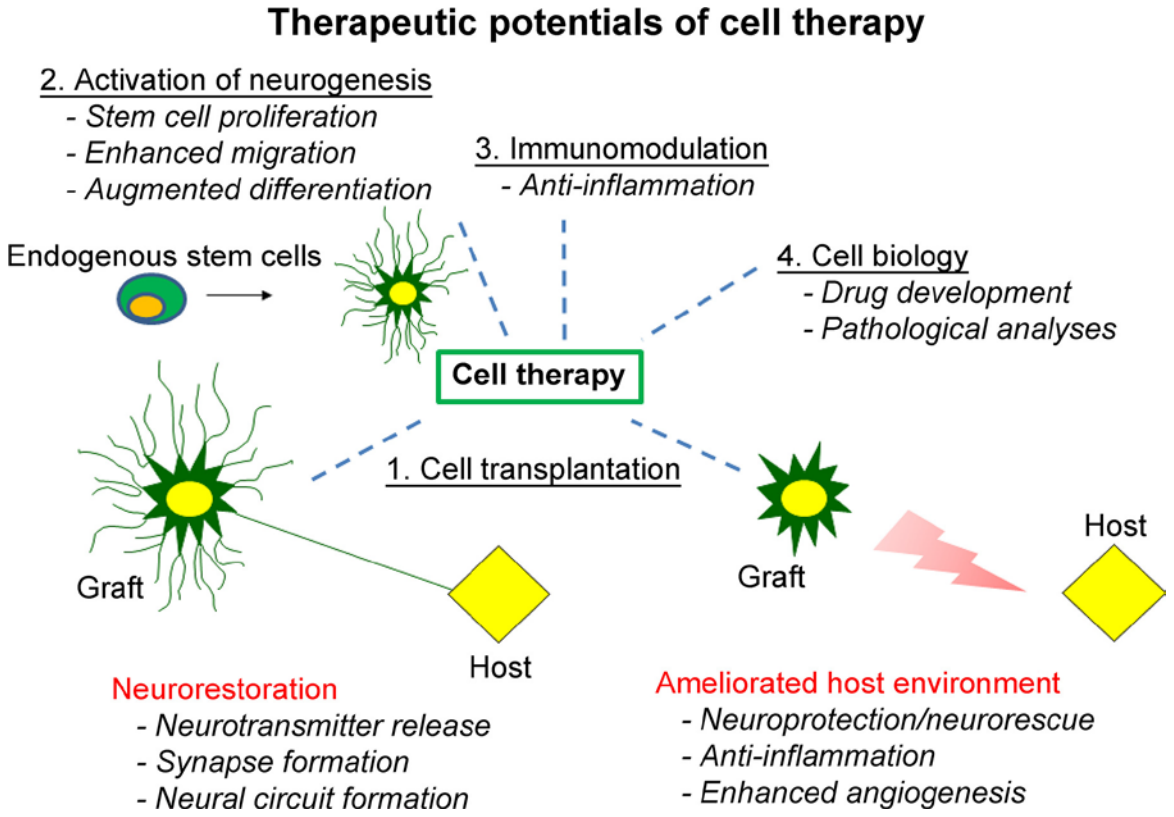
Johns Hopkins Engineering

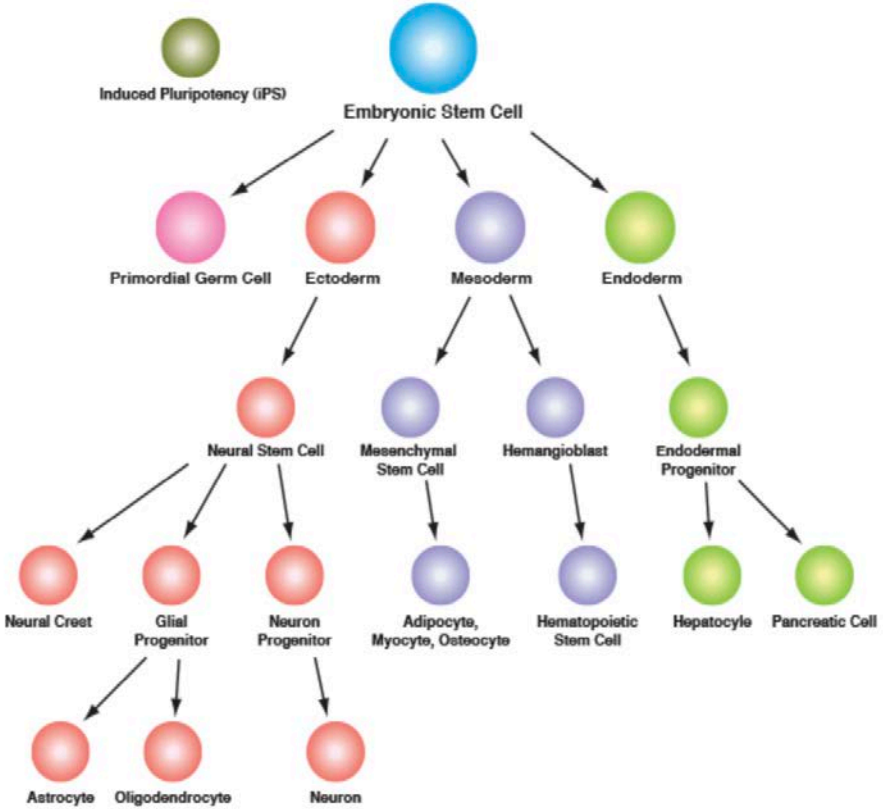
Methods in Neurobiology

Stem Cells Therapy

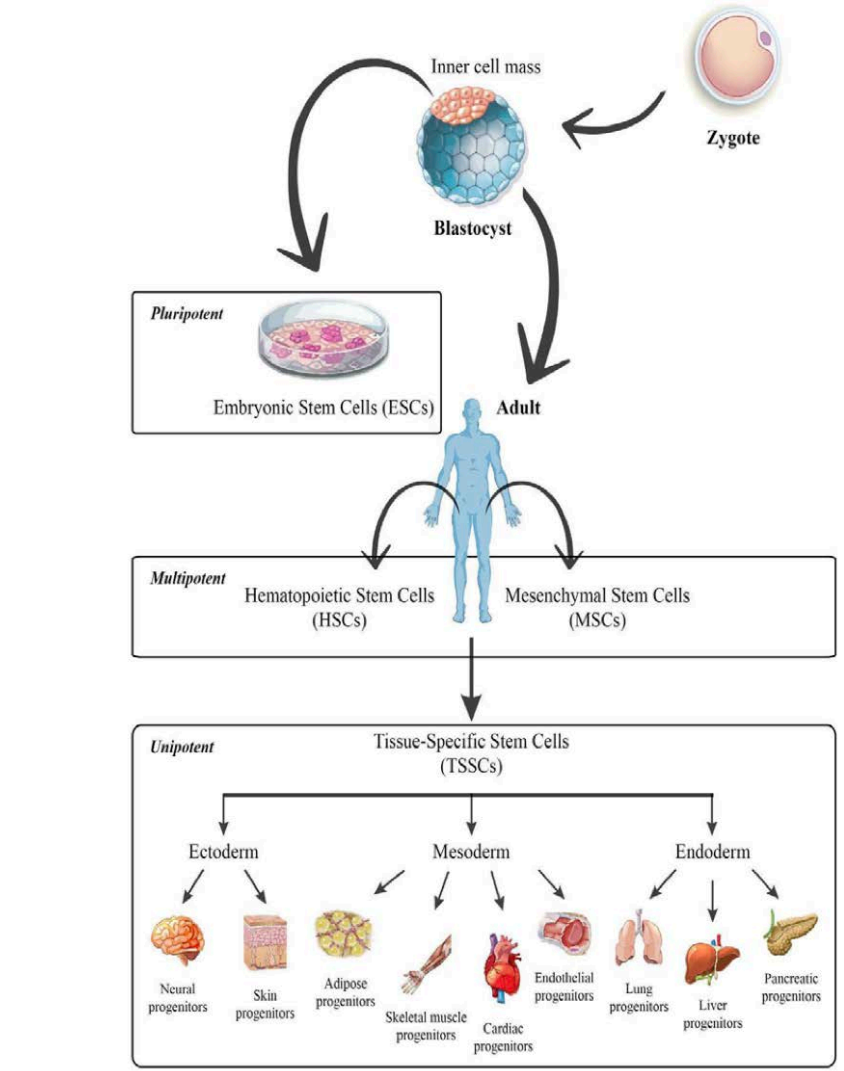
Cell therapy for NS



Stem Cells Lineage

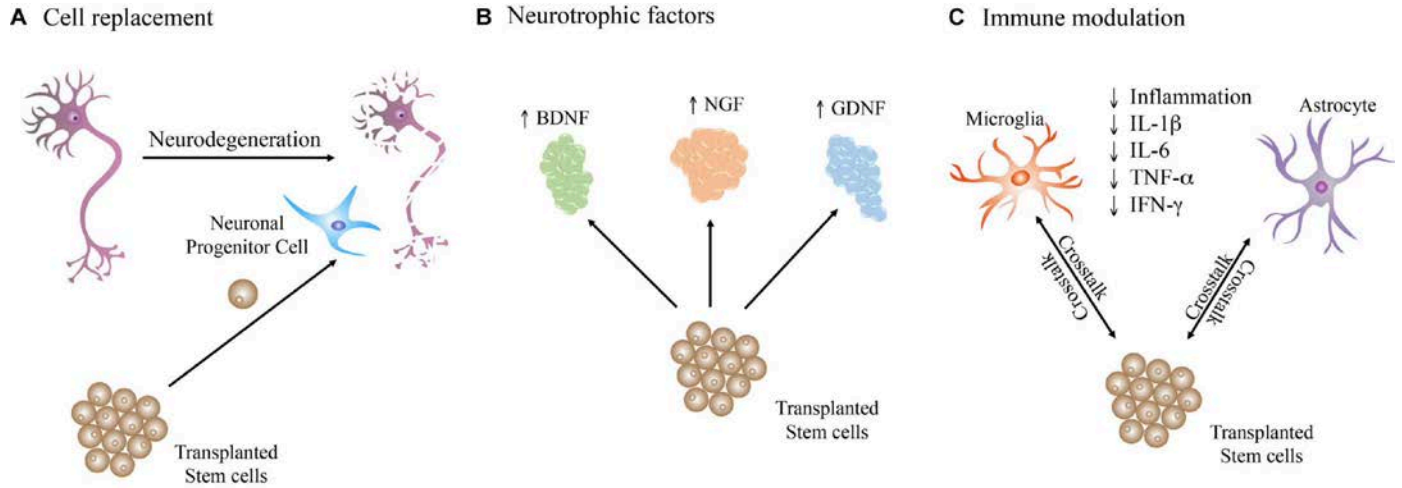


Source of Pluripotent Stem Cells



Important aspects for successful development of cell replacement therapy in the brain

- Good integration of transplanted cells in the host;
- Migration to the site of damage;
- Development of axonal projection to the target.



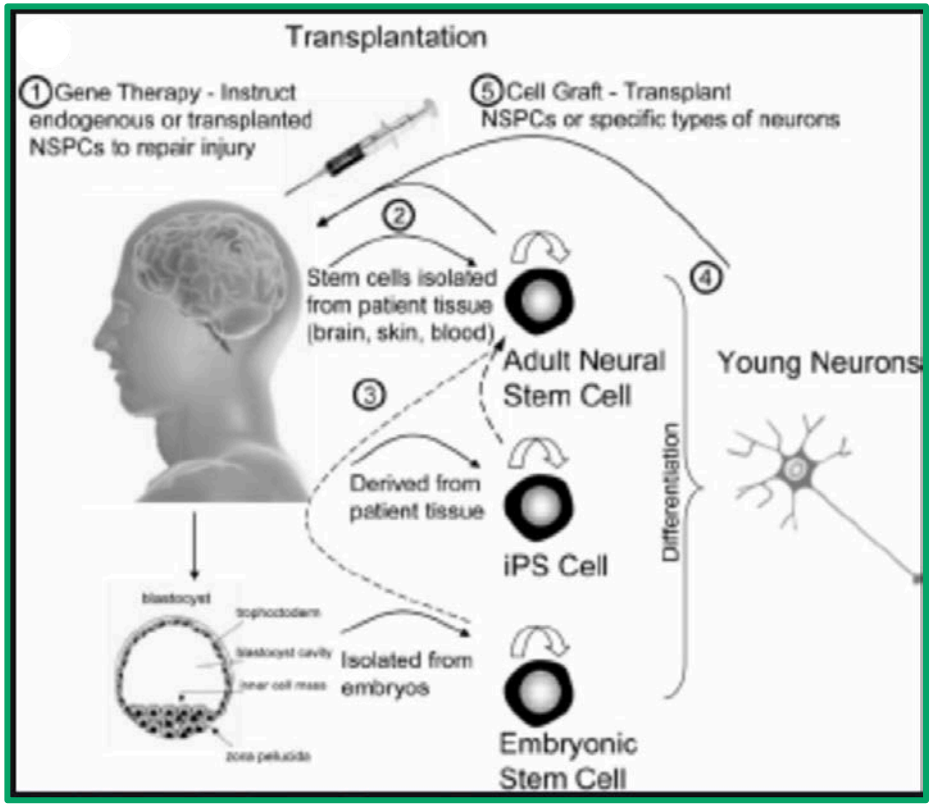
Strategies to improve cell therapy outcome

Target	Strategy	Outcomes	References
Neurotrophic factors (BDNF, NGF, and GDNF)	Expression of Neurotrophic factors by transplanted cells	Survival of host neurons, Survival, migration, and differentiation of transplanted cells	Kamei et al., 2007; Xu et al., 2011; Ma et al., 2012
Cell maturation	Transplant cells with the ideal maturity stage	Increase cell therapy success	Ganat et al., 2012; Payne et al., 2018
Neuroinflammation	Transplantation of cells to decrease neuroinflammation	Reduction of neuronal death	Pluchino et al., 2005, 2009
FGF2 and VEGF	Receptor inhibition; Neutralizing antibodies/receptor-blocking	Enhanced migration	Ladewig et al., 2014
Perineuronal nets (PNNs)	PNNs degradation with CSPGs*-degrading proteases	Render CNS more permissive to axon regeneration	Moon et al., 2001; Lemarchant et al., 2016
Polysialic acid (PSA)	Increase PSA levels: Overexpression of PSA or Overexpression of the enzymes responsible for PSA synthesis	Increased axonal growth	Glaser et al., 2007; Battista et al., 2014
Myelin	Knockdown of Cdh1 to revert myelin associated inhibition of axonal growth	Increased axonal growth	Konishi et al., 2004; Poplawski et al., 2018

CSPGs, chondroitin sulfate proteoglycans.

Risks and limitations

- Safety: tolerability and efficacy;
- Standard operating procedures: type and differentiation level of injected cells; routes of administration, protocols for cells isolation or culture.
- Long term risks:
  1. formation of tumors;
  2. microorganism contamination;
  3. peripheral accumulation in undesired organs;
  4. widespread dissemination.



References

Slide	Reference
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3	Stem cell Lineage and markers. 2019 Cell Signaling Technologies https://www.cellsignal.co.uk/contents/science-cst-pathways-developmental-biology/stem-cell-and-lineage-markers/stem-cell-lineage-markers
4	Pérez, L.M., de Lucas, B., Gálvez, B.G. 2018 Unhealthy Stem Cells: When Health Conditions Upset Stem Cell Properties. *Cell Physiol Biochem*. 46(5):1999-2016
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