Master of Science HES-SO in Life Sciences

ORGANOID TECHNOLOGY TRANSFER IN GLIAX™ PLATFORM

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HES-SO master

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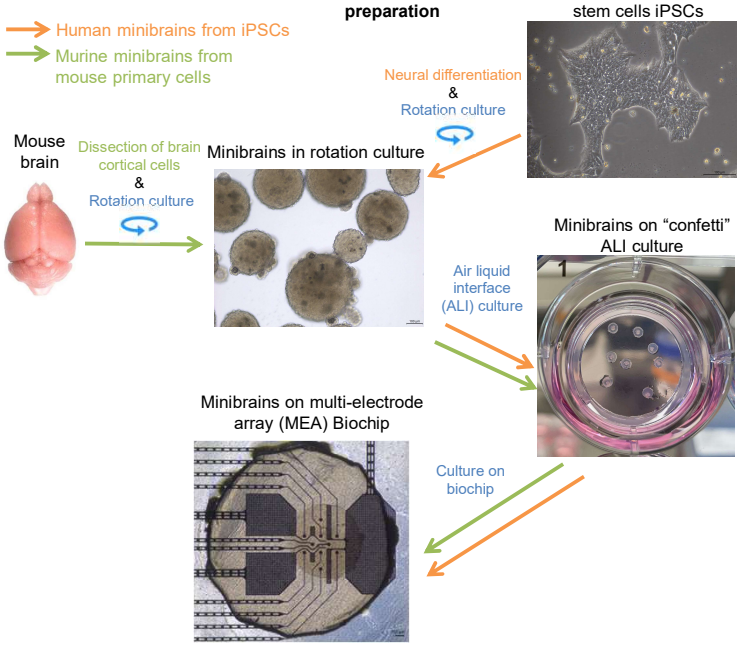
MAIN PURPOSE

Glucose transporter 1 deficiency syndrome (GLUT1 DS) is an orphan disease caused by the mutation of GLUT1 gene that leads to brain hypometabolism and epileptic seizures

- Enhance the GliaPharm GliaX™ drug discovery platform by generating mouse and human 3D minibrains with the implementation of an electrophysiological recording methodology.
- Advance research on GLUT1 DS by evaluating the effect of hypometabolism on electrophysiological activity in the GLUT1 DS mouse minibrain model.

MATERIAL AND METHODS

Minibrains generation and recording preparation

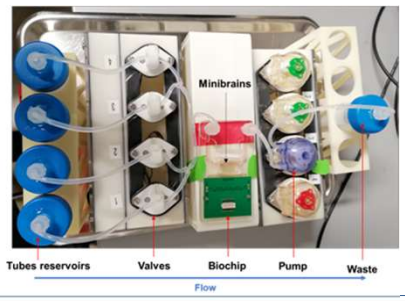


Minibrains connection to the pumping system

The biochip is connected to a pumping system with the 4 tubes reservoir

The setup (biochip + pumping system) is inside an incubator and controlled externally by a tablet and a computer.

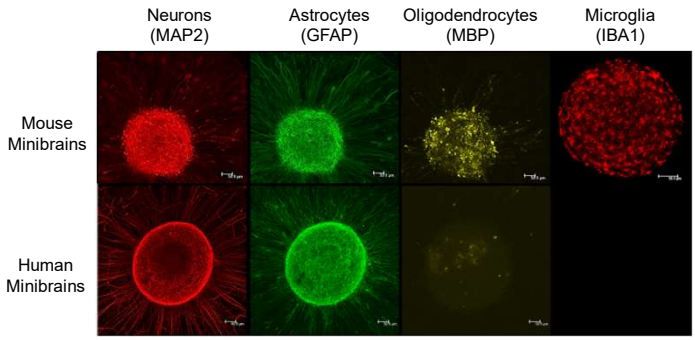
Each medium is brought into contact with minibrains. The recordings are made when the pump is turned off.
The software can extract several visual and quantitative information's from recordings



RESULTS

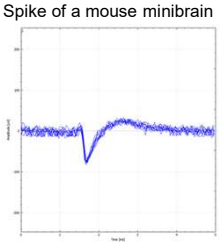
Minibrain characterization

- Mouse minibrains contain mature neurons, astrocytes, oligodendrocytes and microglia
- Human minibrains contain mature neurons, astrocytes and a few immature oligodendrocytes

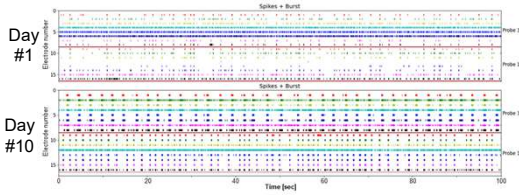


- Mouse minibrains have an electrical activity from 3 weeks of rotation culture
- Human minibrains have an electrical activity from 7 weeks of rotation culture
- Spike are action potential.
- The neuron depolarization, repolarization and hyperpolarization is visible in the spike view
- The minibrains cultured several days on biochips show a network activity (burst firing)

Spike of a mouse minibrain

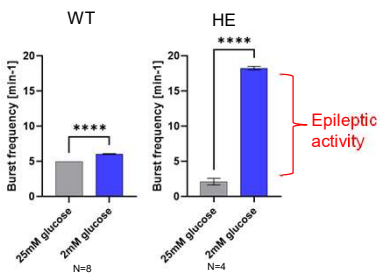


Timestamps of a mouse minibrain as a function of days on biochip

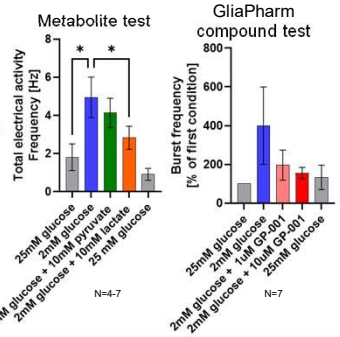


Hypometabolism effect on electrical activity

Mouse minibrains GLUT1 DS



Mouse minibrains GLUT1 DS (HE)



(* p<0.05, *** p<0.0001)

CONCLUSION

- Minibrains can be generated from primary mouse brain cells and derived from human iPSCs.
- Mouse minibrains are composed of mature neurons, astrocytes, oligodendrocytes and microglia. Human minibrains contain mature neurons, astrocytes but immature oligodendrocytes and no microglia.
- Mouse and human minibrains show a synchronised electrical activity
- The electrical activity is increased under hypometabolism conditions (2mM glucose) particularly in minibrain derived from GLUT1 DS HE mouse model, suggesting epileptic activity.
- Pyruvate, lactate and GliaPharm's molecule GP-001 restore the activity at high glucose levels
- This electrophysiological activity methodology in minibrains can be used for the development of drugs in various other neurological diseases

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