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Potential effect of endothelial progenitor cells on pentylenetetrazole-induced seizures in rats: an evaluation of relevant lncRNAs

Key words: Endothelial progenitor cell (EPC); Long noncoding RNA (lncRNA); Pentylenetetrazole (PTZ); Neuronal damage; Seizure

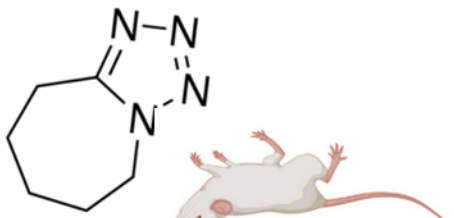
Research Aim

In an attempt to better understand the processes underlying epileptogenesis, and develop more effective treatments for patients with uncontrolled seizures and disabling comorbidities, the present study mainly focused on:

1. Investigation of the potential therapeutic effect of bone marrow-derived **EPCs administration** on **PTZ**-induced kindling, a model of **epilepsy**-induced comorbidities and neurochemical alterations in rats.
2. Profiling brain development- and autophagy-related **lncRNAs** dysregulated in epilepsy.

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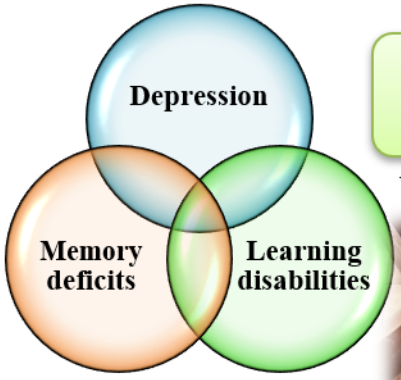
Research Summary



PTZ

PTZ-induced kindling (35 mg/kg) 3 times/week i.p.

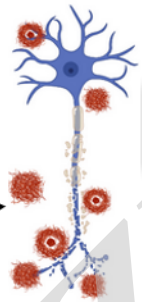
Epilepsy



Cognitive & behavioral comorbidities

Y-maze & OFT





Neuronal damage

S100B protein, NEFH, HSP-70 and UCH-L1



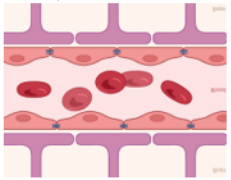
Dysregulated lncRNAs

↓ lncRNAs Evf2, Pnky, Dlx1 APF, HOTAIR and FLJ11812



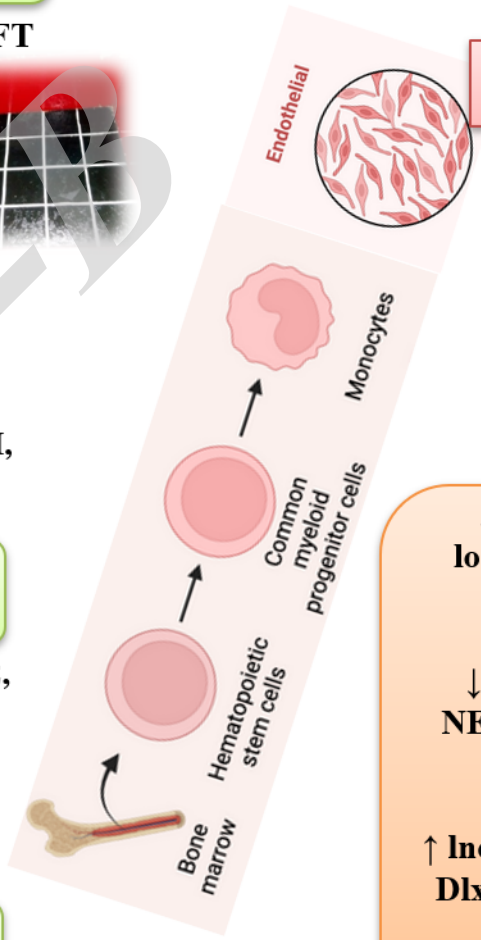
Permanent state of hyperexcitability and hypersynchrony

BBB



Pathologic vascular response

↓ VEGF



Intravenous administration

BM-EPCs (2×10^6 cells)

↓ Memory and locomotor activity deficits

↓ S100B protein, NEFH, HSP-70 and UCH-L1

↑ lncRNAs Evf2, Pnky Dlx1, APF, HOTAIR and FLJ11812

↑VEGF

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Conclusion



- PTZ-induced epilepsy is associated with marked behavioral comorbidities, neuronal damage, vascular abnormalities as well as molecular changes.
- Alterations in the expression of lncRNAs that regulate brain development and autophagy, evoked in PTZ-treated rats, have a central role in the etiology of epilepsy.

- Administration of EPCs significantly reversed most changes associated with epilepsy:
  - Intravenously administered EPCs homed into the epileptic rat hippocampus.
  - EPCs amended the memory and locomotor activity deficits related to epilepsy.
  - EPCs corrected the neuronal damage.
  - EPCs up-regulated expression of lncRNAs that control the CNS development as well as the autophagy process.
  - EPCs mitigated the vascular anomalies.

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The therapeutic application of EPCs in neurological disorders remains constrained, with scant reports in animal models. We want to emphasize the effective potential of EPCs in reducing epileptic activity, offering a hopeful treatment approach that could lessen the impact of the disease and enhance the quality of life for people with epilepsy. Therefore, we encourage more research to improve the utility of using EPCs to treat epilepsy.

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