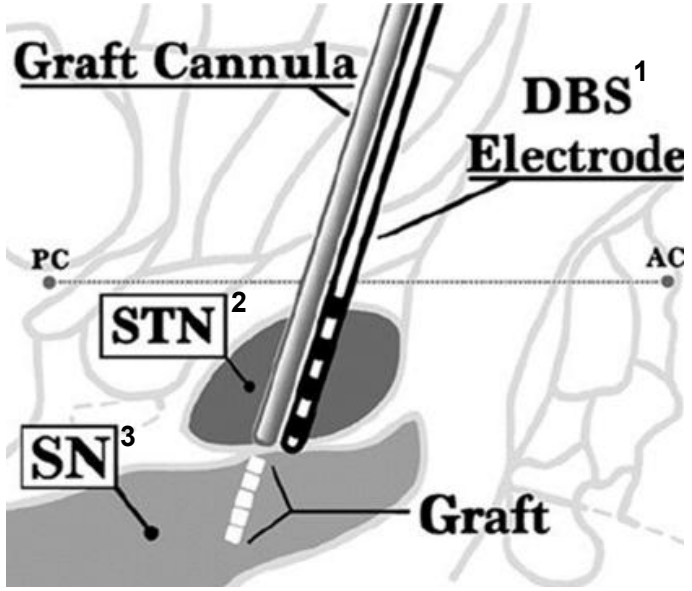
Anschutz | Colorado Clinical and Translational Sciences Institute (CCTSI)

Postmortem Analysis of Peripheral Nerve Autografts to Parkinsons Disease Patients

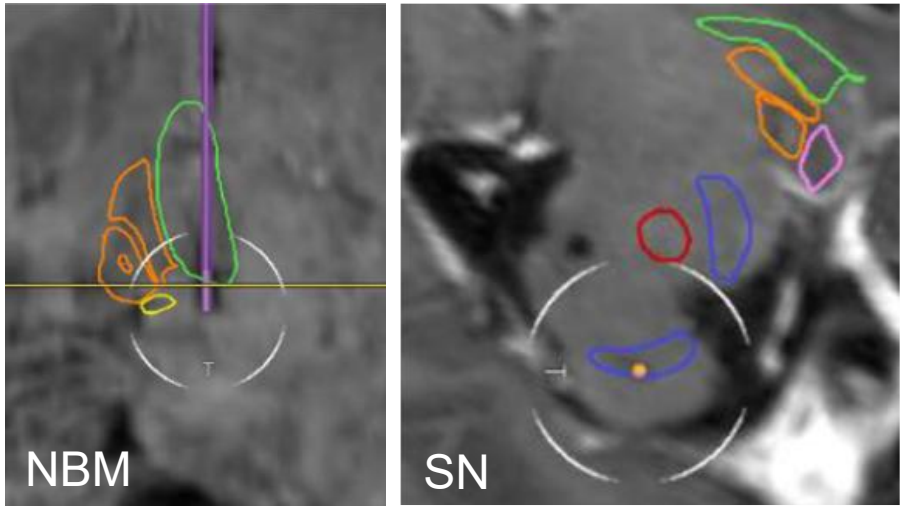
Claire Vrooman
MS candidate SSPPS
Granholm Lab - Neurology

Introduction & Methods:

- Parkinson's disease (PD) - second most common neurodegenerative disorder
- Loss of DA neurons in the substantia nigra (SN) and limbic system
- Currently no known disease modifying treatments
- DBS-plus clinical trial at the University of Kentucky;
  - Autologous sural nerve graft in the SN and/or nucleus basalis of Mynert (NBM)
- Postmortem analysis of 9 grafts in 8 participants
  - Immunofluorescence (IF)
  - Immunohistochemistry (IHC)



MRI Guided Placement Stereotactic Coordinates:



University of Colorado Anschutz

Colorado Clinical and Translational Sciences Institute (CCTSI)

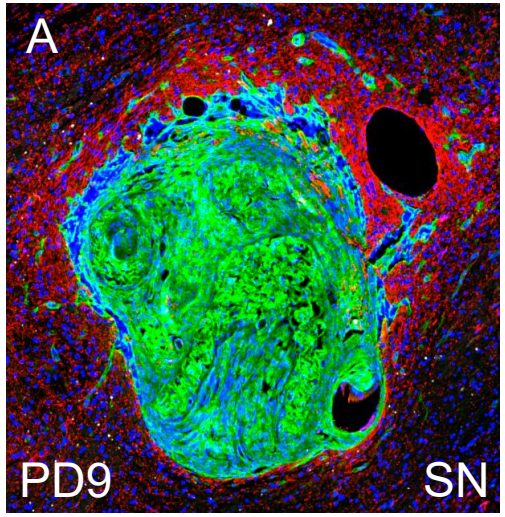
[1] Deep Brain Stimulation
[2] Subthalamic Nucleus
[3] Substantia Nigra

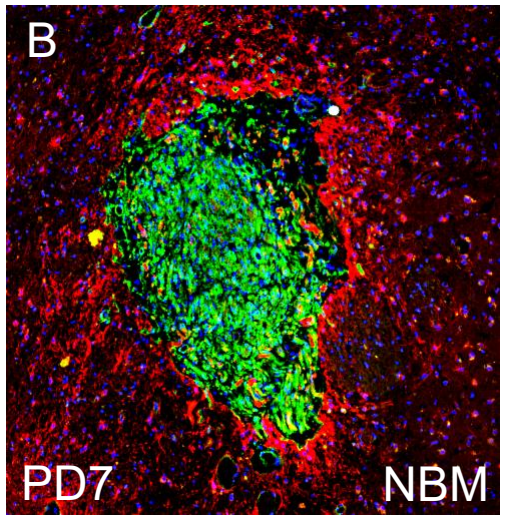
Graft Parameters:

Actual Graft Placement:

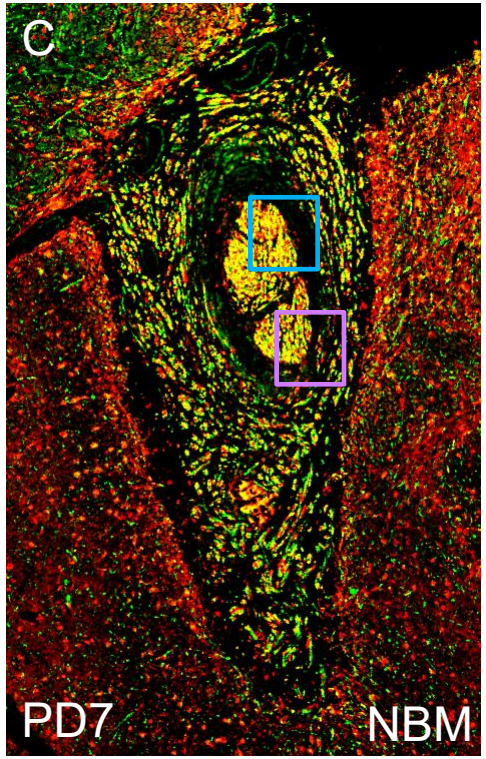
patient	target	Actual location
PD1	SN	SNpc[1]
PD5	SN	SNpc
PD6	SN	SNpr[2]
PD7	SN	SNpc
PD8	SN	SNpc
PD9	SN	SNpc
PD2	NBM	NBM
PD4	NBM	Anterior commissure
PD7	NBM	External medullary lamina

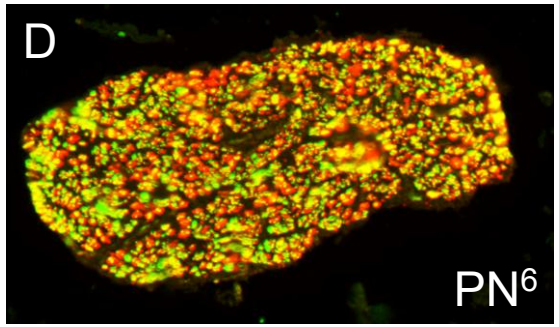
Col1A1[3] & GFAP[4]



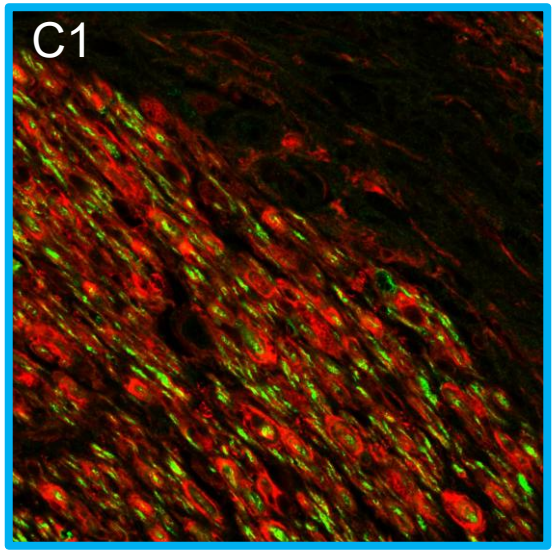


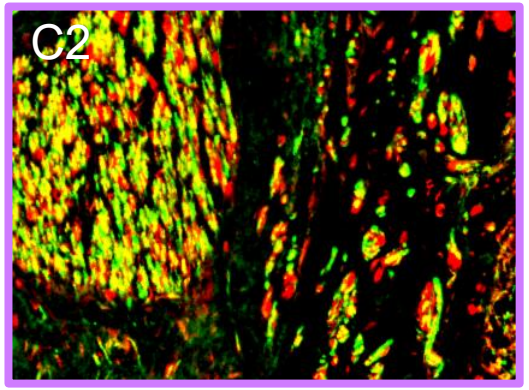
NF[5] & S100B





Schwann cells



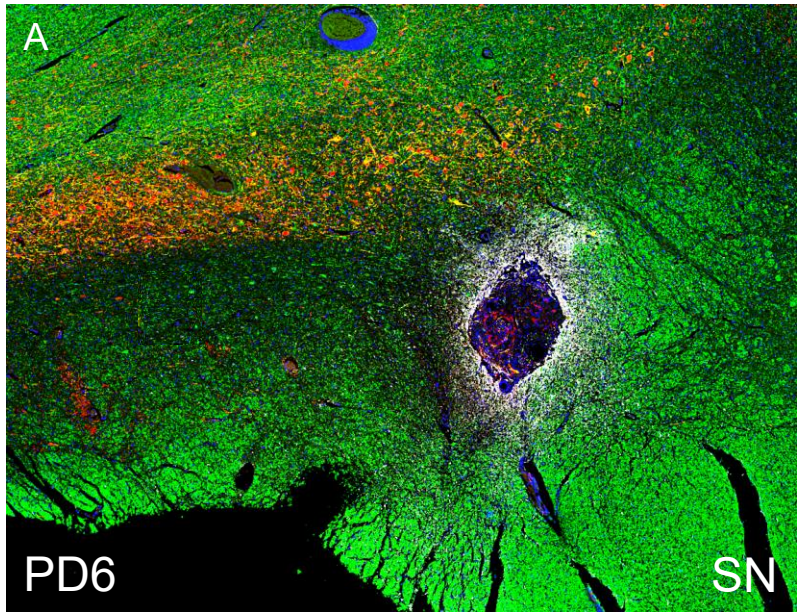


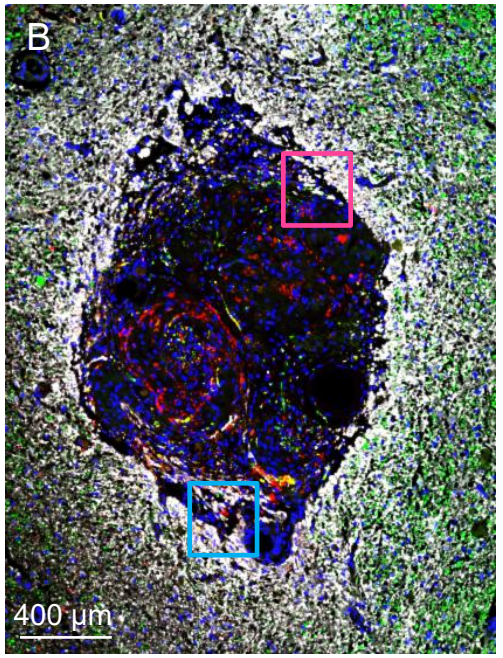
University of Colorado Anschutz

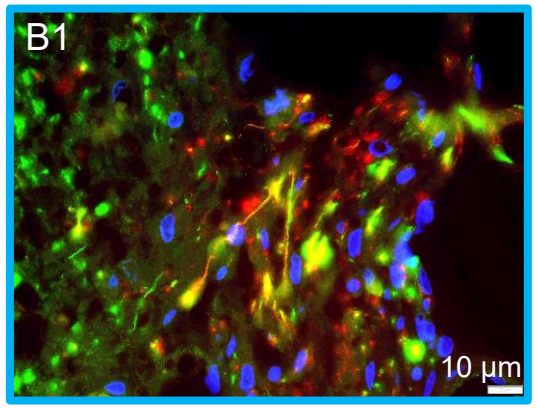
Colorado Clinical and Translational Sciences Institute (CCTSI)

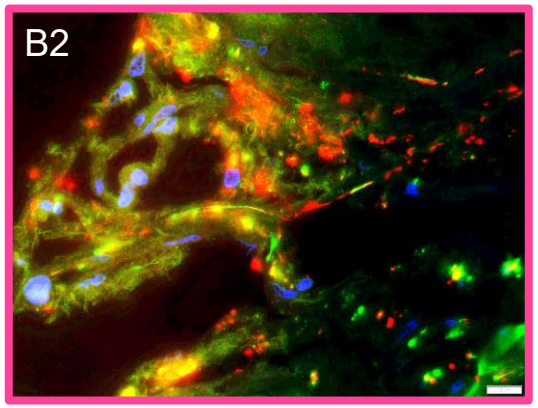
[1]Substantia nigra pars compacta
[2]Substantia nigra pars reticulata
[3]Collagen 1A1
[4]Glial Fibrillary Acidic Protein
[5]Neurofilament
[6]Peripheral Nerve

SN graft Innervation:





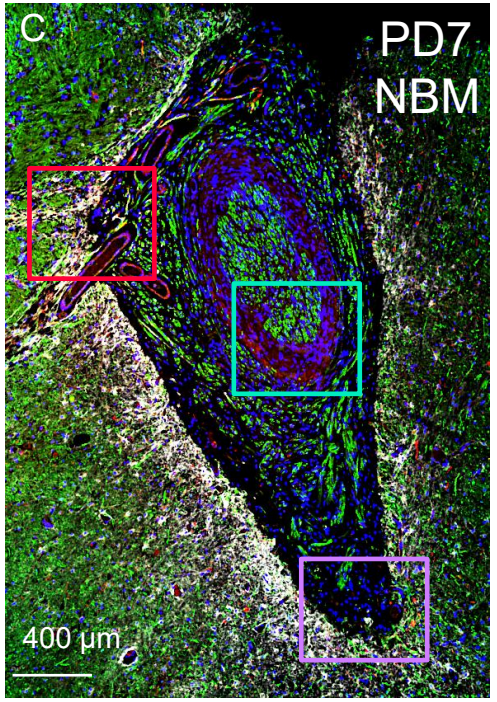


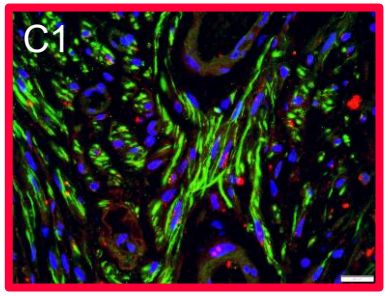


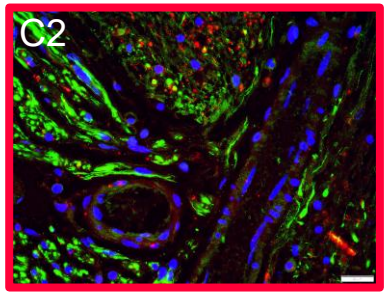
University of Colorado **Anschutz**

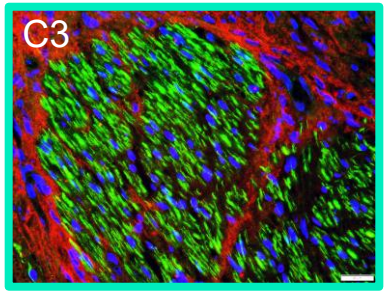
Colorado Clinical and Translational Sciences Institute (CCTSI)

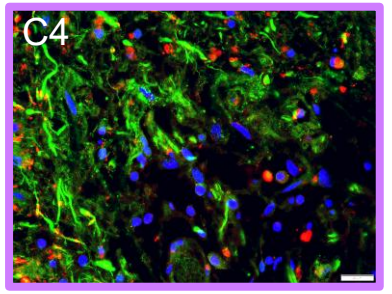
NBM graft Innervation:











Conclusion:

- All 6 SN and 1 of 3 NBM grafts were on target
- All grafts contained Col1A1 positive staining and a halo of GFAP positive astrocytes
- Co-staining indicates surviving Schwann cells
- Complete survival of autologous sural nerve grafts
- Future directions: these studies may lead to a new disease-modifying therapy for PD
  - UPDRS scores and other clinical datapoints

Nerve and vessel entry into PNT graft

THANK YOU

Mentors

Lotta Granholm-Bentley

Greg Gerhardt

Collaborators

Henric Ek Olofsson

Marcella Raust

College of Medicine
Department of Neuroscience

Funding

This work was supported by the National Institute on Aging (R01AG081356) and the Ann Hanley Neuroscience Fund. HEO was supported by The Tegger Foundation and the Elly Berggren Foundation