non-capsid
P1
P2
P3
initiation of translation
3386
5110
7441
949
1765
2480
3833
5372
5987
743
4124
5438
7370
poly (A)
60 ± n
3'
VPg-pU
5'
IRES
polyprotein(247)
termination of translation
P1(97)
P2(65)
P3(84)
VP0(37)
VP3(26)
VP1(34)
2BC(48)
3AB(12)
3CD(72)
2A
VP4(7)
VP2(30)
2C(38)
VPg(2)
3Cpro(20)
3Dpol(52)
2B
3C'(36.4)
3D'(35.6)

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

Research on pathogenicity

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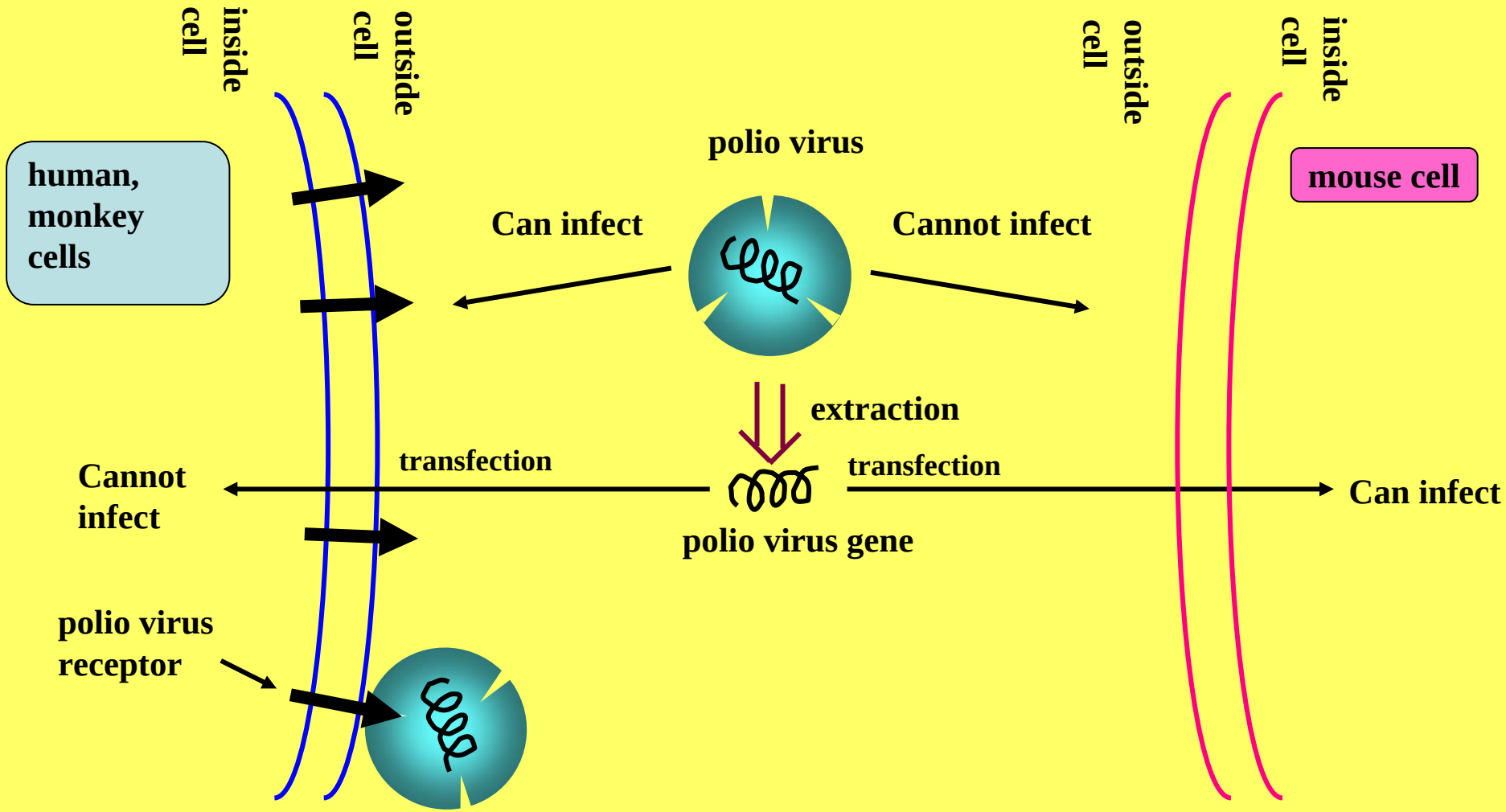
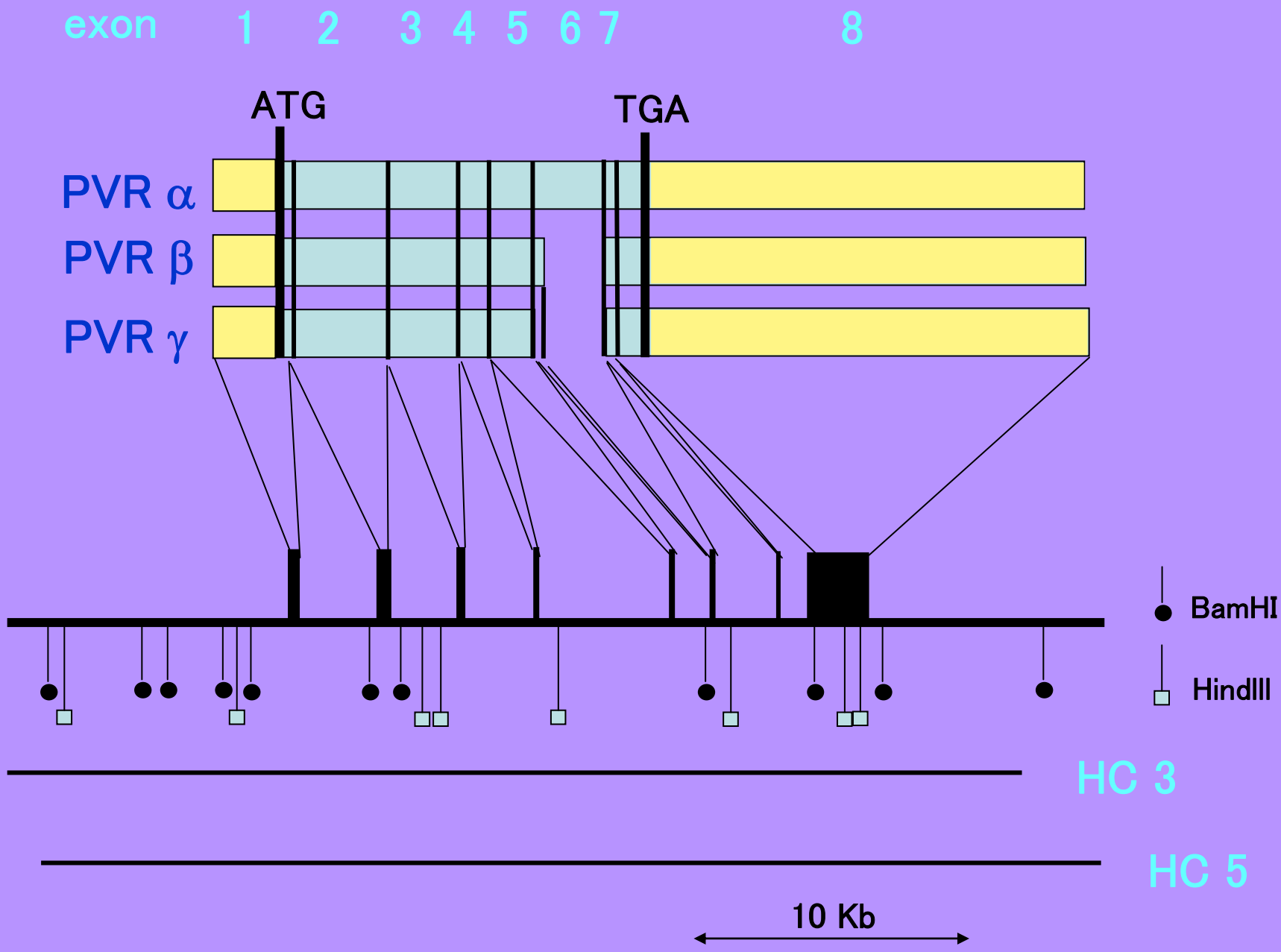
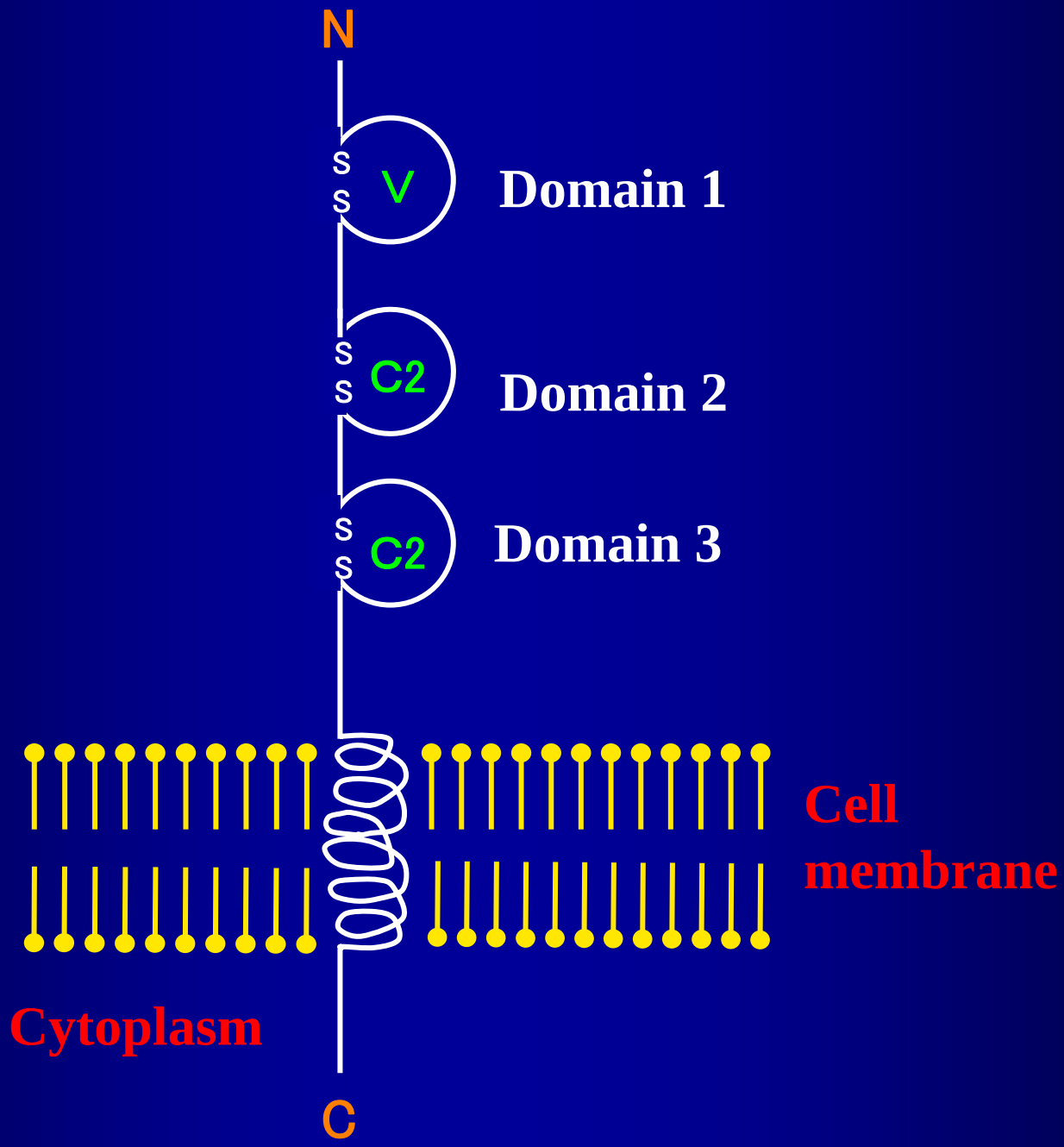
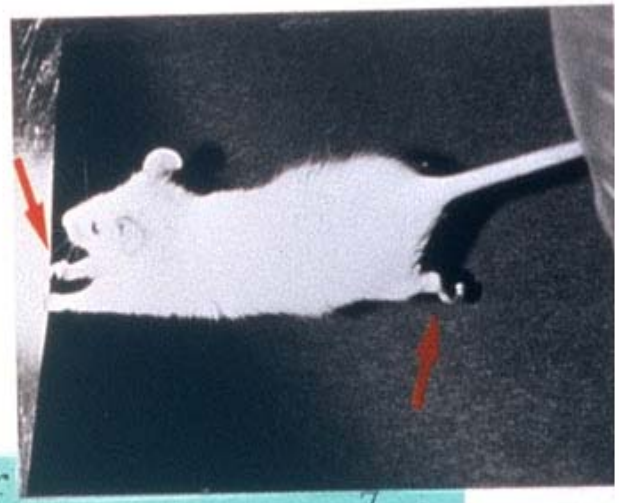
Role of poliovirus receptor during polio virus infection




exon 1 2 3 4 5 6 7 8
ATG
TGA
PVR α
PVR β
PVR γ
BamHI
HindIII
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

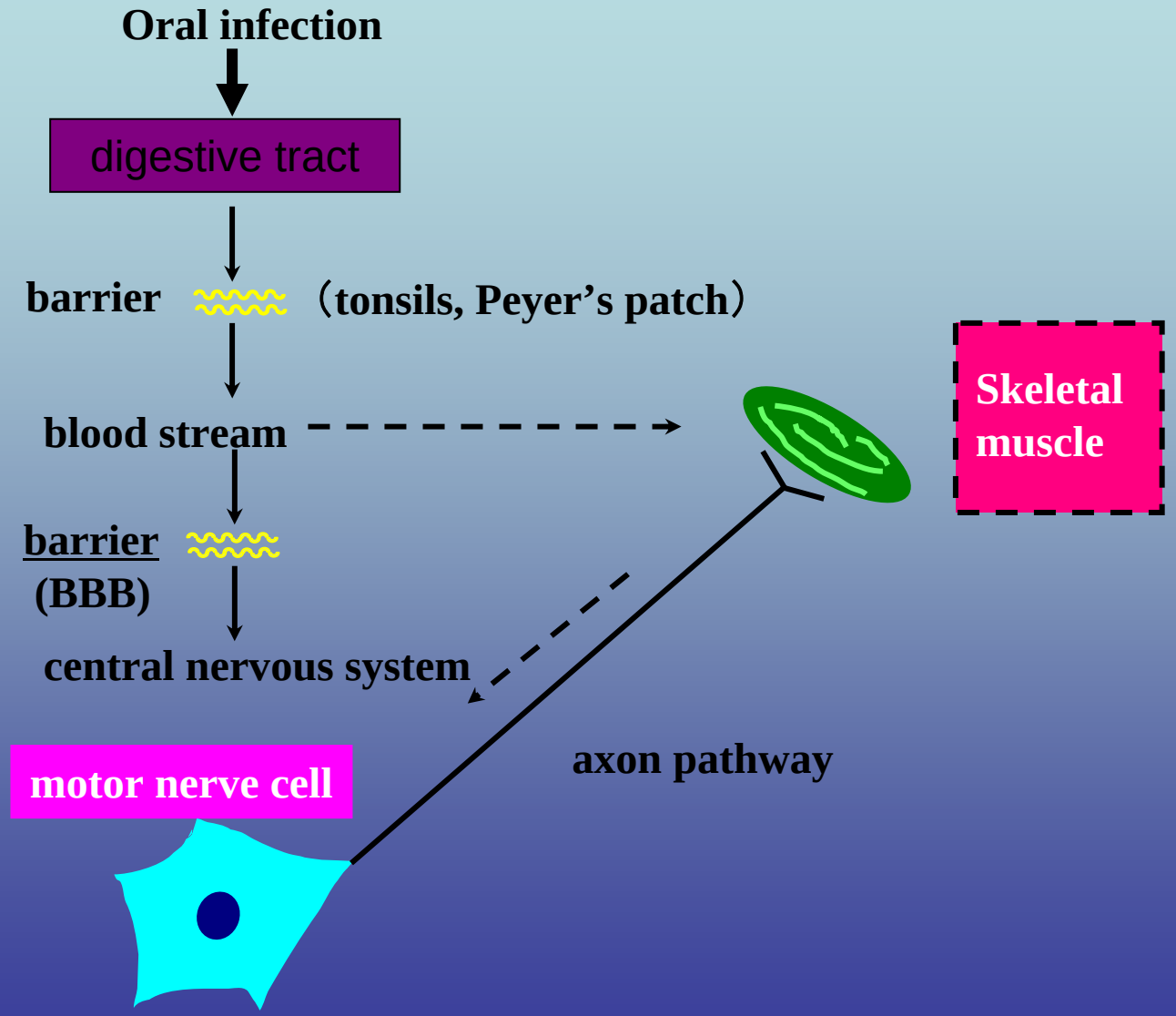
Principles of viral tropism

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

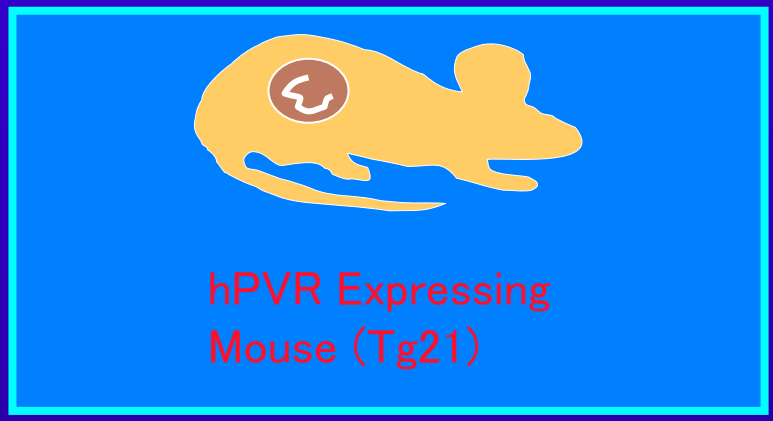
Research on pathogenicity

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



hPVR Expressing
Mouse (Tg21)

	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 (μl / min / 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

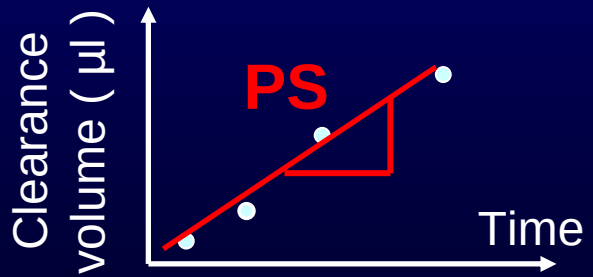
purified PV

fluorescent dye (Alexa Fluor)

fluorescent dyed PV (126.55 μg / ml)

mouse cerebrovascular endothelial cell

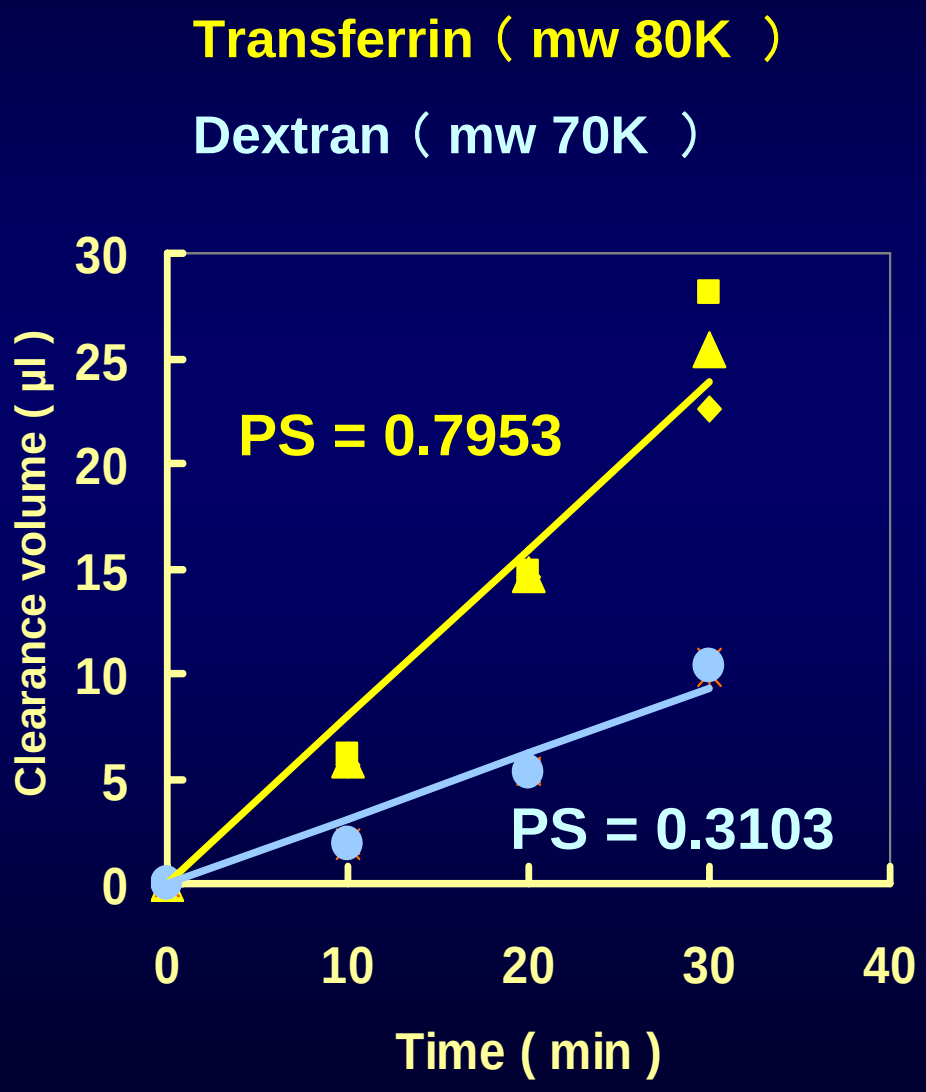
Periodic measurement of fluorescence after PV addition

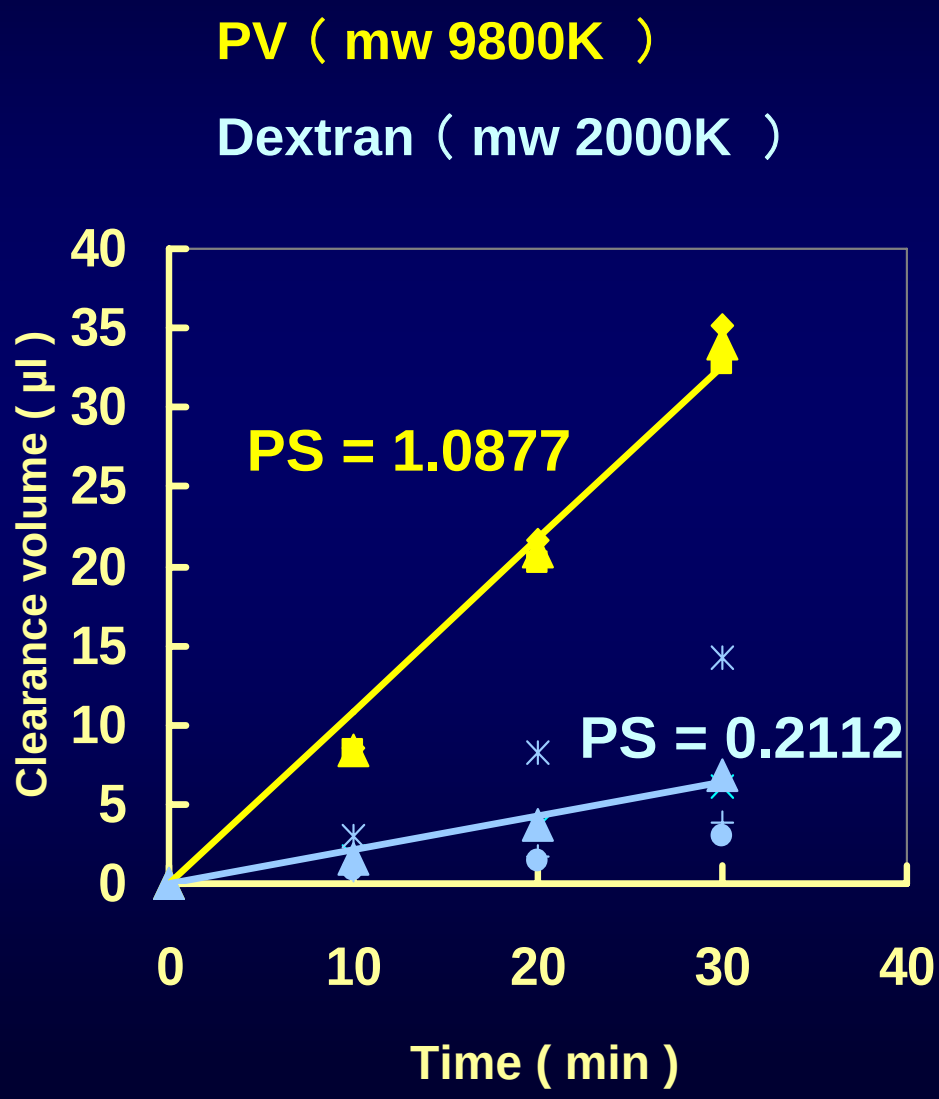


$$\text{Clearance volume (μl)} = \frac{\text{amount of PV moved to basolateral surface (μg)}}{\text{Primary concentration of PV at the luminal surface (μg / μl)}}$$

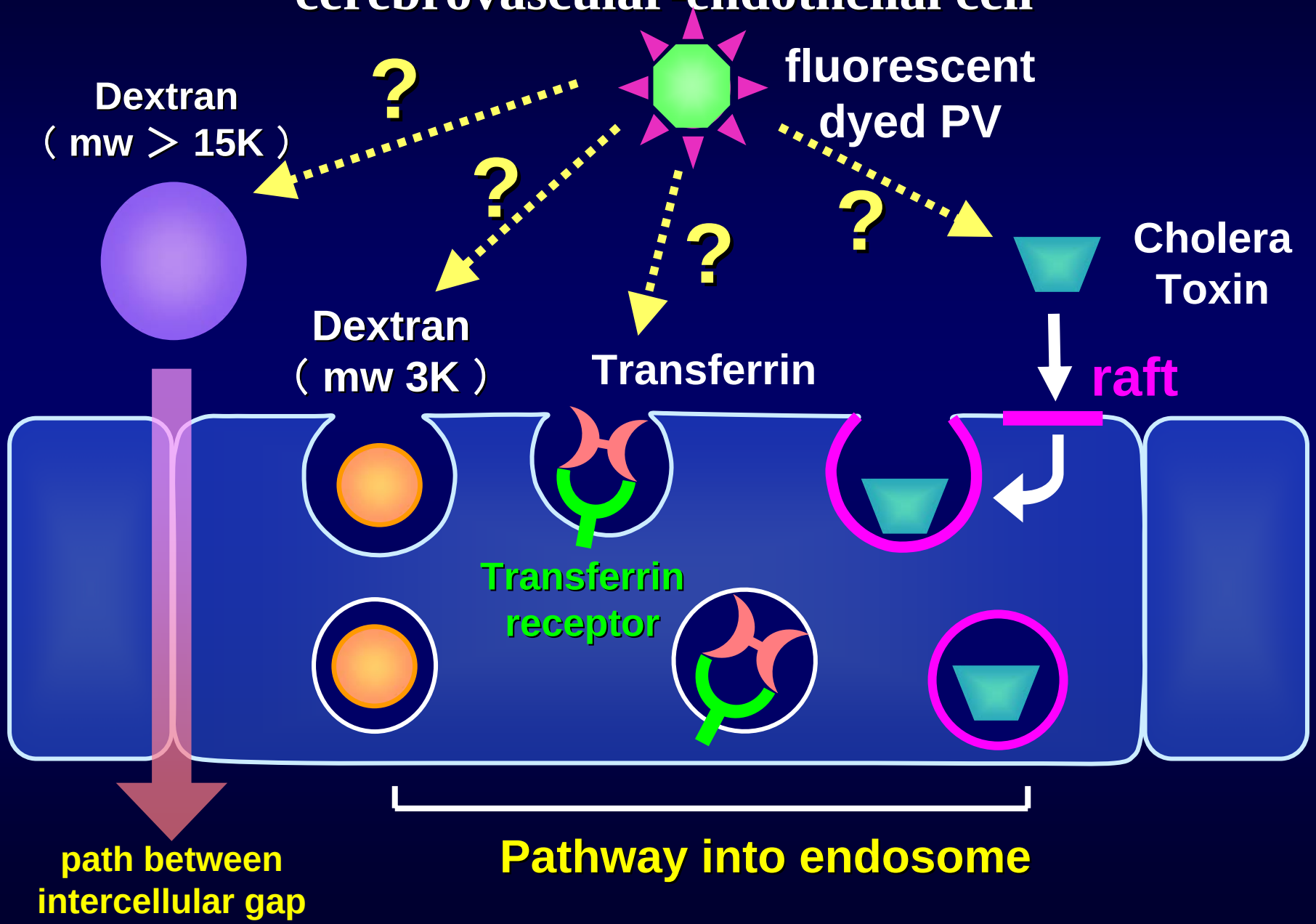
(PS : Permeability-surface area product)

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

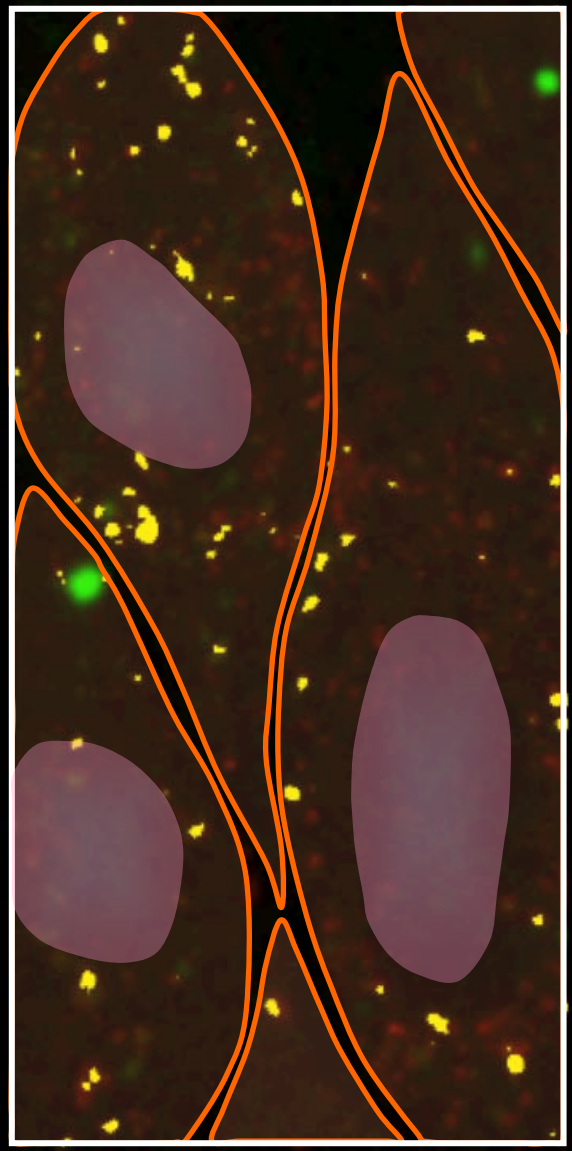




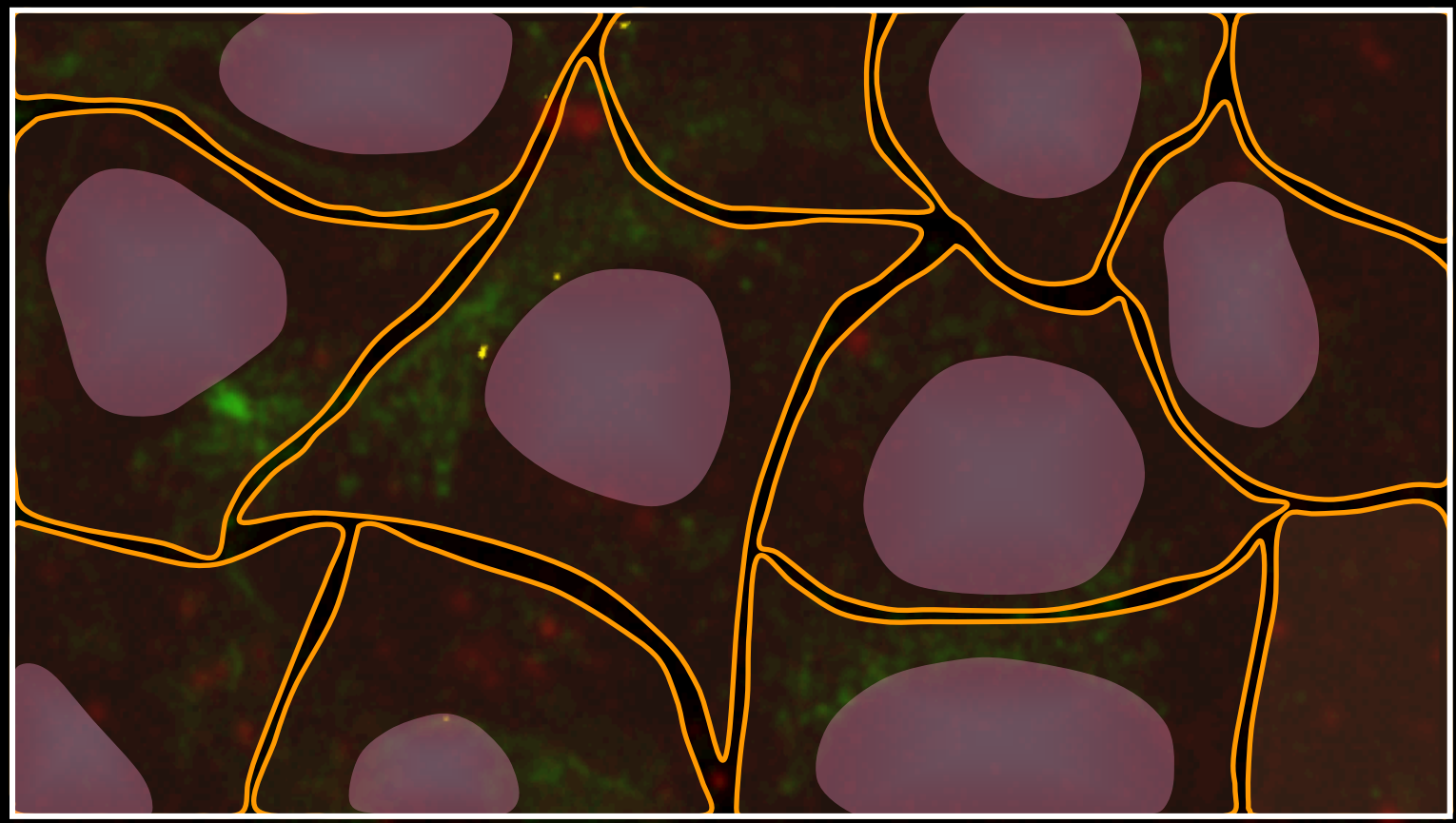
Examination of PV intake into a mouse cerebrovascular-endothelial cell



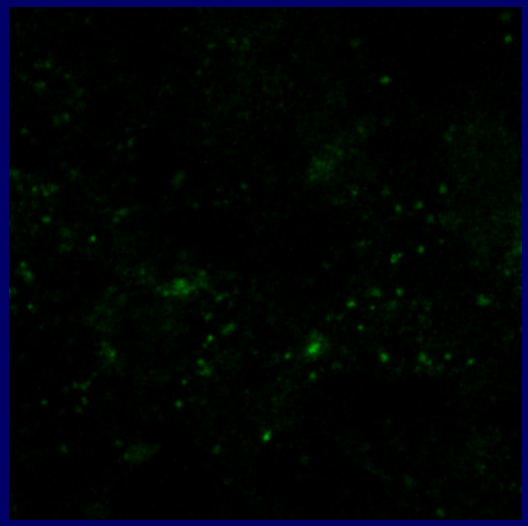
PV + Dextran（mw. 3K ）

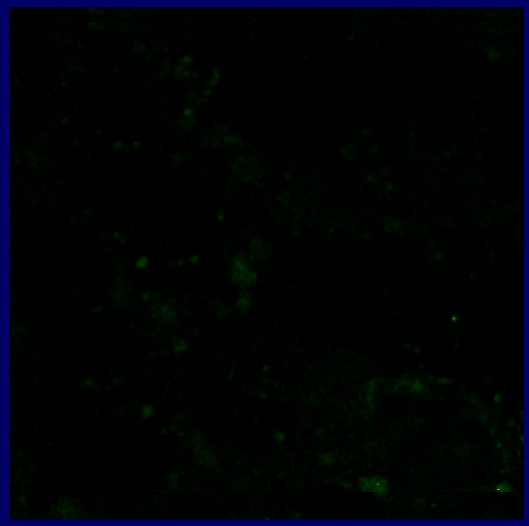


PV + Cholera Toxin



Endocytosis of transferrin (Tf) is inhibited by PV





Alexa 488 - Tf
10μg / ml
(MBEC4 cell)

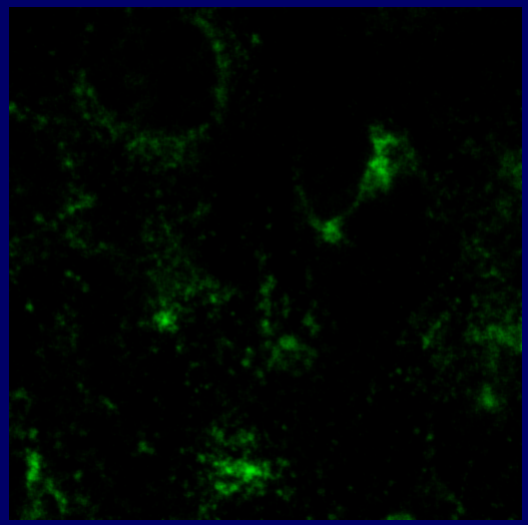
20 μm

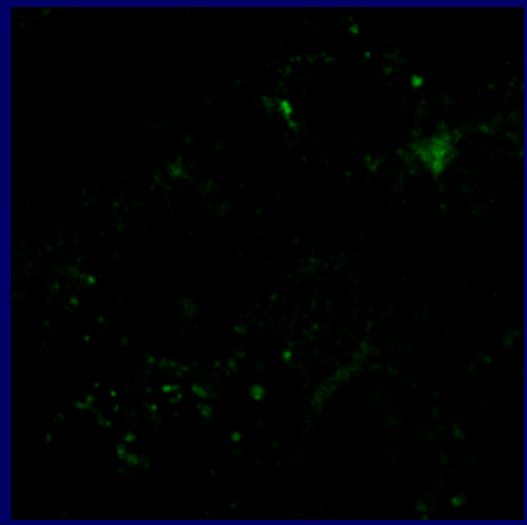
Purified PV

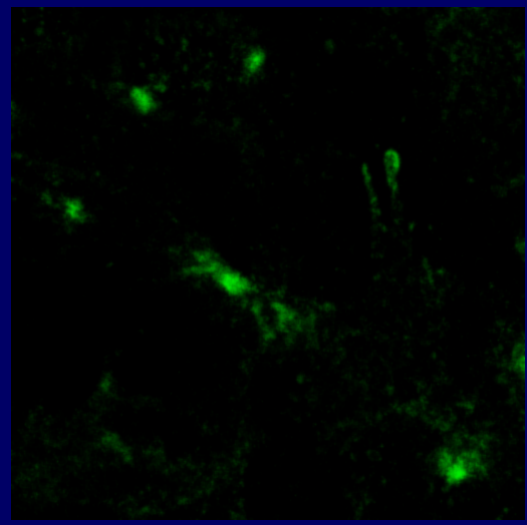
–

m.o.i. 5000

Dextran
(mw
15K - 20K)





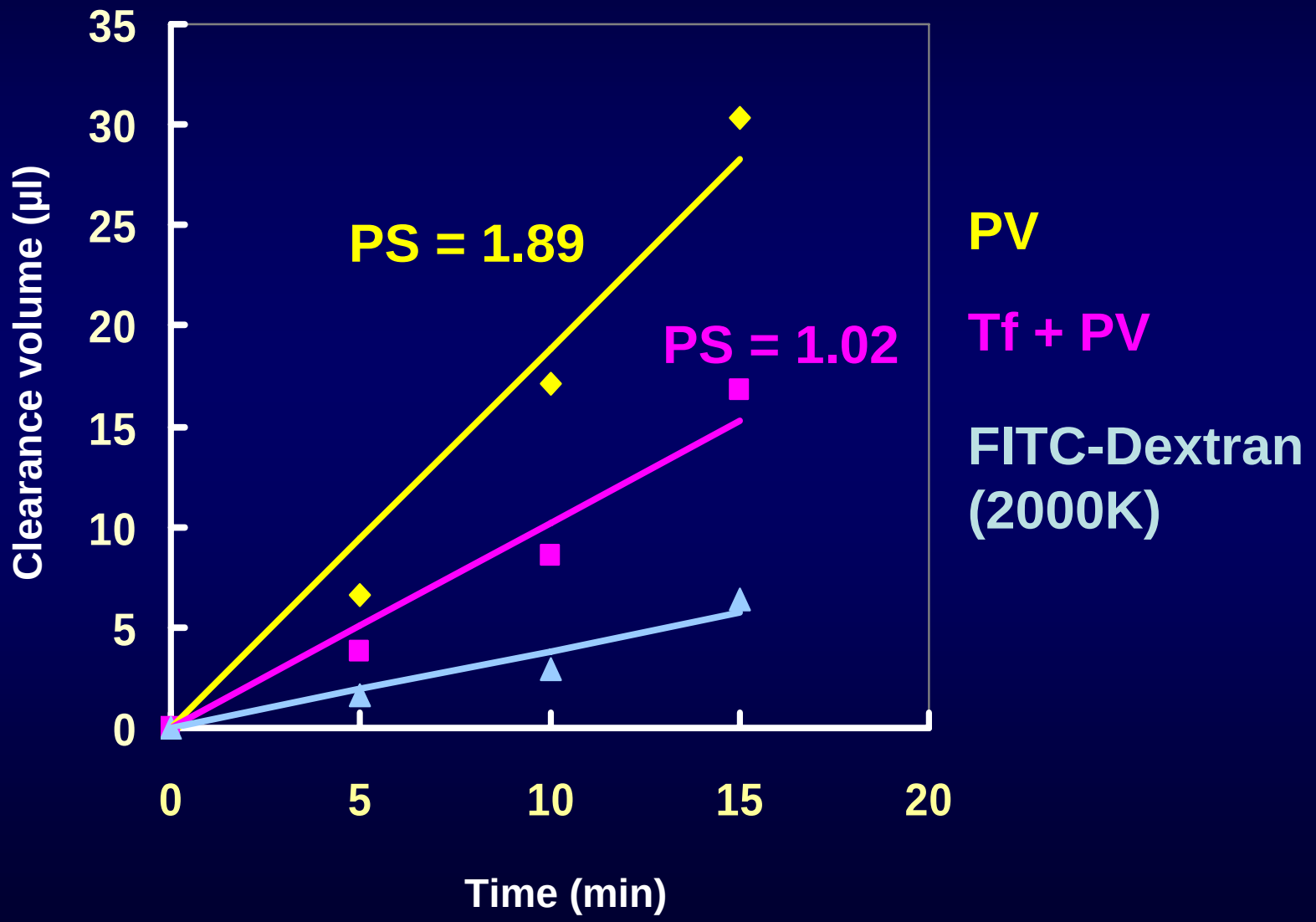


–

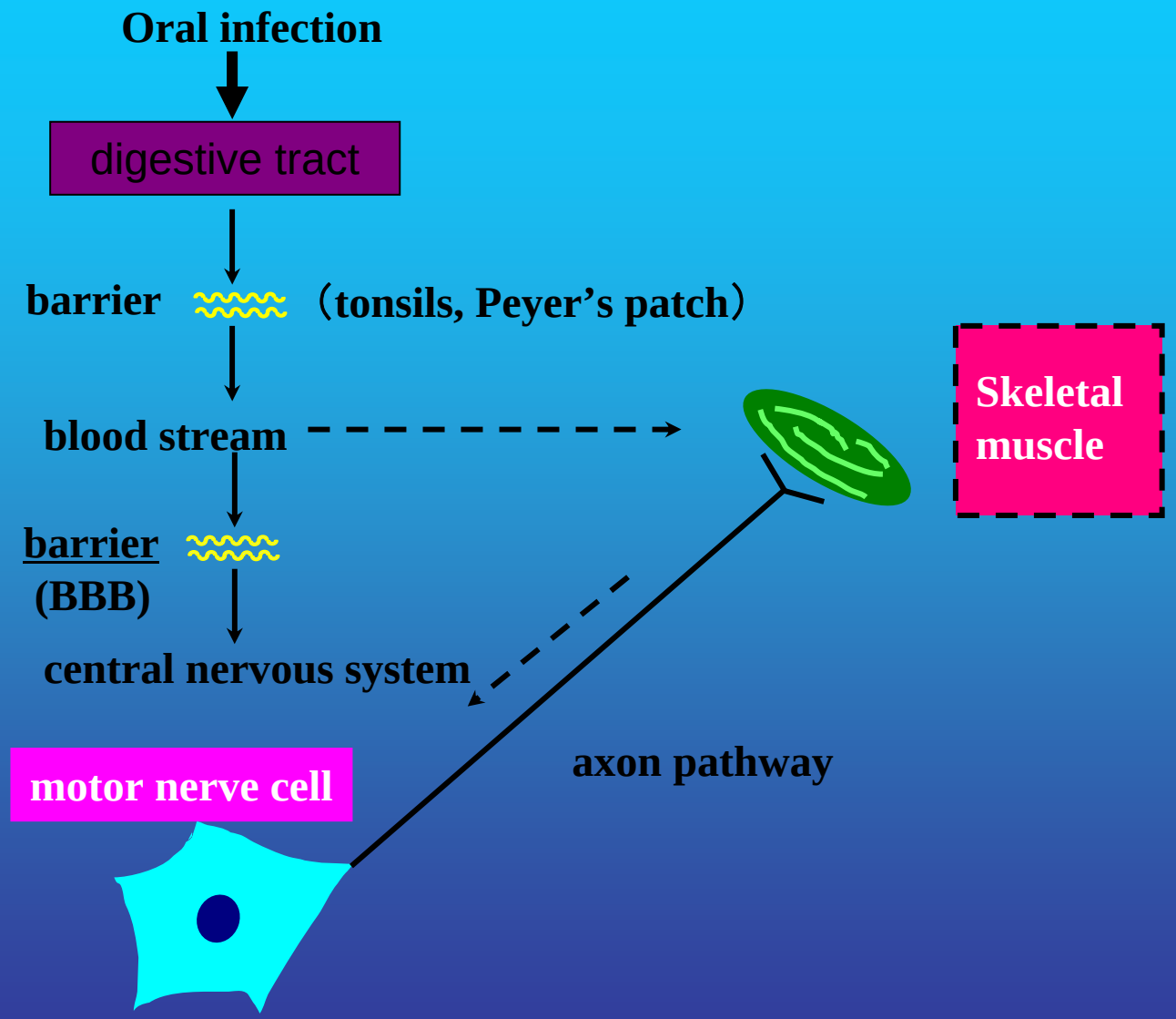
667μg / ml

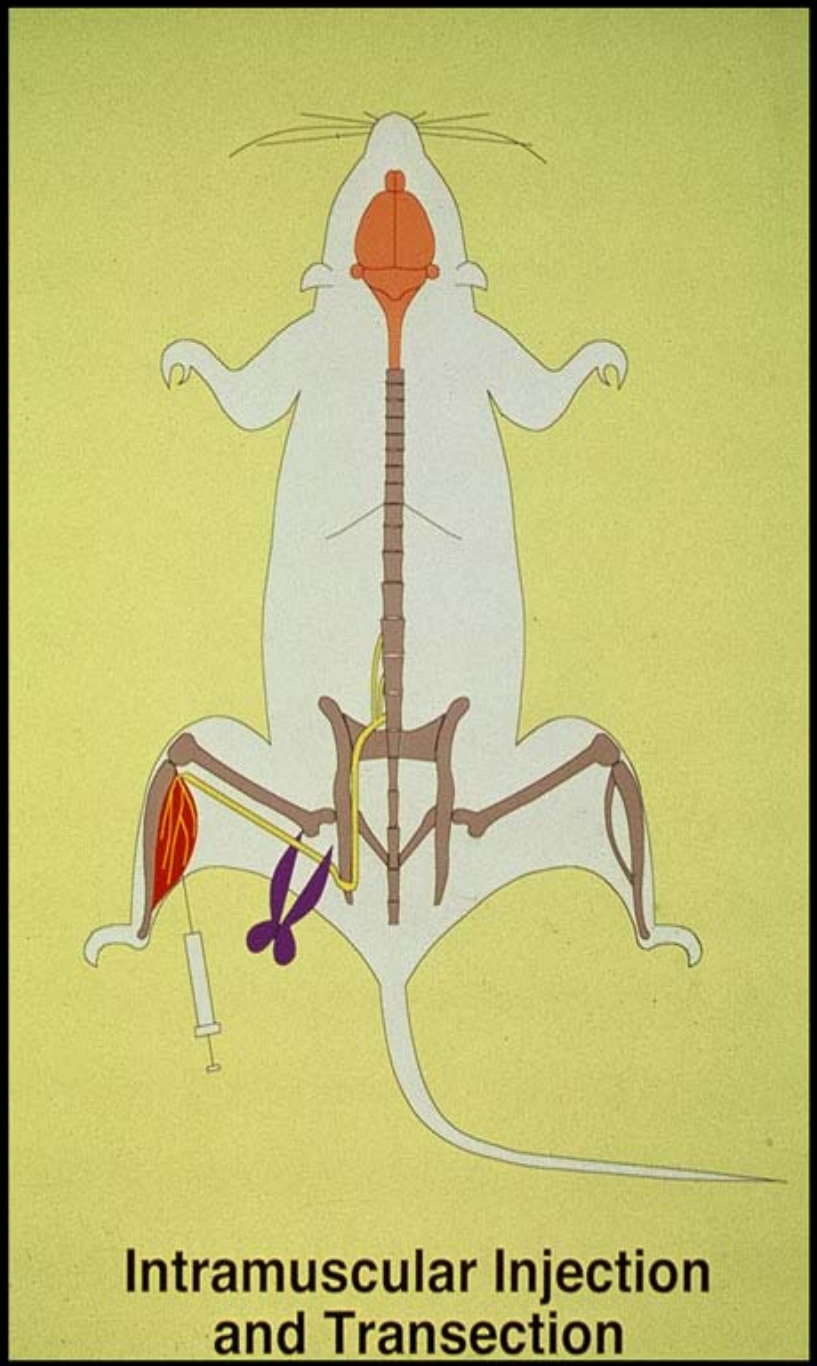
1mg / ml

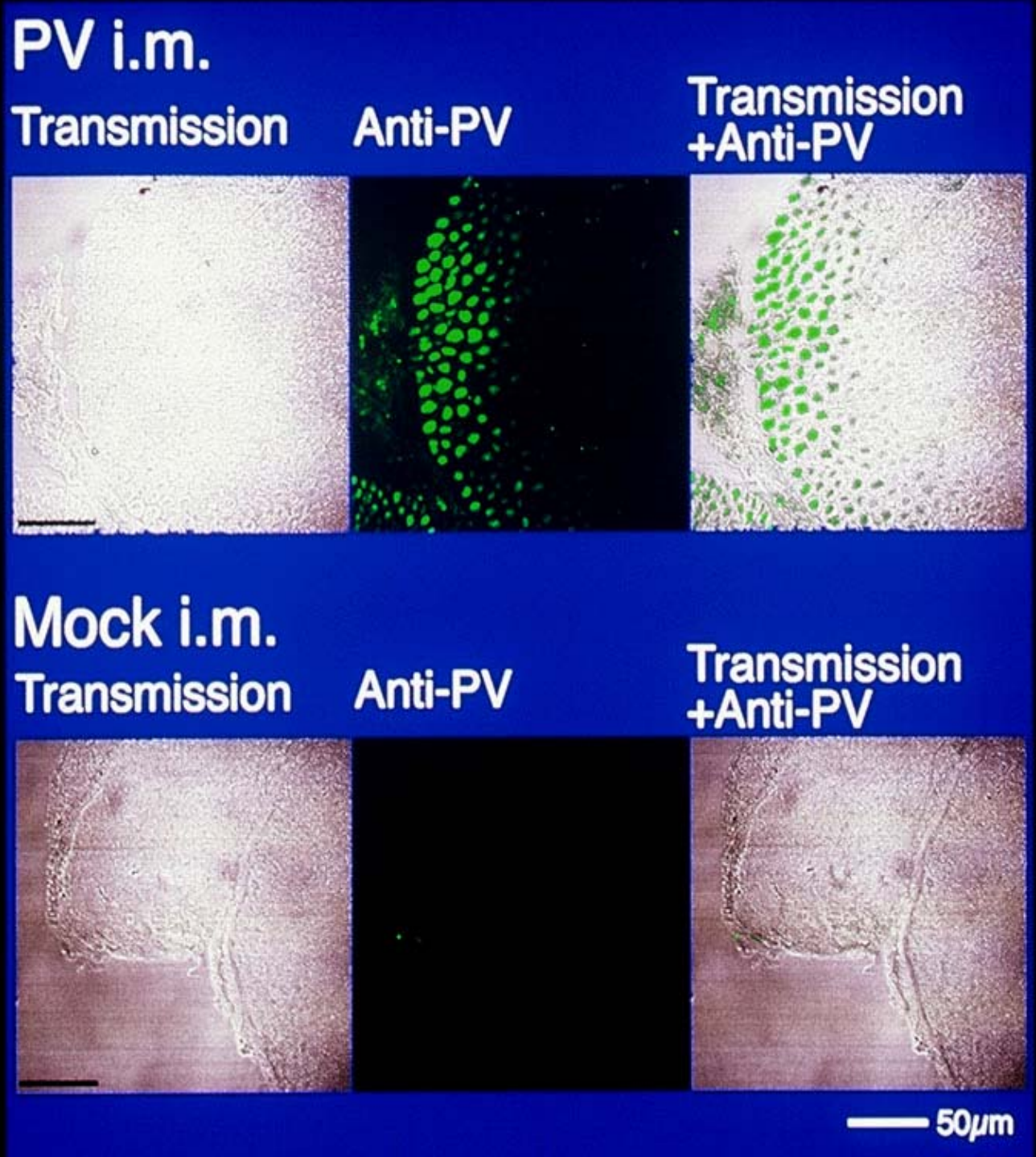
PV percolation in BBB *in vitro* model is lowered by Tf



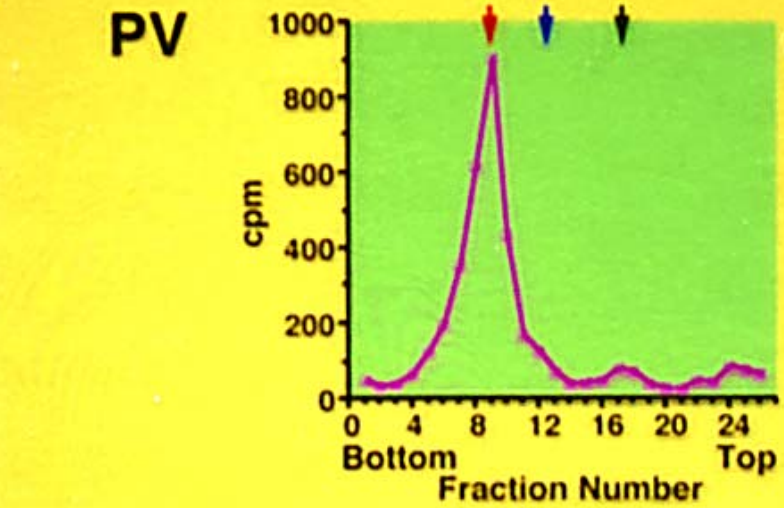
Replication of polio virus and transmission in the body

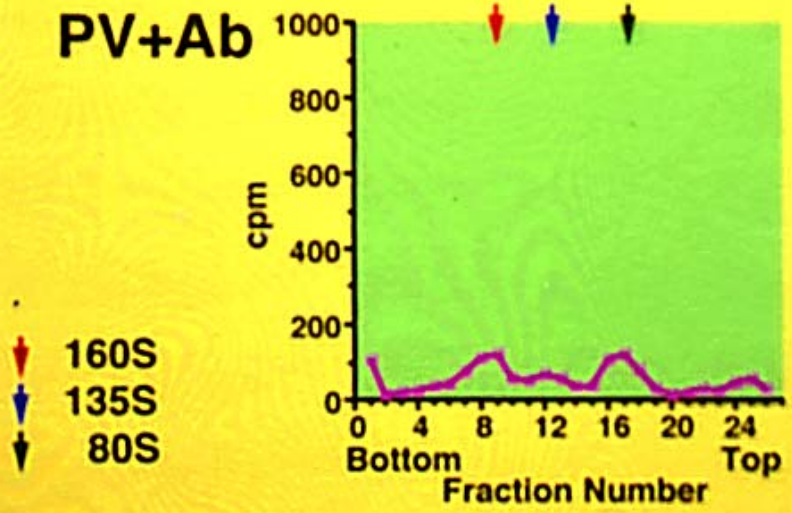



Intramuscular Injection
and Transection


PV i.m.
Transmission
Anti-PV
Transmission
+Anti-PV
Mock i.m.
Transmission
Anti-PV
Transmission
+Anti-PV
50μm

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





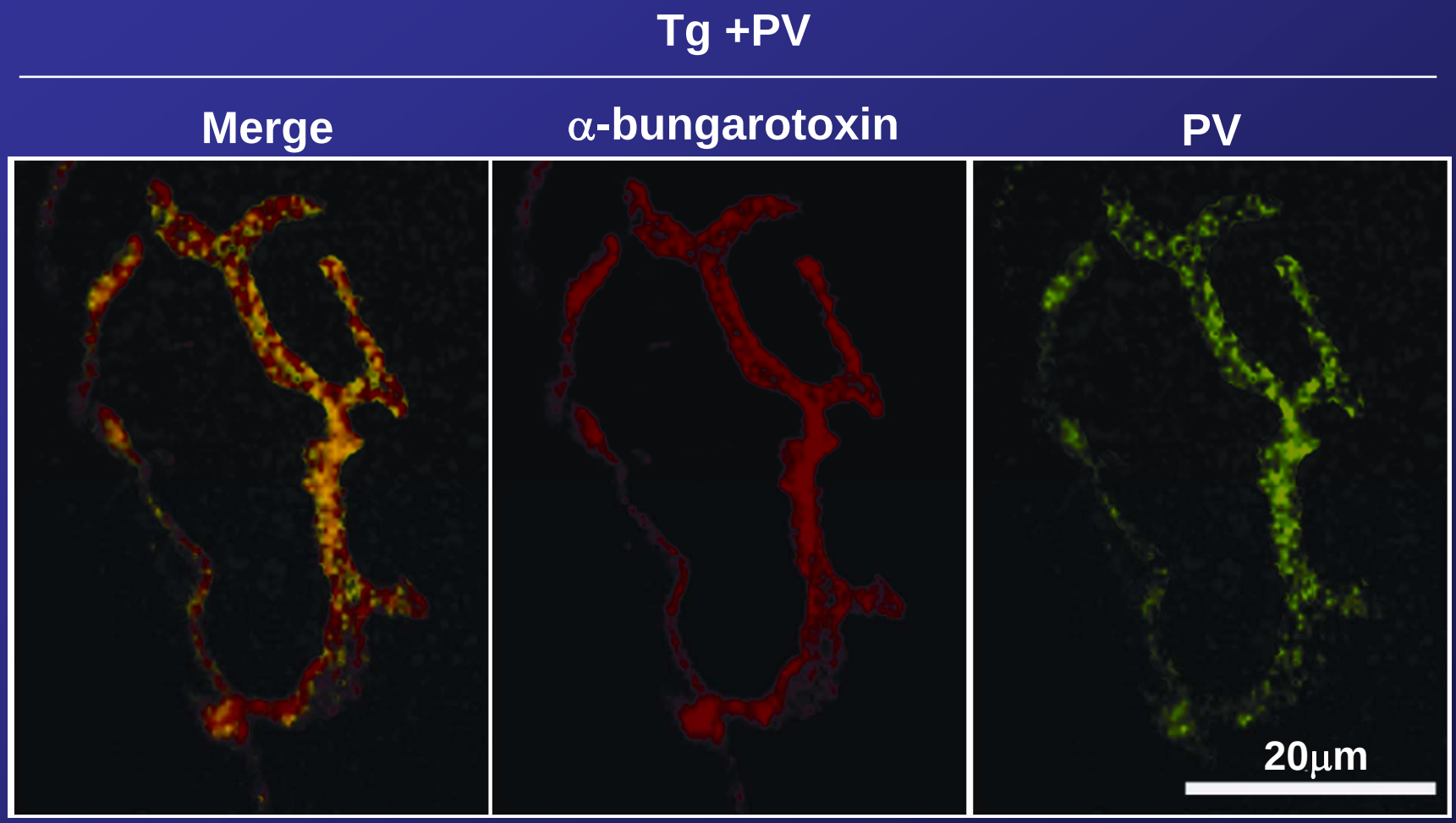
160S
135S
80S

Mouse: Tg21
Virus: 5 x 10^7PFU/20μl (6.9 x 10^5 cpm)
Antibody: Anti-PVR mAb (p286) 42μg/20μl

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

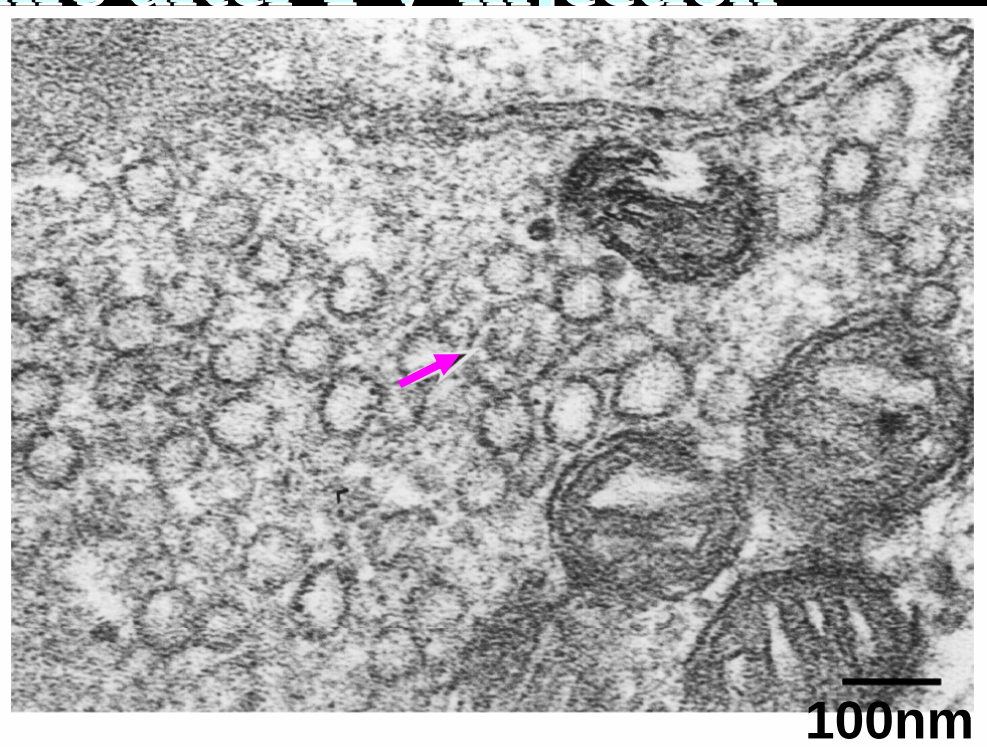
Sampling time	PV antigen
1.5h	− − +
3h	+ + +
6h	+ + +
12h	− ± ±

PV localized at neuromuscular junctions in Tg mice

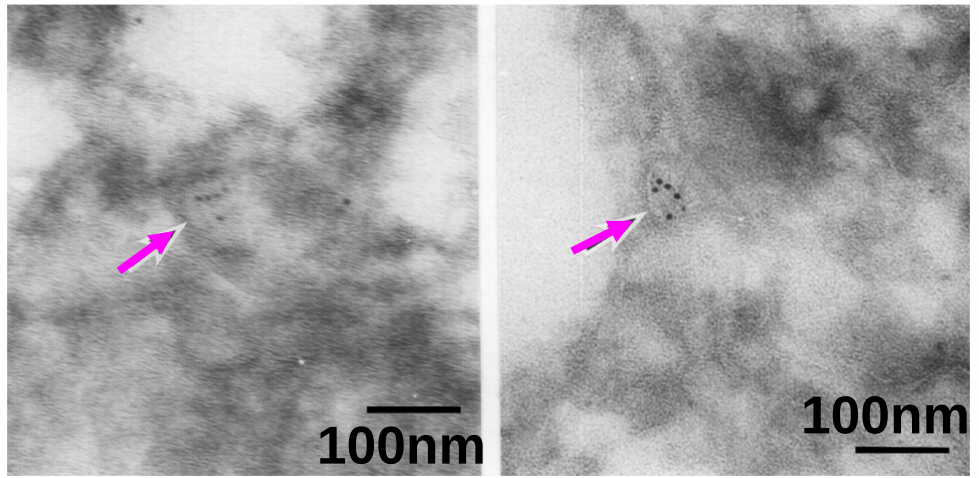


Neuromuscular junction of a Tg mouse 1.5 hrs after PV injection

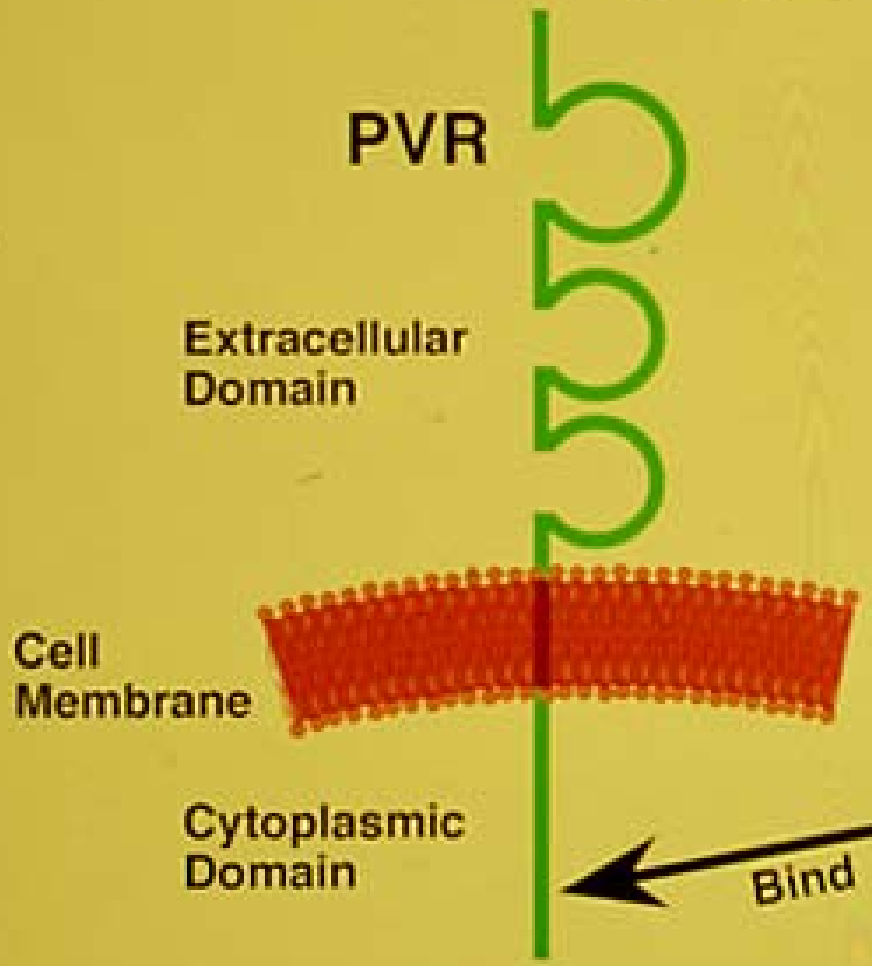
Transmission electron microscope



Immunity electron microscope (detects PV)



Dynein Motor Protein Associates with PVR Cytoplasmic Domain



Tctex-1 (Mouse Dynein Subunit)

TCTEL1 (human homolog)

1 MEDYQAAEETAFVVDEVSNIVKEAIESAIGGNAYQHSKVNQ
41 WTTNVVEQTLSQLTKLGAPFKYIVTCVIMQKNGAGLHTASS
81 CFWDSSTDGSCTVRWENKTMYCIVSAFGLSI