Neuroprotection

Neurorestoration

Remodeling the CNS after stroke and neural injury

MSCs stimulate VEGF expression in astrocytes

MSCs increase vascular density after stroke

MSCs induce neurogenesis in the SVZ
Rewiring the brain

MSCs reduce inhibitory glycoprotein gene expression in peri-infarct astrocytes

MSCs increase axonal density and reorient axons along the border of the infarct

MSCs increase transcallosal axons in the contralateral cortex

Functional recovery is highly correlated with contralateral cortical axonal sprouting 28 days after ischemic stroke
**Axonal sprouting from the intact CST to the denervated side in longitudinal spinal sections**

Functional recovery is highly correlated with axonal outgrowth in the spinal cord

**tPA via astrocytes mediates neurite outgrowth after MSC treatment of stroke**

MSCs increase tPA and decrease PAI-1 in astrocytes post stroke

**No functional benefit from MSCs in tPA-/- mice**

**Sonic Hedgehog**

Stimulates transcription factors which activate many genes involved in CNS modeling during development and remodeling after stroke and neural injury in the adult
MSCs stimulate astrocyte expression of sonic hedgehog (Shh) which drives tPA activity and neurite outgrowth.

Shh increases tPA in astrocytes (mRNA)

Blocking the Shh pathway with Cyclopamine (CP) blocks the functional benefit of MSC treatment of stroke.

Intranasal tPA-7 days post stroke improves neurological function.

Neurological recovery post stroke is significantly correlated with neural remodeling.
MicroRNA biogenesis

Exosomes package and transfer “information” between cells

Ischemic tissue brain extracts increase miR-133b expression in MSC generated exosomes

MiR-133b promotes MSC induced functional recovery

MiR-133b reduces ras homolog gene family member A (RhoA) expression, thus promoting neurite outgrowth and branching

MiR-133b promotes axonal plasticity after stroke

Days after MCAo

Adhesive-Removal Test

% positive area (Mean ± SE)
Neurogenesis  
Angiogenesis  
Exosome  

eRNA  
proteins  

Neurite Remodeling

Intracerebral hemorrhage  
Traumatic brain injury  
Multiple sclerosis  
Peripheral neuropathy

H&E

Modified-Morris Water Maze: tracking-memory and learning

Pre-TBI - 5 day training  
Day 1 after TBI

Thymosin beta 4-actin sequestering protein

TB4 Treatment Improves Spatial Learning Function after TBI in Rat

Time spent in correct quadrant (%)  
Days post TBI
Neurological function after TBI and TB4 treatment is significantly correlated with oligodendrocytes (CNPase) in the CA3

\[ y = 0.1667x + 17.754 \]

\[ R^2 = 0.9062 \]

\[ p < 0.001 \]

Cerebrolysin Treatment Improves Spatial Learning in Rats after Mild Closed Head Injury (MWM Test, 1 Month)

If a relaxing moment turns into the right moment ... will you be ready? To increase cGMP!

Restorative Therapies for Neural Injury