

## VirionBrain™

### Gene Therapy Testing & Virus Invasion Model

Human brain virus organoid model

### Advantages of VirionBrain™

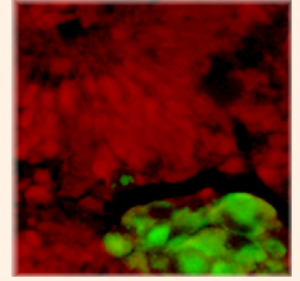
#### Gene therapy testing and virus invasion model

Short & Long term testing

Human 3-dimension tissues

Highly physiological virus - brain organoid interactions

Monitoring viral spreading and affected cell populations



VirionBrain™ is a service for testing the efficiency of gene therapy or anti-viral compounds.

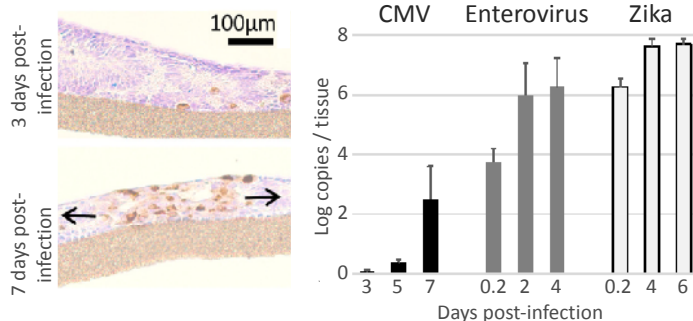
We generate 3-dimensional neural tissue derived from human pluripotent stem cells, these are inoculated with virus.

The long term compound testing, 3D human organoids and physiological neural-virus interactions makes VirionBrain™ advantageous compared to currently used 2D cellular and animal models.

VirionBrain™ represents an ideal tool for gene therapy or anti-viral compound screening and validation through efficiency testing, or deeper histological, proteomic and genomic testing for mechanistic studies.

### Virus spread among neural tissue

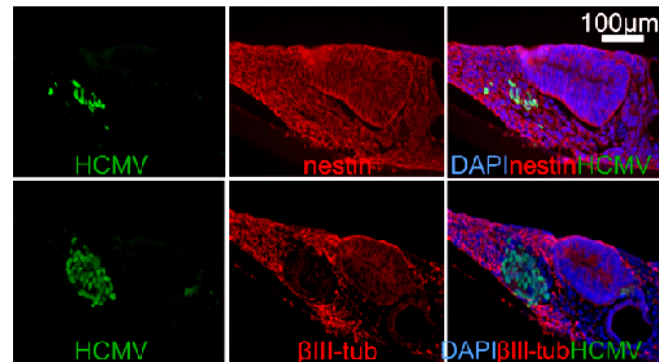
Cytomegalovirus, Enterovirus and Zika virus showed potent invasion in our human neural tissue.



**Fig. A:** Left panel shows progression of the red-stained cytomegalovirus (CMV) in the 3D neural tissue. Right panel display virus copy number following infection of the organoid by CMV (black), Enterovirus D94 (grey) and African Zika (white).

### Monitoring affected cell populations

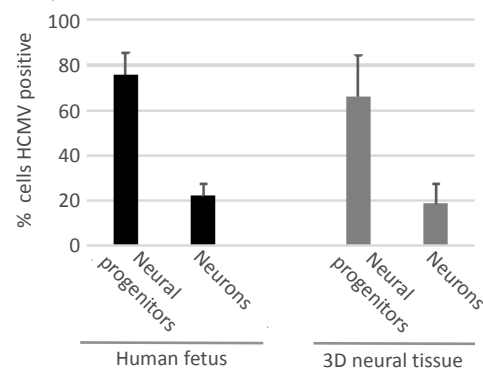
Each virus may infect different cell types. Histological analysis can be performed and shows that CMV specifically affects neural progenitors and weakly neurons.



**Fig. B:** Histological analysis neural tissue infected with CMV. human CMV-infected cells (HCMV), neural progenitors (nestin) and neurons ( $\beta$ III-tub).

### Quantification of infected cell types

CMV infection pattern remains the same between a brain from human fetus and our 3D neural tissue.



**Fig. C:** Cells infected by CMV in a human fetal brain (black) and 3D neural tissue (grey) were compared. CMV infects in equal proportion neural progenitors (nestin marker) and neurons ( $\beta$ III-tubulin marker).

## VirionBrain™ Virus Invasion Model and Gene Therapy Testing - Service specifications

3D neural tissue	Generated from human pluripotent stem cells. Composed of neurons, astrocytes, oligodendrocytes and neural progenitor cells. The latter cells keep generating newborn neurons in a dynamic process.
Production technology	Neurix's Minibrain™ & Neurosphere technology with minimum batch to batch variability guaranteed by extensive quality control of identity (rt-qPCR)
Field of application	High throughput screening and lead treatment validation
Assay window	Short term (7 days) to long term (one month)
Readouts	<ul style="list-style-type: none"><li>- Virus copy number and/or reporter signal</li><li>- 3D reconstruction of infected area and volume quantification</li><li>- Quantification of infected cell number</li><li>- Analysis of infected cell types</li></ul>

### Our publications

Cosset, É. et al. Human three-dimensional engineered neural tissue reveals cellular and molecular events following cytomegalovirus infection. *Biomaterials* 53, 296–308 (2015).

Royston, L. et al. Viral chimeras decrypt the role of enterovirus capsid proteins in viral tropism, acid sensitivity and optimal growth temperature. *PLoS Pathog.* 14, e1006962 (2018).

Cagno, V. et al. Growth of Zika virus in human reconstituted respiratory, intestinal, vaginal and neural tissues. *Clin. Microbiol. Infect. Off. Publ. Eur. Soc. Clin. Microbiol. Infect. Dis.* 25, 1042.e1-1042.e4 (2019).

### Validated assay and protocols

VirionBrain™ service is integrated into a variety of validated assay that can be implemented in drug development for safety and efficacy evaluation of novel compounds:

- Cell viability assays
- Histological analysis (IHC & IF)
- Cell sorting and cell population analysis (FACS)
- Genomic analysis
- Proteomic analysis

### Get in contact with us

Neurix offers customized services for neural applications. These include gene / cell / polymer therapy testing, brain tumor drug testing, neurodegenerative diseases modeling and neurotoxicity assays. Our experienced scientists are happy to work with you in order to understand your needs and meet your objectives.

#### Contact us

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Next generation neuro-engineering