CESAME Institute, Brain, Mind and Health Institute, is located in Lyon, France, and led by Neurodis Foundation. The French Government with the “Investment for Future” program supports the Institute.

CESAME Institute aims at developing research and therapies in neurology and neuropsychiatry for the benefit of patients. The Institute works to bridge brain and mind health creating synergy between: neuroscience, psychiatry and social science and humanities. Its actions come in the following research themes:

- Global understanding of brain functioning: neural development, optogenetics…
- Brain and mind diseases understanding: neural network dysfunctions, degeneration, cognitive disorders, and abnormal brain excitability in pain, epilepsy and mental diseases…
- Therapies enhancements, for example: brain repair, remediation, neuroprotection, readaptation, new technological solutions using brain-computer interfaces…

CESAME Institute gathers five high technological facilities:

- **Cell engineering and gene transfer facility** aims at improving stem cell-based therapeutic strategies of neurodegenerative diseases and implementing gene transfer for restoring vision in non human primates suffering from retinal defects, and for progressing in understanding the mechanisms of brain development and plasticity.
- **Blood-brain interface facility** develops in vitro and ex vivo models for understanding blood-brain interface functions, which is a key issue to improve the bioavailability of Central Nervous System (CNS) therapeutic agents to validate their therapeutic targets and to decrease the side effects of drugs on CNS.
- **Human brain signal facility** permits to record and analyse intracerebral EEG (EEG) in epileptic patients candidates to epilepsy surgery thus offering a unique opportunity to record neural activity throughout the human brain with optimal time and anatomical resolution and permitting a real-time monitoring of interactions between brain and environment.
- **Neuro-immersion facility** develops innovative strategies for rehabilitation of neurological, cognitive and psychiatric disorders via the coupling of next generation immersive virtual reality and neurostimulation systems and state-of-art neuroscience tools.
- **Neuro-imaging facility** develops new radio-ligands and image analysis software for Positon Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) for brain studies using the first fully simultaneous 3Tesla MRI-PET installed in France.

CESAME Institute is open to partnerships for collaborative research and technological developments in:

- Cell therapies, Brain protection, Deep brain and transcranial, Neurostimulation, Functional rehabilitation, Cognitive remediation…
- Virtual reality, Real-time signal processing, software, electrodes (micro electrodes, dry electrodes, etc)...
- Radiotracers, neuroimaging, CNS drug targeting...

4/ references

- François Mauguière (CESAME Leader, Neurodis Foundation Director, Professor of Neurology)

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Cell engineering and gene transfer Platform

This high technological platform is located in the Stem cell and Brain Research Institute in Lyon.

1/ medical & scientific objectives

The platform aims at:

- Improving therapeutic strategies based on stem cells in neurodegenerative diseases,
- Implementing gene transfer for restoring vision in non human primate suffering from retinal defect and for progressing in understanding the brain mechanisms.

2/ presentation

This equipment aims at developing the next generation of human embryonic stem cell (ESCs) and induced pluripotent stem cell (iPSCs). A second part of the facility will develop optogenetic treatment for blindness and neurological disorders. This platform provides:

- A dedicated laboratory with equipment for stem cell development
- A dedicated laboratory for optogenetics on non human primate

The facility has been completed to:

- Develop the next generation of human ESCs and iPSCs with improved self-renewal properties and increased genetic stability,
- Produce somatic and germline chimaeras with pluripotent stem cells in the macaque monkey,
- Develop novel strategies for restoring vision in a non human primate model of blindness,
- Develop novel method and applications for viral vectors in non human primate pathophysiological models of neurological and behavioural disorders

3/ partnerships fields

Partnerships in developing ESCs, iPSCs and optogenetics methods

4/ references

- C. Dehay (Research Director, Stem cells: cortical development and repair team)
- P. Savatier (Research Director, Embryonic Stem Cells: Self-renewal and Early Commitment team) for stem cells development
- J-R. Duhamel (Research Director, Perception and Movement Neurophysiology) in optogenetics

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Human Brain Signal Platform

This high technological platform is open in the epilepsy department, (directed by Prof. Philippe Ryvlin) of the Lyon neurological hospital. Lyon is one of the most advanced centre for investigating the human brain at work.

1/ presentation

Intracerebral EEG (iEEG) recordings in epileptic patients remain the only opportunity to record neural activity throughout the human brain with excellent time and anatomical precision.

This equipment focuses on the human brain signal recordings and interpretations. This platform provide:

• A dedicated iEEG research laboratory with optimal stimulation and recording environment: faraday cage, minimised 50-Hz related artefacts, multimodal sensory and cognitive stimulation platform, eye-tracking system, and high capacity storage system,
• An improved iEEG headbox recorder to allow high frequency (2048 Hz), high throughput (256 channels) and ambulatory recordings.
• A Brain TV system

Equipment:

• Three 256 channels iEEG equipment
• One 128 channels iEEG equipment
• Three on line iEEG signal analysis system (Brain TV)
• One cognitive stimulation system
• One micro-electrode recording system (operational in 2014)

2/ medical & scientific objectives

The platform aims at:

• Understanding the basic issues underlying the fields of cognition and epilepsy,
• Developing micro-electrodes for intracerebral recording in human Brain,
• Developing soft and hard ware system using SEEG recording and stimulation.

3/ partnerships fields

Public research teams: all iEEG protocols dedicated to functional Brain studies
Private partnerships: material support and development: micro-electrode, software linked with iEEG

4/ references

An advisory board organises this platform in the patients’ respect based on a charter of use* (reference to a web site). This board is composed by:

• P. Ryvlin: Neurologist, Epileptologist, Co-director of the team TIGER, CRNL,
• J. Isnard: Neurologist, Epileptologist, Epilepsy Monitoring unit and epilepsy surgery program, team « Central integration of pain in Humans », CRNL,
• O. Bertrand: Research Director, Director of the team « Brain dynamics and cognition » and of the CRNL,
• JP. Lachaux: Research Director, leader of the iEEG research program within team « Brain dynamics and cognition », CRNL.

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Neuro-immersion Platform

1/ medical & scientific objectives
Neuro-immersion is devoted to the study of the brain and the treatment of neurological and psychiatric deficits via the coupling of next-generation immersive virtual reality systems and state-of-art neuroscience tools.
Neuro-immersion allows the full control of multisensory inputs and motor outputs during either brain activity recording or brain stimulation.

2/ presentation
Neuro-immersion: the ever-wanted ideal laboratory that enables to study the basic functioning of physiological and cognitive brain processes of human perception and action, equipped with:

- **Multisensory virtual reality**: wall and head-mounted displays
- **Brain-computer interfaces**: wireless high-density EEG
- **Physiological recordings**: Transcranial Magnetic Stimulation (TMS)-compatible EEG, full-body motion tracking (including face and eyes), haptic robots
- **Neurostimulation**: TMS, transcranial DC stimulation (tDCS), frameless stereotaxic neuro-navigation

3/ services and partnerships
The platform offers engineer-assisted access for research, rehabilitation and industrial applications for:
- Understanding normal and pathological brain functions,
- Developing virtual reality and brain-computer interface based procedures for cognitive enhancement and rehabilitation,
- Developing and testing new technologies and industrial prototypes for health care (patient-tailored treatments), simulation and entertainment industry (e.g., serious games).

4/ references
This high-tech platform is located in the CRNL laboratory (INSERM building) next to the neurological hospital in Lyon.

- Luis Garcia-Larrea, Director of Research INSERM, Head NeuroPain lab at the Centre for Neurosciences of Lyon

- Jacques Luauté, head of department of neurological rehabilitation (Hospices civils de Lyon), Prof. of Physical medicine and rehabilitation (Claude Bernard Lyon 1 University)

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Neuroimaging Platform

This technological platform is based at the CERMEP, an in-vivo multimodal imaging centre dedicated to research, located next to Lyon’s Neurological Hospital.

1/ presentation
The CERMEP offers access to the most advanced in vivo imaging techniques in humans, small animals and non-human primates:

- Positron Emission Tomography, PET (coupled with Computed Tomography: PET/CT)
- Magnetic Resonance Imaging, MRI
- Magneto-Encephalography, MEG
- Scanner (micro-CT)

In 2014, enabled by major grants (“equipment of excellence” Equipex LJL and the Brain and Mental Health Institute CESAME), the CERMEP will open access to the first fully simultaneous hybrid 3T-MRI-PET in France, a breakthrough technology that allows the acquisition of both modalities at the same time for the same part of the body. The CERMEP has a cyclotron, hot cells and a radiochemistry department and can thus produce radiotracers for research and clinical use.

2/ medical & scientific objectives
The neuroimaging platform engages in:

- clinical and preclinical research on ischemic stroke, epilepsy, Alzheimer’s and Parkinson’s disease, neural transplantation, psychiatry and neuropathophysiological mechanisms,
- medical care via Lyon’s Neurological Hospital,
- training and education.

3/ services and partnerships
The platform is open to partnerships including:

- using the imaging facilities: PET, MRI, Scanner/PET-CT, 3T-MRI-PET,
- drug development, developing diagnostics, follow-up care, clinical trials,
- radiochemistry, contrast agent and tracer development,
- data processing and image analysis

4/ references

- A. Hammers, Professor of Functional Neuroimaging, Chair of Excellence, Neurodis Foundation
- N. Costes, Research engineer, Head of PET data analysis, CERMEP
- Olivier Bertrand, Research Director, director of the Lyon Neuroscience Research Centre (CRNL), and head of the DYCOG team

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Blood-Brain Interfaces
Exploratory Platform

Understanding blood-brain interface functions is a key issue to improve CNS drug bioavailability, decrease the side-effects of other non CNS drugs and validate therapeutic targets in these interfaces.

1/ medical and scientific objectives

BIP provides services to:

- study the functions of blood-brain barriers and evaluate neuroprotective strategies restoring barrier efficacy
- evaluate the cerebral bioavailability of drugs and investigate the migration of immune cells and pathogens into the brain

2/ expertise and bioanalytical tools

Ex vivo models of blood-brain interfaces
- for molecular studies (transcripts, proteins)

In vitro model of the blood-CSF barrier
- for functional studies (transport, metabolism, secretion)

Analytical expertise
- HPLC - radiodetection - spectrophotometry - immunocytoLOGY - flux cytometry - ELISA - RNA isolation - protein extraction.

3/ services and partnerships

Drug transport
- Permeability coefficient-based screening
  (small and large drug molecules, contrast agents)
- Identification of transport mechanism
  (diffusional, facilitated, active)

Microorganism invasion, immune cell migration
- Invasion/migration index

Neuroprotective strategies at the blood-brain interfaces
- Anti-oxidant agents
- Anti-inflammatory agents

4/ research & development

- In vitro physiological and pathological models of blood-brain interfaces
- In vivo blood-brain permeability assessment in neonate

5/ references

- Jean-François Ghersi-Egea, Pharmacist, Research Director, Fluids and barrier of the CNS Program, Oncflam Team, Lyon Neuroscience Research Center.
- Nathalie Strazielle, Pharmacist, Cellular and Molecular Biologist, Brain-i

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