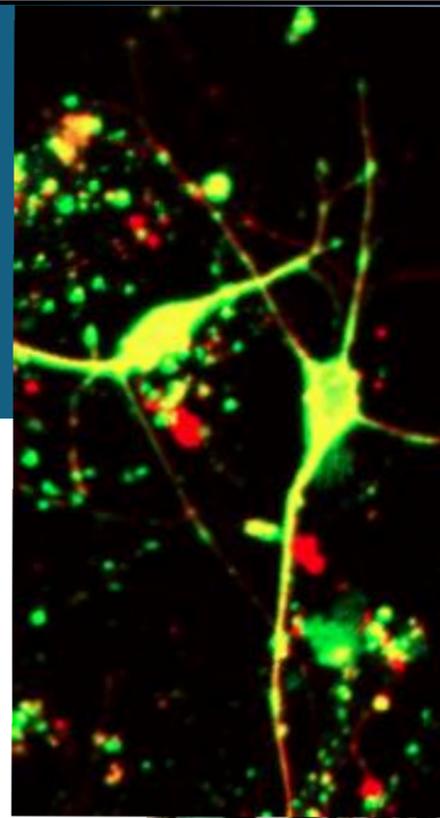


"Protective/Regenerative Activity of iron chelators DFP, DFO and DPD on neuritic degeneration of dopaminergic neurons in PD"



Patricio Pérez Henríquez

BCMN Program
Advisor: Dr. Marco Tulio Nuñez



*Iron and Aging Biology Laboratory
Department of Biology
Faculty of Sciences
University of Chile*

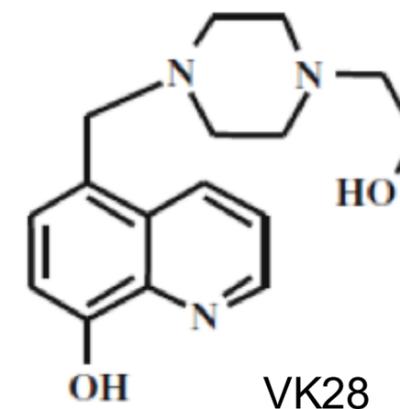
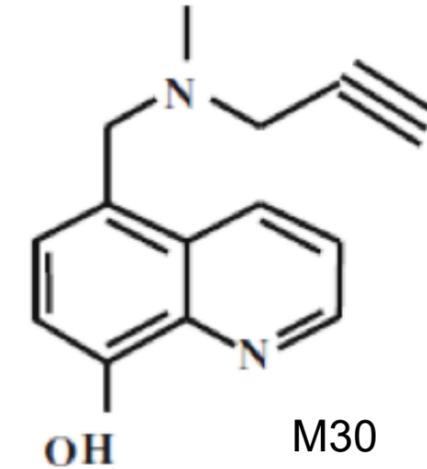
Parkinson's Treatments

- Levodopa
- Surgery
- Selegiline
- Amantadine
- Benztropine
- Rasagiline

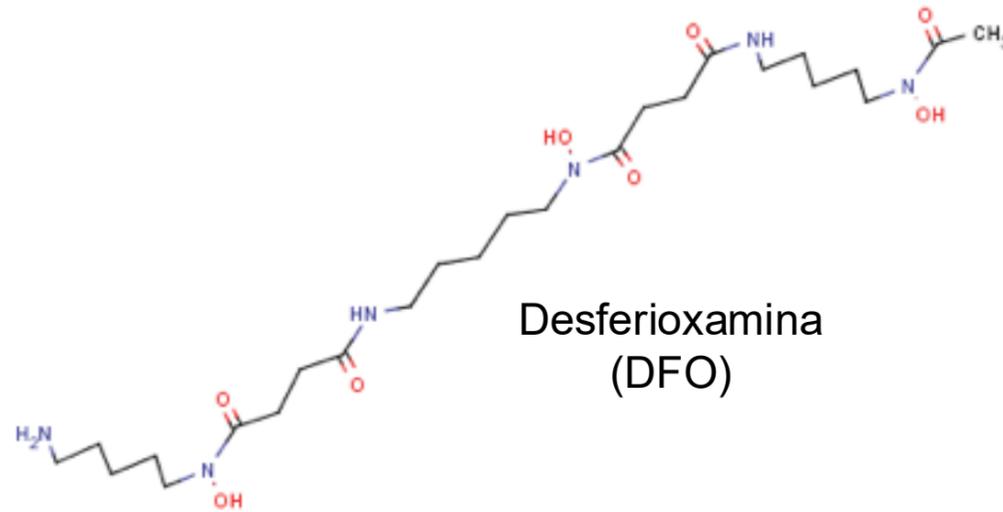
Neurotox Res
DOI 10.1007/s12640-009-9070-9

Restoration of Nigrostriatal Dopamine Neurons in Post-MPTP Treatment by the Novel Multifunctional Brain-Permeable Iron Chelator-Monoamine Oxidase Inhibitor Drug, M30

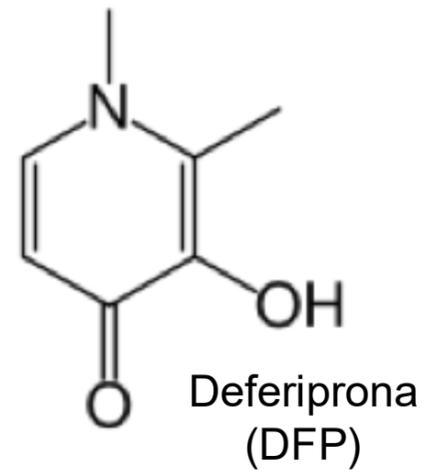
Shunit Gal · Hailin Zheng · Mati Fridkin ·
Moussa B. H. Youdim



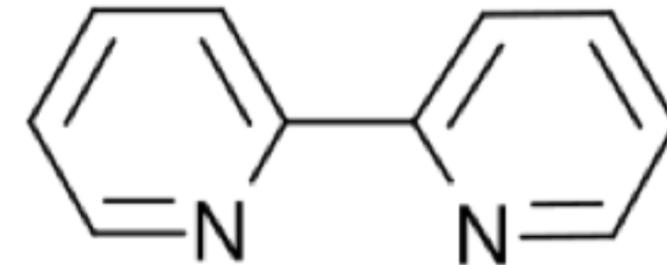
Iron Chelators



Desferioxamina
(DFO)



Deferiprona
(DFP)



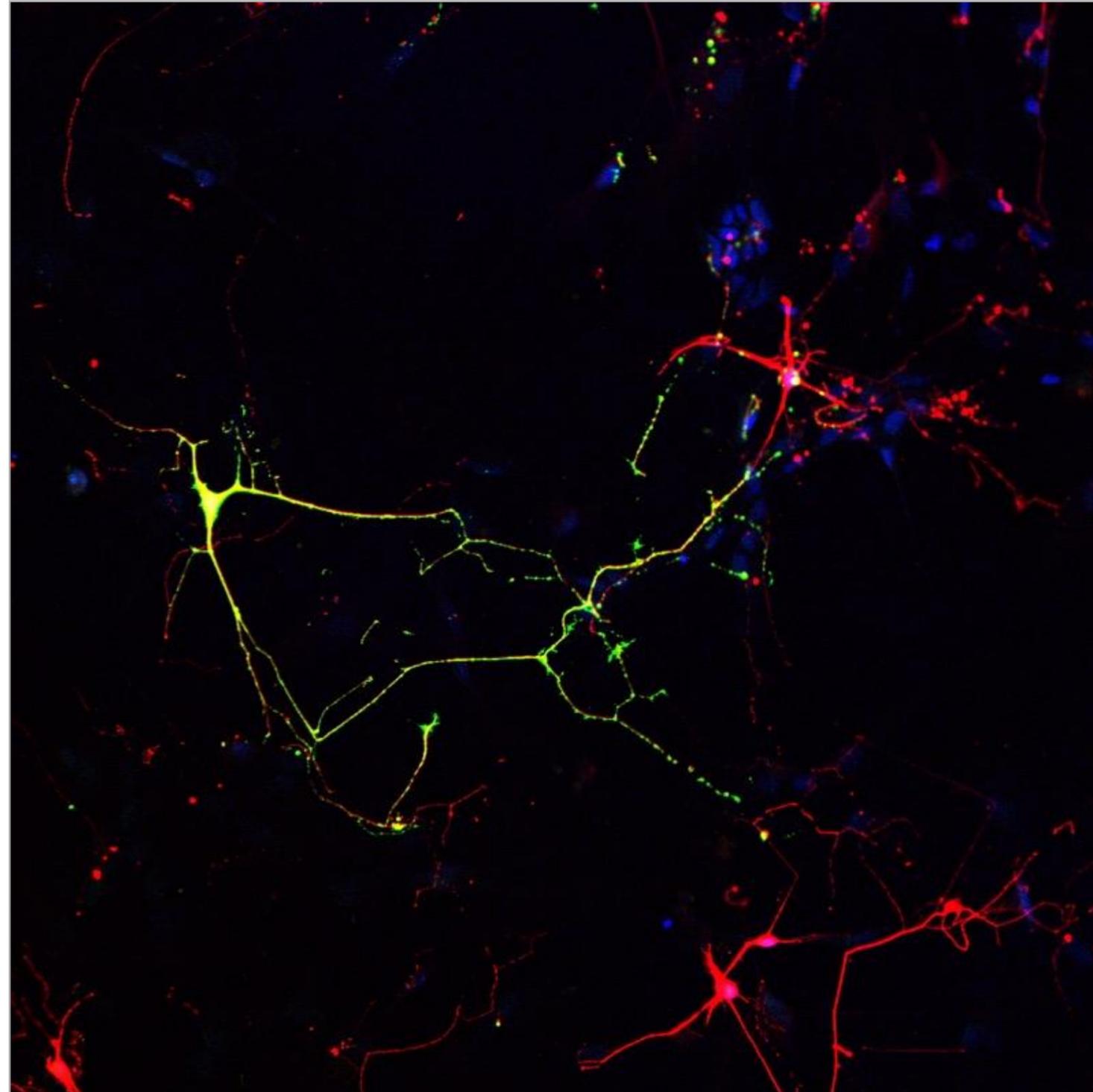
Dipiridilo
(DPD)

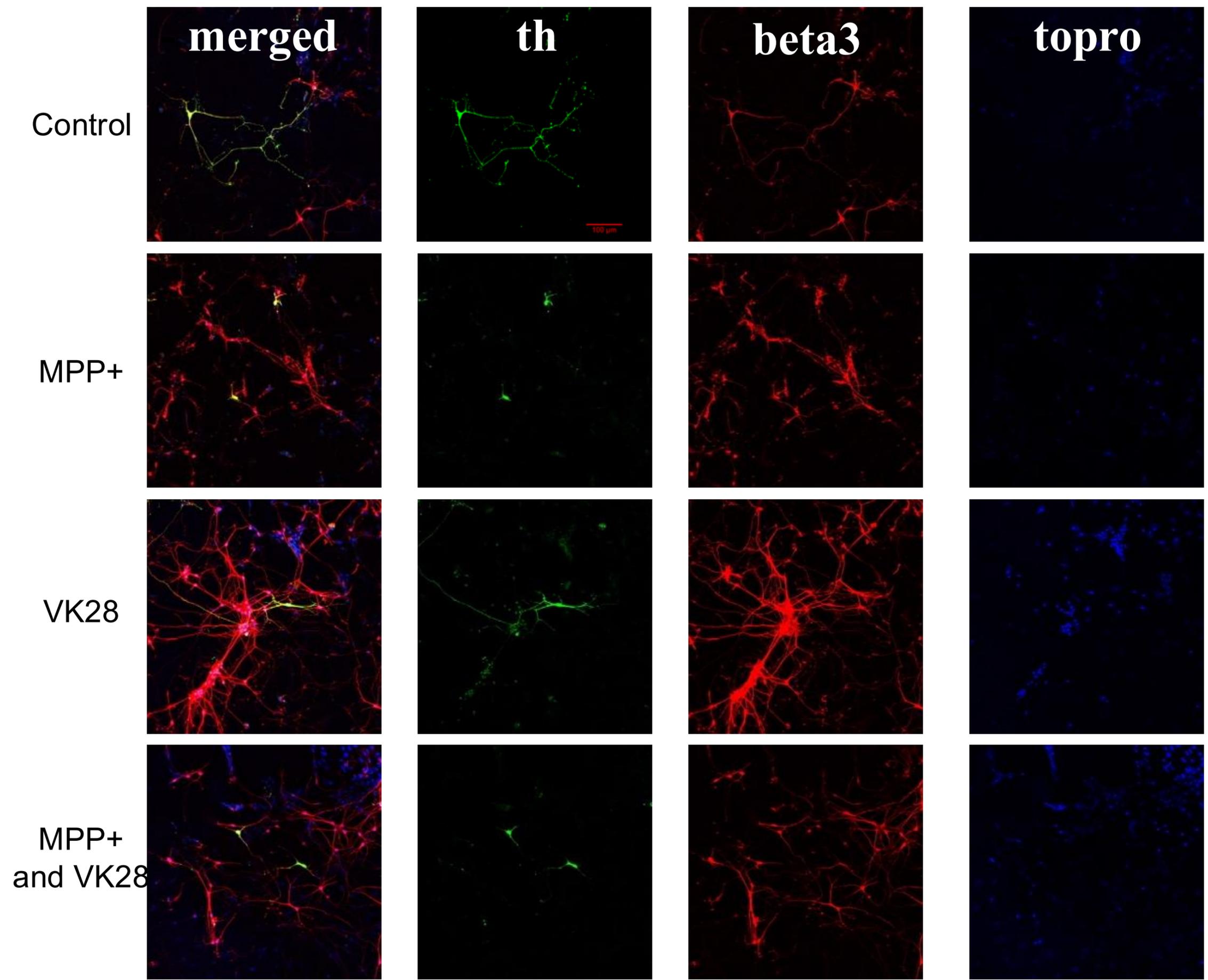
Objective

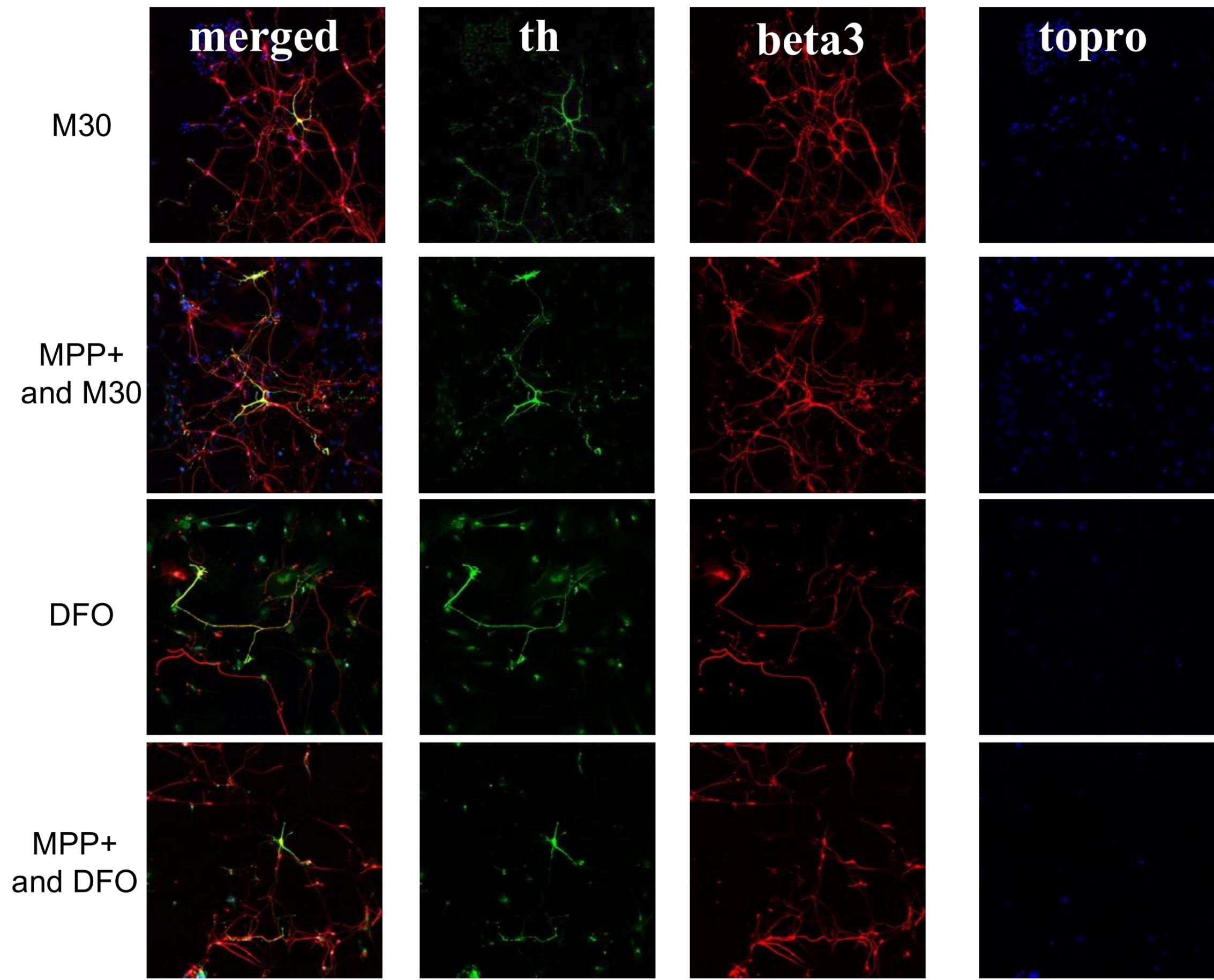
1. Reproduce previous results of the lab on the protection and regeneration caused by compounds M30 and VK28
2. Evaluate the protective/regenerative capacity of iron chelators DFP, DFO, DPD.
3. Evaluate functional neurite regeneration.

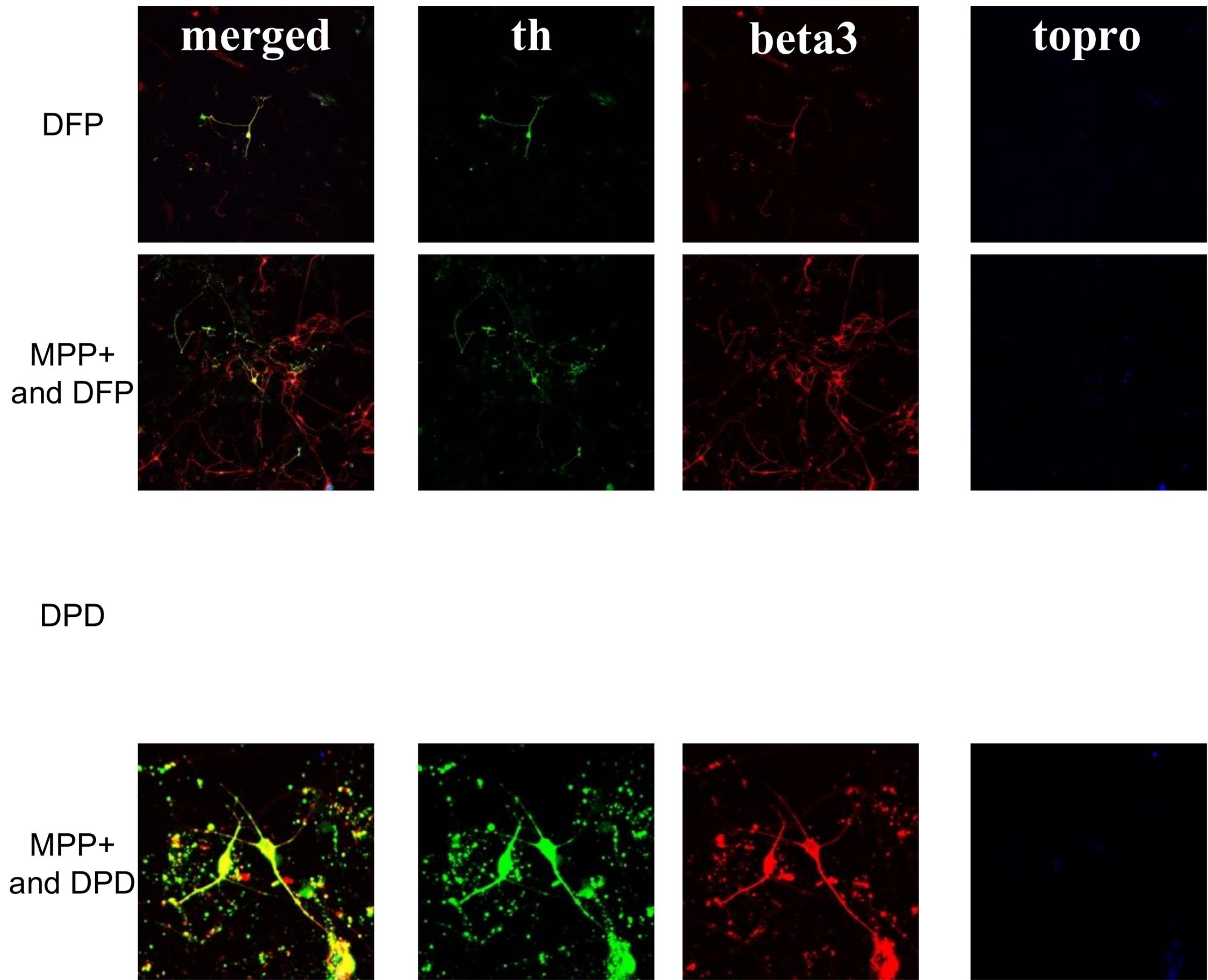
Dopaminergic neurons phenotype DIV10 (Th+)

- beta3
- th
- topro
- merged

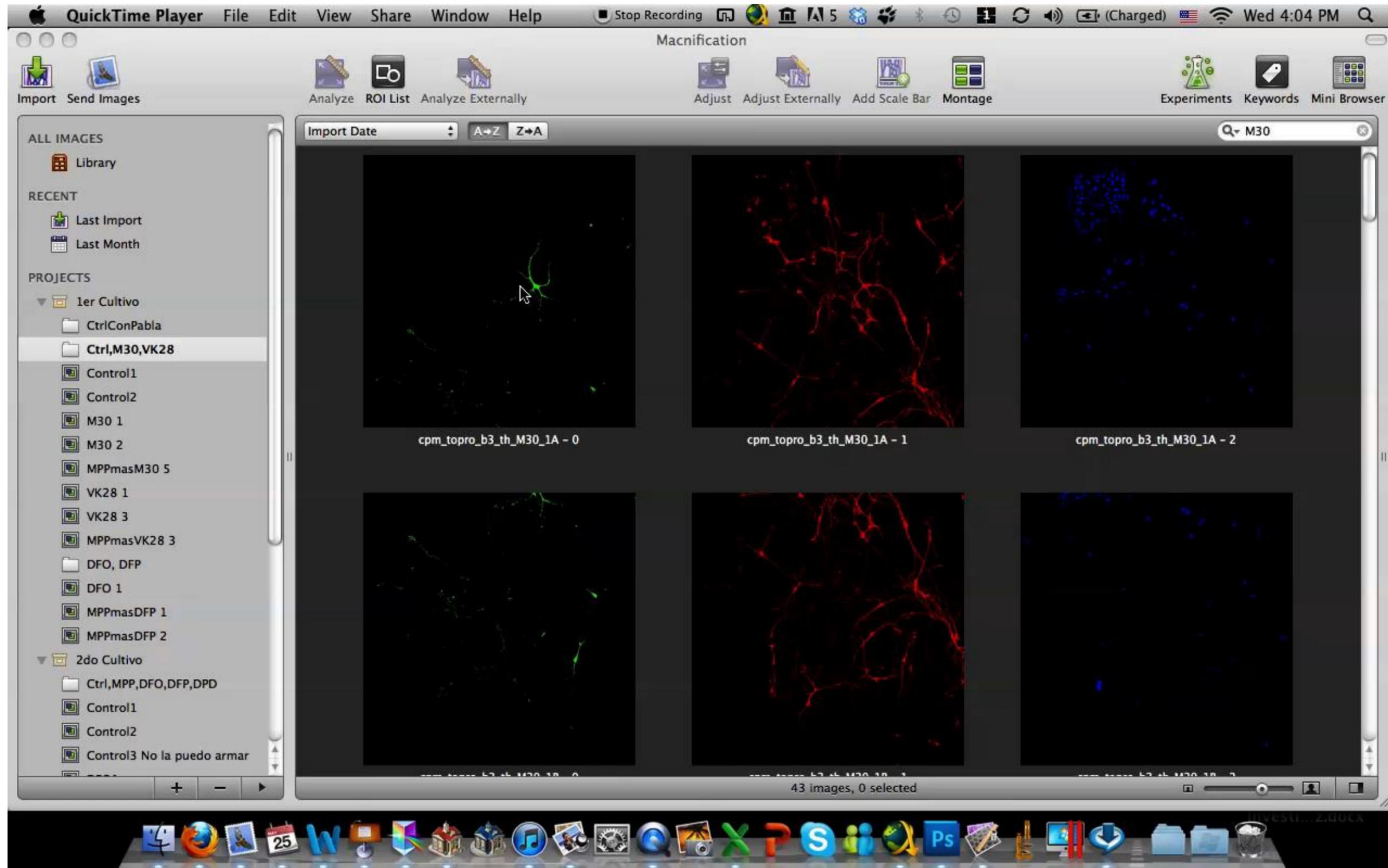




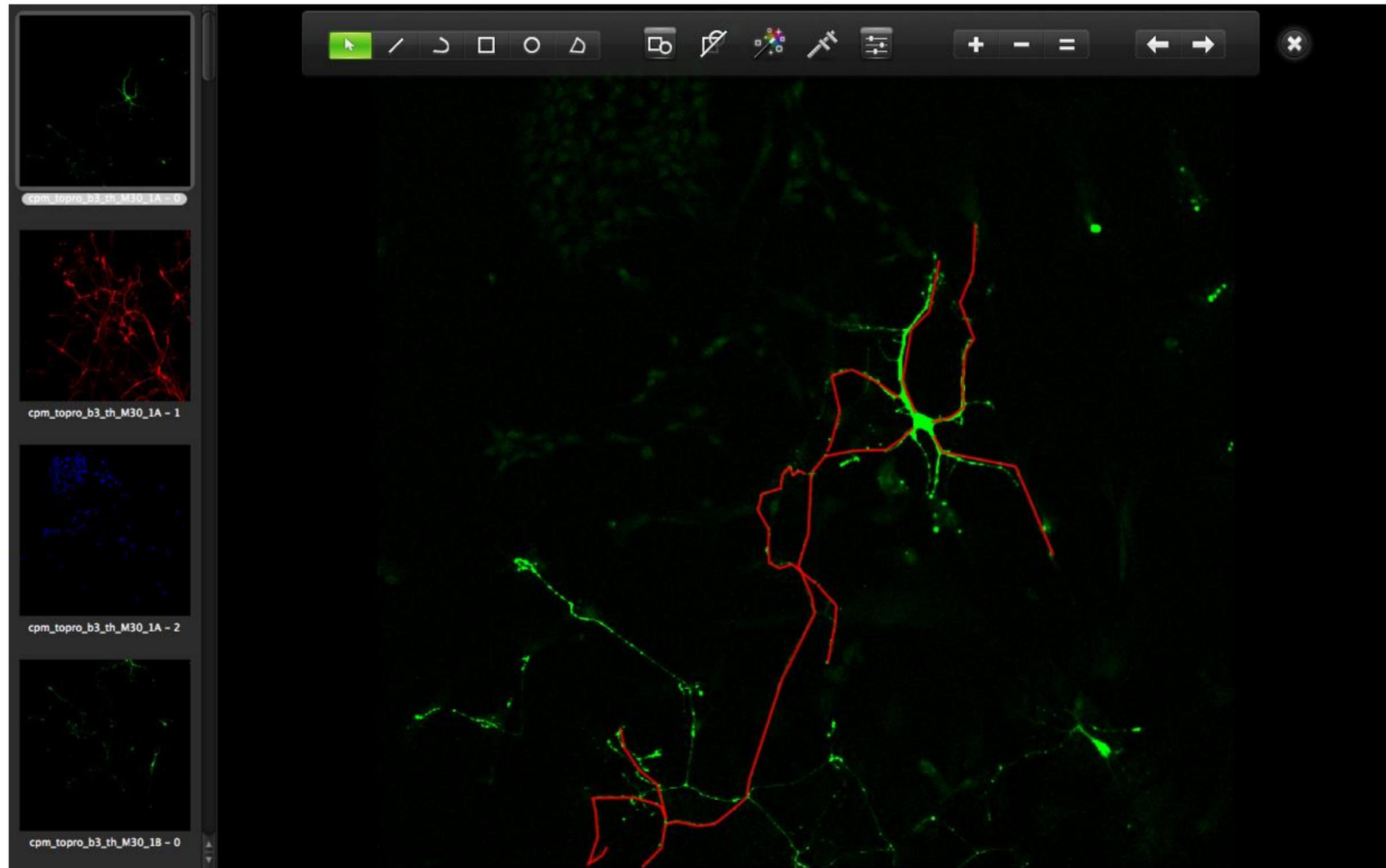




Tracing neurites in stitched image (with macnification)



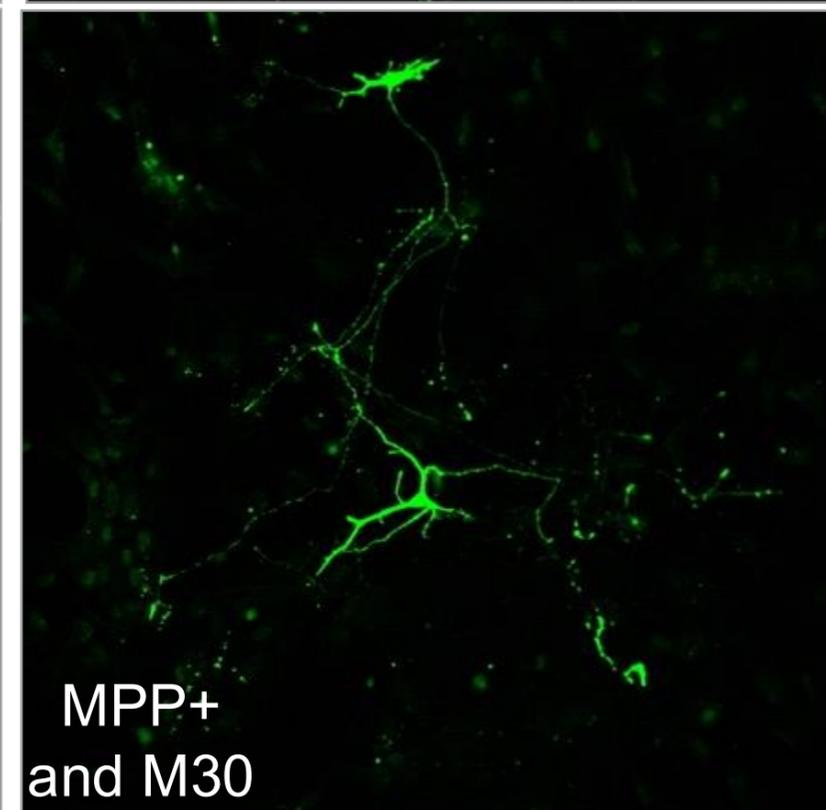
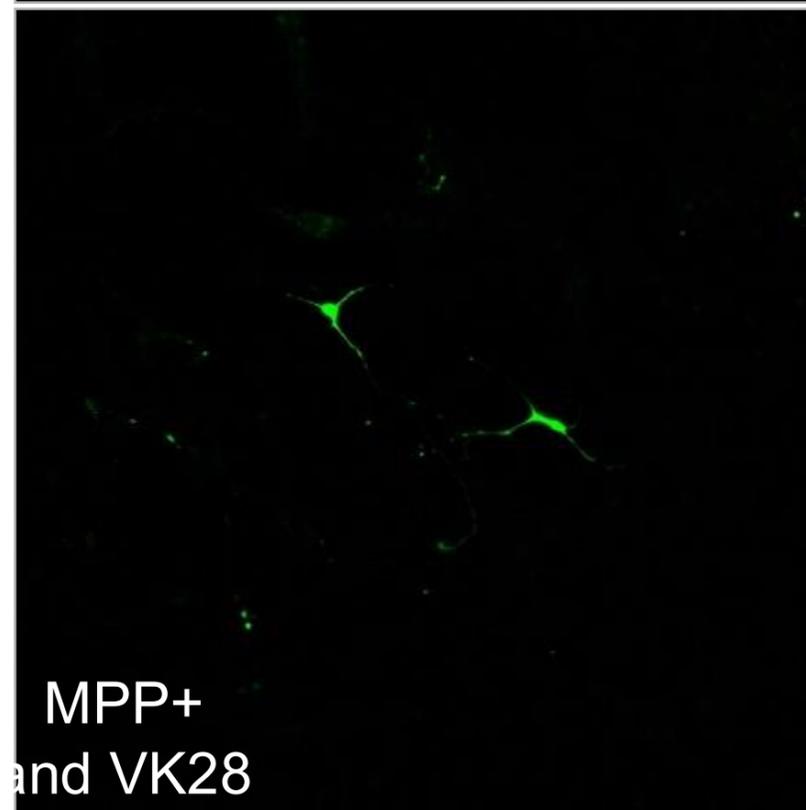
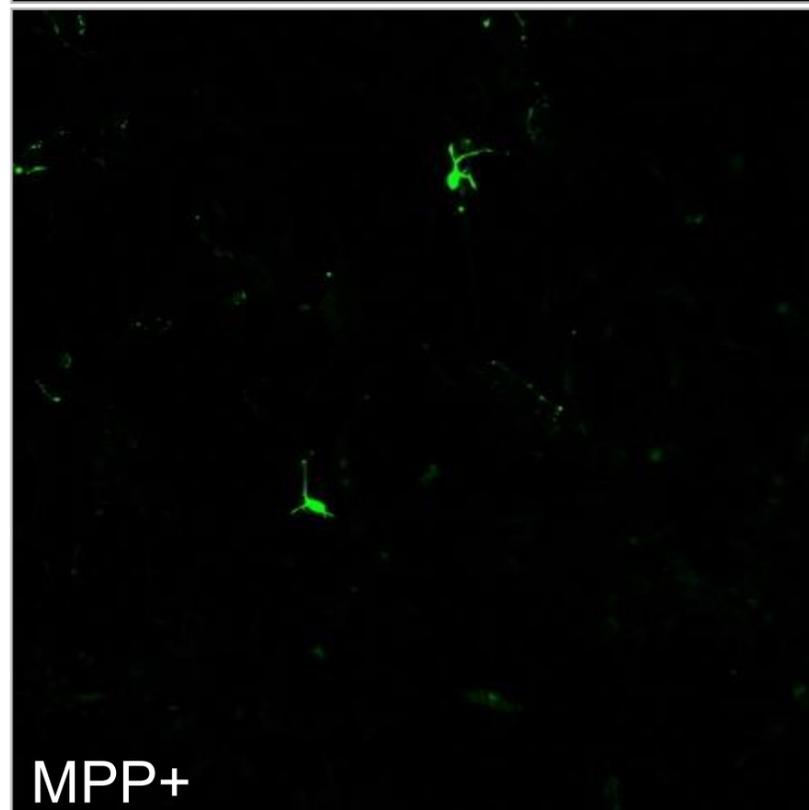
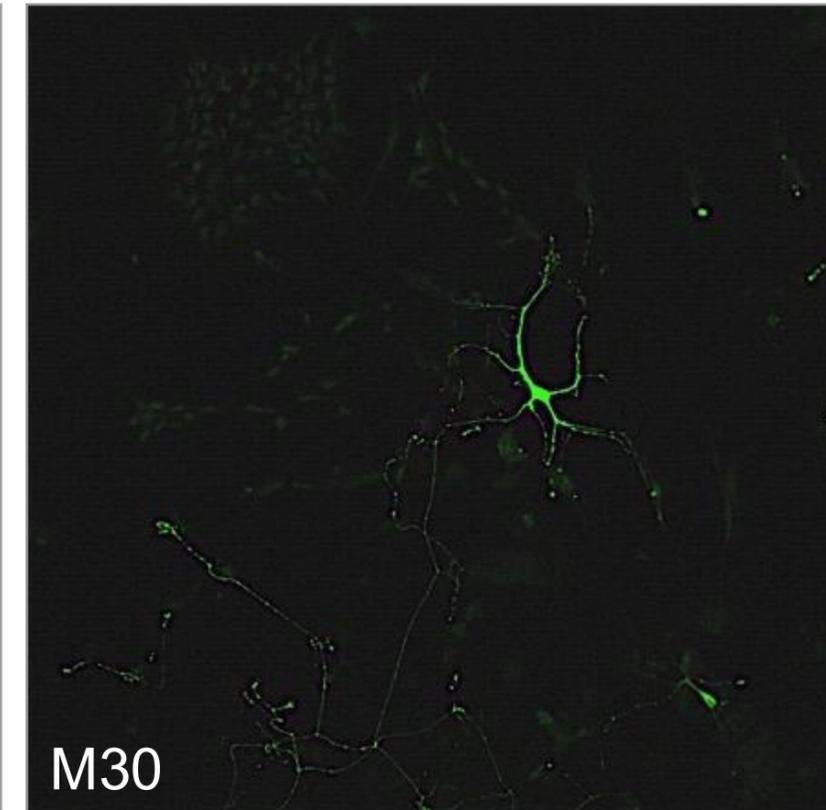
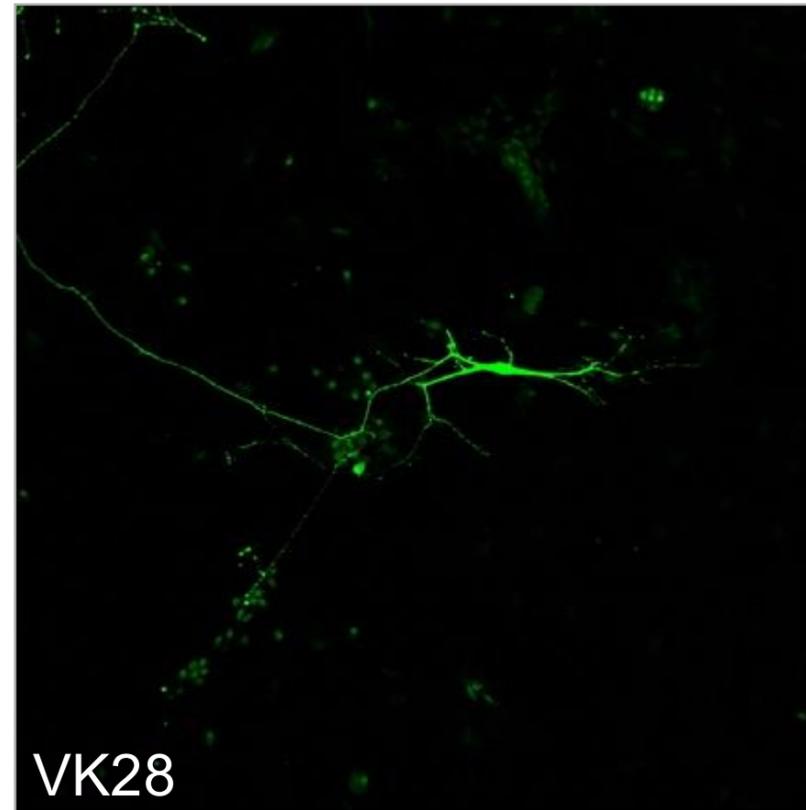
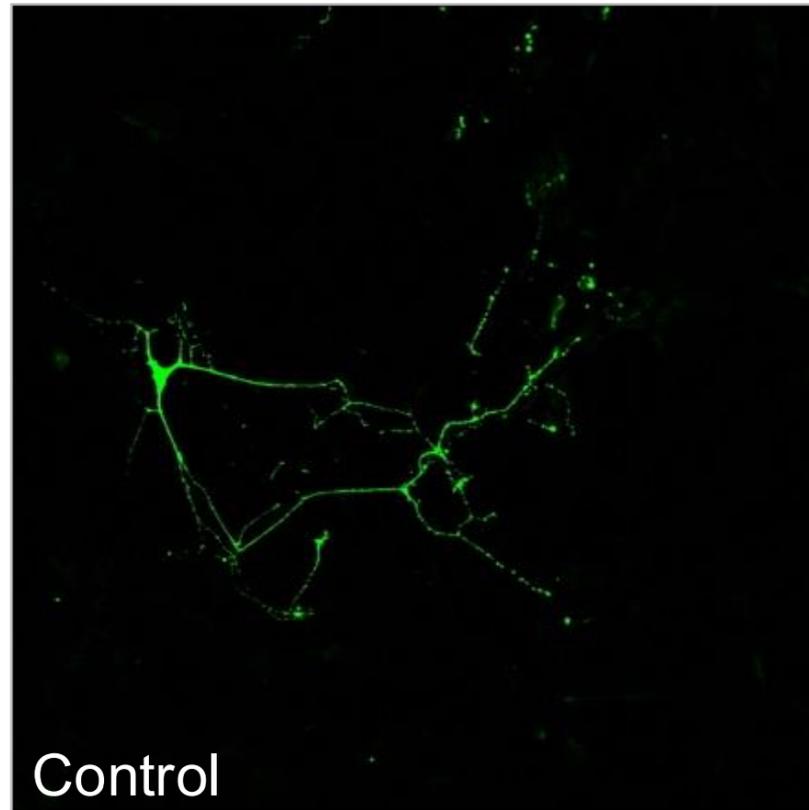
Tracing neurites in stitched image (with macnification)

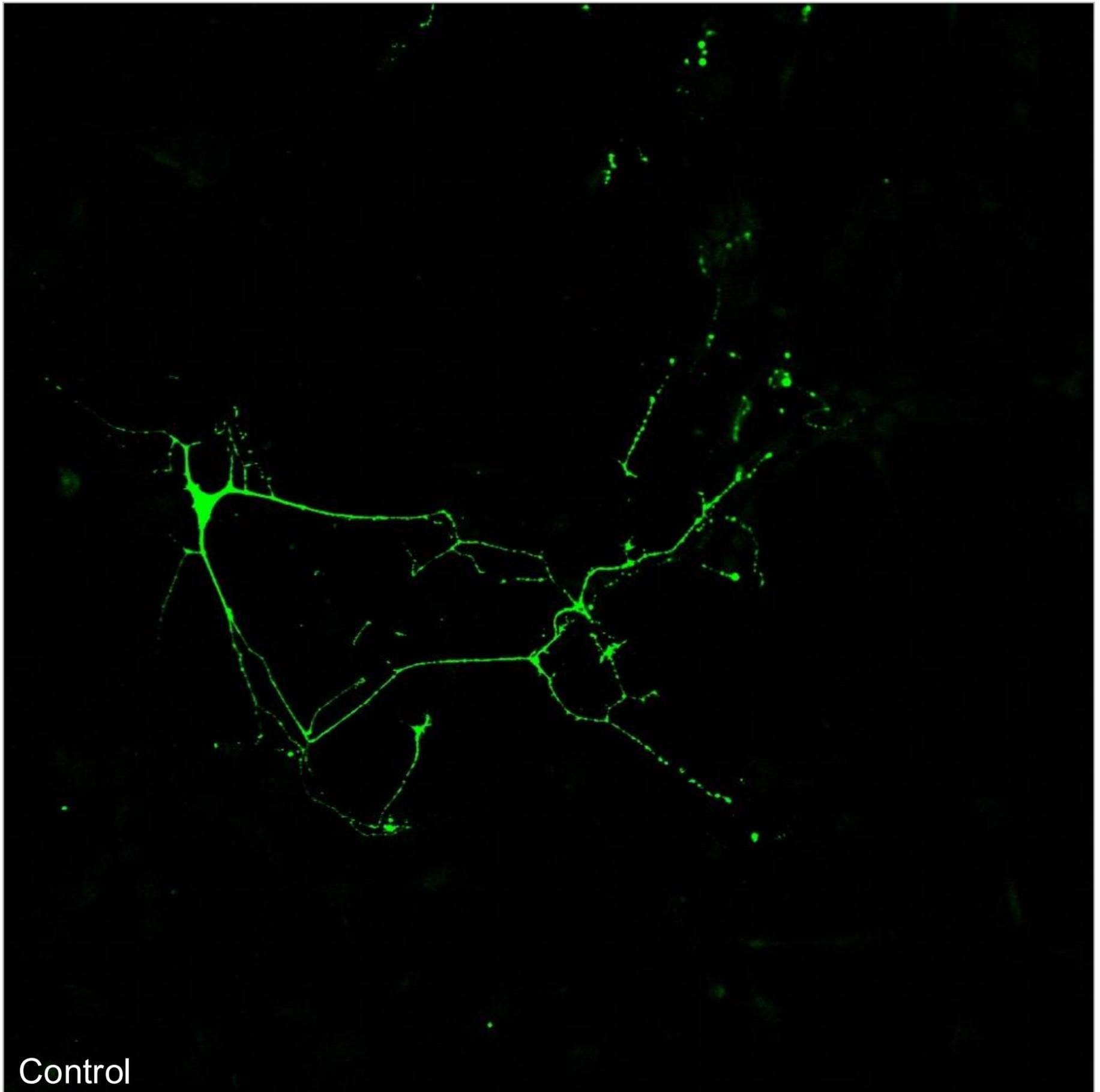


Tracing neurites in stitched image (with macnification)

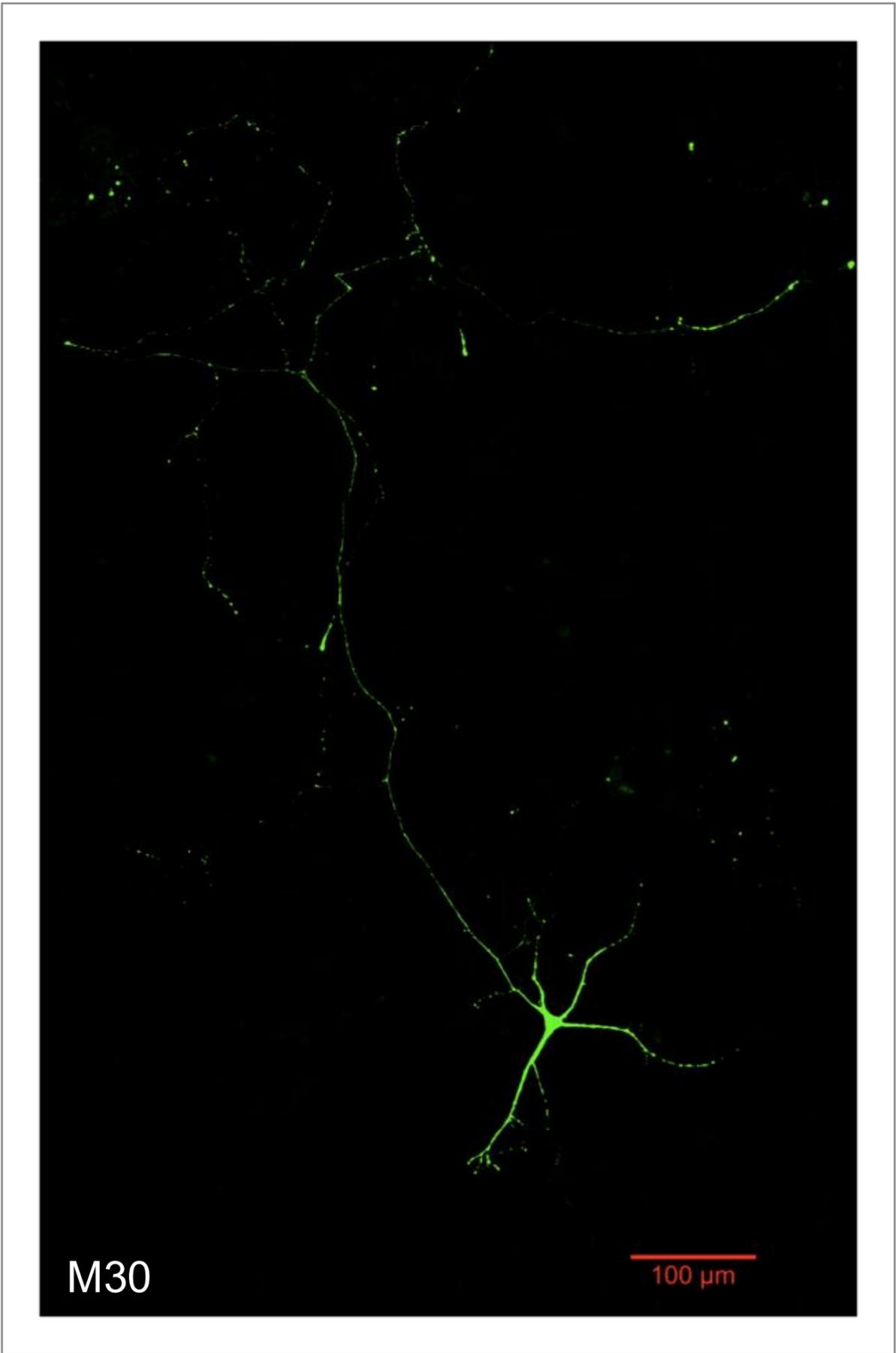


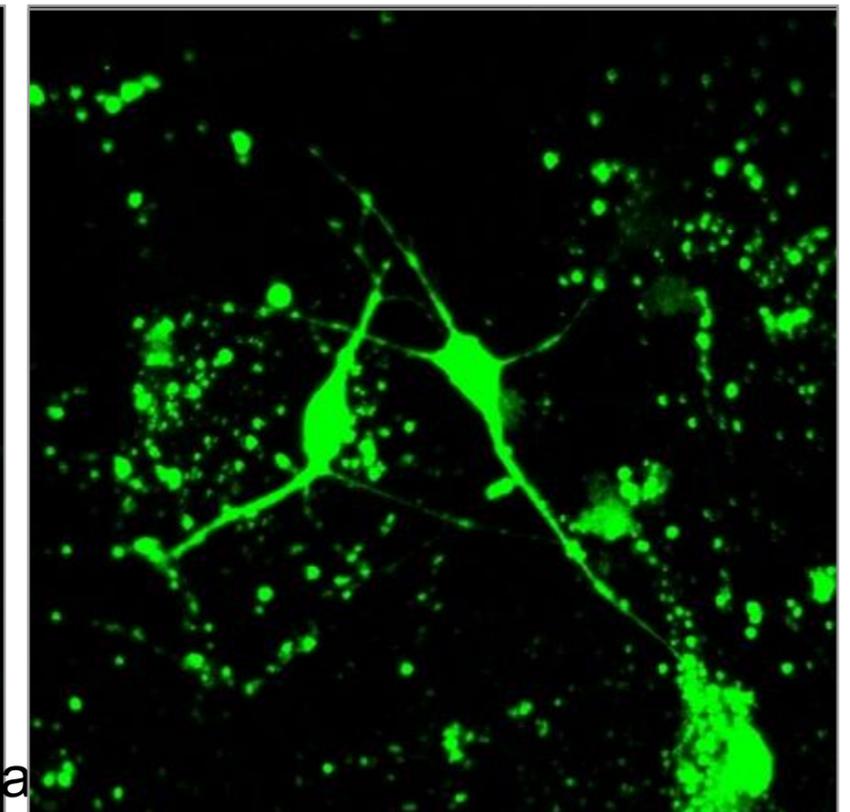
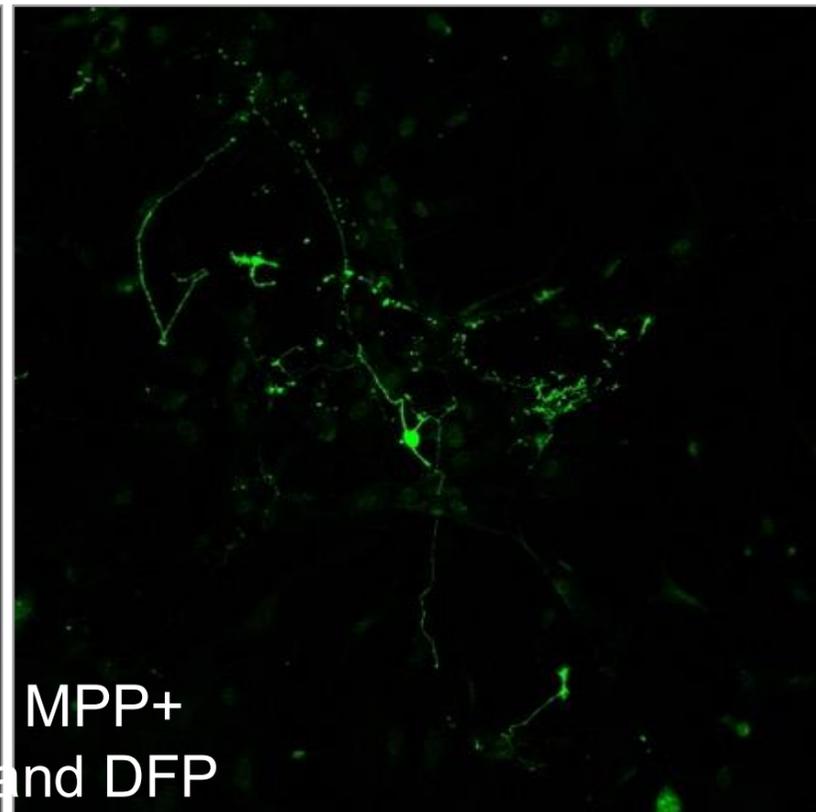
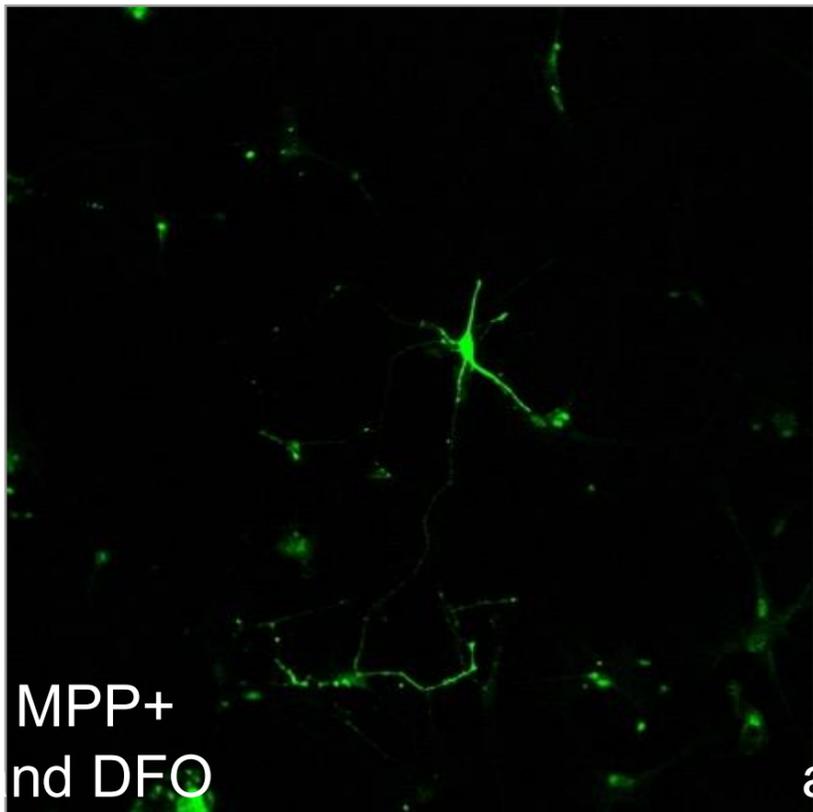
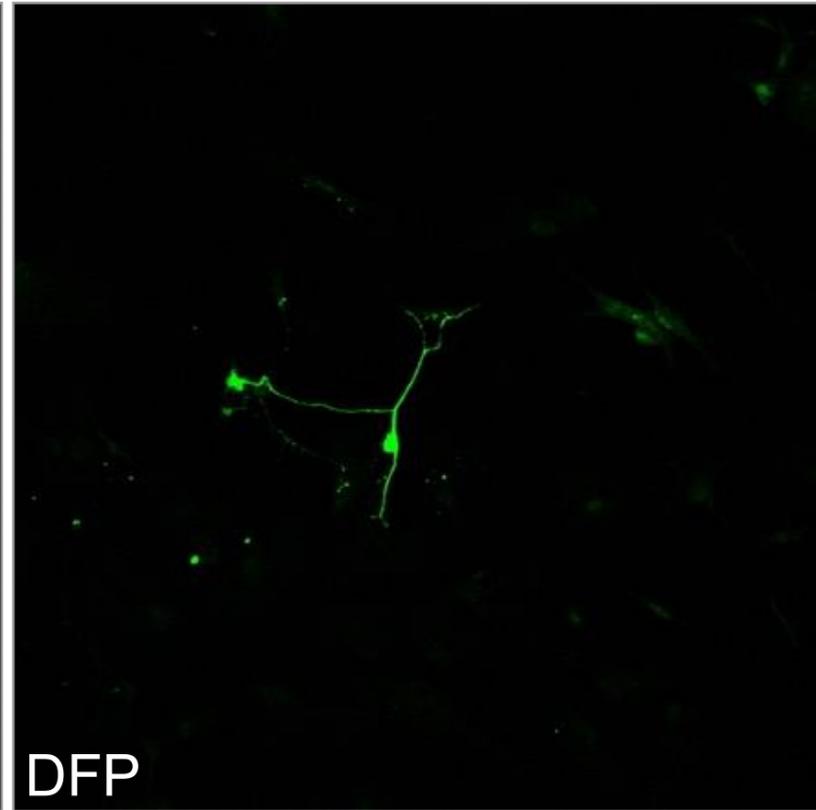
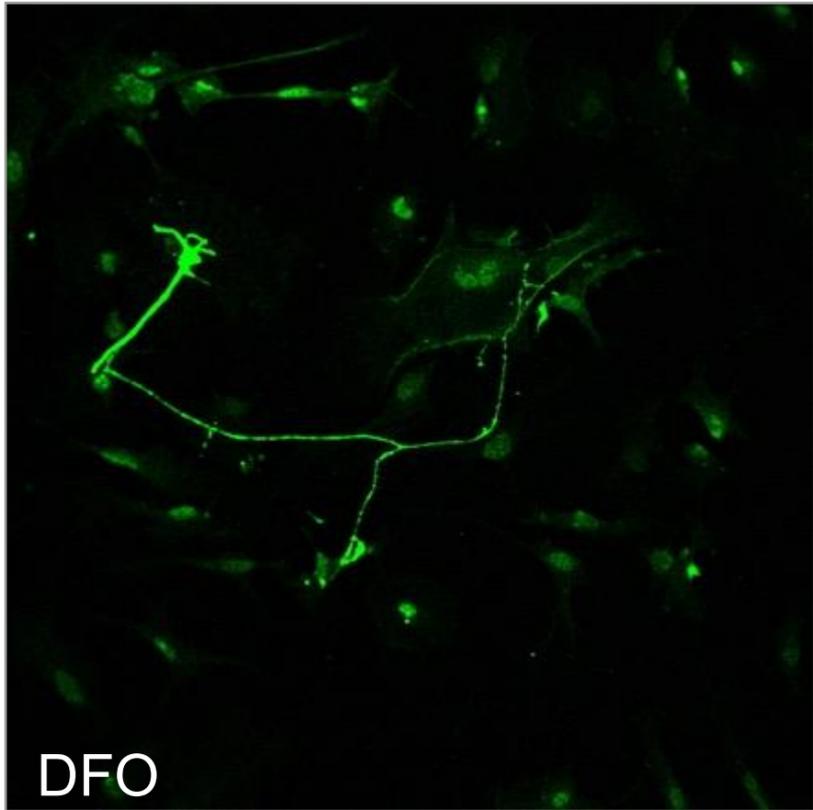
Dopaminergic neurons phenotype DIV10 (Th+)



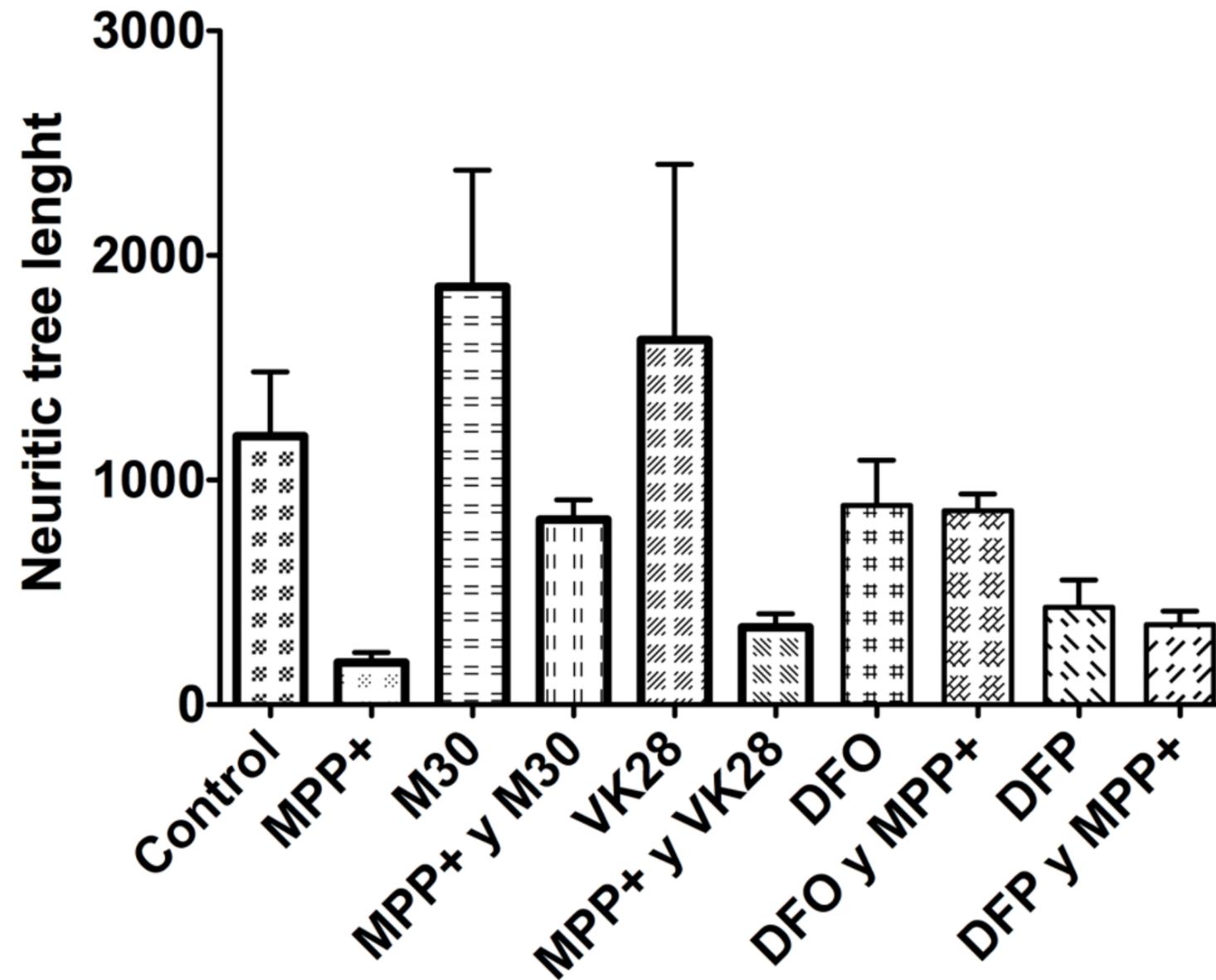


Control



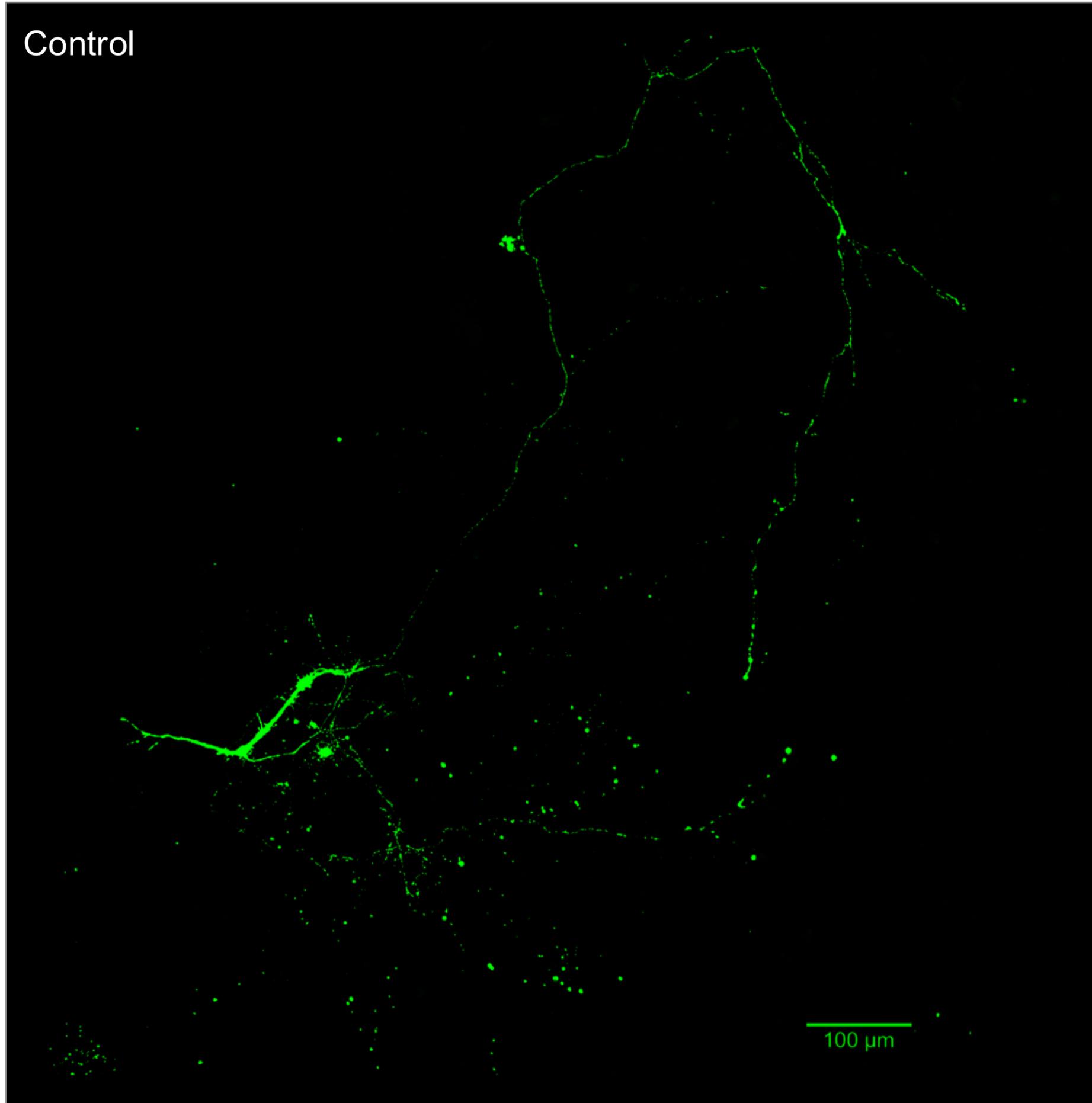


M30 protects better than VK28

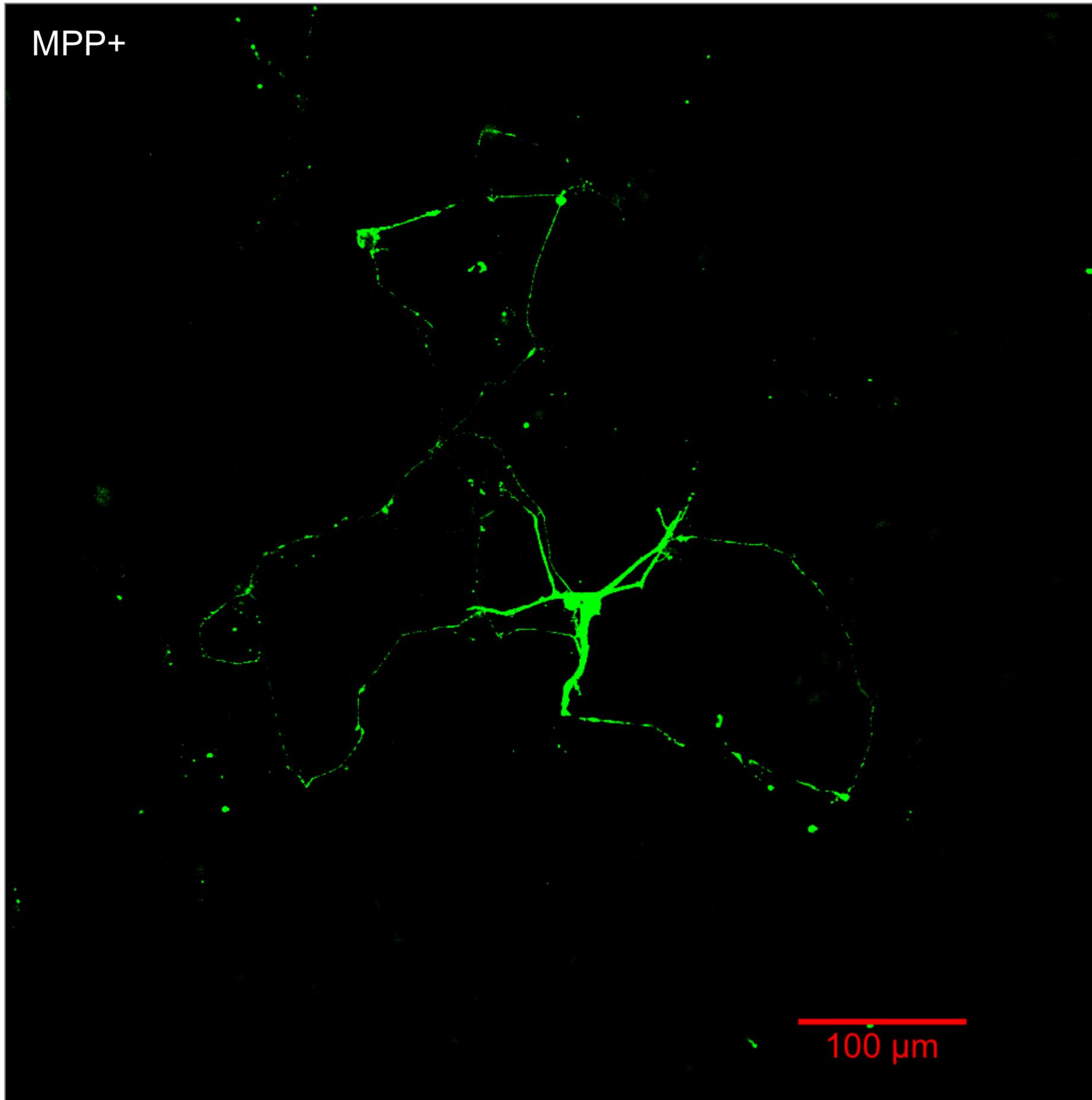


- MPP+ reduces the tree (length)
- M30 and VK28 increase the tree (length)
- M30 protects/regenerates better than VK28
- DFO and DFP mask MPP+

Control

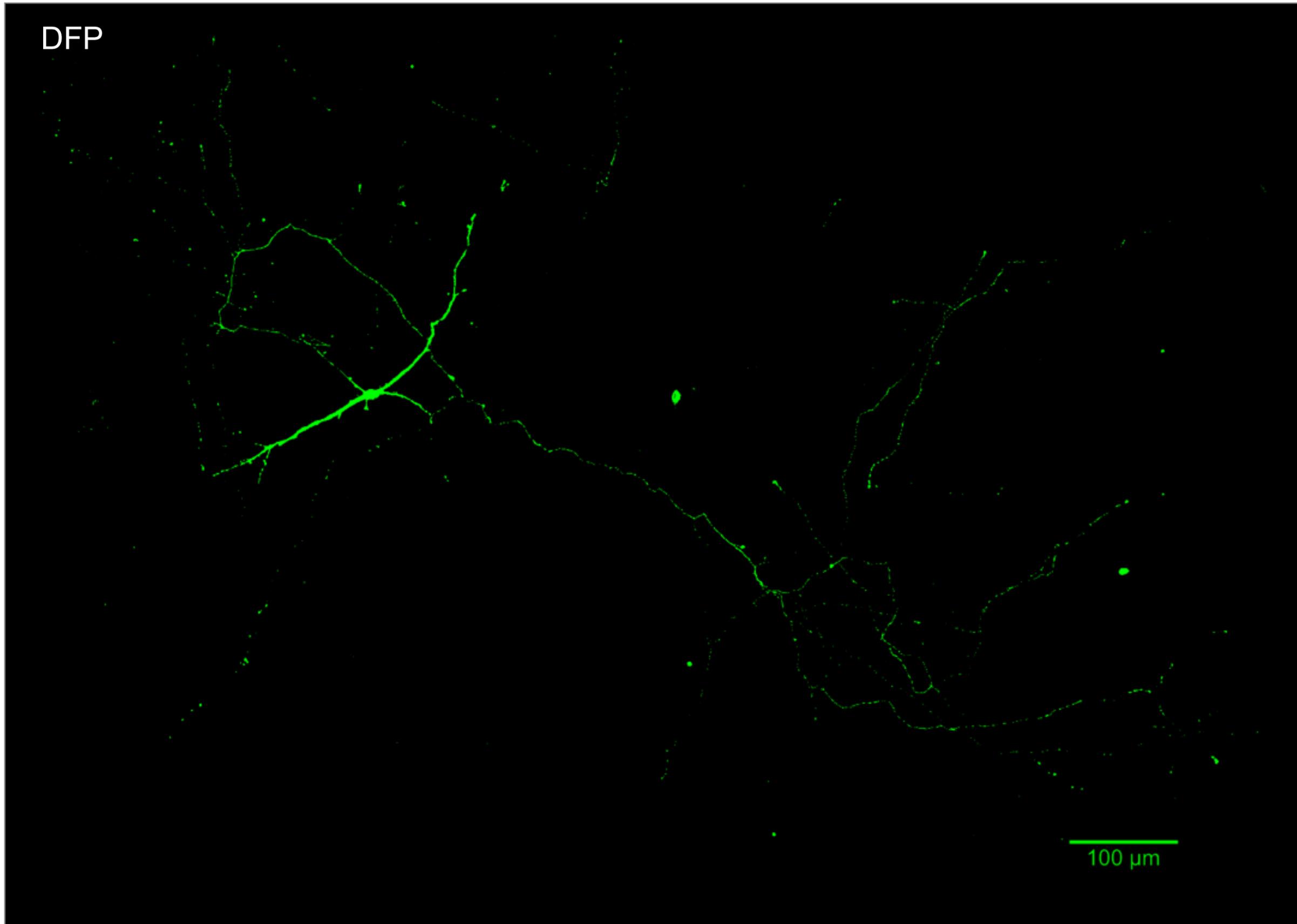


MPP+



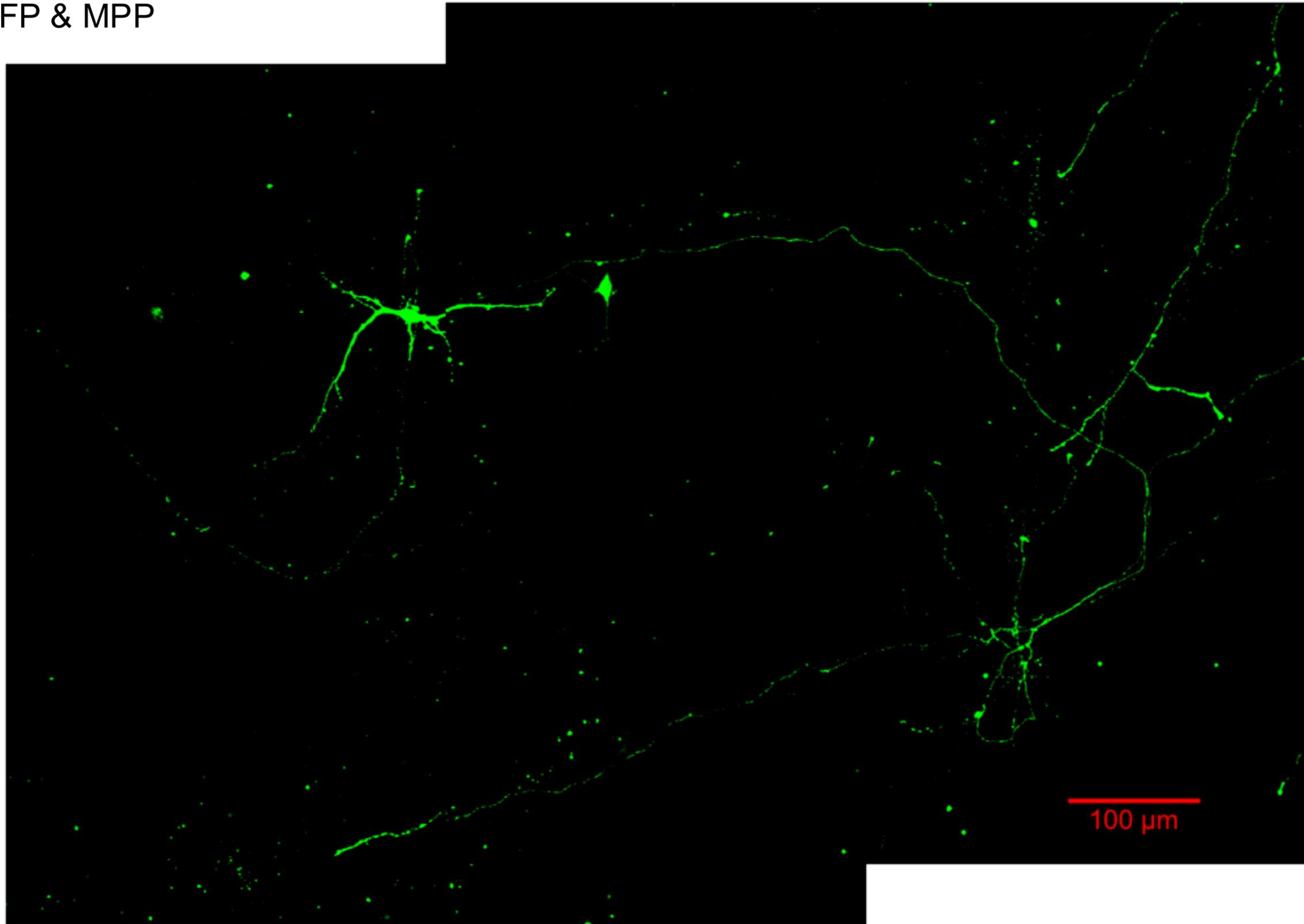
100 μ m

DFP

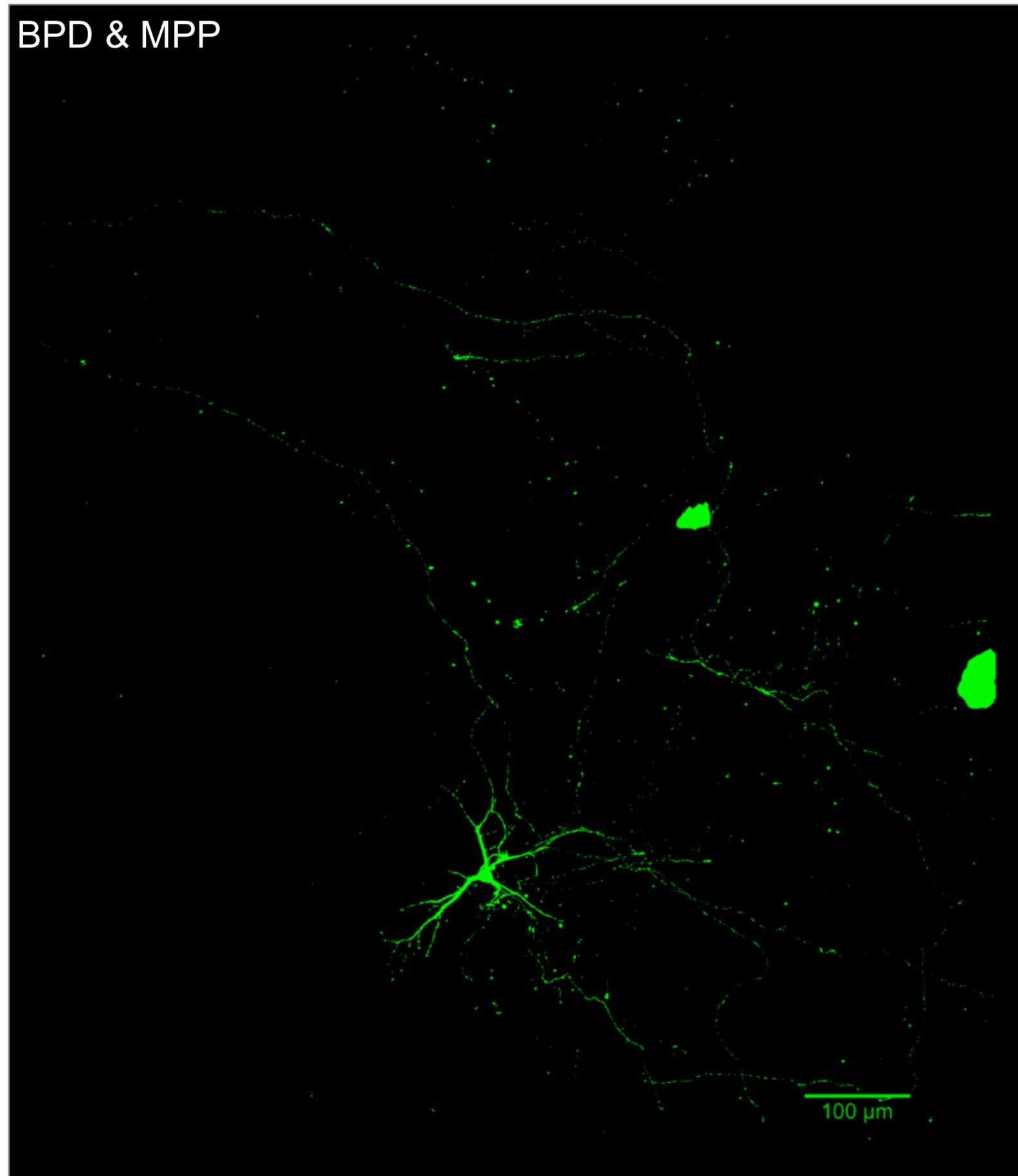


100 μm

DFP & MPP

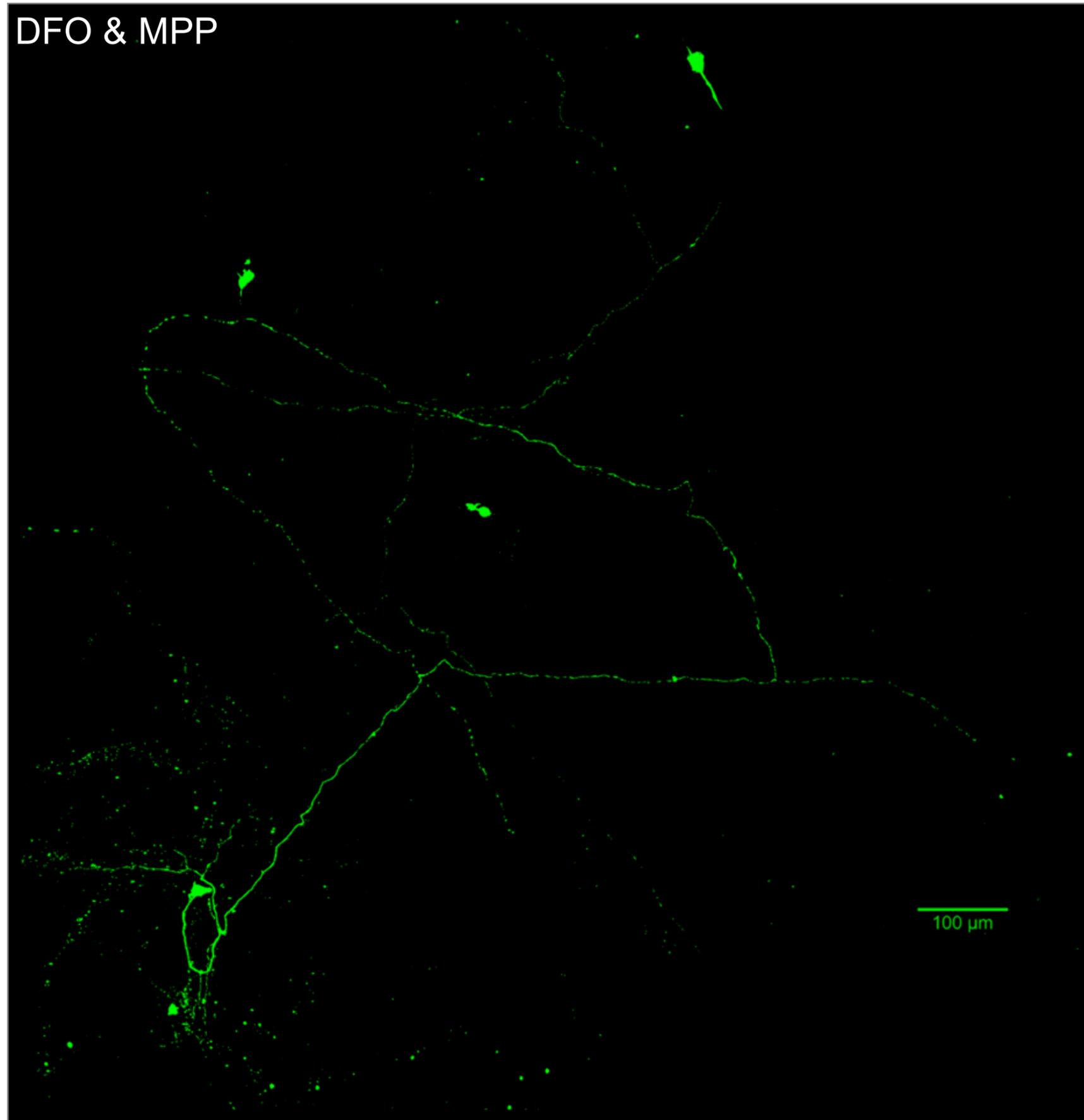


BPD & MPP



100 μm

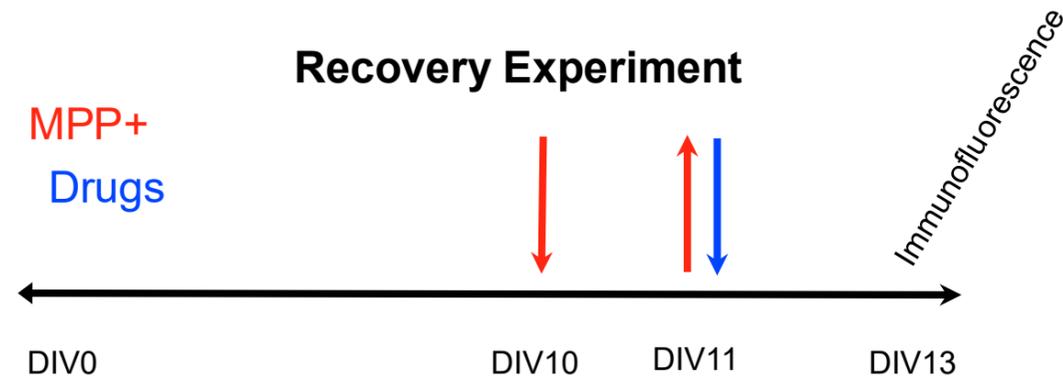
DFO & MPP



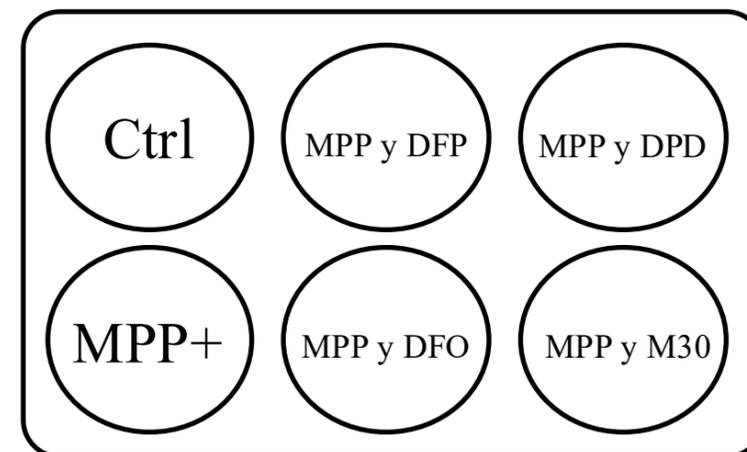
Functional assays

- Identify the nature of the tree generated in recovery experiments under iron chelator treatments

- Remove MPP+
- Extend culture
- Identity of the tree



24 hrs MPP+
48 hrs con drogas



- Th, tau1, MAP2
- Th, Syn, topro
- Th, GAP43, topro

Previously reported

CRMP-2 induces axons in cultured hippocampal neurons

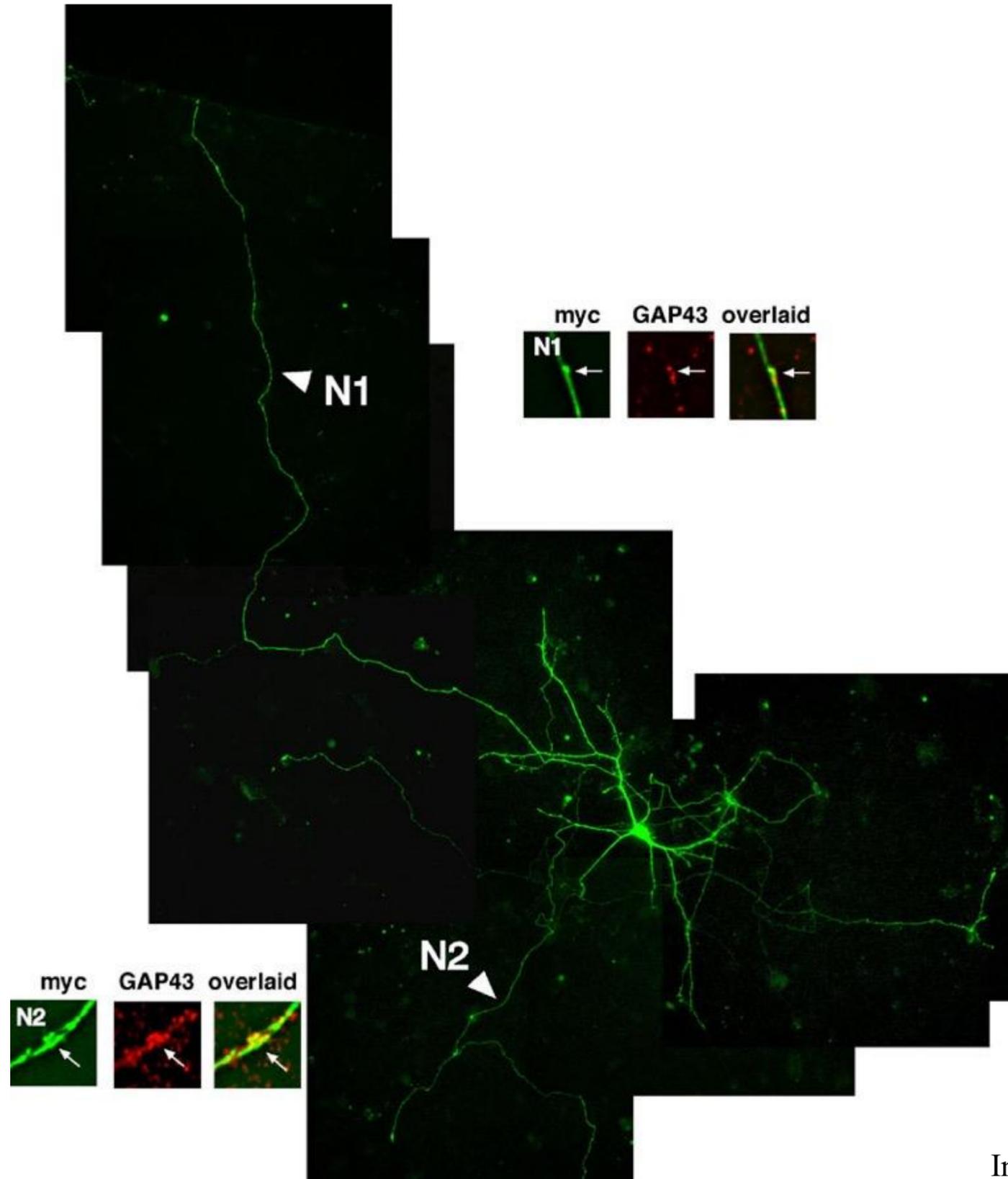
Naoyuki Inagaki^{1,2}, Kazuyasu Chihara¹, Nariko Arimura^{1,3},
Céline Ménager^{1,3}, Yoji Kawano^{1,3}, Naruhiro Matsuo¹,
Takashi Nishimura^{1,3}, Mutsuki Amano^{1,3} and
Ko-ko Kaibuchi^{1,3}

¹ Division of Signal Transduction, Nara Institute of Science and Technology,
Ikoma 630-0101, Japan

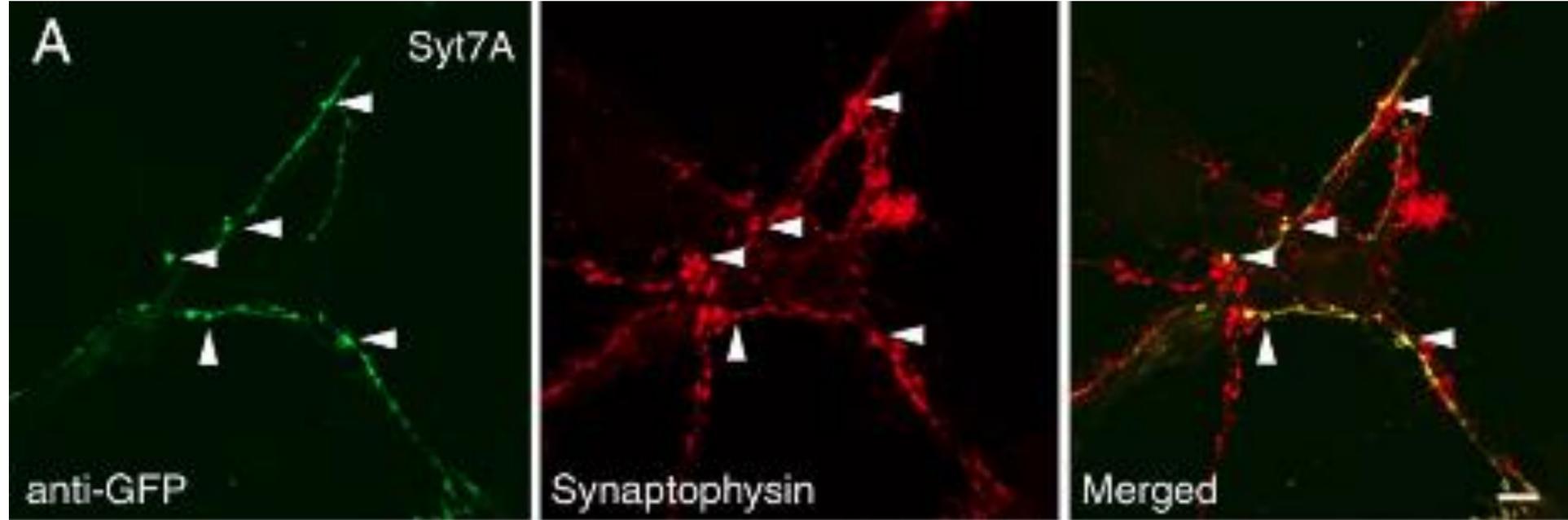
² Recognition and Formation, PRESTO, JST, Kawamato 860-0012, Japan

³ Department of Cell Pharmacology, Nagoya University Graduate School of
Medicine, Nagoya 466-8550, Japan

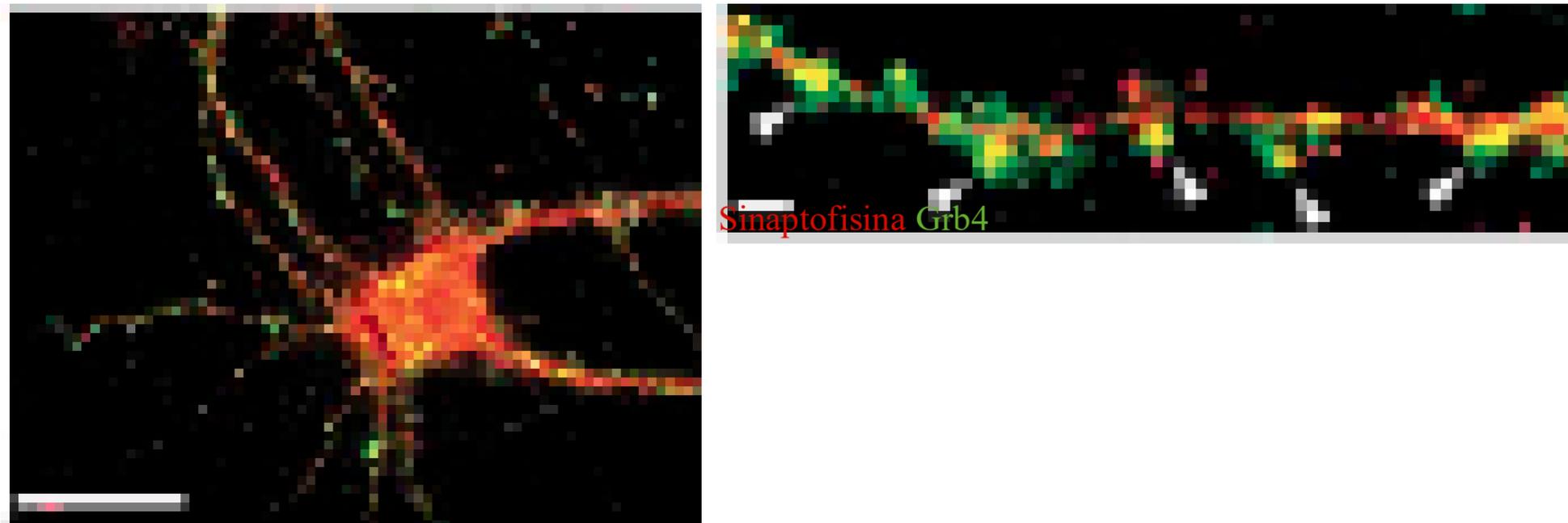
Correspondence should be addressed to K.K. (kaibuchi@med.nagoya-u.ac.jp)



Previously reported

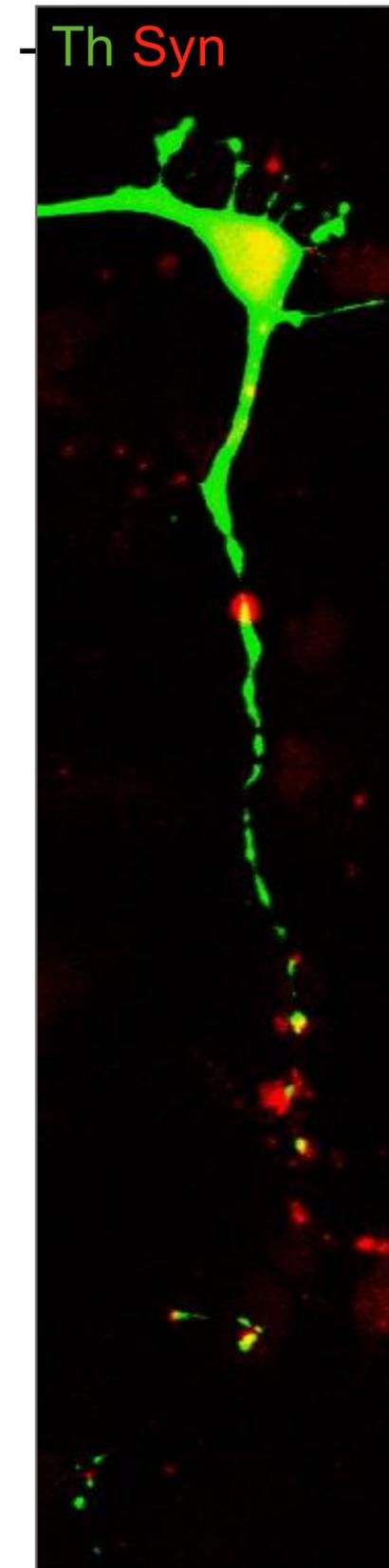
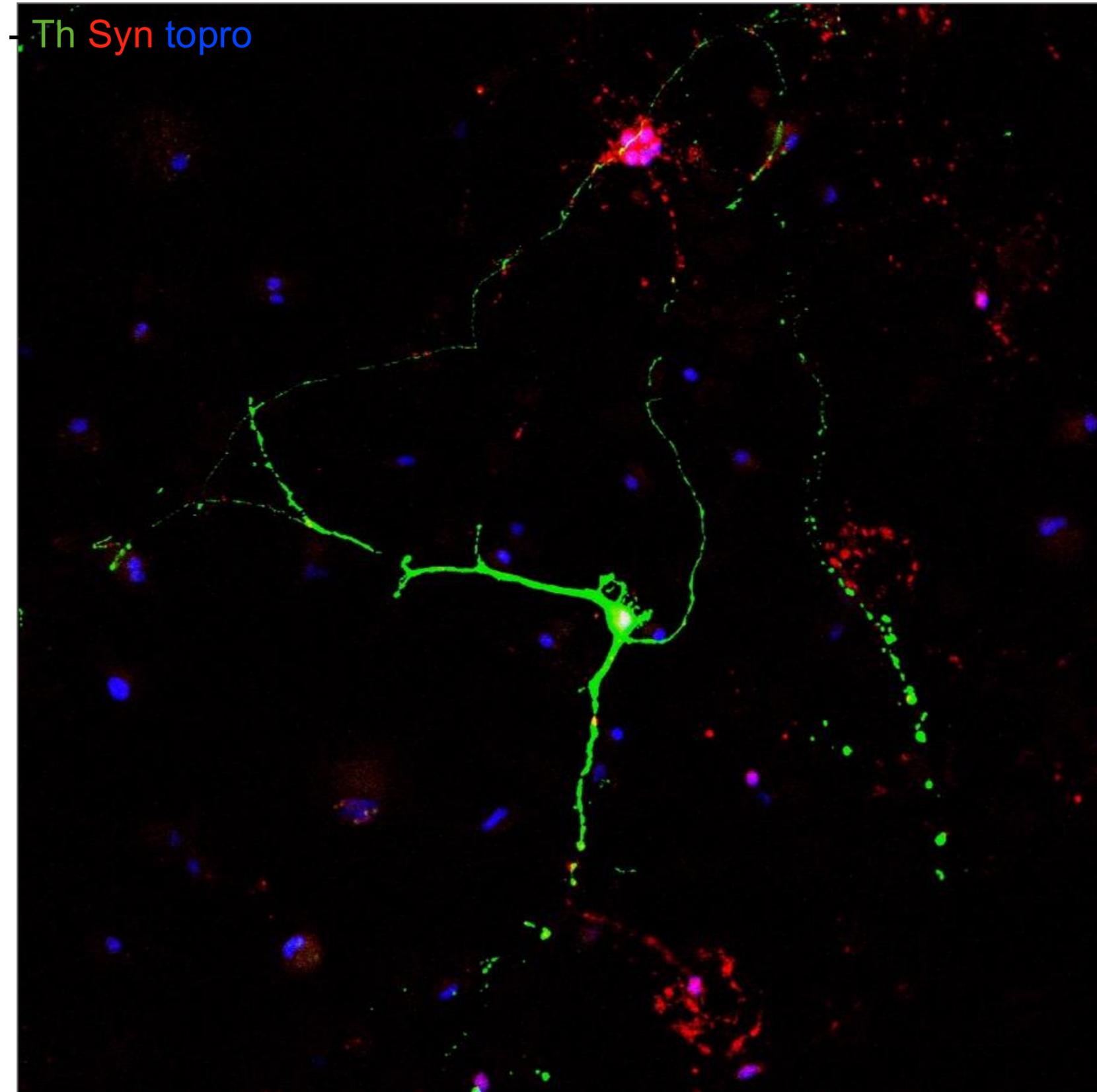


Virmani et al. Synaptotagmin 7 splice variants differentially regulate synaptic vesicle recycling.
EMBO Journal (2003) vol. 22 (20) pp. 5347-57

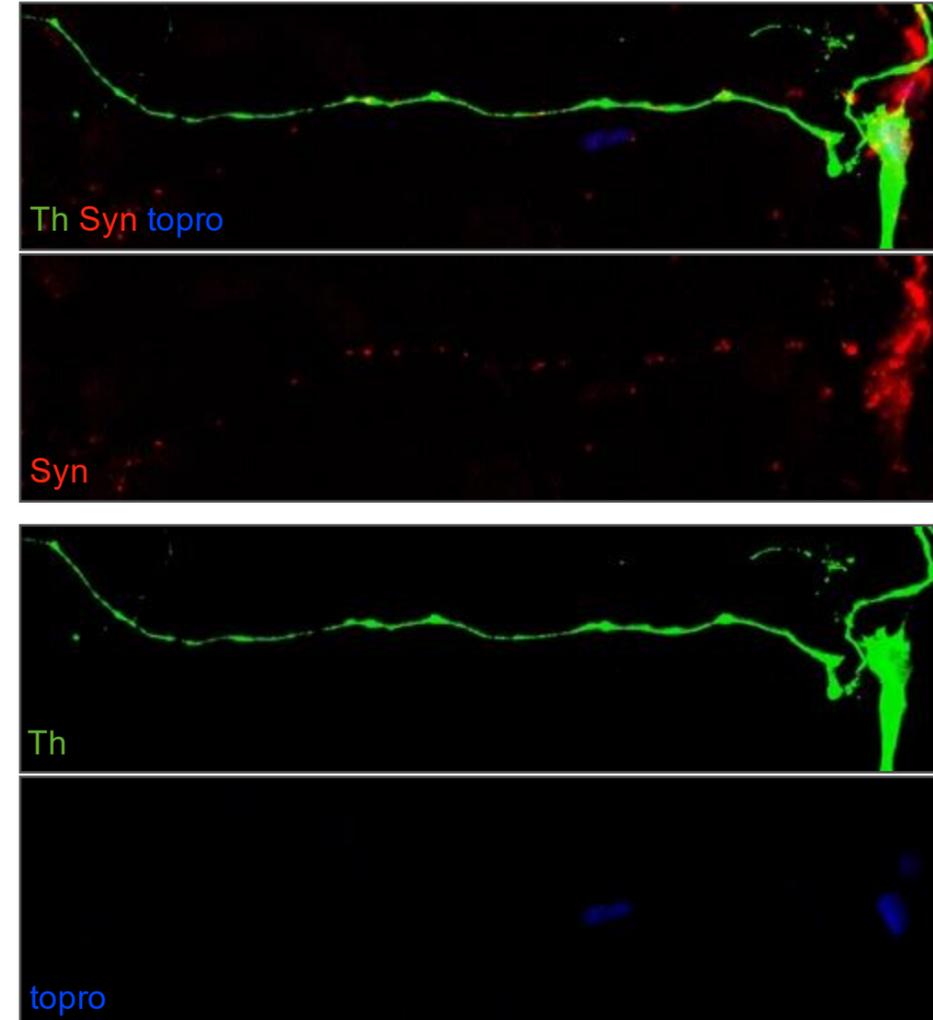
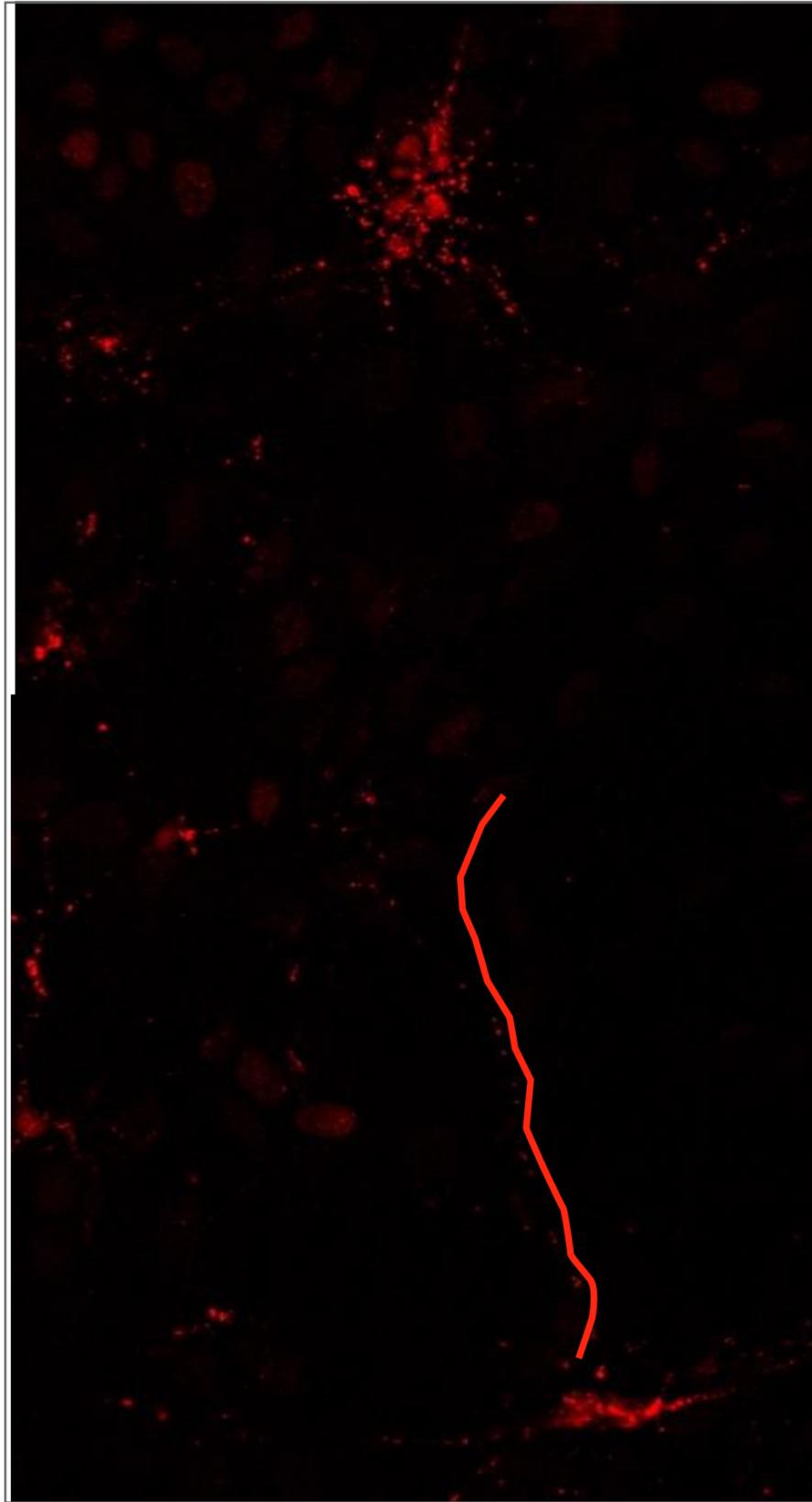


Segura et al. Grb4 and GIT1 transduce ephrinB reverse signals modulating spine morphogenesis and synapse formation.
Nat Neurosci (2007) vol. 10 (3) pp. 301-10

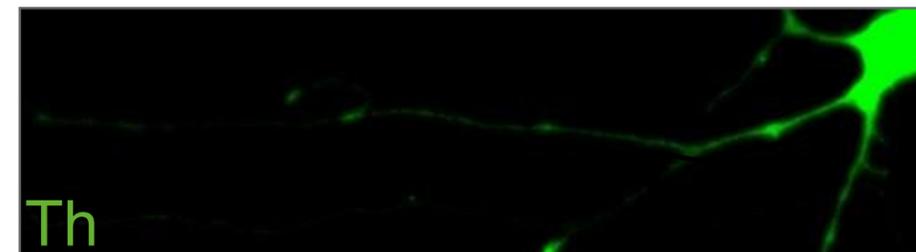
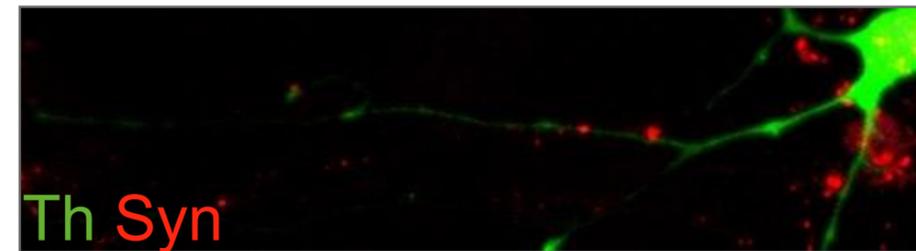
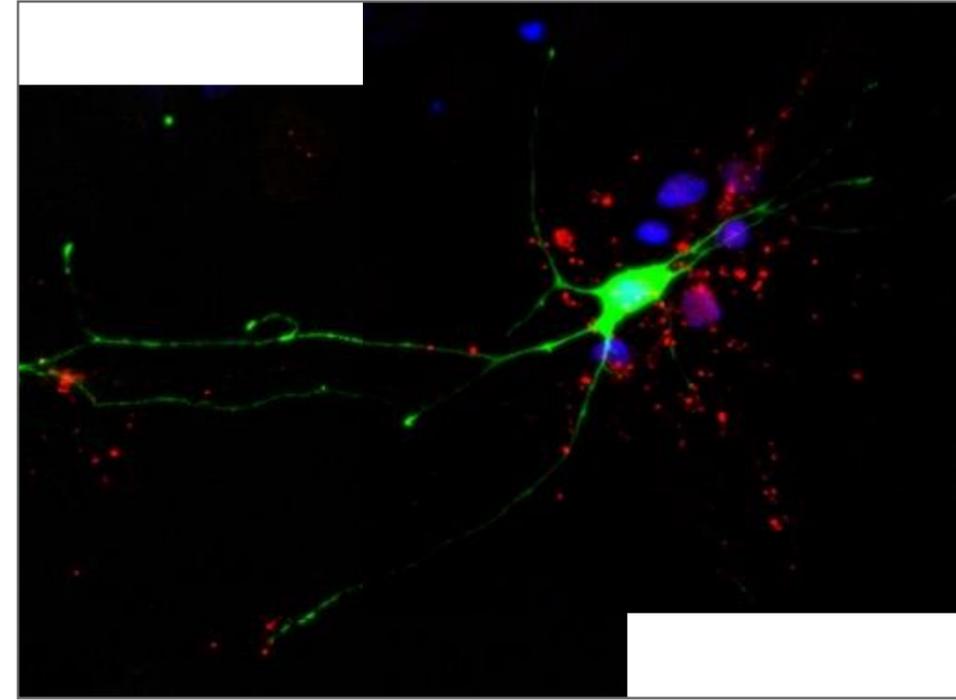
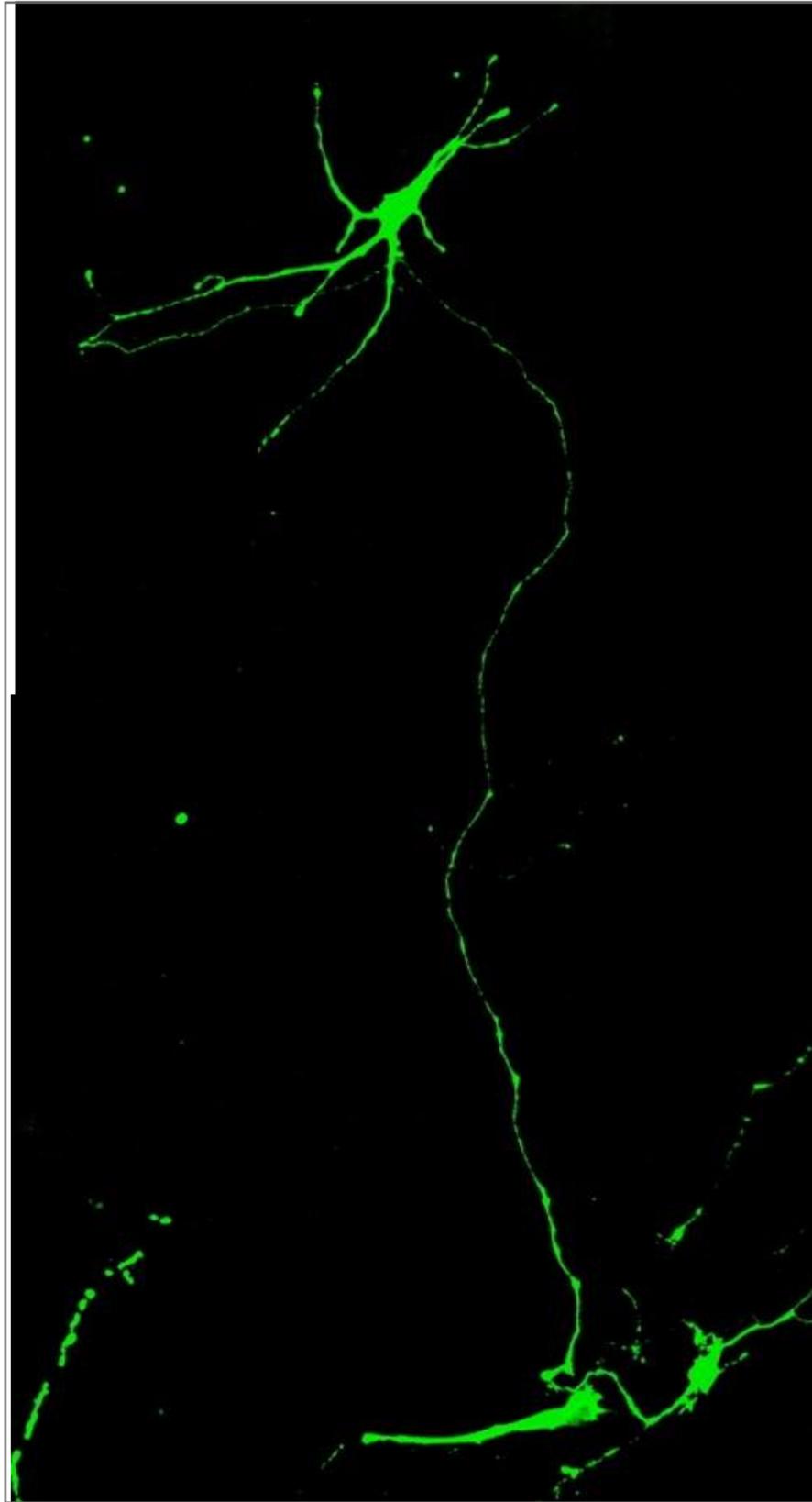
Synaptophysin accumulates around TH+ neurites



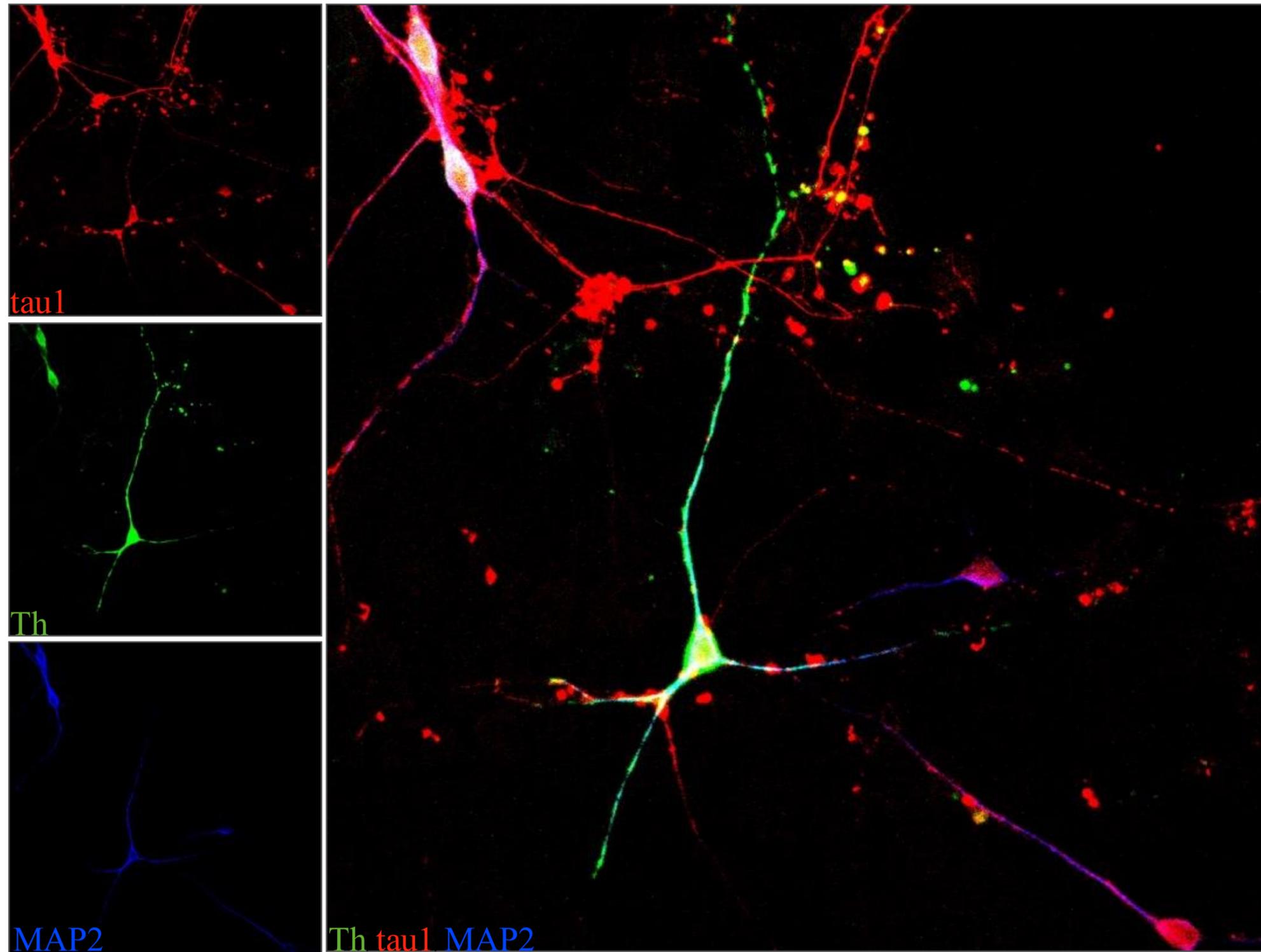
Synaptophysin accumulates around TH+ neurites



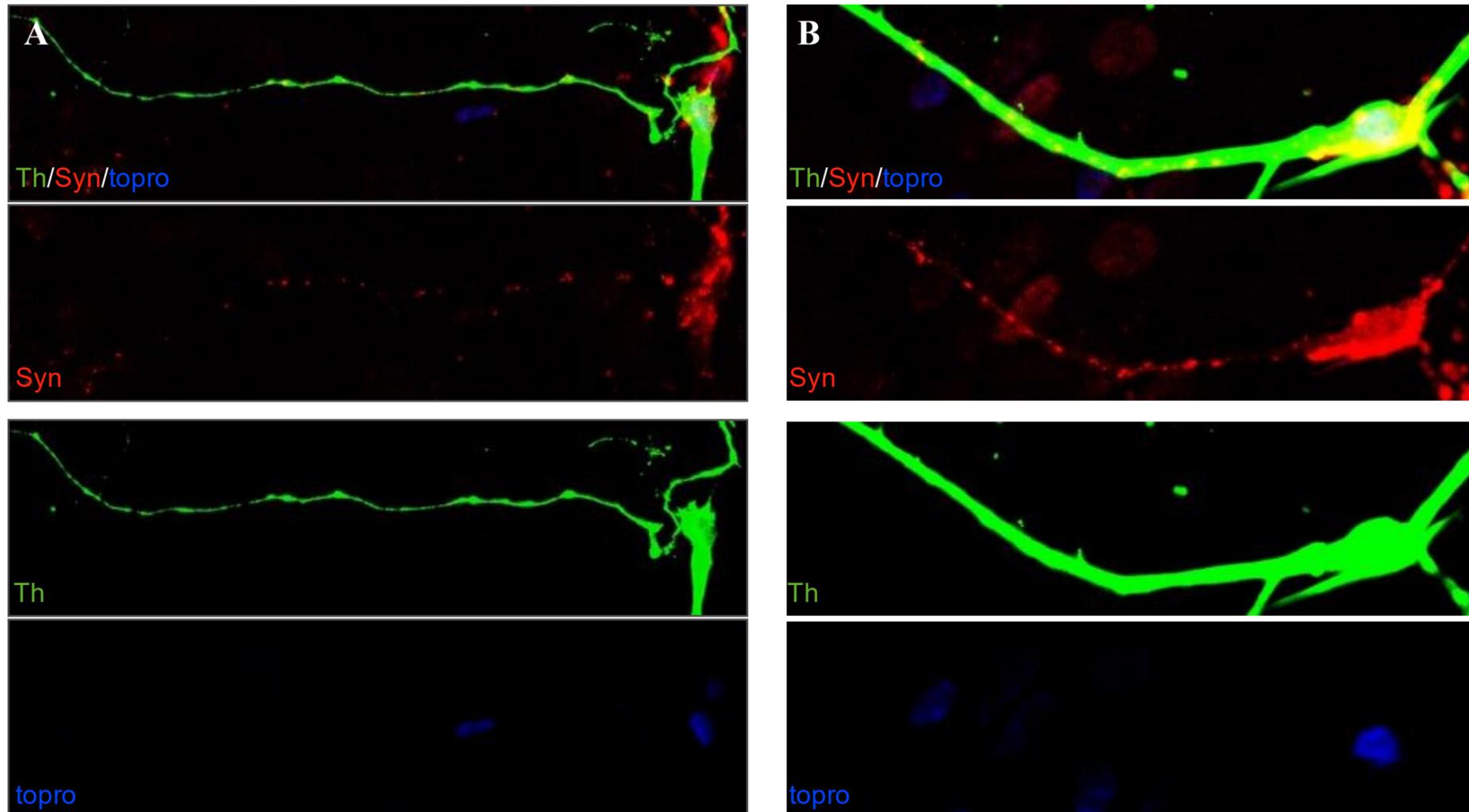
Synaptophysin accumulates around TH+ neurites



tau1 and MAP2 markers did not segregate in 10-day PMC



Synaptophysin accumulates around TH+ neurites



Conclusions

