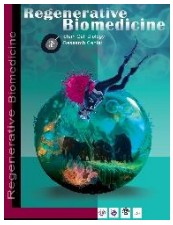

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Mini-Review Article

Integrative Perspectives on In Vitro Neurogenesis; From Fundamental Mechanisms to Clinical Potential

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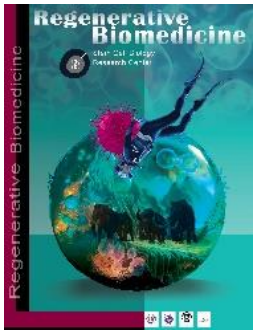
Abstract

In vitro neurogenesis, defined as the differentiation of stem cells into functional neurons under controlled laboratory conditions, represents a pivotal tool in contemporary neuroscience research and regenerative medicine. This approach enables precise modeling of neurodevelopmental processes and neurodegenerative disorders, while also supporting the exploration of novel therapeutic strategies. Stem cell–based platforms, including embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs), and neural stem cells (NSCs), provide versatile and well-characterized sources for generating diverse neuronal lineages. Experimental in vitro models such as neuronal rosettes and neurospheres offer valuable insights into early neural commitment, spatial organization, and lineage specification during neural differentiation. Furthermore, recent advances have highlighted stem cell–derived exosome therapy as a promising cell-free approach for central nervous system (CNS) regeneration. Collectively, this review summarizes major cellular sources, key molecular markers, differentiation mechanisms, and translational applications of in vitro neurogenesis, while also addressing current limitations and outlining future directions in this rapidly evolving field.

Keywords: Embryonic stem cells (ESCs), Exosome therapy, In vitro neurogenesis, Induced pluripotent stem cells (iPSCs), Neural stem cells (NSCs), Progenitors



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Introduction

Neurogenesis occurs both during embryonic development and in limited regions of the adult brain, such as the subventricular zone (SVZ) and subgranular zone (SGZ) of the hippocampus (1). In vitro neurogenesis allows scientists to recreate these processes under controlled conditions, bypassing the complex and variable in vivo environment (2). This approach facilitates a deeper understanding of neural development, disease modeling, and central nervous system (CNS) repair strategies.

Literature Search Strategy

A structured literature search was conducted to identify relevant publications on in vitro neurogenesis and related translational applications. The primary databases used were PubMed and Google Scholar. The search covered studies published between 1990 and 2025. Search terms included combinations of the following keywords: “in vitro neurogenesis,” “neural stem cells,” “embryonic stem cells,” “induced pluripotent stem cells,” “neuronal rosettes,” “neurospheres,” “neuronal differentiation,” and “exosome therapy in CNS.” Only peer-reviewed articles published in English were included. Both original research articles and review papers relevant to neural differentiation mechanisms, cellular markers, disease modeling, and regenerative medicine applications were considered. In addition, the reference lists of selected articles were manually screened to ensure comprehensive coverage of the topic.

Cellular Sources for In Vitro Neurogenesis

Embryonic Stem Cells (ESCs)

ESCs exhibit pluripotency (3, 4) and can differentiate into various neuronal subtypes, including dopaminergic, cholinergic, and GABAergic neurons (5). Their ability to model early neurodevelopment is valuable, though their clinical use is limited by tumorigenicity and ethical concerns.

Induced Pluripotent Stem Cells (iPSCs)

IPSCs share similar properties with ESCs but are reprogrammed from adult somatic cells, making them ethically viable and patient-specific (6, 7). IPSC-derived neurons are now widely used in modeling disorders such as Alzheimer’s, Parkinson’s, and Huntington’s disease (8).

Neural Stem Cells (NSCs)

NSCs derived from fetal or adult CNS tissues can self-renew and give rise to neurons, astrocytes, and oligodendrocytes. They are commonly maintained as neurospheres and have shown potential in CNS regeneration models (9).

Mechanisms of Neuronal Differentiation

Role of Growth Factors

Neurotrophic factors such as brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), and fibroblast growth factor-2 (FGF-2) are critical for supporting neuronal survival, synaptogenesis, and differentiation (10, 11, 12).

Transcriptional and Epigenetic Control

Key transcription factors— Neuronal Differentiation 1 (NEUROD1), Achaete-Scute Family BHLH Transcription Factor 1 (ASCL1), and POU Class 3 Homeobox 2 (BRN2)—initiate neuronal lineage specification. REST/NRSF acts as a repressor

and must be downregulated for neuronal gene expression to proceed (13, 14). Epigenetic mechanisms like DNA methylation and histone acetylation further fine-tune differentiation (13).

Culture Systems: 2D vs. 3D Models

Traditional 2D cultures are valuable but limited in mimicking brain complexity. Three-dimensional (3D) systems such as neurospheres and brain organoids provide more physiologically relevant environments, promoting natural cell–cell interactions and layered architecture (15).

Experimental Models in In Vitro Neurogenesis

Neuronal Progenitor Cells and Early Neural Commitment

Neuronal progenitor cells (NPCs) represent an intermediate stage between pluripotent stem cells and fully differentiated neural cells (Fig. 1). These cells have restricted potential compared to NSCs but are capable of differentiating into major neural lineages, including neurons, astrocytes, and oligodendrocytes. NPCs are essential for early neurodevelopment, contributing to both neural patterning and regional specification.

The early commitment of stem cells to a neural lineage is driven by intrinsic genetic programs and extrinsic signals such as FGF2, BDNF, and retinoic acid, which influence the transcriptional and epigenetic landscape of the cells (16–18). During this stage, cells express characteristic neural progenitor markers including Nestin, PAX6, SOX1, and SOX2, are reflecting their identity and developmental stage (19–22, 1). Morphologically, NPCs often exhibit a bipolar or radial glia-like structure and form organized arrangements in vitro, which serve as the foundation for downstream differentiation models such as rosettes and neurospheres. These models retain the multipotency and self-renewal capacity of NPCs, thereby serving as ideal systems for studying early neurogenesis (23).

Neuronal Rosettes

Neuronal rosettes are radial arrangements of columnar neural progenitor cells that arise during early stages of in vitro differentiation from ESCs or iPSCs. These structures resemble the embryonic neural tube and are considered hallmark indicators of early neuroectodermal commitment (24). They express typical neuroepithelial markers such as PAX6, SOX1, and Nestin (1, 25) , and can be isolated to derive more mature populations of NSCs for further differentiation.

Neurospheres

Neurospheres are spherical clusters (26) of neural stem or progenitor cells grown in suspension cultures, typically in serum-free media supplemented with epidermal growth factor (EGF) and fibroblast growth factor-2. This model allows for expansion, self-renewal, and multipotency testing of NSCs (9, 27). Upon exposure to differentiation conditions (e.g., withdrawal of mitogens), cells from neurospheres can give rise to neurons, astrocytes, and oligodendrocytes. Neurosphere assays are widely used to assess neurogenic potential and study stem cell responses to various stimuli.

Marker Profiles of In Vitro Models

Neuronal rosettes and neurospheres, as representative in vitro models of neurogenesis, exhibit distinct marker expression patterns that reflect their

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developmental status (Table 1). Neuronal rosettes characteristically express early neuroepithelial markers such as PAX6, SOX1, and Nestin, indicating their primitive neural identity and radial organization reminiscent of the neural tube structure (28, 29). In contrast, neurospheres predominantly maintain stemness-associated markers including Nestin, SOX2, and Musashi-1 during their undifferentiated state (27, 30, 31). Following induction of differentiation, these 3D cultures give rise to multiple neural lineages, as demonstrated by the emergence of neuronal, astrocytic, and oligodendroglial markers (32–34), confirming the multipotent capacity of neural stem cell populations.

Neuronal Lineage Markers

The identification of lineage-specific markers plays a crucial role in validating successful neural differentiation in vitro (Table 2).

Nestin

Nestin is an intermediate filament protein expressed predominantly in undifferentiated neural stem cells and early progenitor populations. It serves as a widely accepted indicator of early neural commitment in stem cell-derived cultures (1, 25). As differentiation progresses, Nestin expression gradually declines, reflecting the transition from proliferative progenitors to lineage-restricted cells.

βIII-Tubulin (TUJ1)

βIII-tubulin, detected by the TUJ1 antibody, represents one of the earliest and most reliable markers of neuronal differentiation (35). Its expression indicates post-mitotic neuronal commitment and cytoskeletal reorganization associated with neuronal polarization. Quantification of TUJ1-positive cells is commonly employed to assess neurogenic efficiency in vitro systems.

Applications of In Vitro Neurogenesis

Disease Modeling

Induced PSC-derived neurons have been used to model neurodevelopmental and neurodegenerative diseases, including autism, ALS, and multiple sclerosis (8, 36). These models enable the dissection of molecular pathology and high-throughput drug screening.

CNS Regeneration

NSCs have shown potential in preclinical models of CNS repair. In vitro, they can be directed to generate neurons and glial cells; in vivo, transplanted NSCs can integrate into host circuits and aid functional recovery (9, 37).

Spinal Cord Injury

Stem cell therapies for spinal cord injury (SCI) aim to replace lost neurons, promote axonal regrowth, and restore synaptic connections. Animal studies suggest improved motor function post-transplantation of ESC- or NSC-derived neural precursors (15).

Exosome Therapy as a Product of Stem Cells in Neural Regenerative Therapy

Exosomes are small extracellular vesicles (30–150 nm) secreted by various cell types, including stem cells. These vesicles carry diverse molecular cargos such as proteins, lipids, mRNAs, and microRNAs, enabling intercellular communication and modulation of recipient cell function. In recent years,

Table 1. Comparative summary of key morphological features, molecular markers, and functional roles of in vitro neurogenesis models. These models represent progressive stages in neural differentiation, starting from early progenitor arrangements (rosettes) to multipotent neurospheres and lineage-specific derivatives.

Model	Structure & Growth	Key Markers	Function	References
Neuronal Rosettes	2D radial neural structure	PAX6, SOX1, Nestin	Indicates early neuroectodermal commitment	(24), (25), (28)
Neurospheres	3D NSC cluster	Nestin, SOX1, Musashi-1	Allows NSC expansion and multipotency testing	(27), (30)
Differentiated Neurons	Neurite-bearing post-mitotic cells	TUJ1 (βIII-tubulin)	Indicate successful neuronal commitment	(32), (35)
Glial Derivatives	Mixed adherent cells	GFAP (astrocytes), O4 (oligodendrocytes)	Reflect glial lineage outcome of NSC differentiation	(31), (34)

Table 2. A summary of major components, mechanisms, and translational implications of in vitro neurogenesis based on the integrated content of the updated review article.

Category	Example / Item	Role / Function	Key Reference(s)
Stem Cell Sources	ESCs, iPSCs, NSCs	Source cells for neuronal differentiation	(5–9)
Differentiation Signals	BDNF, NT-3, FGF-2, Retinoic Acid	Promote survival, synaptogenesis, and neuronal lineage specification	(10), (11), (12), (17)
Transcription Factors	NEUROD1, ASCL1, BRN2	Drive neural fate commitment	(13, 14)
Epigenetic Regulators	REST, DNA methylation, histone acetylation	Repress/activate gene expression for neurogenesis	(13, 14)
Culture Models	2D cultures, 3D organoids	Mimic physiological conditions for neuronal development	(15)
Structural Models	Neuronal Rosettes, Neurospheres, Brain Organoids	Models to examine NSC behavior and early differentiation	(24–27), (28), (30)
Neuronal Markers	Nestin, PAX6, TUJ1, GFAP, O4	Identify early progenitors and lineage-specific neural cells	(25), (29), (32–34), (35)
Applications	Disease models, CNS repair, SCI therapy, Exosome-based therapy	Translational uses of in vitro-derived neurons and cell-free regenerative strategies via exosome	(8), (9), (35–38), (40–49)
Challenges	Maturation, reproducibility, microenvironment	Current limitations in achieving clinical-grade neurons	(7, 13, 50)
Future Directions	Bioengineering, CRISPR, patient-specific models	Improve fidelity, personalization, and regenerative potential	(51)

exosomes derived from stem cells have emerged as promising therapeutic tools in neural regenerative medicine due to their capacity to mimic many of the paracrine effects of their parent cells without the associated risks of cell transplantation (38, 39). One major advantage of stem cell-derived exosomes is their ability to cross the blood-brain barrier, allowing them to deliver therapeutic agents directly to affected areas of the CNS (40, 41). Moreover, exosomes exhibit low immunogenicity and eliminate the risks of tumorigenicity or uncontrolled differentiation associated with live stem cell

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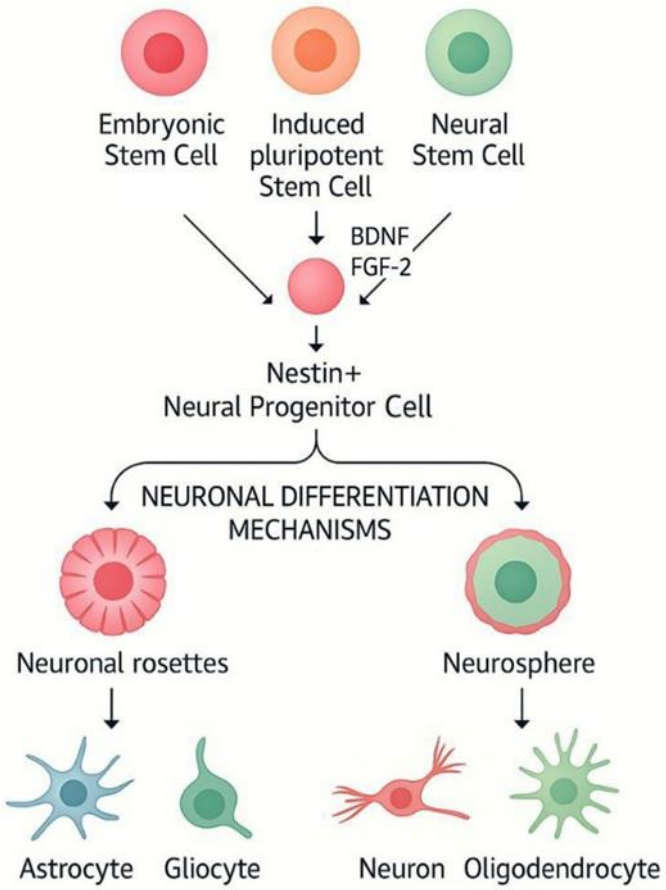

Figure 1. Schematic representation of in vitro neurogenesis. ESCs, iPSCs, and NSCs can differentiate through various neuronal differentiation mechanisms, such as neuronal rosettes and neurospheres. Under the influence of growth factors like BDNF and FGF-2, Nestin-positive neural progenitor cells are generated, which can further differentiate into neurons (TUJ1-positive) and glial lineage cells (GFAP-positive), including astrocytes, gliocytes, and oligodendrocytes.

therapies (38, 42). Their relatively high stability also facilitates storage and transport, which enhances their clinical feasibility (43).

In the context of neurological diseases, exosomes have shown therapeutic potential across several conditions:

- In Alzheimer's and Parkinson's diseases, mesenchymal stem cell (MSC)-derived exosomes have demonstrated neuroprotective effects, including reduced neuro-inflammation and promotion of neurogenesis (44–46).
- In SCI models, exosomes have been shown to support axonal regeneration and functional recovery by modulating local immune responses and stimulating neural repair (47).
- In traumatic brain injury (TBI), exosome treatment has resulted in improved neurological outcomes through enhanced

neurovascular remodeling and suppression of apoptosis (48).

Mechanistically, these effects are attributed to exosome cargo such as BDNF, FGF-2, and miRNAs like miR-133b, which modulate signaling pathways involved in neural differentiation and regeneration (42, 49).

Despite these advantages, several challenges remain. Standardization of isolation and purification methods is critical to ensure reproducibility and efficacy (43). The optimal dosage, frequency, and route of administration also need to be established through preclinical and clinical studies. Finally, deeper mechanistic understanding is necessary to refine and enhance exosome-based interventions for neurological applications (40, 47).

Challenges and Limitations

Despite these advances, several issues remain:

- Maturation deficits: Many in vitro neurons exhibit immature electrophysiological properties (6, 7).
- Variability in differentiation: Protocol inconsistencies across labs affect reproducibility (50).
- Limited micro-environmental mimicry: Lack of vascularization, glial support, and extracellular matrix cues in simplified cultures can limit translational potential (13).

Future Directions

Future work should aim to:

- Enhance neuronal maturation using long-term cultures, electrical stimulation, and co-culture with glial cells.
- Employ bioengineered scaffolds and organoids to better mimic the in vivo brain environment.
- Expand patient-specific applications using iPSC technologies and CRISPR-mediated genetic editing (51).

Conclusion

In vitro neurogenesis stands at the interface of developmental neuroscience, disease modeling, and regenerative medicine. The integration of classical stem cell biology and emerging in vitro models has opened new frontiers for understanding the nervous system and treating its disorders. As challenges are addressed through advanced culture systems, personalized medicine, and bioengineering, the clinical translation of in vitro neurogenesis is steadily becoming a reality.

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References

1. Bond AM, Ming GL, Song H. Adult Mammalian Neural Stem Cells and Neurogenesis: Five Decades Later. Cell Stem Cell. 2015;17(4):385-395.

2. Azari H, Reynolds BA. In vitro models for neurogenesis. Cold Spring Harbor perspectives in biology. 2016 Jun 1;8(6):a021279.

3. Akyash F, Tahajjodi SS, Yazd EF, Hajizadeh-Tafti F, Sadeghian-Nodoushan F, Golzadeh J, Meimandi HH, Moore H, Aflatoonian B. Derivation of new human embryonic stem cell lines (Yazd1-3) and their vitrification using Cryotech and Cryowin tools: A lab resources report. International journal of reproductive biomedicine. 2019 Dec 30;17(12):891.

4. Hajizadeh-Tafti F, Golzadeh J, Akyash F, Tahajjodi SS, Farashahi-Yazd E, Heidarian-Meimandi H, Aflatoonian B. Xeno-free generation of new Yazd human embryonic stem cell lines (Yazd4-7) as a prior stage toward good

https://doi.org/10.22034/jrb.2026.07.V2I1A5

manufacturing practice of clinical-grade raw materials from discarded embryos: A lab resources report. International Journal of Reproductive BioMedicine. 2023 Sep 20;21(8):619.

5. Muguruma K, Sasai Y. In vitro recapitulation of neural development using embryonic stem cells: from neurogenesis to histogenesis. Development, growth & differentiation. 2012 Apr;54(3):349-57.

6. Gordon A, Yoon SJ, Tran SS, et al. Long-term maturation of human cortical organoids matches key early postnatal transitions. Nat Neurosci. 2021;24(3):331-342.

7. Paşca SP, Panagiotakos G, Dolmetsch RE. Generating human neurons in vitro and using them to understand neuropsychiatric disease. Annual review of neuroscience. 2014 Jul 8;37(1):479-501.

8. Baldassari S, Musante I, Iacomino M, Zara F, Salpietro V, Scudieri P. Brain organoids as model systems for genetic neurodevelopmental disorders. Frontiers in Cell and Developmental Biology. 2020 Oct 12;8:590119.

9. da Silva Siqueira L, Majolo F, da Silva AP, da Costa JC, Marinowic DR. Neurospheres: a potential in vitro model for the study of central nervous system disorders. Molecular Biology Reports. 2021 Apr;48:3649-63.

10. El Ouaamari Y, Van den Bos J, Willekens B, Cools N, Wens I. Neurotrophic factors as regenerative therapy for neurodegenerative diseases: Current status, challenges and future perspectives. International journal of molecular sciences. 2023 Feb 15;24(4):3866.

11. Mitre M, Mariga A, Chao MV. Neurotrophin signalling: novel insights into mechanisms and pathophysiology. Clinical science. 2017 Jan 1;131(1):13-23.

12. Pincus DW, Keyoung HM, Harrison-Restelli C, Goodman RR, Fraser RA, Edgar M, Sakakibara SI, Okano H, Nedergaard M, Goldman SA. Fibroblast growth factor-2/brain-derived neurotrophic factor–associated maturation of new neurons generated from adult human subependymal cells. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 1998 May;43(5):576-85.

13. Juliandi B, Abematsu M, Nakashima K. Epigenetic regulation in neural stem cell differentiation. Development, growth & differentiation. 2010 Aug;52(6):493-504.

14. Ballas N, Grunseich C, Lu DD, Speh JC, Mandel G. REST and its corepressors mediate plasticity of neuronal gene chromatin throughout neurogenesis. Cell. 2005 May 20;121(4):645-57.

15. Tetzlaff W, Okon EB, Karimi-Abdolrezaee S, Hill CE, Sparling JS, Plemel JR, Plunet WT, Tsai EC, Baptiste D, Smithson LJ, Kawaja MD. A systematic review of cellular transplantation therapies for spinal cord injury. Journal of neurotrauma. 2011 Aug 1;28(8):1611-82.

16. Gupta S, M-Redmond T, Meng F, Tidball A, Akil H, Watson S, Parent JM, Uhler M. Fibroblast growth factor 2 regulates activity and gene expression of human post-mitotic excitatory neurons. Journal of neurochemistry. 2018 May;145(3):188-203.

17. Chen K, Henry RA, Hughes SM, Connor B. Creating a neurogenic environment: the role of BDNF and FGF2. Molecular and Cellular Neuroscience. 2007 Sep 1;36(1):108-20.

18. Kubickova B, Martinkova S, Bohaciakova D, Nezvedova M, Liu R, Brozman O, Spáčil Z, Hilscherova K. Effects of all-trans and 9-cis retinoic acid on differentiating human neural stem cells in vitro. Toxicology. 2023 Mar 15;487:153461.

19. Graham V, Khudyakov J, Ellis P, Pevny L. SOX2 functions to maintain neural progenitor identity. Neuron. 2003 Aug 28;39(5):749-65.

20. Venere M, Han YG, Bell R, Song JS, Alvarez-Buylla A, Blelloch R. Sox1 marks an activated neural stem/progenitor cell in the hippocampus. Development. 2012 Nov 1;139(21):3938-49.

21. Suter DM, Tirefort D, Julien S, Krause KH. A Sox1 to Pax6 switch drives neuroectoderm to radial glia progression during differentiation of mouse embryonic stem cells. Stem Cells. 2009 Jan 1;27(1):49-58.

22. Galiakberova AA, Dashinimaev EB. Neural stem cells and methods for their generation from induced pluripotent stem cells in vitro. Frontiers in cell and developmental biology. 2020 Oct 8;8:815.

23. Oliveira SL, Pillat MM, Cheffer A, Lameu C, Schwindt TT, Ulrich H. Functions of neurotrophins and growth factors in neurogenesis and brain repair. Cytometry Part A. 2013 Jan;83(1):76-89.

24. Gaspard N, Vanderhaeghen P. From stem cells to neural networks: recent advances and perspectives for neurodevelopmental disorders. Developmental Medicine & Child Neurology. 2011 Jan;53(1):13-7.

25. Lendahl U, Zimmerman LB, McKay RD. CNS stem cells express a new class of intermediate filament protein. Cell. 1990 Feb 23;60(4):585-95.

26. Aflatoonian B, Moore H. Human primordial germ cells and embryonic germ cells, and their use in cell therapy. Current opinion in Biotechnology. 2005 Oct 1;16(5):530-5.

27. Reynolds BA, Weiss S. Generation of neurons and astrocytes from isolated cells of the adult mammalian central nervous system. science. 1992 Mar 27;255(5052):1707-10.

28. Elkabetz Y, Panagiotakos G, Al Shamy G, Socci ND, Tabar V, Studer L. Human ES cell-derived neural rosettes reveal a functionally distinct early neural stem cell stage. Genes & development. 2008 Jan 15;22(2):152-65.

29. Chandrasekaran A, Avci HX, Ochalek A, Rösingh LN, Molnár K, László L, Bellák T, Téglási A, Pesti K, Mike A, Phanthong P. Comparison of 2D and 3D neural induction methods for the generation of neural progenitor cells from human induced pluripotent stem cells. Stem cell research. 2017 Dec 1; 25:139-51.

30. Conti L, Cattaneo E. Neural stem cell systems: physiological players or in vitro entities? Nature Reviews Neuroscience. 2010 Mar;11(3):176-87.

31. Singh SK, Clarke ID, Terasaki M, Bonn VE, Hawkins C, Squire J, Dirks PB. Identification of a cancer stem cell in human brain tumors. Cancer research. 2003 Sep 15;63(18):5821-8.

32. Zhang SC, Wernig M, Duncan ID, Brüstle O, Thomson JA. In vitro differentiation of transplantable neural precursors from human embryonic stem cells. Nature biotechnology. 2001 Dec 1;19(12):1129-33.

33. Kaneko Y, Sakakibara S, Imai T, Suzuki A, Nakamura Y, Sawamoto K, Ogawa Y, Toyama Y, Miyata T, Okano H. Musashi1: an evolutionally conserved marker for CNS progenitor cells including neural stem cells. Developmental neuroscience. 2000 Feb 15;22(1-2):139-53.

34. Perrier AL, Tabar V, Barberi T, Rubio ME, Bruses J, Topf N, Harrison NL, Studer L. Derivation of midbrain dopamine neurons from human embryonic stem cells. Proceedings of the National Academy of Sciences. 2004 Aug 24;101(34):12543-8.

35. Katsetos CD, Reginato MJ, Baas PW, D'Agostino L, Legido A, Tuszyn JA, Draberova E, Dráber P. Emerging microtubule targets in glioma therapy. InSeminars in pediatric neurology 2015 Mar 1 (Vol. 22, No. 1, pp. 49-72). WB Saunders.

36. Livesey FJ. Human stem cell models of dementia. Human molecular genetics. 2014 Sep 15;23(R1):R35-9.

37. Tornero D. Neuronal circuitry reconstruction after stem cell therapy in damaged brain. Neural Regeneration Research. 2022 Sep 1;17(9):1959-60.

38. Kalluri R, LeBleu VS. The biology, function, and biomedical applications of exosomes. Science. 2020;367(6478):eaau6977.

39. Zhang B, Yeo RW, Tan KH, Lim SK. Focus on extracellular vesicles: therapeutic potential of stem cell-derived extracellular vesicles. Int J Mol Sci. 2016;17(2):174.

40. Gotoh S, Kawabori M, Fujimura M. Intranasal administration of stem cell-derived exosomes for central nervous system diseases. Neural Regen Res. 2024;19(6):1249-1255.

41. Rahmanifar, F. Exosome Therapy Using Mesenchymal Stromal/Stem Cells: A Mini-Review. Regenerative Biomedicine, 2024; 1(1): 17-22.

42. Xin H, Li Y, Buller B, Katakowski M, Zhang Y, Wang X, et al. Exosome-mediated transfer of miR-133b from multipotent mesenchymal stromal cells to neural cells

https://doi.org/10.22034/jrb.2026.07.V2I1A5

contributes to neurite outgrowth. Stem Cells. 2012;30(7):1556–64.

43. Lai RC, Yeo RW, Tan KH, Lim SK. Exosomes for drug delivery—a novel application for the mesenchymal stem cell. Biotechnol Adv. 2013;31(5):543–51.

44. Zhong L, Wang J, Wang P, Liu X, Liu P, Cheng X, Cao L, Wu H, Chen J, Zhou L. Neural stem cell-derived exosomes and regeneration: cell-free therapeutic strategies for traumatic brain injury. Stem cell research & therapy. 2023 Aug 8;14(1):198.

45. Salehpour A, Karimi Z, Ghasemi Zadeh M, Afshar M, Kameli A, Mooseli F, Zare M, Afshar A. Therapeutic potential of mesenchymal stem cell-derived exosomes and miRNAs in neuronal regeneration and rejuvenation in neurological disorders: A mini review. Frontiers in Cellular Neuroscience. 2024 Oct 4;18:1427525.

46. Hoseini,S. M., Azad, F. S., Zare, E., Montazeri, F. Therapeutic Potential of Amniotic Fluid and Amniotic Fluid-Derived Stem Cells in Regenerative Medicine. Regenerative Biomedicine, 2025; 1(2): 85-105.

47. Liu MW, Li H, Xiong GF, Zhang BR, Zhang QJ, Gao SJ, Zhu YL, Zhang LM. Mesenchymal stem cell exosomes therapy for the treatment of traumatic brain injury: mechanism, progress, challenges and prospects. Journal of Translational Medicine. 2025 Apr 11;23(1):427.

48. Wang YY, Cheng J, Liu YD, Wang YP, Yang QW, Zhou N. Exosome-based regenerative rehabilitation: a novel ice breaker for neurological disorders. Biomedicine & Pharmacotherapy. 2023 Dec 31;169:115920.

49. Katakowski M, Buller B, Zheng X, Lu Y, Rogers T, Osobamiro O, Shu W, Jiang F, Chopp M. Exosomes from marrow stromal cells expressing miR-146b inhibit glioma growth. Cancer letters. 2013 Jul 10;335(1):201-4.

50. Andrews MG, Kriegstein AR. Challenges of Organoid Research. Annu Rev Neurosci. 2022;45:23-39.

51. Sato M, Saitoh I, Inada E. Efficient CRISPR/Cas9-based gene correction in induced pluripotent stem cells established from fibroblasts of patients with sickle cell disease. Stem cell investigation. 2016 Nov 14; 3:78.