

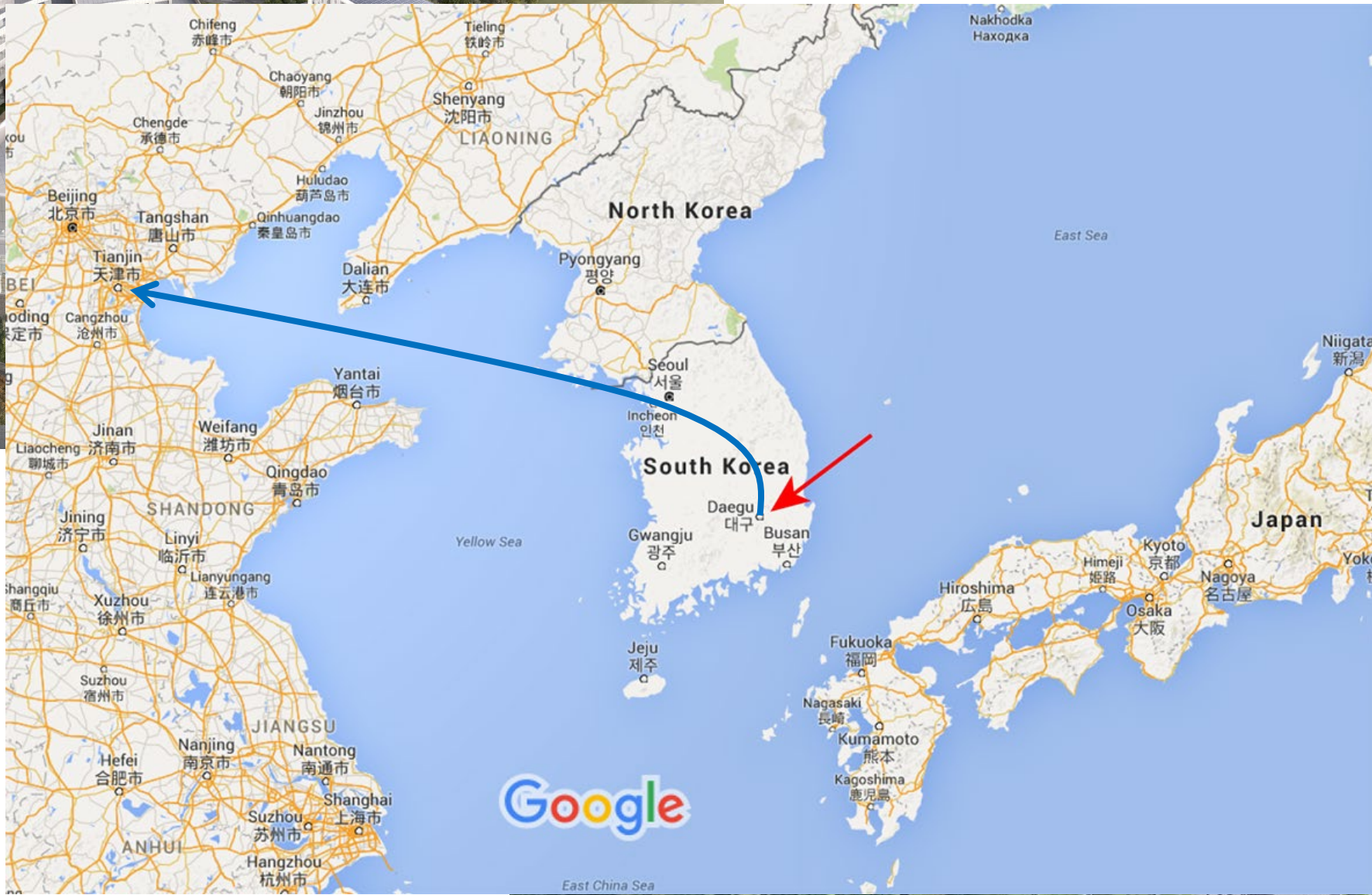
# Parkinson's disease progression from a neurovascular perspective

Tianjin, China  
2025. 11. 22.

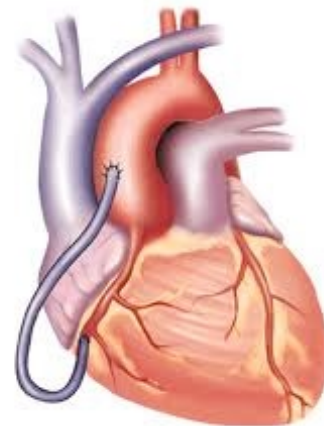
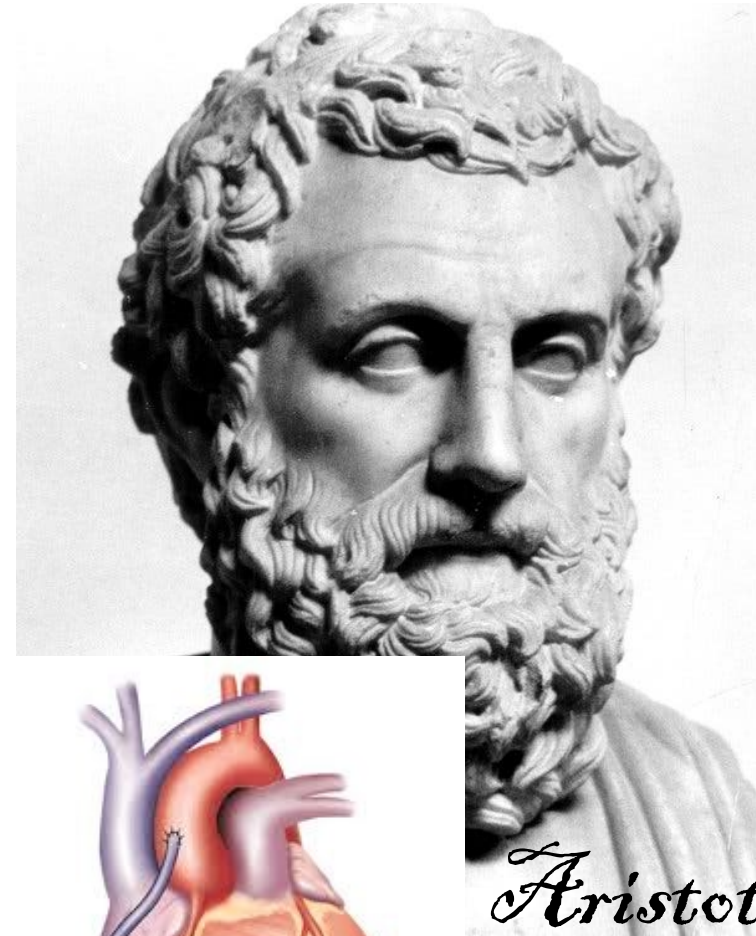
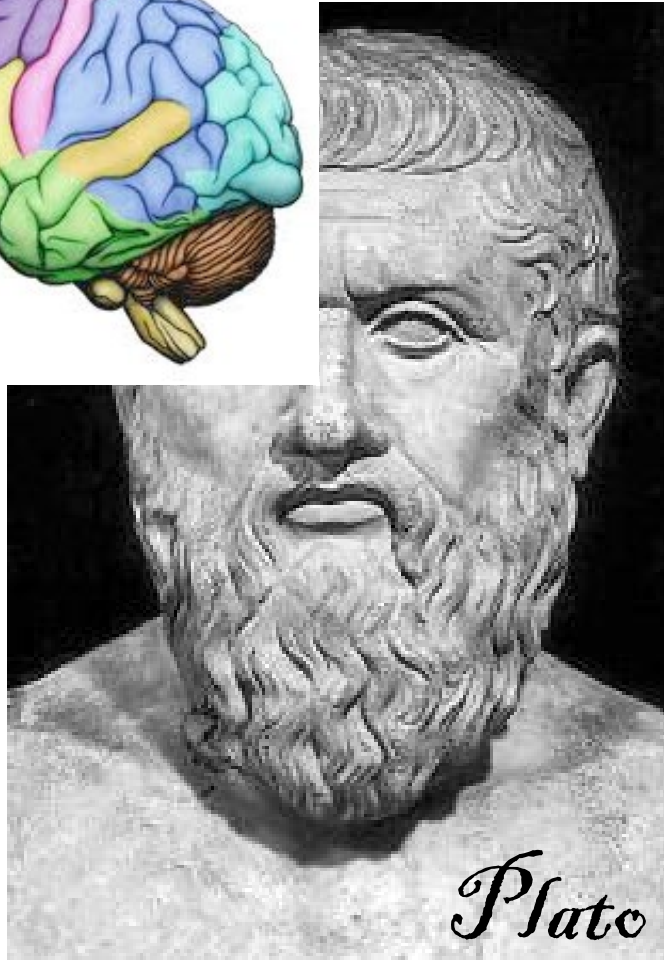
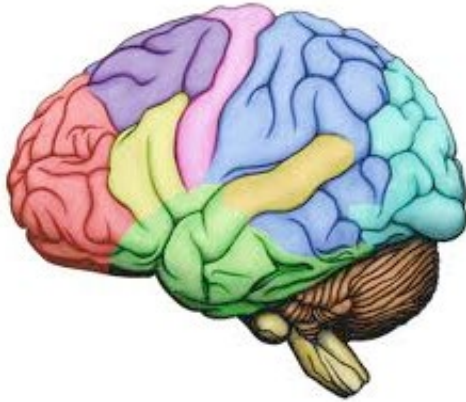
OH, WON-JONG  
오 원 종 (吳源鐘)

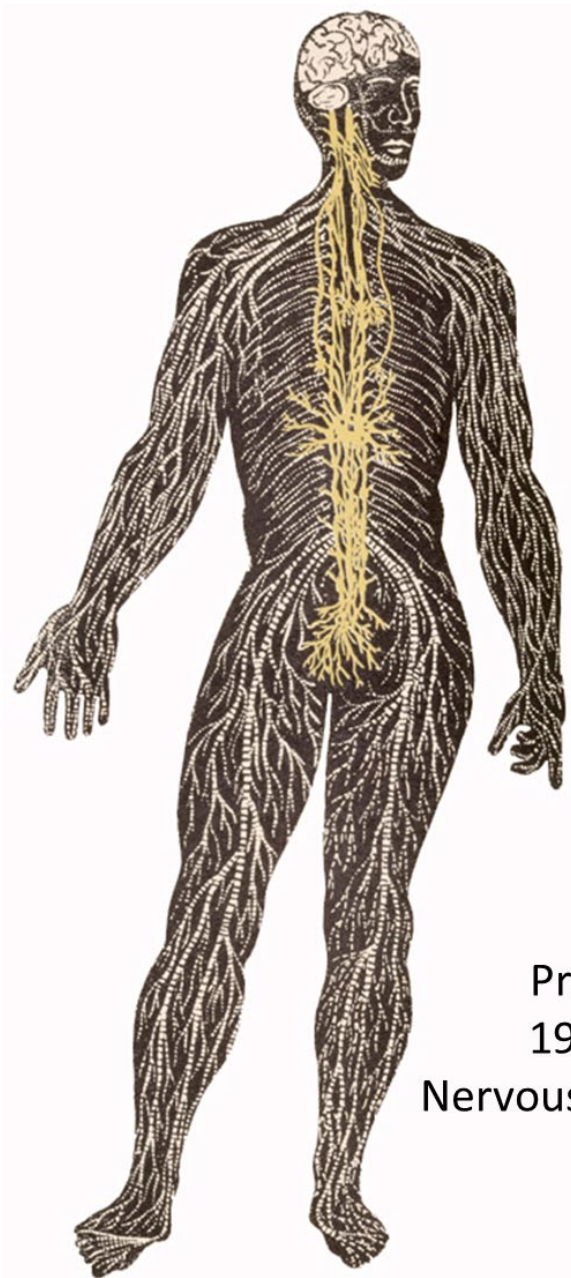
Neurovascular Unit Research Group  
Korea Brain Research Institute



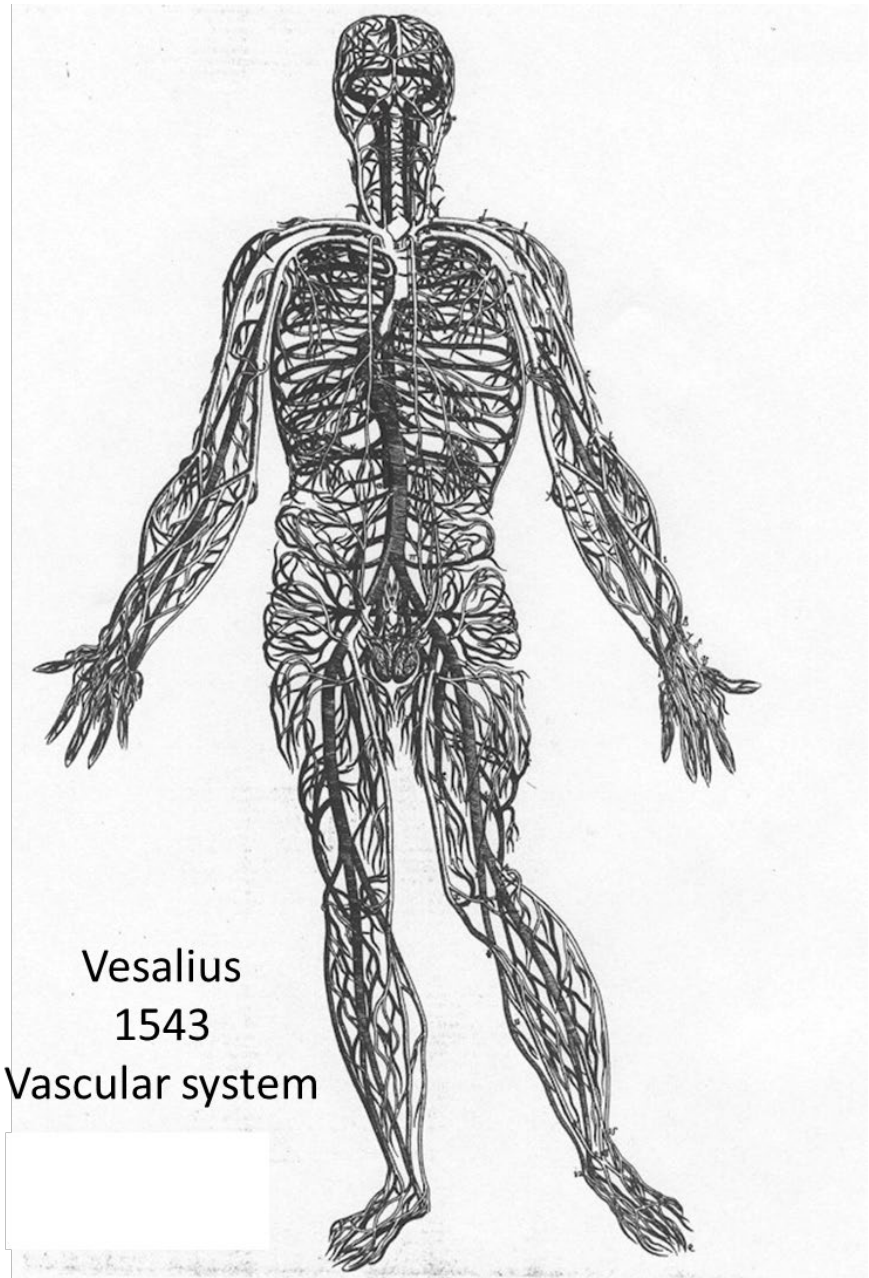


# *Where is the intellect? Brain vs. Heart*



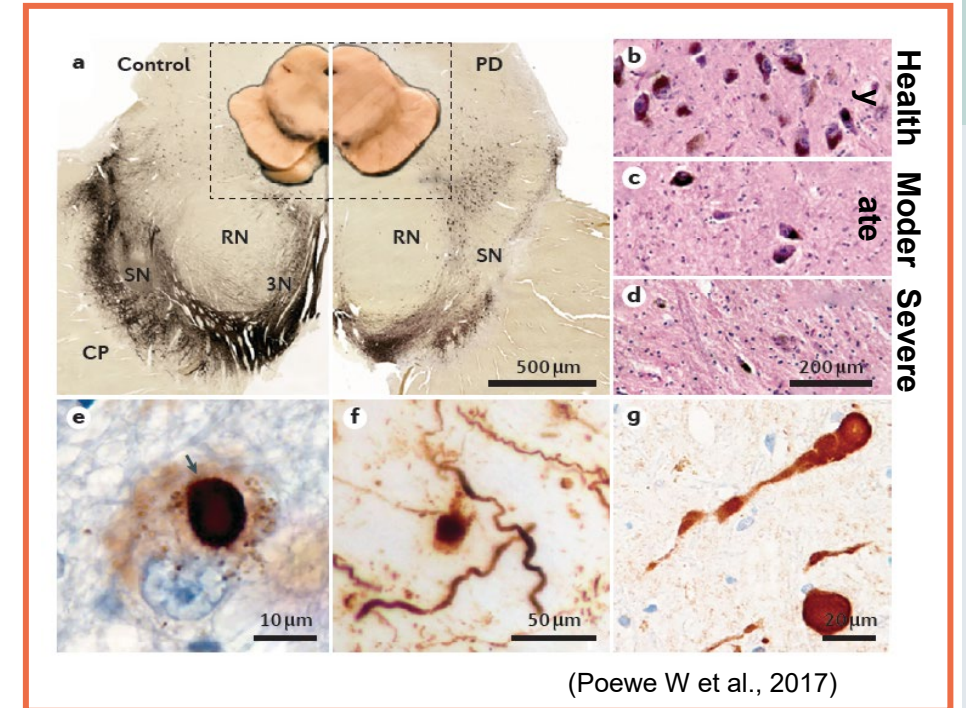
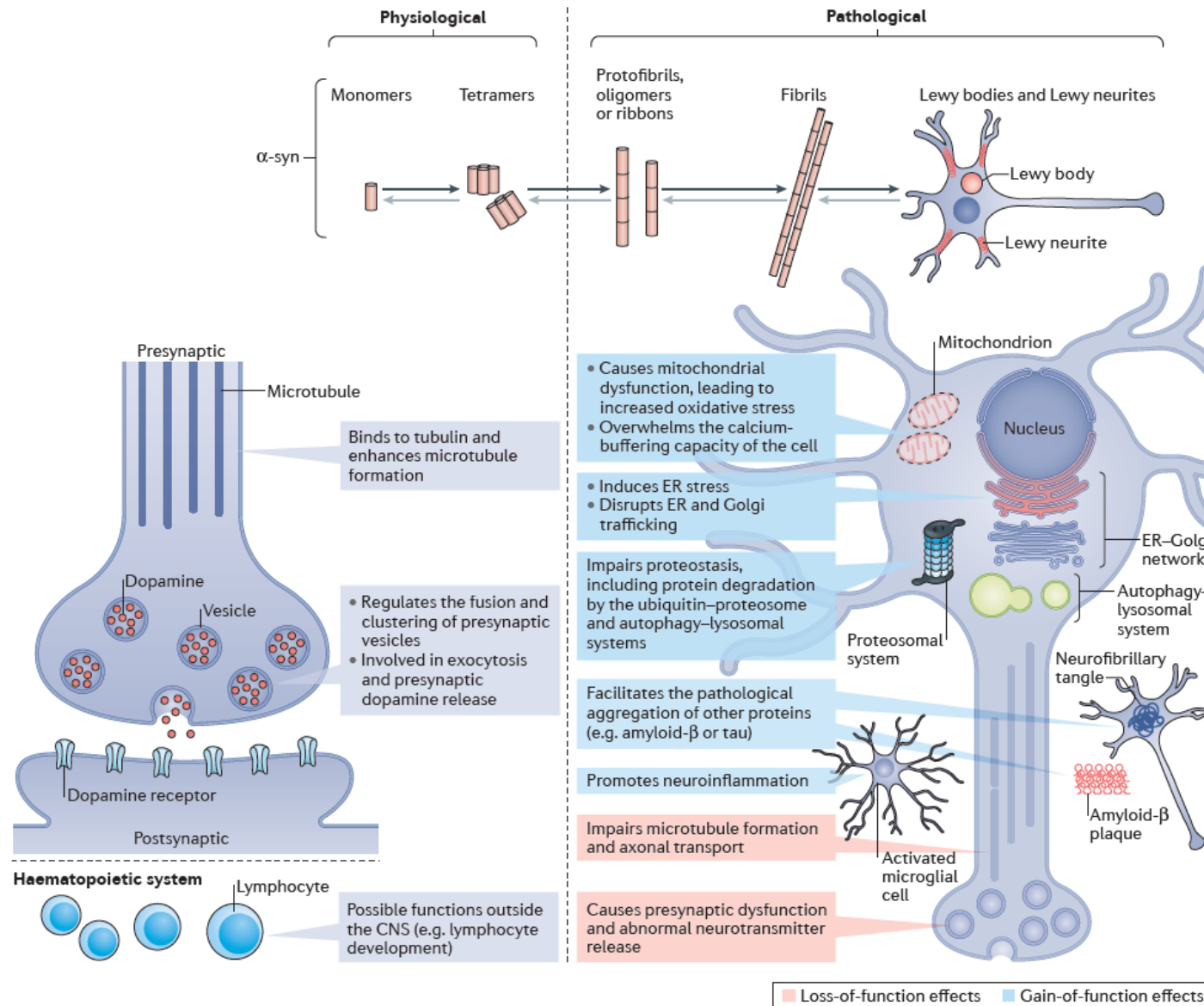


Pratt  
1901  
Nervous System



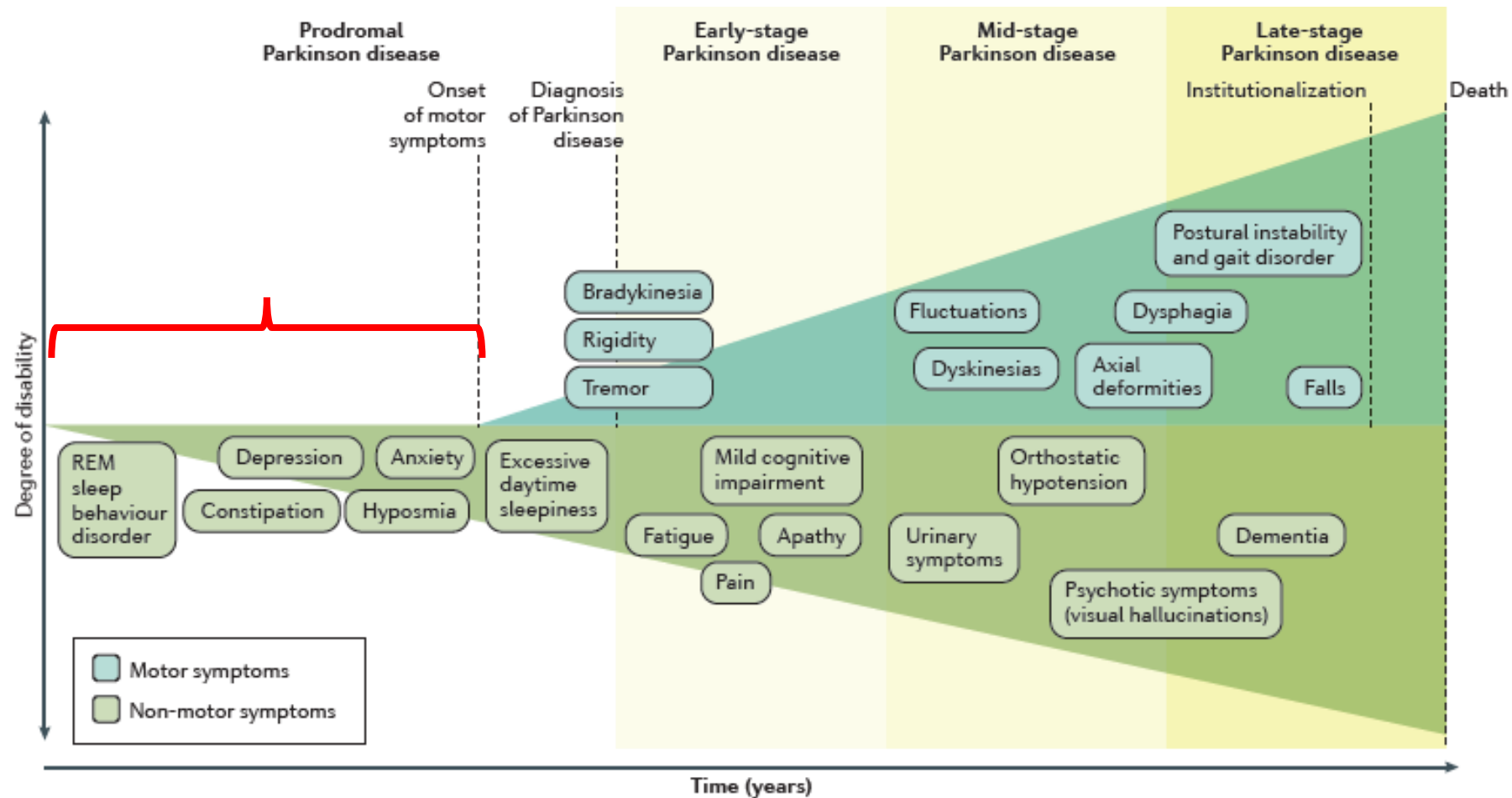
Vesalius  
1543  
Vascular system

# Pathology of $\alpha$ -synuclein for PD progression



(Koprich JB et al., 2017)

# Clinical symptoms associated with Parkinson's Disease



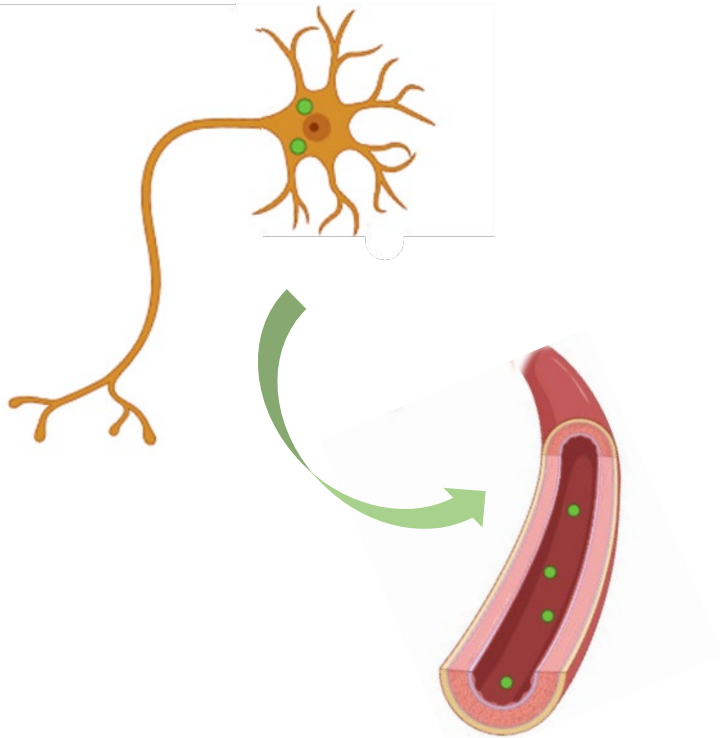
(Poewe W et al., 2017)

# Brain vascular dysfunction associated with $\alpha$ -synuclein

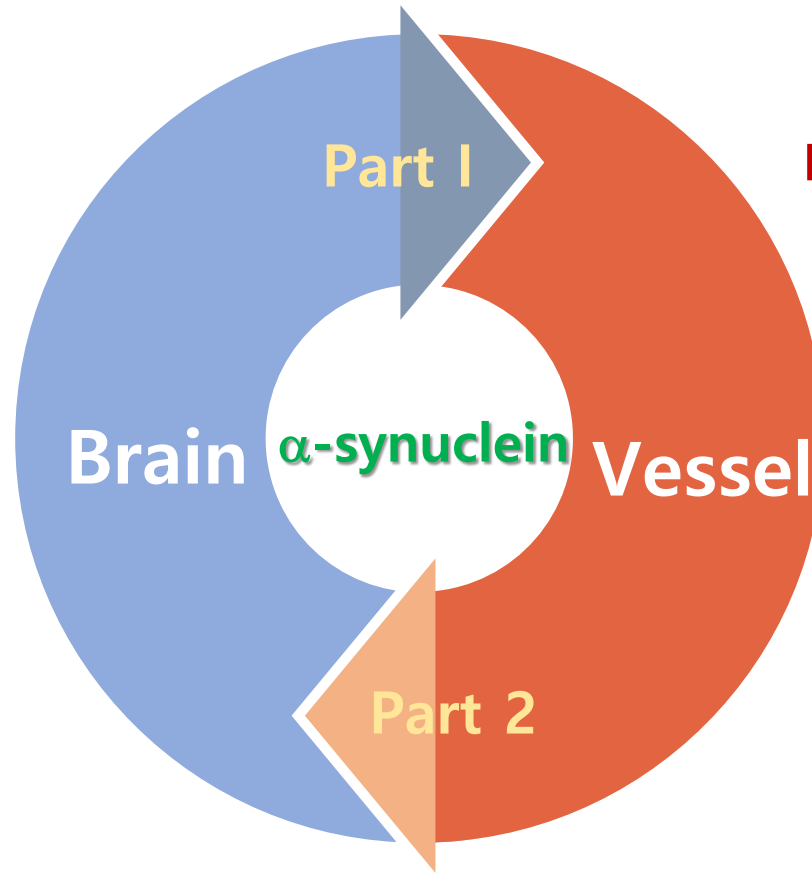
| Disorder                       | Key features                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Selected references                                                                                                                                                                                    |
|--------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Altered BBB and angiogenesis   | <ul style="list-style-type: none"> <li>– Increased vessel density, BBB leakage and VEGF-A release.</li> <li>– Decreased TJ molecules including occludin and claudin-5.</li> <li>– Rodent model of HD revealed increased transcytosis and paracellular transport in brain ECs with TJ imbalance.</li> <li>– mHtt aggregates localized in ECs, smooth muscle cells and perivascular macrophages.</li> <li>– iPSCs-derived HD BMECs show increased angiogenesis, altered barrier properties and impaired Wnt/<math>\beta</math>-catenin signaling.</li> </ul>                                              | Stevenson et al., 2020; Drouin-Ouellet et al., 2015; Di Pardo et al., 2017; Lim et al., 2017                                                                                                           |
| <b>PD</b>                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                        |
| Altered CBF                    | <ul style="list-style-type: none"> <li>– Decreased CBF in frontal, parietal and occipital areas.</li> <li>– PD patients with dementia show left temporo-parietal hypoperfusion.</li> <li>– PD patients without dementia display hypoperfusion in the posterior cortical regions.</li> <li>– Hypoperfusion is positively correlated with cognitive performance and motor impairment.</li> </ul>                                                                                                                                                                                                          | Derejko et al., 2006; Kamagata et al., 2011; Fernandez-Seara et al., 2012; Madhyastha et al., 2015; Syrimi et al., 2017                                                                                |
| Altered CBF, BBB, angiogenesis |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                        |
| Altered BBB and angiogenesis   | <ul style="list-style-type: none"> <li>– BBB disruption in the SNc with increased permeability in the post-commissural putamen.</li> <li>– Down regulation of TJ proteins (ZO-1) and higher number of EC nuclei in the SNc.</li> <li>– String vessel formation in brain capillary networks.</li> <li>– Upregulation of VEGF, and parkinsonian traits following VEGF administration in rodent models.</li> <li>– Formation of endothelial clusters, capillary network damage, loss of capillary connections in the SN, basement membrane thickening, vacuolization, and pericyte degradation.</li> </ul> | Farkas et al., 2000; Barcia et al., 2005; Kortekaas et al., 2005; Wada et al., 2006; Rite et al., 2007; Chao et al., 2009; Patel et al., 2011; Guan et al., 2013; Yang et al., 2015; Kuan et al., 2016 |

# Contents

## Effect of neuronal $\alpha$ -synuclein on cerebral blood vessels

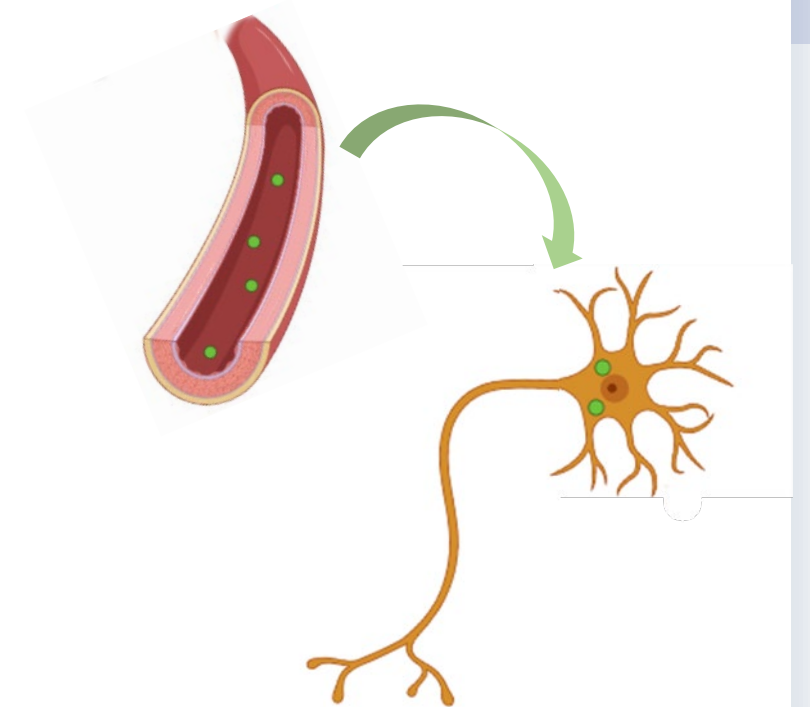


(Jeong JY et. al., 2023, *Sci Reports*)



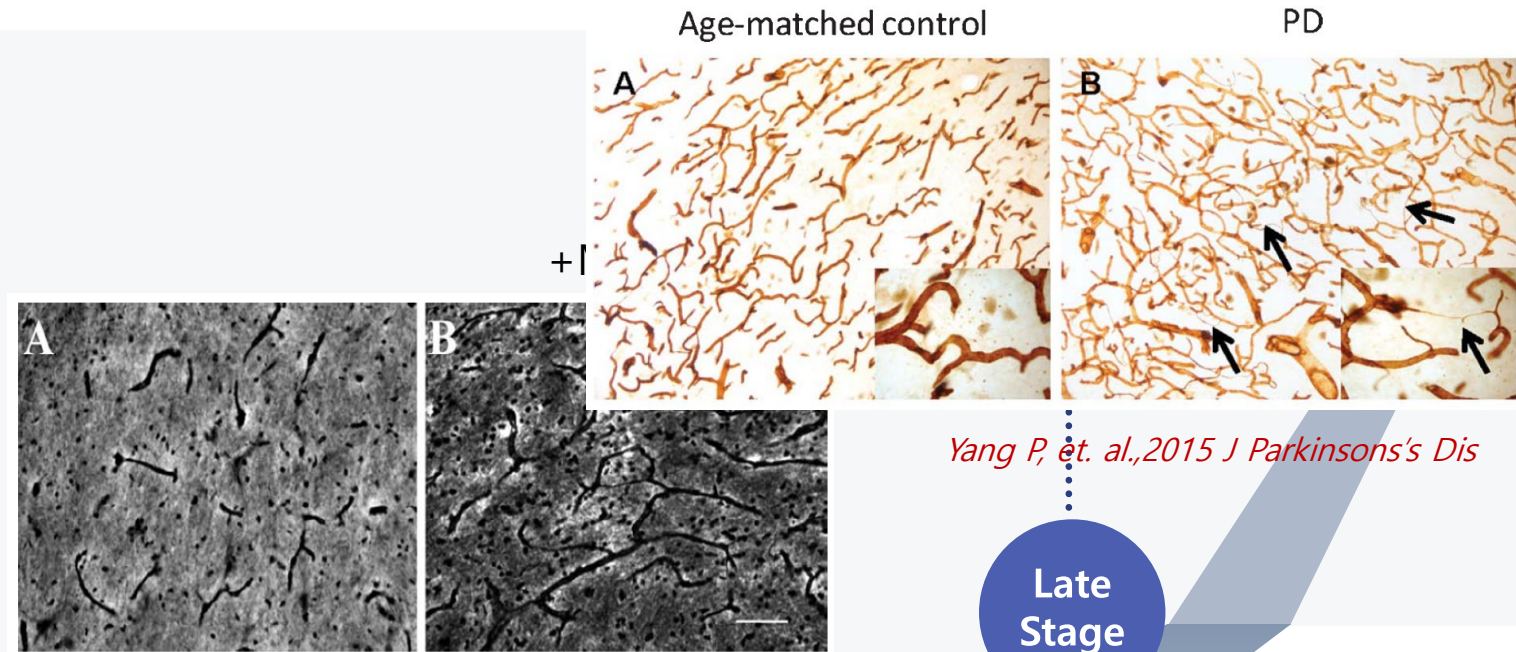
**PD pathology**

## Role of $\alpha$ -synuclein in the blood plasma in synucleinopathy



(Jeong JY & Kim N et. al., 2025, *npj Parkinson's Disease*)

# Two distinct histological findings regarding cerebrovascular formation in PD



Barcia C, et. al., 2005 J Neural Transm

Moderate Stage

Late Stage

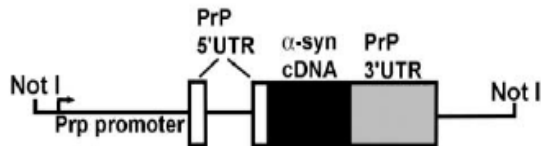
“

To investigate whether  $\alpha$ -Syn overexpression affects the structural defects of brain vasculature in M83 PD mouse model.

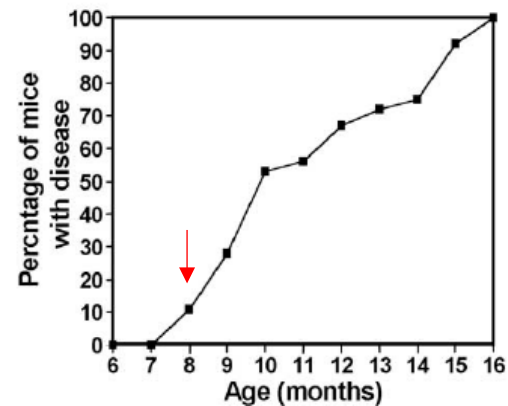
# SNCA<sup>A53T</sup> mouse (M83 line) model

## SNCA<sup>A53T</sup> (M83 line) mouse

- Familial mutant A53T point mutation

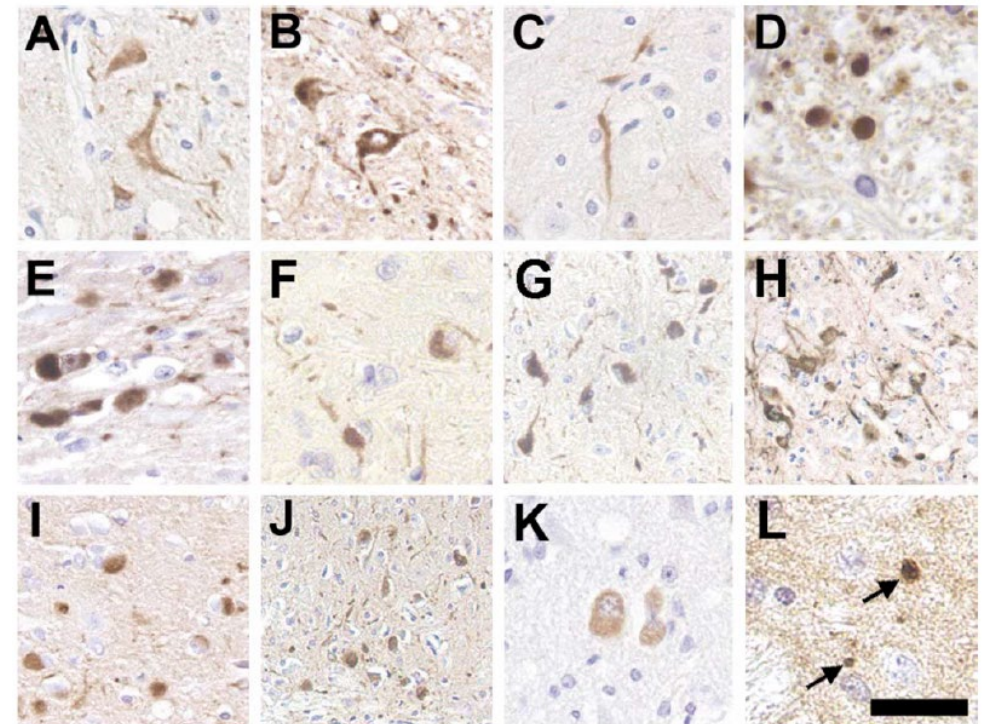


- The targeting vector design for A53T transgenic mouse



- Onset of **motor phenotype** in M83 homozygous mice (n=40)

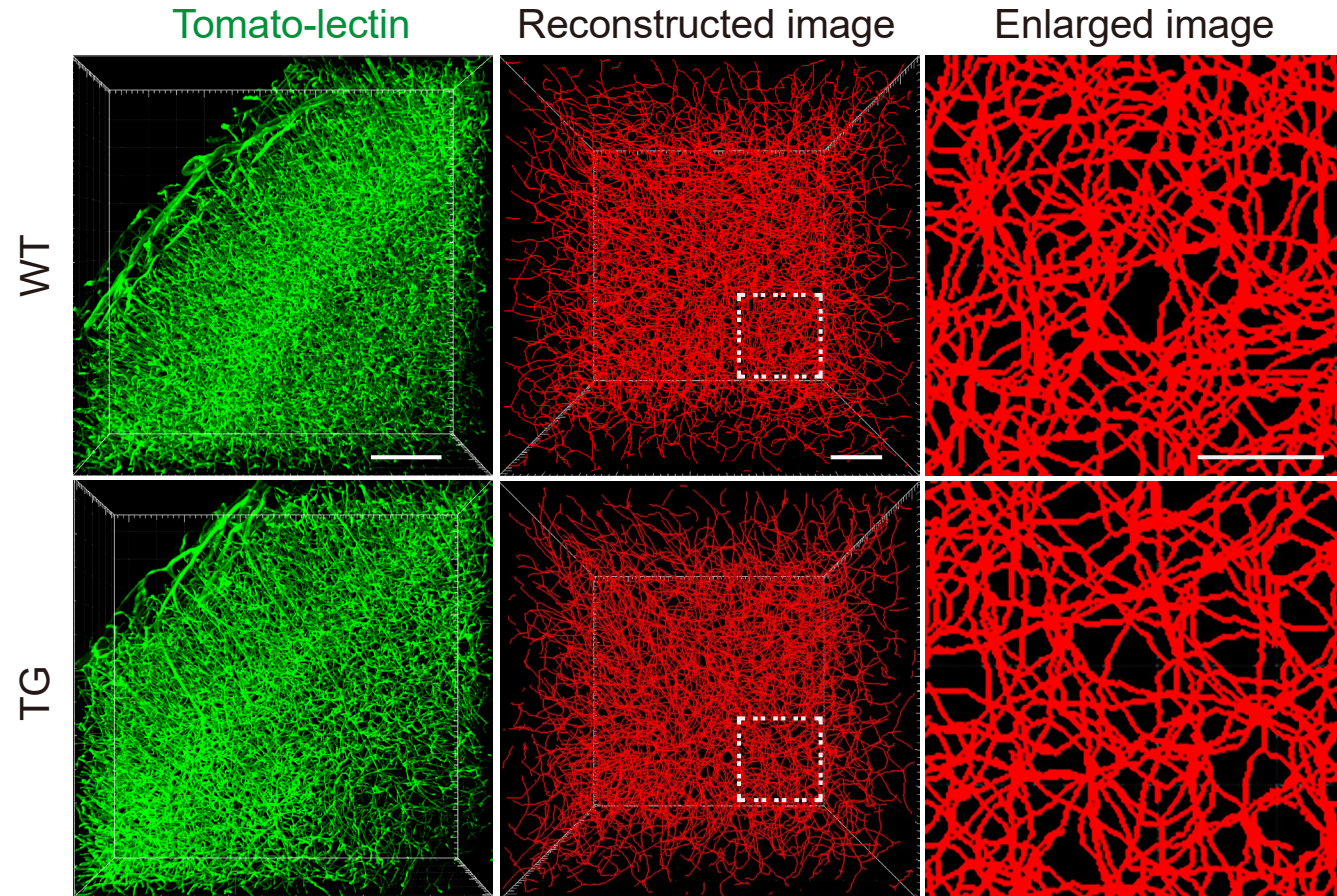
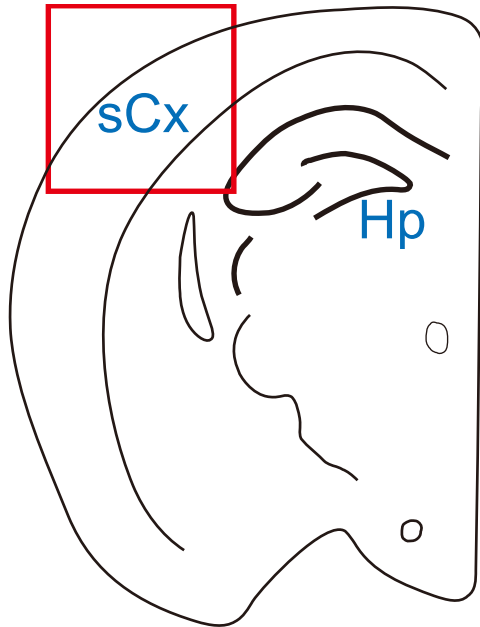
- SNCA<sup>A53T</sup> mouse model show increased
- Lewy bodies** from 9-month old



(Giasson BI et al., 2002, Neuron)

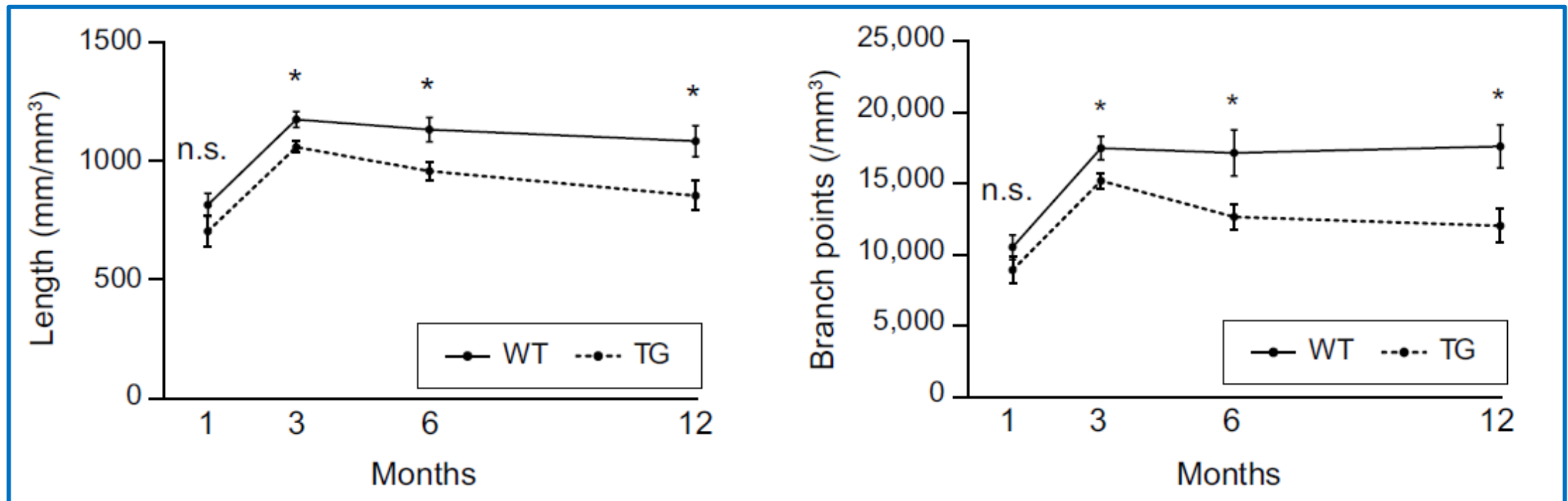
# M83 PD mouse model shows reduced cerebrovascular patterning

- Label blood vessels with tomato-lectin-488 and clearing by using ECI methods
- 3-month-old homozygous (TG) and age-matched control (WT)

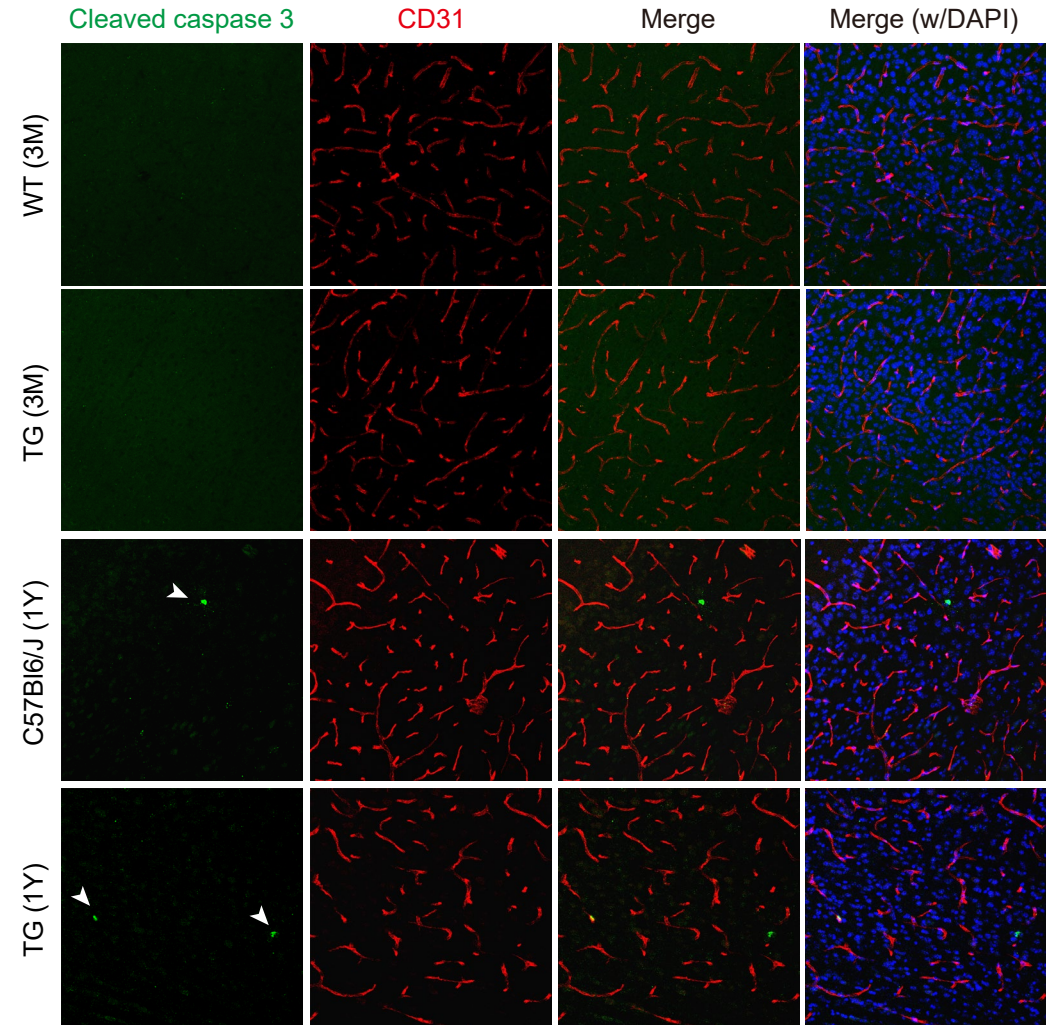
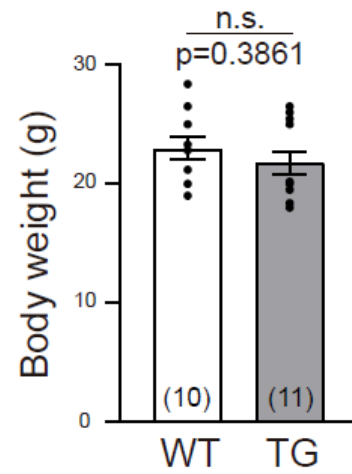
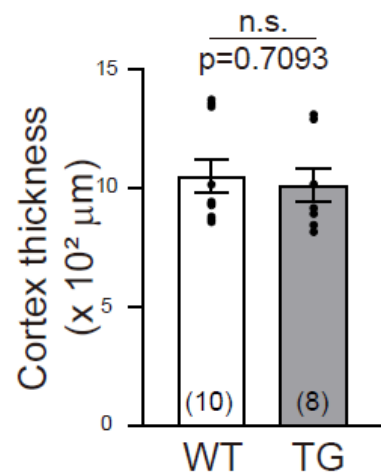
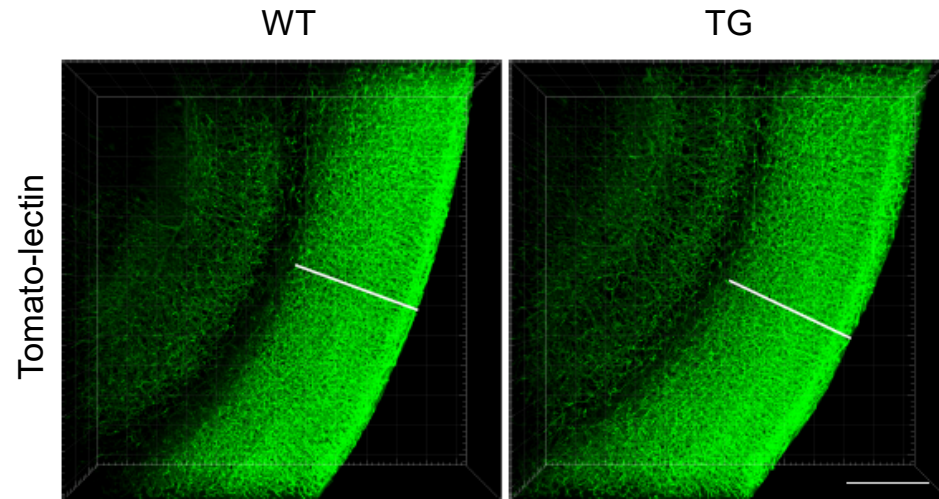


# M83 PD mouse model shows reduced cerebrovascular patterning

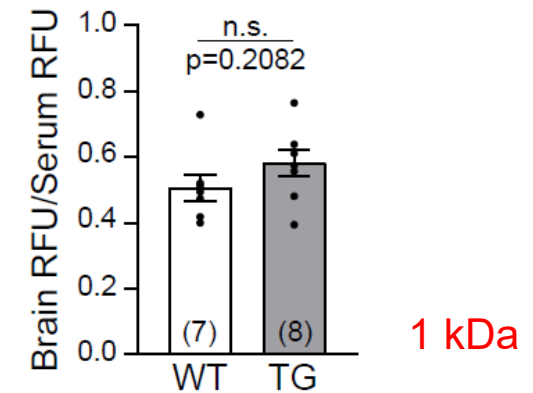
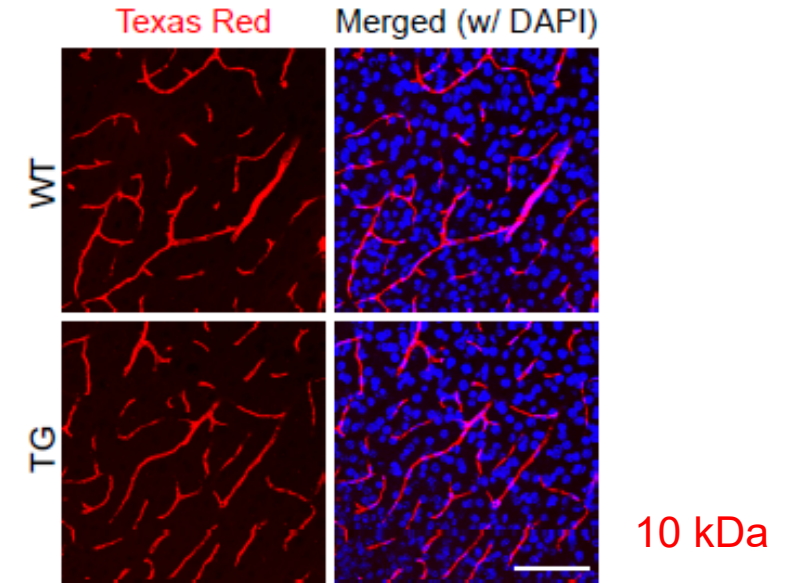
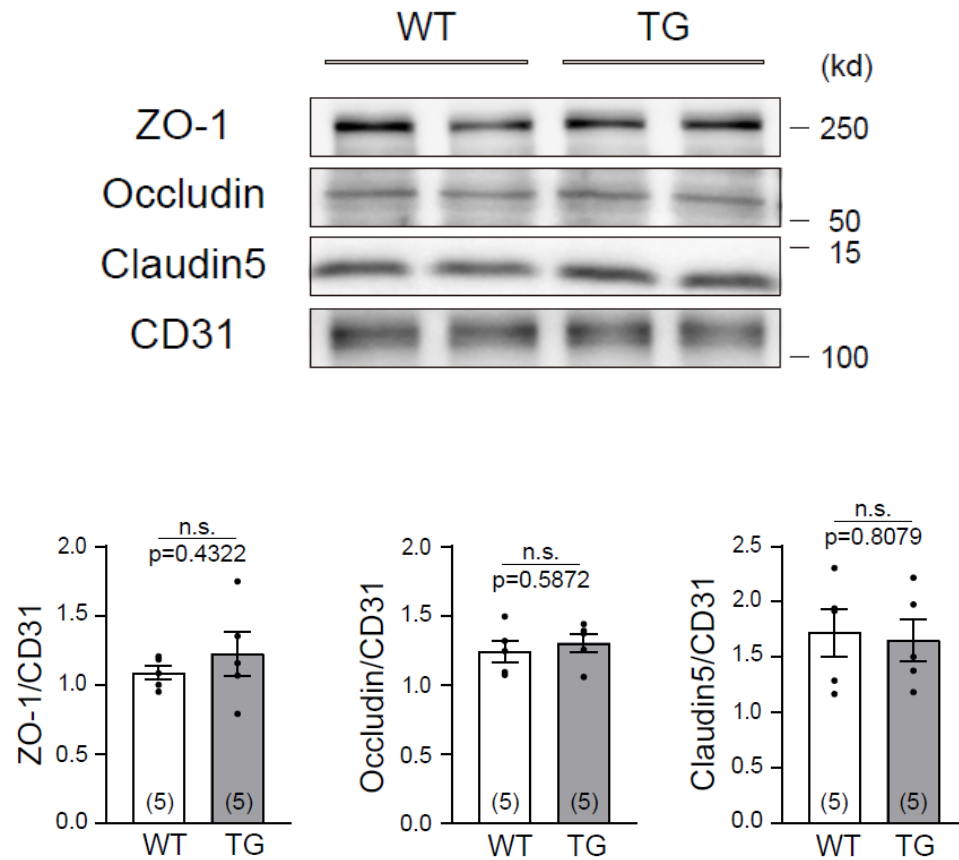
- Label blood vessels with tomato-lectin-488 and clearing by using ECI methods
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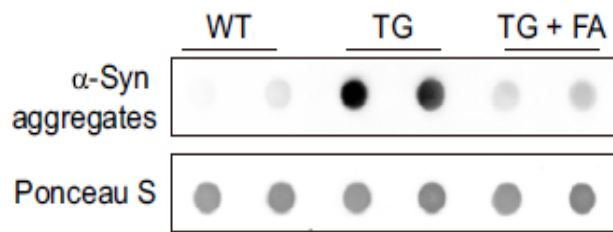
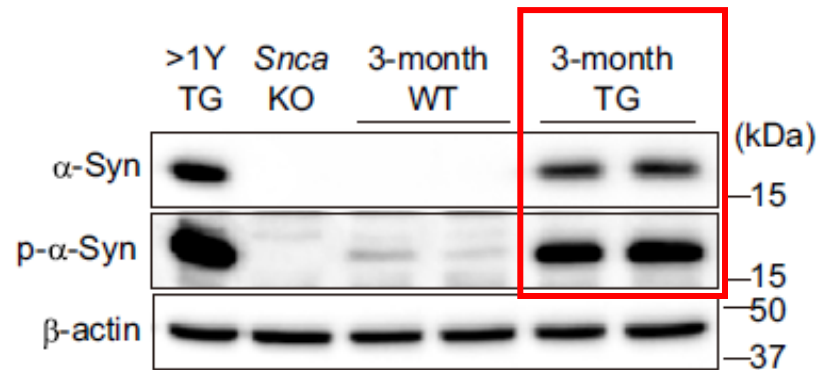
# The reduced cerebrovascular network in PD model is not caused by developmental retardation or vascular damage



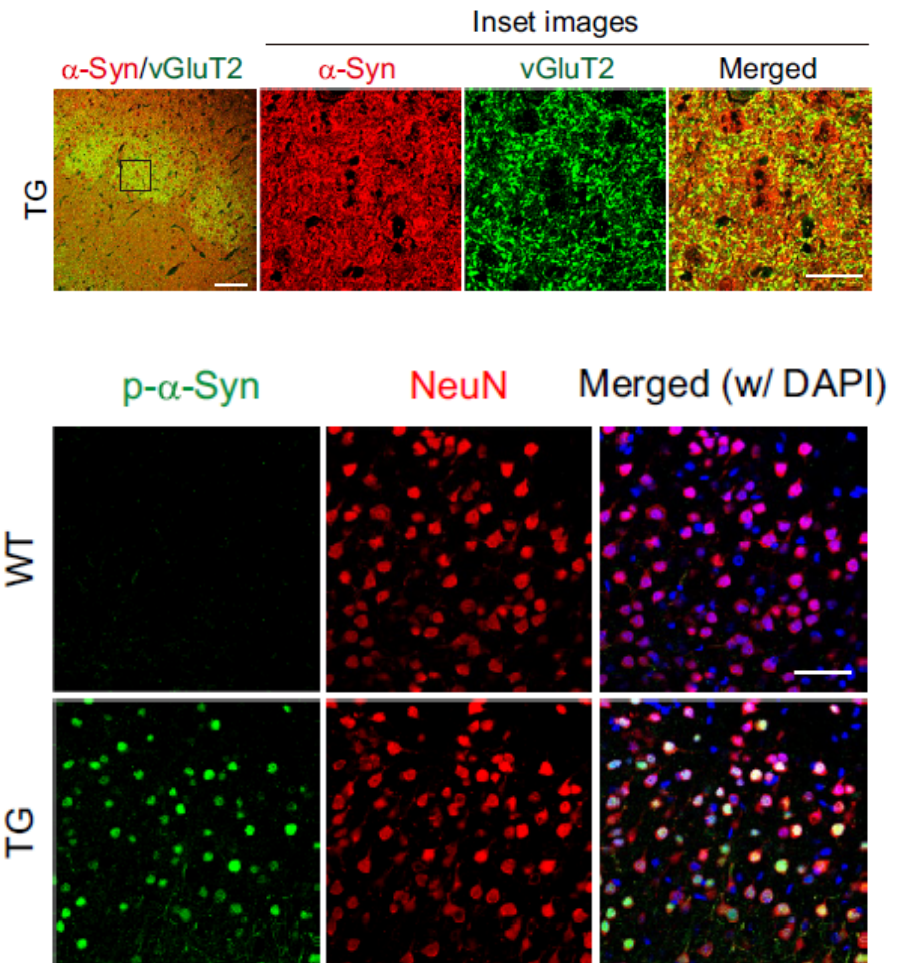
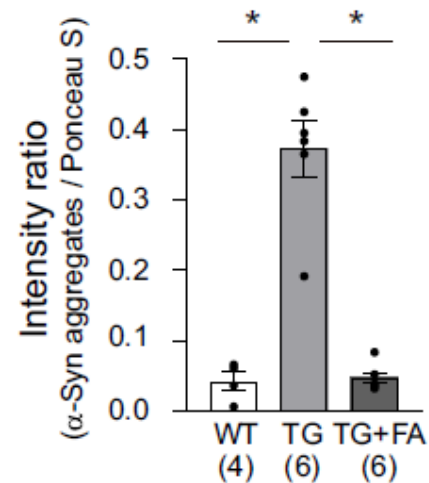
# Young M83 PD mice show normal blood-brain barrier formation and function



# Young PD mouse model shows increased levels of phosphorylated and aggregated form of $\alpha$ -syn

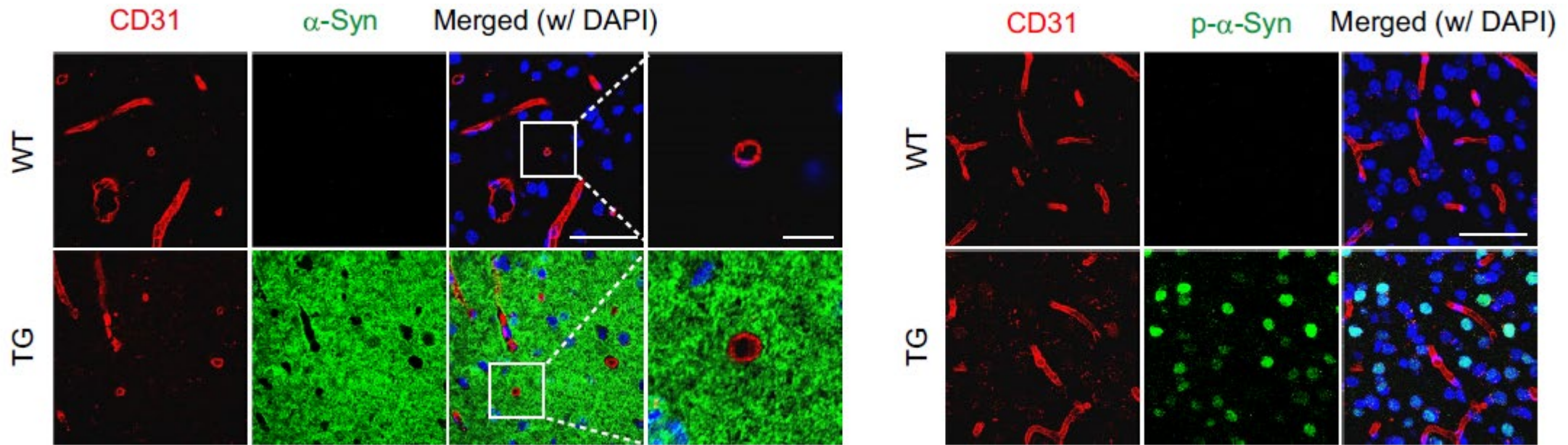


\*Formic acid



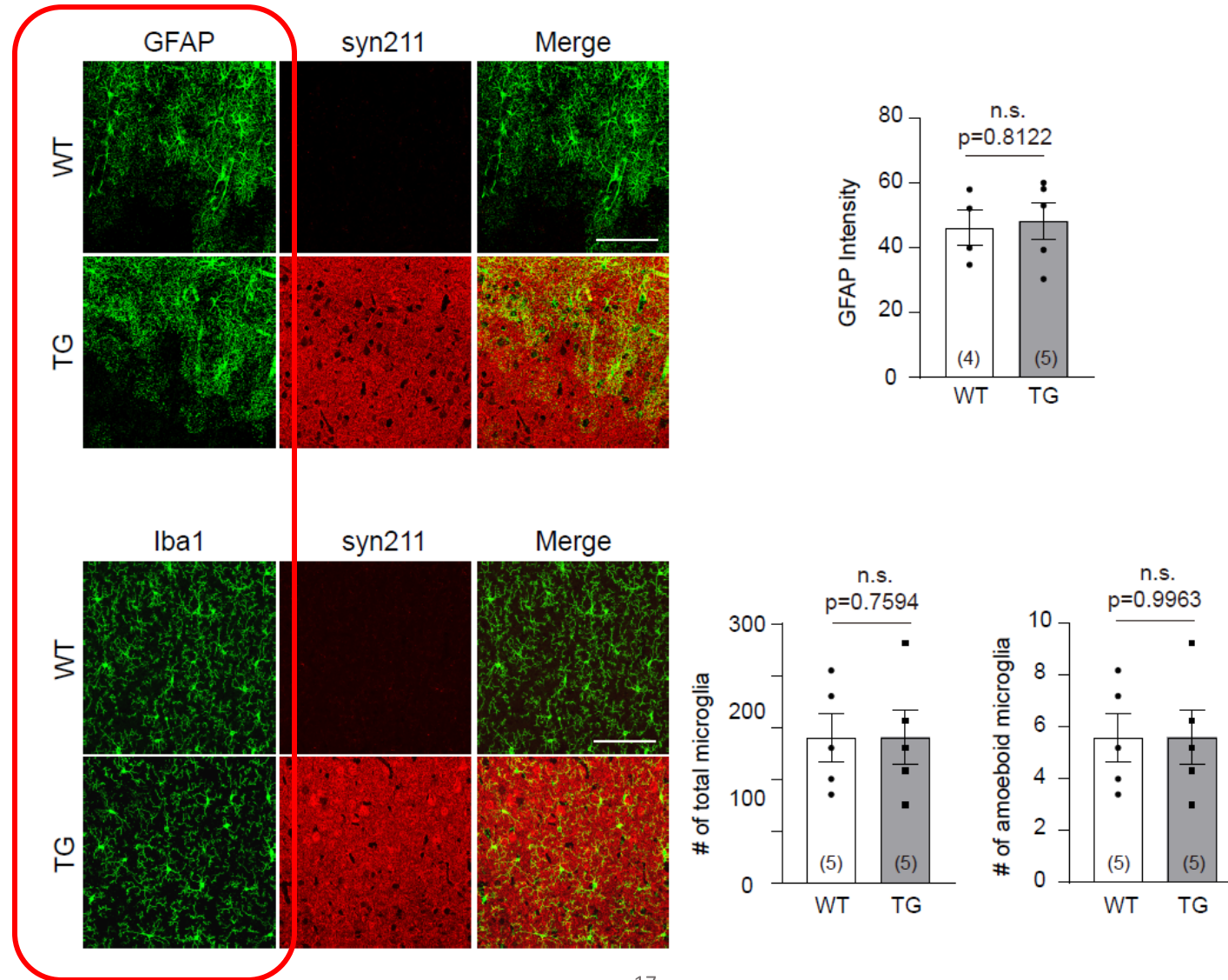
# The pathological form of human $\alpha$ -synuclein does not directly contact with blood vessels

- 3-month-old homozygous (TG) and age-matched control (WT)



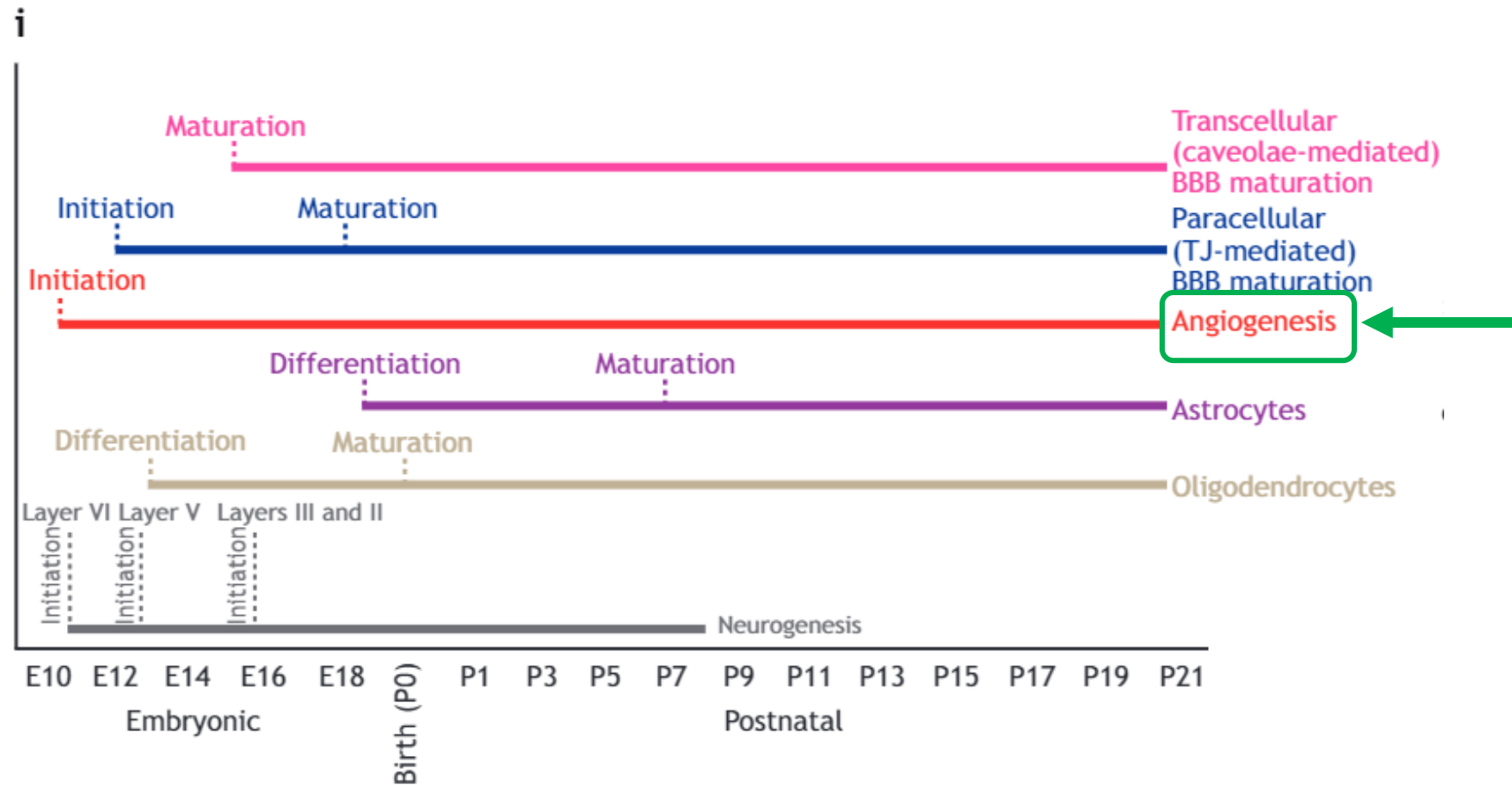
CD31, endothelial cell marker

# Overexpressed human $\alpha$ -synuclein does not induce abnormal inflammatory responses in young PD mice



# Vigorous brain endothelial proliferation from embryonic to early post-natal period

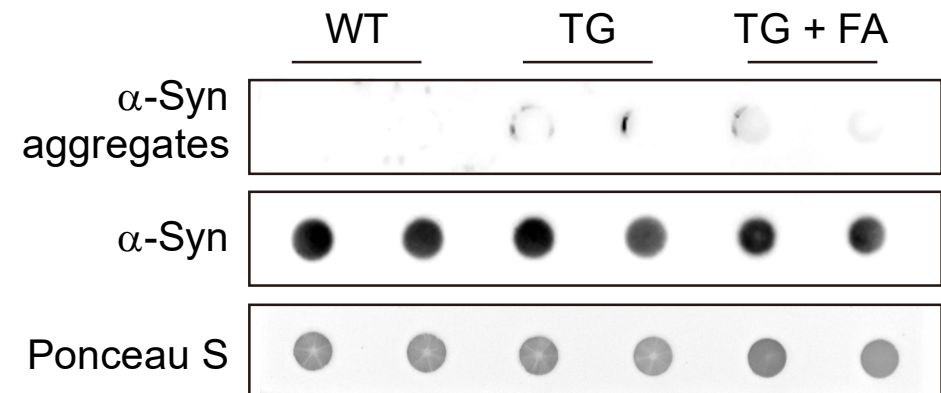
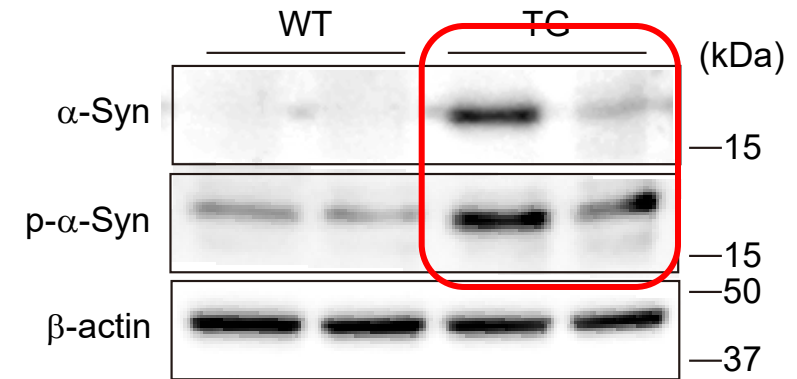
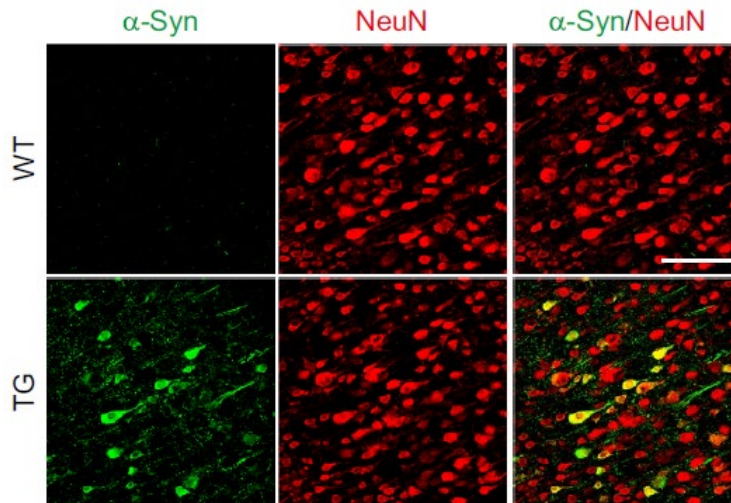
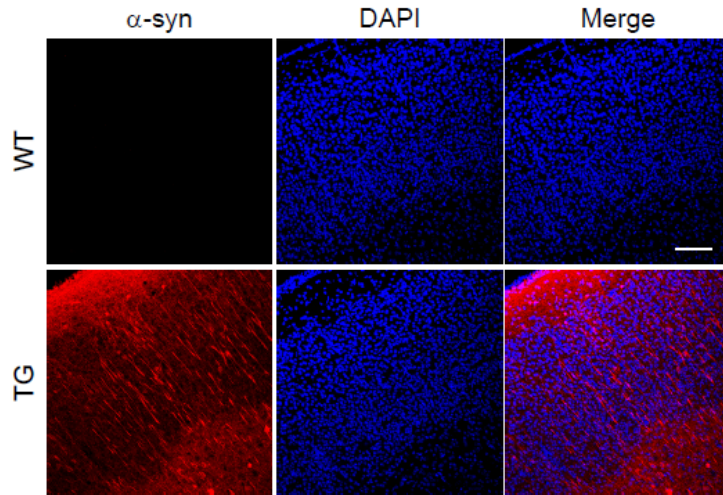
## A Cerebral cortex



(Biswas S et al., 2020)

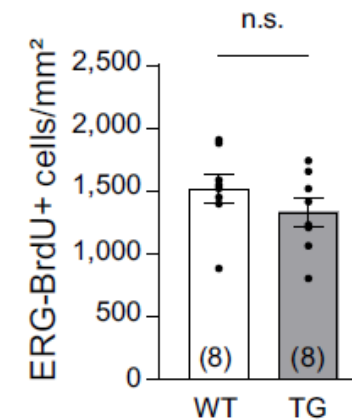
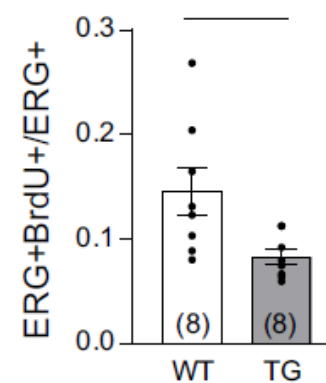
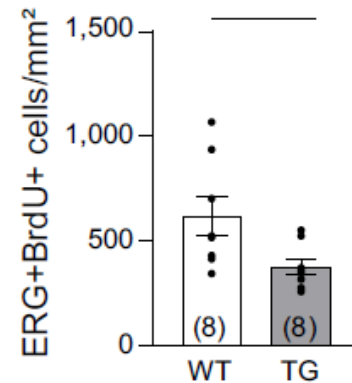
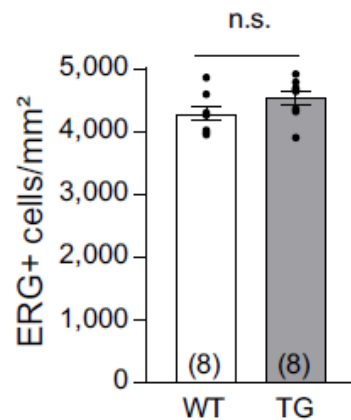
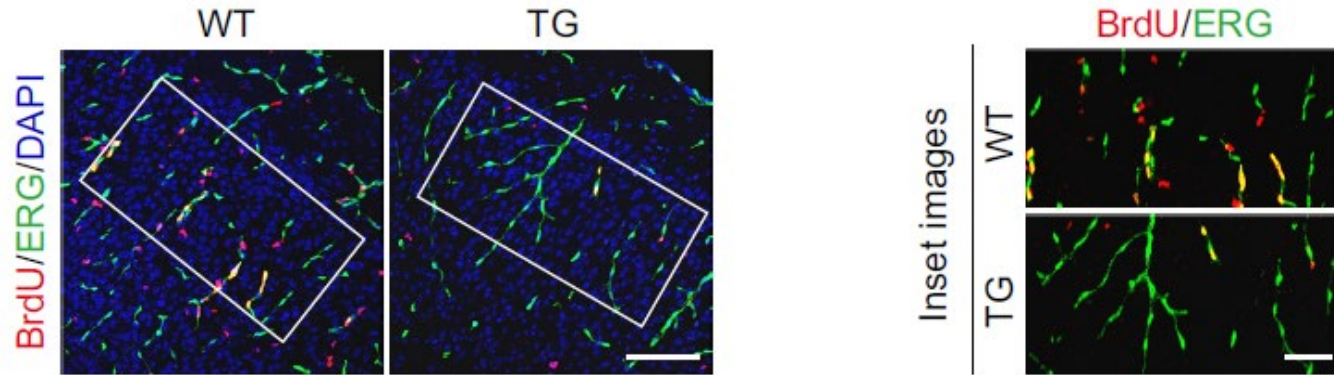
# Neonatal M83 PD pups express high levels of human $\alpha$ -synuclein expression and its phosphorylated form

P10



# Reduced proliferation rate of brain endothelial cell in neonatal stage of PD model

P10



**ERG**, ETS-related gene, a transcription factor in endothelial cells  
**BrdU**, bromodeoxyuridine

# Do vascular abnormalities in young PD mice correlate with reduced neuronal activation?

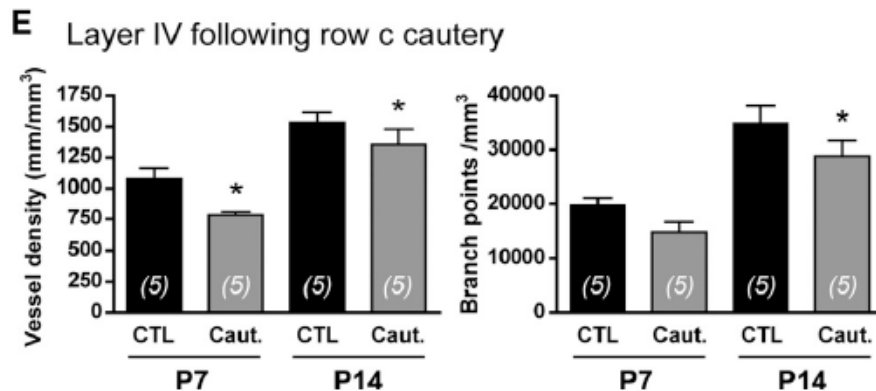


# Neural activity regulates cerebrovascular angiogenesis during a postnatal critical period

## Neuron Article

### Sensory-Related Neural Activity Regulates the Structure of Vascular Networks in the Cerebral Cortex

Baptiste Lacoste,<sup>1</sup> Cesar H. Comin,<sup>2</sup> Ayal Ben-Zvi,<sup>1</sup> Pascal S. Kaeser,<sup>1</sup> Xiaoyin Xu,<sup>3</sup> Luciano da F. Costa,<sup>2</sup> and Chenghua Gu<sup>1,\*</sup>

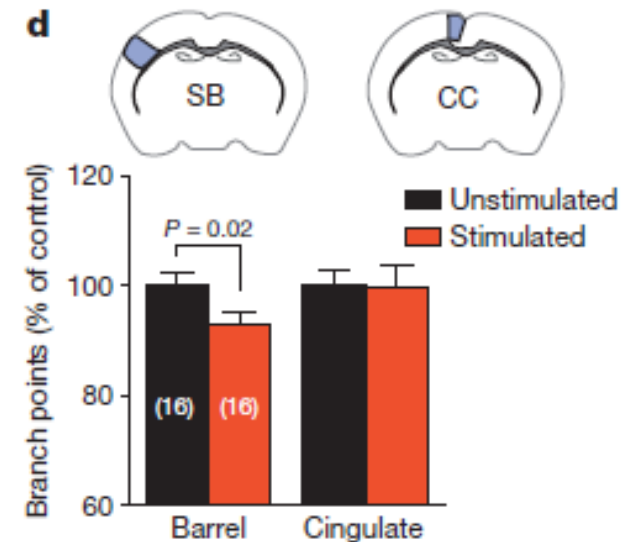


## LETTER

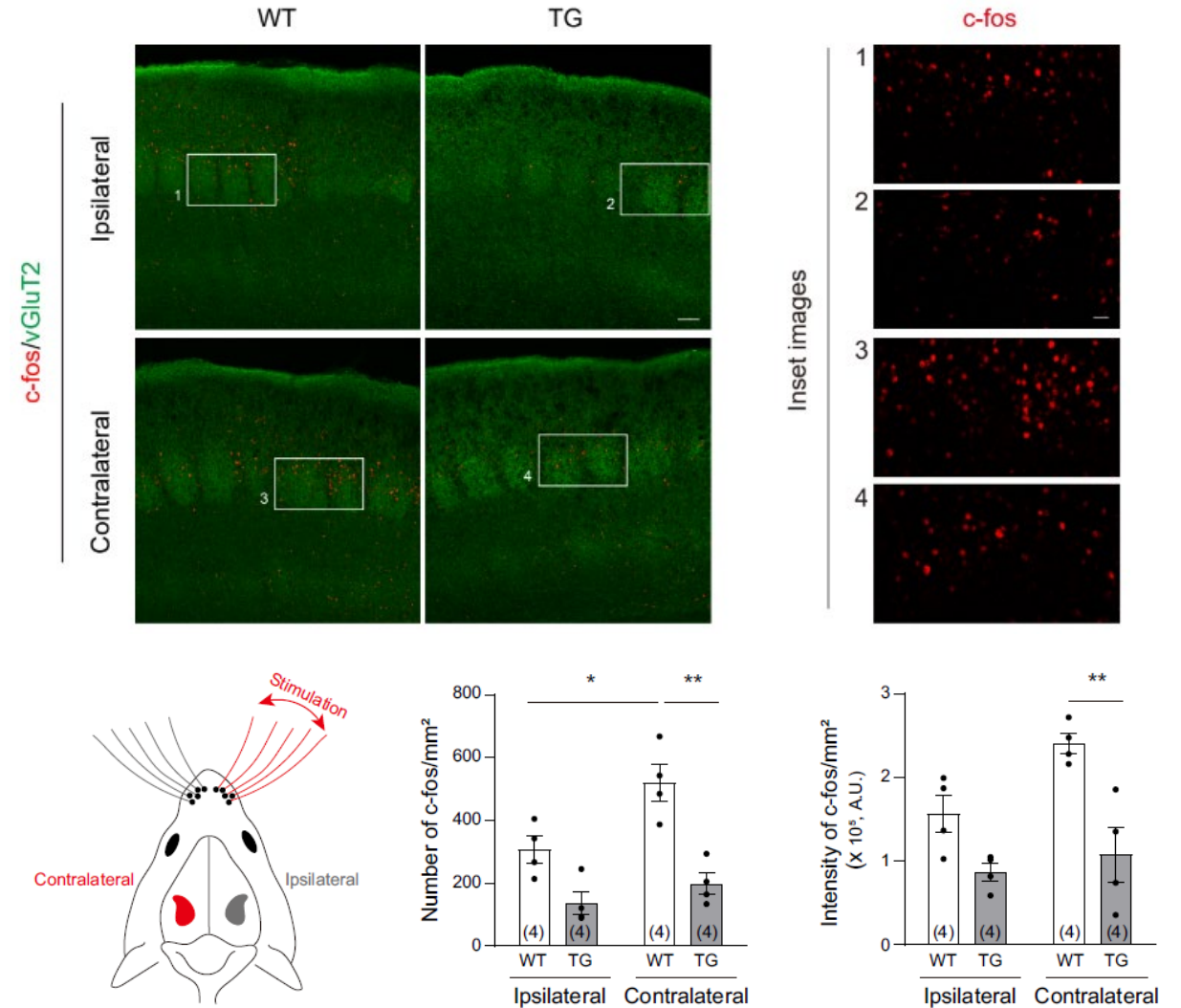
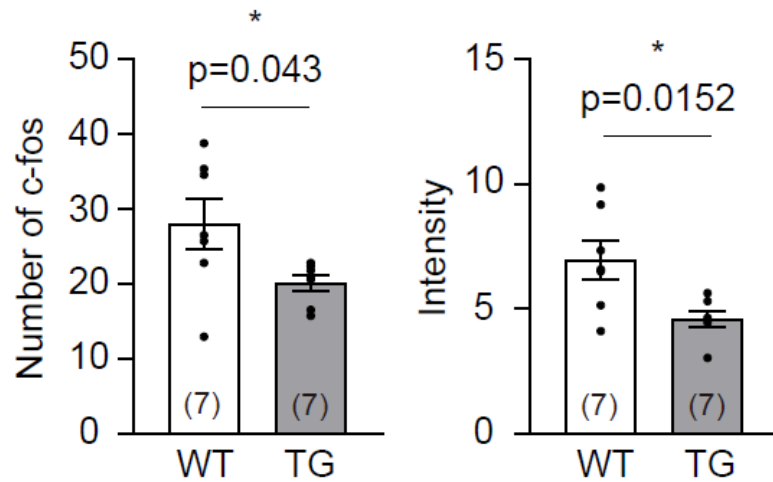
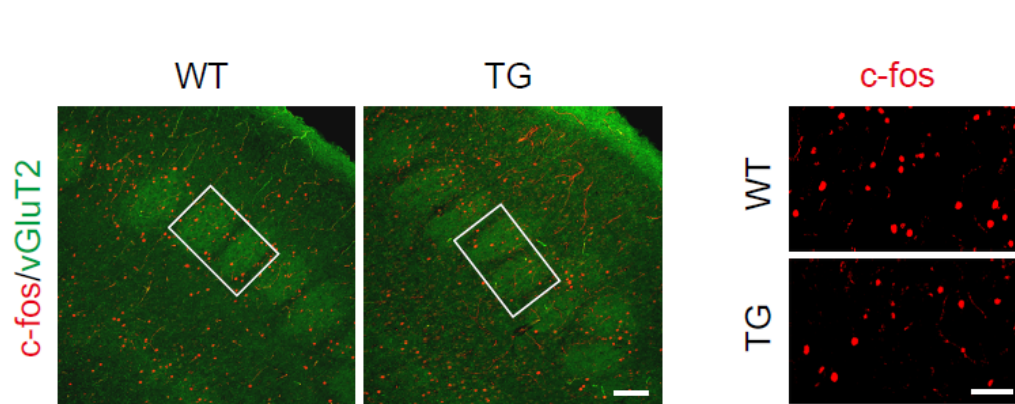
doi:10.1038/nature12821

### Perturbed neural activity disrupts cerebral angiogenesis during a postnatal critical period

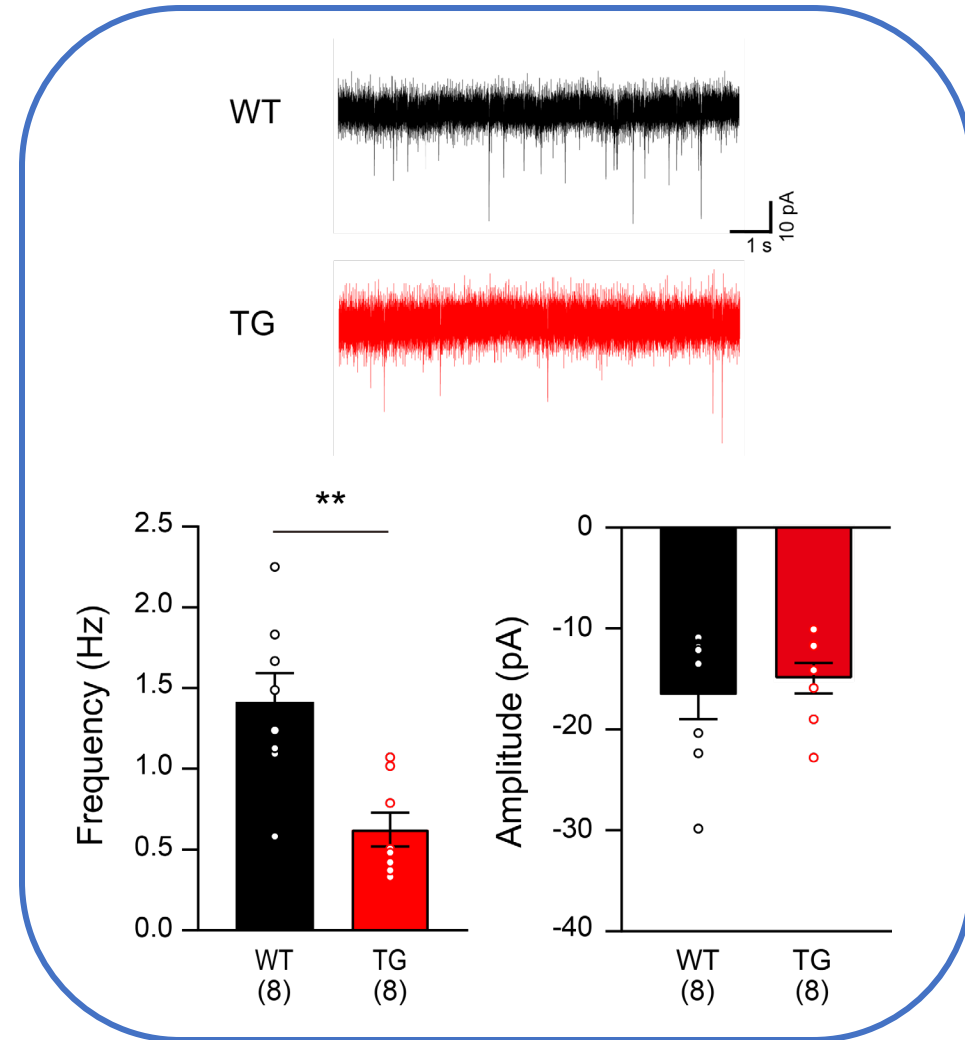
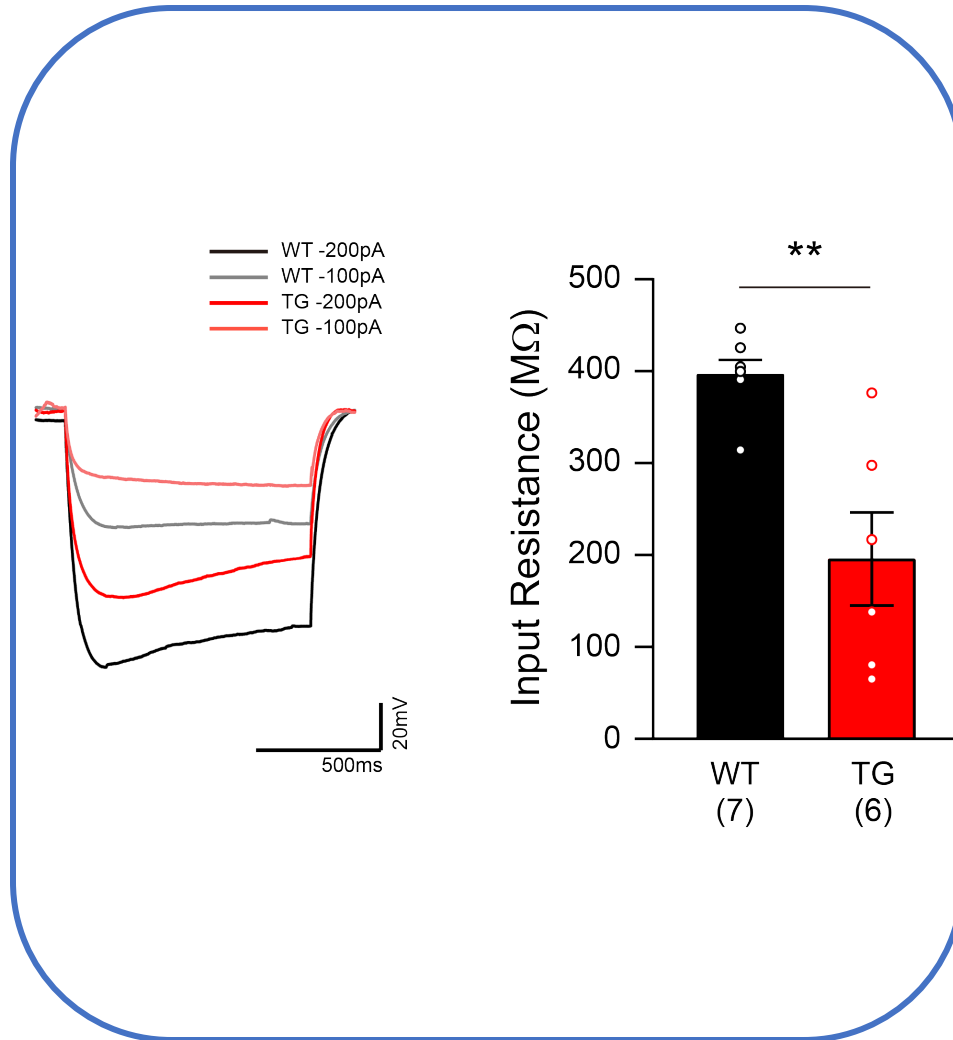
Christina Whiteus<sup>1,2</sup>, Catarina Freitas<sup>1</sup> & Jaime Grutzendler<sup>1,2</sup>



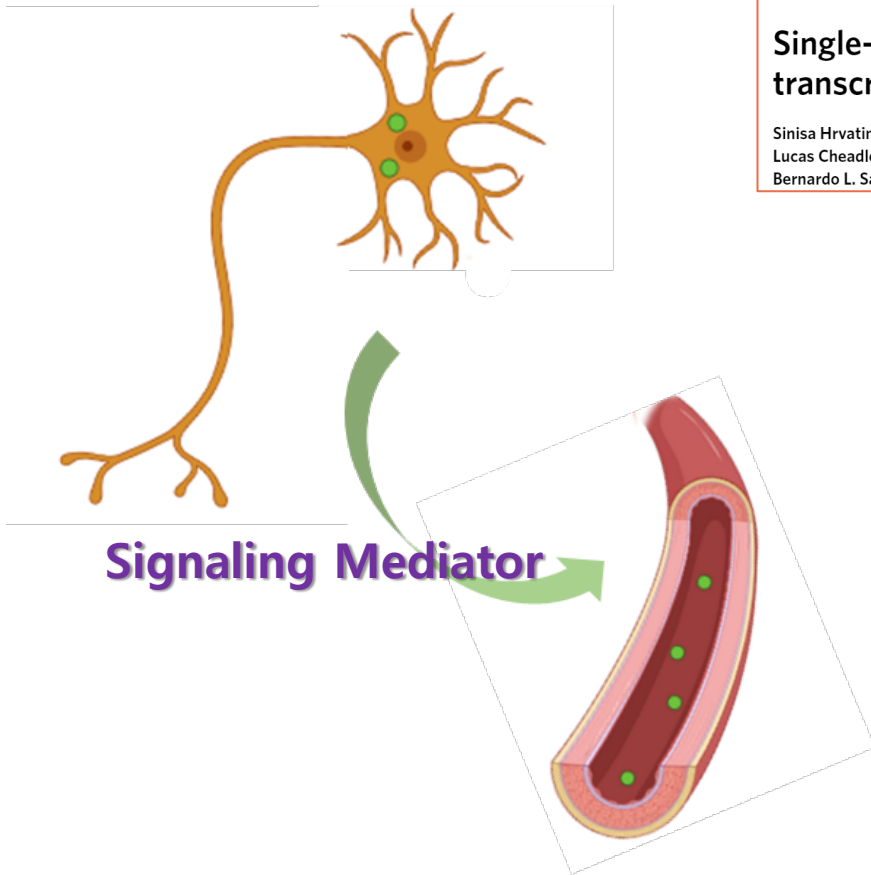
# PD neonates show the reduction of neural activity



# The activation of neocortical neurons involved in sensory processing is downregulated in the young PD mouse (P10)



# Potential angiogenic candidates in brain endothelial cells in response to neuronal activation



## RESOURCE

<https://doi.org/10.1038/s41593-017-0029-5>

nature  
neuroscience

Corrected: Publisher Correction

## Single-cell analysis of experience-dependent transcriptomic states in the mouse visual cortex

Sinisa Hrvatin<sup>1</sup>, Daniel R. Hochbaum<sup>2,3</sup>, M. Aurel Nagy<sup>1</sup>, Marcelo Cicconet<sup>4</sup>, Keiramarie Robertson<sup>3</sup>, Lucas Cheadle<sup>1</sup>, Rapolas Zilionis<sup>5,6</sup>, Alex Ratner<sup>7</sup>, Rebeca Borges-Monroy<sup>8</sup>, Allon M. Klein<sup>5</sup>, Bernardo L. Sabatini<sup>3\*</sup> and Michael E. Greenberg<sup>1\*</sup>

(Hrvatin S et al., 2018)

## Neuron

CellPress

## Article

## Neuronal Activity Regulates Blood-Brain Barrier Efflux Transport through Endothelial Circadian Genes

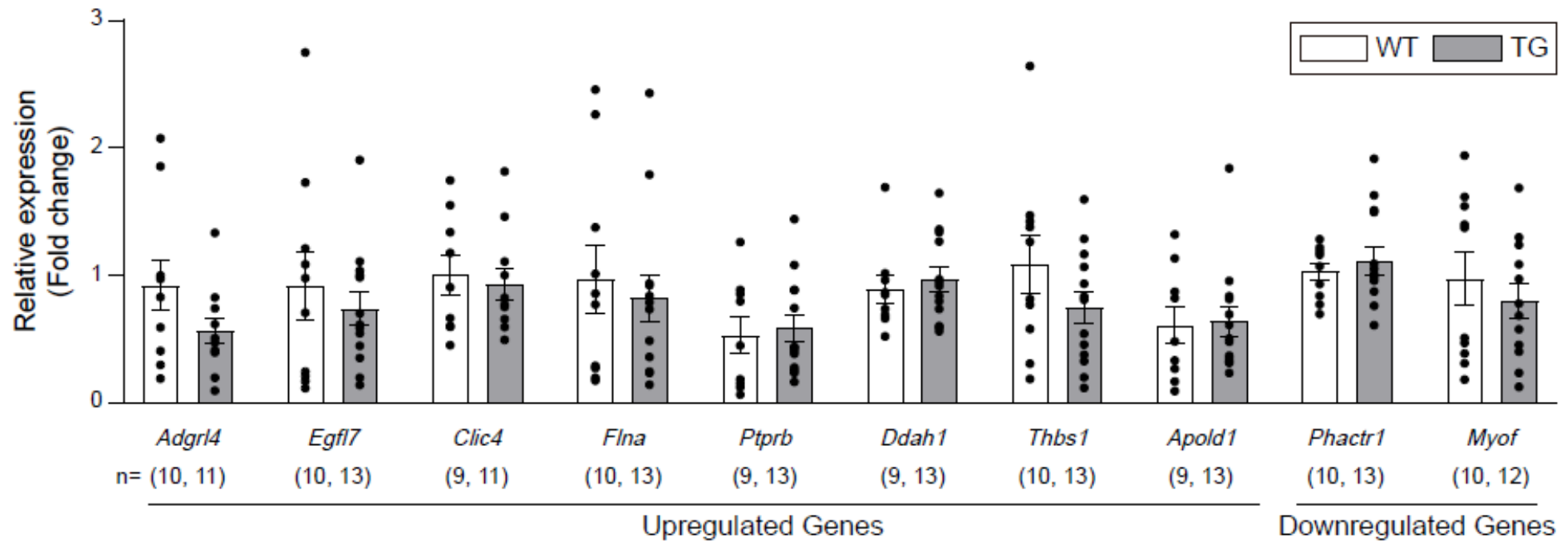
Robert S. Pulido<sup>1,\*</sup>, Roeben N. Munji<sup>1</sup>, Tamara C. Chan<sup>1</sup>, Clare R. Quirk<sup>2</sup>, Geoffrey A. Weiner<sup>1</sup>, Benjamin D. Weger<sup>3</sup>, Meghan J. Rossi<sup>1</sup>, Sara Elmsaoui<sup>1</sup>, Mario Malfavon<sup>1</sup>, Aaron Deng<sup>1</sup>, Caterina P. Profaci<sup>1</sup>, Marie Blanchette<sup>1</sup>, Tongcheng Qian<sup>4</sup>, Koji L. Foreman<sup>4</sup>, Eric V. Shusta<sup>4,5</sup>, Michael R. Gorman<sup>6</sup>, Frédéric Gachon<sup>3</sup>, Stefan Leutgeb<sup>2</sup> and Richard Daneman<sup>1,7,8,\*</sup>

(Pulido RS et al., 2020)

| Up-regulated genes | Down-regulated genes |
|--------------------|----------------------|
| <i>Ptprb</i>       | <i>Myof</i>          |
| <i>Egfl7</i>       | <i>Phactr1</i>       |
| <i>Clic4</i>       |                      |
| <i>Ddah1</i>       |                      |
| <i>Adgrl4</i>      |                      |
| <i>Flna</i>        |                      |
| <i>Thbs1</i>       |                      |
| <i>Apold1</i>      |                      |

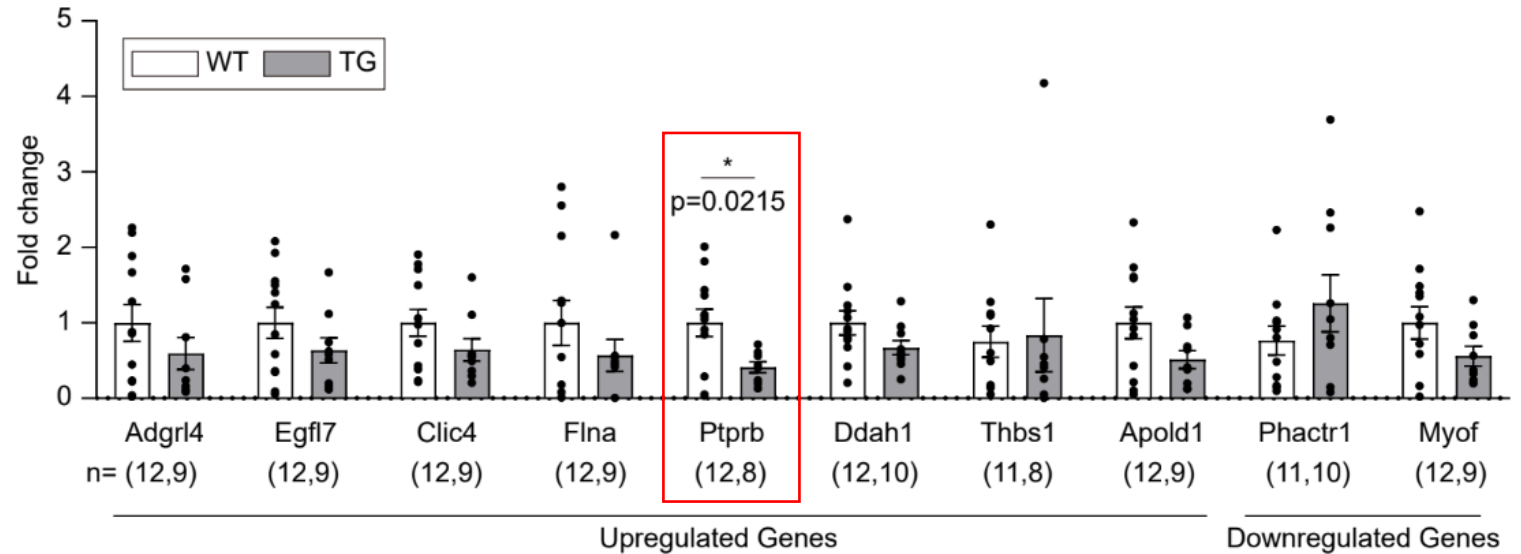
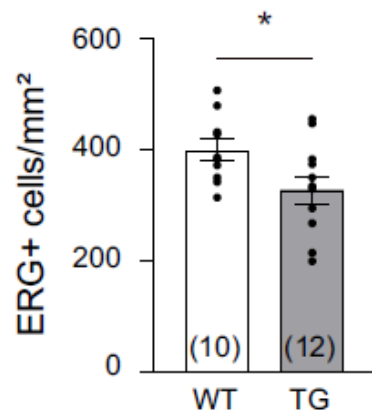
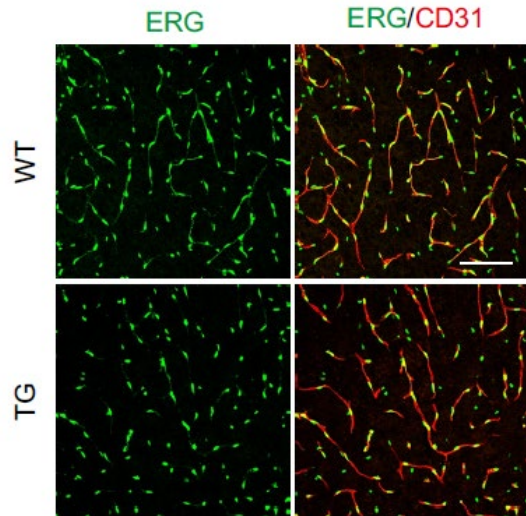
# No significant changes in the anticipated EC gene expression patterns at P10 due to the strong developmental variations

- Isolated P10 capillary endothelial cells from somatosensory cortex



# More apparent changes in the anticipated EC gene expression patterns at 1 month of age

- Isolated P30 capillary endothelial cells from somatosensory cortex



## Ptpnb (VE-PTP)

- Vascular endothelial protein tyrosine phosphatase
- Control vascular development and barrier function by regulating junctional proteins and signaling receptors

# Summary and Clinical relevance

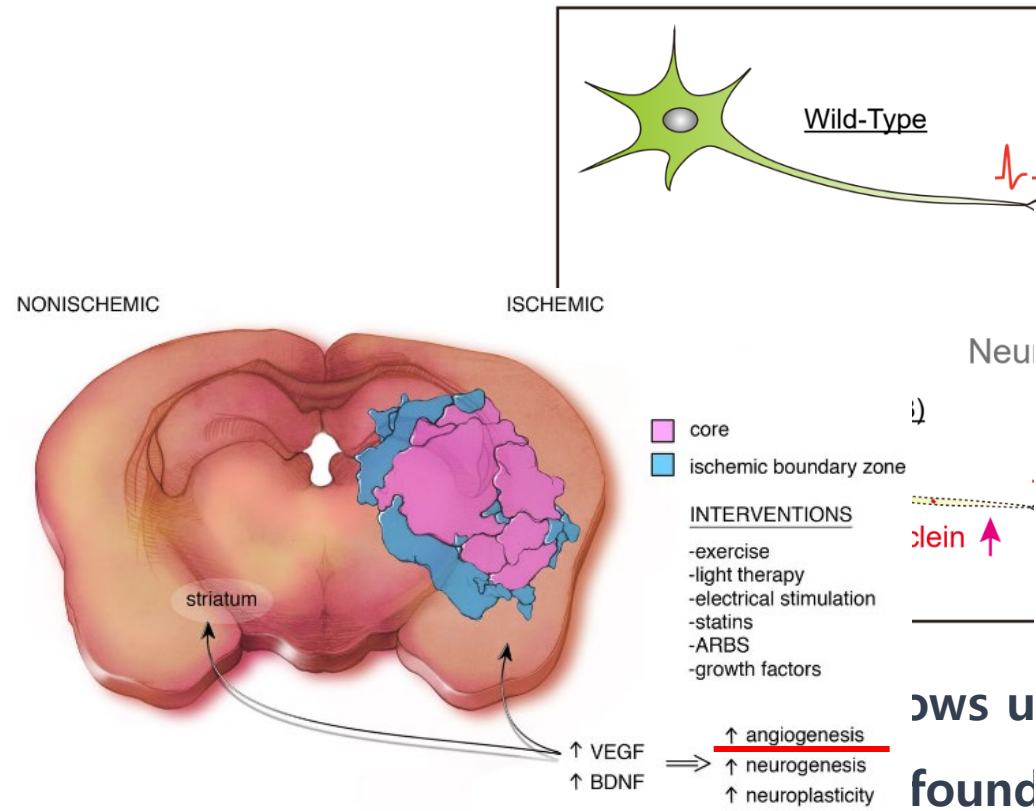


**Table 3.** Number of ischemic stroke events and the hazard ratio of stroke for the matched Parkinson's disease (PD) and non-PD groups.

|                                  | PD group             | Non-PD group        |
|----------------------------------|----------------------|---------------------|
| Variables                        | (N = 2204)           | (N = 2204)          |
| Ischemic stroke events, N        | 328                  | 156                 |
| Risk per 1000 person-yr (95% CI) | 70.9 (63.4 to 79.0)  | 30.2 (25.6 to 35.3) |
| Hazard Ratio (95% CI)            | 2.37 (1.92 to 2.93)* | 1.00                |

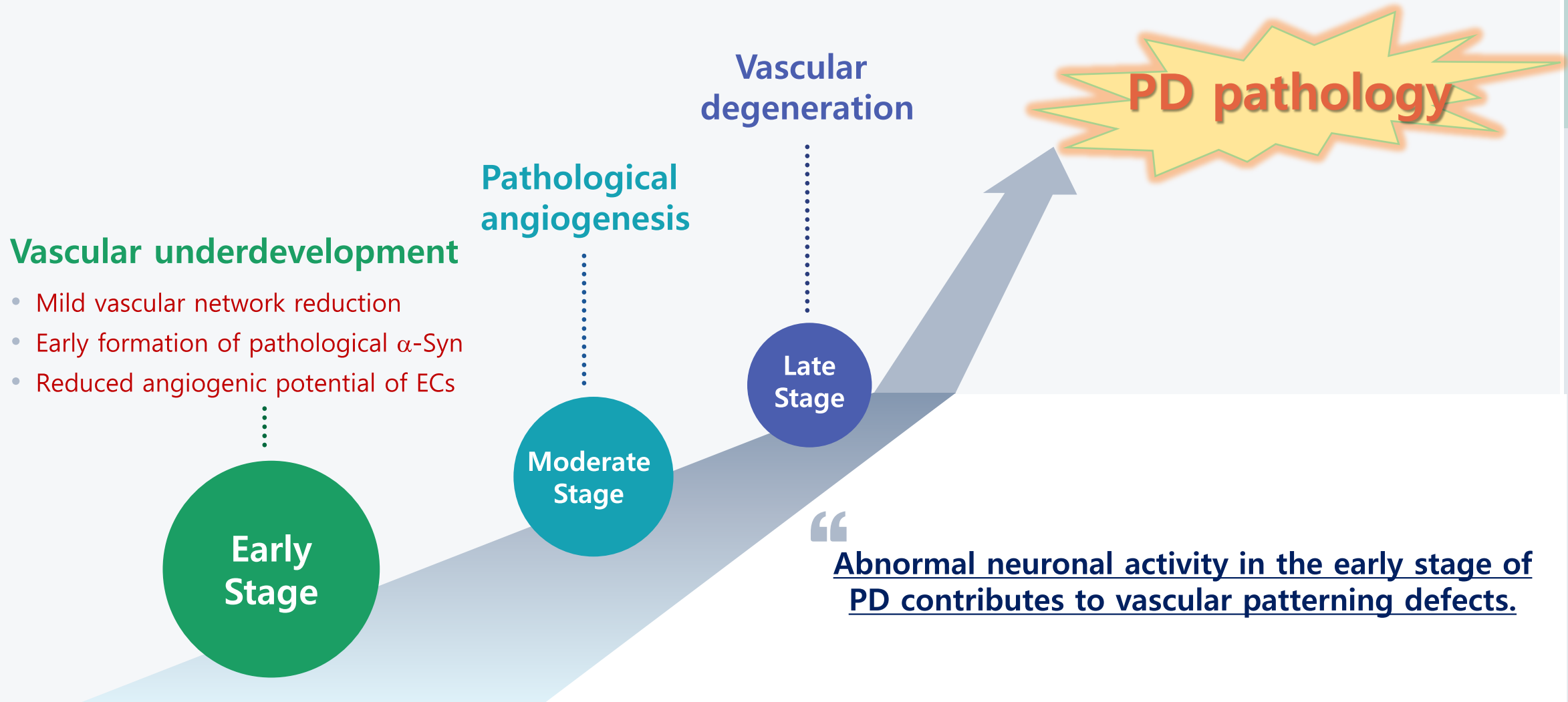
\*P<0.0001.

doi:10.1371/journal.pone.0068314.t003

activity in the early stage of PD

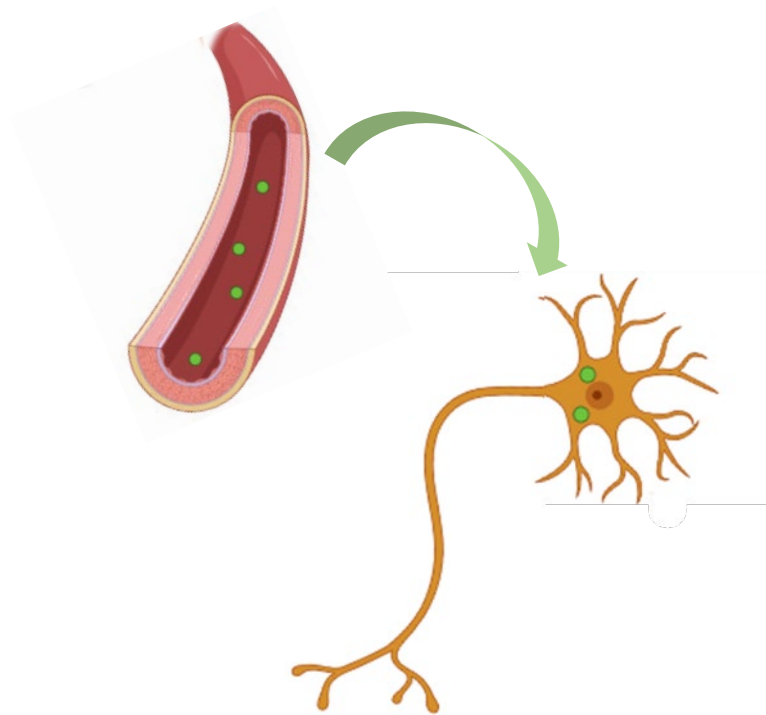
- Downregulation of neuronal activity can reduce angiogenic potential through changes in activity-dependent genes of endothelial cells

# New findings regarding cerebrovascular formation in PD

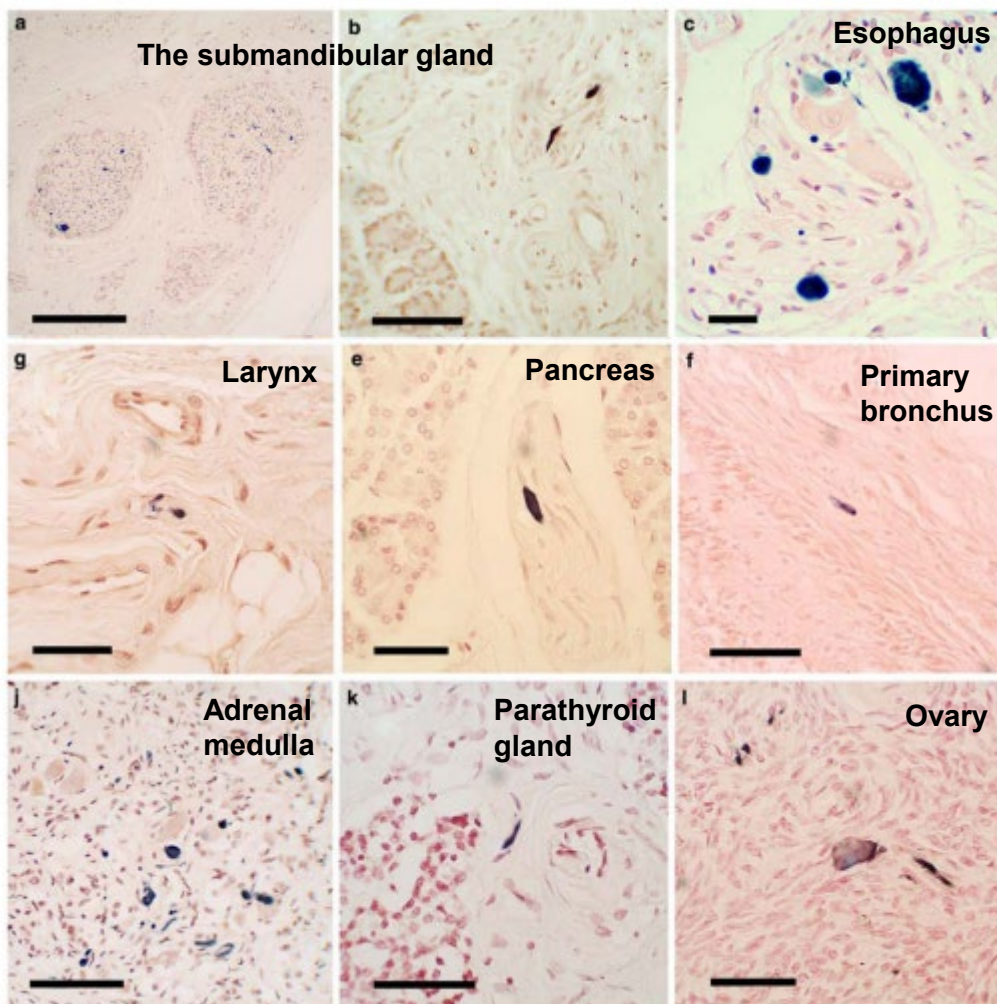


## Part II

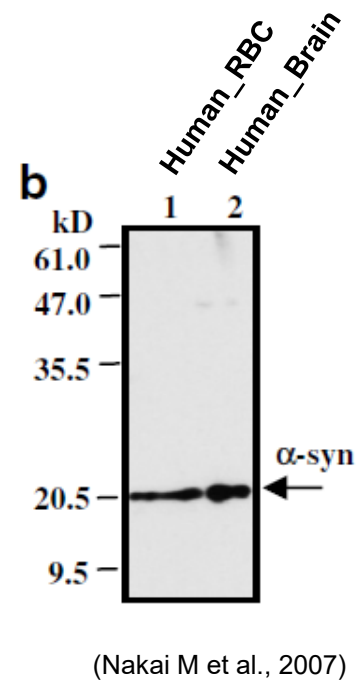
# Role of $\alpha$ -synuclein in the blood plasma in synucleinopathy



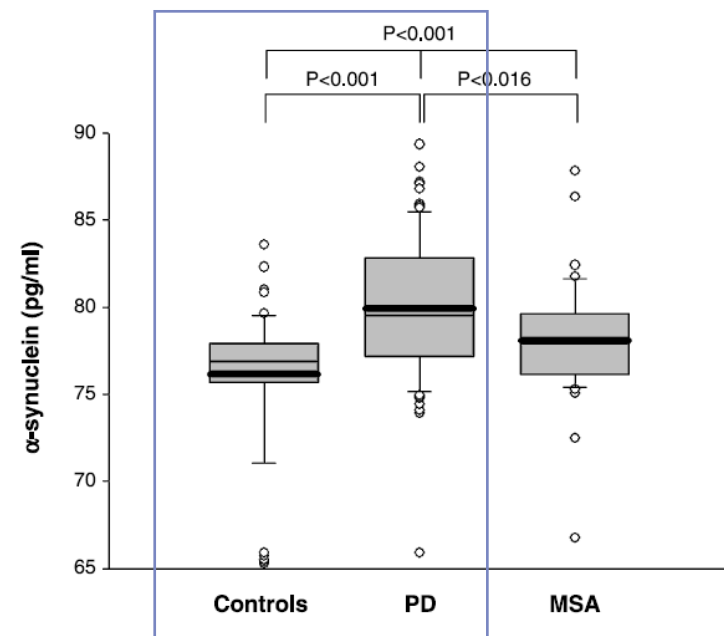
# Multi-organ distribution of $\alpha$ -synuclein including blood RBC



(Beach TG W et al., 2011)

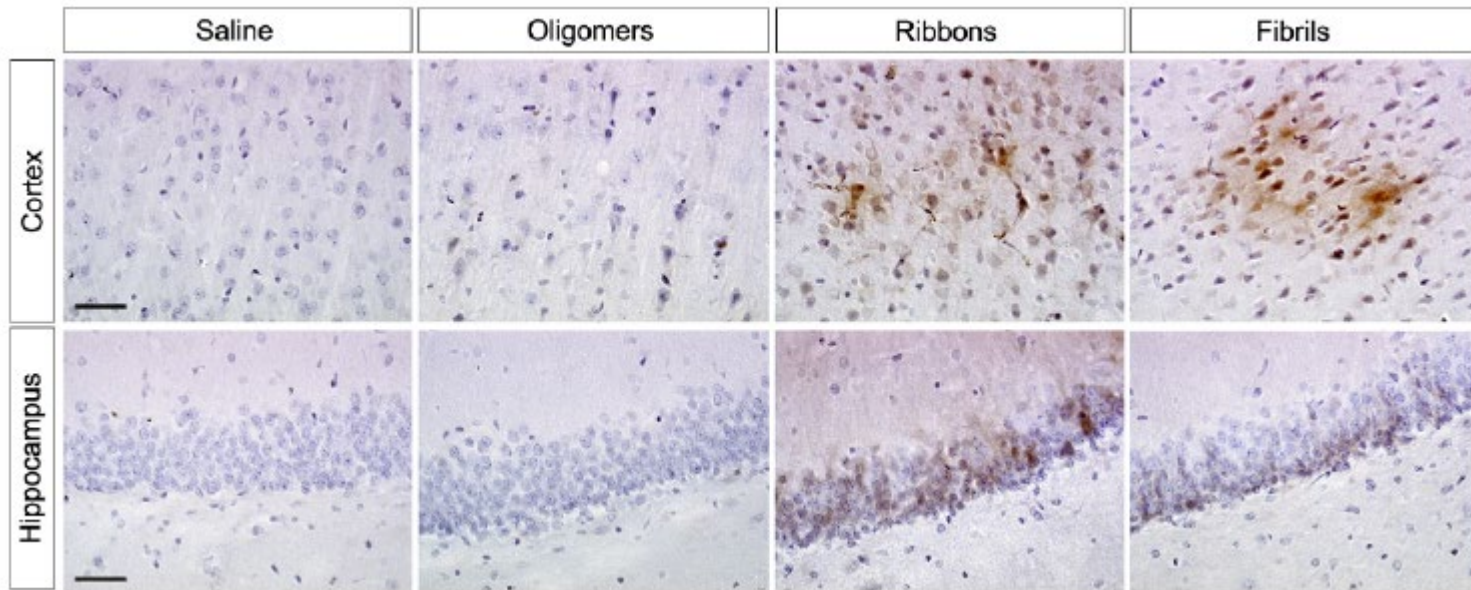


<Plasma>



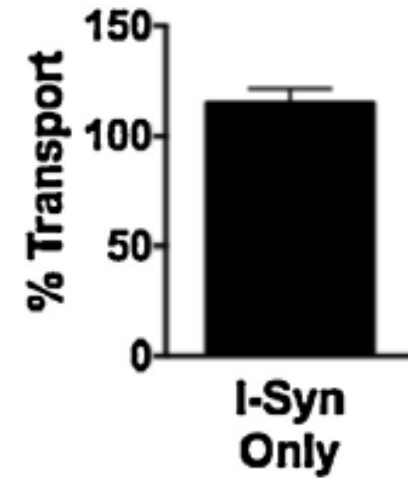
(Lee PH et al., 2006)

# Bi-directional movements of $\alpha$ -synuclein between blood and brain



(Peelaerts W et al., 2015)

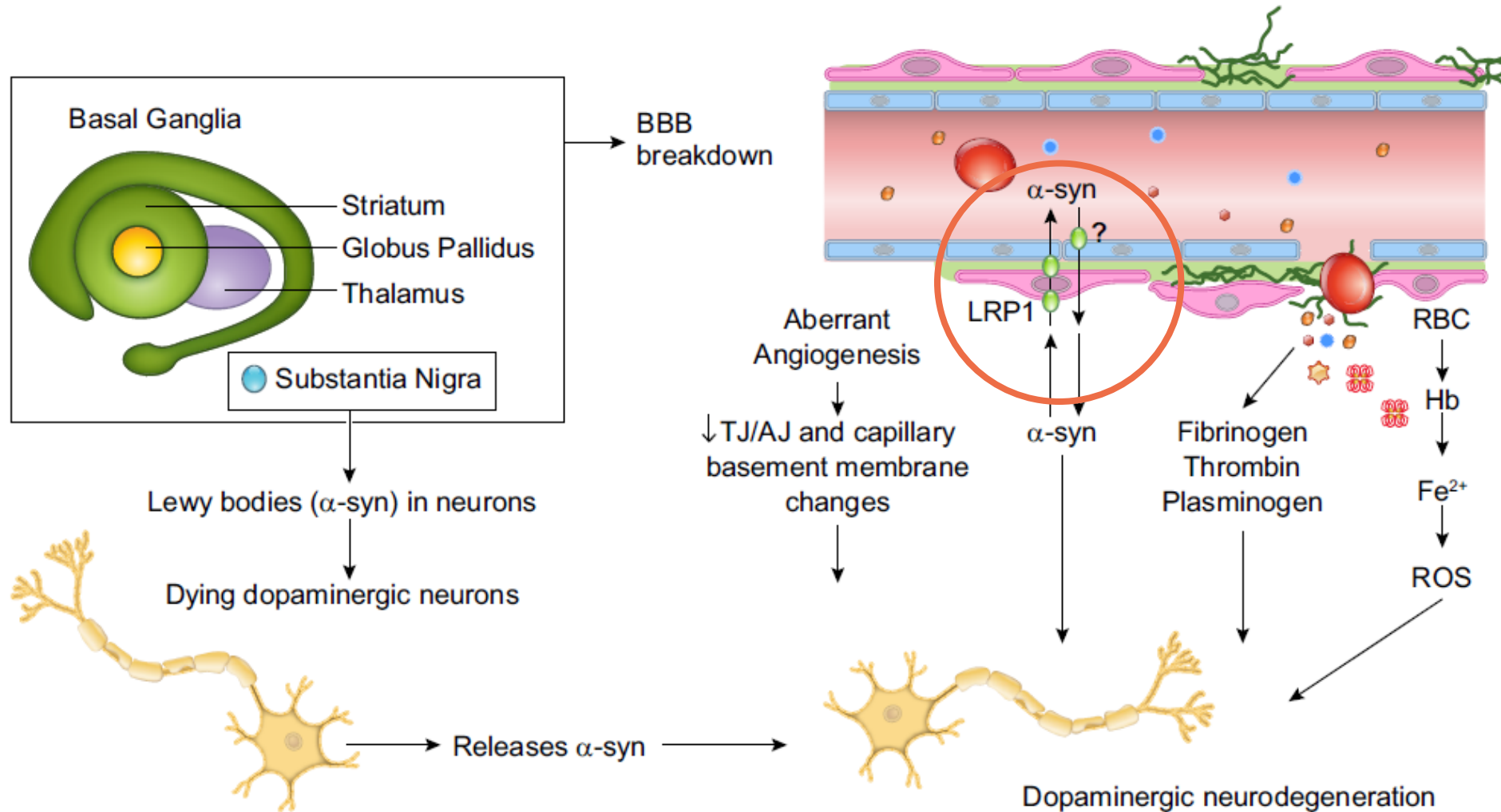
Blood to Brain



(Sui YT et al., 2014)

Brain to Blood

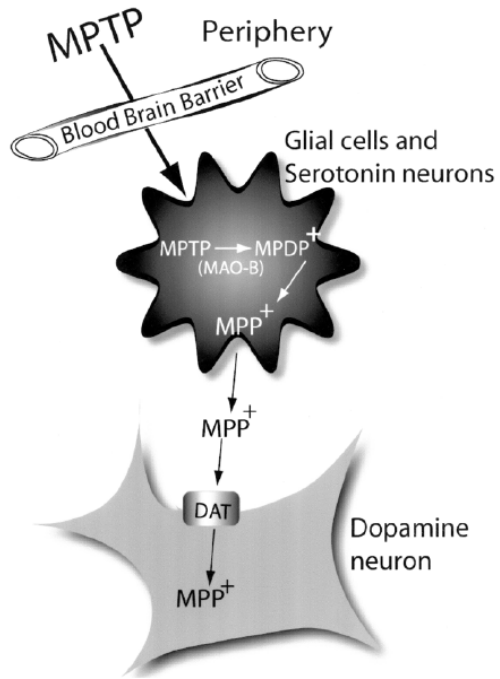
# PD progression via abnormal function of $\alpha$ -synuclein in the neurovascular system



(Sweeney MD et al., 2019)

# Current PD model systems

## Toxic-induced model



(Przedborski S W et al., 2003)

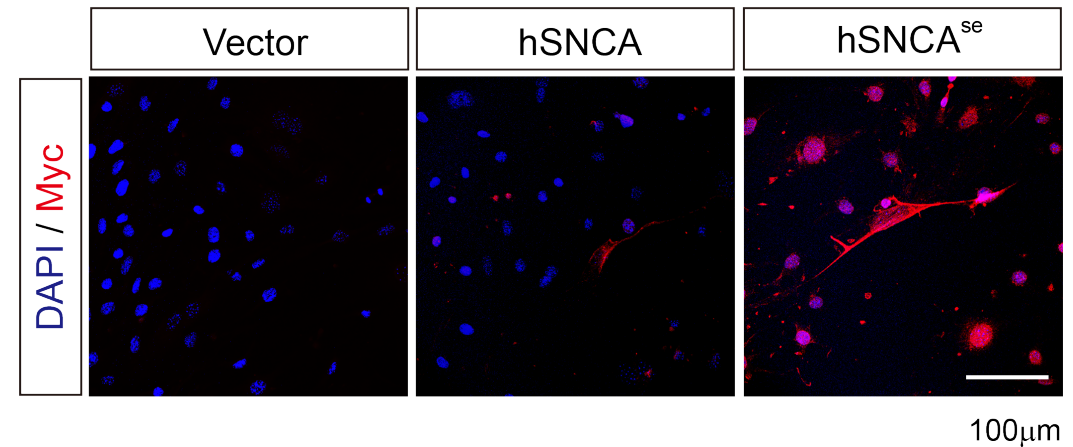
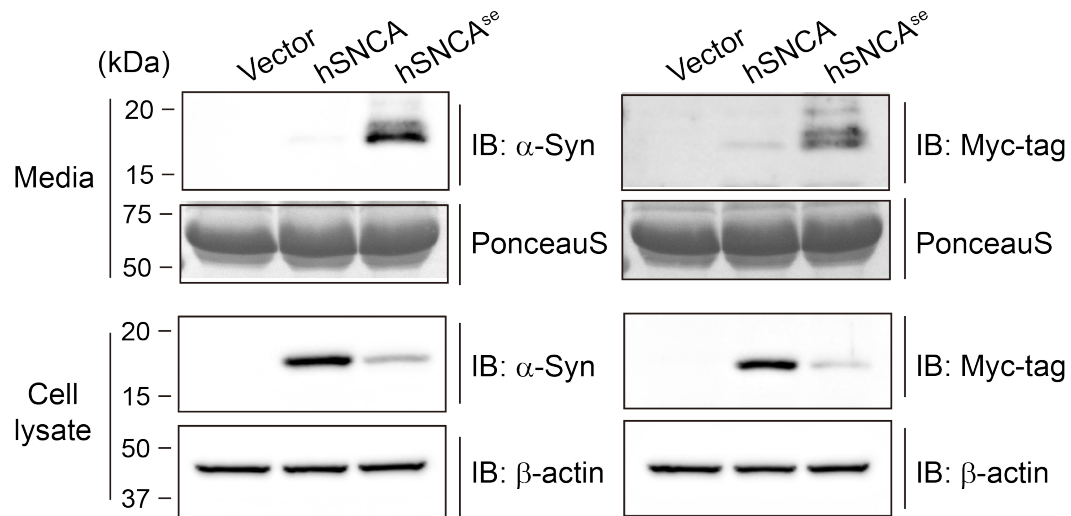
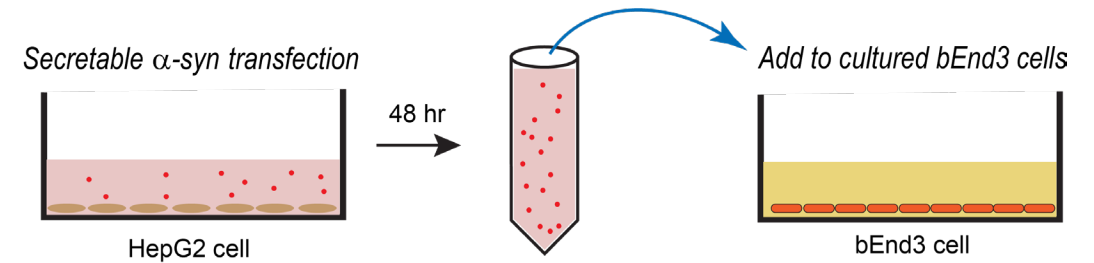
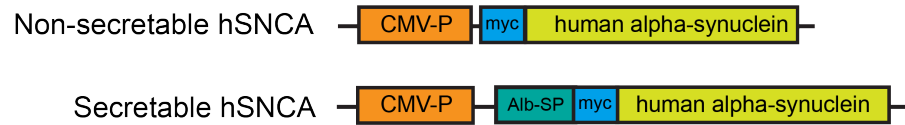
- Chemical ablation of dopaminergic neuron
- Recapitulate a sporadic PD
- Trigger motor defects
- Does not induce the LB formation

## Genetic model

| Model                   | Promoter | Endogenous protein | Synucleinopathy | Neurodegeneration | Motor deficits | Non-motor deficits |
|-------------------------|----------|--------------------|-----------------|-------------------|----------------|--------------------|
| SNCA                    |          |                    |                 |                   |                |                    |
| Mouse                   |          |                    |                 |                   |                |                    |
| msyn KO                 | —        | A                  | —               | Mild <sup>b</sup> | ND             | Y                  |
| PAC-hsyn-wt             | PAC      | A                  | ND              | ND                | ND             | ND                 |
| PAC-hA53T               | PAC      | A                  | Y <sup>a</sup>  | ND                | Y              | Y                  |
| PAC-hA30P               | PAC      | A                  | Y <sup>a</sup>  | ND                | ND             | Y                  |
| BAC-hsyn-A30P           | BAC      | A                  | ND              | ND                | ND             | ND                 |
| CAM-tTA-hwt             | Cam-tTA  | P                  | ND              | Mild              | Mild           | Y                  |
| CAM-tTA-hA53T           | Cam-tTA  | P                  | Y <sup>b</sup>  | ND <sup>c</sup>   | ND             | Y                  |
| PDGFb-hsyn-wt           | mPDGFb   | P                  | Y               | Y <sup>d</sup>    | Y              | Y                  |
| Pitx3-tTA-hsyn-A53T     | Pitx3    | P                  | Y               | Y                 | Y              | Y                  |
| Prp-hsyn-wt             | mPrp     | P                  | ND              | ND                | ND             | —                  |
| Prp-hsyn-A53T           | mPrp     | P                  | Y <sup>e</sup>  | Y <sup>b</sup>    | Y <sup>b</sup> | Y                  |
| Prp-hsyn-E46K           | mPrp     | P                  | Y <sup>e</sup>  | ND                | Y <sup>b</sup> | —                  |
| ROSA26-hsyn-wt(1-119)   | mROSA26  | P                  | —               | ND                | —              | —                  |
| ROSA26-hsyn-A53T(1-119) | mROSA26  | P                  | —               | ND                | —              | —                  |
| ROSA26-hsyn-E46K(1-119) | mROSA26  | —                  | —               | —                 | —              | —                  |
| TH-hsyn-wt              | rTH      | A/P <sup>f</sup>   | ND              | Y <sup>b</sup>    | ND             | —                  |
| TH-hsyn-wt(1-120)       | rTH      | P                  | Y               | ND                | Y <sup>b</sup> | —                  |
| TH-hsyn-A53T            | rTH      | P                  | ND              | ND                | ND             | —                  |
| TH-hsyn-A53T(1-130)     | rTH      | P                  | NR              | Y                 | Y              | —                  |
| TH-hsyn-A30P            | rTH      | P                  | ND              | ND                | —              | —                  |
| TH-hsyn-A53T/A30P       | rTH      | P                  | ND              | ND                | N              | —                  |
| THy1-hwt                | mThy1    | P                  | Y <sup>b</sup>  | Y <sup>d</sup>    | Y <sup>b</sup> | Y                  |
| Thy1-hsyn-A53T          | mThy1    | P                  | Y <sup>b</sup>  | Y <sup>b</sup>    | Y <sup>g</sup> | —                  |
| THy1-hsyn-A30P          | mThy1    | P                  | Y <sup>e</sup>  | ND                | Y <sup>g</sup> | Y                  |

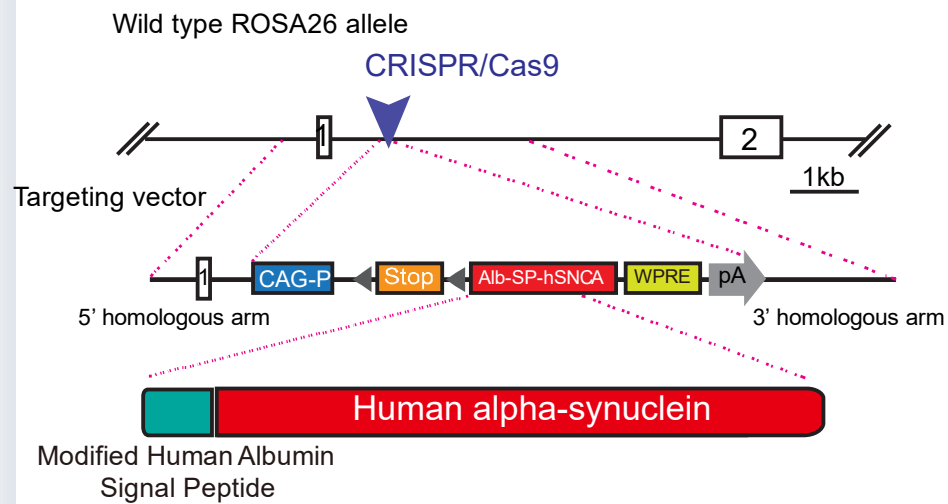
(Breger LS et al., 2018)

# Secretable $\alpha$ -synuclein by attaching signal peptide

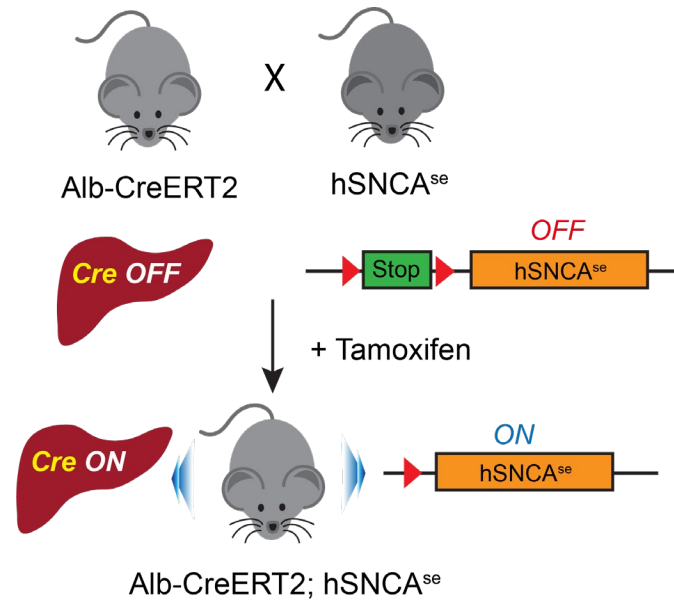


# Generation of secretable human $\alpha$ -synuclein mouse model (hSNCA<sup>se</sup>) to increase blood $\alpha$ -synuclein level via liver

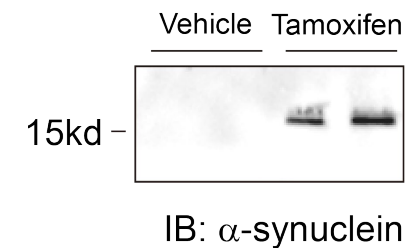
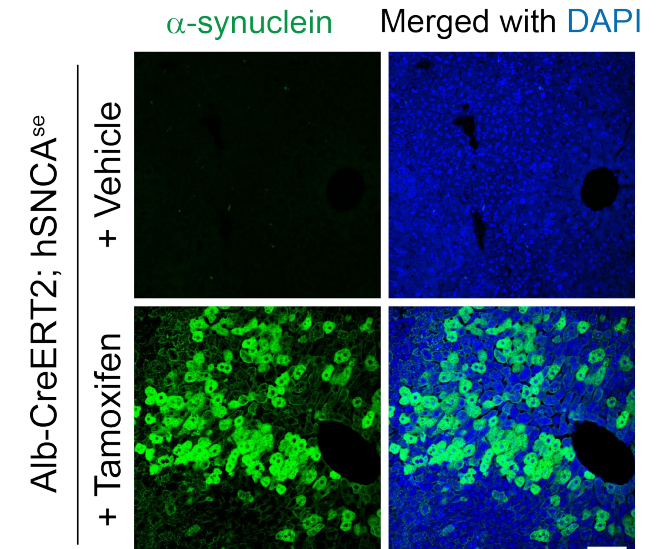
## hSNCA<sup>se</sup> Mouse targeting scheme



## Breeding scheme



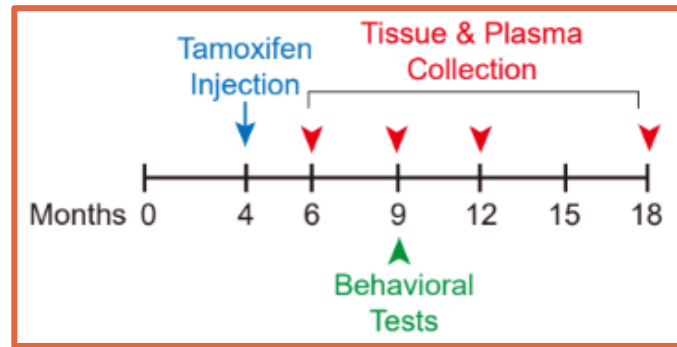
## Liver



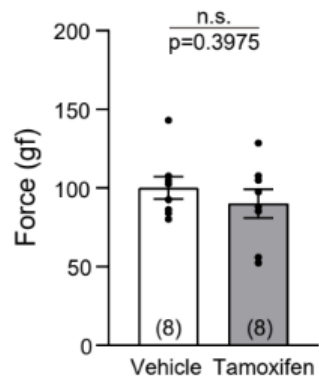
## Blood

(Jeong JY & Kim N et. al., 2025, npj Parkinson's Disease)

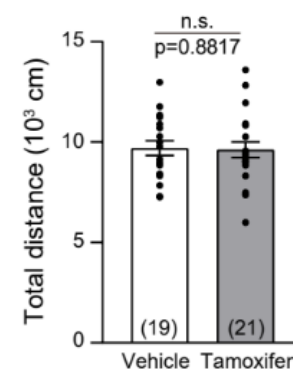
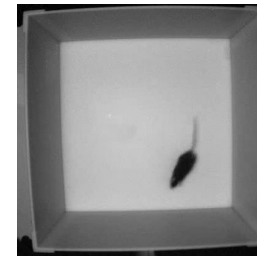
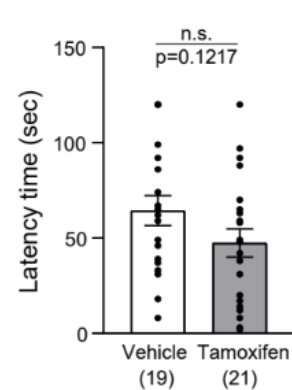
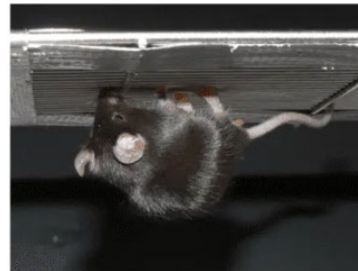
# Elevation of human $\alpha$ -synuclein in blood does not induce behavioral defects



## Grip strength assay

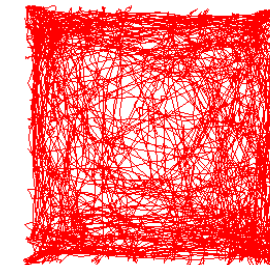


## Wire hanging test

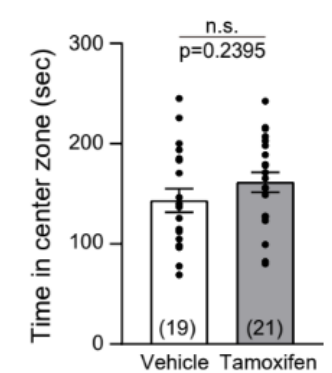
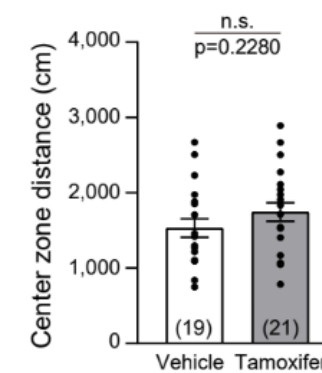


## Open field test

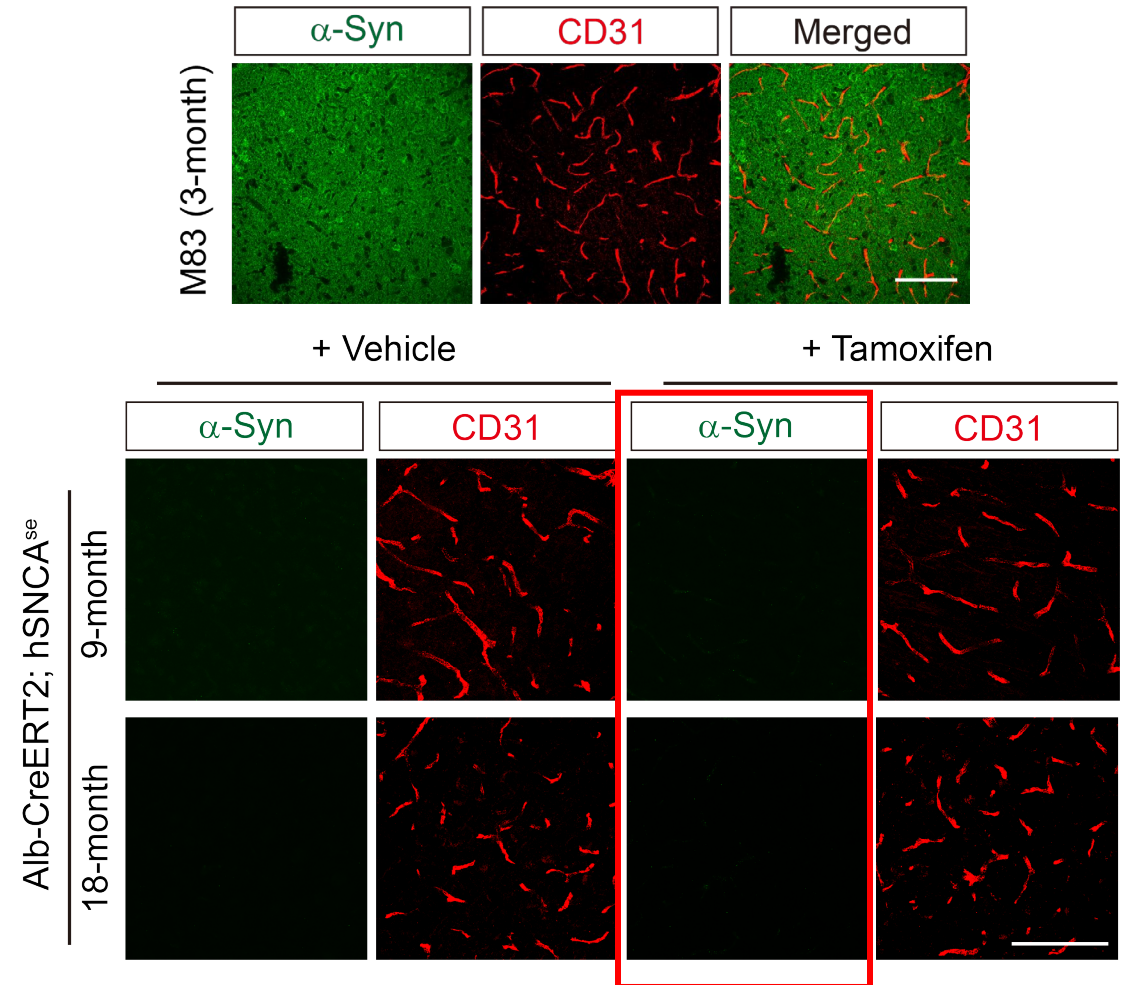
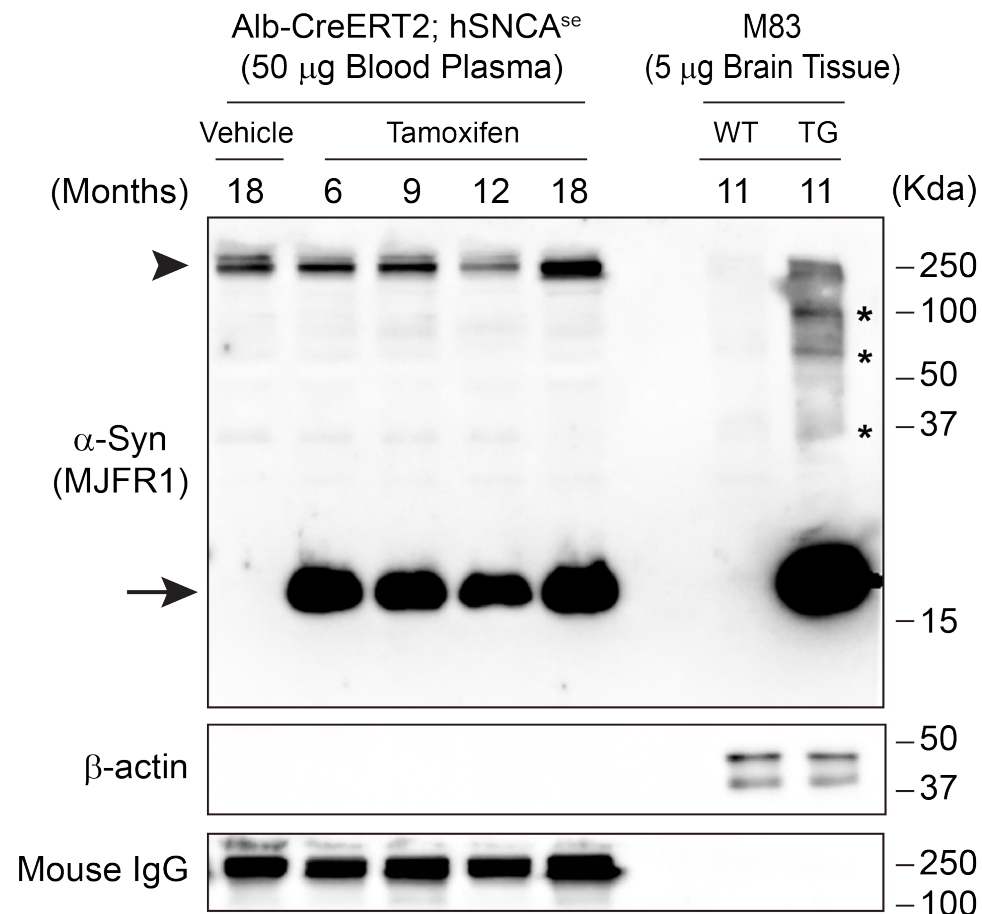
Vehicle



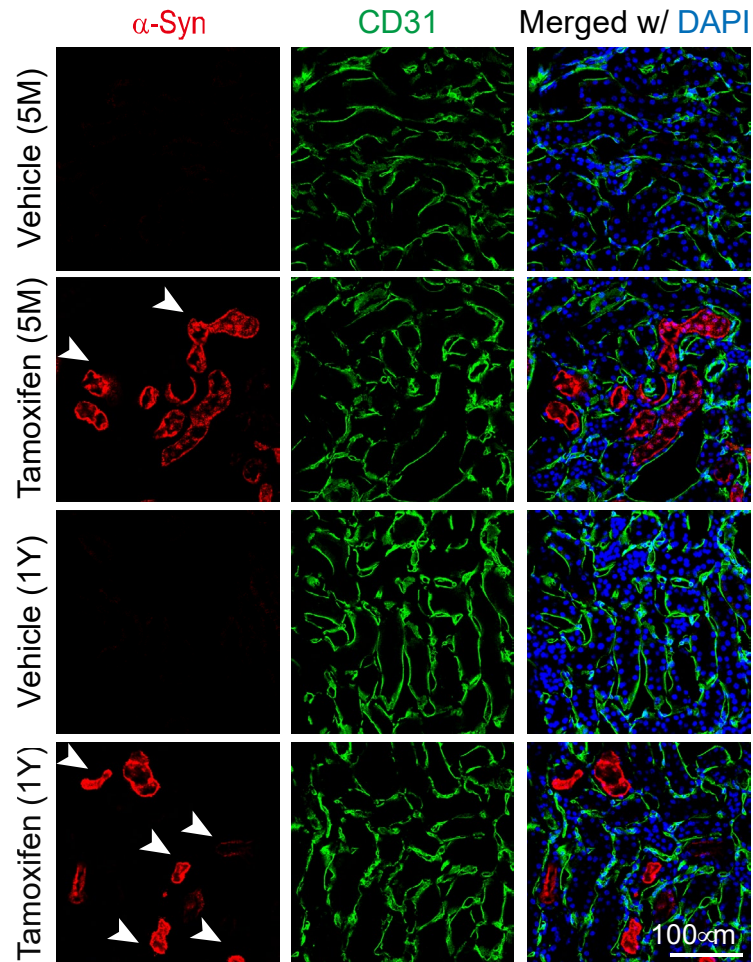
Tamoxifen



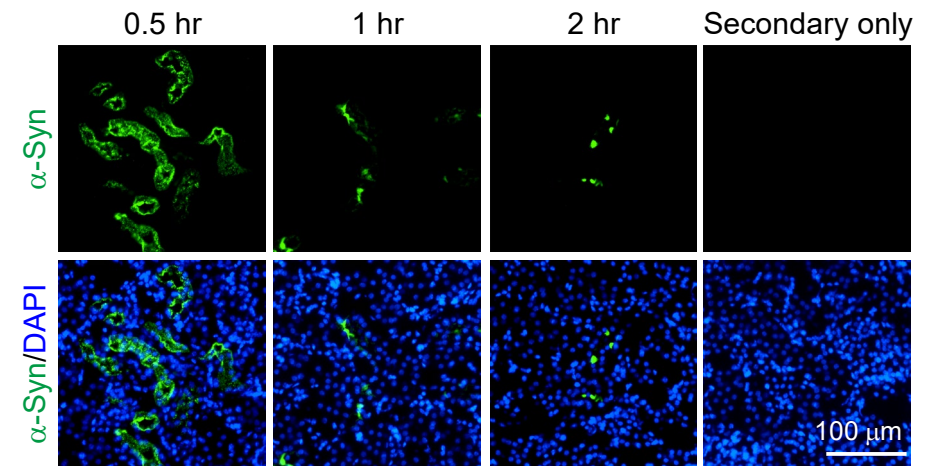
# Elevated levels of human $\alpha$ -synuclein in the blood do not cause pathological aggregation of $\alpha$ -synuclein or its entry into the brain



# Rapid elimination of plasma $\alpha$ -synuclein via kidney



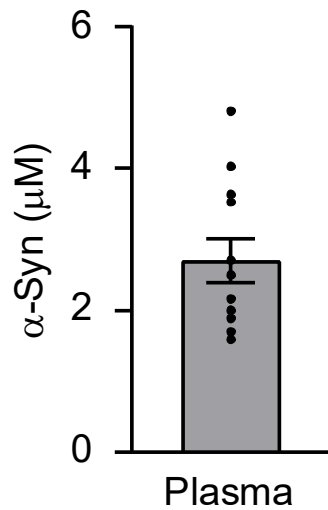
## Tracing injected $\alpha$ -synuclein in Kidney



# What factors prevent hSNCA<sup>se</sup> mice from exhibiting pathological symptoms?

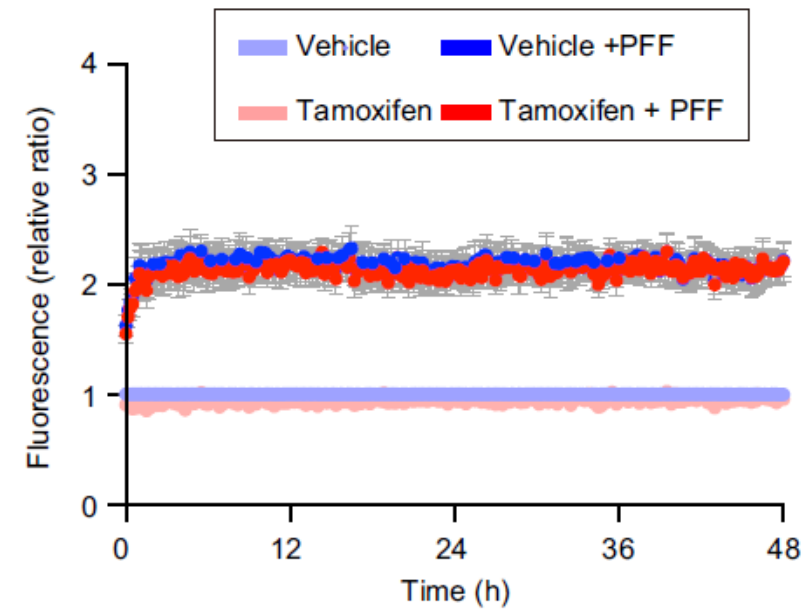
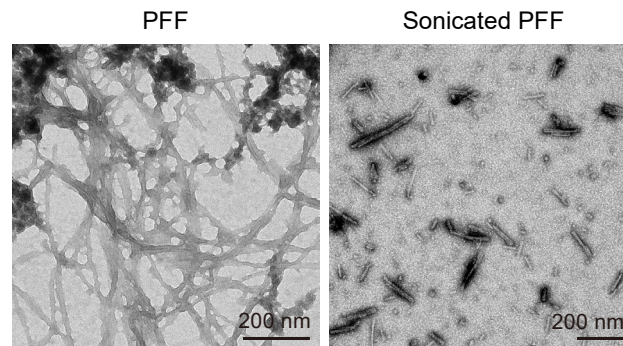
in vitro aggregation study (Afitska K. et al., 2019)

- Critical concentration of  $\alpha$ -synuclein fibril growth is  $\sim 0.4 \mu\text{M}$  in the presence of seeds
- Without seeds, fibrils are formed only at monomer concentrations higher than  $10 \mu\text{M}$



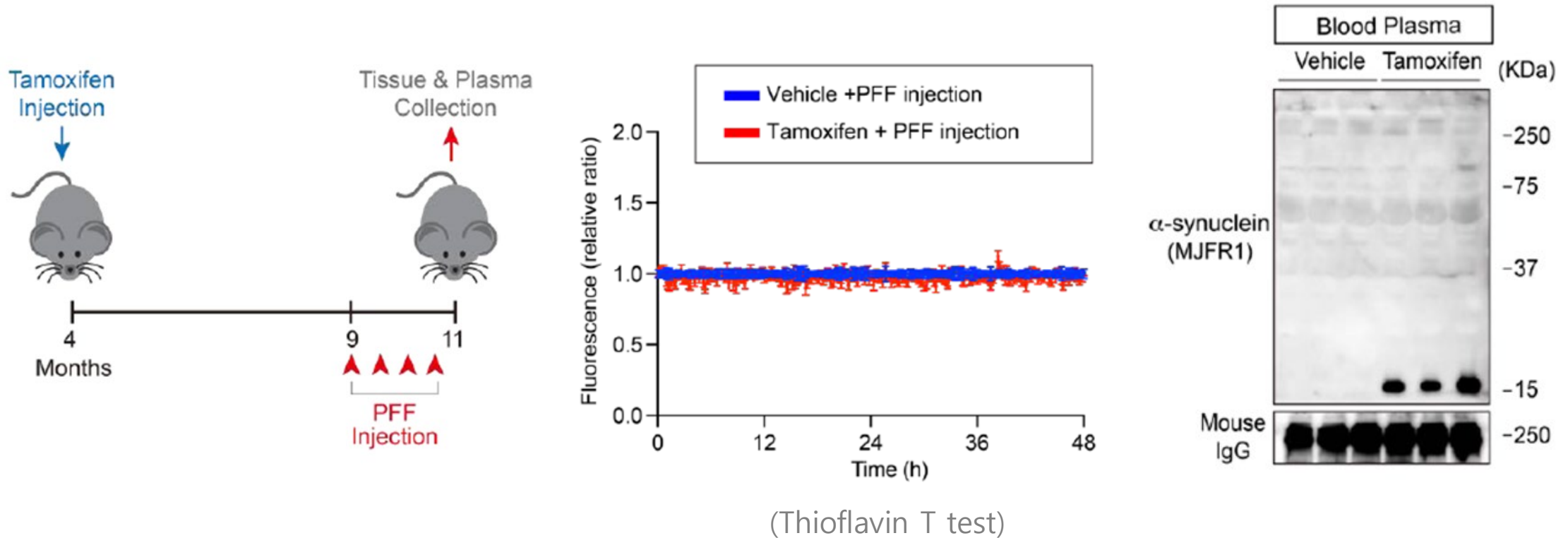
**N=10,  $\sim 2.7 \mu\text{M}$**

Prefibrillar form of  $\alpha$ -synuclein



(Thioflavin T test)

# Intravenous administration of $\alpha$ -synuclein PFF showed no detectable aggregation



# What factors prevent hSNCA<sup>se</sup> mice from exhibiting pathological symptoms?

## Single-Molecule Characterization of the Interactions between Extracellular Chaperones and Toxic $\alpha$ -Synuclein Oligomers

Daniel R. Whiten,<sup>1,2</sup> Dezeray Cox,<sup>2,4</sup> Mathew H. Horrocks,<sup>1,2,5,6</sup> Christopher G. Taylor,<sup>1</sup> Suman De,<sup>1</sup> Patrick Flagmeier,<sup>1</sup> Laura Tosatto,<sup>1,7</sup> Janet R. Kumita,<sup>1</sup> Heath Ecroyd,<sup>2</sup> Christopher M. Dobson,<sup>1</sup> David Klenerman,<sup>1,3,8,\*</sup> and Mark R. Wilson<sup>2,\*</sup>

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<sup>7</sup>Present address: Centre for Integrative Biology, Università degli Studi di Trento, via Sommarive 9, 38123 Trento, Italy

<sup>8</sup>Lead Contact

*Cell Reports (2018)*

## Cerebrospinal fluid lipoproteins inhibit $\alpha$ -synuclein aggregation by interacting with oligomeric species in seed amplification assays

Giovanni Bellomo<sup>1\*</sup>, Silvia Paciotti<sup>1</sup>, Luis Concha-Marambio<sup>2</sup>, Domenico Rizzo<sup>3,4</sup>, Anna Lidia Wojdata<sup>1</sup>, Davide Chiasserini<sup>5</sup>, Leonardo Gatticchi<sup>5</sup>, Linda Cerofolini<sup>3,6</sup>, Stefano Giuntini<sup>3</sup>, Chiara Maria Giulia De Luca<sup>7</sup>, Yihua Ma<sup>2</sup>, Carly M. Farris<sup>2</sup>, Giuseppe Pieraccini<sup>8</sup>, Sara Bologna<sup>3</sup>, Marta Filidei<sup>1</sup>, Enrico Ravera<sup>3,4,6</sup>, Moreno Lelli<sup>3,4,6</sup>, Fabio Moda<sup>7</sup>, Marco Fragai<sup>3,4,6</sup>, Lucilla Parnetti<sup>1</sup> and Claudio Luchinat<sup>3,4,6\*</sup>

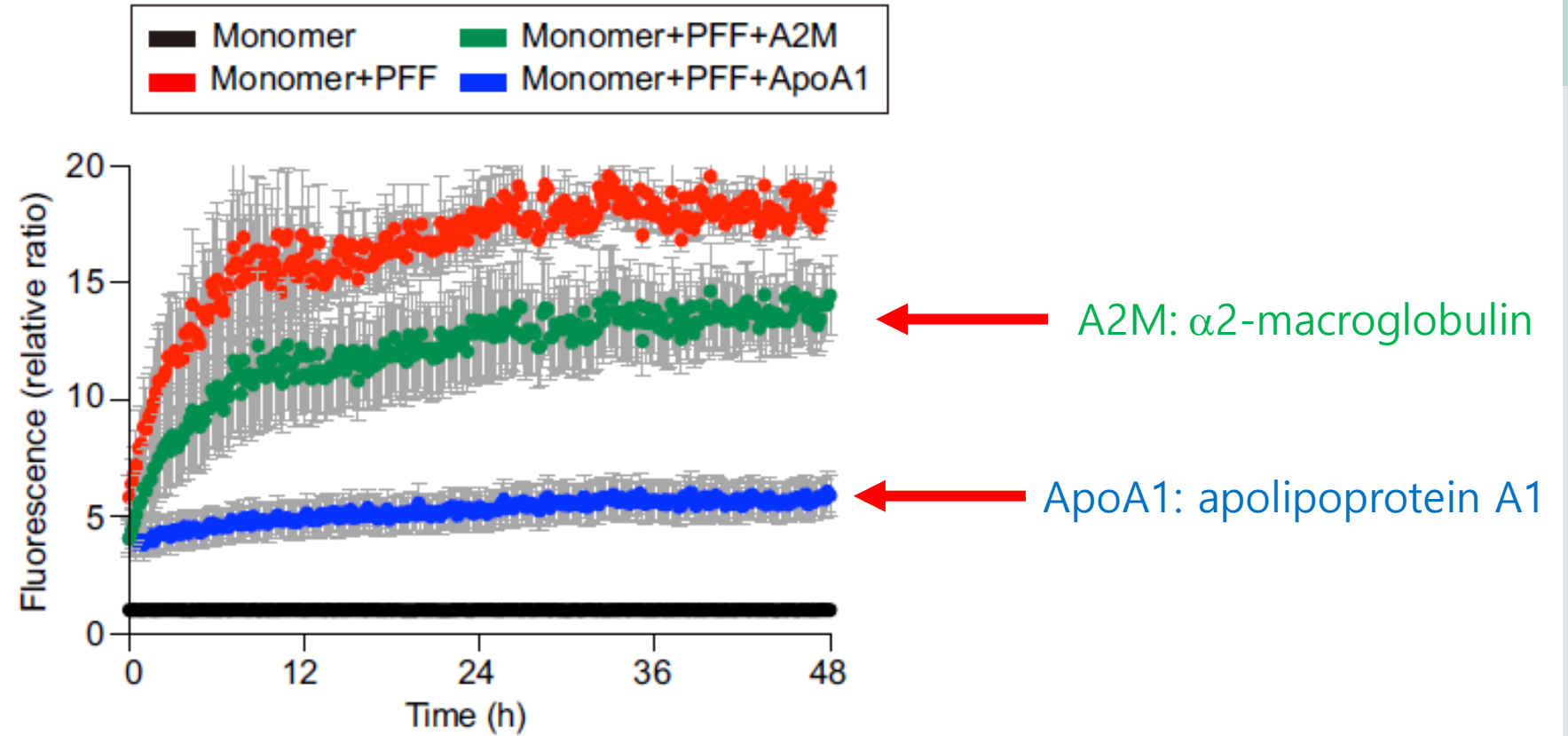
*Molecular Neurodegeneration (2023)*



**Some extracellular proteins interact with  $\alpha$ -synuclein to prevent its pathological aggregation and toxicity**



# Apolipoprotein A1 dramatically suppressed $\alpha$ -synuclein aggregation



# Summary

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- A recent meta-analysis of 32 published article examining blood  $\alpha$ -synuclein levels in PD patients revealed a significant increase in total  $\alpha$ -synuclein levels in PD patients (Zubelzu, M. et. al., 2022, *Park. Relat. Disord*)
  - Elevated levels of  $\alpha$ -synuclein exclusively in the blood do not seem to induce PD pathology under healthy conditions
- Both monomeric and oligomeric forms of  $\alpha$ -synuclein can be released in the extracellular space through unconventional exocytosis (Lee, H.-J. et. al., 2005, *J. Neurosci*; Wu, S. et. al., 2023, *eLife*)
  - *hSNCA*<sup>se</sup> mouse model could be a good system to investigate the pathological mechanism of extracellular  $\alpha$ -synuclein

*In a groundbreaking study that challenges long-standing assumptions in neurodegenerative research, scientists have unveiled compelling evidence indicating that elevated levels of alpha-synuclein protein in the plasma are not a requisite factor for the development or progression of Parkinson's disease pathology.* This revelation, published in the prestigious npj Parkinson's Disease journal, marks a significant departure from decades of prevailing thought that positioned alpha-synuclein accumulation as a central driver and biomarker of Parkinson's disease (.....)

The study's findings underscore an evolving paradigm in Parkinson's disease research where the pathophysiological landscape is perceived with greater sophistication, recognizing the limitations of oversimplified biomarkers. They stimulate a broader conversation about the reliability of peripheral fluid markers in reflecting brain-specific disease processes across neurodegenerative diseases, inviting comparative studies and cross-disease insights (.....)

Ultimately, this study charts a new course for future investigations aiming to identify truly representative biomarkers and develop precision therapies. *By challenging entrenched dogma, it empowers researchers to think beyond conventional frameworks and embrace new scientific horizons that promise better diagnostic and therapeutic outcomes for patients afflicted by Parkinson's disease* (.....)

*Scienmag, Aug 4<sup>th</sup>, 2025*

# Acknowledgements

## KBRI **Neurovascular Biology** Lab (Current Lab members)

- Namsuk Kim, PhD
- Yan Li, PhD
- Eunyoung Choi, MS
- Jun-Mo Moon, MS

## (Former Lab member)

- Jin-Young Jeong, PhD

## Funding

- KBRI Intramural Grants (KBRI 25-BR-01-02, 25-BR-05-06)
- Korea NRF (2020M3E5D9079766, 2022M3E5E8017701)



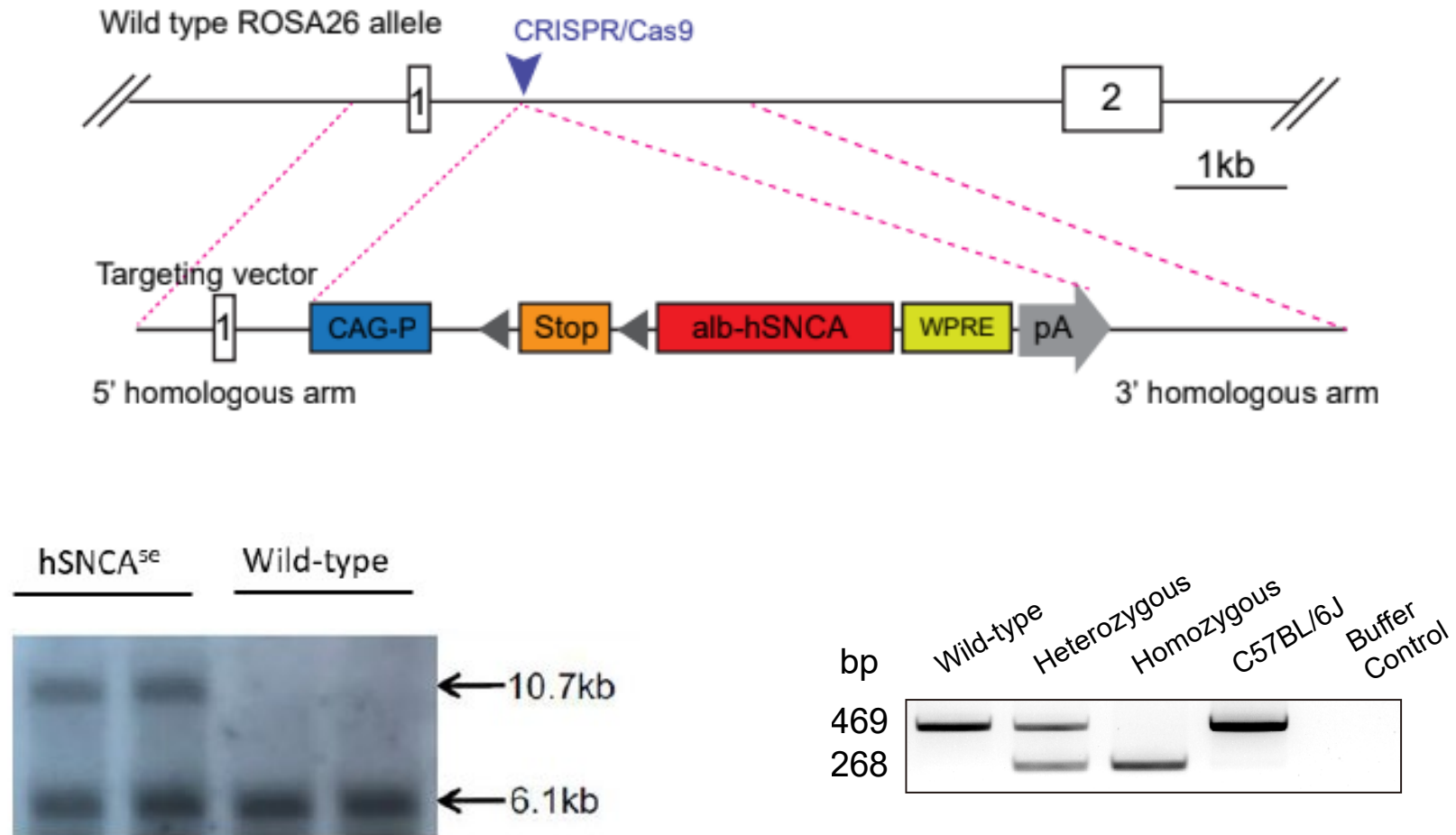
## Collaborators

- Jong-Cheol Rah, PhD (KBRI)
- Hyong-Kyu Kim, PhD  
Doo-Jin Kim, PhD  
(Chungbuk National Univ.)



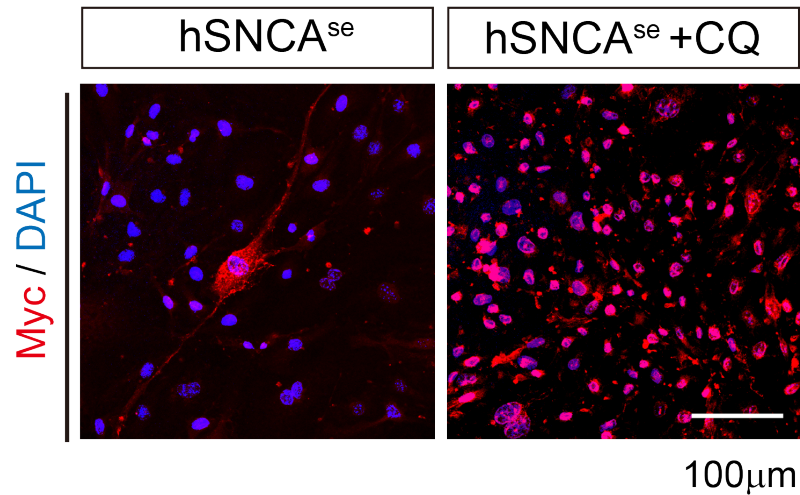
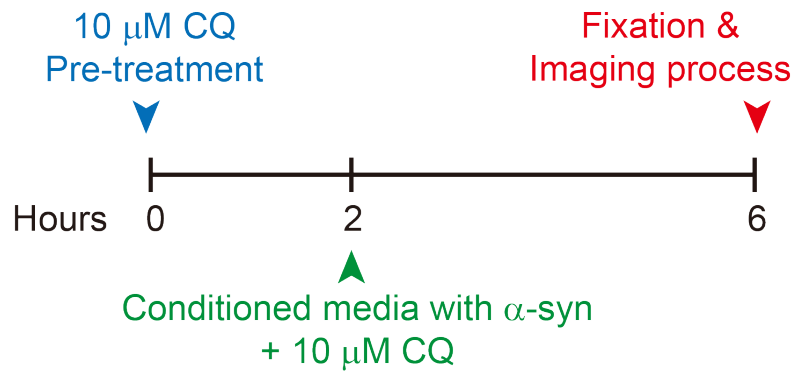
Q & A

# Generation of secretable human $\alpha$ -synuclein mouse model (hSNCA<sup>se</sup>)

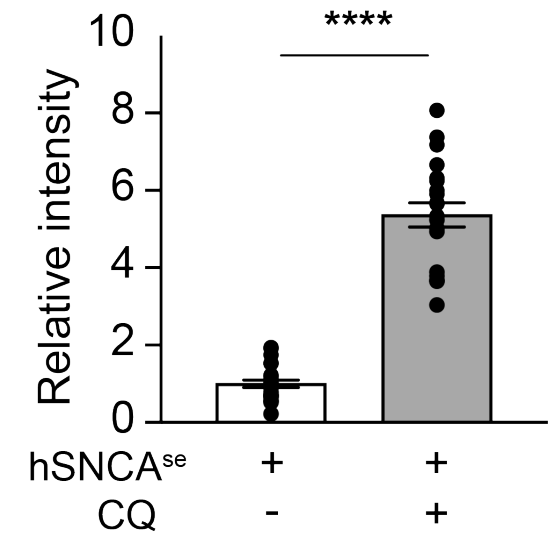


(Jeong JY & Kim N et. al., 2025, npj Parkinson's Disease)

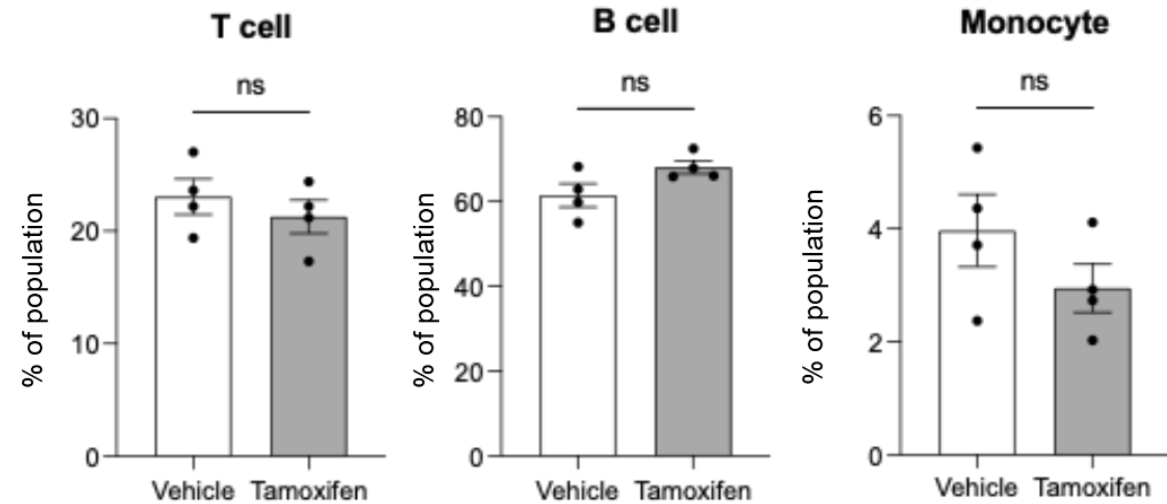
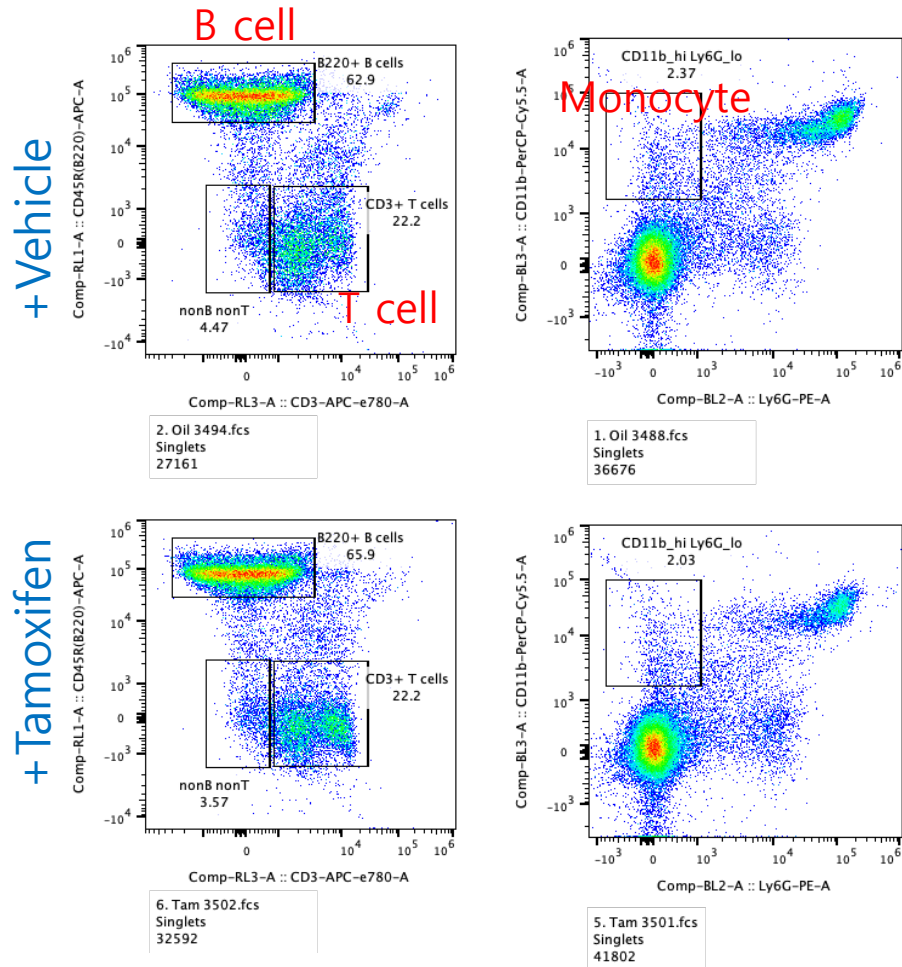
# Rapid degradation of endocytosed $\alpha$ -synuclein in brain ECs



\*Chloroquine: Lysosomal inhibitor



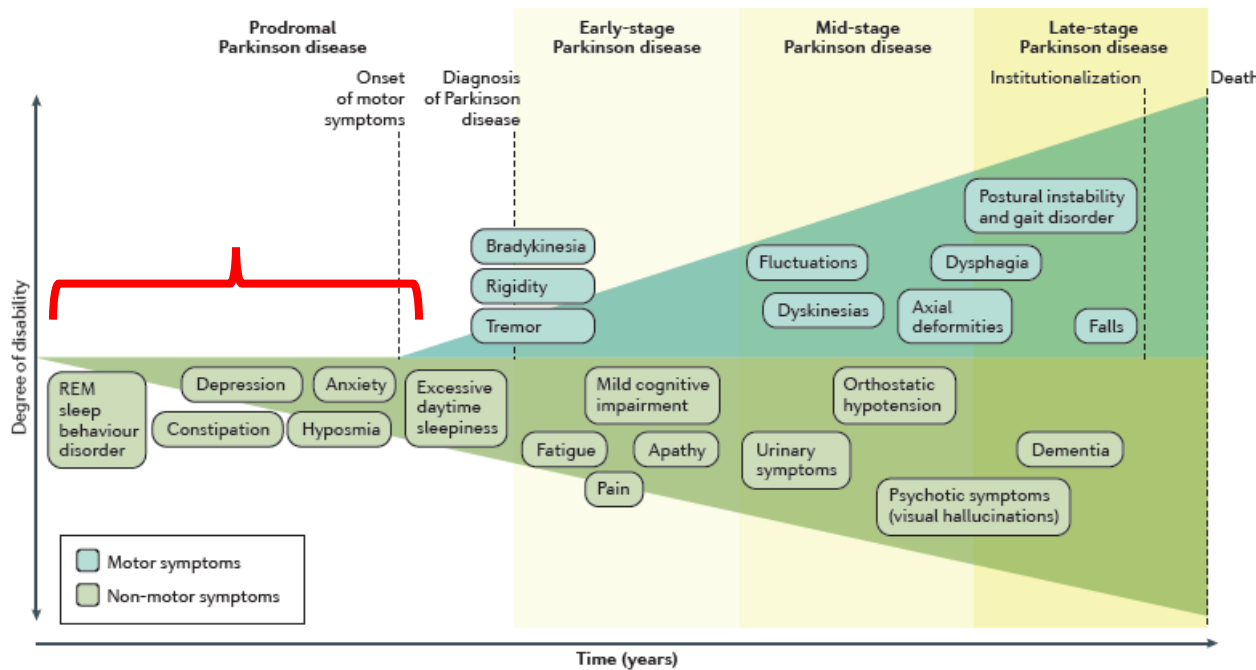
# No significant activation of immune cells in the secreted $\alpha$ -Syn model



By Doo-Jin Kim, PhD, Chungbuk Nat. Univ.

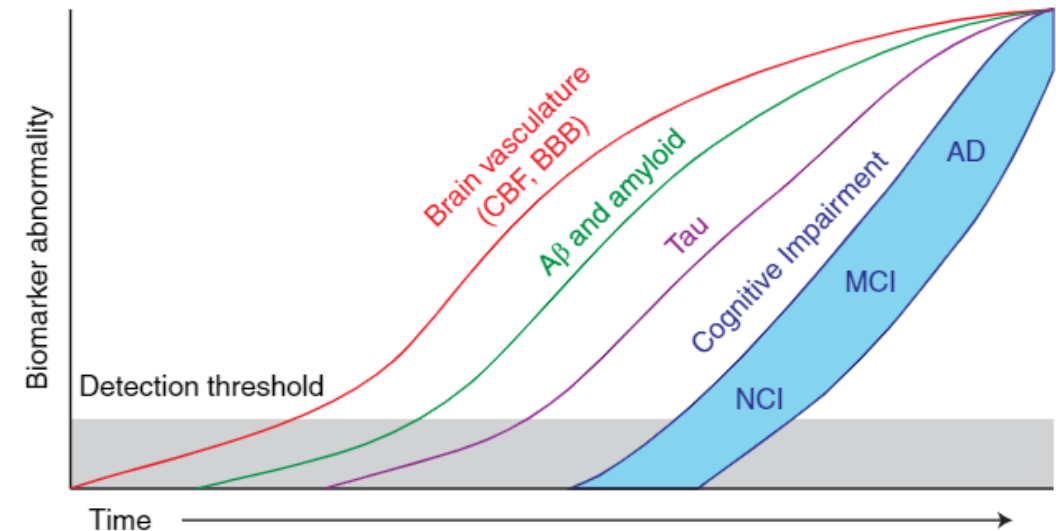
# Possibility of vascular dysfunction as an etiologic factor for early onset of PD

## Clinical symptoms associated with PD



(Poewe W et al., 2017)

## Hypothetical model of Alzheimer's disease (AD) biomarker changes



(Sweeney MD et al., 2018)

