Development of luminescent human iPSC-derived neurospheroids

Created on: 21-11-2022 - Last modified on: 02-01-2023

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Organisation

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SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research
Type of method	In vitro - Ex vivo
Specify the type of cells/tissues/organs	human induced pluripotent stem cell-derived neurospheroids

DESCRIPTION

Method keywords

neurospheroid
Bioluminescence
IPSC
organoid
neurotoxicity

Scientific area keywords

3D organoid models
Induced pluripotent stem cells
ischemic stroke

Method description

This method relates to the development of highly reproducible human iPSC-derived neurospheroids equipped with intrinsic bioluminescence for an easy and longitudinal follow-up of the viability and growth of these neurospheroids over time. The luminescent neurospheroids have been applied in ischemic stroke research, where this model enabled modeling of neurotoxicity after oxygen-glucose deprivation. The easy neural survival

read-out may also enable the evaluation of potential neuroprotective agents (in high-throughput).

Lab equipment

- Laminar flow cabinet;
- Shaker;
- Microplate reader (Luminometer).

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

- Three-dimensional model;
- human-based model;
- longitudinal measurements of neurospheroid viability (i.e. does not require a single endpoint and/or disruption of neurospheroids);
- highly reproducible;
- amenable to high-throughput drug screening.

Challenges

- Maturity of neurospheroids and lack of glial cell types;
- Hypoxic/necrotic core development;
- Potential transgene silencing associated with lentiviral vector transduction.

Modifications

- Optimization of culture conditions of neurospheroids (i.e. increasing culture time, other media types, use of bioreactors, etc.);
- Addition of microglia-progenitors to neurospheroids;
- Modification of genetic engineering strategy (e.g. CRISPR/Cas9).

Future & Other applications

- Neurotoxicity, neurotrauma and neurodegenerative disease modeling;
- Evaluation of candidate neuroprotective therapies (in high-throughput).

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Van Breedam E, Nijak A, Buyle-Huybrecht T, Di Stefano J, Boeren M, Govaerts J, et al. Luminescent Human iPSC-Derived Neurospheroids Enable Modeling of Neurotoxicity After Oxygen-glucose Deprivation. Neurotherapeutics. 2022.

Links

Luminescent Human iPSC-Derived Neurospheroids Enable Modeling of Neurotoxicity …

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