5D brain
Alzheimer disease model

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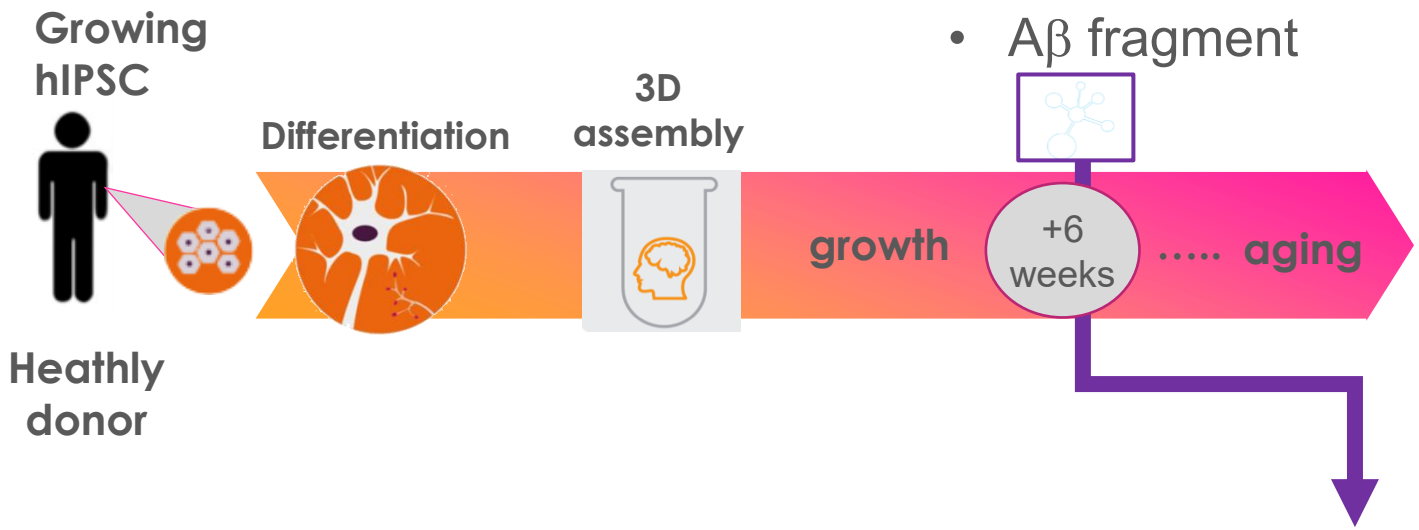
5D Brain – AD Model



Effects on neuronal activity

Visualize cell response

Transcriptomic response

Dosage of Inflammation and toxicity markers

US patents: US 9,080,148 B2 & US 10,041,936 B2

Pautot S. et al. Nature Methods (2008)
Platen M. et al., Biomacromelecules (2015)
Lück S. et al., Biomaterials (2016)

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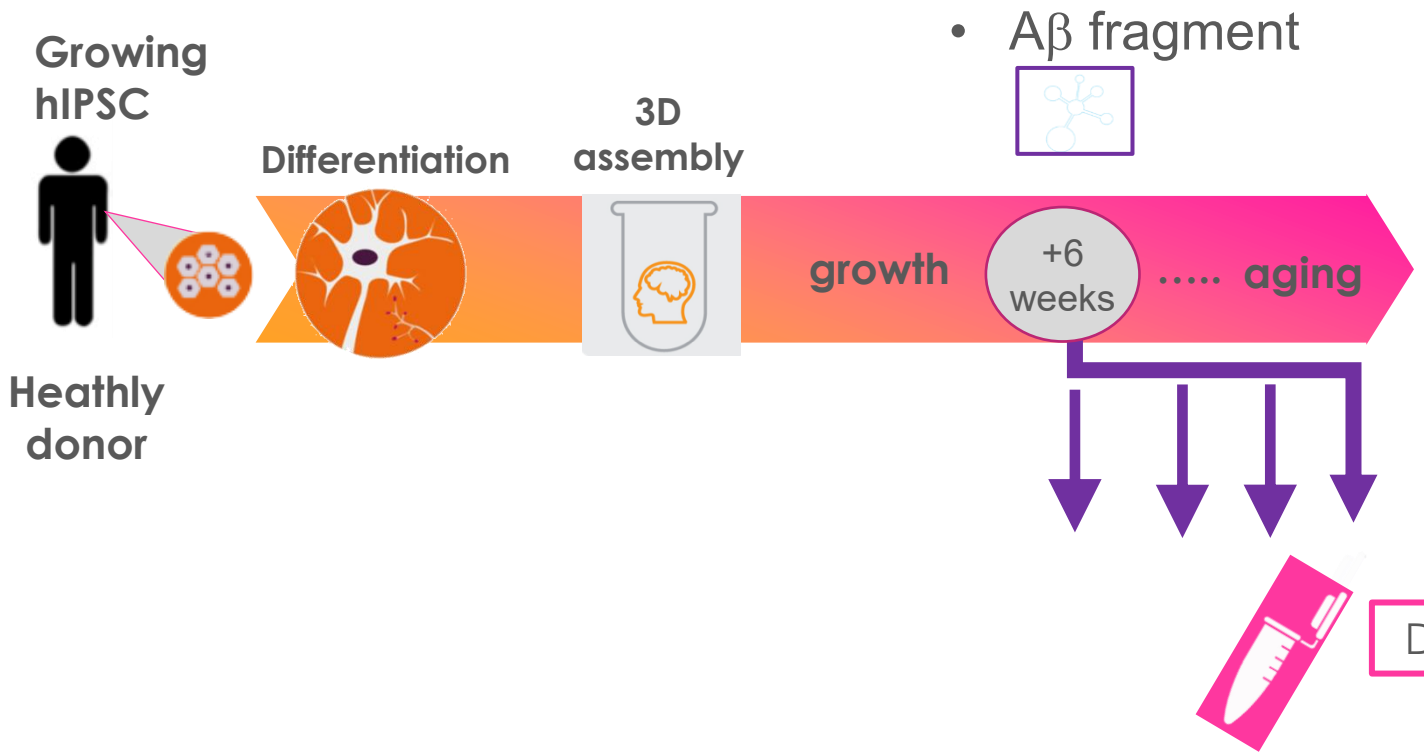
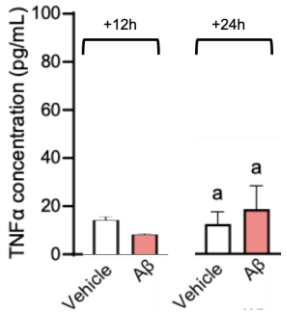
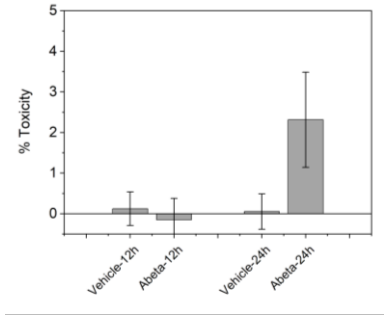
5D Brain – AD Model



Elisa detecttion



LDH



Dosage of Inflammation and toxicity markers

Aβ neuroinflammatory and neurotoxic effect start to be measurable 24h after treatment

US patents: US 9,080,148 B2 & US 10,041,936 B2

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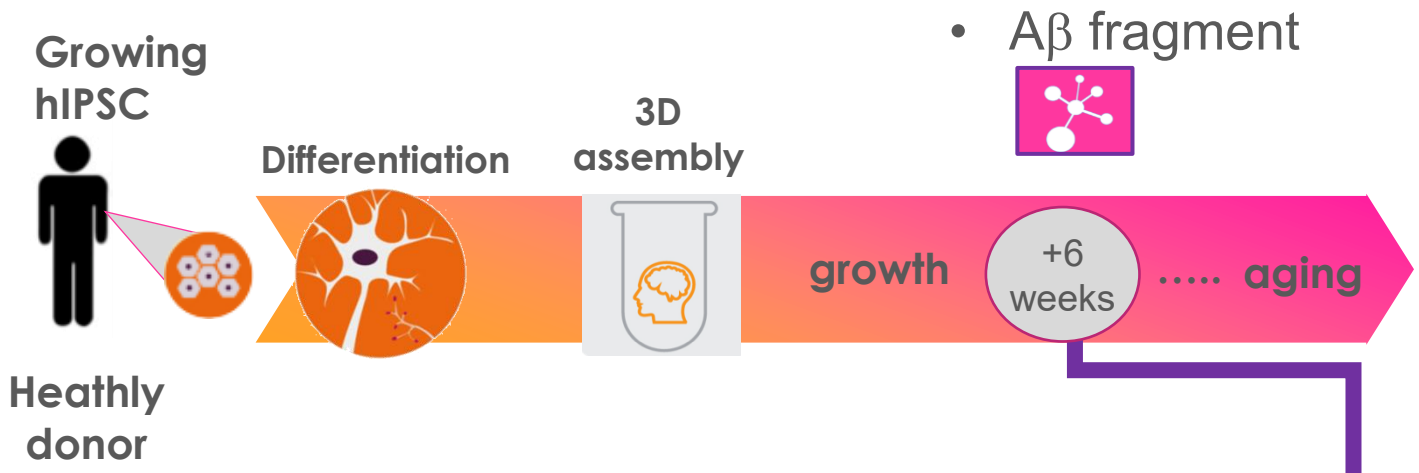
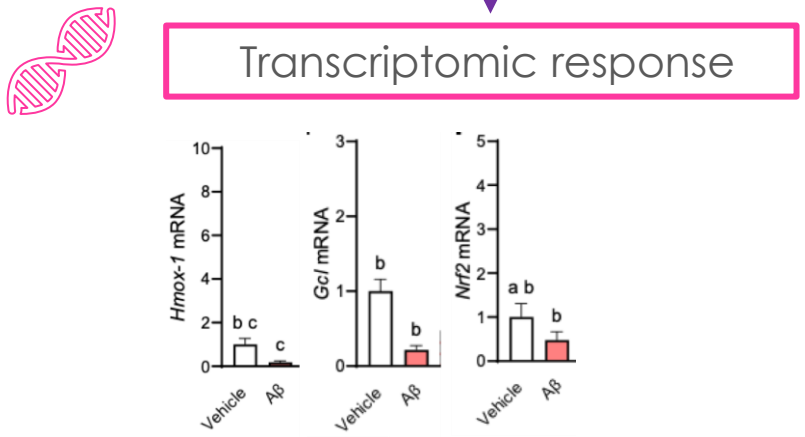
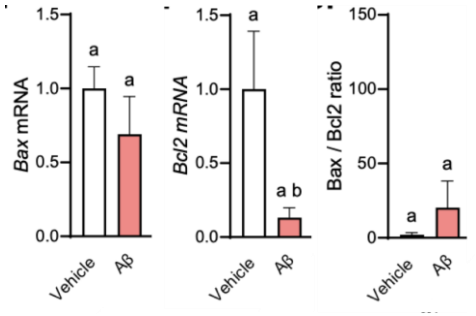
5D Brain – AD Model



- Aβ fragment



qPCR analysis



Aβ Apoptotic effect start to be measurable 24h after treatment

US patents: US 9,080,148 B2 & US 10,041,936 B2

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Lück S. et al., Biomaterials (2016)

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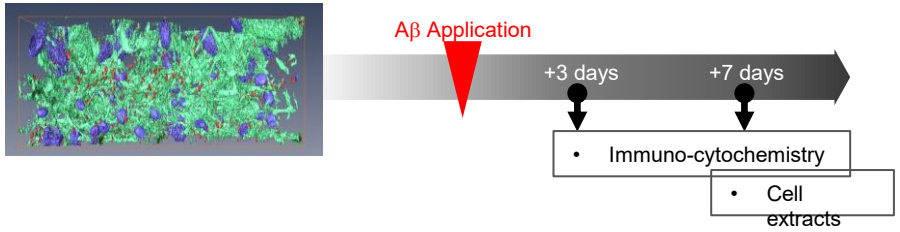
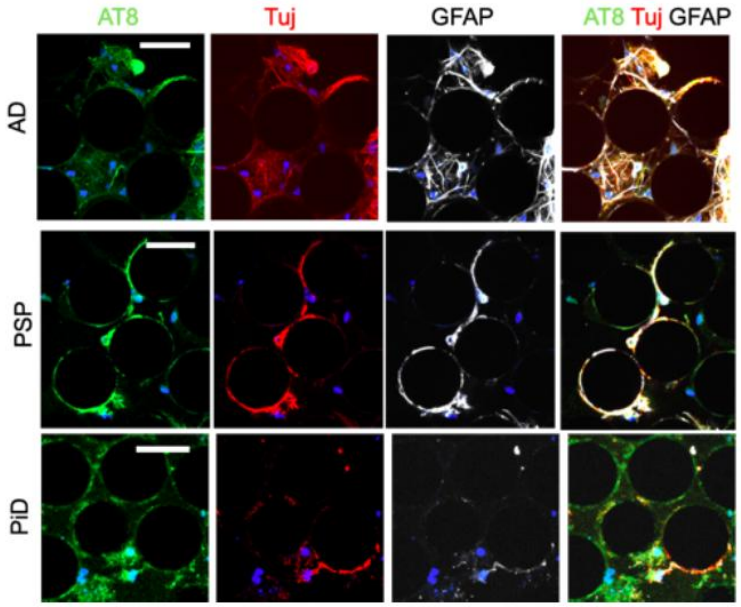
“5D-brain” recapitulates Tauopathies phenotype in vitro

- **5 weeks-old mature rat mini-brain replicate in vivo tissues** with all Tau isoforms, ECMs, density
- **Normalized sample**: 150k cells
- extract treated



Histology phenotype of Tauopathies 7 days post-treatment with “extracts”



AD phenotype: triple positive AT8/tuj/GAFP cells with astrocytic response

PSP phenotype: triple positive AT8/tuj/GAFP cells and presence of AT8 in other cells

PiD phenotype: few triple positive AT8/tuj/GAFP cells but AT8 mainly localized in other cells. Astrocyte are less abundant

Institut du Cerveau ICM

FONDATION RECHERCHE ALZHEIMER

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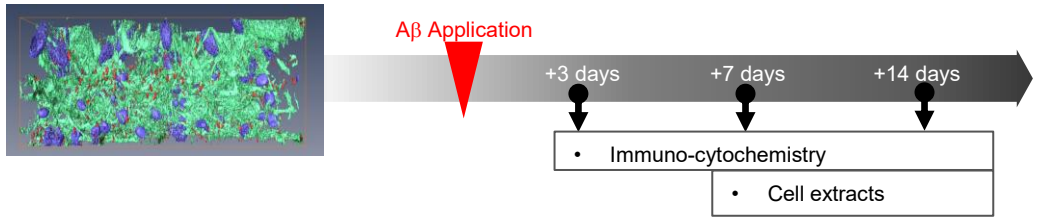
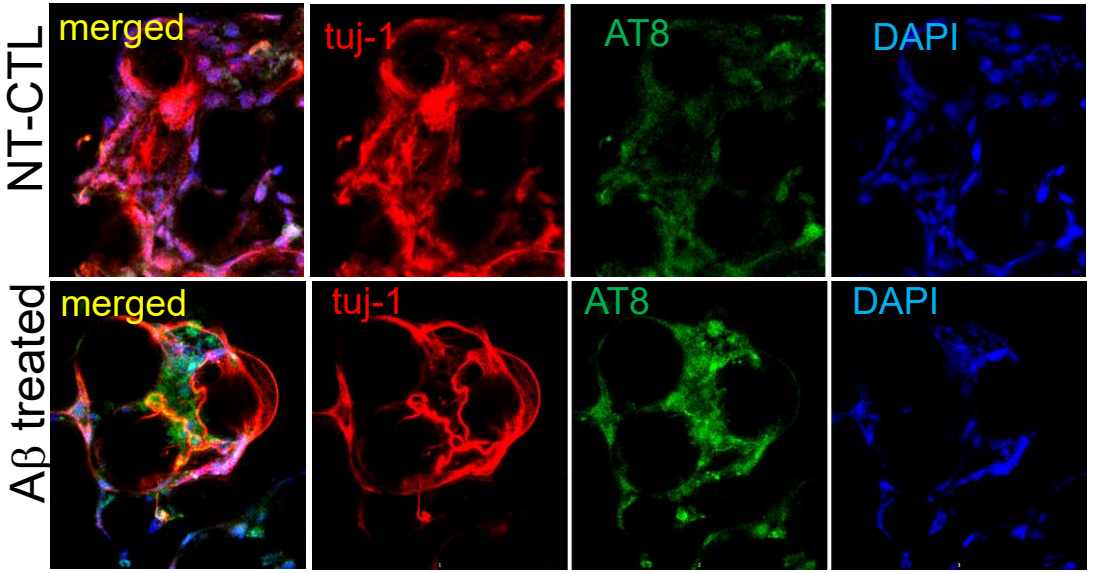
“5D-brain” recapitulates Alzheimer disease phenotype in vitro

- **6 weeks-old mature human mini-brain replicate in vivo tissues** with all Tau isoforms, ECMs, density
- **Normalized sample**: 150k cells
- Aβ 42 treated for 24h @1uM



Histology phenotype for Alzheimer didease 7 days post-treatment with Aβ42 peptide



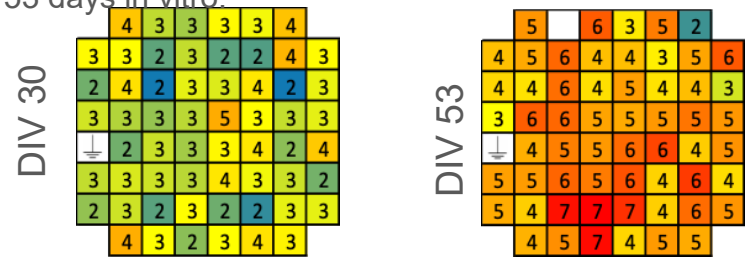
Neuronal activity differences between healthy and Alzheimer human mini-brains

Mini-brain from healthy donor human IPSCs

First the spiking activity increases stochastically before the firing rate show small bursts after div 30.

Raster plot of the spiking pattern observed for one of the 60 electrodes

Evolution of neuronal activity over time for one mini-brain.
Color coded map of the neuronal activity (blue lowest spiking frequency, red highest spiking frequency) after 30 day in vitro and after 53 days in vitro.

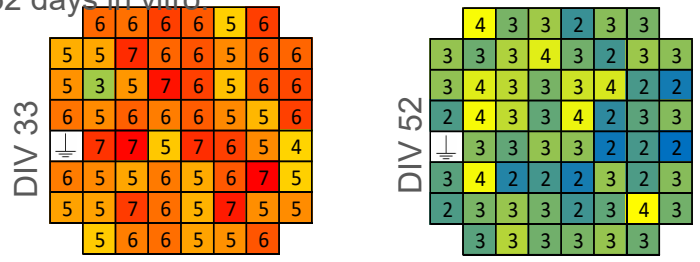


Mini-brain from Alzheimer Patient-derived human IPSCs

Patient-derived human IPSCs (Tauopathy) showed an earlier and stronger spontaneous spiking activity that receded over time when compared to normal cells. Burst activity remains unstructured.

Raster plot of the spiking pattern observed for one of the 60 electrodes

Evolution of neuronal activity over time for one mini-brain.
Color coded map of the neuronal activity (blue lowest spiking frequency, red highest spiking frequency) after 33 day in vitro and after 52 days in vitro.



Healthy neuronal networks exhibited a long-term viability with no apparent decay in neuronal activity, while diseases networks progressively declined

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360o “Compound” characterization in a model representative of the in vivo complexity

Cytotoxicity test

LDH release

Cell type targeted

Imaging

Molecular & cell signalling pathways

qPCR, WB

Neuronal activity

Electrophysiology

Spontaneous activity recording

Pharmacology

Electrophysiology

- Dose response
- Comparison with a reference compound

Customized disease model

Chemically induced or hiPSCs from patients

On request after discussion

Compound tested:

- small molecules,
- anti-bodies,
- cellular extract,
- conditioned medium,
- extracellular vesicles,
- virus (AAV, Lenti)

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