

2021

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

STROKE

Patient-derived glial enriched progenitors repair functional deficits due to white matter stroke and vascular dementia in rodents

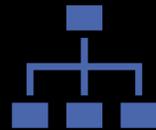
Irene L. Llorente^{1†}, Yuan Xie^{2†}, Jose A. Mazzitelli¹, Emily A. Hatanaka^{1,3}, Jessica Cinkornpumin³, David R. Miller¹, Ying Lin³, William E. Lowry^{3*}, S. Thomas Carmichael^{1*}

Présenté par Nasser Bouhalassa

Plan



INTRODUCTION



MÉTHODES

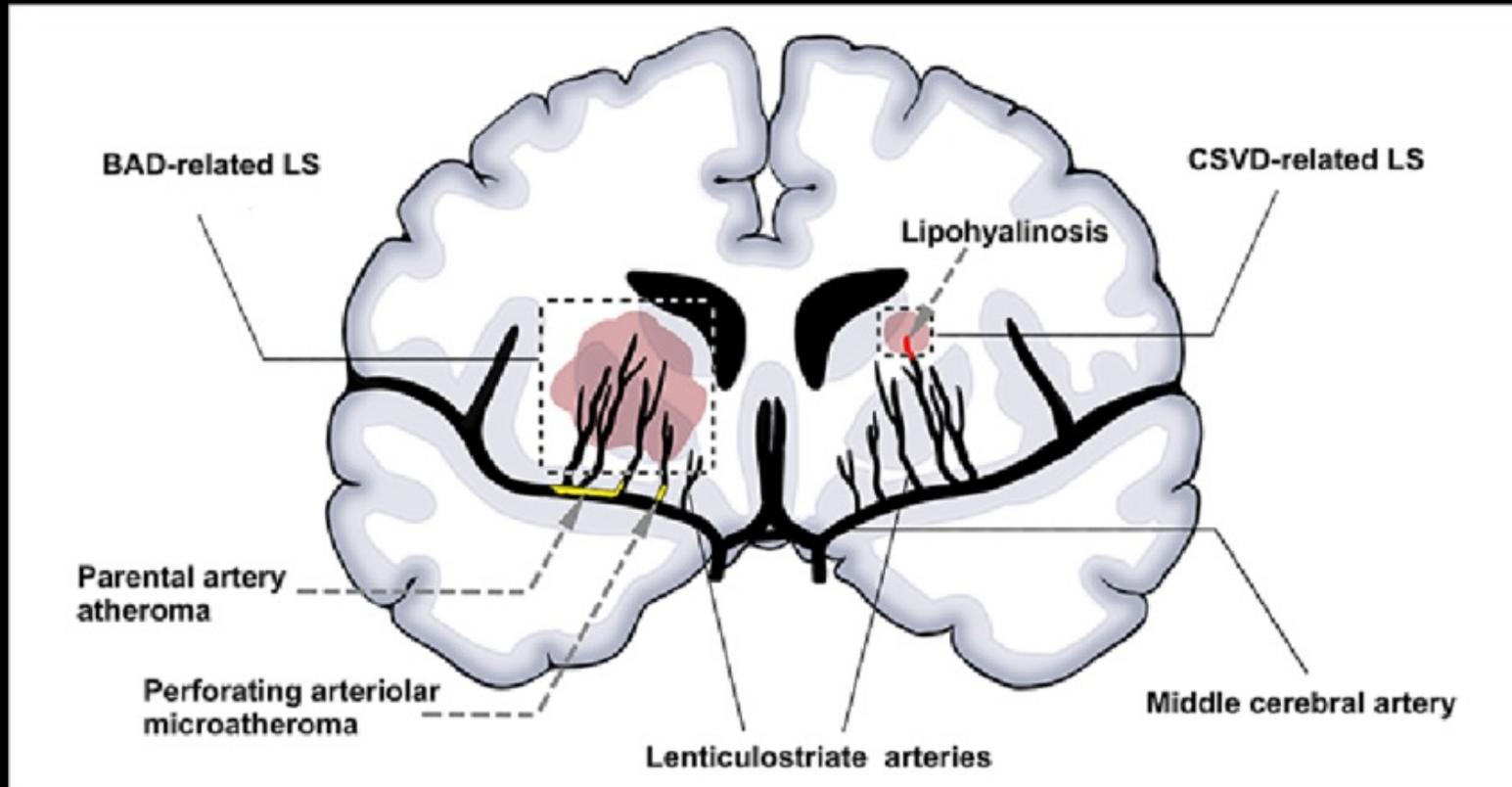


RÉSULTATS



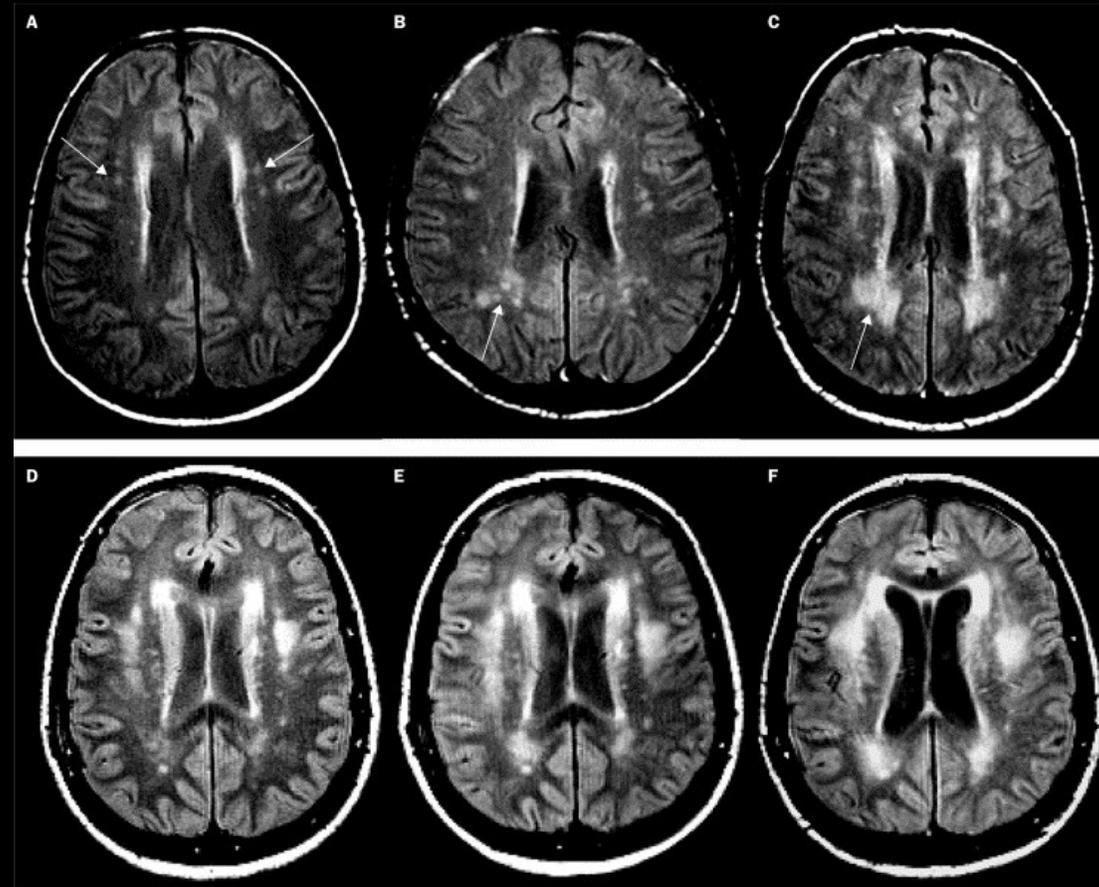
CONCLUSIONS

AVC de la substance blanche



- Artères perforantes
- 30% de tous les AVC
- Progression dans le temps
- Démence vasculaire

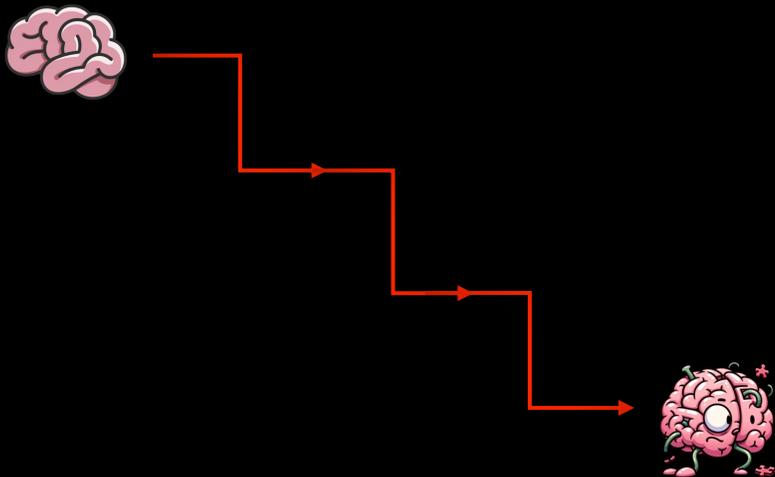
AVC de la substance blanche



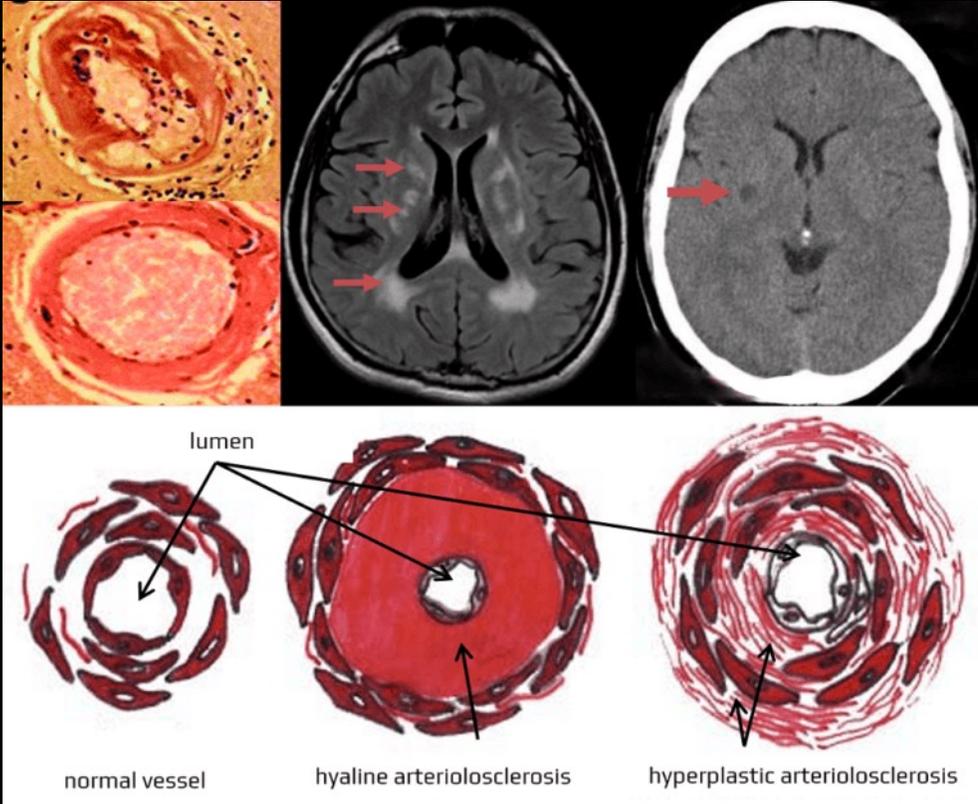
Schmidt R, Enzinger C, Ropele S, Schmidt H, Fazekas F; Austrian Stroke Prevention Study. Progression of cerebral white matter lesions: 6-year results of the Austrian Stroke Prevention Study. *Lancet*. 2003 Jun 14;361(9374):2046-8. doi: 10.1016/s0140-6736(03)13616-1

Démence vasculaire

- Déficit cognitif, sensoriel, moteur
- Pas de traitement !
- Pathophysiologie mal comprise

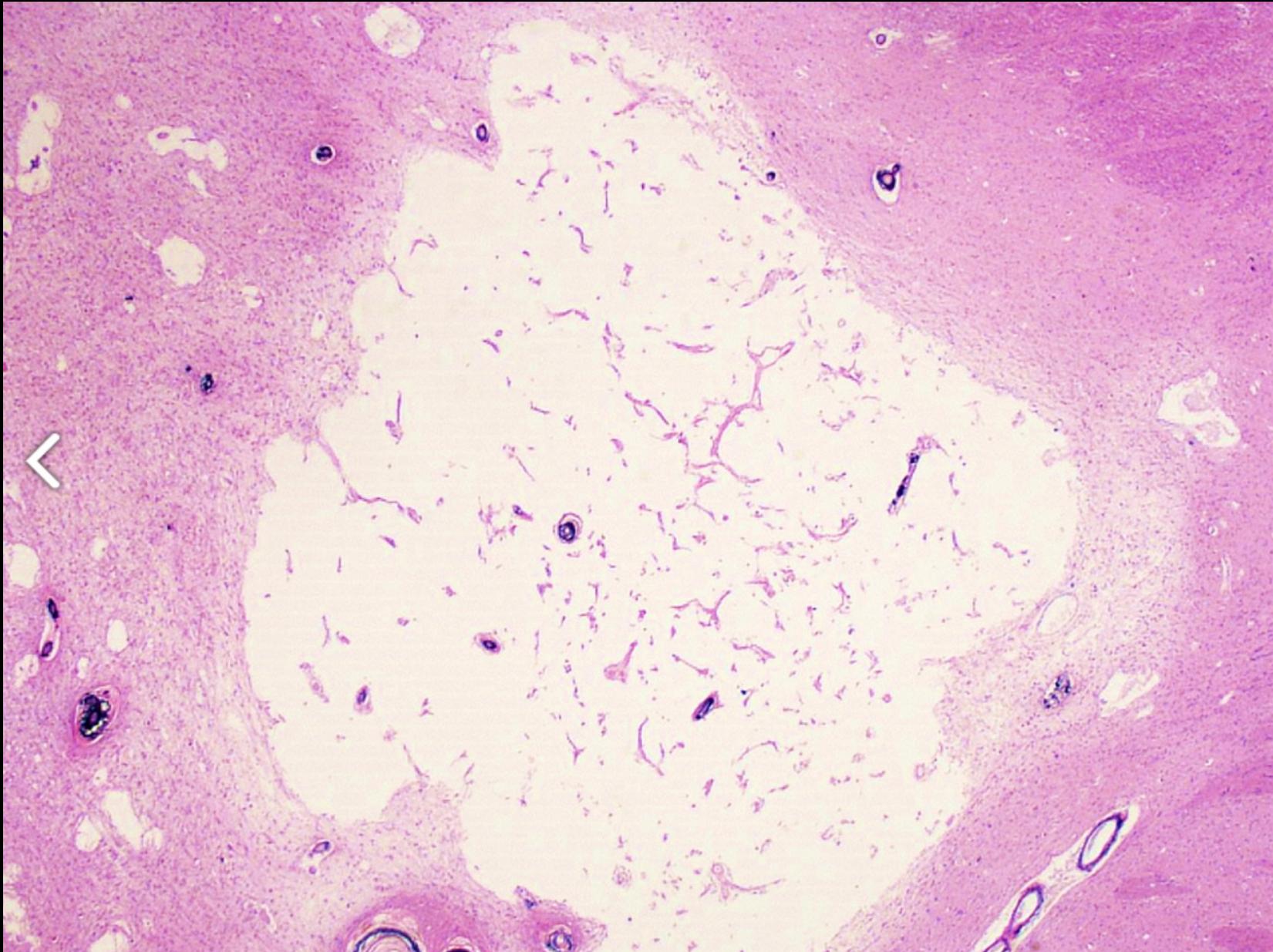


AVC lacunaire

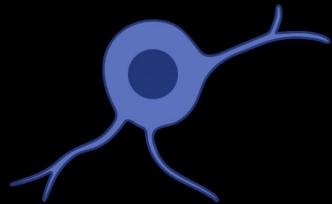


Lacunar stroke | stroke manual [En ligne]. 2022 [cité le 8 mars 2024]. Disponible: <https://www.stroke-manual.com/lacunar-stroke/>

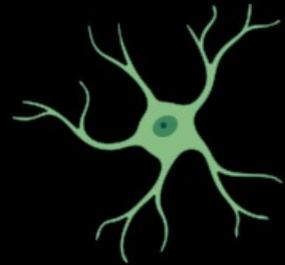
Caplan LR. Lacunar infarction and small vessel disease: pathology and pathophysiology. *J Stroke*. 2015 Jan;17(1):2-6. doi: 10.5853/jos.2015.17.1.2



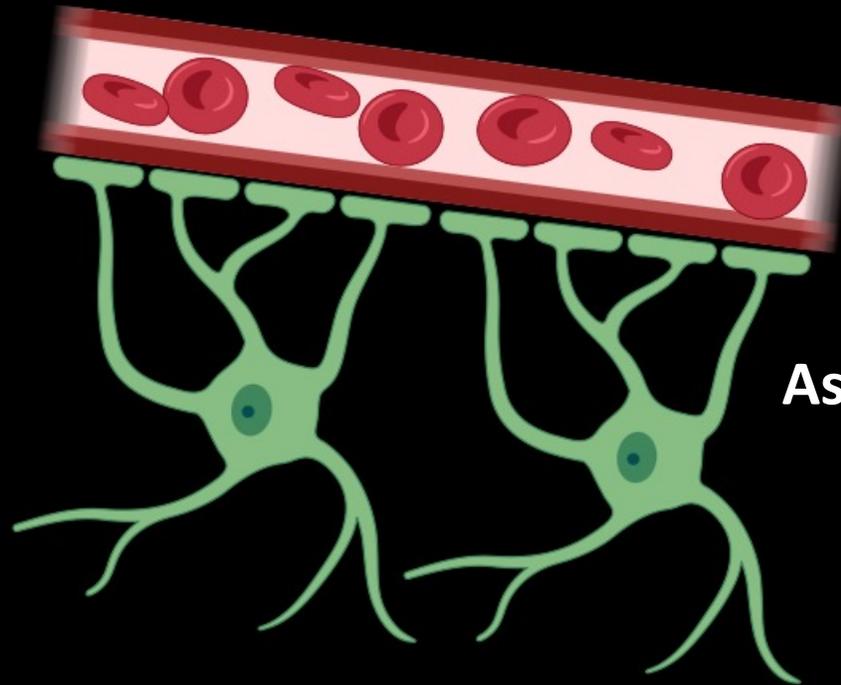
Ischemic stroke / infarct. [En ligne]. [cité le 8 mars 2024]. Disponible: <https://www.pathologyoutlines.com/topic/cnsstroke.html>



OPC

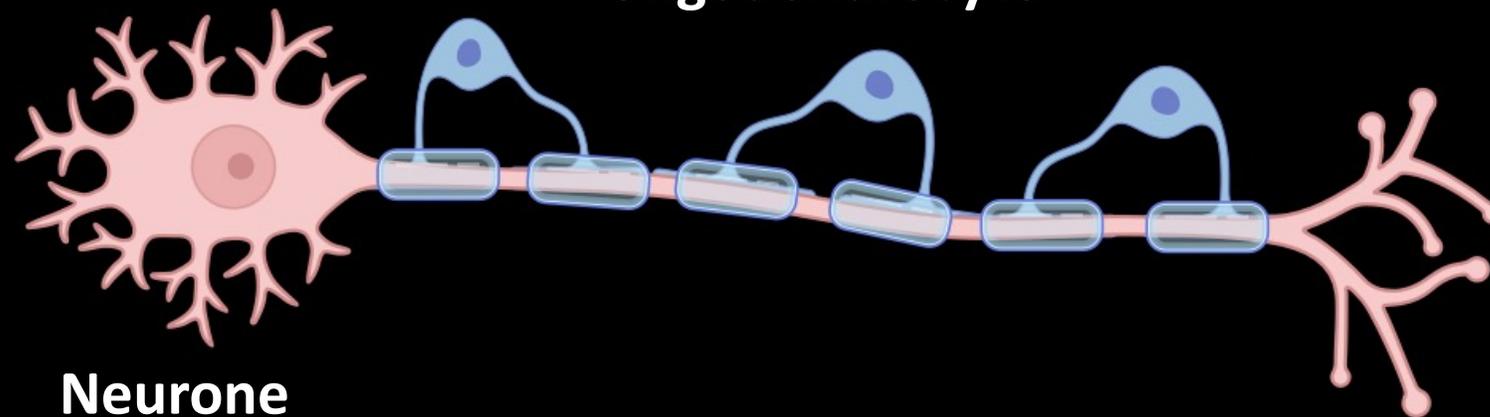


Microglie

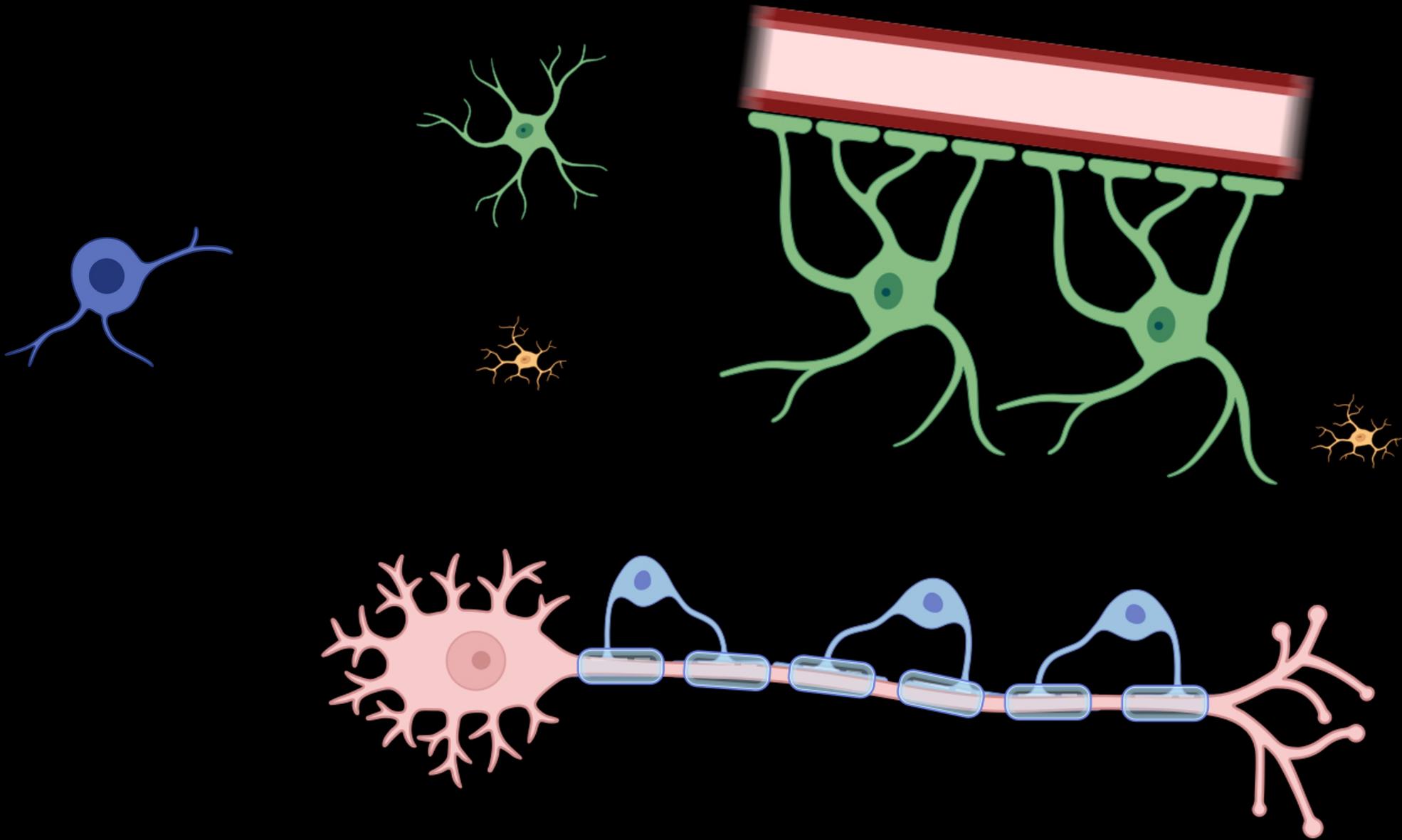


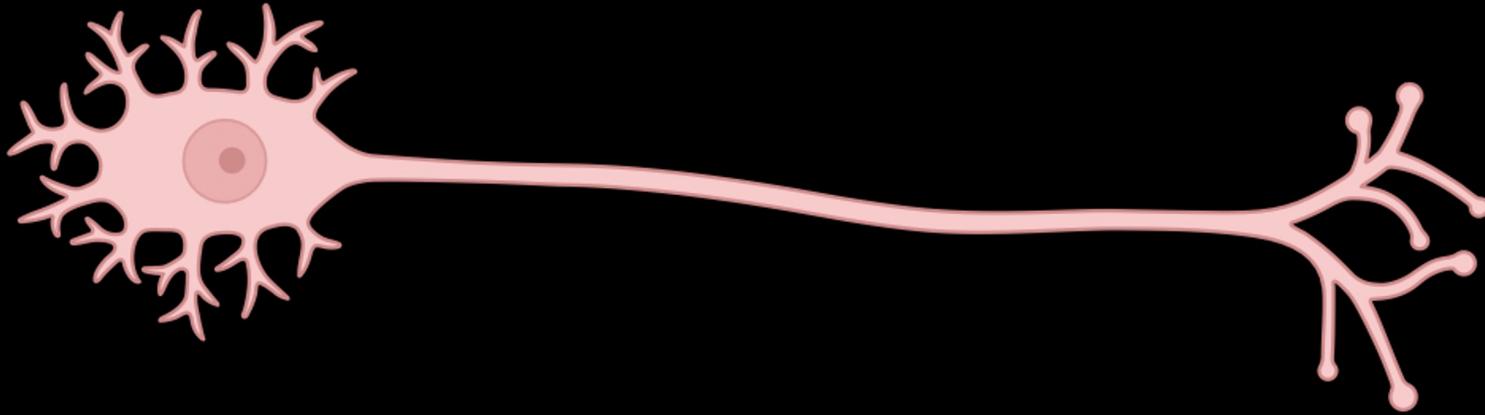
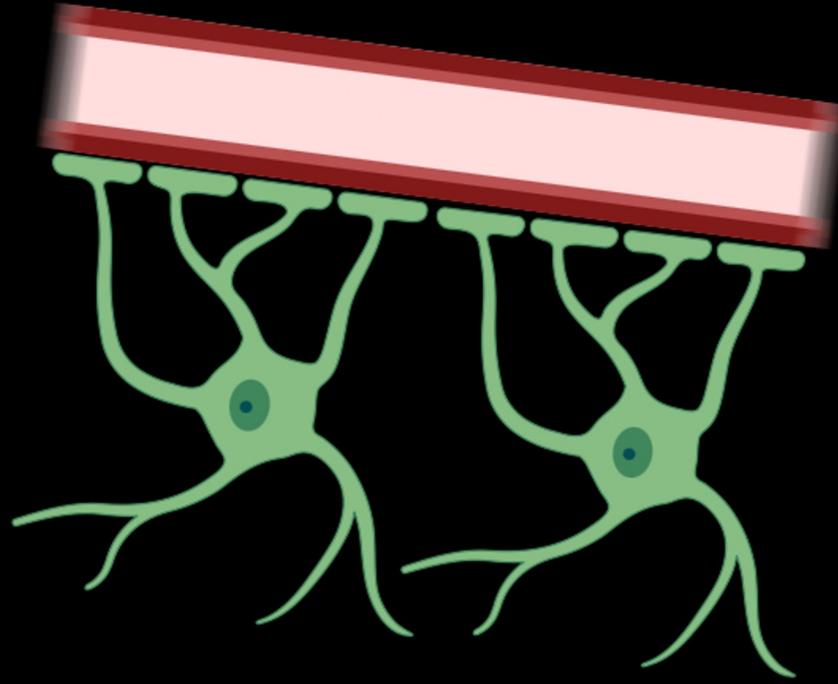
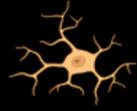
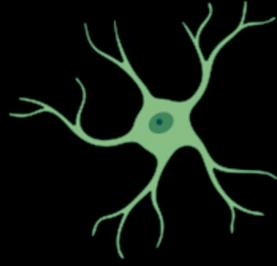
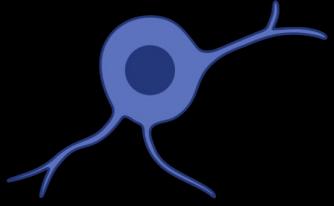
Astrocyte

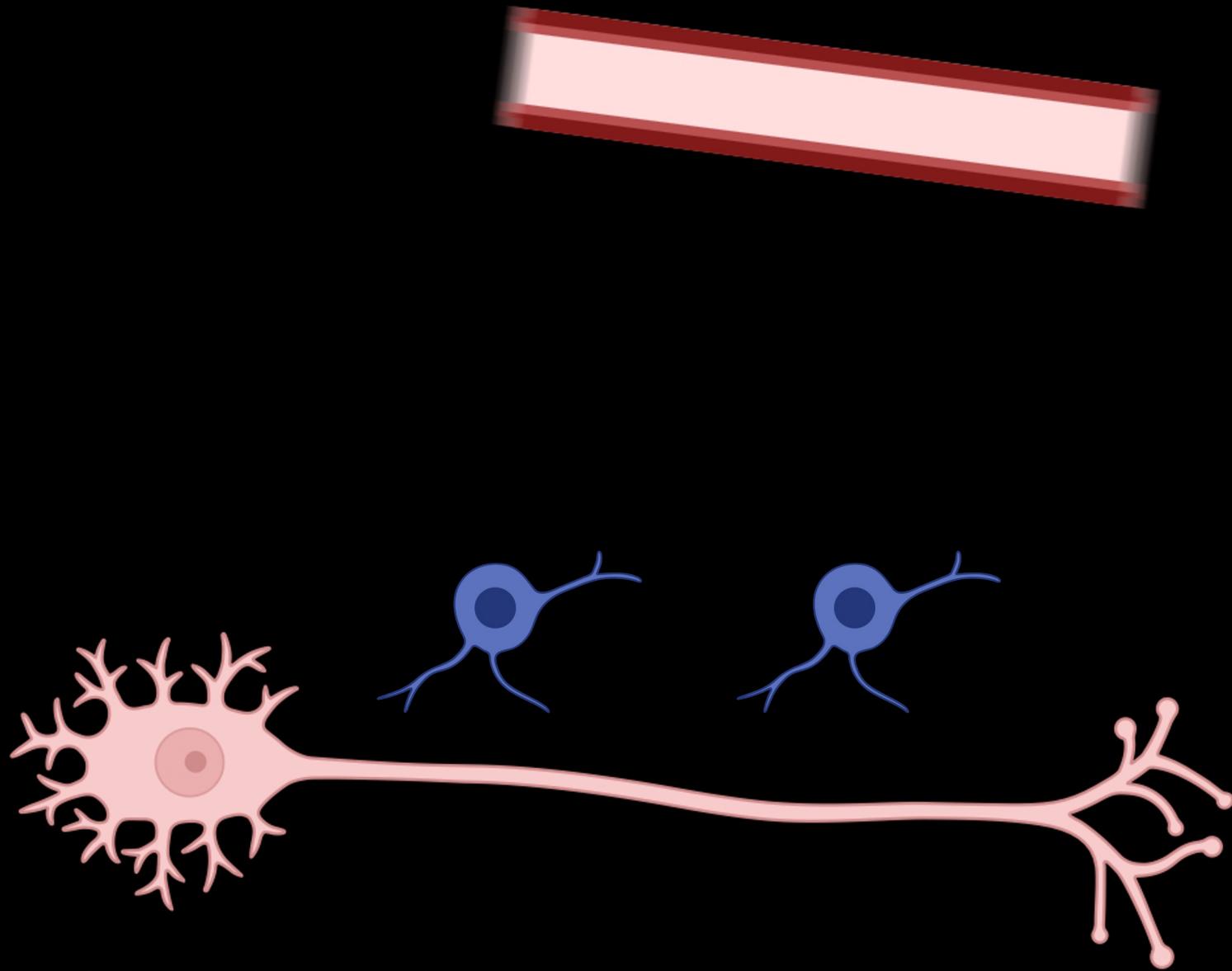
Oligodendrocyte



Neurone





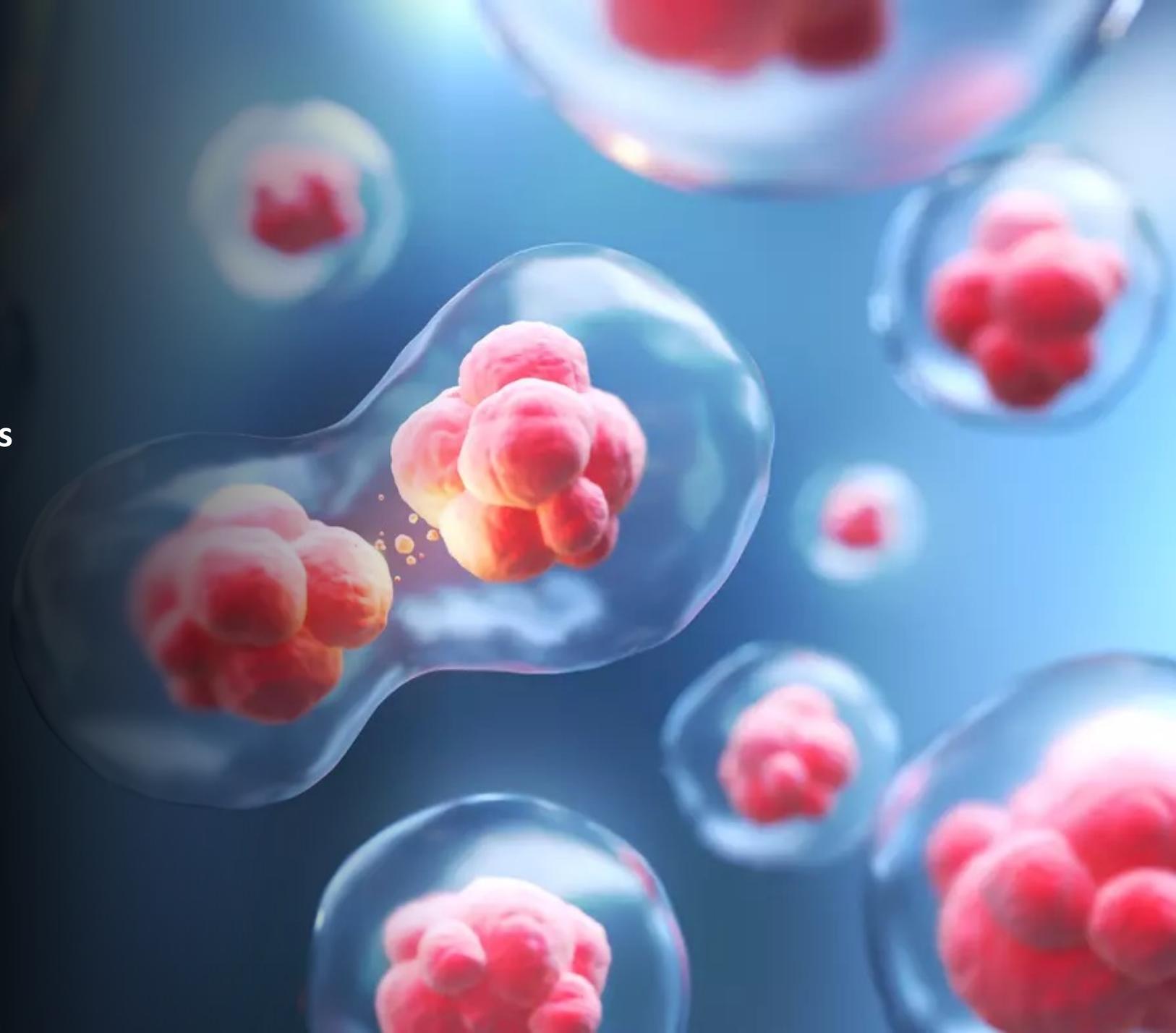


Comment réparer les lésions de la
substance blanche à partir du **potentiel
endogène** du système nerveux ?

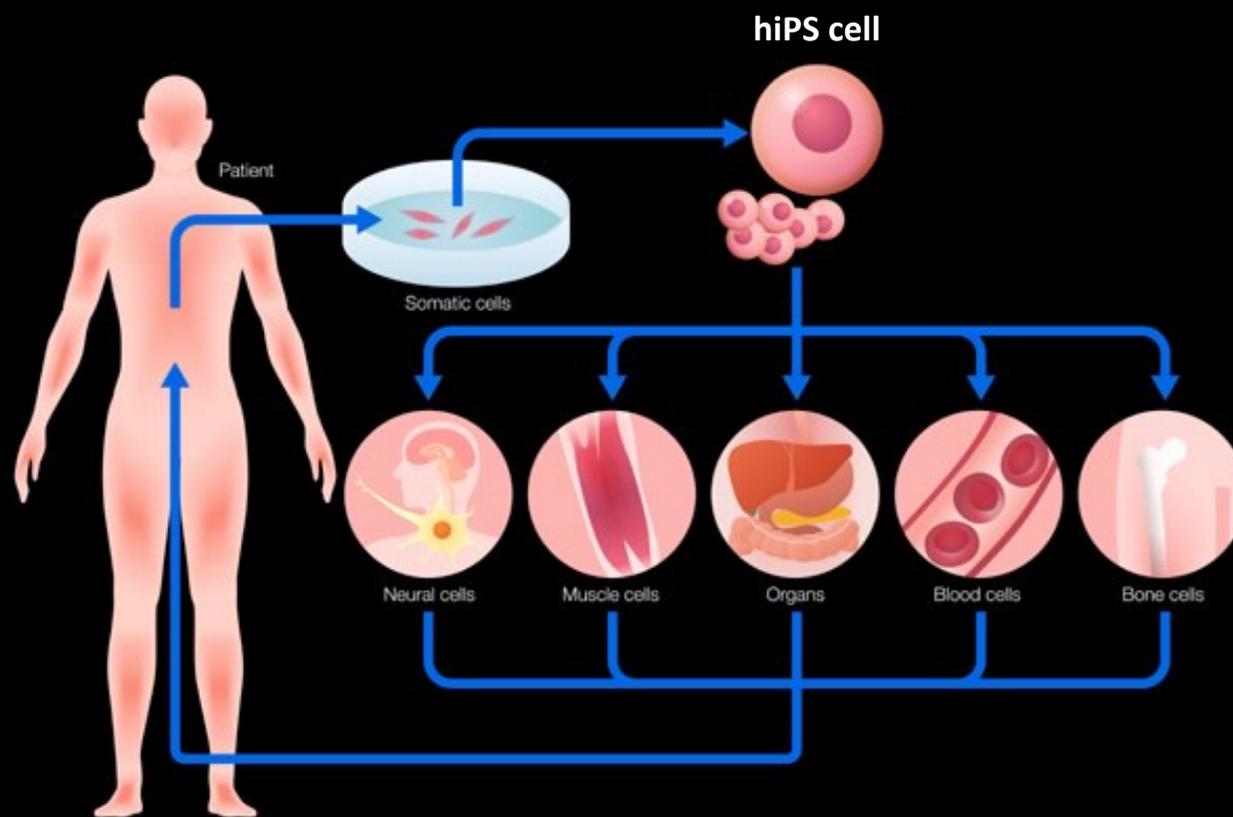
Objectifs de l'étude

Promouvoir le potentiel des oligodendrocytes pour réparer les dommages des AVC de la substance blanche

- **Potentiel des hiPSC-GEP**

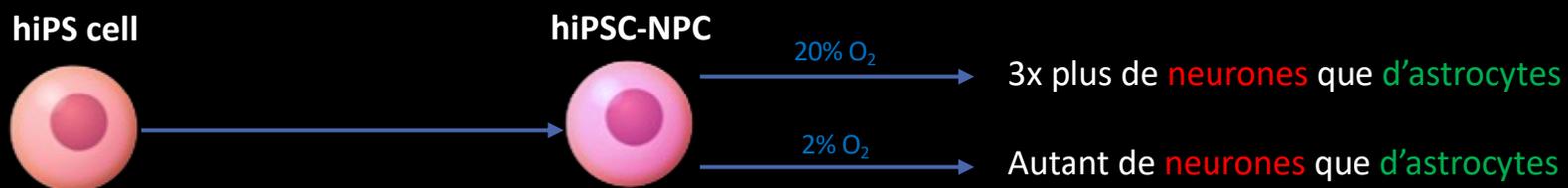


Génération des hiPSC-GEP



P, Surat. 2019. Induced Pluripotent Stem (iPS) Cells in Medicine and Research. News-Medical, [En ligne]. 2019 [cité le 8 Mars 2024], Disponible: <https://www.news-medical.net/life-sciences/Induced-Pluripotent-Stem-Cells-in-Medicine-and-Research.aspx>.

Génération des hiPSC-GEP

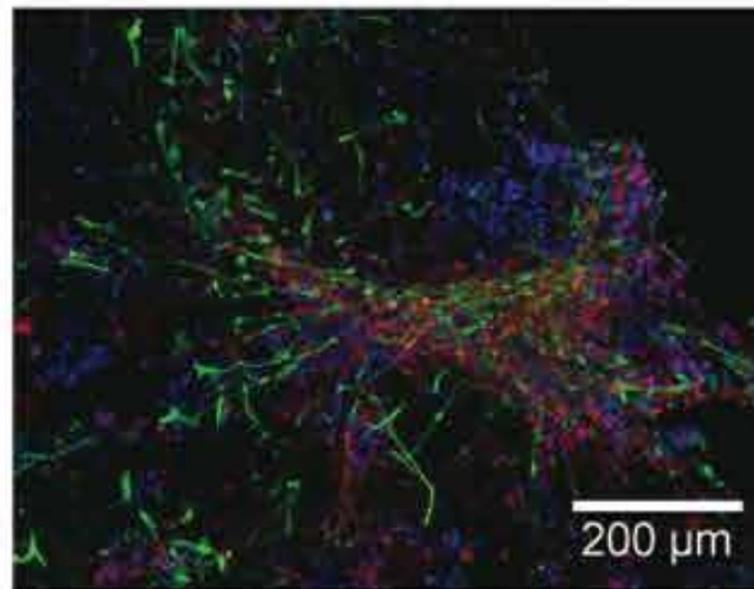
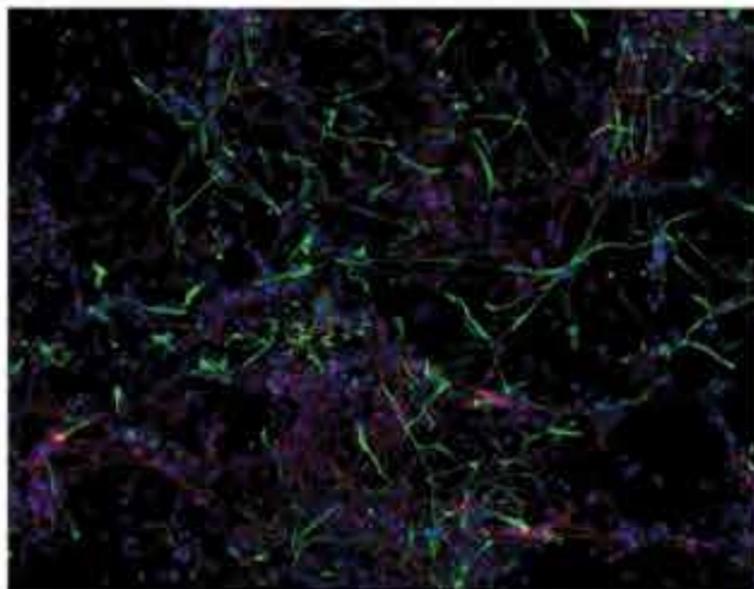
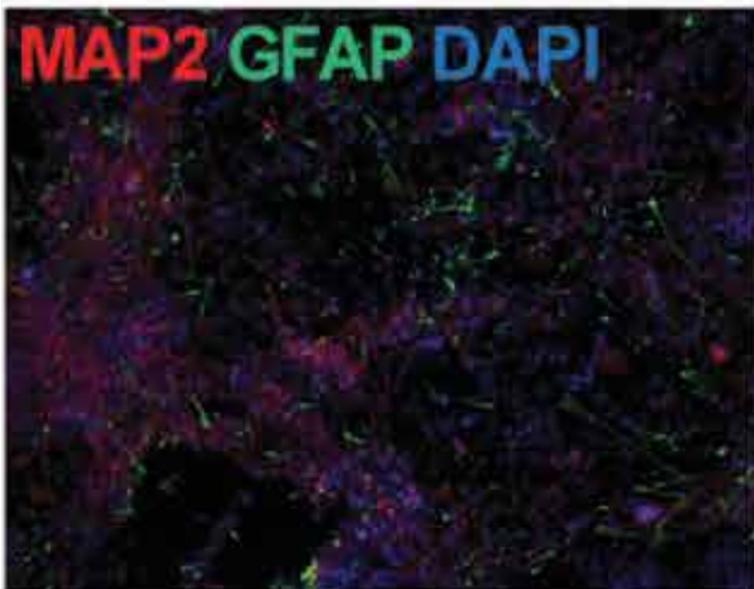


20% O₂

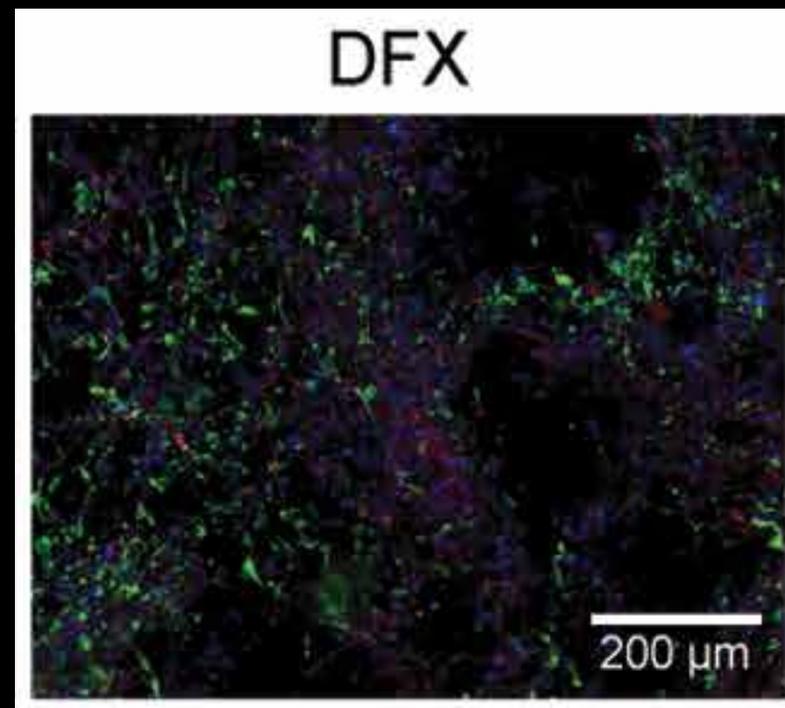
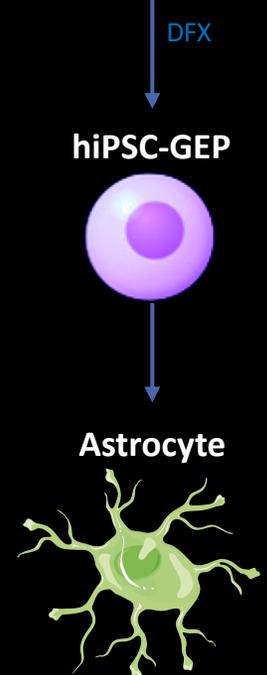
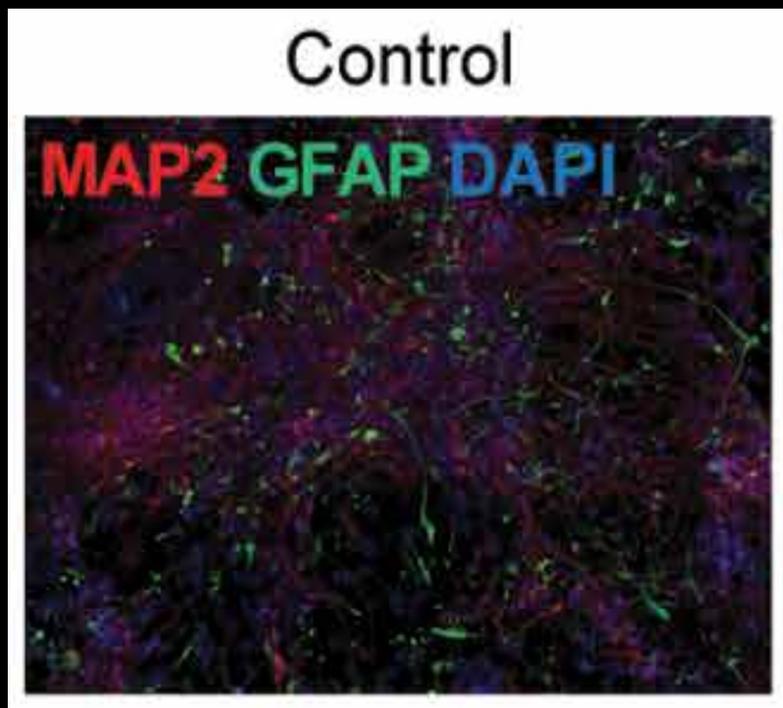
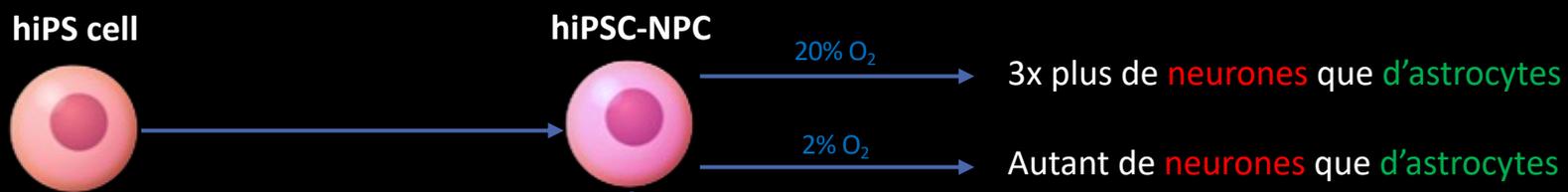
2% O₂

2% → 20% O₂

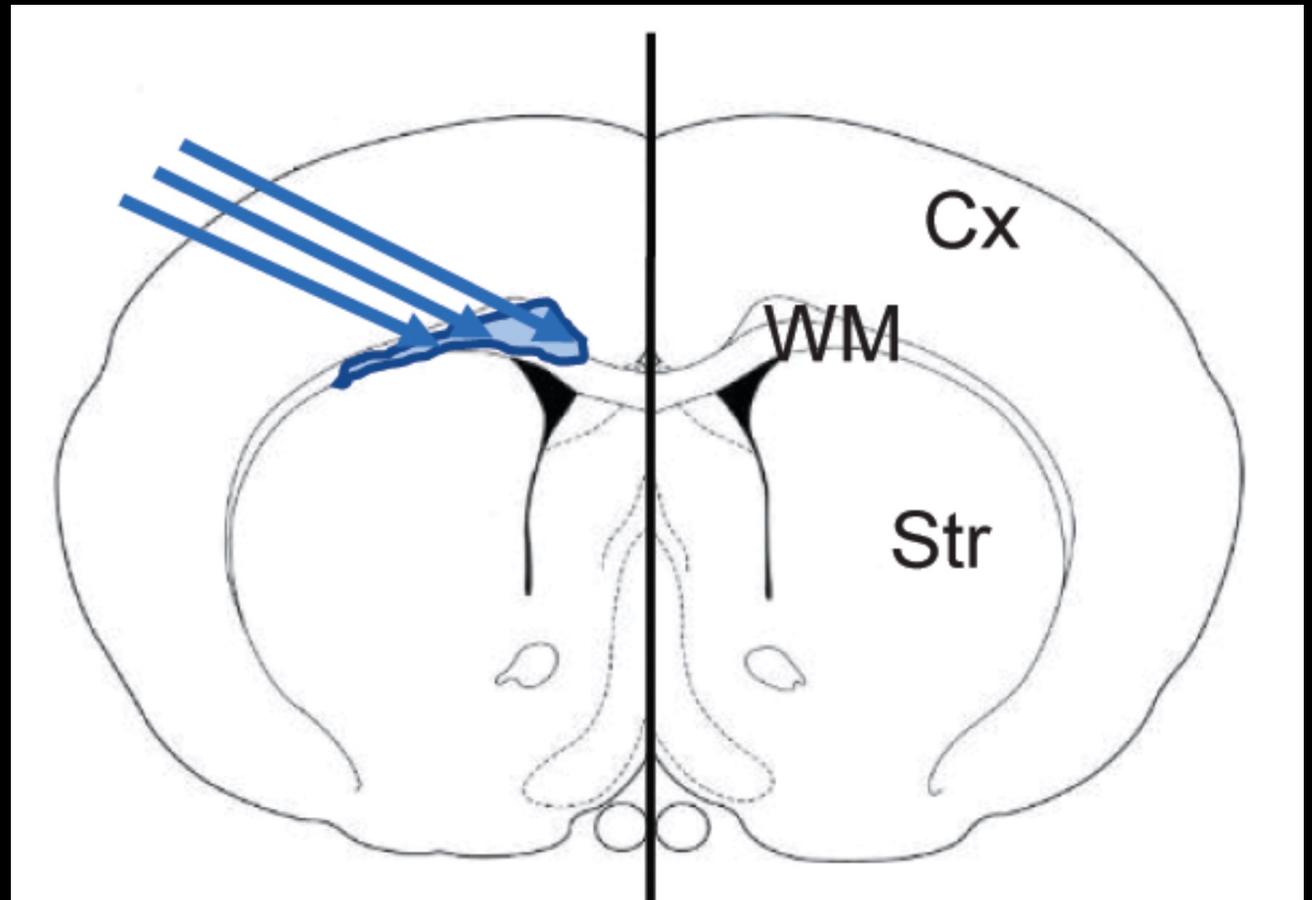
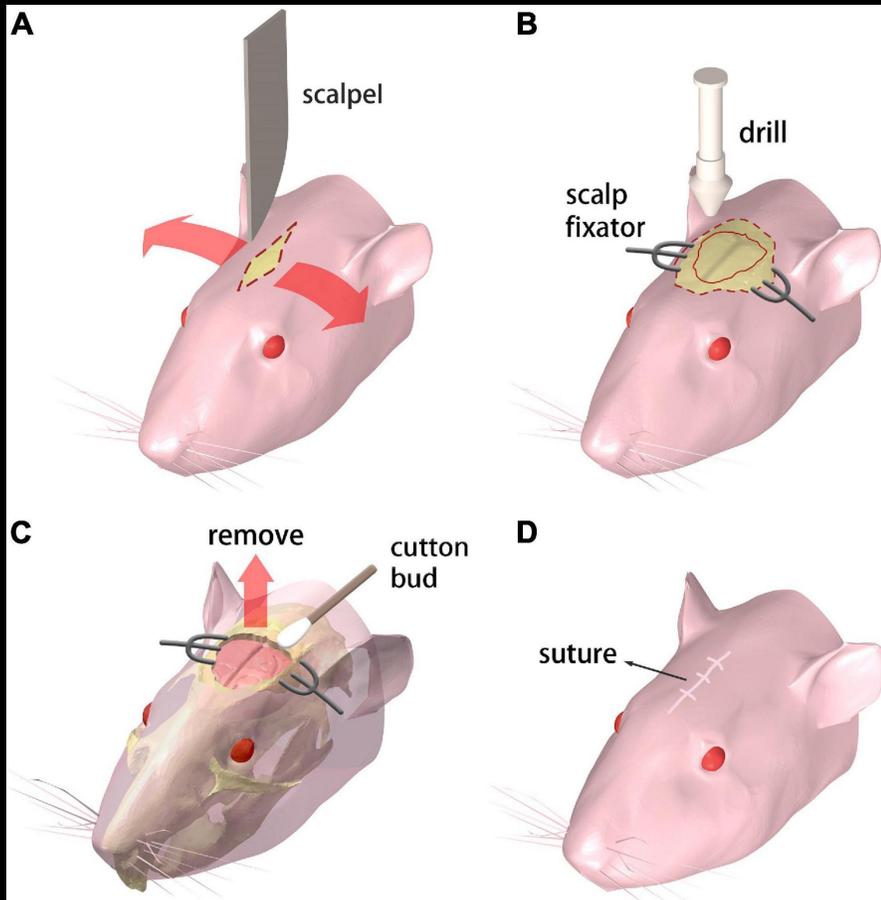
MAP2 GFAP DAPI



Génération des hiPSC-GEP

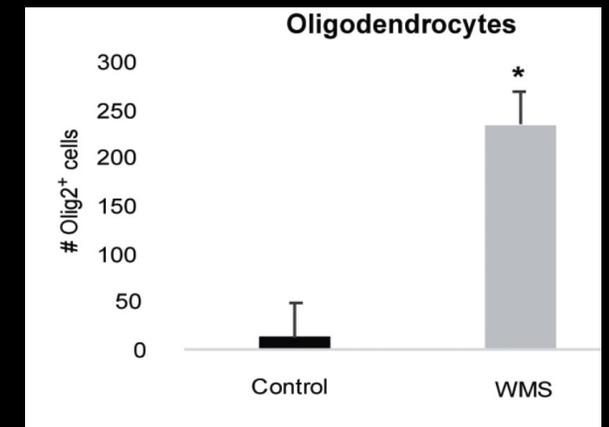
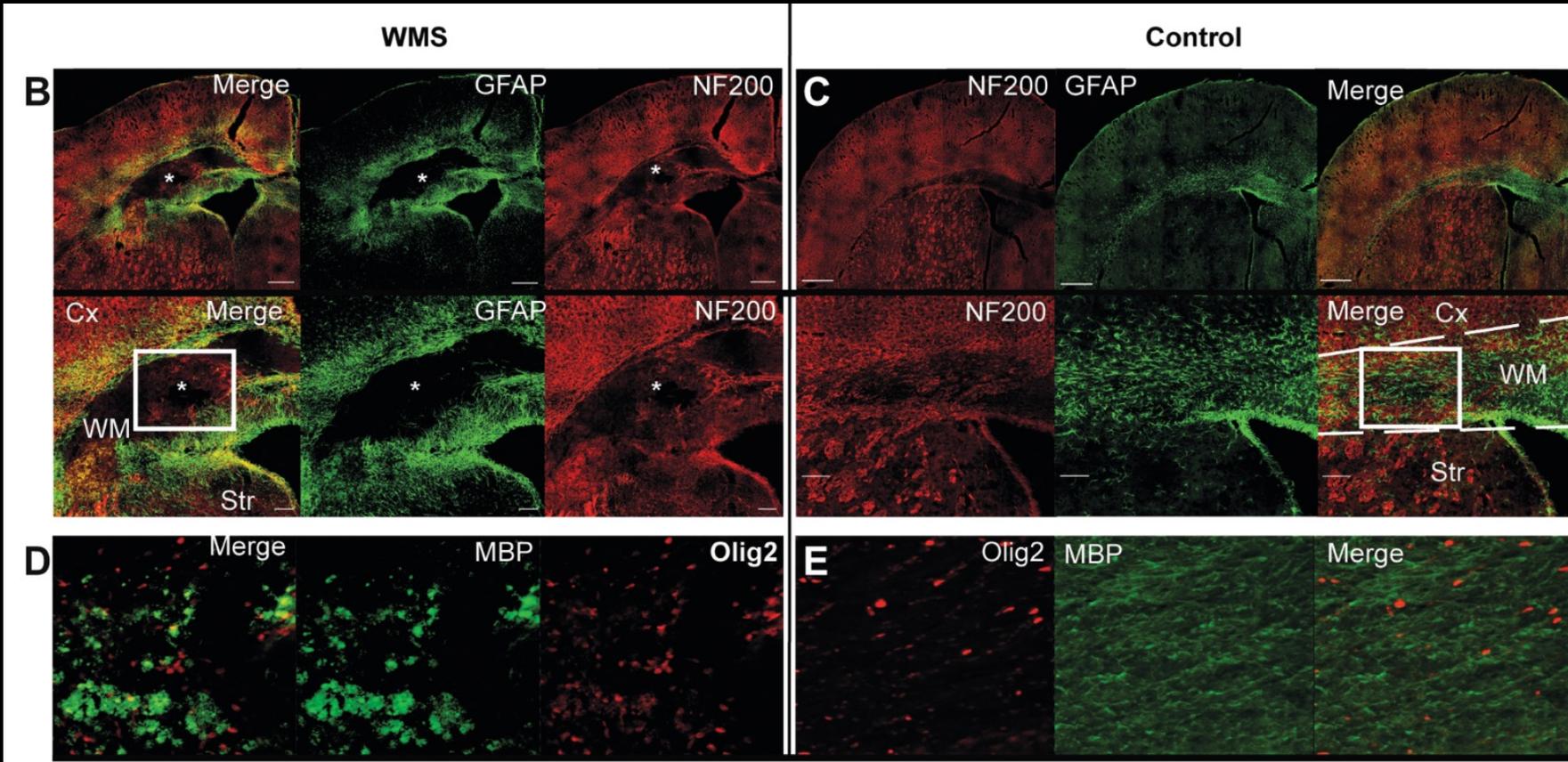


Comment induire un
AVC chez l'animal ?

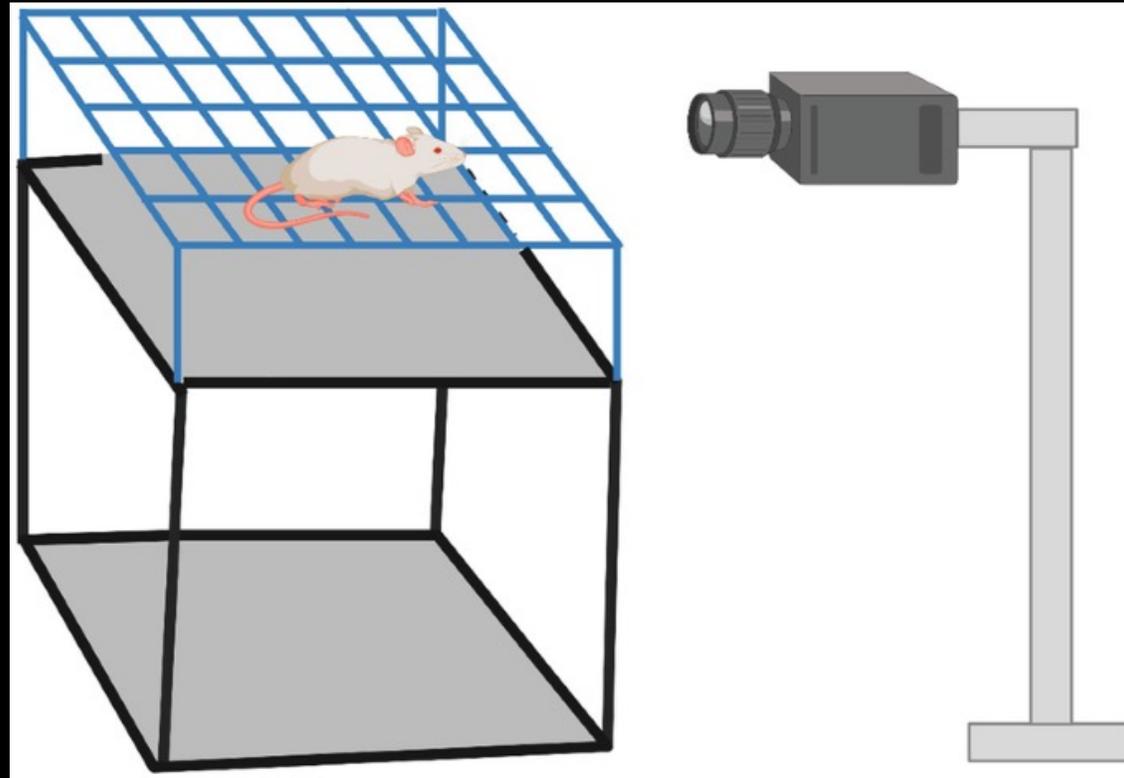


Wang X, Luo Y, Chen Y, Chen C, Yin L, Yu T, He W, Ma C. A Skull-Removed Chronic Cranial Window for Ultrasound and Photoacoustic Imaging of the Rodent Brain. *Front Neurosci.* 2021 May 31;15:673740. doi: 10.3389/fnins.2021.673740

Évaluation structurelle



Évaluation fonctionnelle



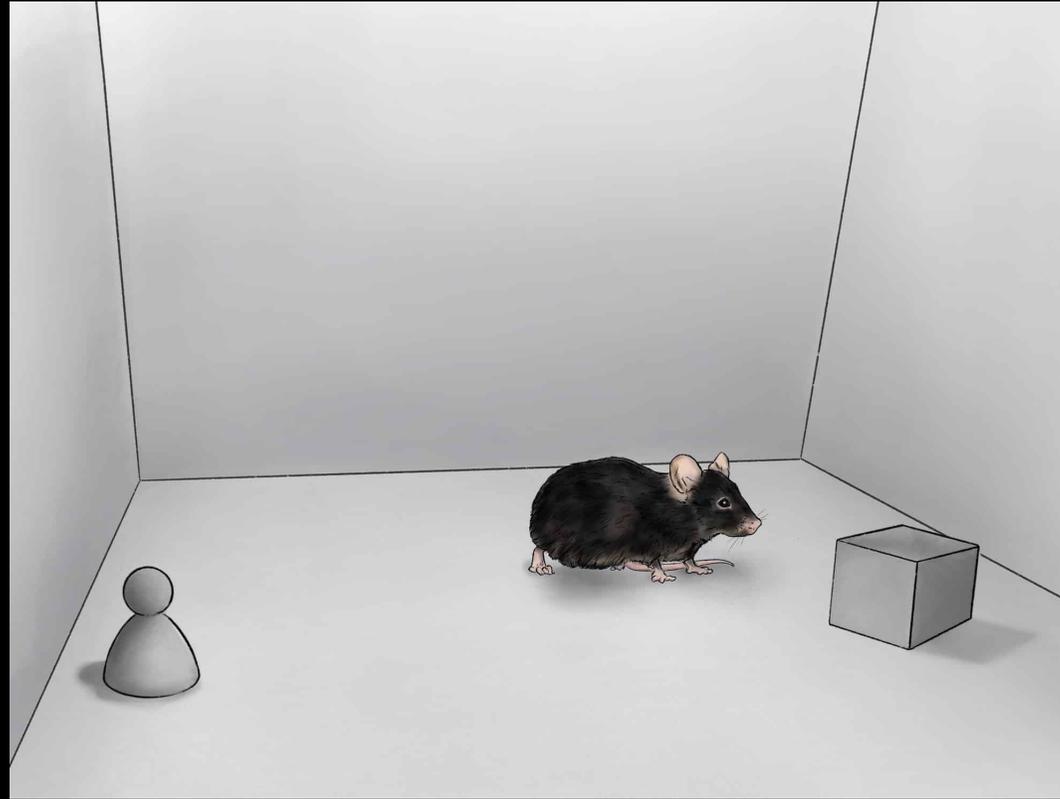
Syera N, Bagchi S, Al Shoyaib A, Karamyan ST, Alamri FF, Karamyan VT. The Finer Aspects of Grid-Walking and Cylinder Tests for Experimental Stroke Recovery Studies in Mice. *Methods Mol Biol.* 2023;2616:345-353. doi: 10.1007/978-1-0716-2926-0_23

Évaluation fonctionnelle



Scantox [En ligne]. Cylinder test; 2024 [cité le 8 mars 2024]. Disponible:
<https://scantoxneuro.com/in-vivo-services/behavioral-tests/lateral-lesion-tests/cylinder-test/>

Évaluation fonctionnelle



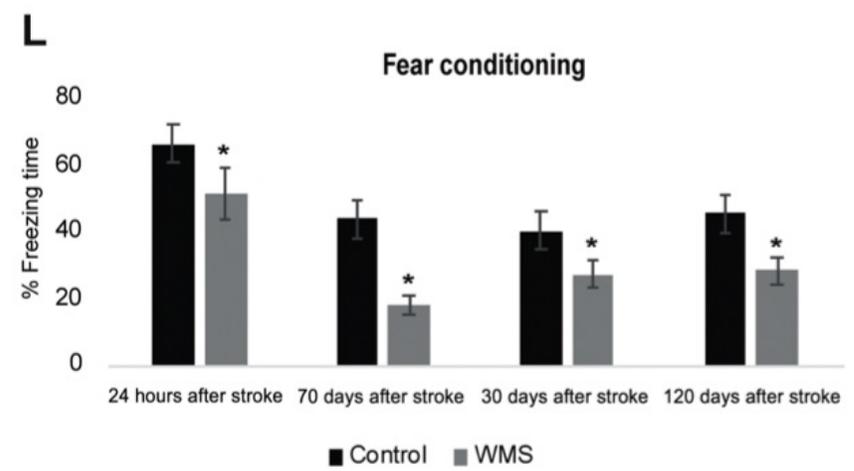
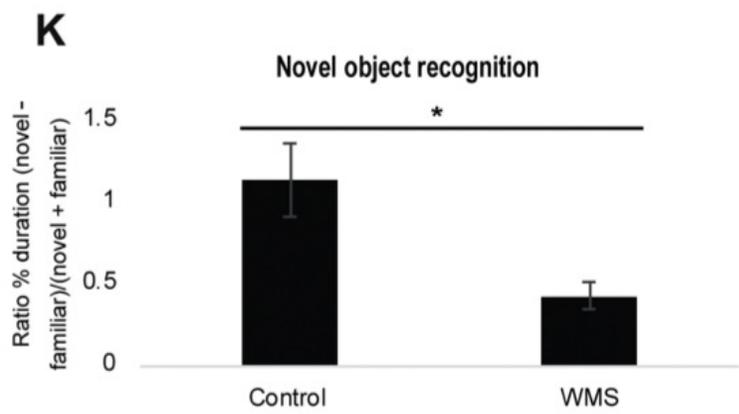
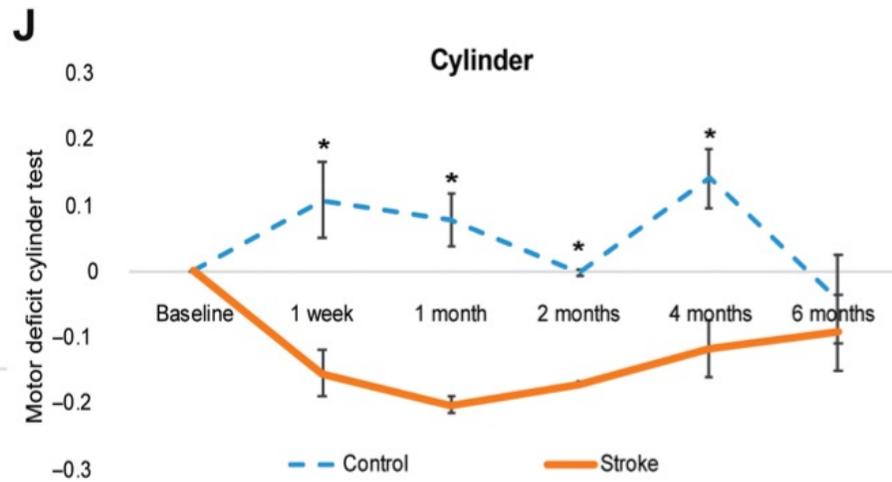
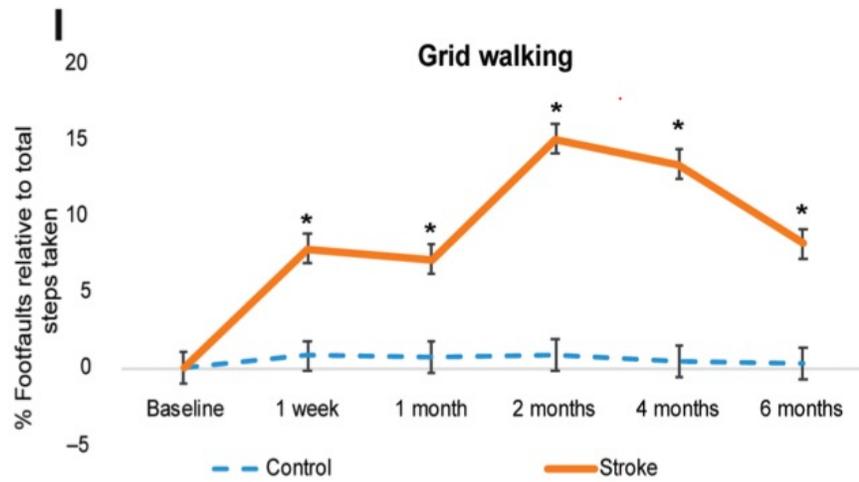
Scantox [En ligne]. Novel object recognition test; 2024 [cité le 8 mars 2024]. Disponible: <https://scantoxneuro.com/in-vivo-services/behavioral-tests/cognitive-tests/novel-object-recognition-test/>

Évaluation fonctionnelle



Scantox [En ligne]. Contextual fear conditioning test; 2024 [cité le 8 mars 2024]. Disponible: <https://scantoxneuro.com/in-vivo-services/behavioral-tests/cognitive-tests/contextual-fear-conditioning-test/>

Évaluation fonctionnelle



Test de l'hypothèse

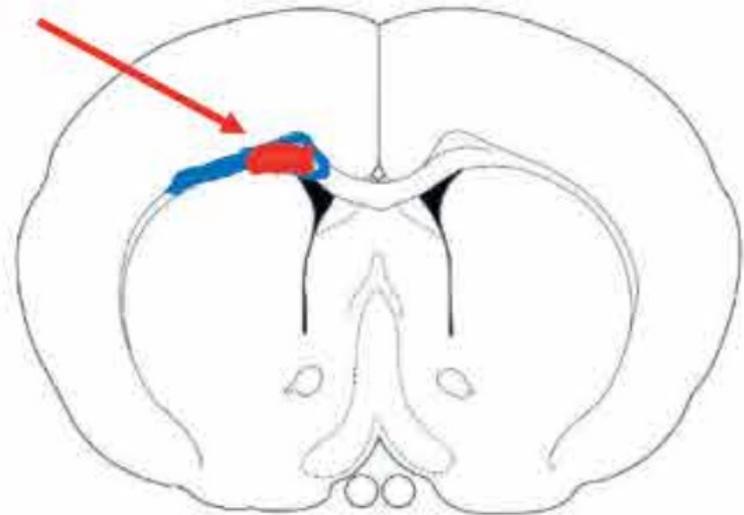
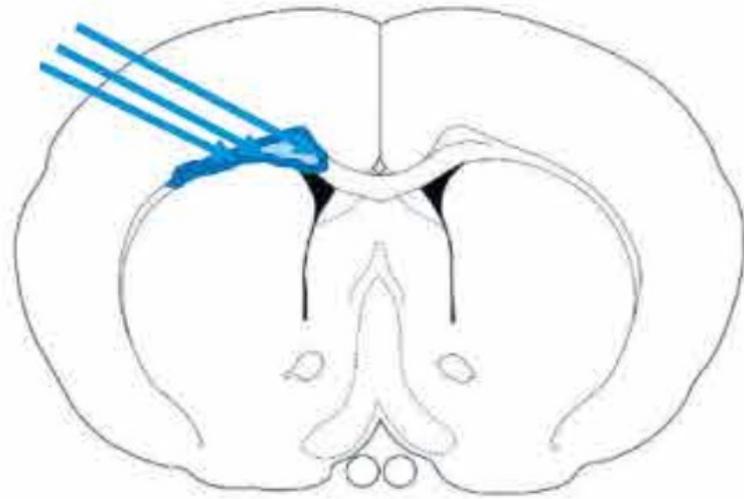


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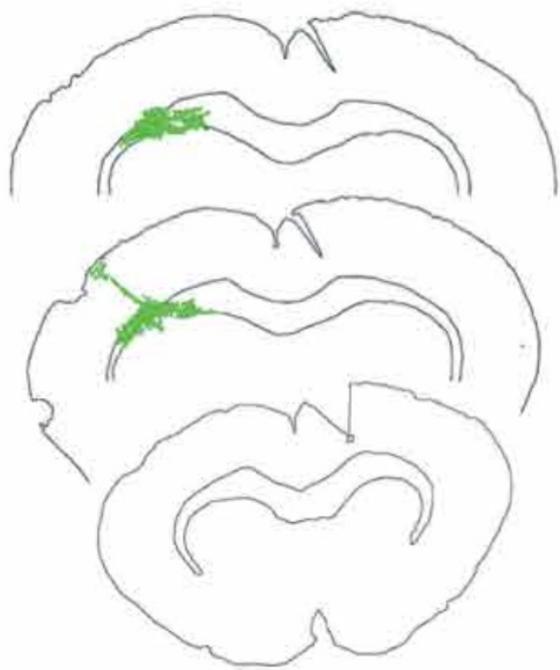


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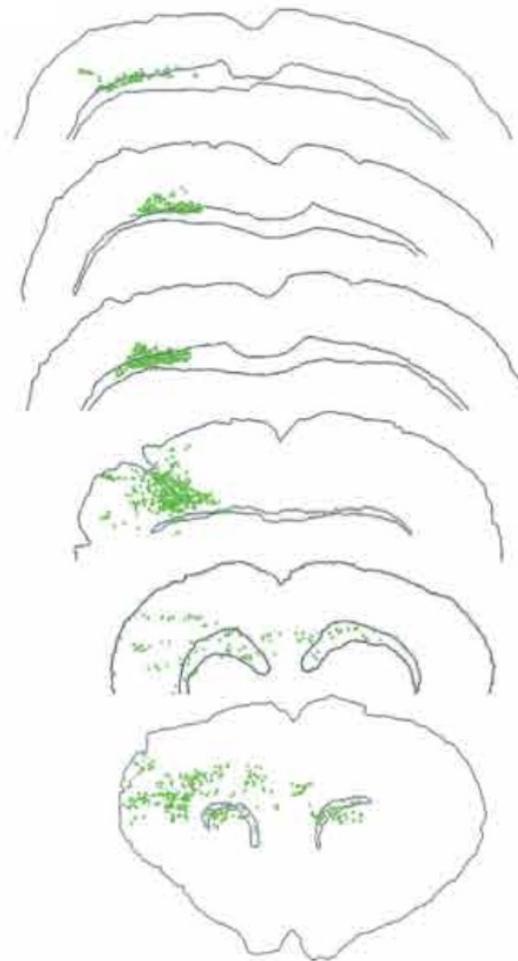




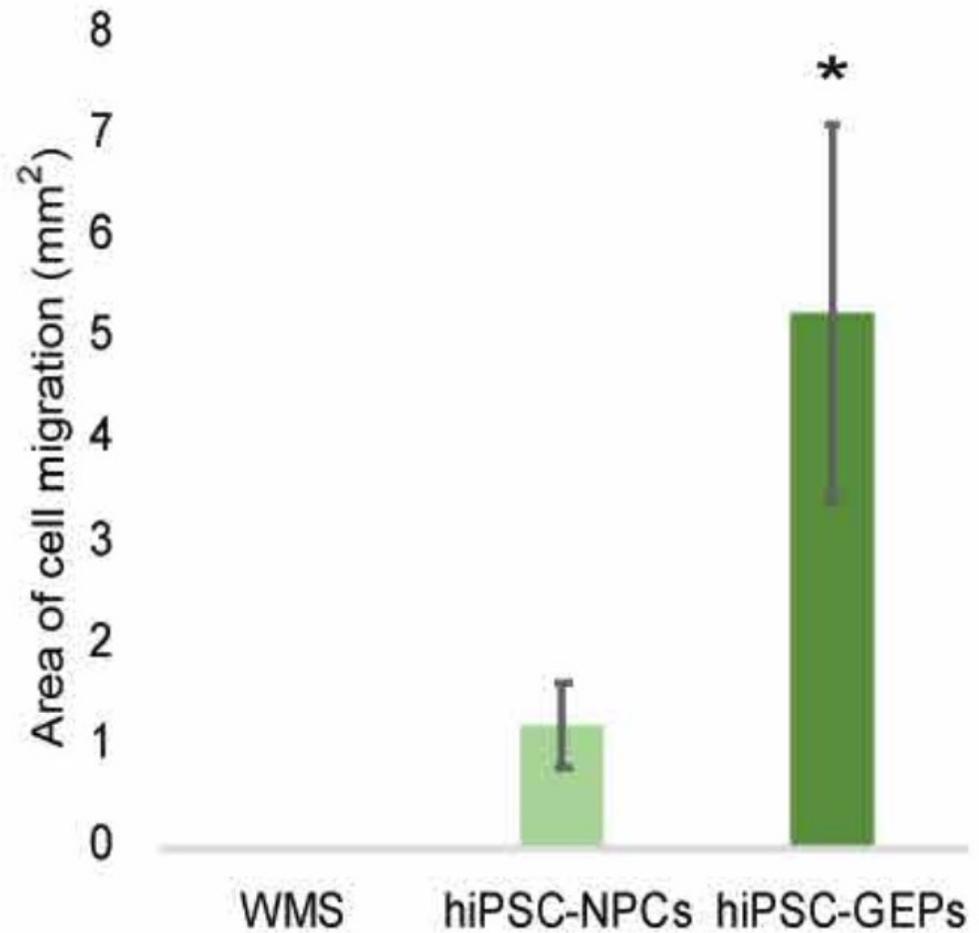
hiPSC-NPCs



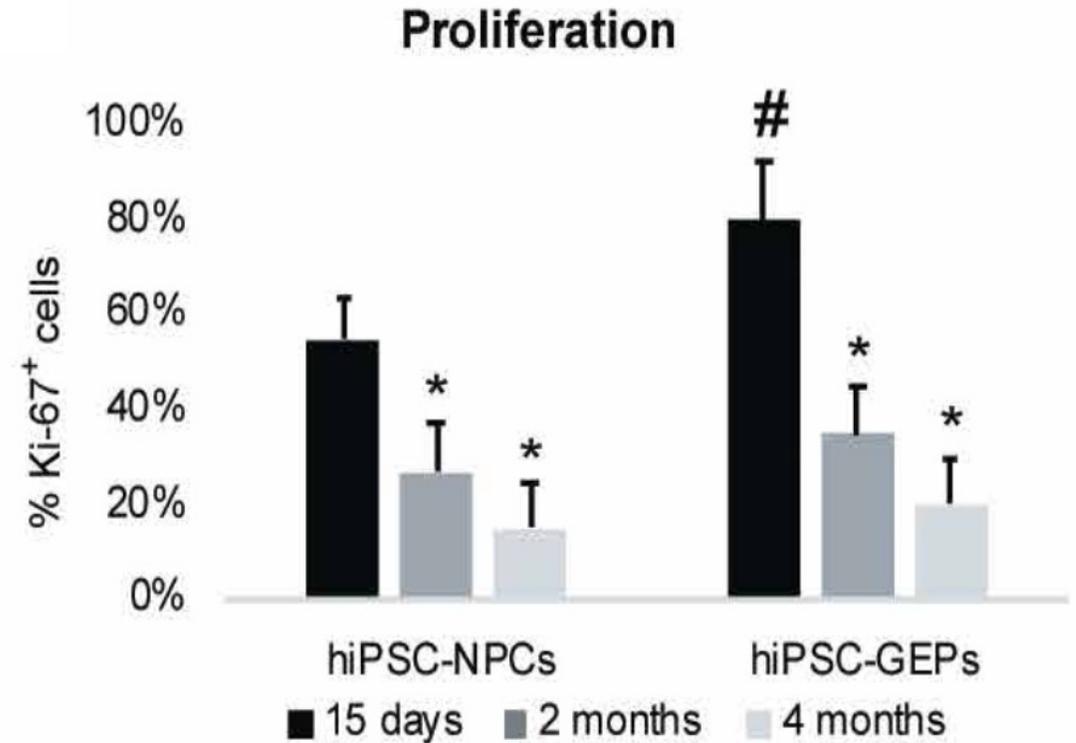
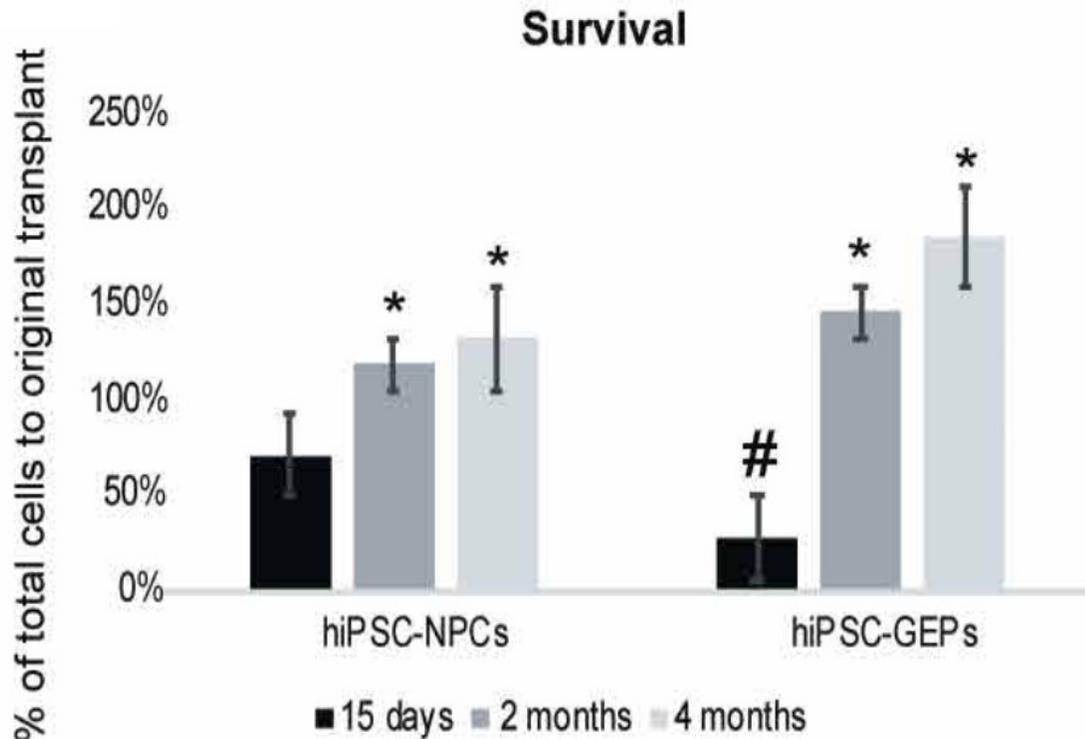
hiPSC-GEPs



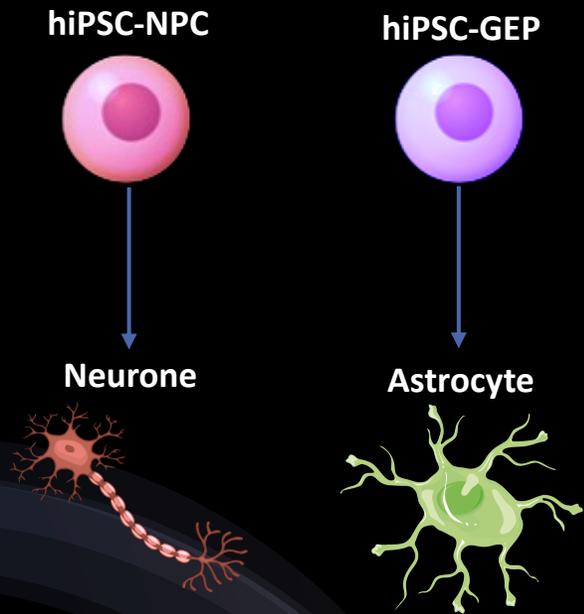
Cell migration



Évaluation de l'évolution des cellules

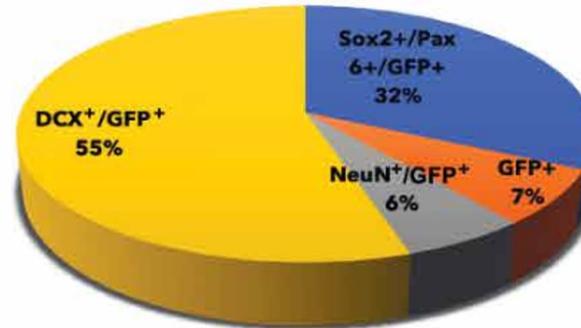


Destinée cellulaire

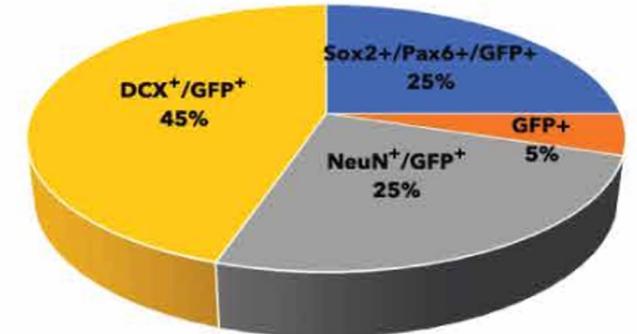


hiPSC-NPCs

2 months

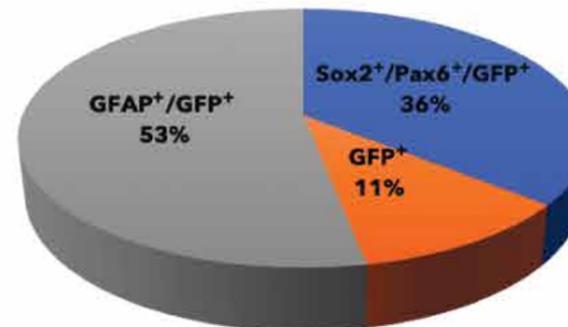


4 months

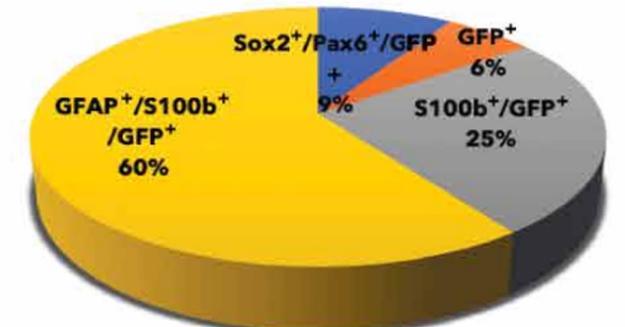


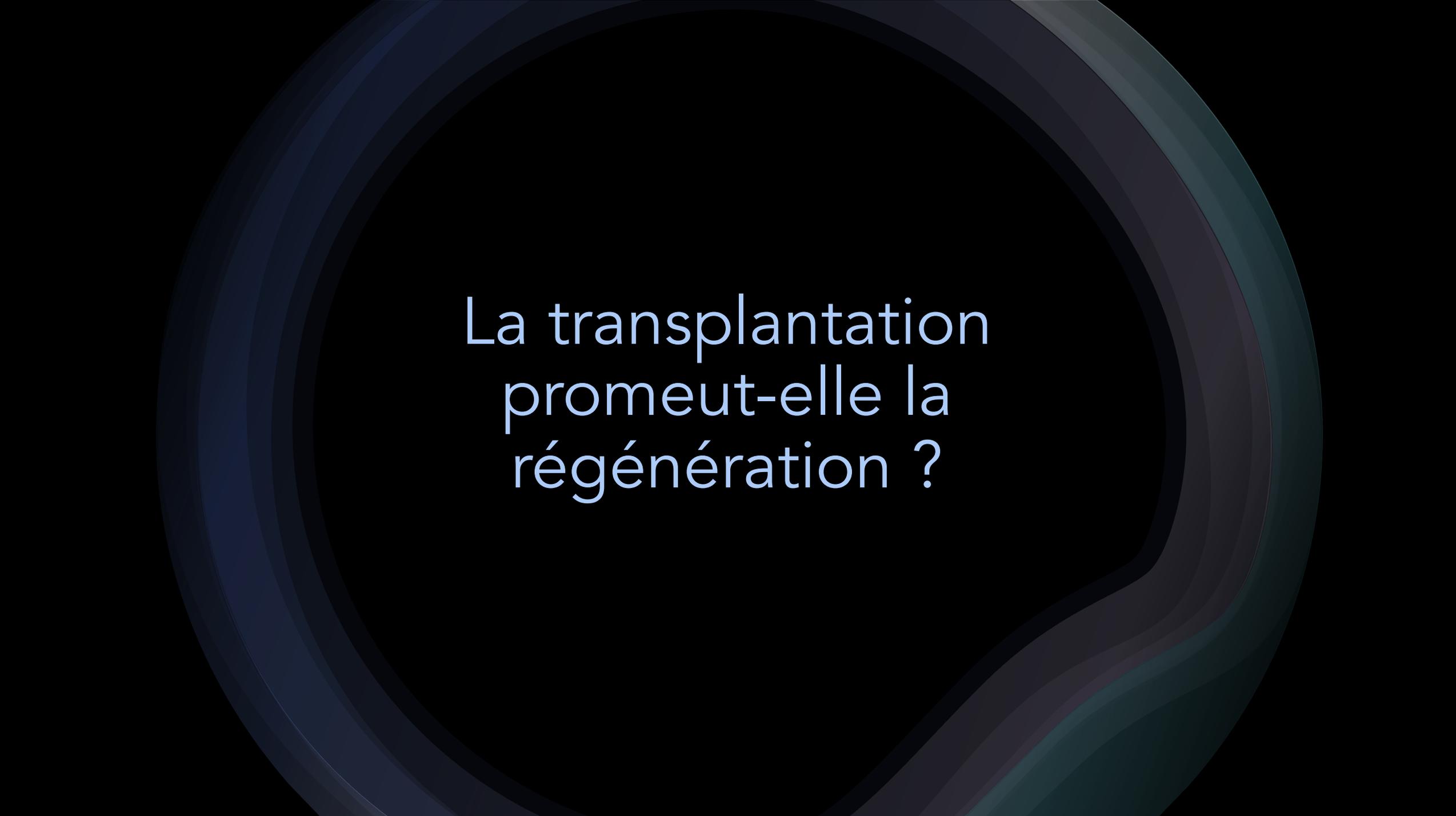
hiPSC-GEPs

2 months



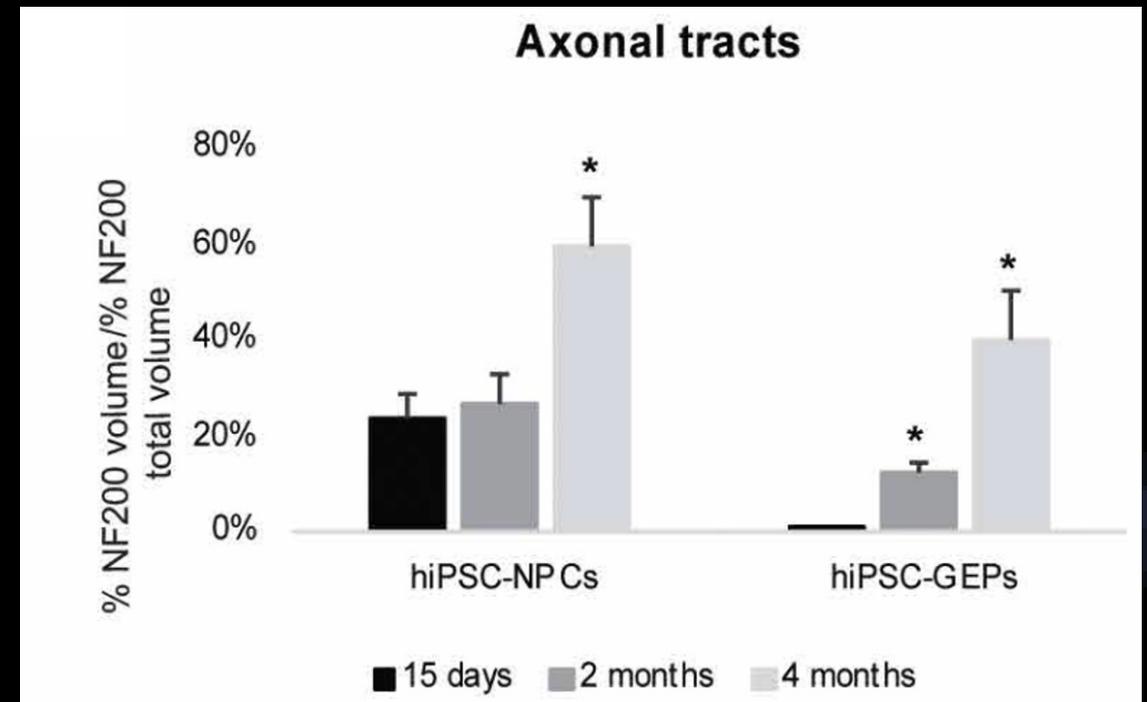
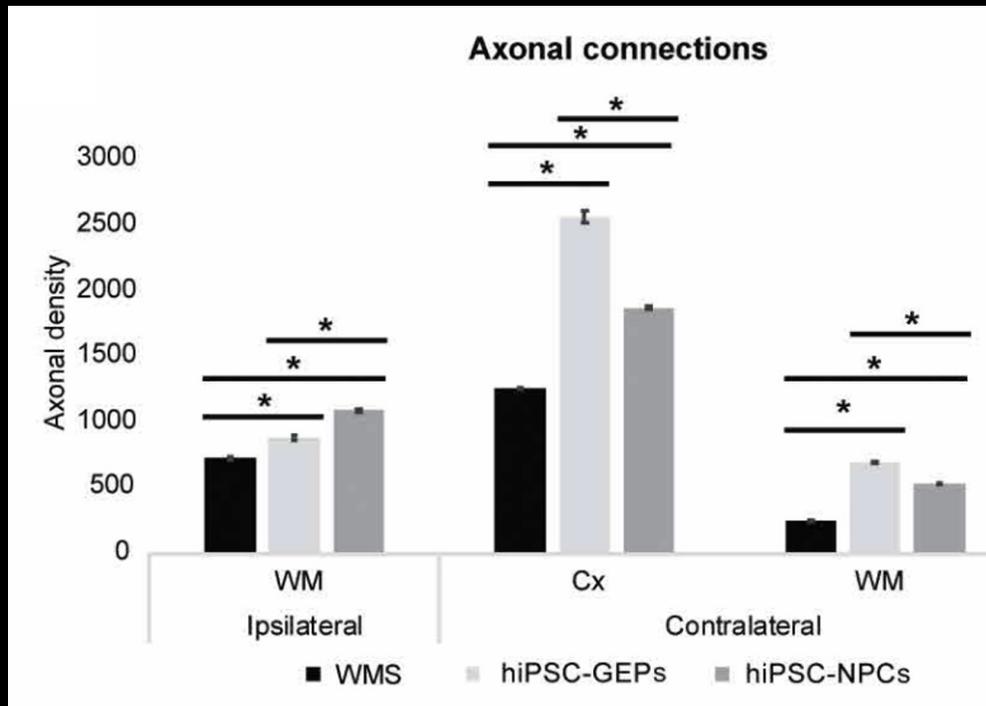
4 months



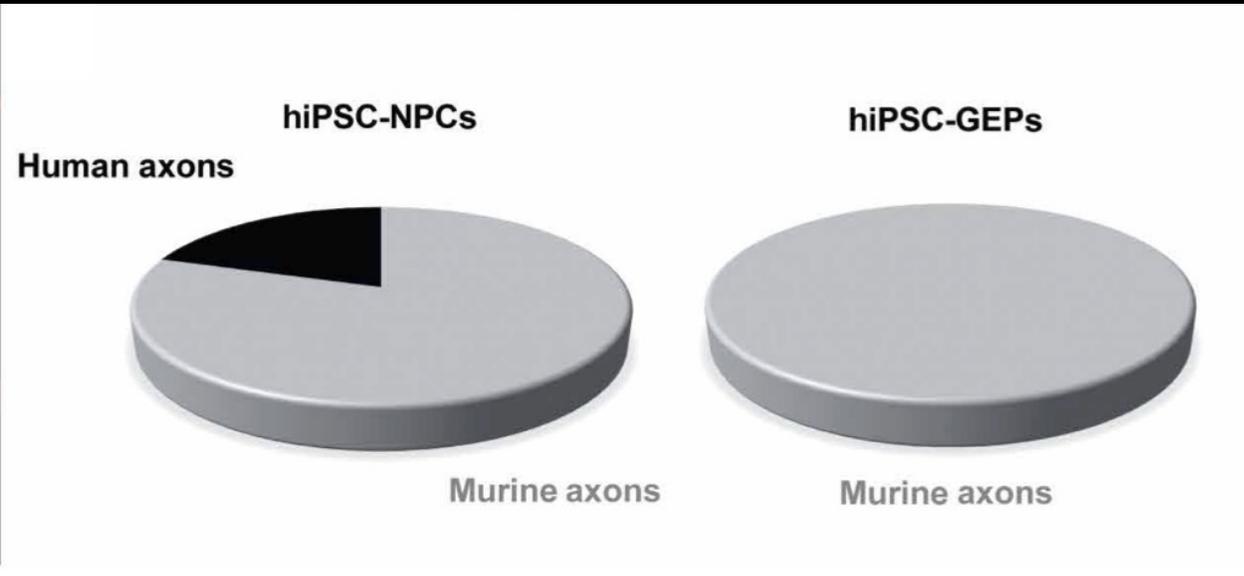
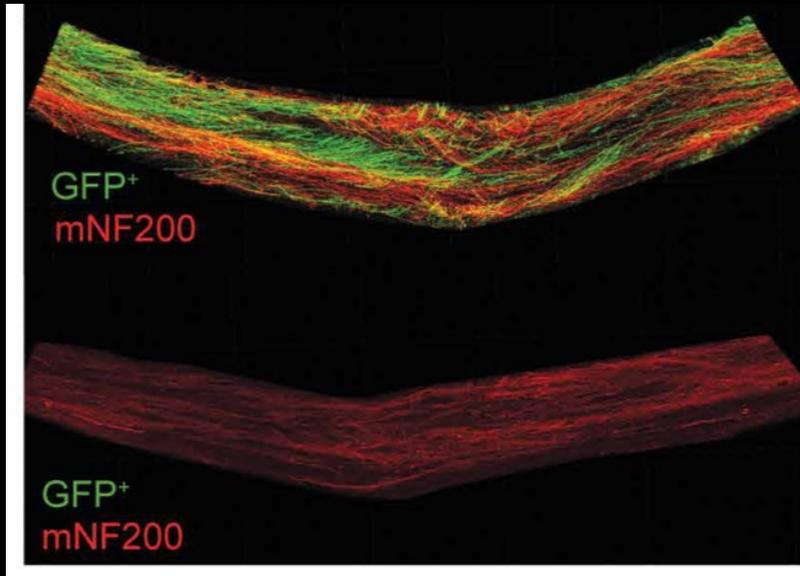


La transplantation
promeut-elle la
régénération ?

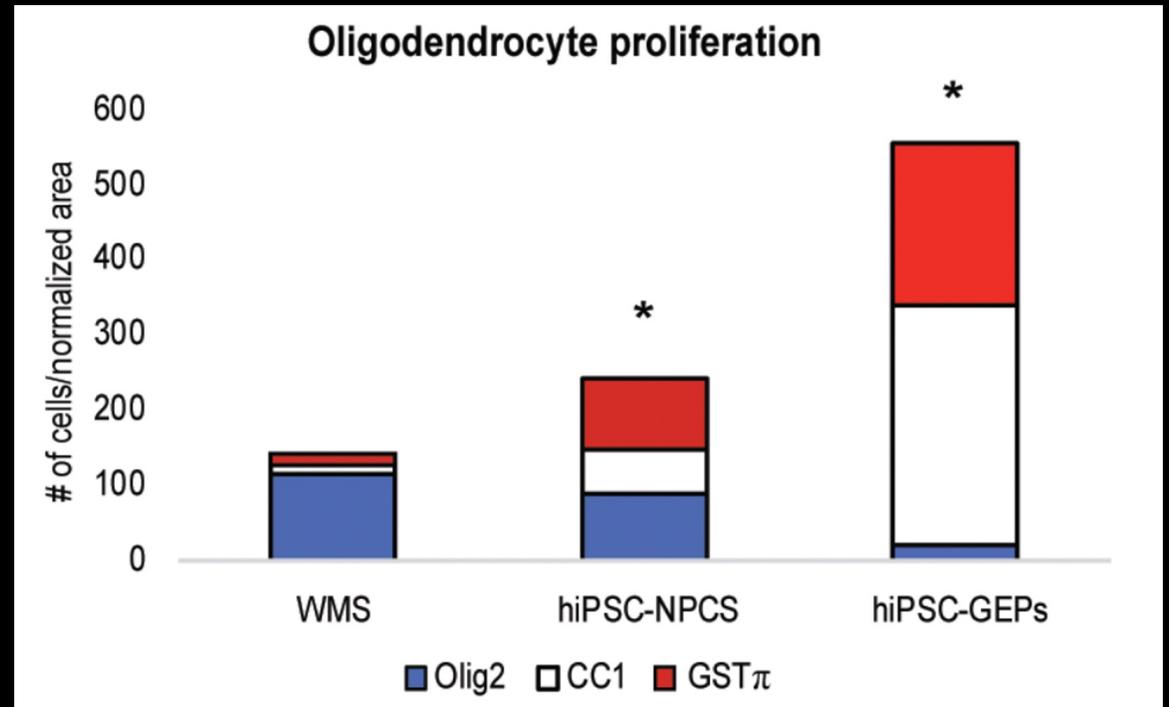
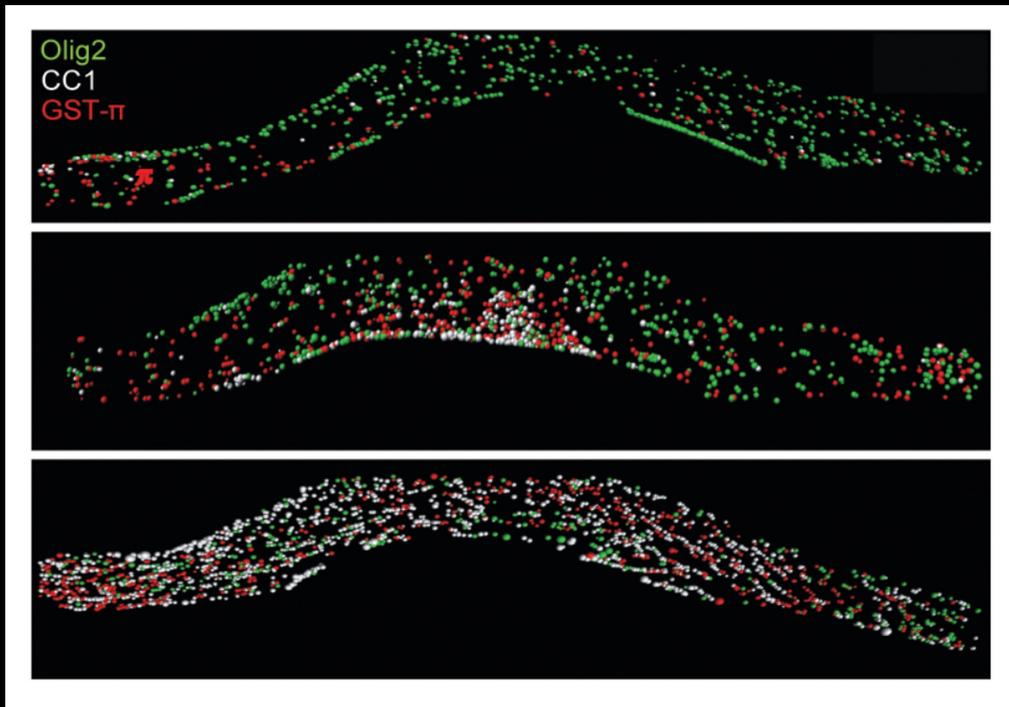
Résultats



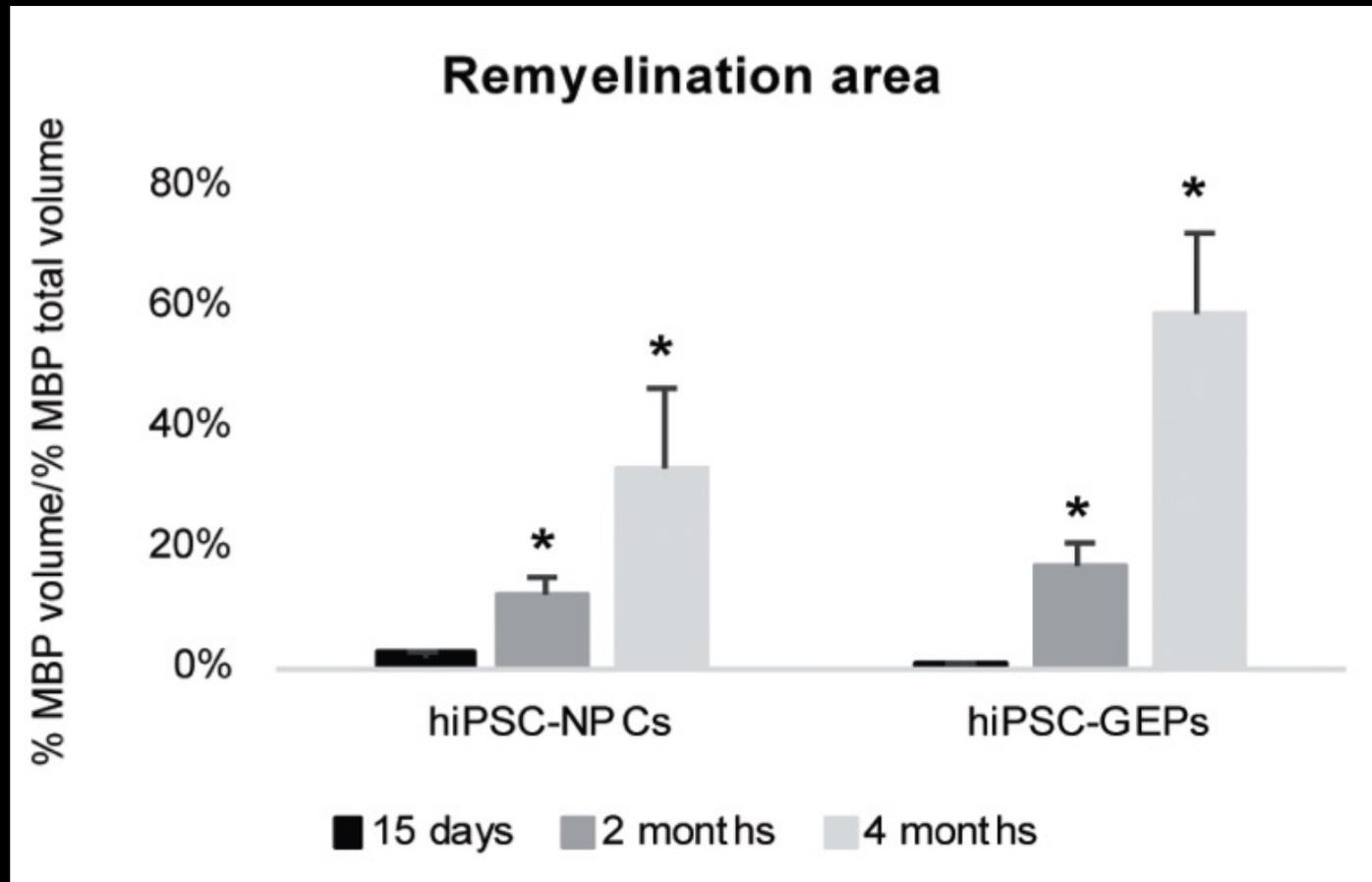
Évaluation structurelle de la transplantation



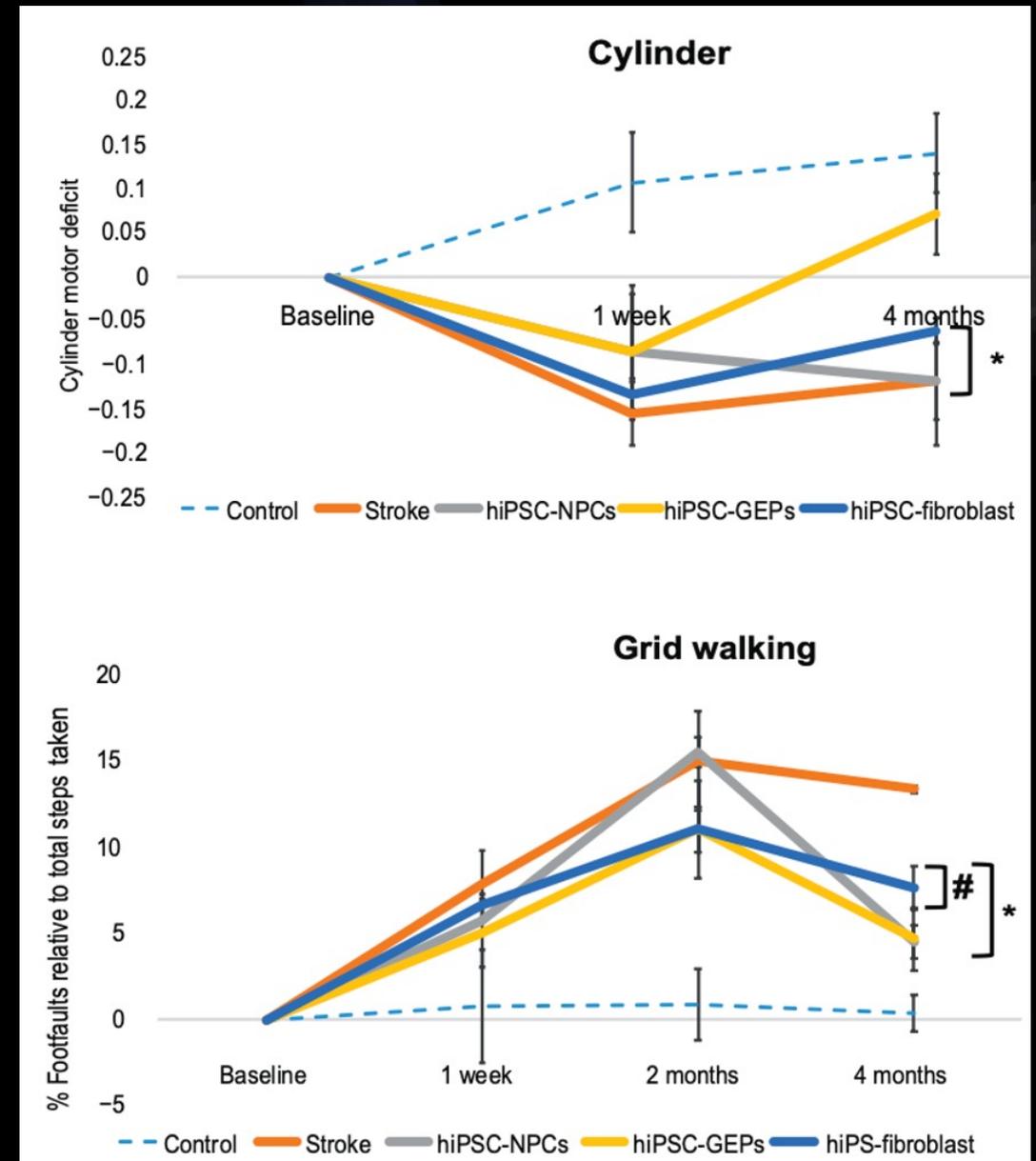
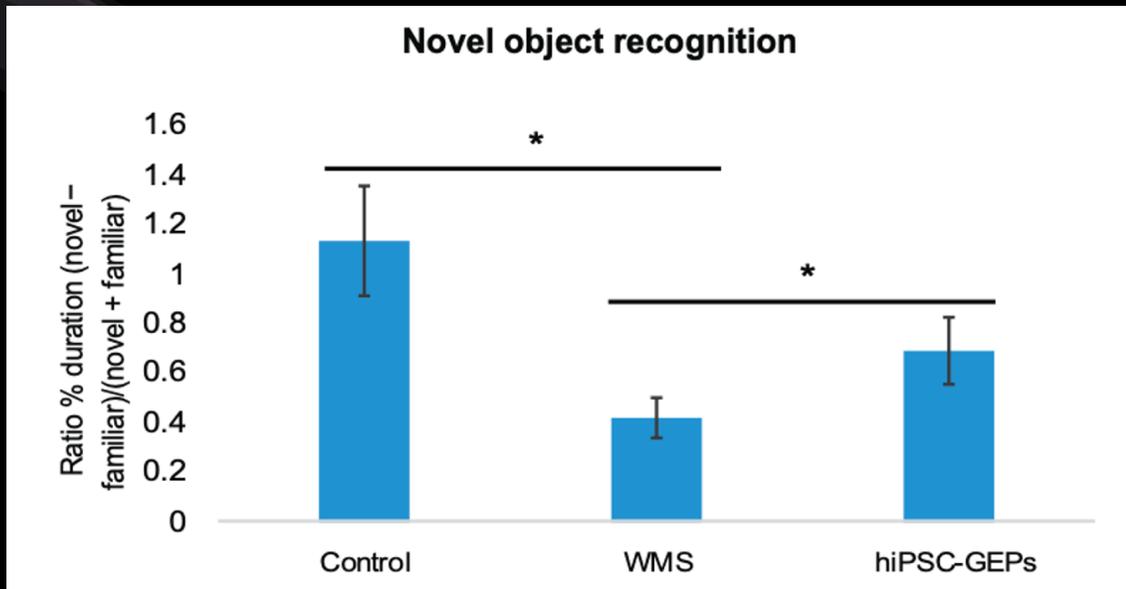
Évaluation structurelle de la transplantation



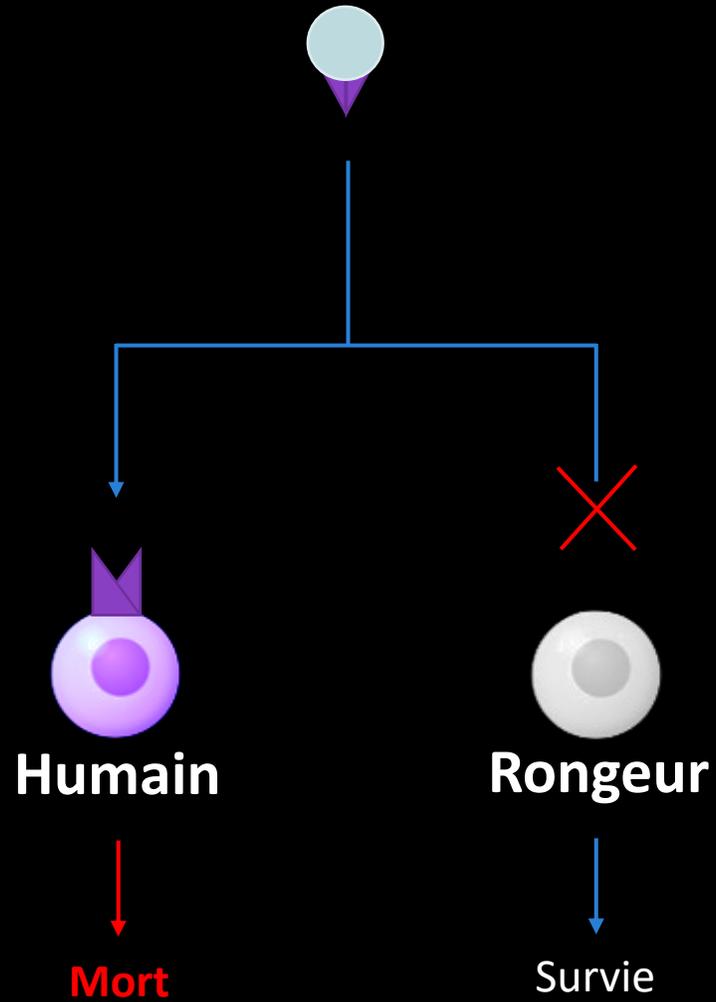
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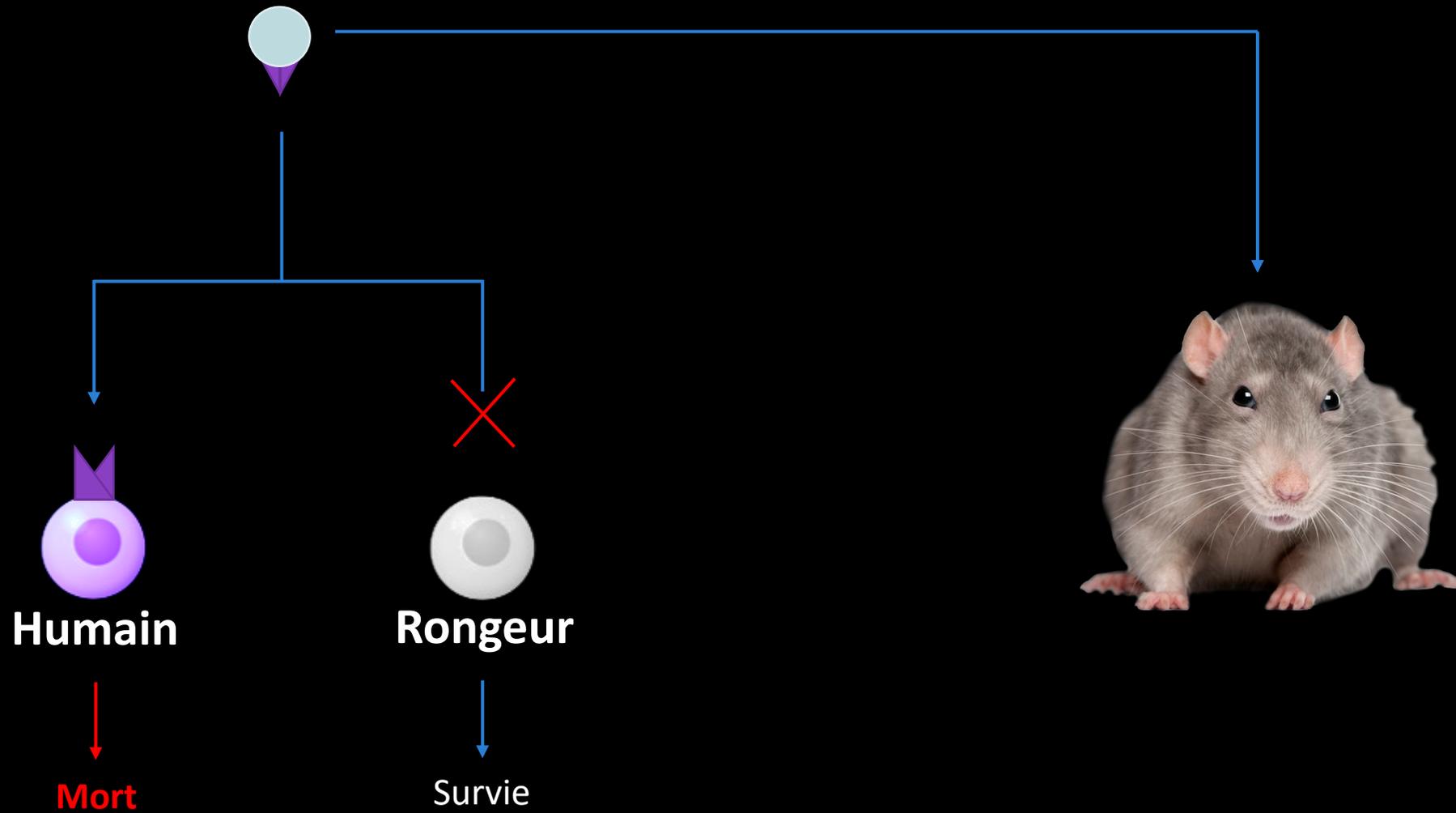
Évaluation fonctionnelle de la transplantation



Toxine diphtérique



Toxine diphtérique



Analyse critique

Perspectives



Conclusion personnelle

Merci !

