Modified oligodendroglia cell-derived exosomes as nanotherapeutics for multiple sclerosis

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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, Education and training, Translational - Applied Research
Type of method	In vitro - Ex vivo
Species from which cells/tissues/organs are derived	human, rodents

Type of cells/tissues/organs	Oligodendroglia cells, astrocytes, microglia, brain, PBMC, MSC, neuronal cell lines

DESCRIPTION

Method keywords

extracellular vesicles

autophagy

Gene expression

RNA sequencing

peptide sequencing

lipidomics

Endocytosis

Scientific area keywords

Engineerd extracellular vesicles

genetically modified exosomes

Nanotherapeutics

small chaperones

Method description

Characterization of Human Oligodendroglia derived-EV-rich in sHSPs (HOG-EV-sHSPs). Establish HSPB1/B8 stably expressing cell lines for the production of sHSPs rich-EV cell culture conditioned medium. Human Oligodendroglia cell lines (HOG) were stably transduced with pLenti-HSPBs gene constructs following a well-established protocol, and are successfully cultured to produce HOG-EV-sHSPs. Current approaches for the production of EV are based on classical cell culture (2D culture). However, these cells do not reflect biological conditions. For therapeutic applications, we will culture cells in a Hollow Fibercell Bioreactor. This is a 3D culture system with an EV yield up to 100 times higher. We have optimized and validated the use of FiberCell bioreactor. Pilot experiments showed

the feasibility of mass exosomes production in the bioreactor.

Lab equipment

- SPR ;
- NTA ;
- TEM ;
- Miseq ;
- SEC ;
- Ultracentrifuge.

Method status

Still in development

Internally validated

Currently submitted for further validation by an external party (e.g. OECD, EURL ECVAM,…)

PROS, CONS & FUTURE POTENTIAL

Advantages

- Non-invasive biomarker for chronic diseases ;
- Future studies focused on modified exosomes as nanotherapeutics will contribute to the development of MS-phenotype targeted cell-free based therapeutics.

Challenges

- Heterogenous EV subtypes ;
- Homogeneity in Exosome production and purification.

Modifications

The use of modified mesenchymal stem cells (MSC) for exosome production.

Future & Other applications

- Personalized targeted treatment ;
- EV as a diagnostic tool ;
- EV as a therapeutic tool ;
- Use of Exosomes in diagnosis ;
- Use of EV to identify (non-)responders to treatment ;
- Cell-free based therapy ;
- The targeted treatment could have a significant impact on the well-being and productivity of the affected patients and their families and on reducing the lifetime costs for the individual, family, and society.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Van den Broek B, Pintelon I, Hamad I, Haidar M, Hellings N, Hendriks J, Kleinewietfeld M, Timmerman V, Timmermans JP, Somers V, Michiels L, Irobi J. Microglial derived extracellular vesicles activate autophagy and mediate multi-target signaling to maintain cellular homeostasis. (under review, 2020, Journal Extracellular Vesicles), IF: 11