Abril 28, 2011. F. Pfizer/ISCiii. Hotel Eurostar, Madrid
Grandes retos actuales en la Investigación Biomédica e instrumentos para el desarrollo de una investigación de vanguardia en España

Neurodegeneración y neuroprotección en el sistema nervioso adulto

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Human brain

Neuronal networks

Neurodegeneration: Progressive loss of neurons without an apparent cause (traumatic, infectious or ischemic) normally associated with age

Enfermedades neurodegenerativas más frecuentes

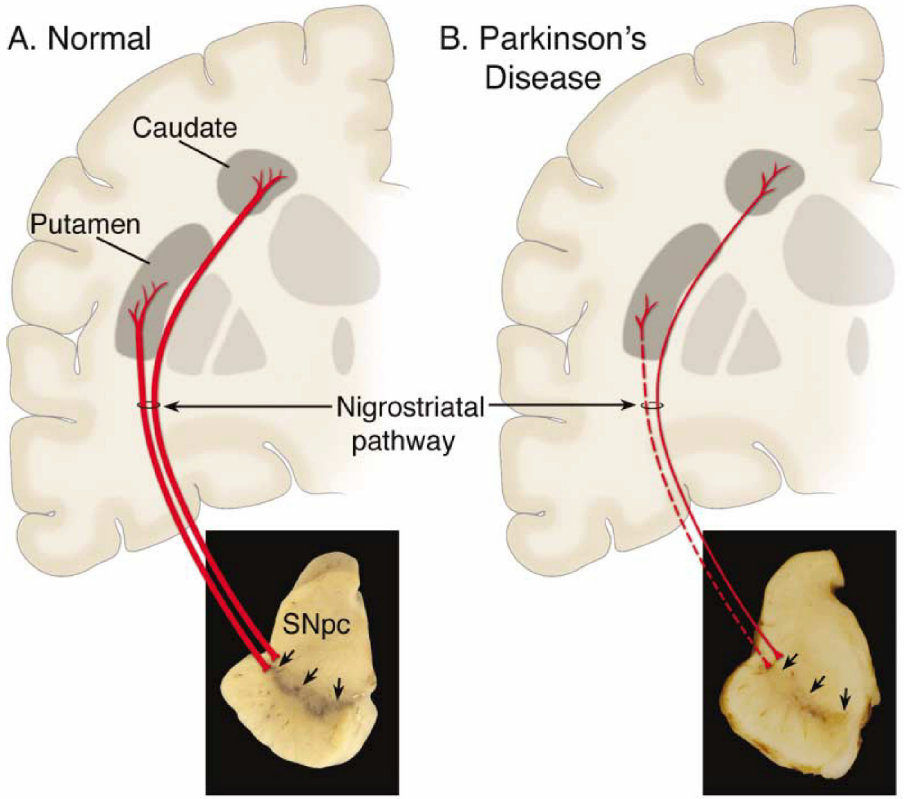
Enfermedad de Alzheimer y otras demencias
Enfermedad de Parkinson
Otras (Coreas, Ataxias, Esclerosis lateral amiotrófica…)

(Pérdida progresiva de neuronas y atrofia cerebral. Alteración de las funciones motoras, sensoriales, emocionales y cognitivas)

Neurodegeneración: reto biomédico del siglo XXI

(Problemas muy frecuentes. Curso crónico e invalidante. Alto coste para las personas, el enfermo y sus familiares, social y sanitario)

Neuronal loss in Parkinson's disease



Cuerpos de Lewy

D. Tremor-rigidity-bradykinesia (*Shaking palsy*)

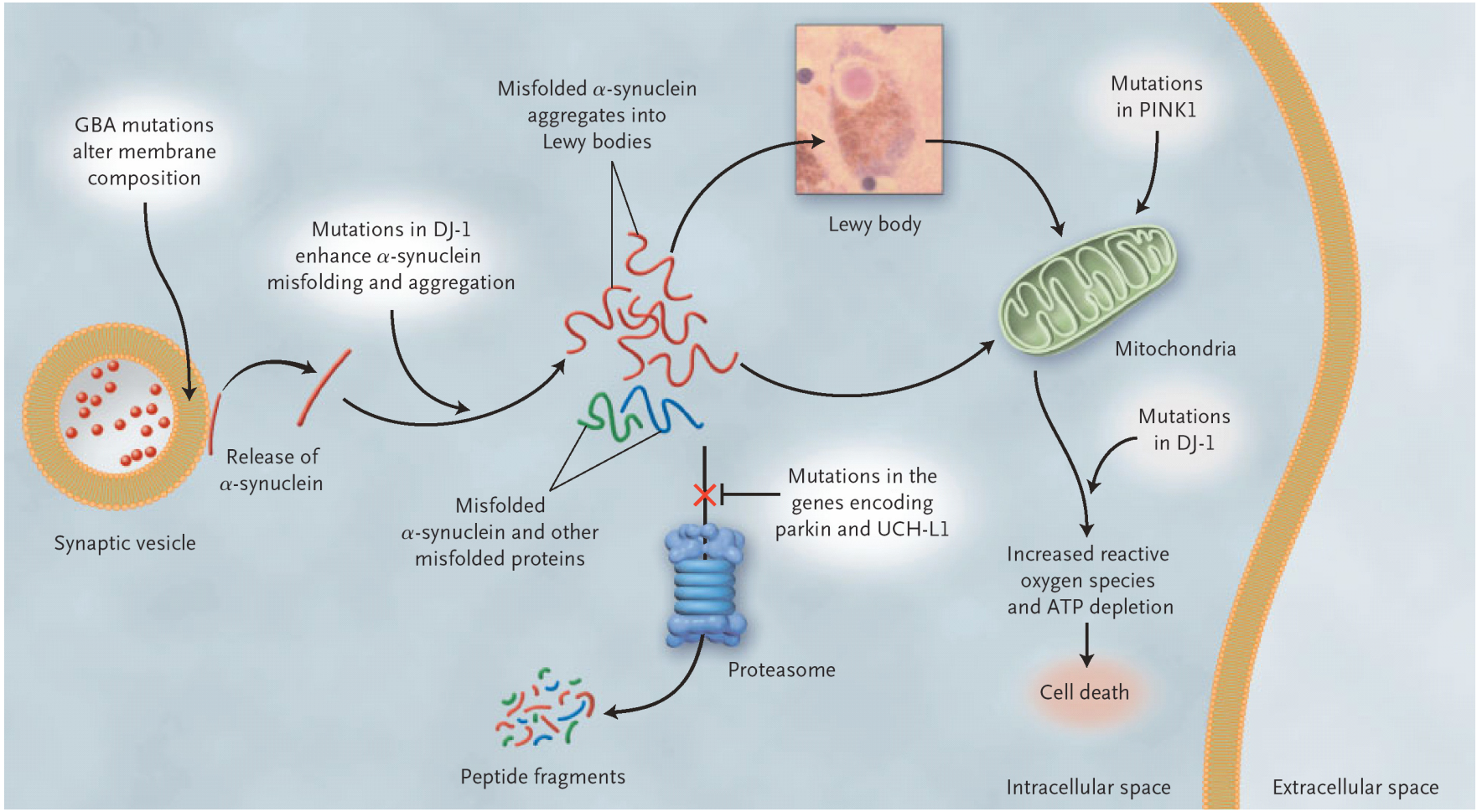
Dauer et al. Neuron (2003)

Grandes retos en la investigación sobre enfermedades neurodegenerativas

- Comprender la etiopatogenia (Pathogenesis)
  - factores etiológicos y nuevas dianas farmacológicas
  - modelos que recapitulen la enfermedad

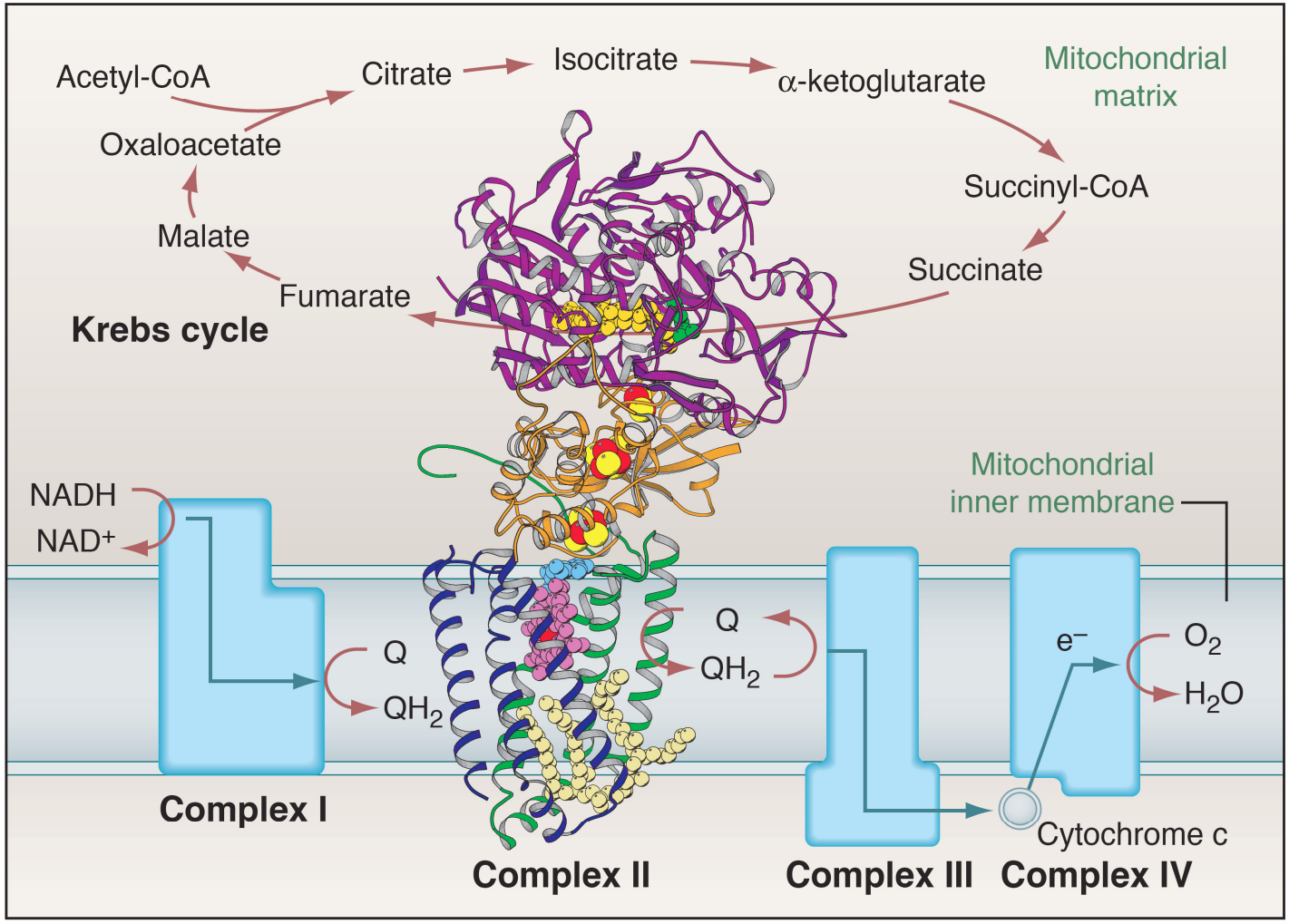
- Terapias avanzadas (Advanced therapies)

Pathogenesis of Parkinson's disease



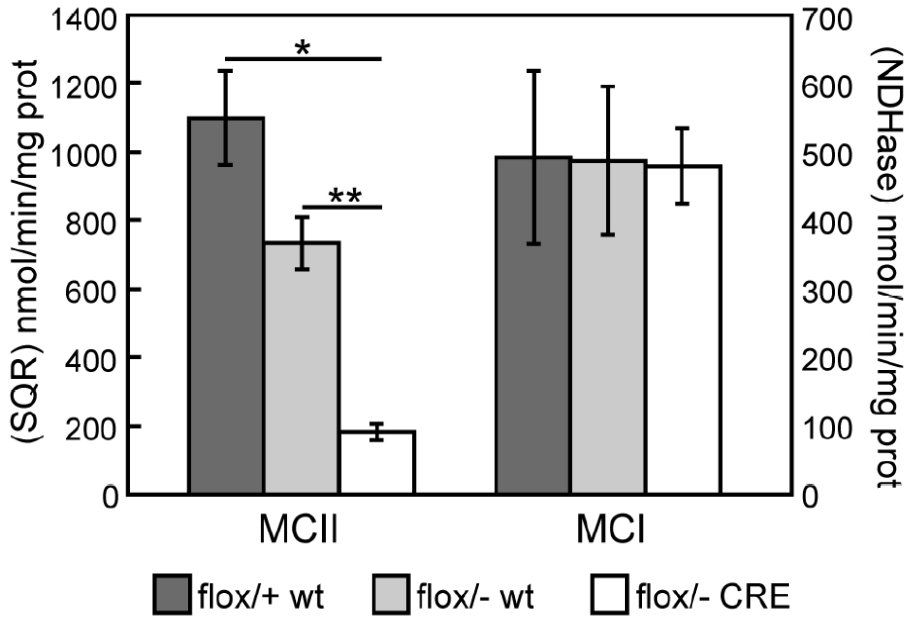
Feany, New England Journal of Medicine (2004)

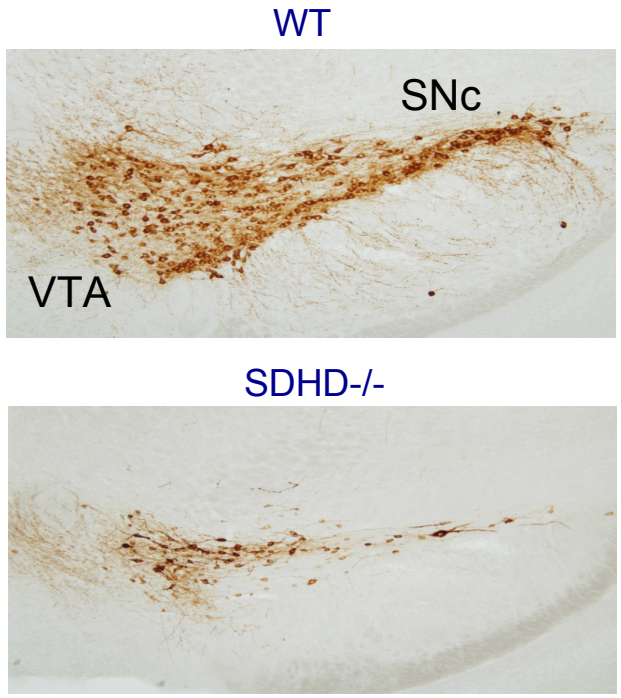
Mitochondrial complex II (Succinate dehydrogenase)



Hederstedt, Science (2003)

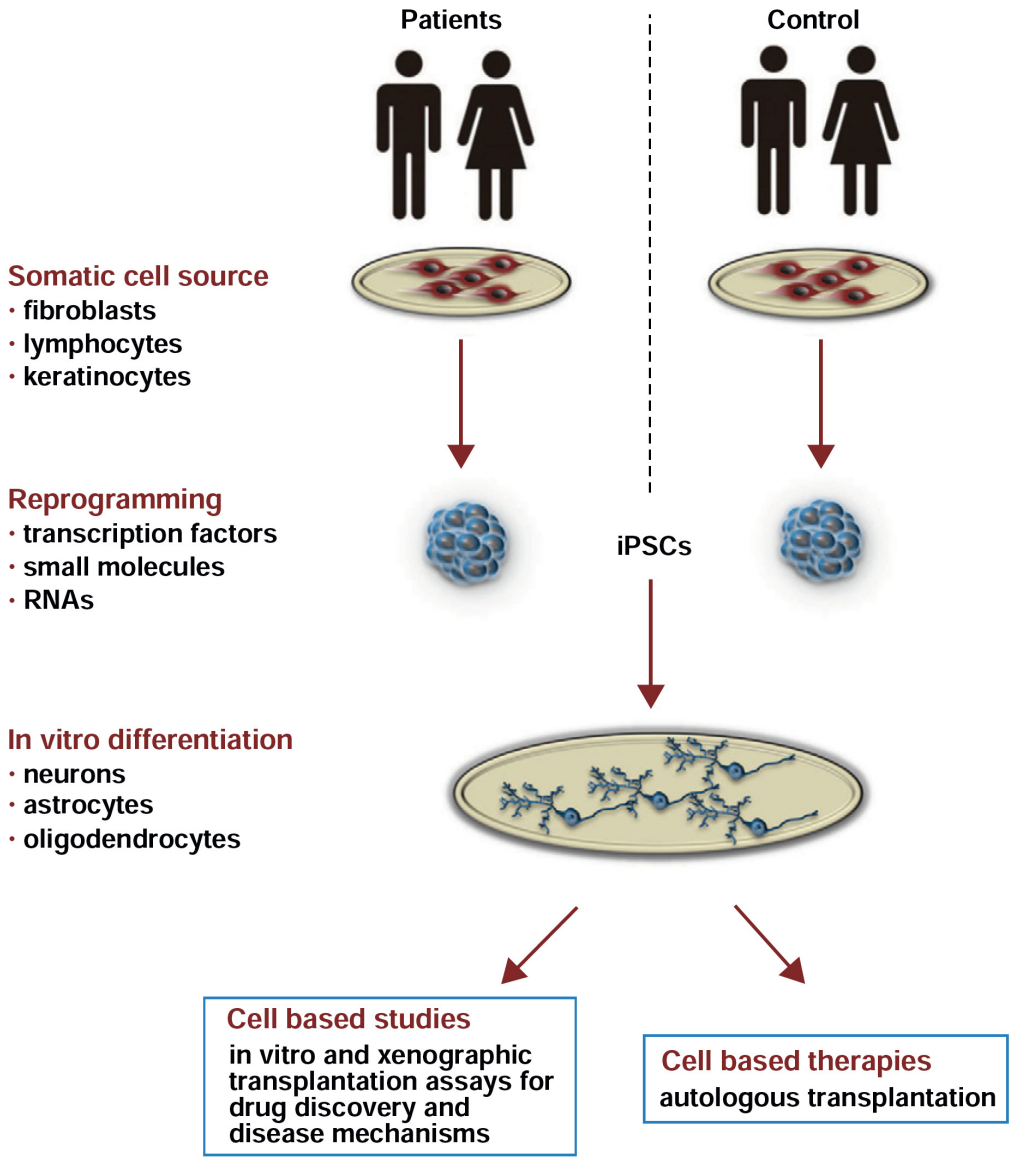
Selective dopaminergic neuronal death in SDHD KO mouse





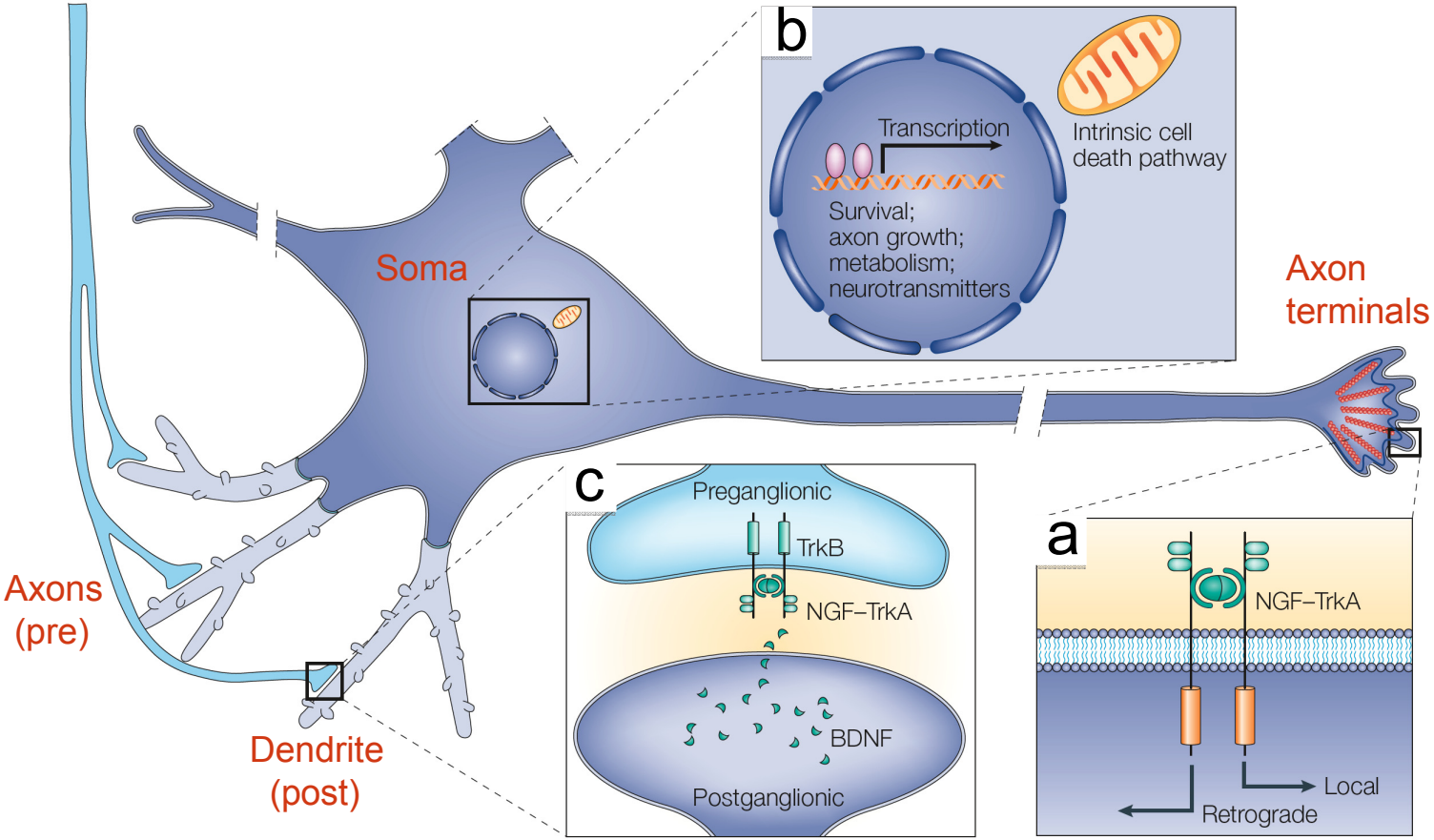
Patient-specific induced pluripotent stem cells and dopaminergic neurons

CIBERNED's "Parkinson Cooperative Project"



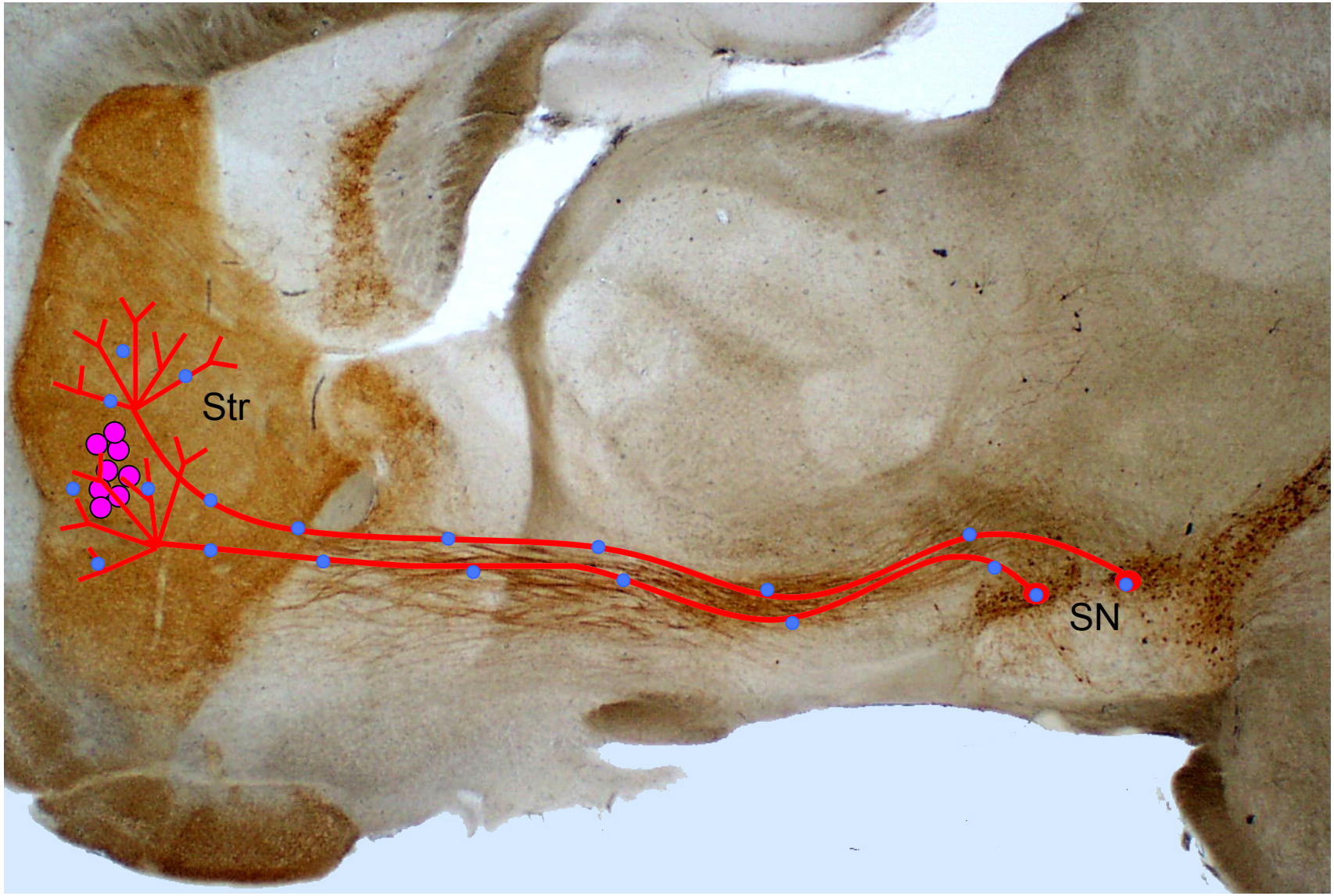
Cundiff and Anderson, Current Opinion in Genetics and Development (2011)

Local and retrograde signalling of neurotrophic factors



Sweifel et al., Nature Reviews Neuroscience (2005)

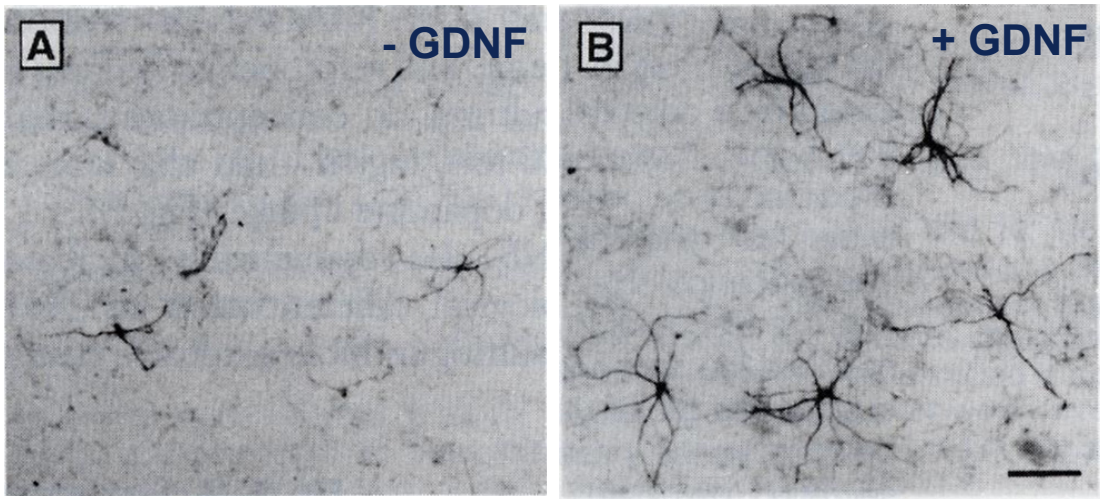
Effect of trophic factors on the nigrostriatal pathway



Toledo-Aral et al., unpublished

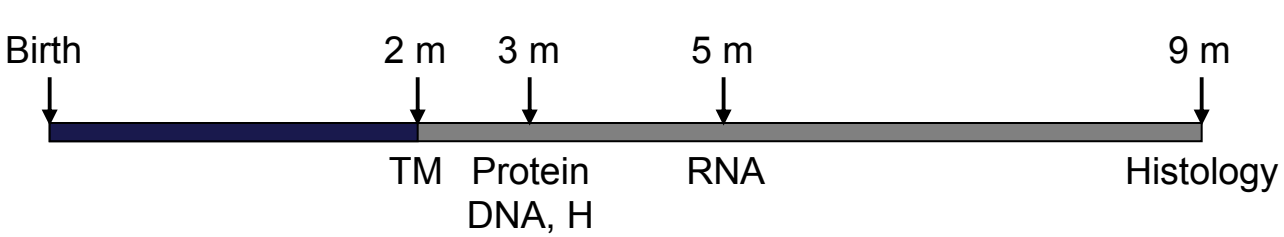
The glial cell line-derived neurotrophic factor (GDNF) is a potent dopaminergic neuroprotective agent

Embryonic mesencephalic neurons

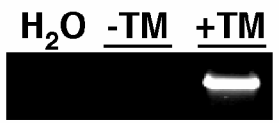


Lin et al., Science (1993)

Conditional GDNF "knock out" mouse

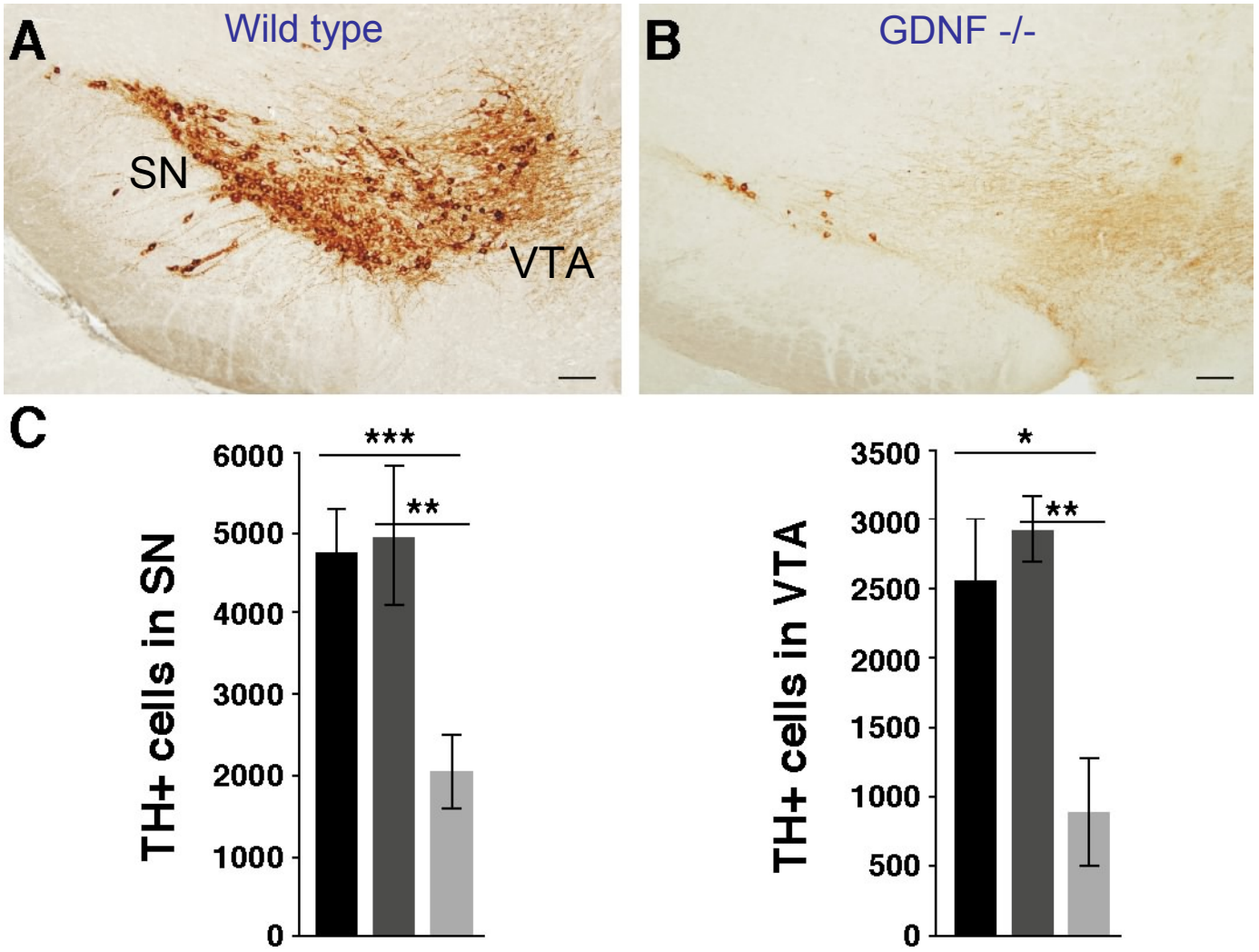


Striatal DNA



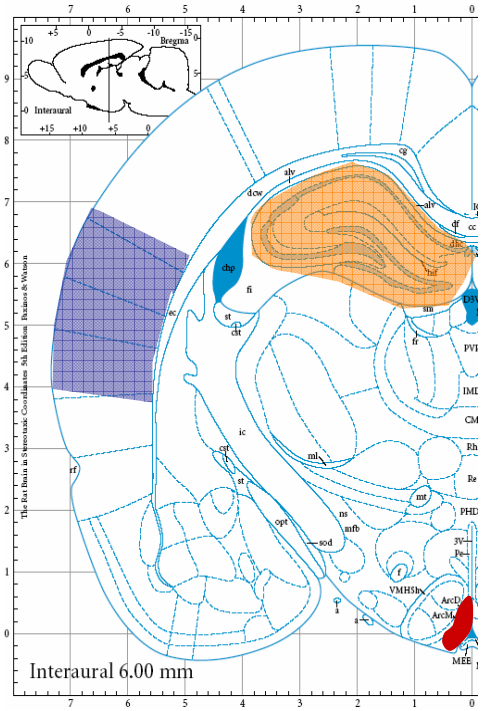
Pascual et al., Nature Neuroscience (2008)

Death of mesencephalic dopaminergic neurons in the adult conditional GDNF knock out mice



Pascual et al., Nature Neuroscience (2008)

Adult conditional GDNF knock out mice



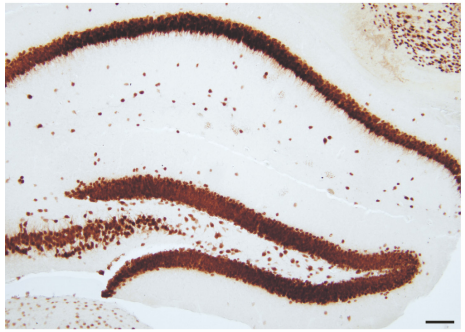
Hippocampus

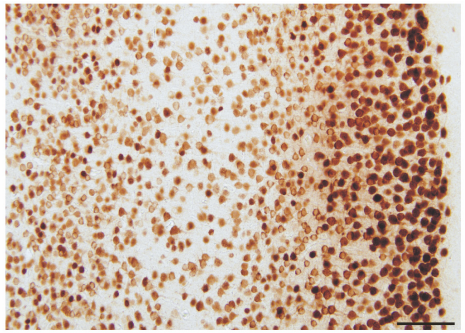
Cortex

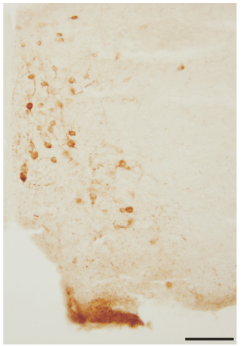
Arcuate N.

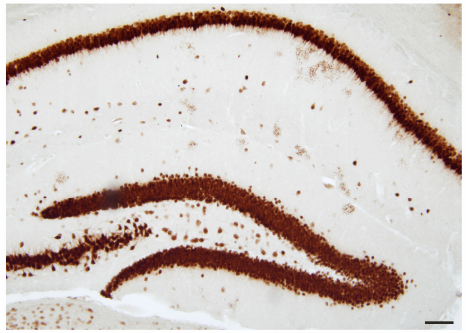
WT

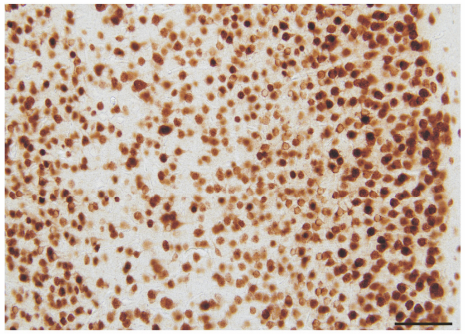
GDNF^{KO}

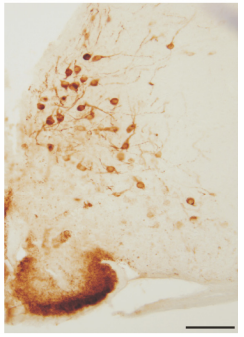






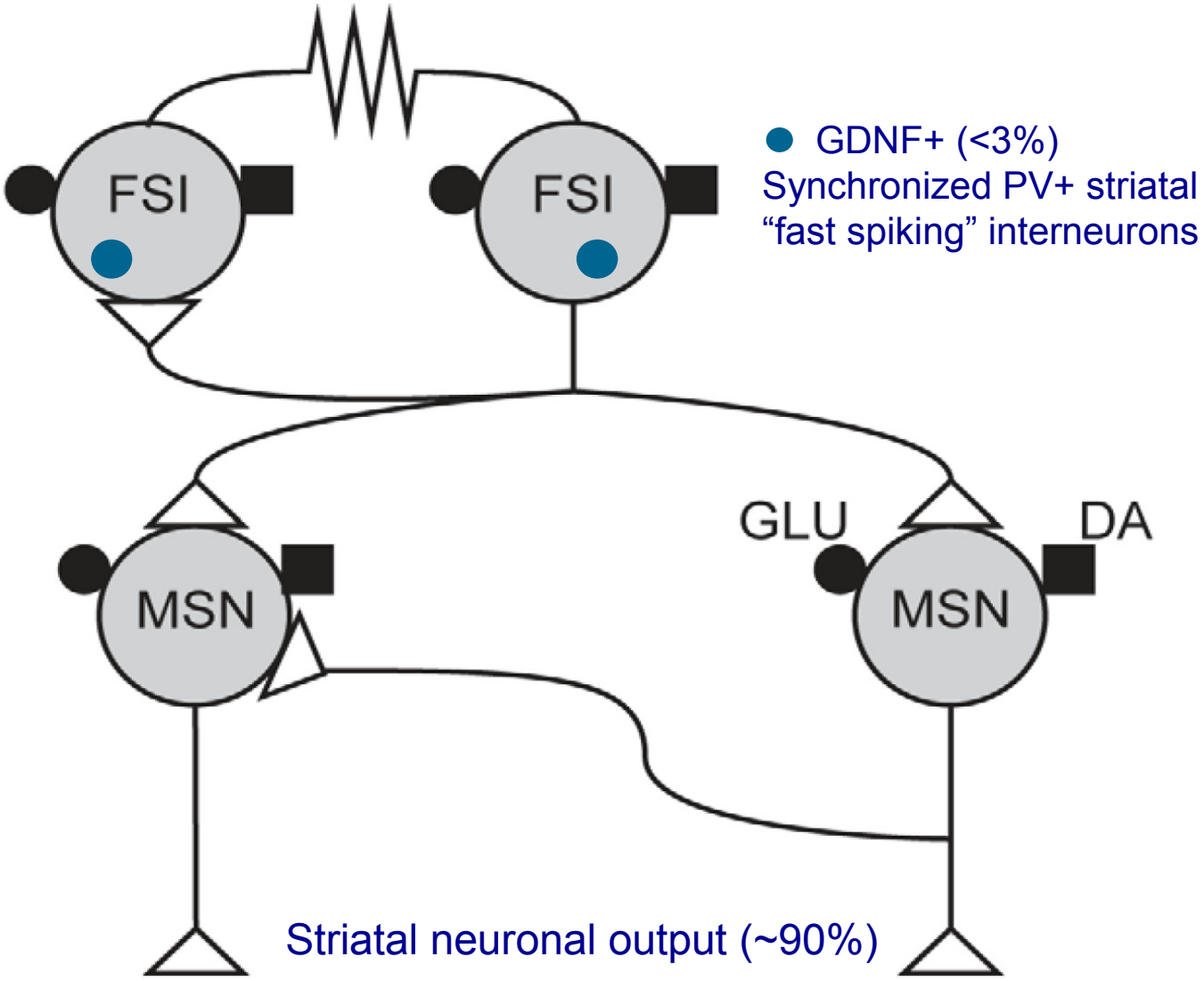






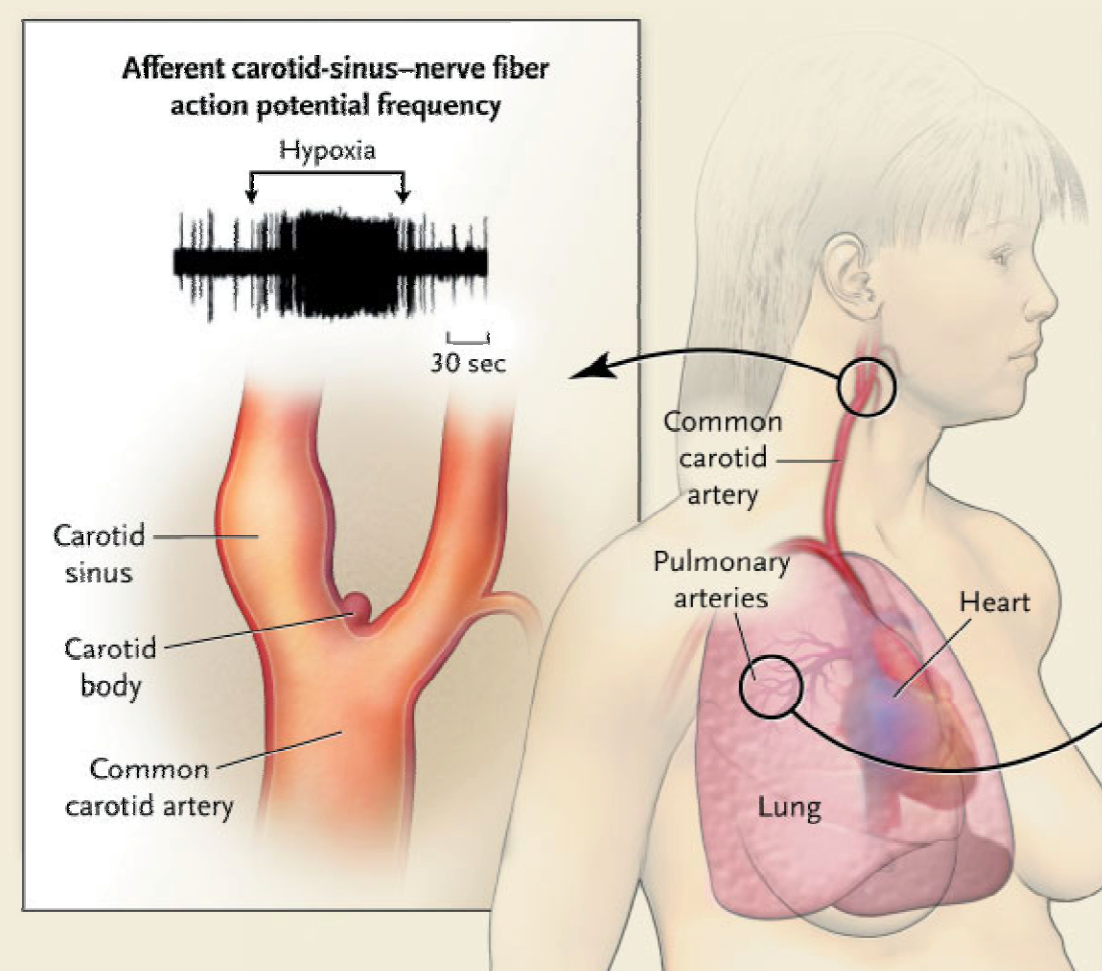
Pascual et al., Nature Neuroscience, 2008

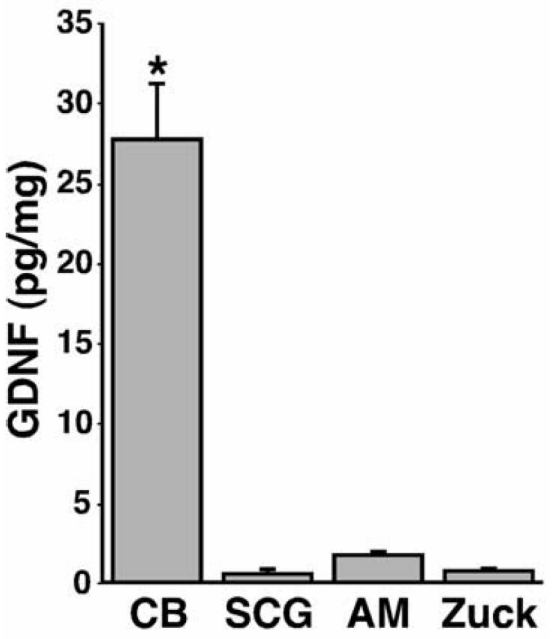
Selective GDNF expression in the striatal connectome



Humphries et al., PLoS Computer Biology (2010)

The human carotid body; an abundant source of GDNF

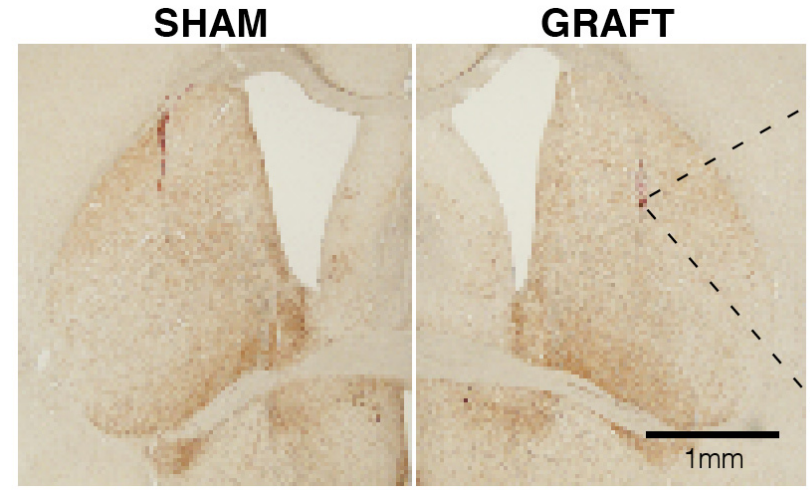


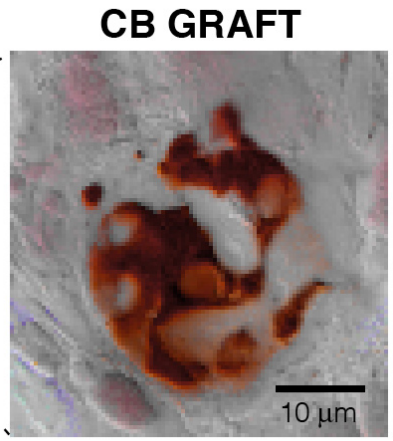


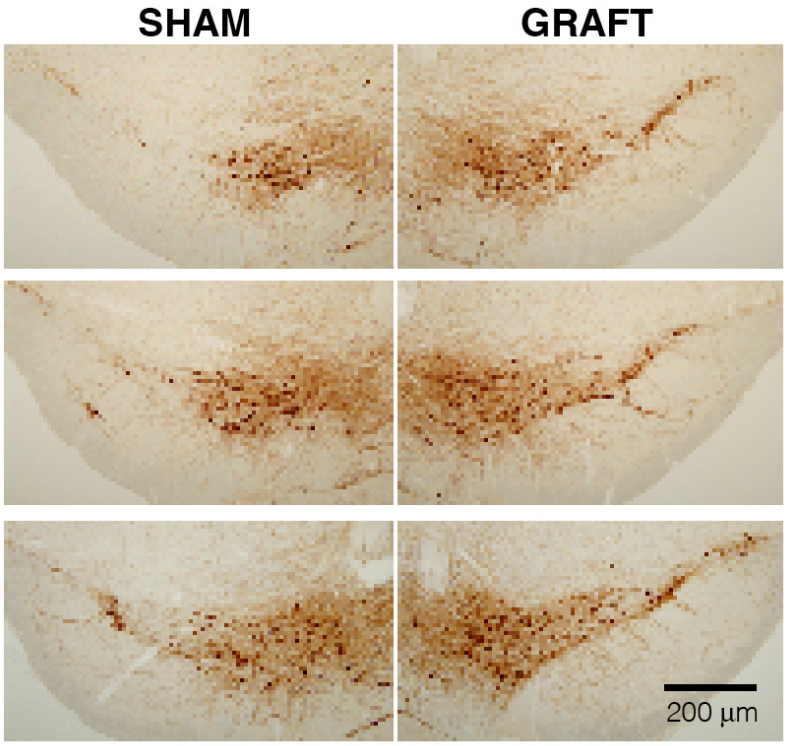
Weir, López-Barneo, Buckler & Archer, New England Journal of Medicine (2005)

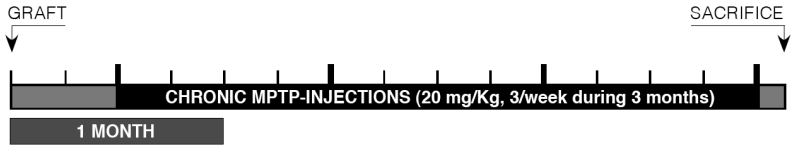
Villadiego et al., Journal of Neuroscience (2005)

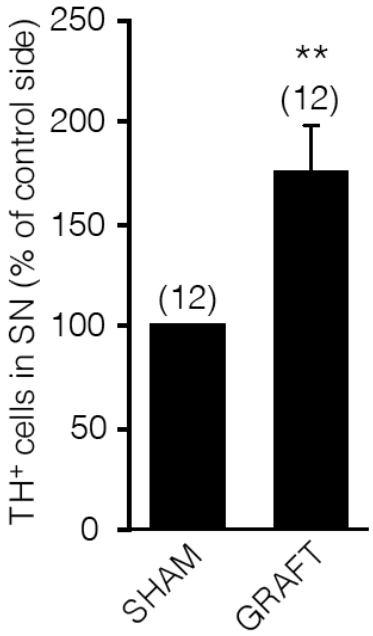
Neuroprotective effect of intrastriatal CB transplantation



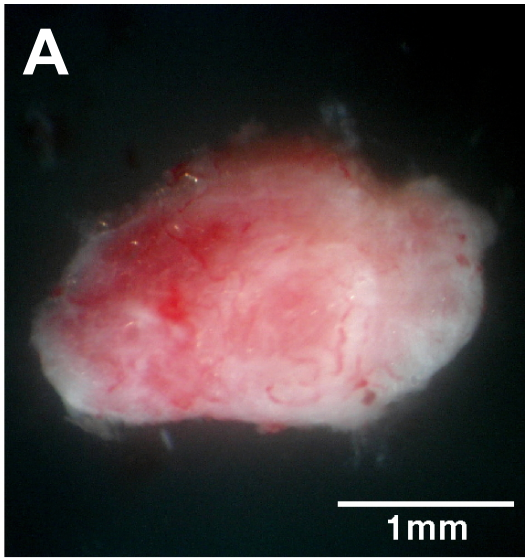


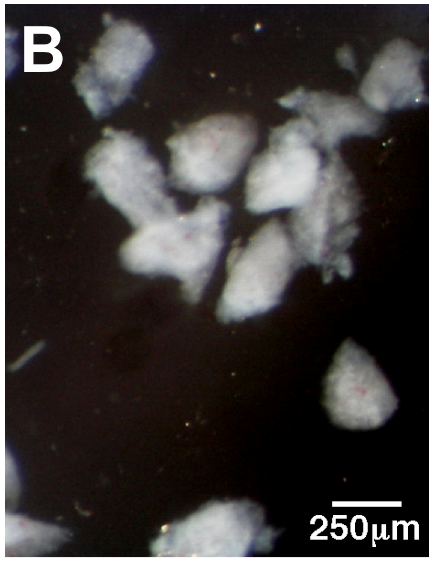


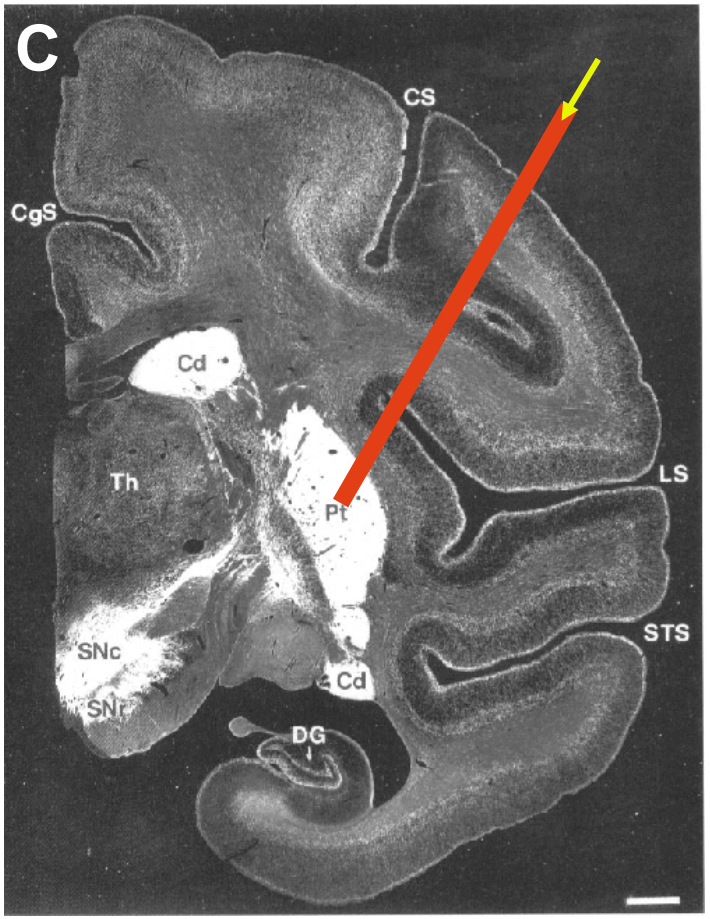




Autotransplantation of CB cell aggregates in PD patients



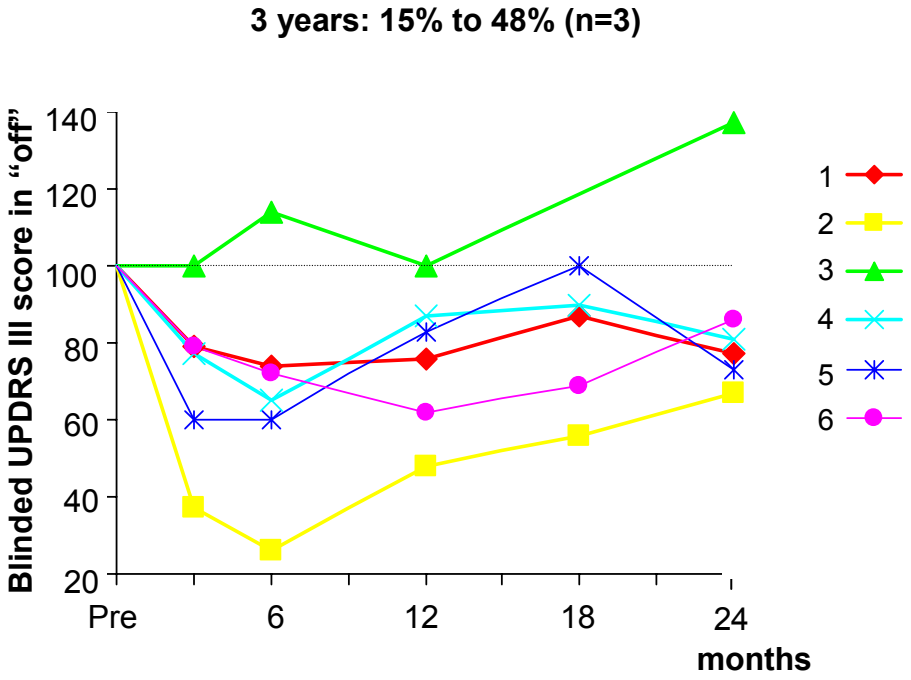




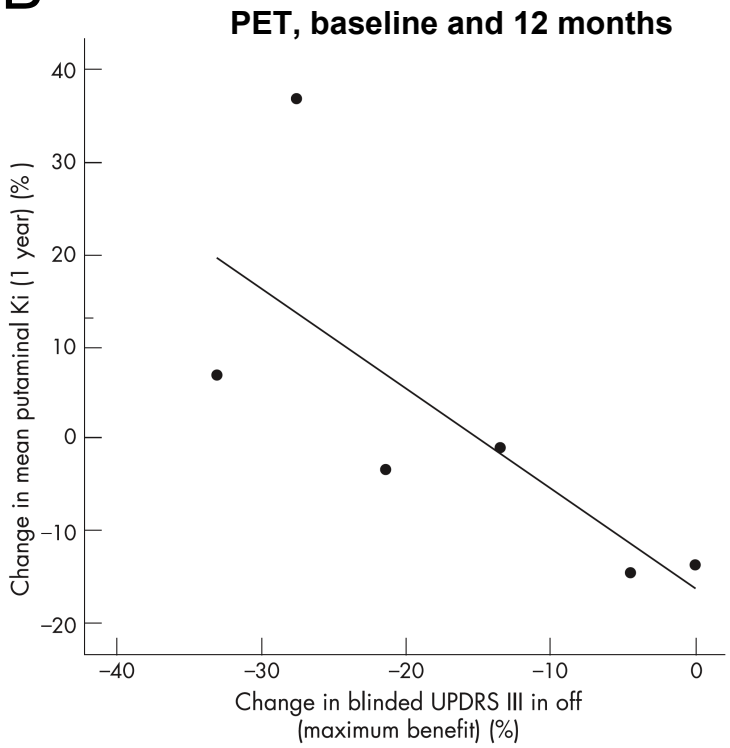
Arjona et al., Neurosurgery (2003)

Clinical and neurochemical outcomes of CB transplanted PD patients

A

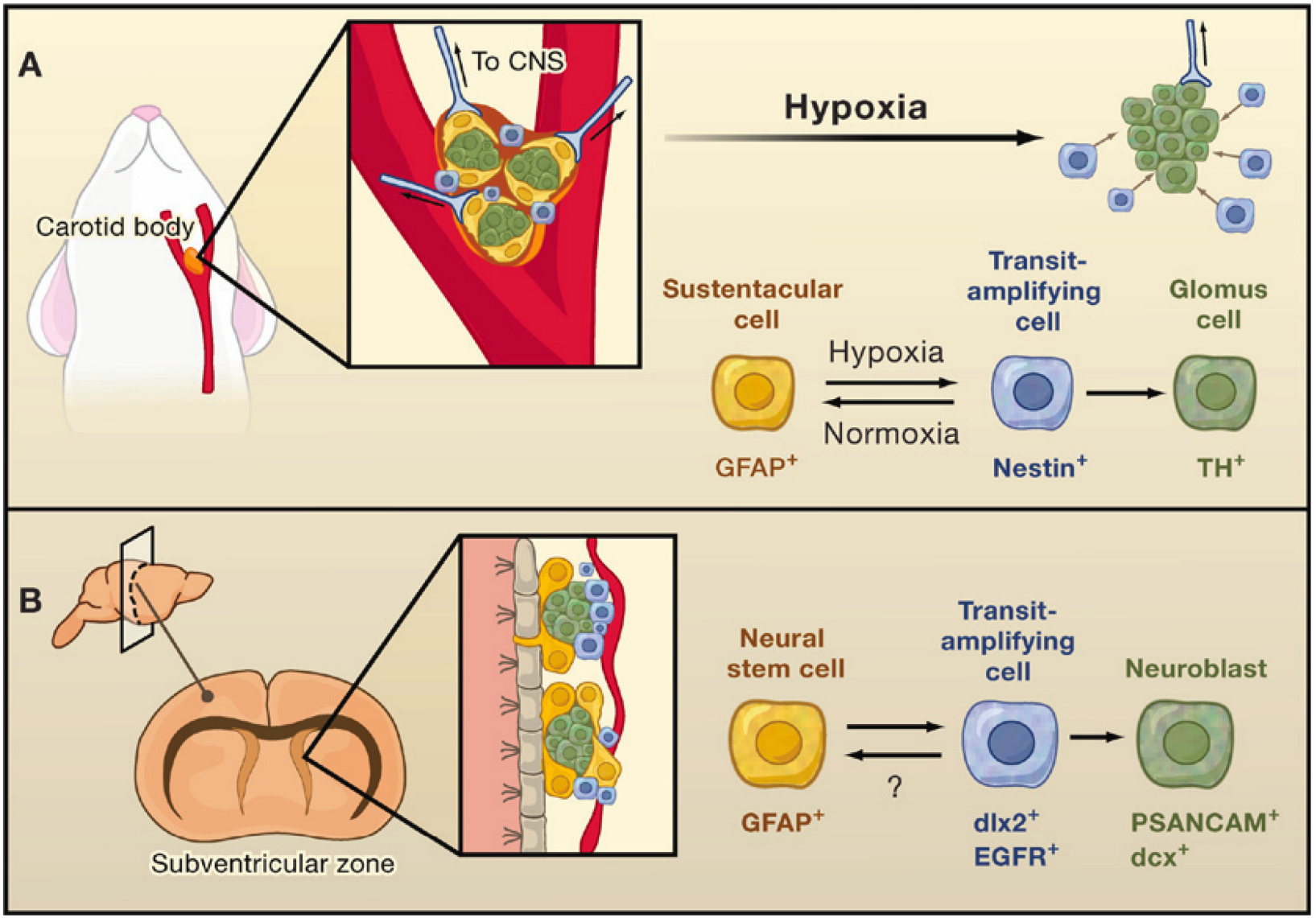


B



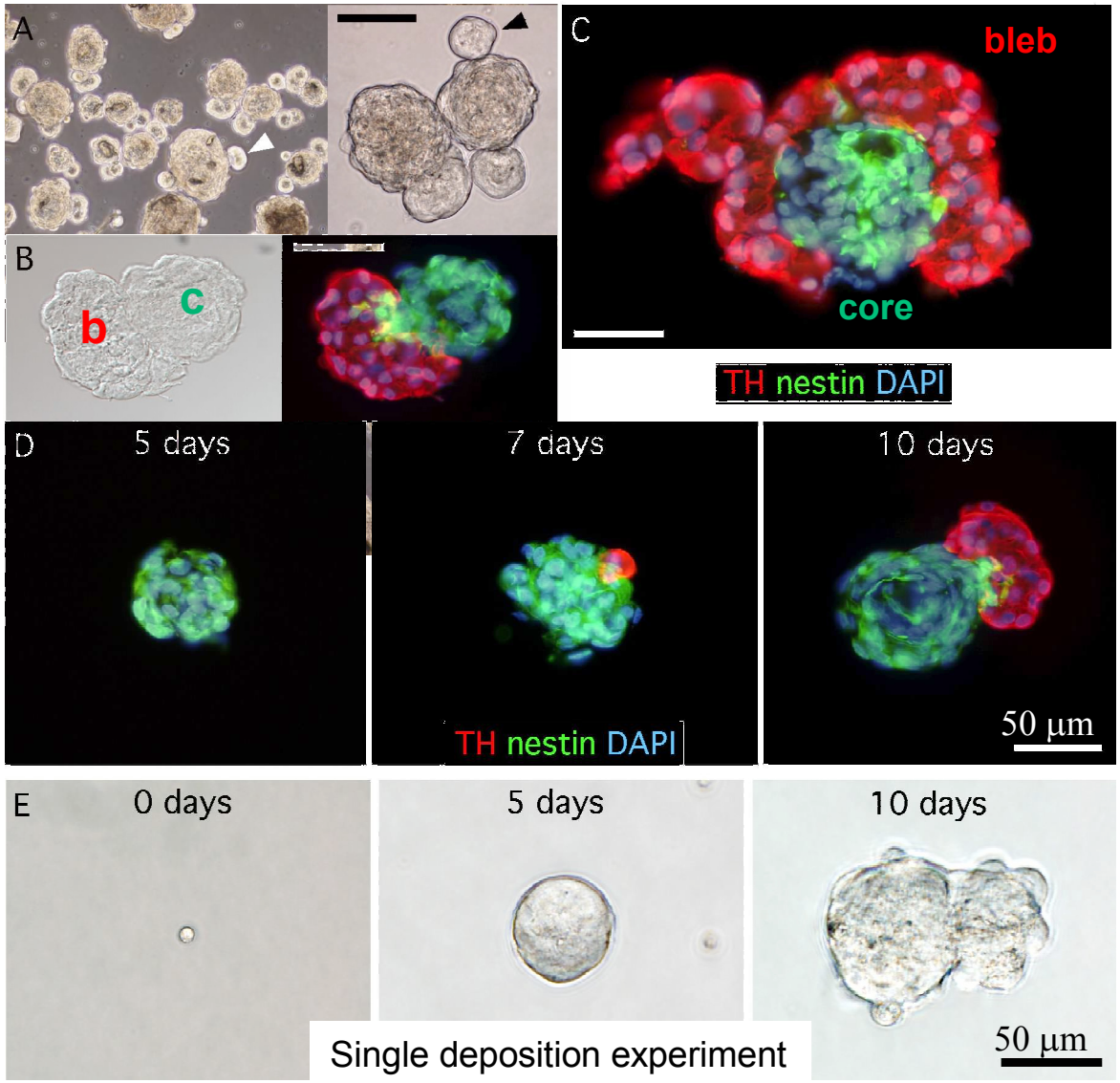
Arjona et al., Neurosurgery (2003)
Mínguez-Castellanos et al., Journal of Neurology, Neurosurgery & Psychiatry (2007)

Neurogenic niches in the adult central and peripheral nervous system



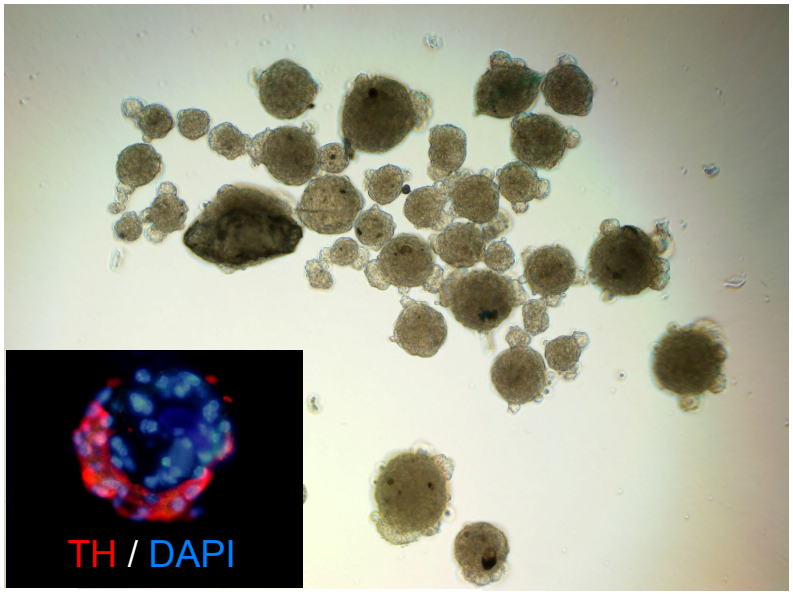
Kokovay and Temple, Cell (2007)

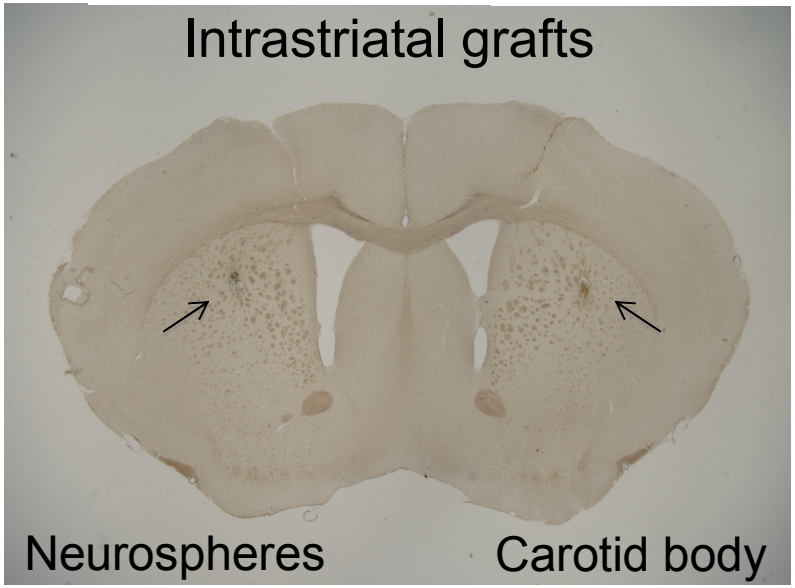
Identification of stem/progenitor cells in the adult carotid body (neurosphere assay)



Pardal et al., Cell (2007)

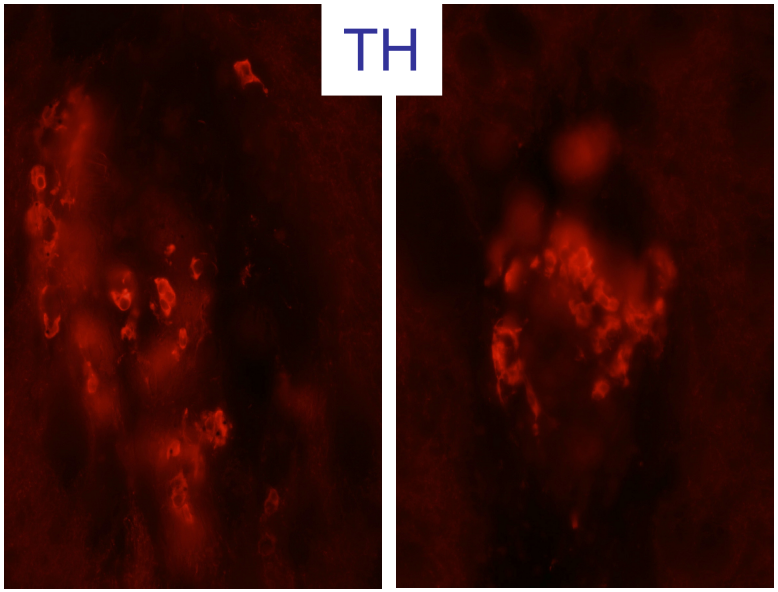
Mouse carotid body neurospheres

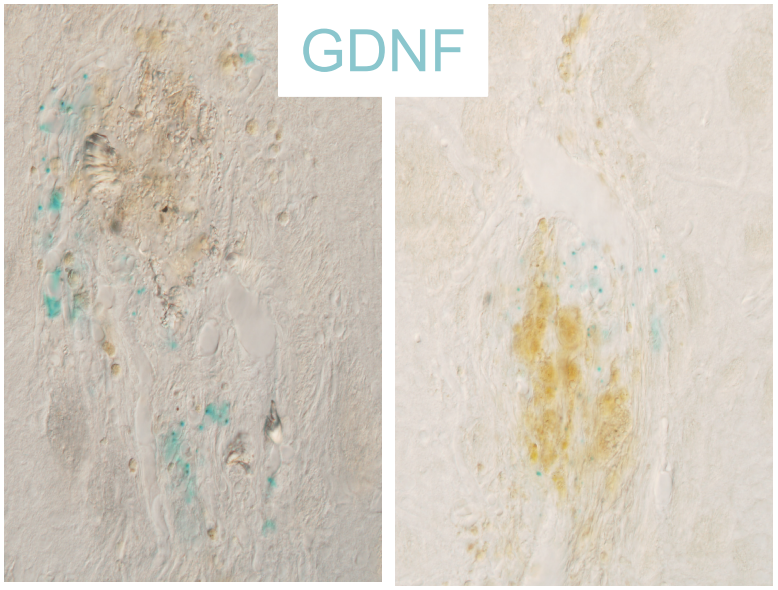




Lopez-Barneo et al., unpublished

Neurospheres Carotid body





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