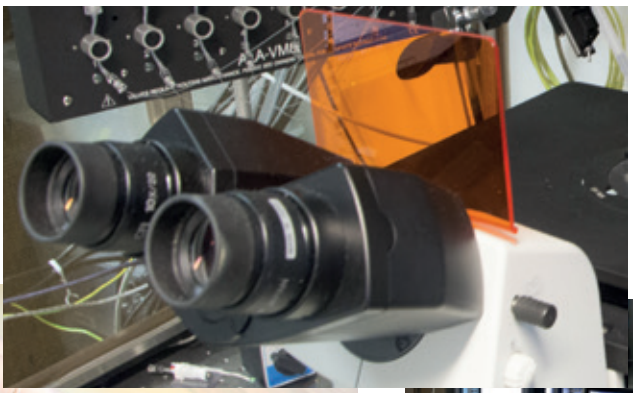
Paris Brain Institute
ICM
Search, find, cure, for you, with you

Research teams and core facilities



“The Paris Brain institute has become a leading neuroscience institute and major breakthroughs are and will be made there on the brain and its pathologies. To go further, we must continue to recruit the most talented people to nurture a dynamic ecosystem. Focus on the development of new technologies, have the most powerful tools, because they are the ones that allow us to push back the boundaries. We also need to approach questions related to the functioning and pathologies of the nervous system from different angles; for this we need specialists from various disciplines. Our ability to get researchers and clinicians to work together at the interface of their discipline brings new concepts to life.”

Prof Alexis Brice,
Executive Director of the Paris Brain Institute

“The ambition of the Paris Brain Institute to become the world’s leading brain research institute depends on two main pillars that we are currently building. First, encouraging research that questions dogma, takes risks, research that is allowed to fail and try once more, and recruiting and rewarding people who dare to challenge existing models. Second, creating an open environment in which people who take an interest in the brain as a whole, from molecules to networks, cognition and disease, work together to create a virtuous circle of knowledge from patients’ bedsides to a laboratory environment.”

Prof Bassem Hassan,
Scientific Director of the Paris Brain Institute

About Paris Brain Institute

The Paris Brain Institute is an international center of scientific excellence, located on the site of the Pitié-Salpêtrière University Hospital in Paris, an exceptional multidisciplinary center, ranging from basic to clinical research and dedicated to the central nervous system. An association between the public and private sectors united by a unique entrepreneurial spirit. The Paris Brain Institute is an institute “at the service of knowledge and patients”, which brings together, on the same site, patients, clinicians and researchers with a common aim: make rapid advances in research and accelerate the discovery of innovative treatments.

The institute hosts about 700 researchers, faculty members, clinicians, engineers, technicians, post-doctoral fellows, students and administrative staff, working in 25 research teams. The latter have access to 10 cutting-edge core facilities.
The scientific missions and priorities meet the challenges of the next decade: understanding how the brain works, preventing and curing neurological and psychiatric diseases. The Paris Brain Institute succeeds in bringing together fundamental neuroscience research and world-class clinical research expertise in one place.

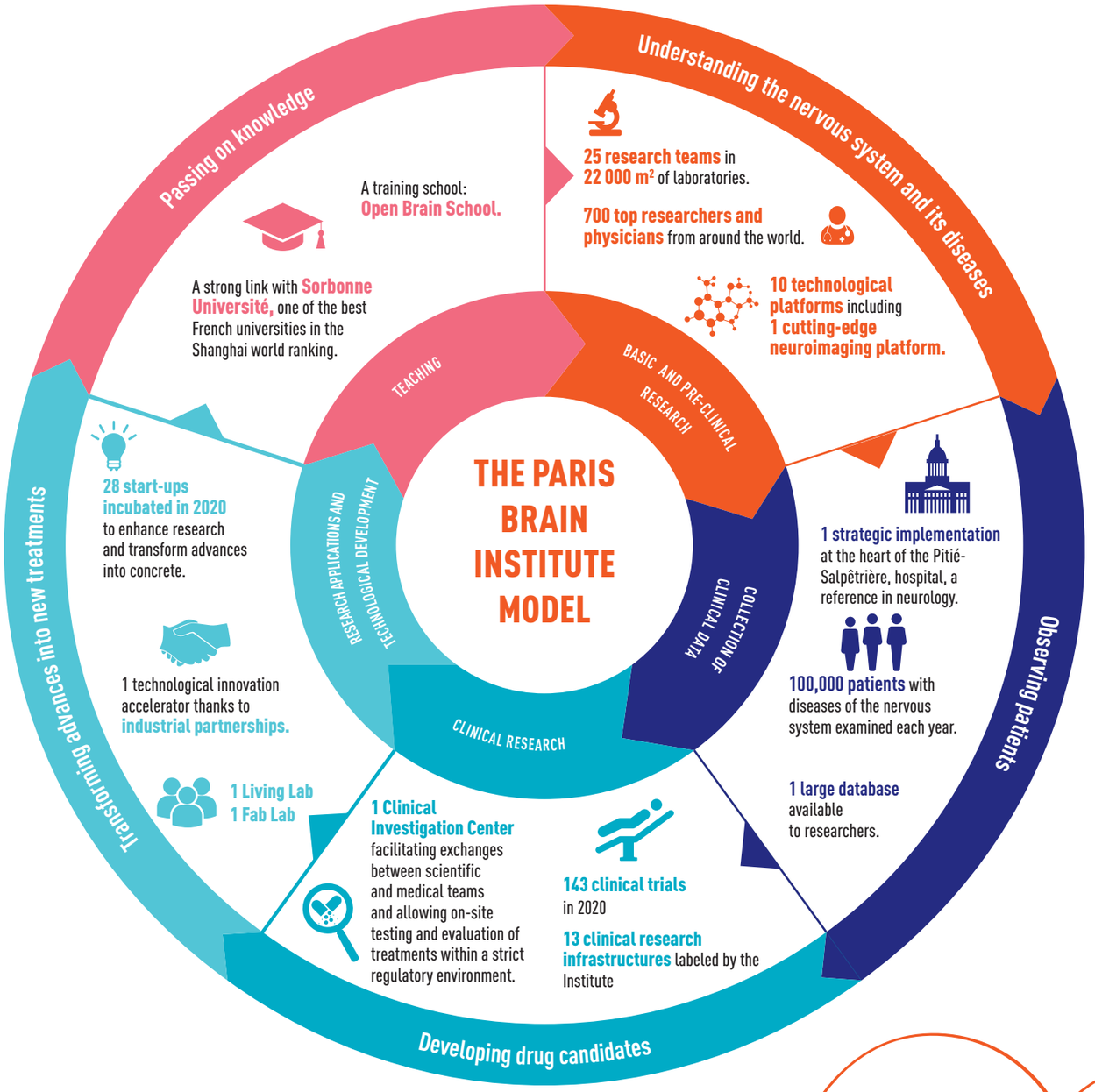
Faced with the challenges of research on the brain and its pathologies, the Institute’s objectives are:
- Develop cutting-edge basic research in neuroscience;
- Be leader in the prevention and treatment of nervous system diseases;
- Be at the forefront of technological innovation and its medical applications.

TO DO SO, THE INSTITUTE:

- Attracts the best international researchers;
- Develops cutting-edge core facilities;
- Promotes entrepreneurial research;
- Creates a unique, attractive, international and open-to-society training venue.

Our ambitious strategy aims to include a multidisciplinary approach. Paris Brain Institute is organized in five major fields: molecular and cellular, neurophysiology, cognition, clinical and translational, and computational neurosciences. High flexibility between these fields is a cornerstone of our scientific and medical development. Many in-house actions, including the Big Brain Theory program, help accelerate interactions between research areas. Our scientific and medical strategy also relies on strengthening the already strong relationship between research teams, core facilities, and clinical research with our own clinical research infrastructure network.

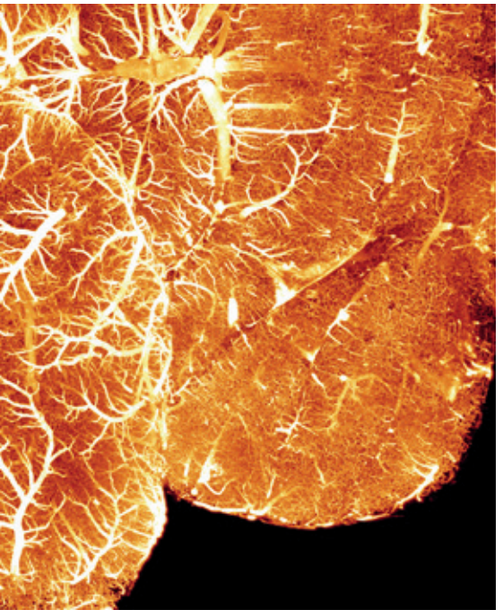
A unique performing ecosystem



Summary

Our research domains

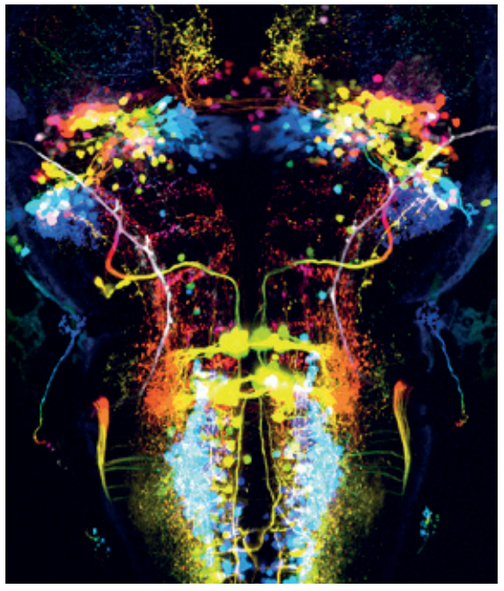
The Paris Brain Institute is organized into 5 research domains: molecular and cellular, neurophysiology, cognition, clinical and translational. The great flexibility between these fields is a cornerstone of our scientific and medical growth.



Cellular and molecular domain

The teams of this domain use largely molecular and cellular approaches to understand the genetic, molecular and cellular basis of central nervous system development, function and disease. In more details, the major aims are:

- Unravel how the central nervous system generates cellular diversity and how these cells interconnect and interact to produce the brain and ensure its health throughout life, and how different pathophysiological mechanisms impact various brain areas at different ages.
- Dissect the impact of genetic mutations using animal and human healthy and disease models to decipher the cellular and molecular mechanisms that take place under normal and pathological conditions including aging, neurodegenerative diseases, multiple sclerosis, epilepsy, cortical malformations and brain tumors.
- Exploit molecular and cellular based approaches to explore and develop new targeted therapies to correct damaged brain networks.

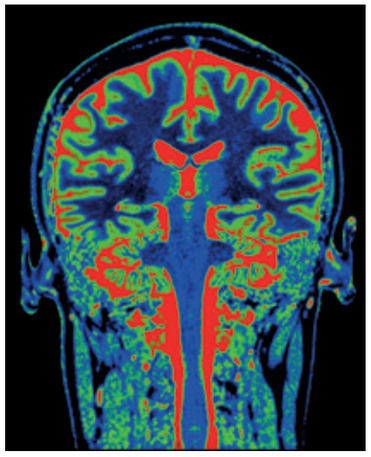


Integrative Neurophysiology domain

The teams in this field aim to determine how neural activity at different scales underlies behavior in healthy organisms, and to decipher the mechanisms by which neural activity becomes dysfunctional in neurological disorders such as epilepsy, Parkinson's disease (PD) and obsessive-compulsive disorder (OCD).
The approaches shared by the Institute's different teams include the use of multiscale imaging and electrophysiological approaches as well as cutting-edge computational modeling in zebrafish, rodents, non-human primates and humans to study sensory processing and motor control at the synaptic, microcircuit and whole-brain network levels.

Cognitive neuroscience domain

The teams in this field aim at a better understanding of how neural networks on the whole brain scale underpin cognitive, affective, contextual, and motivational processes, and through it translate into behavior. In more detail, the teams combine behavioral testing and clinical assessments with neurophysiology and brain stimulation methods (EEG, TMS, MEG), functional and structural MRI, and mathematical modeling in human and animal models. They investigate how the neural mechanisms of cognitive, affective, contextual, and motivational determinants of behavior are affected by mood disorders, apathy, dementia, consciousness disorders, tumor and vascular lesions causing aphasia, neglect and dysexecutive syndrome.



Clinical and translational neuroscience domain

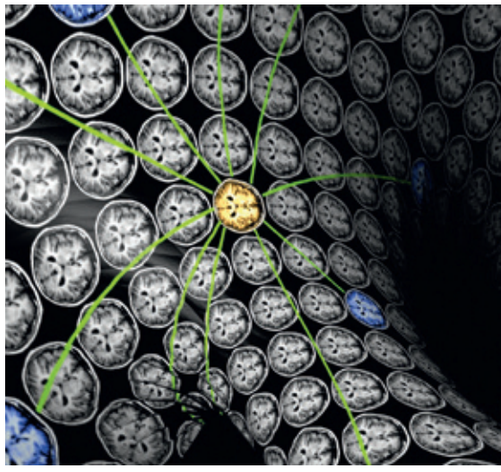
The aim of clinical and translational research is to enable the development of predictive or progression markers and treatments for neurological and psychiatric diseases, from identification in simple laboratory modelling to clinical trials at the Clinical Investigation Center, iCRIN teams, in relationship with clinical teams of the DMU Neurosciences clinical units. The teams aim at:

- Providing innovative tools for clinical assessments of symptoms of neurological and psychiatric disease, diagnosis or progression biomarkers, and new therapeutics for patients. The domain embraces translational research from bench to bedside and vice versa.
- Based on the use of human diseases as models to better understand brain physiology or pathophysiology, the teams also nourish basic research of the Institute by disease modelling, brain mapping, biological samples and cell lines with their counterpart in animal models of neurological and psychiatric diseases.
- Developing well-phenotype and biologically characterized (stratified) cohorts of patients with specific neurologic and psychiatric diseases, including rare diseases, markers and modulation techniques of brain activity, and of innovative molecular imaging tools aiming at quantifying neurodegenerative mechanisms.
- Developing innovative therapeutics and molecular screening strategies (biotherapy systems).

Computational modelling in neuroscience domain

The major aims of the teams focused on this line of research are:

- Mathematical modeling of multi-scale brain mechanisms ranging from molecular/cellular processes, large-scale integrated structure and dynamics (eg, anatomo-functional interactions), to cognition and behavior.
- Development of data-mining methods including network science, signal/image processing, machine learning and AI, for data interpretation and analysis and for better diagnosis and prognosis in neurological and psychiatric diseases;
- Development of scientific software and engineering tools for neuroscience applications.



RE-SEARCH TEAMS

Cellular physiology of cortical microcircuits

Alberto Bacci's team investigates the microcircuits of the cerebral cortex. In particular, the team is interested in the synaptic and plasticity properties of synapses originating from a highly diverse population of neurons forming stereotyped cortical circuits. To this aim, the lab uses a battery of ex vivo and in vivo neurophysiological approaches.

Four major projects:
- The identification of layer- and interneuron-specific forms of plasticity, their molecular mechanisms and functional roles;
- The functional role of an elusive inhibitory interneuron subtype during sensory processing;
- The search of the cellular and molecular determinants of dendritic inhibitory synapses;
- The identification of the physiological role of perineuronal nets (PNNs) and the synaptic mechanism by which they restrict cortical plasticity.

MAJOR PUBLICATIONS

1. Zorrilla de San Martin J, Donato C, Peixoto J, Aguirre A, Choudhary V, De Stasi AM, Lourenço J, Potier MC, Bacci A (2020) Alterations of specific cortical GABAergic circuits underlie abnormal network activity in a mouse model of Down syndrome eLife 2020;9:e58731
2. Lourenço J, De Stasi AM, Deleuze C, Bigot M, Pazienti A, Aguirre A, Giugliano M, Ostojic S, Bacci A (2020) Modulation of coordinated activity across cortical layers by plasticity of inhibitory synapses onto layer 5 pyramidal neurons Cell Reports, 30(3):630-641.e5.
3. Deleuze C, Bhumbra GS, Pazienti A, Lourenço J, Mailhes, C, Aguirre A, Beato M*, Bacci A* (2019) Strong preference for autaptic self-connectivity of neocortical PV interneurons facilitates their tuning to γ-oscillations PLoS Biol. 2019 Sep 4;17(9):e3000419 (*Co-senior authors)
4. Faini G., Aguirre A., Landi S., Lamers D., Pizzorusso T., Ratto G.M., Deleuze C., Bacci A. (2018) Perineuronal nets control visual input via thalamic recruitment of cortical PV interneurons eLife 7:e41520.
5. Lourenço J., Pacioni S., Rebola N., van Woerden G.M., Marinelli S., DiGregorio D., Bacci A. (2014) Non associative potentiation of perisomatic inhibition alters the temporal coding of neocortical layer 5 pyramidal neurons PLoS Biology 12:e1001903.

MAIN DOMAIN

NEUROPHYSIOLOGY

Alberto BACCI, PhD
Neurophysiology

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PRINCIPAL INVESTIGATORS

- **Joana LOURENÇO,** PhD
  Role of CB1/CCK interneurons and GABAergic plasticity during sensory processing. In vivo and in vitro 2P imaging, electrophysiology
- **Laurence CATHALA**, PhD
  PNNs and PV cells, synaptic biophysics, 2P imaging electrophysiology

Genetics and physiopathology of epilepsy

Stéphanie Baulac & Eric Leguern's team aims to unravel the molecular and cellular mechanisms underlying focal epilepsies with malformations of the cortical development, Developmental & Epileptic Encephalopathies and genetic generalized epilepsies.

Main goals are:
- To understand how mutations in the mTOR pathway genes contribute to epileptogenesis and seizures using diverse disease models (patient iPSCS, human brain spheroids, in utero electroporation)
- To assess the role of brain somatic mutations in human epileptic tissues by means of deep NGS and single cell OMICS;
- To identify susceptibility genes contributing to genetic generalized epilepsies by means of NGS.

MAJOR PUBLICATIONS

1. Baldassari S, Ribierre T, Marsan E, Adle-Biassette H, Ferrand-Sorbets S, Bulteau C, Dorison N, Fohlen M, Polivka M, Weckhuysen S, Dorfmüller G, Chipaux M, and Baulac S (2019). Dissecting the genetic basis of focal cortical dysplasia: a large cohort study. Acta Neuropathologica, Dec;138(6):885-900

2. Ribierre T., Deleuze C., Bacq A., Baldassari S., Marsan E., Chipaux M., Muraca G., Roussel D., Navarro V., Leguern E., Miles R. and Baulac S. (2018). Second-hit mosaic mutation in mTORC1 repressor DEPDC5 causes focal cortical dysplasia-associated epilepsy. Journal of Clinical Investigation, Jun 1;128(6):2452-2458. Highlighted by the editor in the "JCI This Month".

3. Baulac S., Ishida S., Marsan E., Miquel C., Biraben A., Nguyen D.K., Nordli D., Cossette P., Nguyen S., Lambrecq V., Vlaicu M., Daniau M., Bielle F., Andermann E., Andermann F., Leguern E., Chassoux F., Picard F. (2015). Familial focal epilepsy with focal cortical dysplasia due to DEPDC5 mutations. Ann Neurol. Apr;77(4):675-83. Highlighted as Best Advances of 2015 by the Neurology Today Editorial Advisory Board.

4. Boillot M., Huneau C., Marsan E., Lehongre K., Navarro V., Ishida S., Dufresnois B., Ozkaynak E., Garrigue J., Miles R., Martin B., Leguern E., Anderson M. and Baulac S. (2014). Glutamatergic neuron-targeted loss of Lgi1-epilepsy gene results in seizures. Brain, Nov;137(Pt 11):2984-96.

5. Nava C., Dalle C., Rastetter A., Striano P., de Kovel C.G., Nabbout R., Cancès C., Ville D., Brilstra E.H., Gobbi G., Raffo E., Bouteiller D., Marie Y., Trouillard O., Robbiano A., Keren B., Agher D., Roze E., Lesage S., Nicolas A., Brice A., Baulac M., Vogt C., El Hajj N., Schneider E., Suls A., Weckhuysen S., Gormley P., Lehesjoki A.E., De Jonghe P., Helbig I., Baulac S., Zara F., Koeleman B.P.; EuroEPINOMICS RES Consortium, Haaf T., Leguern E., Depienne C (2014). De novo mutations in HCN1 cause early infantile epileptic encephalopathy. Nat Genet. Jun;46(6):640-5.

6. Ishida S., Picard F, Rudolf G., Noé E., Achaz G., Thomas P., Genton P., Mundwiller E., Wolff M., Marescaux C., Miles R., Baulac M., Hirsch E., Leguern E. and Baulac S. (2013). Mutations of DEPDC5 cause autosomal dominant focal epilepsies. Nat Genet, Apr 26;45(5):552-5. Highlighted in Nature reviews.

MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCE

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Stéphanie BAULAC, PhD
Genetic focal epilepsies & Focal Cortical Dysplasia (FCD); Scientific manager of iGenSeq core facility

Eric LEGUERN, MD, PhD
Genetic generalized epilepsies

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PRINCIPAL INVESTIGATOR

- **Christel DEPIENNE,** PhD (Prof of Human Genetics at University Hospital Essen) Developmental & Epileptic Encephalopathies

AFFILIATED CLINICIANS

- **Michel BAULAC,** MD Adult patient recruitment
- **Cyril MIGNOT,** MD Child patient recruitment
- **Mathilde CHIPAUX,** MD PhD Epilepsy surgery patient recruitment

ALS causes and mechanisms of motor neuron degeneration

Séverine Boillée's team investigates mechanisms of motor neuron (MN) degeneration in Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's disease) resulting from pathological interactions between MNs and microglia/macrophages to find therapeutically promising pathways to slow disease progression through two main aims:

- To understand how known/new ALS genes, identified using dedicated genetic approaches, lead to MN death and deregulated microglial responses, with the goal to identify and functionally validate common/divergent pathological pathways, using iPSc-derived MNs/microglia, mouse models and human post-mortem tissues;
- Focusing on the unique characteristics of spinal MNs, to assess impact and ALS disease modifying capacities of peripheral nerve macrophages (vs CNS microglia), using gene profiling in ALS mice and patient's bloodand iPSc-derived microglia/macrophages. The final goal being to find disease modifying targets at the periphery, therapeutically easier to reach than in the CNS.

MAJOR PUBLICATIONS

1. Chiot A., Zaïdi S., Iltis C., Ribon M., Berriat F., Schiaffino L., Jolly A., de la Grange P., Mallat M., Bohl D., Millecamps S., Seilhean D., Lobsiger C.S., Boillée S. Modifying macrophages at the periphery has the capacity to change microglial reactivity and to extend ALS survival. Nat Neurosci. 2020.

2. Amador M.d.M., Muratet F., Teyssou E., Banneau G., Danel-Brunaud V., Allart E., Antoine J.-C., Camdessanché J.-P., Anheim M., Rudolf G., Tranchant C., Fleury M.-C., Bernard E., Stevanin G. & Millecamps S. Spastic paraplegia due to recessive or dominant mutations in ERLIN2 can convert to ALS, Neurology: Genetics, 5 (6):e374 (2019).

3. Teyssou E.*, Chartier L.*, Amador M.d.M., Lam R., Lautrette G., Nicol M., Machat S., Da Barroca S., Moigneu C., Mairey M., Larmonier T., Saker S., Dussert C., Forlani S., Fontaine B., Seilhean D., Bohl D., Boillée S., Meininger V., Couratier P., Salachas F., Stevanin G., Millecamps S. Novel UBQLN2 mutations linked to Amyotrophic Lateral Sclerosis and atypical Hereditary Spastic Paraplegia phenotype through defective HSP70-mediated proteolysis. Neurobiology of Aging, 58:239.e11-239.e20. (2017). *equal contribution.

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5. Toli D., Buttigieg D., Blanchard S., Lemonnier T., Lamotte d'Incamps B., Bellouze S., Baillat G., Bohl D.*, Haase G.* Modeling amyotrophic lateral sclerosis in pure human iPSc-derived motor neurons isolated by a novel FACS double selection technique. Neurobiol. Dis., 82:269-80 (2015). *co-authors and co-corresponding authors.

MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCE

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Séverine BOILLÉE, PhD
ALS mechanisms, ALS, neuroinflammation, animal models

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PRINCIPAL INVESTIGATORS

- **Delphine BOHL,** PhD ALS mechanisms, iPSc ALS models; Scientific manager of CELIS-iPSc core facility
- **Stéphanie MILLECAMPS,** PharmD, PhD ALS genetics, cellular and animal models
- **Christian LOBSIGER,** PhD Neuro-glia interactions, transcriptomics, animal models

AFFILITIATED CLINICIANS

- **François SALACHAS,** MD ALS clinician, Neurologist/ Head of Pitié-Salpêtrière ALS reference center
- **Danielle SEILHEAN,** MD, PhD Neuropathologist, Head of the Neuropathology department of Pitié-Salpêtrière
- **Maria DEL MAR AMADOR,** MD ALS clinician

Neurophysiology of repetitive behaviors

Eric Burguière's team aims to implement an ambitious translational approach to characterize neurofunctional basis of normal and pathological repetitive behaviors. The main focus of the team is to study neurophysiological dynamics underlying the automatization of motivated behaviours and their contextual adaptation. The team has access to both patients and animal models suffering from pathological repetitive behaviors such as compulsion/impulsion and stereotypies.

The three main objectives are:
- To characterize the behavioural components underlying normal and pathological repetitive behaviors;
- To determine the neural circuits which participate to the acquisition and regulation of repetitive behaviors;
- To identify the micro-circuitry which modulate the neural activity within these circuits.

MAJOR PUBLICATIONS

1. Senova S, Mallet L, ..., Pelissolo A, Palfi S, Domenech P. Severe Obsessive-Compulsive Disorder Secondary to Neurodegeneration With Brain Iron Accumulation: Complete Remission After Subthalamic Nuclei Deep Brain Stimulation. Biol Psychiatry, 2020 Jun 15;87(12):e39-e41.
2. Welter M.L., Houeto J.L., Thobois S., ..., Jalenques I., Karachi C., Mallet L. Anterior pallidal deep brain stimulation for Tourette's syndrome: a double-blind randomised parallel controlled trial. Lancet Neurology 2017, S1474-4422(17)30160-6.
3. Mondragon, L., & Burguiere, E. Bio-inspired benchmark generator for extracellular multi-unit recordings. Scientific Reports, 2017 Jan; 7, 43253.
4. Domenech P., Redoute J., Koechlin E. and Dreher J.C. The Neuro-Computational Architecture of Value-Based Selection in the Human Brain. Cerebral Cortex, 2017 Jan; 1-17.
5. Burbaud P., Clair A.H., ..., Welter M.L., Mallet L. Neuronal activity correlated with checking behaviour in the subthalamic nucleus of patients with obsessive-compulsive disorder. Brain, 2013 Jan;136(Pt 1):304-17.
6. Burguière E., Monteiro P., Feng G., Graybiel A.M. Optogenetic stimulation of lateral orbitofrontostriatal pathway suppresses compulsive behaviors. Science, 2013 Jun 7;340(6137):1243-6.

MAIN DOMAIN

NEUROPHYSIOLOGY

SUBDOMAIN

COGNITION

Eric BURGUIÈRE, PhD
Behavior, neurophysiology and optogenetic in rodents

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PRINCIPAL INVESTIGATORS

- **Luc MALLET,** MD, PhD
Neurophysiology and DBS in patients, Psychiatry
- **Philippe DOMENECH,** MD, PhD
Computational neuroscience, neurophysiology, Psychiatry

Dynamics of epileptic networks and neuronal excitability

The team investigates the pathophysiological processes making the brain epileptic (epileptogenesis) and how the mechanisms responsible for the occurrence of seizures (ictogenesis). These two dimensions of epileptic diseases are explored using a translational and multiscale strategy: from validated animal models to clinical semiology and from single neurons to large scale networks. Specifically, the research includes in vivo EEG and cell recordings from both human epileptic patients and animal models exhibiting spontaneous (genetic models) or provoked (drugs or stimulation-induced) seizures.

The central goal of their team is to establish mechanistic-causal links between single neuron properties and large-scale brain dynamics, an approach requires to elucidate the different facets of the pathophysiology of focal to generalized epilepsies. In complement of this research, the team explores extreme brain conditions with abnormal and sustained electrical activities (from isoelectric status to status epilepticus, up to near-death states).

MAJOR PUBLICATIONS

1. Schramm AE, Carton-Leclercq A, Diallo S, Navarro V, Chavez M, Mahon S, Charpier S (2020). Identifying neuronal correlates of dying and resuscitation in a model of reversible brain anoxia. Prog Neurobiol. 185:101733.
2. Lambrecq V., Lehongre K., Adam C., Frazzini V., Mathon B., Clemenceau S., Hasboun D., Charpier S., Baulac M., Navarro V., Le Van Quyen M. (2017) Single-unit activities during the transition to seizures in deep mesial structures. Ann Neurol.;82(6):1022-1028.
3. Williams M., Altwegg-Boussac T., Chavez M., Lecas S., Mahon S. and Charpier S. (2016). Integrative properties and transfer function of cortical neurons initiating absence seizures in a rat genetic model. J Physiol. (London) 594: 6733-6751. This article was featured at the journal's perspectives: Polack, P.O. (2016). J Physiol. (London) 594:6439-6751, 2016.
4. Navarro V., Dagron C., Elie C., Lamhaut L., Demeret S., Urien S., An K., Bolgert F., Tréluyer J.M., Baulac M., Carli P. (2016) Levetiracetam and clonazepam in status epilepticus: A prehospital doubleblind randomised trial. Lancet Neurology 15: 47-55.
5. Lopez-Persem A, Bastin J, Petton M, Abitbol R, Lehongre K, Adam C, Navarro V, Rheims S, Kahane P, Domenech P, Pessiglione (2020). Four core properties of the human brain valuation system demonstrated in intracranial signals. Nat Neurosci. 23(5): 664-675.

MAIN DOMAIN

NEUROPHYSIOLOGY

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Stéphane CHARPIER, PhD
In vivo multi-scale electrophysiology on animal models

Mario CHAVEZ, PhD
Networks dynamics & signal processing

Vincent NAVARRO, MD, PhD
In vivo multi-scale electrophysiology on epileptic patients and animal models of focal epilepsy

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PRINCIPAL INVESTIGATORS

- **Séverine MAHON,** PhD
In vivo multi-scale electrophysiology on animal models
- **Virginie LAMBRECQ,** MD, PhD
Cellular & network analysis of epileptic seizures in patients

Algorithms, models and methods for images and signals of the human brain

Olivier Colliot & Stanley Durrleman's team, aims to build numerical models of brain diseases from multimodal patient data, based on the development of specific data-driven approaches.

The main research axes are:
- Integrate multimodal neuroimaging data (PET, microstructure, ASL) to fully characterize alterations;
- Model the temporal dynamics of disease;
- Model brain networks;
- Integrate imaging with other types of data (in particular omics and clinical data).

MAJOR PUBLICATIONS

1. Samper-González J., Burgos N., Bottani S., Fontanella S., Lu P., Marcoux A., Routier A., Guillon J., Bacci M., Wen J., Bertrand A., Bertin H., Habert M.O., Durrleman S., Evgeniou T., Colliot O. ADNI; AIBL. Reproducible evaluation of classification methods in Alzheimer's disease: Framework and application to MRI and PET data. Neuroimage 2018.

2. Schiratti J.-B., Allassonniere S., Colliot O., Durrleman S. A Bayesian mixed-efects model to learn trajectories of changes from repeated manifold-valued observations. Journal of Machine Learning Research (JMLR) 18(1), 4840-4872. 2017.

3. Obando C., De Vico Fallani F. A statistical model for brain networks inferred from largescale electrophysiological signals. Journal of the Royal Society Interface.

4. Bertrand A., Wen J., Rinaldi D., Houot M., Sayah S., Camuzat A., Fournier C., Fontanella S., Routier A., Couratier P., Pasquier F., Habert M.O., Hannequin D., Martinaud O., Caroppo P., Levy R., Dubois B., Brice A., Durrleman S., Colliot O. Early Cognitive, Structural, and Microstructural Changes in Presymptomatic C9orf72 Carriers Younger Than 40 Years. JAMA neurology 75(2);236-245, 2018.

5. De Vico Fallani F., Richiardi J., Chavez M., and Achard S. Graph analysis of functional brain networks: practical issues in translational neuroscience. Philosophical Transactions of the Royal Society of London Series B, Biological Sciences, 369:1653, 2014.

MAIN DOMAIN

COMPUTATIONAL MODELLING IN NEUROSCIENCE

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Olivier COLLIOT, PhD
Medical image computing, machine learning, applications to neurodegenerative diseases

Stanley DURRLEMAN, PhD
Medical image computing, statistical & machine learning, computer vision. Coordinator of ICM Centre for Neuroinformatics

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PRINCIPAL INVESTIGATORS

- **Fabrizio DE VICO FALLANI,** PhD
  Complex network theory, brain connectivity, functional brain imaging
- **Ninon BURGOS,** PhD
  Multimodal neuroimaging, machine learning
- **Daniel RACOCEANU,** PhD
  histological imaging, machine learning, digital pathology
- **Stéphane EPELBAUM,** MD, PhD
  Neurology, Alzheimer's disease
- **Didier DORMONT,** MD, PhD
  Brain imaging neuroradiology, dementia

Molecular pathophysiology of Parkinson's disease

Olga Corti & Jean-Christophe Corvol's team proposes a multidimensional clinical, genetic/genomic and cell biology-based program aimed at deciphering and integrating the molecular heterogeneity and biological complexity of Parkinson's Disease (PD) towards translation to clinical research.

Specific aims are:
- To identify new molecular determinants of PD including genes, modifiers of progression or response to treatment and non-coding genetic elements accounting for cell-specific effects;
- To explore pathways to disease, with a focus on PINK1/Parkin dysregulation and its impact on neuronal vulnerability to stress and immune cell function;
- To use new findings to develop clinical-genetic models for predictive/precision medicine.

MAJOR PUBLICATIONS

1. Lesage S, Lunati A, Houot M, Romdhan SB, Clot F, Tesson C, Mangone G, Toullec BL, Courtin T, Larcher K, et al., French Parkinson disease Genetics Study Group (PDG). Characterization of recessive Parkinson's disease in a large multicenter study. Ann Neurol. 2020.

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MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCE

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

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Molecular and cellular mechanisms, mitochondrial exploration

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- **Louise-Laure MARIANI,** MD, PhD
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  Clinical aspects

The Diane Barrière Chair "Molecular physiology of synaptic bioenergetics"

Jaime de Juan-Sanz's team investigates mitochondrial dysfunction as a primary cause in epilepsy. Mitochondria plays a pivotal role for neuronal function, controlling three fundamental mechanisms that are essential for neuronal biology and synaptic transmission:
1. ATP production,
2. Ca2+ homeostasis and
3. apoptotic cell death.

Using cutting-edge optical techniques to study bioenergetics in firing synapses in combination with precise metabolic and genetic manipulations, the team will work on developing a detailed molecular understanding of the role of synaptic mitochondrial metabolism in controlling neuronal function in health and disease.

This will:
- Improve the limited understanding of the neurophysiological role of mitochondria in maintaining synaptic metabolic integrity;
- Provide a solid molecular framework to unravel the poorly understood molecular link between mitochondrial dysfunction and metabolic epilepsies;
- Help frame future investigations focused on improving mitochondrial bioenergetics in neurological diseases caused by dysfunctional mitochondria.

MAJOR PUBLICATIONS

1. Ashrafi, G.*, de Juan-Sanz, J*, Farrell, R.J. and Ryan T.A. (2020). Molecular tuning of the axonal mitochondrial Ca2+ uniporter ensures metabolic flexibility of neurotransmission. Neuron, 105(4):678-687.e5. * Co-first authors.
2. De la Rocha-Muñoz, A., Núñez, E., Gómez-López, S., López-Corcuera B., de Juan-Sanz J* and Aragón C (2020). The presynaptic glycine transporter GlyT2 is regulated by the Hedgehog pathway in vitro and in vivo. * Corresponding author. BioRxiv.doi:https://doi.org/10.1101/2020.07.28.224659.
3. De la Rocha-Muñoz A., Núñez, E., Arribas-González, E., LópezyCorcuera, B., Aragón, C* and de Juan-Sanz J* (2019). E3 ubiquitin ligases LNX1 and LNX2 are major regulators of the presynaptic glycine transporter GlyT2. * Co-corresponding authors. Scientific Reports. Sci Rep 9, 14944
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5. de Juan-Sanz, J., Holt, G. T., Schreiter, E. R., de Juan, F., Kim, D. S., & Ryan, T. A. (2017). Axonal endoplasmic reticulum Ca 2+ content controls release probability in CNS nerve terminals. Neuron, 93(4), 867-881.

MAIN DOMAIN

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Basic to translational neurogenetics

Alexandra Durr & Giovanni Stevanin's team focus on inherited neurogenetic diseases, such as spinocerebellar degenerations, frontotemporal lobar degenerations and Huntington Disease. These rare conditions share clinical, genetic and functional characteristics, such as selective neurodegeneration, but are extremely heterogeneous regarding their molecular, clinical and histopathological features.

Specific aims are:
- To identify novel causative genes/molecular defects and modifying factors in improving the genomic analysis of familial forms;
- To investigate common pathological mechanisms such as dysfunction of lysosomes and autophagy;
- To uncover new pathological pathways using unbiased methods (RNASeq, lipidomics, metabolomics...);
- To implement innovative therapeutic strategies, including gene therapy, using biomarkers identified in longitudinal studies of patients and premanifest gene mutation carriers.

MAJOR PUBLICATIONS

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2. Roux T, Barbier M, Papin M, Davoine CS, Sayah S, Coarelli G, Charles P, Marelli C, Parodi L, Tranchant C, Goizet C, Klebe S, Lohmann E, Van Maldergen L, van Broeckhoven C, Coutelier M, Tesson C, Stevanin G, Duyckaerts C, Brice A, Durr A; SPATAX network. Clinical, neuropathological, and genetic characterization of STUB1 variants in cerebellar ataxias: a frequent cause of predominant cognitive impairment. Genet Med. 2020 Jul 27.
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5. Duchesne A, Vaiman A, Frah M, Floriot S, Legoueix-Rodriguez S, Desmazières A, Fritz S, Beauvallet C, Albaric O, Venot E, Bertaud M, Saintilan R, Guatteo R, Esquerré D, Branchu J, Fleming A, Brice A, Darios F, Vilotte JL, Stevanin G, Boichard D, El Hachimi KH. Progressive ataxia of Charolais cattle highlights a role of KIF1C in sustainable myelination. PLoS Genet. 2018;14(8):e1007550.

MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCE

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- **Isabelle LE BER,** MD, PhD
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- **Solveig HEIDE,** MD
  Medical genetics

Control - interoception - attention

Liane Schmidt & Philippe Fossati's team aims to understand how cognitive control processes integrate external and internal signals, and how this integration takes place on behavioral and neural levels, in healthy subjects and patients with impaired cognitive control (i.e., in depression and obesity).

The team will:
- Investigate the neurocognitive mechanisms that mediate the effect of expectancies and mindsets on judgment and behavior
- Explore the role of motivation and cognitive biases on response to medical treatments;
- Attempt to disentangle impaired cognitive control in the establishment of depression or obesity.

MAJOR PUBLICATIONS

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MAIN DOMAIN

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- **Jean-Yves ROTGE,** MD, PhD
  Clinical expertise, brain imaging & experimental psychology
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  Neuroeconomics, brain imaging, behavior

Brain development

Bassem Hassan's team investigates the formation of neurons and neural circuits during brain development, focusing on the transcriptional control of stem cells fate during early neurogenesis using Drosophila, mouse, and human models, and on the emergence of individuality in Drosophila visual circuits and behavior.

The 3 main aims are:
- To unravel the role of proneural proteins in generation and diversification of neurons from neural progenitors;
- To investigate the link between wiring variability and individualized innate behavior;
- To understand the normal physiological function of human disease genes during brain development.

MAJOR PUBLICATIONS

1. Linneweber GA, Andriatsilavo M, Dutta SB, et al. A neurodevelopmental origin of behavioral individuality in the Drosophila visual system. Science. 2020. 367(6482):1112-19.

2. Ramaekers A, Claeys A, Kapun M, et al. Altering the Temporal Regulation of One Transcription Factor Drives Evolutionary Trade-Offs between Head Sensory Organs. Dev Cell. 2019. 50(6):780-92.e7.

3. Mora N., Oliva C., Fiers M., Ejsmont R., Soldano A., et al. A Temporal Transcriptional Switch Governs Stem Cell Division, Neuronal Numbers, and Maintenance of Differentiation. Dev Cell. 2018. 45(1):53-66.e5.

4. Quan X.J., Yuan L., Tiberi L., Claeys A., De Geest N., et al. Post-translational Control of the Temporal Dynamics of Transcription Factor Activity Regulates Neurogenesis. Cell. 2016. 164(3):460-75.

5. Langen M., Koch M., Yan J., De Geest N., Erfurth M.L., et al. Mutual inhibition among postmitotic neurons regulates robustness of brain wiring in Drosophila. Elife. 2013. 2:e00337.

MAIN DOMAIN

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PRINCIPAL INVESTIGATOR

- **Carlos PARRAS,** PhD
  Transcriptional control of mouse brain development

Genetics and development of nervous system tumors

Emmanuelle Huillard & Marc Sanson's team proposes to identify new mutations and biomarkers, and understand the development of brain tumors with four major aims:

- To improve diagnosis and treatment by expanding their molecular database and feed new translational projects;
- To characterize the function of newly identified mutations in gliomas by using the "mutation to function" pipeline successfully implemented by the team;
- To characterize the cell intrinsic and environmental mechanisms governing brain tumor initiation and progression;
- To develop new mouse and patient-derived models to identify actionable targets and new treatments.

MAJOR PUBLICATIONS

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2. Di Stefano AL et al. Clinical, Molecular and Radiomic Profile of Gliomas With FGFR3-TACC3 Fusions. Neuro Oncol 2020 May 15:noaa121. doi: 10.1093/neuonc/noaa121.
3. D'Angelo F et al. The molecular landscape of glioma in patients with Neurofibromatosis 1. Nat Med. 2019 Jan;25(1):176-187.
4. Idbaih A et al. Safety and Feasibility of Repeated and Transient Blood-Brain Barrier Disruption by Pulsed Ultrasound in Patients with Recurrent Glioblastoma. Clin Cancer Res. 2019 Jul 1;25(13):3793-3801.
5. Rosenberg S et al. A recurrent point mutation in PRKCA is a hallmark of chordoid gliomas. Nat Commun. 2018 Jun 18;9(1):2371
6. Labreche K et al. Diffuse gliomas classified by 1p/19q co-deletion, TERT promoter and IDH mutation status are associated with specific genetic risk loci. Acta Neuropathol. 2018 May;135(5):743-755.
7. Peyre M, et al. Progestin-associated shift of meningioma mutational landscape. Ann Oncol 2018 Mar 1;29(3):681-686.
8. Frattini V et al. A metabolic function of FGFR3-TACC3 gene fusions in cancer. Nature. 2018 Jan 11;553(7687):222-227.

MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCES

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Developmental neurobiology, mouse models, transcription factors

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- **Karima MOKHTARI,** MD
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- **Mathieu PEYRE,** MD, PhD
  Meningioma tumorigenesis, neurosurgery
- **Anna Luisa DI STEFANO,** MD, PhD
  Genetics of brain tumors, cerebral lymphomas

Experimental therapeutics of Parkinson's disease

Etienne Hirsch & Stéphane Hunot's team aims to understand the mechanisms underlying disease progression in Parkinsons disease (PD) and to identify and validate new disease-modifying treatments. Besides intrinsic neuronal mechanisms and transneuronal propagation of the proteinopathy, the team posits that disease progression also relies on a complex pathological cell-cell interaction network.

The specific aims of the team are to better describe:
- How pathological protein assemblies (a-Syn and Tau) and other inflammatory cues shape microglial cell responses?
- How disease-associated brain vascular changes modulate neuroinflammation and clearance of pathological protein assemblies?
- How progressive dysfunction of non-DA neurotransmitter systems impacts on neurodegeneration and on immune cell polarization and function?
- How disease-relevant environmental factors impact PD pathogenesis?

MAJOR PUBLICATIONS

1. Dos-Santos-Pereira M, Guimarães FS, Del-Bel E, Raisman-Vozari R, Michel PP. Cannabidiol prevents LPS-induced microglial inflammation by inhibiting ROS/NF-γB-dependent signaling and glucose consumption. Glia. 2020 68(3):561-573.
2. Parillaud VR, Lornet G, Monnet Y, Privat AL, Haddad AT, Brochard V, Bekaert A, de Chanville CB, Hirsch EC, Combadière C, Hunot S, Lobsiger CS. Analysis of monocyte infiltration in MPTP mice reveals that microglial CX3CR1 protects against neurotoxic over-induction of monocyte-attracting CCL2 by astrocytes. J Neuroinflammation. 2017 21;14(1):60.
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4. Mécharles S., Herrmann C., Poullain P., Tran T.H., Deschamps N., Mathon G., Landais A., Breurec S., Lannuzel A. Acute myelitis due to Zika virus infection. Lancet. 2016 2; 387(10026):1481.
5. Michel P.P., Hirsch E.C., Hunot S. Understanding Dopaminergic Cell Death Pathways in Parkinson Disease. Neuron. 2016 18; 90:675-91.

MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCE

SUBDOMAIN

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Pathophysiology of PD

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Animal models of PD and Neuroimmunology

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  Clinical studies, cohorts of patients with atypical forms of PD

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- **Alice DEMOLY,** MD
  Clinical studies on Progressive Supranuclear Palsy
- **Hugo CHAUMONT,** MD
  Clinical studies

Frontal function and pathology, FRONTLAB

The activities of the FRONTLAB team is a true collective research structured in 4 main tracks, all focused on the anatomical and functional organisation of the frontal lobes and associated networks for higher-order cognition in health and disease.

The first track (human cognition) studies on how the human brain generates and valuates creative ideas. Computational modeling combined with cognitive tasks, neuroimaging, intraoperative recordings of brain activity in awake surgery and non-invasive brain stimulation are applied to investigate interaction between the processes of generating new ideas and those required to evaluate their appropriateness and originality.

The second track (human behaviour), addresses how goal-directed behaviour is generated and what are the pathophysiological mechanisms underlying abnormally expressed goal-directed behaviours, in particular, disinhibition and apathy). Our approach relies on classical approaches combined with the analysis of human behaviour in close to real-life situations using simulated scenarios in the lab or wired tracking devices at home.

The third track (human brain organisation), investigates at the network level the causal structural and neurophysiological basis of cognitive functions and their impairments in healthy individuals and neurosurgical patients. It also addresses the characterization of activity states subtending the allocation, control and transient loss of sustained attention and its modulation with invasive and non-invasive brain stimulation technologies.

The fourth track ("bench to bedside") is a translational clinical program aiming to characterize genetic, molecular, neurophysiological and anatomical impairments leading to neuropsychiatric symptoms impacting frontal networks or explaining disease vulnerability. Multimodal approaches are applied to phenotype large cohorts of FTLD patients and on such basis contain their progression or reverse its symptoms with or molecular approaches or non-invasive brain stimulation (rTMS, tDCS, tACS).

MAJOR PUBLICATIONS

1. Migliaccio R et al. Cognitive and behavioural inhibition deficits in neurodegenerative dementias. Cortex 2020 (e-pub, ehead of print)
2. Montembeault M et al. Cognitive inhibition impairments in presymptomatic C9orf72 carriers. J Neurol Neurosurg Psychiatry. 2020;91(4):366-372.
3. Toba MN et al. Revisiting 'brain modes' in a new computational era: Approaches for the characterization of brain-behavioural associations. Brain 2020 ;143(4):1088-1098.
4. Batrancourt B et al. Exploration deficit in ecological condition as a marker of apathy in frontotemporal dementia. Front. Neurol 2019; 10:941.
5. Alves P et al. An improved neuroanatomical model of the default-mode network reconciles previous neuroimaging and neuropathological findings. Communications Biology, 2019. 2, 370.
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9. Foulon C et al. Advanced lesion symptom mapping analyses and implementation as BCBtoolkit. GigaScience 2018 7; 1-17
10. Bendetowicz D et al. Two critical brain networks for generation and combination of remote associations. Brain 2018 141 : 217-233
11. Bertrand A et al. Early cognitive, structural and microstructural changes in c9orf72 presymptomatic carriers before 40 years of age. JAMA Neurology 2018 75; 236-245

MAIN DOMAIN

COGNITION

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  Behavior, structural & functional imaging analysis
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  Brain-behavior relationship, neurosurgery
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  Functional connectivity, brain stimulation and neuromodulation
- **Emmanuelle VOLLE,** MD, PhD
  Cognition, neuroimaging analysis
- **Bénédicte BATRANCOURT,** PhD
  Behavioral tracking analysis tools, biomedical informatics

Repair in multiple sclerosis: From biology to clinical translation

Catherine Lubetzki & Bruno Stankoff's team aims to tackle the mechanisms of CNS myelin repair through complementary approaches and expertise in Multiple sclerosis and demyelinating disorders.

The team has recently developed several in vitro and in vivo approaches and models in order:
- To investigate myelination processes in various species (mice, Xenopus, humans);
- To select new targets and validate new pharmacological compounds based on their complementary remyelinating models;
- To understand the molecular components and dynamics of glia-neuron interactions during remyelination;
- To gain insight into inflammation, de/remyelination as well as energy dysregulation using molecular imaging, with the goal to determine the influence of different components on neurodegeneration in MS patients;
- To identify novel imaging signatures characterizing the key phases of demyelinating diseases and to stratify patients for innovative clinical trials.

MAJOR PUBLICATIONS

1. Lubetzki C, Zalc B, Williams A, Stadelmann C, Stankoff B. Remyelination in multiple sclerosis: from basic science to clinical translation. Lancet Neurol. 2020 Aug;19(8):678-688
2. Bodini B*, Poirion E*, Tonietto M, Benoit M, Palladino R, Maillart E, Portera E, Battaglini M, Bera G, Kuhnast B, Louapre C, Bottlaender M, Stankoff B. Individual mapping of innate immune cell activation is a candidate marker of patient-specific trajectories of disability worsening in Multiple Sclerosis. J Nuc Med, 2020;61(7):1043-1049
3. Dubessy AL, Mazuir E, Rappeneau Q, Ou S, Abi Ghanem C, Piquand K, Aigrot MS, Thétiot M,Desmazières A, Chan E, Fitzgibbon M, Fleming M, Krauss R, Zalc B, Ranscht B, Lubetzki C, Sol-Foulon N. Role of a Contactin multi-molecular complex secreted by oligodendrocytes in nodal protein clustering in the CNS. Glia. 2019 Dec;67(12):2248-2263
4. Bodini B., Veronese M., Garcia-Lorenzo D., Battaglini M., Poirion E., Chardain A., Freeman L., Louapre C., Tchikviladze, Papeix C., Dolle F., Zalc B., Lubetzki C., Bottlaender M., Turkeimer F., Stankoff B. Dynamic imaging of individual remyelination profiles in multiple sclerosis. Ann Neurol, 2016 Feb 18. (cited in the Jan 2017 issue of Lancet Neurology as one of the best 5 papers in MS in 2016).
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MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCE

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Catherine LUBETZKI, MD, PhD
Mechanisms of repair and target identification. Head of the Neuroscience Medical-University department Pitié-Salpêtrière hospital. Medical director of Paris Brain Institute

Bruno STANKOFF, MD, PhD
Imaging of tissue damage and repair in MS and target identification. Head of St Antoine hospital MS clinic

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PRINCIPAL INVESTIGATORS

- **Nathalie SOL-FOULON**, PharmD, PhD
  Neuron-glia interactions during myelination
- **Anne DESMAZIERES,** PhD
  Formation/reformation of Nodes of Ranvier
- **Marc DAVENNE,** PhD
  Axonal initial segment in MS and experimental models
- **Bernard ZALC,** PhD
  Validation of remyelinating targets, triggers of myelination
- **Céline LOUAPRE,** MD, PhD
  Clinical and MRI research
- **Benedetta BODINI,** MD, PhD
  MS imaging

AFFILIATED CLINICIANS

- **Caroline PAPEIX,** MD, PhD
  Clinical research, cohort studies
- **Elisabeth MAILLART,** MD
  Clinical research, cohort studies

"Mov'It" Movements, Investigation, Therapeutics

Marie Vidailhet & Stéphane Lehéricy's team aims at further investigating network dysfunctions and pathophysiology in movement and behavioral disorders using translational, neuroimaging, neurophysiological, and genetic/metabolic approaches from animals to patients.

The four main objectives are:
- To explore motor pathways and pathophysiology in dystonia (AMEDYST);
- To investigate high order motor integration disorders (Agent10, COGIT) and motor consolidation during sleep (MEMOdream);
- To perform a prospective study (ICEBERG) aiming to build a dynamic progression model of PD for predictive medicine;
- develop automated diagnostic algorithms for atypical Parkinsonism (PARK ATYPIQUE)
- To develop innovative therapeutic approaches in movement disorders using focused ultrasound, non-invasive stimulation and drugs targeting metabolic dysfunctions.

MAJOR PUBLICATIONS

1. Biondetti E, Gaurav R, Yahia-Cherif L, Mangone G, Pyatigorskaya N,..., Vidailhet M, Lehéricy S Spatiotemporal changes in substantia nigra neuromelanin content in Parkinson's disease. Brain. 2020 Aug 28:awaa216.
2. Mochel F, Delorme C, Czernecki V, ..., Roze E, Labauge P, Nguyen S. J Haematopoietic stem cell transplantation in CSF1R-related adult-onset leukoencephalopathy with axonal spheroids and pigmented glia. Neurol Neurosurg Psychiatry. 2019 Dec;90(12):1375-1376.
3. Dizeux A, Gesnik M, Ahnine H, Blaize K, Arcizet F, Picaud S, Sahel JA, Deffieux T, Pouget P, Tanter M. Nat Commun. 2019 Mar 28;10(1):1400.
4. Lacaux C, Izabelle C,..., Arnulf I, Oudiette D. Increased creative thinking in narcolepsy. Brain. 2019 Jul 1;142(7):1988-1999.
5. Kemlin C, Moulton E, Lamy JC,..., Brochard V, Corvol JC, Samson Y, Rosso C. Elucidating the Structural and Functional Correlates of Upper-Limb Poststroke Motor Impairment. Stroke. 2019 Dec;50(12):3647-3649.
6. Méneret A, Franz EA, Trouillard O,..., Brice A, Chédotal A, Dusart I, Roze E, Markie D.J Mutations in the netrin-1 gene cause congenital mirror movements. J Clin Invest. 2017 Nov 1;127(11):3923-3936.
7. Sliwa J, Freiwald WA. A dedicated network for social interaction processing in the primate brain. Science. 2017 May 19;356(6339):745-749.
8. Gallea C., Popa T,..., Fernández-Vidal S., Bardinet E., Roze E., Lehéricy S., Vidailhet M., Meunier S. Intrinsic signature of essential tremor in the cerebello-frontal network. Brain. 2015 Oct;138(Pt 10):2920-33.

MAIN DOMAIN

NEUROPHYSIOLOGY

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Marie VIDAILHET, MD, PhD
Clinical neurology, pathophysiology movement disorders, Coordinator of the Reference Centre for rare Diseases Dystonia and Abnormal Movements, member of ERN

Stéphane LEHÉRICY, MD, PhD
Neuroimaging in humans, Parkinson and movement disorders. Head of the neuroimaging center (CENIR)


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PRINCIPAL INVESTIGATORS

- **Isabelle ARNULF,** MD, PhD. Neurophysiology: sleep disorders, movement disorders
- **Andreas HARTMANN,** MD, PhD. Clinical neurology and movement disorders. Coordinator of the Tourette syndrome reference center
- **Fanny MOCHEL,** MD, PhD. Coordinator Reference Centre on Adult Neurometabolic diseases genetics, neurometabolism and movement disorders
- **Yulia WORBE,** MD, PhD. Clinical neurology, behavior and movement disorders
- **Charlotte ROSSO,** MD, PhD. Stroke, Rehabilitation, Neurophysiology: non-invasive stimulation (TMS, tDCS, tACS)
- **Emmanuel ROZE,** MD, PhD. Clinical neurology, genetics and movement disorders
- **Pierre POUGET,** PhD Primate animal models and behavior
- **Cécile GALLEA,** PhD Neuroimaging in humans and movement disorders
- **Delphine OUDIETTE** PhD. Neurophysiology of sleep and sleep disorders
- **Sabine MEUNIER,** MD, PhD. Neurophysiology, movement disorders
- **Julia SLIWA,** PhD. Primate animal models and behavior
- **Emmanuelle APARTIS-BOURDIEU,** MD, PhD. Neurophysiology: non-invasive stimulation (TMS, tDCS, tACS)
- **Nadya PYATIGORSKAYA,** MD, PhD. Neuroimaging, Parkinsonism
- **Aurelie MENERET** MD, PhD. Clinical neurology, movement disorders, genetics
- **Elodie HAINQUE** MD, PhD. Clinical neurology, Parkinson, neurophysiology

Physiological investigation of clinically normal and impaired cognition

Laurent Cohen, Lionel Naccache & Paolo Bartolomeo's team explores the neural bases of cognitive functions in humans. They work with both healthy and brain-damaged persons, using behavioral methods and a full panel of brain imaging techniques (anatomical, functional and diffusion-based MRI, EEG, MEG, intracerebral recordings).

Their goal is not only the fundamental deciphering of cognitive functions, but also the development of clinically useful tools for the diagnosis and rehabilitation of patients. They focus their research on:
- The generality of conscious access, the relationships between brain-body interactions and states-of-consciousness, the exploration of stream of consciousness through the dynamics of conscious states. The team will design patterns of brain stimulation to improve conscious state of non-communicating patients, and implement a novel translational tool for real time and web-based metrics of consciousness for clinical care;
- Cognitive functions and brain plasticity, investigating the cerebral mechanisms of word reading, as well as the novel functions of the visual cortex of congenitally blind individuals;
- Investigation of the precise dynamics of frontoparietal networks that control visuospatial attention.

MAJOR PUBLICATIONS

1. Hermann, B., A. Ben Salah, V. Perlbarg, M. Valente, N. Pyatigorskaia, M.O. Habert, F. Raimondo, J. Stender, D. Galanaud, A. Kas, L. Puybasset, P. Perez, S. J.D., B. Rohaut, and L. Naccache, Habituation of auditory startle reflex is a new sign of minimally conscious state. Brain, 2020. 143(7): p. 2154–2172.
2. Abboud S, Cohen L. Distinctive Interaction Between Cognitive Networks and the Visual Cortex in Early Blind Individuals. Cereb Cortex. 2019 Dec 17;29(11):4725-4742.
3. Demertzi A, Tagliazucchi E, Dehaene S, Deco G, Barttfeld P, Raimondo F, Martial C, Fernández-Espejo D, Rohaut B, Voss HU, Schiff ND, Owen AM, Laureys S, Naccache L, Sitt JD. Human consciousness is supported by dynamic complex patterns of brain signal coordination. Sci Adv. 2019 Feb 6;5(2):eaat7603.
4. Bouhali, F., Thiebaut de Schotten, M., Pinel, P., Poupon, C., Mangin, J.F., Dehaene, S., and Cohen, L. (2014). Anatomical connections of the visual word form area. The Journal of Neuroscience 34, 15402-15414.
5. Lunven, M., Thiebaut De Schotten, M., Bourlon, C., Duret, C., Migliaccio, R., Rode, G., and Bartolomeo, P. (2015). White matter lesional predictors of chronic visual neglect: a longitudinal study. Brain 138, 746-760.

MAIN DOMAIN

COGNITION

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE
COMPUTATIONAL MODELLING IN NEUROSCIENCE

Laurent COHEN, MD, PhD
Language, reading and perception

Paolo BARTOLOMEO, MD, PhD
Attention and perception

Lionel NACCACHE, MD, PhD
Consciousness
Principal investigators



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PRINCIPAL INVESTIGATORS

- **Jacobo SITT,** MD, PhD Consciousness
- **Benjamin ROHAUT,** MD, PhD Consciouness

Motivation, brain and behavior

Mathias Pessiglione, Jean Daunizeau & Sébastien Bouret's team aims to build a neuro-computational model of how the brain motivates behavior, which would explain irrational behaviors in the normal population, and motivational disorders in pathological conditions. Motivation is conceived as a cost-benefit arbitrage that drives the behavior.

The team combines human brain imaging, clinical neuropsychology, monkey neurophysiology and computational modeling:
- To understand how costs and benefits variables are represented in the brain;
- To explain how choice is arbitrated through cognitive control;
- To investigate how the arbitrage is influenced by emotion and fatigue;
- To specify how it varies with clinical conditions and treatments.

MAJOR PUBLICATIONS

1. Lopez-Persem A, Bastin J, Petton M, Abitbol R, Lehongre K, Adam C, Navarro V, Rheims S, Kahane P, Domenech P, Pessiglione M. Four core properties of the human brain valuation system demonstrated in intracranial signals. Nat Neurosci. 2020 May;23(5):664-675.
2. Forgeot d'Arc B, Devaine M, Daunizeau J. Social behavioural adaptation in Autism. PLoS Comp. Biol. (2020), 16(3): e1007700.
3. Borderies N, Bornert P., Gilardeau S., Bouret S. Pharmacological evidence for the implication of noradrenaline in effort. PLoS Biol. (2020)
4. Blain B, Schmit C, Aubry A, Hausswirth C, Le Meur Y, Pessiglione M. Neuro-computational Impact of Physical Training Overload on Economic Decision-Making. Curr Biol. 2019 Oct 7;29(19):3289-3297.e4.
5. Vinckier F, Rigoux L, Oudiette D, Pessiglione M. Neuro-computational account of how mood fluctuations arise and affect decision making. Nat Commun. 2018 Apr 26;9(1):1708.
6. Pessiglione M, Vinckier F, Bouret S, Daunizeau J, Le Bouc R. Why not try harder? Computational approach to motivation deficits in neuro-psychiatric diseases. Brain. 2018 Mar 1;141(3):629-650.
7. San-Galli A, Varazzani C, Abitbol R, Pessiglione M, Bouret S. Primate Ventromedial Prefrontal Cortex Neurons Continuously Encode the Willingness to Engage in Reward-Directed Behavior. Cereb Cortex. 2018 Jan 1;28(1):73-89.

MAIN DOMAIN

COGNITION

SUBDOMAIN

COMPUTATIONAL MODELLING IN NEUROSCIENCE

Mathias PESSIGLIONE, PhD
Neuroimaging and neuropsychology in humans

Jean DAUNIZEAU, PhD
Computational and statistical modeling

Sébastien BOURET, PhD
Neurophysiology and pharmacology in monkeys

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PRINCIPAL INVESTIGATORS

- **Fabien VINCKIER,** MD, PhD
  Clinical psychiatry
- **Raphaël LE BOUC,** MD, PhD
  Clinical neurology

Structural plasticity of cerebral networks

Nicolas Renier's plan is to develop and use cutting-edge 3D whole brain imaging and genetic tools aimed at elucidating how neuronal and vascular networks in the adult brain can be remodeled.

The team will:
- Investigate the molecular mechanisms of axon and branch dynamics in the adult brain;
- Gain new information on neuro-vascular interaction during plastic events;
- Develop correlative 3D imaging of live calcium imaging in the behaving animal with whole brain mapping of neuronal markers and connectivity;
- Determine the role of structural plasticity to support behavioral plasticity in the mouse.

MAJOR PUBLICATIONS

1. Kirst, C., Skriabine, S., Vieites-Prado, A., Topilko, T., Bertin, P., Gerschenfeld, G., Verny, F., Topilko, P., Michalski, N., Tessier-Lavigne, M., Renier, N. (2020). Mapping the Fine-Scale Organization and Plasticity of the Brain Vasculature Cell 180(4), 780-795.e25. (IF=28.7).
2. Renier N., Dominici C., Erzurumlu R.S., Kratochwil C.F., Rijli F.M., Gaspar P. & Chédotal A. (2017). A mutant with bilateral whisker to barrel inputs unveils somatosensory mapping rules in the cerebral cortex. eLife, 6, 700. (IF=8.3).
3. Renier N.*, Adams E. L.*, Kirst C.*, Wu Z.*, Azevedo R., Kohl J., et al. (2016). Mapping of Brain Activity by Automated Volume Analysis of Immediate Early Genes. Cell, 165(7), 1789–1802. (IF=28.7).
4. Renier N.*, Wu Z.*, Simon D.J., Yang J., Ariel P., & Tessier-Lavigne M. (2014). iDISCO: a simple,rapid method to immunolabel large tissue samples for volume imaging. Cell, 159(4), 896–910. (IF=28.7).
5. Xu K.*, Wu Z.*, Renier N.*, Antipenko A., Tzvetkova-Robev D., Xu Y., et al. (2014). Structures of netrin-1 bound to two receptors provide insight into its axon guidance mechanism. Science, 344(6189), 1275–1279. (IF=34.7).

MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCES

Nicolas RENIER, PhD
Expertise in developmental biology, microscopy, histology, neuro-anatomy

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Sensory spinal signaling & descending control of locomotion

Claire Wyart's team investigates the neuromodulatory pathways in the brain and spinal cord and their effects on locomotion and posture. The team is particularly interested in sensory feedback and the descending command that triggers locomotion in the hindbrain by projecting onto spinal circuits.

The main objectives are:
- To study how inner physiological states via neuromodulation and release of peptides change the activity of brainstem neurons;
- To pursue the investigation of the mechanisms linking CSF and body-axis formation, scoliosis and host defense;
- To constitute novel translational paths providing insights into the mechanisms of recovery after torsion of the spine, spinal injury or pathogen invasion in the CSF.

MAJOR PUBLICATIONS (2018-2020)

1. Antinucci*, P, Dumitrescu*, AS, Deleuze, C, Morley, HJ, Leung, K, Hagley, T, Kubo, F, Baier, H, Bianco, IH#, Wyart, C#. A calibrated optogenetic toolbox of stable zebrafish opsin lines, eLife 2020;9:e54937.
2. Orts-Del'Immagine, A, Cantaut-Belarif, Y,*, Thouvenin, O, Roussel, J, Baskaran, A, Langui, D, Koeth, F, Bivas, P, Lejeune, FX, Bardet, PL, WYART C# [2020]. Sensory neurons contacting the cerebrospinal fluid require the Reissner fiber to detect spinal curvature in vivo. Current Biology 9;30(5):827-839.e4.
3. Thouvenin, O, Keiser, L, Cantaut-Belarif, Y, Carbo-Tano, M, Verweij, F, Jurisch-Yaksi, N, Bardet, PL, Van Niel, G, Gallaire, F, Wyart, C# [2020]. Origin and role of the cerebrospinal fluid bidirectional flow in the central canal. eLife, pii: e47699.
4. Sternberg, JR, Prendergast, AE#, Brosse, L, Cantaut-Belarif, Y, Thouvenin, O, Orts-Dell'Immagine, A, Castillo, L, Djenoune, L, Kurisu, S, McDearmid, JR, Bardet, PL, Boccara, C, Okamoto, H, Delmas, P, Wyart, C # [2018] Pkd2l1 is required for mechanoception in cerebrospinal fluid-contacting neurons and maintenance of spine curvature. Nature Communications 2018, 9:3804.
5. Cantaut-Belarif Y, Sternberg J, Thouvenin O, WYART C#, Bardet PL# [2018]. The Reissner fiber in the cerebrospinal fluid controls morphogenesis of the body axis [2018]. Current Biology 28:2479-2486.e4.

MAIN DOMAIN

NEUROPHYSIOLOGY

SUBDOMAIN

MOLECULAR & CELLULAR NEUROSCIENCE

Claire WYART, PhD
Biophysics, neuroscience, physiology, imaging

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PRINCIPAL INVESTIGATOR

- **Yasmine CANTAUT-BELARIF,** PhD
  Development, Genetics, Cell biology

AFFILIATED CLINICIANS

- **Hugues PASCAL-MOUSSELARD,** MD
  Human spinal cord

Gene and cell therapy

Nathalie Cartier's team develops gene therapy strategies for severe neurodegenerative diseases including Huntington's disease, spinocerebellar ataxias, Alzheimer's disease and genetic leukodystrophies. Research includes proof of concept in animal models and translational steps to clinical applications. The team aims to propose a phase I/II therapeutic trial in 2020 for Huntington disease. The team will also develop tools for the delivery of therapeutic molecules in the brain (use of microglia, optimization of AAV for intravenous administration, optogenerapy for time-controlled delivery).

MAJOR PUBLICATIONS

1. Nóbrega C, Mendonça L, Marcelo A, Lamazière A, Tomé S, Despres G, Matos CA, Mechmet F, Langui D, den Dunnen W, de Almeida LP, Cartier N, Alves S. Restoring brain cholesterol turnover improves autophagy and has therapeutic potential in mouse models of spinocerebellar ataxia. Acta Neuropathol. 2019 Nov;138(5):837-858.
2. Boussicault L.*, Alves S.*, Lamazière A., Planques A., Heck N., Moumné L., Despres G., Bolte S., -Hue A., Pagès C., Galvan L., Piguet F., Aubourg P., Cartier N.*, Caboche J.* and Betuing S.*. Cyp46-A1, the rate-limiting enzyme for cholesterol degradation, is neuroprotective in Huntington's Disease. Brain 2016 Mar;139(Pt 3):953-70.
3. Fol R., Braudeau J., Ludewig S., Abel T., Weyer S.W., Roederer J.P., Brod F., Audrain M, Bemelmans A.P., Buchholz C.J., Korte M., Cartier N.*#, Müller U.C.*#. Viral gene transfer of APPsy rescues synaptic failure in an Alzheimers disease mouse model. Acta Neuropathol. 2015 Nov 4.
4. Burlot M.A., Braudeau J., Michaelsen-Preusse K., Potier B., Ayciriex S., Varin J, Gautier B., Djelti F., Audrain M., Dauphinot L., Fernandez-Gomez F.J., Laprévote O., Bièche I., Auzeil N., Potier M.C., Dutar P., Korte M., Buée L., Blum D., Cartier N. Cholesterol24-hydroxylase defect is implicated in memory impairments of Alzheimer-like Tau pathology. Hum Mol Genet. 2015: 24: 5965-76.
5. Djelti F., Braudeau J., Hudry E., Dhenain M., Varin J., Bièche I., Marquer C., Chali F., S Ayciriex, Auzeil N., Alves S., Langui D., Potier M.C., Laprevote O., Vidaud M., Duyckaerts C., Miles R., Aubourg P.*, Cartier N.* Cholesterol-24-hydroxylase (CYP46a1) inhibition and accumulation of neuronal cholesterol in hippocampus leads to amyloid production, neurodegeneration and paves the way for Alzheimer's disease. Brain 2015: 138: 2383-98.

MAIN DOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

SUBDOMAIN

MOLECULAR & CELLULAR NEUROSCIENCE

Nathalie CARTIER, MD, PhD
Gene and therapy for rare diseases

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PRINCIPAL INVESTIGATORS

- **Françoise PIGUET,** PhD
  Gene therapy for rare diseases
- **Corinne BESNARD-GUERIN,** PhD
  ALS physiopathology

AFFILIATED CLINICIANS

- **Caroline SEVIN,** MD
  Gene therapy for leukodystrophies
- **Michel ZERAH,** MD, PhD
  In vivo clinical gene therapy for CNS diseases in patients (MLD, MPS3A, MPS3B) and preclinical work in primate; neurocsurgery delivery clinical protocols
- **Arthur ANDRE,** MD
  Primate experiments and clinical program for Huntington's disease
- **Timothée DE SAINT DENIS,** MD
  Primate experiments and neurosurgery delivery clinical protocols

Alzheimer's disease and prion diseases

The team has a strong background in Alzheimer's disease and prions diseases and brings together researchers specialized on both diseases with the complementary skills and strategies to foster emerging approaches and study common mechanisms. It notably relies on the central role of the investigators in brain banking (Neuro-CEB) and national centers of reference for prion diseases, and on the transversal knowledge from neuropathology to animal and cellular models both in Alzheimer and in prion's fields.

The scientific objectives of the team have been to study (i) mechanisms of misfolded proteins production and toxicity associated to Aß and prion pathologies with a specific focus on the role of lipids, particularly cholesterol and ApoE in AD; (ii) amyloid and tau pathologies interplay; (iii) seeding and spreading of prion and Alzheimer's pathologies including the characterization and understanding of of the strain phenomenon and (iv) to develop innovative approaches for the diagnosis and treatment of both diseases.

To reach these goals the team set up transversal approaches combining complementary expertise and technology including (i) cellular models of prion propagation and Aß production and spreading; (ii) protein misfolding amplification technologies; (iii) mouse and C. elegans models of misfolded proteins propagation and toxicity at the functional and neuropathological levels with a special focus on early events; (iv) clinical, genetic and post-mortem studies in patients for translating the team's results to diagnosis and treatments in Alzheimer and prion's diseases.

The involvement of the team in innovative approaches and translational research is exemplified by (i) numerous collaborations with industrials and biotechs; (ii) patents on technologies and treatments, one of them awarded by the CNRS Cristal Medal; (iii) transfer of technology through licensing of patent to the industry (SATT Lutech Trophées 2017).

MAJOR PUBLICATIONS

1. Brandel JP, Bustuchina-Vlaicu M, Culeux A, Belondrade M, Bougard D, Grznarova K, Denouel, A, Plu I, Bouaziz-Amar E, Seilhean D, Levasseur M & Haïk S. Variant Creutzfeldt-Jakob Disease Diagnosed 7.5 Years after Occupational Exposure. N Engl J Med. 2020 Jul 2;383(1):83-85.
2. Thierry M, Boluda S, Delatour B, Marty S, Seilhean D; Brainbank Neuro-CEB Neuropathology Network, Potier MC, Duyckaerts C. Human subiculo-fornico-mamillary system in Alzheimer's disease: Tau seeding by the pillar of the fornix. Acta Neuropathol. 2020 Mar;139(3):443-461.
3. Xicota L, Ichou F, Lejeune FX, Colsch B, Tenenhaus A, Leroy I, Fontaine G, Lhomme M, Bertin H, Habert MO, Epelbaum S, Dubois B, Mochel F, Potier MC; INSIGHT study group. Multi-omics signature of brain amyloid deposition in asymptomatic individuals at-risk for Alzheimer's disease: The INSIGHT-preAD study. EBioMedicine. 2019 Sep;47:518-528.
4. Androuin A., Potier B., Nägerl U.V., Cattaert D., Danglot L., Thierry M., Youssef I., Triller A., Duyckaerts C., El Hachimi K.H., Dutar P., Delatour B., Marty S. Evidence for altered dendritic spine compartmentalization in Alzheimer's disease and functional effects in a mouse model. Acta Neuropathol. 2018 Jun;135(6):839-854.
5. Haik S., Marcon G., Mallet A., Tettamanti M., Welaratne A., Giaccone G., Azimi S., Pietrini V., Fabreguettes J.R., Imperiale D., Cesaro P., Buffa C., Aucan C., Lucca U., Peckeu L., Suardi S., Tranchant, C., Zerr, I., Houillier, C., Redaelli, V., Vespignani, H., Campanella A., Sellal, F., Krasnianski, A., Seilhean, D., Heinemann, U., Sedel, F., Canovi, M., Gobbi, M., Di Fede G., Laplanche J.L., Pocchiari M., Salmona M., Forloni G., Brandel J.P. & Tagliavini F. (2014) Doxycycline in Creutzfeldt- Jakob disease: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet Neurol. 13, 150- 158.

MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCE

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Marie-Claude POTIER, PharmD, PhD
Molecular and cellular biology, Down syndrome and Alzheimer's disease

Stéphane HAIK, MD, PhD
Neurobiology & neurology of prion and prion-like disorders

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PRINCIPAL INVESTIGATORS

- **Nicolas BIZAT,** PhD
  C.Elegans model
- **Jean-Léon THOMAS,** PhD
  Cellular and molecular mechanism, neurovascular system, in vivo models
- **Benoit DELATOUR,** PhD
  In vivo rodent models, behavior, histology, stereotaxy
- **Serge MARTY,** PhD
  Histology, electron microscopy, synapse
- **Susana BOLUDA,** MD, PhD
  Neuropathology, in vivo models of propagation
- **Jean-Philippe BRANDEL,** MD
  CJD neurology and epidemiology
- **Charles DUYCKAERTS,** MD, PhD
  Neuropathology
- **Jean-Maurice DELABAR,** PhD
  Down syndrome

RESEARCH TEAMS

Experimental neurosurgery

Brian Lau & Carine Karachi's team aims to characterize the subcortico-cortical anatomy and physiology of brain networks involved in motor control, with the long-term goal of developing new therapies including novel applications of deep brain stimulation (DBS).

The team's future research is focused on:
- Anatomo-functional comprehension of networks involving DBS targets;
- Comprehension of these targets using behavioral tasks coupled with electrophysiology;
- Development of new therapies such as understanding how neurofeedback can be used to ameliorate movement disorders in Parkinson's disease.

MAJOR PUBLICATIONS

1. Lau B., Meier N., Serra G., Czernecki V., Schuepbach M., Navarro S., Cornu P., Grabli D., Agid Y., Vidailhet M., Karachi C., Welter M.-L. (2019): Axial symptoms predict mortality in patients with Parkinson disease and subthalamic stimulation. Neurology. 92: 2559-2570.
2. Karachi C., Cormier-Dequaire F., Grabli D., Lau B., Belaid H., Navarro S., Vidailhet M., Bardinet E., Fernandez-Vidal S., Welter M.-L. (2019): Clinical and anatomical predictors for freezing of gait and falls after subthalamic deep brain stimulation in Parkinson's disease patients. Parkinsonism & Related Disorders. 62: 91-97.
3. Sébille S.*, Rolland A.-S.*, Faillot M., Perez-Garcia F., Colomb-Clerc A., Lau B., Dumas S., Fernandez Vidal S., Welter M.-L., Francois C., Bardinet E., Karachi C. (2019): Normal and pathological neuronal distribution of the human mesencephalic locomotor region. Movement Disorders. 34: 218-227.
4. Welter M.-L., Houeto J.L., Thobois S., Bataille B., Guenot M., Worbe Y., Hartmann A., Czernecki V., Bardinet E., Yelnik J., Tezenas du Montcel S., Agid Y., Vidailhet M., Cornu P., Tanguy A., Ansquer S., Jaafari N., Poulet E., Serra G., Burbaud P., Cuny E., Aouizerate B., Pollak P., Chabardes S., Polosan M., Borg M., Fontaine D., Giordana B., Raoul S., Rouaud T., Sauvaget A., Jalenques I., Karachi C., Mallet L., for the STIC study group. (2017): Anterior pallidal deep brain stimulation for Tourette's syndrome: a double-blind randomized parallel controlled trial. Lancet Neurology. 16:610-619.
5. Sébille S.*, Belaid H.*, Philippe A., André A., Lau B., François F., Karachi C., Bardinet E. (2016): Anatomical evidence for functional diversity in the mesencephalic locomotor region of primates. NeuroImage. 147: 66-78.
6. Lau B., Welter M.-L., Belaid H., Fernandez Vidal S., Bardinet E., Grabli D., Karachi C. (2015): The integrative role of the pedunculopontine nucleus in human gait. Brain. 138: 1284–1296.

MAIN DOMAIN

NEUROPHYSIOLOGY

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Brian LAU, PhD
Neurophysiology

Carine KARACHI, MD, PhD
Neurosurgery, anatomy, models of Parkinson's Disease.

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PRINCIPAL INVESTIGATORS

- **Marie-Laure WELTER,** MD, PhD
  Human intracranial electrophysiology, biomechanics
- **Nathalie GEORGE,** PhD
  EEG-MEG brain imaging

Myelin plasticity and regeneration

Brahim Nait Oumesmar & Violetta Zujovic's team aims at providing better insight into the mechanisms of myelin plasticity and regeneration. Compelling evidences indicate that oligodendrocyte progenitor cells (OPCs) sense neuronal activity and immune cells signaling, highlighting the importance of these crosstalk's in (re)-myelination.

Therefore, our research project will rely on three major aims to decipher:
- The role of 1) neuronal activity and 2) immune cells in oligodendrocyte differentiation, regeneration and myelin repair, unraveling their relevance in human oligodendrocyte differentiation;
- To develop innovative tools to identify and assess the therapeutic value of new pro-myelinating compounds.

MAJOR PUBLICATIONS

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2. Chew LJ, Ming X, McEllin B, Dupree J, Hong E, Catron M, Fauveau M, Nait-Oumesmar B, Gallo V (2019) Sox17 Regulates a Program of Oligodendrocyte Progenitor Cell Expansion and Differentiation during Development and Repair. Cell Rep 29(10):3173-3186.
3. Garcia-Diaz B, Bachelin C, Coulpier F, Gerschenfeld G, Deboux C, Zujovic V, Charnay P, Topilko P, Baron-Van Evercooren A (2019) Blood vessels guide Schwann cell migration in the adult demyelinated CNS through Eph/ephrin signaling. Acta Neuropathol. 138(3):457-476.
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5. El Behi M.*, Sanson C.*, Bachelin C., Guillot-Noël L., Fransson J., Stankoff B., Maillart E., Sarrazin N., Guillemot V., Abdi H., Cournu-Rebeix I.**, Fontaine B.**, Zujovic V.** (2015) Adaptive human immunity drives remyelination in a mouse model of demyelination. Brain 140(4):967-98. *Equally contributed

MAIN DOMAIN

CELLULAR & MOLECULAR NEUROSCIENCE

SUBDOMAIN

CLINICAL & TRANSLATIONAL NEUROSCIENCE

Brahim NAIT-OUMESMAR, PhD
Oligodendrocyte development and regeneration

Violetta ZUJOVIC, PhD
Immune cell functions in remyelination

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PRINCIPAL INVESTIGATORS

- **Anne BARON VAN-EVERCOOREN,** PhD
  Human stem/progenitor cells
- **Lamia BOUSLAMA,** PhD
  Developmental myelination

Cellular mechanisms of sensory processing

The human brain is composed by millions of neurons that communicate with each other using an even greater number of synapses. An open question is how those neurons with all its connections give rise to most of animal and human behavior? In the lab we investigate the cellular and network mechanisms at the origin of sensory perception.

From the drowsiness of a daydreaming commuter in his suburb train, to the heightened vigilance of a rock climber executing a difficult move, sensation during wakefulness takes place under drastically different conditions, themselves associated to various perceptual outcomes. A remarkable property of sensory systems is therefore to provide a flexible strategy to process afferent information in a context-dependent manner. Such a flexibility in the computation of incoming signals appears to be a key feature of cortical processing in the healthy brain. Indeed, reduced context-dependent sensory processing and adaptability underlies several brain disorders like Schizophrenia and Depression. Yet, the combination of circuit and cellular features shaping such modulations is still poorly understood.

In the lab we use a multidisciplinary approach, involving, electrophysiology, brain imaging (two-photon), optogenetics both in vivo and in vitro as well as computer modeling to understand how neuronal networks process sensory information and how this process is influenced by context. Working in the primary somatosensory cortex of mice we try to identify previously unnoticed cellular mechanisms that are essential for information processing by the brain.

Our goal is also to investigate how such cellular mechanisms are modified or altered in the pathological brain and eventually uncover new molecular targets with potential therapeutical value.

MAJOR PUBLICATIONS

1. Rebola N, Reva M, Kirizs T, Szoboszlay M, Lőrincz A, Moneron G, Nusser Z, DiGregorio DA. Distinct Nanoscale Calcium Channel and Synaptic Vesicle Topographies Contribute to the Diversity of Synaptic Function. Neuron. 2019 Nov 20;104(4):693-710.e9.
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5. Carta M*, Lanore F*, Rebola N*, Szabo Z, Viana Da Silva S, Lourenço J, Verraes A, Nadler A, Schultz C, Blanchet C, Mulle, C. Membrane lipids tune synaptic transmission by direct modulation of presynaptic potassium channels, Neuron. 2014, 81(4):787-99. *-Co-first authors
6. Rebola N, Carta M, Lanore F, Blanchet C, Mulle C. NMDA receptor-dependent metaplasticity at hippocampal mossy fiber synapses. Nature Neurosci. 2011Jun.;14(6):691–3.
7. Rebola N, Luján R, Cunha RA, Mulle C. Adenosine A2A Receptors Are Essential for Long-Term Potentiation of NMDA-EPSCs at Hippocampal Mossy Fiber Synapses. Neuron. 2008 Jan.;57(1):121–34.
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MAIN DOMAIN

NEUROPHYSIOLOGY

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Funding opportunities and prestigious prizes

International attractiveness

At Paris Brain Institute, we know that our diversity and strong ties with our collaborators around the world are a driving force to improve our work and make it more efficient. Our institute brings together individuals from 43 countries, committed to advancing brain research. More than 70% of postdocs are internationally recruited, from 40 nationalities. We build international cooperation with DRI-UK, DZNE-Germany, VIB- Belgium MNI Montreal, UCSF San Francisco, Yale - New Haven – USA, Stanford University – USA, MIT -USA, Florey Institute Melbourne. 62% of our funded research collaborations carried out with foreign institutions (2016-2018) and 40% of our industrial collaborations are with foreign companies. We host undergraduate students from Stanford Palo Alto, MIT Cambridge and St. John University New-York. Every year, the Paris Brain Institute is proud to welcome more than 80 invited speakers for high-level scientific lectures.

MAJOR GRANTS OBTAINED BY OUR RESEARCHERS

15 ERC + 2 POC grants
21 Marie Sklodowska-Curie Actions IF
2 ITN
17 FP7-H2020 (PHC, IMI, HBP)

107 ANR national grants
316 from national Associations foundations

55 Grants from internationally renowned foundations
6 NIH grants

SOME OF THE PRESTIGIOUS PRIZES WON BY OUR RESEARCHERS

Allen distinguished investigator award
Bassem Hassan, PhD

Roger de Spoelberg Prize
Bassem Hassan, PhD
Alexis Brice, MD

NYSCF Prize
Claire Wyart, PhD

Michael J. Fox Foundation's Edmond J. Safra Fellowship in Movement Disorders
Jean -Christophe Corvol, MD, PhD

International Peter and Patricia Gruber Award from the Society for Neuroscience
Julia Sliwa, PhD

Cor Baayen Young Researcher Award
Ninon Burgos, PhD

Inria - French Academy of Science Award
Stanley Durrleman, PhD

Inserm excellence Award
Mathias Pessiglione, PhD

Michael prize 2019 for Epileptology
Stéphanie Baulac, PhD

Prix Lamonica de Neurologie
Alexandra Durr, MD, PhD
Lionel Naccache, MD, PhD

Prix Halphen
Philippe Fossati, MD, PhD
Luc Mallet, MD, PhD
Mathias Pessiglione, PhD

Rita Levi-Montalcini Award
Benedetta Bodini, MD, PhD

Charcot Award from the Multiple Sclerosis International Federation (MSIF)
Catherine Lubetzki, MD, PhD

A community devoted to neuroscience

The AJITES, the Youth Organization and Associates

The AJITES association was founded in 2012. It is deeply involved in the organization of many activities for Paris Brain Institute's staff, both scientific and social, with a particular focus on PhD students and Post-doctorate fellows.

In particular, the association aims to help develop presentation skills by organizing annual scientific events such as the Best Poster Awards and a Workshop where PhD students and Postdoc get to present their projects on a casual and friendly atmosphere. The association also contributes to include the institute in the Paris scientific scene by inviting external speakers during a monthly Science-Pizza and organizing Professional Breakfasts with other scientific institute around the city. Furthermore, the association is deeply involved in giving a unique opportunity to Young Researchers to meet and interact with worldwide invited speakers over a casual lunch, every Monday. The association also aims to develop and tighten interactions on site, among Paris Brain Institute's staff, by offering frequent social events including Happy Hours and a photography contest, opened to all employees of the institute. Finally, the AJITES association contributes to the wellbeing of many at Paris Brain Institute by offering activities such as yoga, salsa dancing and theater.

The AJITES association is bringing a constant driving push to the institute by innovating and frequently presenting new ideas to energize the institute scientific and social life. For those constantly on the lookout for new projects and who enjoy meeting new people, Paris Brain Institute is a unique opportunity to think differently, open up our approach and ways of working, and to innovate. Working at the institute means belonging to something greater: a community dedicated to Neuroscience.

Education and training at the heart of the Institute's missions: The Open Brain School

To share knowledge at national and international levels, Paris Brain Institute created a training school, the Open Brain School, with the ambition to be a new international leader in neuroscience-based training. The Institute proposes to open up neuroscience education to people outside of research as well as continue developing training for the highly-skilled professionals in research and patient care through the Open Brain School. The long-term goal of Paris Brain Institute is to contribute to the training of both "neuro-citizens" and neuro-experts. To open neuroscience to people from diverse backgrounds interested in learning more about the brain and its role in our identity and our behavior and to provide high-quality training to brain researchers, doctors, and medical staff. One of the reasons for the creation of the Open Brain School is to consolidate and give more visibility to the Institute's educational programs both on national and international levels. The Open Brain School is organized around 4 pillars:

PILLAR 1
Dedicated to programs focused on research and cutting-edge technology

PILLAR 2
Dedicated to clinical and translational research

PILLAR 3
Dedicated to transversal expertise such as soft skills

PILLAR 4
Dedicated to new teaching methods and technologies

The International human resources office

With about 700 people of 43 nationalities working at Paris Brain Institute, our international human resources office is dedicated to support staff in all the procedures in relation with integration and daily life on all HR aspects: employment contract, remuneration, administrative formalities, training, career management...

CORE FACILITIES

Core facilities of Paris Brain Institute

The progress and quality of science depends as much on technological progress as it does on good ideas. At Paris Brain Institute, researchers and core facility managers work together to continuously monitor technological advances to offer the most advanced equipment and techniques operated by highly competent staff to move brain research forward.
Beyond providing innovative equipment, the mission of the core facilities at Paris Brain Institute is to pool skills and provide services and expertise for the entire scientific community: Institute research teams, external scientific teams, incubated companies and outside companies as well.
Basic equipment is distributed according to research areas and their scale of analysis: molecular exploration, cellular exploration, imaging, preclinical functional exploration, functional exploration, bioinformatics and biobanks.
The main activities of Paris Brain Institute are three-fold:

- Supplying equipment and services from project design to results analysis;
- Maintaining cutting-edge technological research and development in each area of expertise;
- Training for equipment use or implementing techniques.

10 Core facilities and biobanks

iGenSeq
Next generation sequencing of RNA and DNA

iVector
customized lenti, adenovirus, Crispr

CELIS
Screening, cell culture, iPSC, electrophysiology

Histomics
processing of histological animal and human material

ICMQuant
conventional fluorescence microscopy, microscopy confocal laser scanning, bi-photonic microscopy, confocal rotating disk microscopy or transmission electron microscope

PhenoPark
Preclinical functional exploration, behavioural analyses, surgery, electrophysiology

CENIR
Center for NeuroImaging Research:
3T MRI, PET-MRI, TMS, MEG-EEG, Gait analysis

PRISME
cognitive and social evaluation in ecological conditions and virtual reality

DAC
Genomics, Bioinformatics and Biostatistics

Biobanks
biological ressource collection, DNA, plasma, cells, brain tissue

© : N Renier

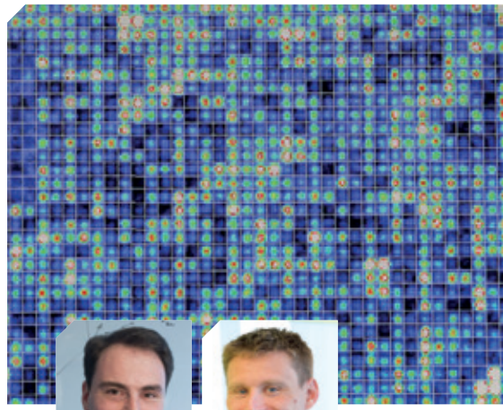
DAC

Data analysis core

The Data Analysis Core develops, maintains and makes available methods for analysis of brained focused data. It runs its own R&D, and assists scientists and clinicians in their research projects by providing both technological solutions and methodological expertise, from the experimental design of studies to data management, processing, integration and analysis, up to the interpretation of results.

These activities include:
- Data management support (curation, standardization, structuration, integration and visualization);
- Development and deployment of bioinformatics pipelines to process genetics and (epi)genomics data;
- Support in statistical analysis, including the development and application of advanced methods for the integrative analysis of multimodal data

DAC provides support ranging from mere consulting to basic bioinformatics and biostatistics services, up to full-scale scientific projects, on a collaborative basis. The IHU program supports this activity. Projects can be funded through joint grants or through fee-for-service.



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BIOBANKS

DNA & cell bank

Biological samples from blood, biopsies or surgery are a highly precious source of information for research on diseases. Founded in 1990, Paris Brain Institute DNA and cell bank is a Biological Resource Centre (BRC) which manages numerous collections of biological samples and associated data to enhance the medical research on neurological and psychiatric diseases.
The bank provides the technical support and expertise to collect samples, record, process, store and make them available to the scientific community, with certification of its NF S96-900 quality management since 2009. The collections gather a total of 62, 000 registered subjects, in cohorts among the largest of international ones for spinocerebellar degenerations (10,500), Parkinson's disease (6,700), psychiatric disorders (8,650) and frontotemporal dementia (5,950). Samples are mostly nucleic acids (DNA but also RNA), blood cells and fibroblasts, and biological fluids (plasma, serum and cerebrospinal fluid).

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CELIS

Cell culture core facility

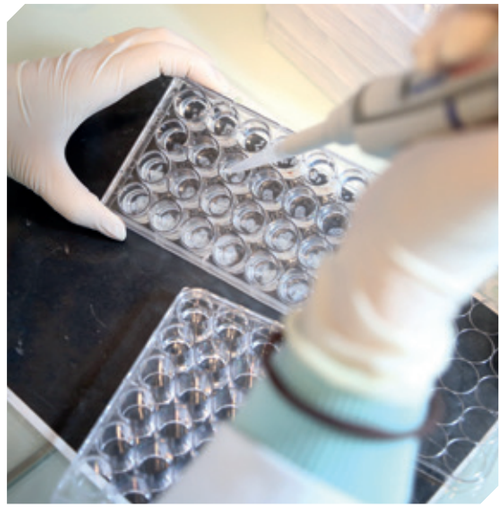
This core facility makes available a large panel of cell and tissue culture models and up-to-date equipment to academic researchers, biotech companies and industrials that pursue experimental projects on pathologies of the brain and spinal cord. The platform is structured around 3 types of activities:

- CELIS: Basic cell culture operations and high-content or conventional fluorescence imaging.
- CELIS iPS: induced-pluripotent stem cell production characterization along with genome editing.
- CELIS-ePhyS: recordings from isolated cells, brain slices and Zebrafish larvae.

The facility is supported by “Investissements d’avenir” IHU programme and NeurATRIS.

CELIS-cell culture

CELIS delivers full services in cell culture, providing training on equipment and scientific/technical assistance on demand, as well as fully equipped culture box and consumables and essential reagents, at cost price. Regarding its imaging operations, the core facility provides guidance in equipment selection for imaging, implementation of protocols for image acquisition with high-content imaging systems and other inverted microscopes, development of personalized analysis tools for cell/tissue culture samples and assistance with result interpretation and protocol writing.



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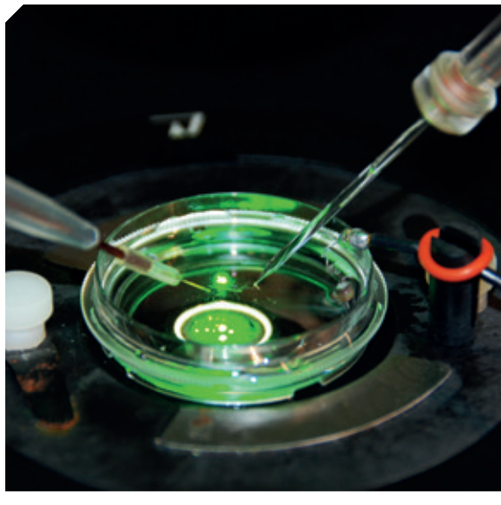
CELIS-ePhys

CELIS-ePhys is a core facility with extensive expertise and resources for in vitro electrophysiology and optogenetics. The facility is equipped with patch-clamp and multielectrode array (MEA) systems suitable for recordings from neuronal cultures, human induced pluripotent stem cells (iPSC)-derived neurons, rodent acute brain slice and zebrafish. The facility is involved in the characterization of electrophysiological aspects of both basic and clinical research projects. Part of CELIS-ePhys activity is dedicated to R&D. The IHU program funding supports this activity.



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Charlotte DELEUZE, PhD

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CELIS-iPS

Stem cells core facility

To model in a culture dish degenerative disorders of the brain and the spinal cord, CELIS-iPS produces and genetically modifies Human induced-pluripotent stem (iPS) cells. This aim is to better investigate the molecular and cellular mechanisms underlying these disorders and to develop a screening approach for drugs of therapeutical interest.

The specific goals of the core facility are three-fold:

1. To generate and characterize iPS cells through genetic reprogramming of skin or blood cells from patients and healthy volunteers;
2. To correct or introduce mutations of interest using CRISPR/CAS9 technology;
3. To offer access to a L2 cell culture box equipped for human iPSc culture.

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ICMQuant

Bioimaging core facility

This core facility makes available to academic researchers and industrial partners a large panel of imaging technologies. Optical microscopy part of the facility includes widefield, confocal (point-scanning and spinning disk), light-sheet and multiphoton microscopes. Electron microscopy part is equipped with a transmission electron microscope. All the imaging systems as well as the sample preparation spaces, devices and image processing computers are available for autonomous usage. Specific activities of ICM Quant staff include trainings and assistance as well as design of experimental procedures involving electron and photonic microscopy approaches. The facility is supported by Neuratris, a research infrastructure aiming to accelerate the translation of discoveries from basic research into medical innovations for treatment of nervous system diseases. The facility possesses the Ibisa national label and is a part of the Sorbonne Université network of the facilities.

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HISTOMICS

Histology core facility

Histomics is a technical support center open to researchers of the Paris Brain Institute and to academic/ industrial partners. It is accessible on a space-rent or service basis and uses standardized protocols and up-to date equipment for the processing of histological (animal and human) material. The staff offers technical and scientific support and services, to train users to histological techniques and to perform work for specific projects. Histomics facilitates translational research projects.

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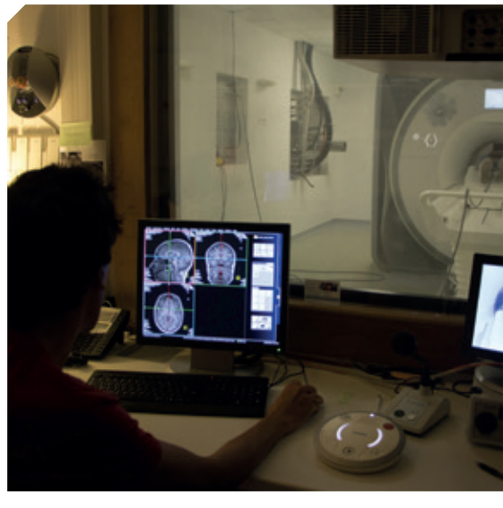
CENIR-MRI

Neuroimaging core facility

CENIR (Center for NeuroImaging Research) is the Paris Brain Institute main in vivo imaging core facility. With a set of expertise around neurological diseases, cognitive neuroscience and image analysis, it offers academic and industrial investigators high quality imaging tools for investigating the human brain and spinal cord. Personnel with complementary expertise (neuroimaging, neurology, neuroscience, MRI, MR spectroscopy, clinical trials, high intensity focused ultrasound, image processing, data analysis) design protocols and run the imaging equipment for more than 80 projects each year. The use of 3T MRI, focused Ultrasound techniques and MRI-compatible EEG creates the perfect environment to conduct neuroimaging projects.



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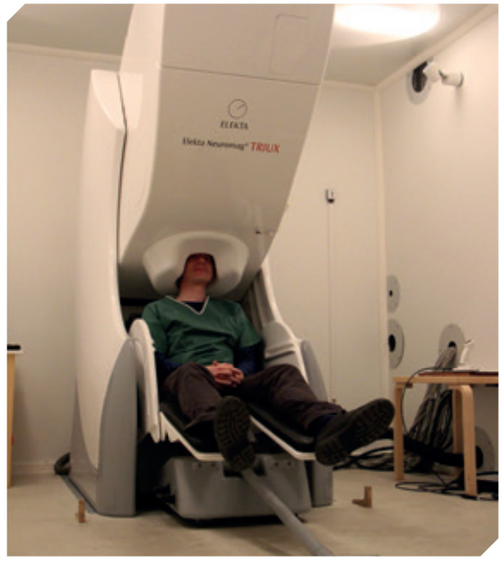
CENIR-MEG/EEG

MEG and EEG core facility

The CENIR Magnetoencephalography (MEG) and Electroencephalography (EEG) core facility is part of the Center for NeuroImaging Research (CENIR). The core facility aims to develop non-invasive methods that allow visualizing human brain activity on a millisecond time scale in normal or pathological conditions. With the latest equipment, the highly skilled team brings support to academic and industrial partners who wish to undergo clinical or fundamental research, at every stage of experimental protocols from study setup to advanced data processing, and develop integrated analysis tools for multi-level electrophysiological data. The CENIR MEG-EEG is part of the Paris Brain Institute core facility network (MRI, PANAM, PRISME...) which facilitates translational research projects.



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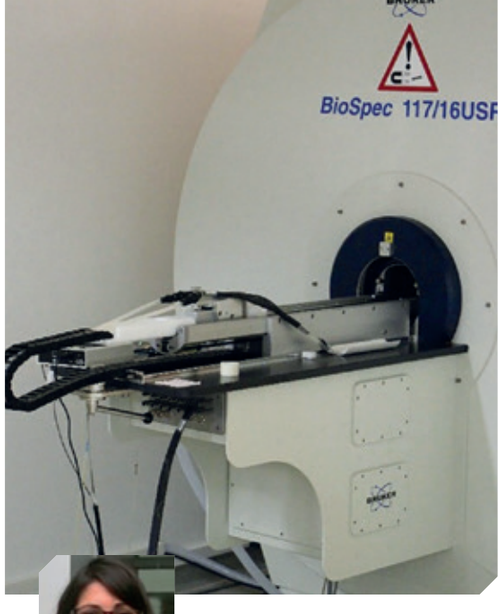
CENIR–SA MRI

Small animal MRI core facility

The SA MRI core facility is part of the Center for Neuroimaging Research (CENIR). This core facility is dedicated to imaging experimental models of diseases (mainly rodents and potentially any species small enough to fit inside the magnet). A very high magnetic field (11,7 T), associated with high quality probes (Cryoprobe™ for mice), a wide range of imaging protocols and support to data analysis, bring the quality needed for a small animal MRI core facility. CENIR-SA MRI is part of the Paris Brain Institute core facility network (PHENO-ICMice, PHENO-PRIMR...) which facilitates translational research projects.



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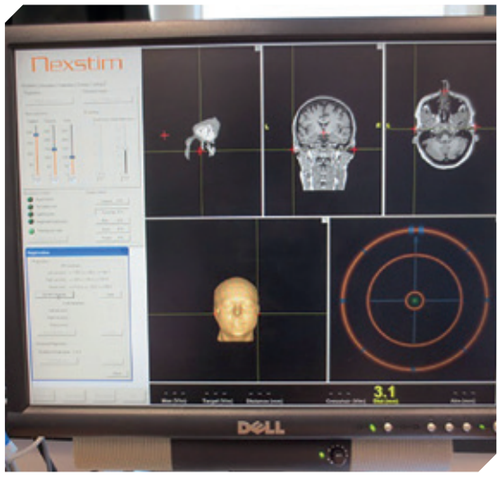
CENIR-PANAM

Physiology and analysis of movement core facility

The PANAM core facility is part of the Center for Neuroimaging Research (CENIR) and focuses on two axis:

1. Clinical research and therapeutics using non-invasive cerebral/spinal stimulations in neurological and psychiatric diseases;
2. The study of movement, gait and balance in patients with neurological diseases. In addition, the facility develops new technics of non-invasive cerebellar stimulation, TMS/MRI, LFP-EEG coupled recordings.



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CENIR-STIM

Stereotaxy core facility

STIM is part of the Center for Neuroimaging Research (CENIR) and is dedicated to supporting research done on stereotactic data. It provides specific software development, data analysis, and expertise in neuroimaging processing and electrophysiology. Its main application fields are deep brain stimulation (DBS), surgery (pre, per and post-operatively) and SEEG procedures.. The YeB Atlas, developed by Jérôme YELNIK and Éric BARDINET, is a strong support for data analysis. The core facility is involved in several DBS protocols in collaboration with other research institutes and industrials and coordinates the research protocols conducted on epileptic patients of the Pitié-Salpêtrière. Interaction with the Pitié-Salpêtrière hospital departments such as neuroradiology, neurosurgery and neurology, adds up to the expertise of the core facility. Stereotactic software and models developed by the STIM core facility are available to academic partners. CENIR-STIM is part of the Paris Brain Institute core facility network (MRI, MEG/EEG, PANAM, PRISME...) which facilitates translational research projects.

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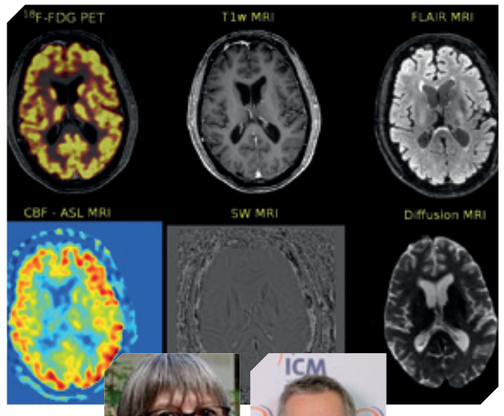
CENIR-PET MRI

Combined PET and MRI core facility

A hybrid PET/MRI scanner is available in the nuclear medicine department of the hospital La Pitié-Salpêtrière. Combining nuclear imaging with Magnetic Resonance Imaging (MRI) allows acquiring anatomical, functional and molecular images, thus providing a good anatomical reference for a better diagnosis, a shorter time spent in the scanner for the patient as well as a reduced radiation dose. This GE SIGNA integrated PET/ MR system allows simultaneous PET and 3T MR imaging without moving the subject in addition to being able to measure the time of flight of the PET emission data. The combination of PET and MR imaging raises new methodological challenges, like photon attenuation correction, but also offers new opportunities such as motion correction, MR-guided PET image reconstruction and multi-parametric imaging.



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PRISME

Human Behavior Core Facility

PRISME is the Paris Brain Institute core facility dedicated to the exploration of human behavior and cognition.

It supports cognitive neuroscience, clinical research, and industrial studies by providing testing rooms, data acquisition equipment, technical support, and scientific guidance. PRISME is unique for its focus toward developing human behavioral research with a high real-life translational prospect on human cognitive functions, motor performance, and social interactions. PRISME offers a variety of tools for experimental psychology and ambulatory physiological recordings in laboratory, semi-ecological as well as virtual environments.



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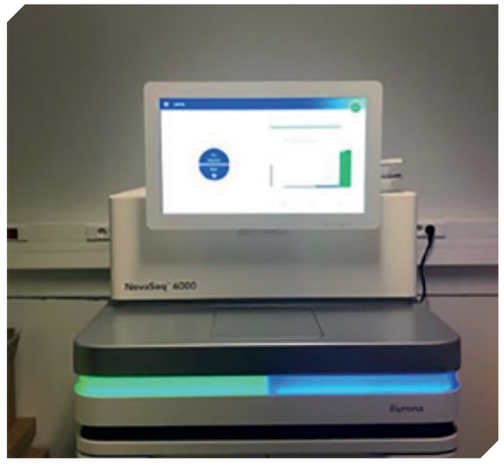
iGENSEQ

Genotyping and sequencing core facility

iGenSeq provides tools and services for genome analysis to academics or industrials. More specifically, services include real-time PCR, digital PCR, sequencing, 10X Genomics technology, as well as purification and analysis of nucleic acids. Each project submitted to the core facility is discussed with the investigator to optimize the design, the feasibility and the cost. This core facility has expertise with high throughput and single cell sequencing.

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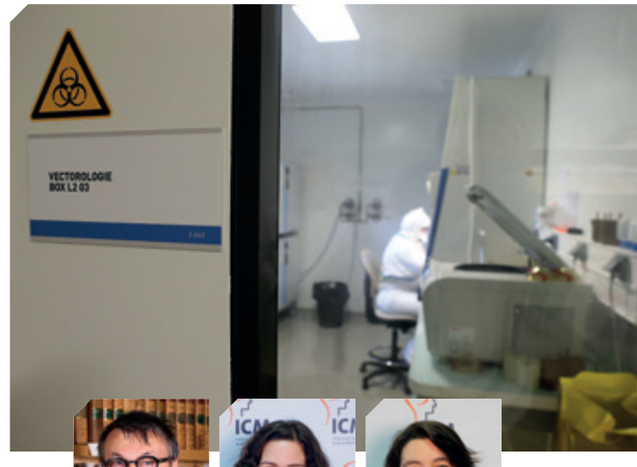
iVECTOR

Vectorology core facility

The Vector core facility produces viral tools for gene transfer highly concentrated under different scales. iVector is specialized in lentiviral systems. Since the use of adenoviruses and AAV systems in the field of research in neurobiology is constantly increasing, iVector has developed production of AAV (serotypes 1, 2, 5, 6, 7, 8, r10, PHP-eB, PHP-A, PHP-S, retro2) in addition to its lentiviral system. iVector is making these tools available for any academic and indus- trial partner. iVector implements continuously in his ser- vices portfolio gene transfer innovative technologies (ie: CRISPRs, Split-reporters, DNA/RNA based libraries...) to allow new approaches in basic research and lead to new applications in genetic engineering, curative and regenerative medicine (gene and cell therapy, tissue engineering and vaccines). iVector premises for production and manipulation of viral particles were designed to match both Biosafety Level 2 (BSL2) and Biosafety Level 3 (BSL3) in accordance to national and European regulations. We have access to, we develop, a large and various collection of viral vectors that allows us to provide quickly a tailored solution that fits researchers' needs.





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PHENOPARC

Preclinical functional exploration

The preclinical functional exploration core facility houses experimental animals and contributes to the development of research projects involving experimentation on animal models. Studies on these models profit from multiple techniques: behavioral analyses, surgery and electrophysiology. The equipment and the experts present on the core facility provide very high-quality support for teams inside and outside the Paris Brain Institute.




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CLINI-CAL RE-SEARCH

Clinical research at Paris Brain Institute

Clinical Research is one of the major activities of Paris Brain Institute. The Institute is located in Pitié-Salpêtrière University Hospital, one of the largest university hospitals in Europe dedicated to neurological diseases.

Neurology-related clinical research programs at Paris Brain Institute, aim at better understanding the physiopathology of the diseases, identifying potential biomarkers or targets, and learning about long-term outcomes in order to propose new diagnostic and therapeutic strategies.

The Institute uses the latest cutting-edge genetic, biochemical, neuropsychology and neuroimaging technology available to study various neurological and psychiatric disorders. Several first-class scientific research teams in a rich variety of related research fields — from cognition to neuroimaging to genetics — work from bench to bedside. Long-term cohorts are constituted and therapeutic clinical trials are conducted to test new molecules or novel technologies. Our unique environment allows preclinical researchers and clinical scientists to better collaborate and work together. This enables living growing translational research supported by private-public partnerships to improve human health and treat disease.

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CIC: The Clinical Investigation Centre

The CIC is a clinical research platform at the interface between Paris Brain Institute's researchers, the neurologists and psychiatrists of the medical-university neurosciences department. The CIC is also highly involved in national and international clinical research networks. It is an outstanding gateway between research and care, offering innovative treatments to patients affected by neurological and psychiatric diseases, with 143 ongoing clinical trials in 2020.

The CIC activity is connected to the neurological care units of the Pitié-Salpêtrière University Hospital, and to the co-localized core facilities, including the most advanced tools such as EEG, MEG, 3T MRI and a PET-MRI scan. The CIC collaborates with preclinical groups and core facilities, promoting innovative and active translational research.

The Neuroscience Medical-University Department (DMU)

The Neuroscience Medical-University Department includes 13 services or departments, for a total of 34 functional units. It is made up of 4 pillars:

- "Neurology" (Saint Antoine and Pitié-Salpêtrière hospitals);
- "Adult Psychiatry - Addictology" (Saint Antoine, Tenon, Pitié-Salpêtrière, Charles Foix hospitals);
- "Physical medicine rehabilitation, Follow-up rehabilitation care (MPR-SSR)" (Rothschild and Pitié-Salpêtrière hospitals);
- « Neurophysiology-neuropathology" (Saint Antoine, Pitié-Salpêtrière, Charles Foix hospitals).

The Neuroscience DMU has the considerable advantage of having a very strong thematic consistency and backing by very large research institutions (Paris Brain Institute, Institute of Myology), and of being part of the Paris Brain Institute, the only Neuroscience IHU in the country. The integration of new units is an opportunity. By strengthening the adult psychiatry-addiction and MPR-SSR units, it becomes possible to develop a true "pillar-based strategy" for the fields of "adult psychiatry" and "Physical medicine and rehabilitation", alongside the already large "Neurology" pillar.

The department has 541 beds and spots, 249 medical staff and 1054 paramedical and administrative staff. The DMU also takes part in 14 rare disease reference centers (including 8 as coordinator or constitutive center) and 2 rare cancer reference centers (coordinators).

"Clinical and basic research is above all research! In both cases, there is a question asked, a methodology that must be strict in order to have interpretable results and a team. It is also an asset of the Paris Brain Institute to get clinicians and researchers working together. To work together, it is essential to know each other, to know what the other is doing. Each must nourish the other. The iCRIN, Paris Brain Institute's Neuroscience Clinical Research Infrastructures, are truly a springboard for attracting clinicians and caregivers to research."

Prof. Catherine Lubetzki, Director of the University Medical Neurosciences Department of the Pitié-Salpêtrière Hospital and Medical Director of the Paris Brain Institute.

iCRIN: The Paris Brain Institute Clinical Research Network

The aim of iCRIN infrastructures is to develop interactions and knowledge-sharing between team members of the Neuroscience Medical-University Department and Paris Brain Institute research teams. The winners of this call for projects received "Clinical research infrastructure of the Paris Brain Institute" certification paired with funding to develop their project within the hospital.

The launch of the iCRINs now makes it possible to support numerous clinical research projects in the clinical services of the Neuroscience Medical University Department directly or indirectly linked to the Paris Brain Institute. This adds to the Institute's historical partner services new prospects for collaboration with other services at the Pitié-Salpêtrière Hospital (sleep, neurosurgery) but also at Saint Antoine (psychiatry, neurology, addictology), Rothschild Hospital (rehabilitation) and Tenon Hospital (outpatient psychiatry). Paris Brain Institute's Clinical Investigation Centre team coordinates this activity by organising monthly meetings with the ICRIN referents for each theme to share experience, set up common procedures and report activity indicators.

Alzheimer and associated diseases

In collaboration with that the Institute of Alzheimer and Associated diseases (IM2A), this project aims to prepare to the development of curative treatment in neurodegenerative dementias. IM2A has a longstanding expertise in the domain of care management of dementias, a very important flow of patients and a tight relationship with research teams and core facilities, at the Paris Brain Institute.

The goals are three-fold:
- Identify new cognitive markers based on our recognized expertise in the field of cognition, neuropsychology and behavior and also clusterizing specific populations of patients;
- Reciprocal transfer of knowledge from bench to beside and vice versa through dialogue with fundamental research team;
- Develop clinical applications, by increasing preclinical and clinical trials, and proof of concepts studies.

For that, we are building-up and following-up cohorts of patients suffering from neurodegenerative diseases (NDs), diagnosed with a high degree of certainty and for whom a comprehensive and homogeneous set of clinical, biological and neuroimaging data will be organized into an easily accessible databank.

COORDINATOR

Richard LEVY, MD, PhD

Parkinson's disease and movement disorders

The iCRIN dedicated to Parkinson's disease and movement disorders benefits from synergies between the two ICM teams dedicated to these topics: (i) Molecular Pathophysiology of PD led by Prof Corvol and Dr Corti and (ii) Normal and abnormal motor control: movement disorders and experimental therapeutics led by Prof Vidailhet and Prof Lehéricy. These teams share common approaches to empower clinical research.

The two main axes of clinical research are:
- Identification of clinical/genetic/brain imaging markers of disease severity, disease progression and drug response in PD;
- Deciphering pathophysiological mechanisms underlying behavioral and high order motor control disorders in rare human movement disorders.

COORDINATOR

David GRABLI, MD, PhD

Amyotrophic lateral sclerosis

The Paris ALS/MND center is one of the most important ALS centers in Europe both in terms of new patients and caseload; it is dedicated to providing excellence in clinical care for patients with ALS and other motor neuron diseases, researching the causes and finding treatments. The Paris ALS reference center has fruitfully collaborated with several members of Dr Boillée's research team at the Paris Brain Institute for several years.

The clinical research project is made of four axis:
- Elucidate the initial trigger of ALS and identify biomarkers;
- Understand the spreading phenomenon of motor neuron dysfunction;
- Uncover the molecular mechanisms by which compensatory reinnervation, a critical process for motor function and survival, is maintained over time in some ALS patients;
- Study the effect of focused ultrasounds for blood brain barriers opening in ALS.

COORDINATOR

François SALACHAS, MD

Neurological intensive care

The Neurological Intensive Care Unit is a unique structure, highly experienced in the acute care of severe neurologically ill patients, presenting with peripheral and/ or central nervous system disease. Its clinical research activity focuses on four major pathologies, in close collaboration with teams from the Paris Brain Institute:

- Disorders of consciousness: multimodal assessment (e.g. dedicated clinical scales, HD-EEG, evoked potentials, MRI, PET-scan) to better categorize the patients' consciousness state and track recovery and stimulation of brain activity to improve recovery, in collaboration with Prof Naccache's team.
- Status epilepticus: conduct diagnostic and therapeutic studies and original bench to bedside researches (in collaboration with Prof Charpier & Prof Navarro's team).
- Encephalitis: develop early diagnosis and therapeutic strategy for the outcome of these severe diseases, both in terms of mortality and neurological sequelae.
- Myasthenia Gravis: creation of a large database for clinical and therapeutic studies in this rare disease.

COORDINATOR

Sophie DEMERET, MD

Neurosurgery

The neurosurgical department of the Pitié-Salpêtrière Sorbonne University hospital performs more than 4,000 surgical procedures per year in 10 different clinical/ research activities, in strong collaboration with several other clinical departments of the Pitié-Salpêtrière but also in Europe and in the USA. Nearly all of the clinical activities have research programs with specific research teams and core facilities from the Paris Brain Institute.

The research strategy aims to insure the development and maintenance of multimodal databases (big data) and the feasibility of future clinical trials. The goal is also to reinforce five major lines of research:
- Factors predicting morbimortality in cohorts of patients with brain tumors and in patients with aneurysms;
- New deep brain stimulation targets and brain-machine interfaces;
- Blood brain barrier opening in various intractable pathologies;
- New therapeutic approaches for meningiomas;
- Ex vivo human tissue for cellular electrophysiology.

COORDINATORS

Carine KARACHI, MD, PhD
Alexandre CARPENTIER, MD, PhD

Neurogenetics

The clinical research core facility NEUROLOP aims to enhance clinical research spanning phenotypes from fetus to adults, by reunifying data, samples and organizing therapeutic trials. NEUROLOP will tackle three disease groups: Huntington disease, spinocerebellar ataxias and intellectual deficiencies. Metabolic dysfunctions are implicated in all three groups, at different levels and sometimes solely responsible for the phenotype.

The final goal is to create an infrastructure dedicated to clinical research including actors from the Hospital and the Paris Brain Institute. It will increase exchange between clinicians actively involved in:
- Clinical deciphering of phenotypic spectra of the same genes involved at birth and an adult age;
- Search for clinical, imaging, biological and genetic biomarkers;
- Therapeutic trials in small cohorts of rare diseases with adaptive and innovative designs;
- Transition of developmental defects to neuro- degeneration in link with fundamental research.

COORDINATOR

Alexandra DURR, MD, PhD

Neuro-oncology

The neuro-oncology department, headed by Prof Hoang- Xuan, is a leading center for clinical and translational research in neuro-oncology in Europe. Indeed, it launches clinical trials contributing to define standard of care and is one of the most important contributors in academic and industrial multicenter clinical trials in neuro-oncology. The group has optimal resources to develop bench to bedside programs, including a dedicated research team at the Paris Brain Institute (headed by Pr Sanson and Dr Huillard, a unique tumor bank connected to a clinic-biological database (Onconeurotek), a preclinical therapeutic research group for gliomas (GlioTex, headed by Prof Idbaih) and an Institut National du Cancer-certified for early phase clinical trials and cancer innovative therapies (CLIP2 Galilée).

The current projects are to strengthen the link between clinics, clinical research, translational research and basic research, to accelerate the transfer of innovations from the laboratory to clinical applications, by identifying new biomarkers and innovative therapies, and to enlarge translational research to yet underexplored fields.

COORDINATOR

Ahmed IDBAIH, MD, PhD

Stroke

The Pitié-Salpêtrière Stroke center has been involved in many of clinical trials as well as in various registries of patients, crucial to monitor the safety/efficacy profile of the intensive care unit, build prognosis models, and in many academic research projects. The overall goal of this iCRIN is to develop pathophysiological and therapeutic research on acute stroke but also on functional recovery at the subacute and chronic stages by combining the strength and the knowledge of both the Paris Brain Institute and the stroke center. More specifically:

- Participation/coordination of Randomized Controlled trials (RCTs) and use big data to build a dynamic disease prognostic model of stroke outcome;
- Identification of new structural and functional markers for stroke outcome (independency, motor and language, motivation, and ethics);
- Development of innovative therapeutic approaches in recovery and secondary prevention such as non-invasive brain stimulation techniques, ludic and innovative strategies in recovery (serious games, neurofeedback) or pharmacological treatment in restorative strategies.

COORDINATORS

Yves SAMSON, MD
Charlotte ROSSO, MD, PhD

Orthopedic surgery

The Orthopedic department at the Pitié-Salpêtrière hospital is known in the surgical community as a reference in various surgical fields: spine surgery and sport surgery being the major two. The clinical project focuses on three major topics:

- The genetic etiology of idiopathic scoliosis, in collaboration with the Dr Wyart's team at the Paris Brain Institute;
- Implement a systematic record of neurologic status data, before and after surgery (at different times: immediate post-operative, each consultation) to all patients of the Spine-Unit; and to computerize all these data, in order to facilitate current and further studies;
- Develop various protocols of prospective analysis by linking neuroscience and sports surgery (proprioceptive analysis of the etiologies of ACL rupture), or to spinal cord injuries.

COORDINATOR

Hugues PASCAL-MOUSSELARD, MD, PhD

Adult psychiatry

The iCRIN Psychiatry proposes a multimodal approach combining brain stimulation with other therapeutic options (i.e. pharmacotherapy or psychotherapy) in addition to the usual recommended treatments with the permanent concern to reciprocally benefit both clinical practice and research. It represents a strong interface between clinical departments and the Paris Brain Institute for basic research, more specifically with the "Control—Interoception—Attention" team, headed by Prof Fossati and Dr Schmidt. The objective is to articulate brain basic pathophysiological knowledge with innovative therapeutic strategies for the improvement of mental disorder outcomes. The iCRIN focuses more specifically on the cortico-striatal circuitry due to its particular importance in the pathogenesis of these disorders and by the ability of stimulation technique to correct these dysfunctions. Two streams of research are currently explored:

- Development of pragmatic trials in disorders related to stress dysregulation such as Post-Traumatic Stress Disorder (PTSD);
- Exploration of networks' neuromodulation in psychiatric and substance use disorders (SUD).

COORDINATOR

Bruno MILLET, MD, PhD

Traumatic brain injuries

New approaches to integrate data from multiple source are crucial to monitor brain vulnerability, individual trajectories and the course of traumatic brain injuries (TBI) at large over time, including, but not limited to, three pillars: genomics and biological biomarkers, MRI, clinical markers and social-economic determinants.

Directly stemming from its local (Pitié-Salpêtrière Hospital, Sorbonne University & Paris Brain Institute), regional, national and international expertise and collaboration networks, the iCRIN for TBI aims to address these multiple challenges with the objective to:

- Structure and expand an expert phenotyped prospective follow-up cohort of persons with TBI (TBI-multimodal registry);
- Develop modeling of multidomain outcomes, including use of statistical learning technics leveraging excellent collaborations that have been tied over years.

COORDINATOR

Éléonore BAYEN, MD, PhD

Multiple sclerosis

The clinical research activity dedicated to multiple sclerosis associates different structures: a research team at the Paris Brain Institute, coordinated by Prof Lubetzki and Prof Stankoff, the clinical investigation center and the imaging core facilities. These structures are closely linked to the Pitié-Salpêtrière MS clinic and the joint St Antoine and Pitié-Salpêtrière CRC (resources and competences center) labeled in 2017, gathering an active file of 4,000 patients.

The goals are to achieve:

- Translational development of remyelination strategies to prevent disability progression, based on molecules or pathways identified in experimental models;
- Development of novel imaging tools to evaluate these repair strategies in patients with MS;
- Development of new imaging methods centered on the use of PET scan imaging to tackle the innate immune system activation;
- Optimization and enlargement of several cohorts;
- Development of academic and industry supported therapies impacting the immune system;
- Detection and understanding of the pathophysiology of some MS symptoms, such as respiratory symptoms, and developing novel connected tools for a more accurate evaluation of disability evolution.

COORDINATORS

Catherine LUBETZKI, MD, PhD
Bruno STANKOFF, MD, PhD

Sleep

In the rapidly evolving field of sleep physiology and medicine, this center tightly couples medical care and clinical research. Plus, being a sleep center in the Paris hospital with the highest number of neurological patients and departments, allows to develop a sleep medicine and a clinical research based on neurological sleep disorders, with the idea of optimal diagnosis and treatment, but also using these neurological disorders as models to under- stand normal sleep mechanisms.

As National Reference Center for Rare Hypersomnias, it takes in charge the highest number of patients with rare hypersomnias (narcolepsy, idiopathic hypersomnia and Kleine-Levin syndrome). Research is focused on:

- Better describing the semiology of these disorders, their genetic, neurophysiological and brain imaging markers, and their optimal treatment;
- Understanding the mechanisms of normal sleep and dreaming;
- Determine if a function (e.g., memory, insight, emotion desensitization) is linked to Non-REM or REM sleep;
- Study preclinical neurodegeneration and try neuro- protective approaches in patients with idiopathic RBD (prodrome of Parkinson's disease and dementia with Lewy bodies), reaching the general interest of all the Movement Disorders teams of the Paris Brain Institute.

COORDINATOR

Isabelle ARNULF, MD, PhD

The Paris Brain Institute is the embodiment
of a new model in neuroscience research.

Located at the Pitié-Salpêtrière hospital in Paris,
this 22,000 m² international research institute,
one of a kind, is at the heart of the care process.

Government authorities, companies and donors
are joining hands to bring together patients,
doctors and the world's leading researchers to work
together and find new treatments for diseases
of the nervous system.

Paris Brain Institute — ICM

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