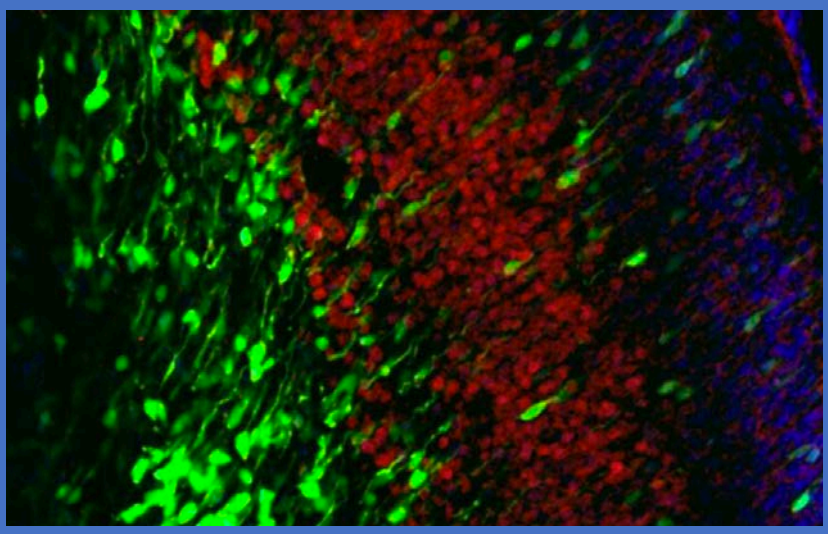
MMDN
INSERM U1198
MONTPELLIER

Molecular Mechanisms in Neurodegenerative Diseases

Scientific Report 2019



Objectives

Organization

Research teams

Research facilities

Science and Society

Université de Montpellier
MUSE MONTPELLIER UNIVERSITY OF EXCELLENCE
Inserm Institut national de la santé et de la recherche médicale
École Pratique des Hautes Études

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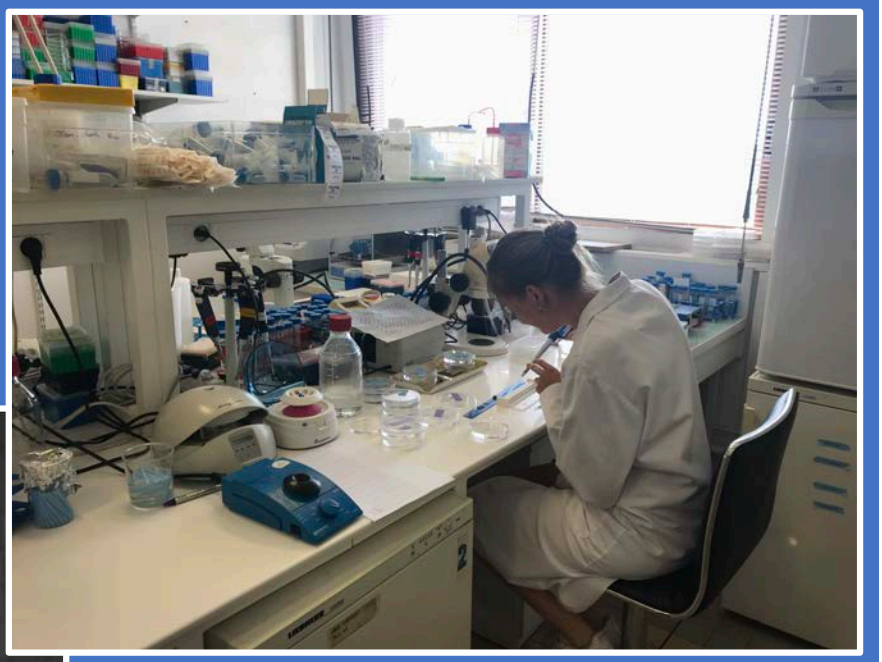
Contents



Forewords

The MMDN laboratory has been created 15 years ago by Jean-Michel VERDIER with the scientific vision that interdisciplinary approaches are the only effective means to advance knowledge in the biology of ageing and neurodegenerative diseases. Our expertise now covers physiological ageing and several neurodegenerative disorders in numerous animal models and Human. From the cellular level to animal models and human clinic, we develop innovative strategies, identifying pathological mechanisms, proposing novel biomarkers and exploring promising therapies. Our catalog of animal models, a hallmark of MMDN, includes genetic, transitory, pharmacological and surgical models in several animal species.

Research at MMDN is developed through leading projects from basic aspects of neuroscience and neurodegenerative processes to human clinic and epidemiology. They are sustained by a very dynamic dialog with socio-economic partners and the public. Our broader interest for both physiological and pathological aspects of ageing using multidisciplinary approaches including neuroscience, demography, epidemiology and socio-economic aspects, has strengthened the interdisciplinary science in MMDN. The laboratory thanks the University of Montpellier, INSERM and EPHE for continuous support.

Today, MMDN appears as an attractive and dynamic laboratory in the local landscape, benefiting from a solid network of technological platforms established within the laboratory, in the university or locally, with the BioCampus facilities. MMDN develops dynamic interactions with other local institutes, faculties or university hospitals. Moreover, our researchers developed a large network of national and international collaborations, illustrated by numerous co-authorships of published work, high number of invitations to international meetings and worldwide recognized expertise in several fields. Finally, MMDN is engaged in numerous technology transfer projects, actively working with the local SATT agency, patenting results of the research and initiating transfer to the clinic.

This strong scientific background and the dynamism of all lab members will stimulate the novel Direction Team to set the optimal conditions for future major therapeutic discoveries and accelerate their benefit for the patients. This brochure, based on the last quinquenal period achievements, will give you a rapid outlook on our research and means and hopefully stimulate your wish to interact directly with us in a near future.

Tangui MAURICE
Director

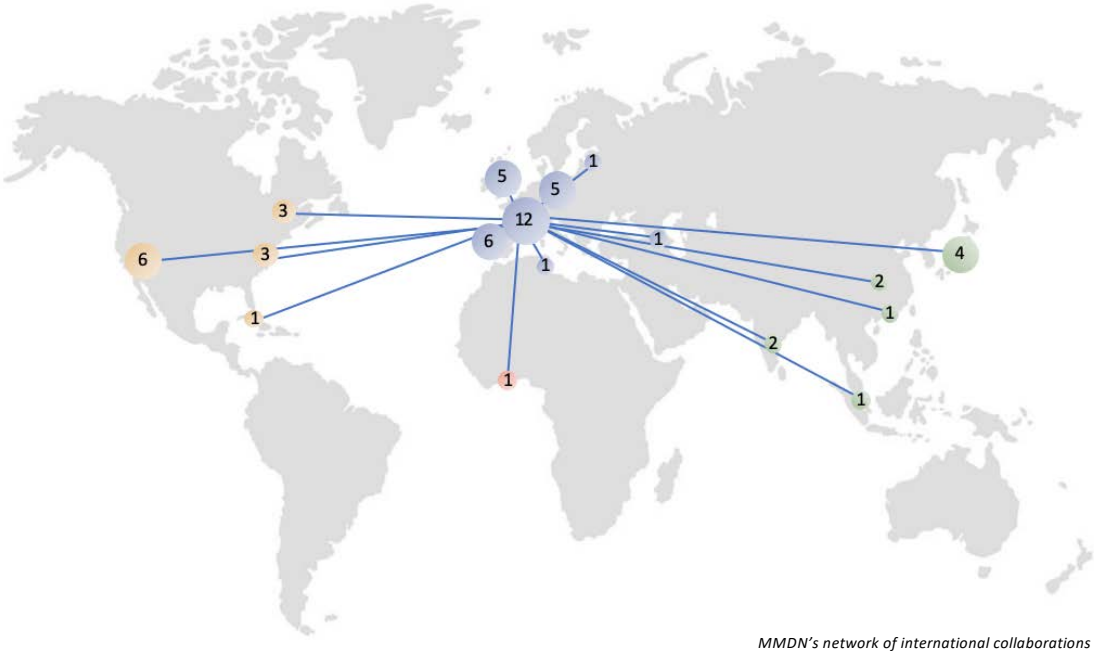
Nadine MESTRE-FRANCES
Deputy Director

The laboratory

MMDN is an interdisciplinary laboratory dedicated to research in the biology of ageing and neurodegenerative and neurotraumatic diseases, from cellular level to human disorder. Our expertise covers pathologies such as Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, prion diseases, genetic diseases, or spinal cord injury. We master numerous animal models, including genetic models in *Drosophila*, zebrafish or rodents, transitory models or pharmacological and surgical models in rodents or non-human primates (*Microcebus murinus)*. These means already allowed us to identify novel pathological mechanisms, innovative biomarkers and promising therapies. MMDN is engaged in several technology transfer projects, with SATT AxLR, patenting results of the research, initiating novel Start-Ups and initiating transfer to the clinic.

The research projects in MMDN covers a large spectrum of activities, including basic aspects of neuroscience and neurodegenerative processes, development of new animal models, and identification of innovative biomarkers and therapeutic strategies. We cover both physiological and pathological aspects of ageing, using multidisciplinary approaches including neurosciences, demography, epidemiology and socio-economic aspects.

The laboratory occupies a 750 m^2 surface at the 3rd floor of the Biology & Health building N°24 of the *Campus Triolet* of the University. Laboratory rooms occupy 300 m^2, offices for researchers, research supporting staff and students almost 300 m^2 and 85 m^2 are devoted to platforms (L2 laboratory, Ze-Neuro, ZebraSens). We have also access to University platforms in separate buildings of the campus (BioNanoNMRI, CECEMA) with additional experimental space for rodent behavior experiments, for instance (40 m^2 in 4 rooms), or animal housing. Therefore, we have the resources to continue growing smoothly and accommodate new teams.



MMDN's network of international collaborations

Data-in-brief

MMDN in numbers, for the 2015-2019 period

900 m² of lab space, including the main lab and platforms

6 teams

4 platforms

150 researchers, teacher-researchers, clinicians, engineers, technicians, students and administrative personnels (40 permanent staff)

250 original, review and clinical articles

16 book chapters

92 invited or oral communications in meetings

112 poster communications in meetings

6 patents

1 orphan drug designation

11 industry R&D contracts

1 CRO created

1 Start-Up in project

29 PhD theses

67 internships

18 habilited HDR

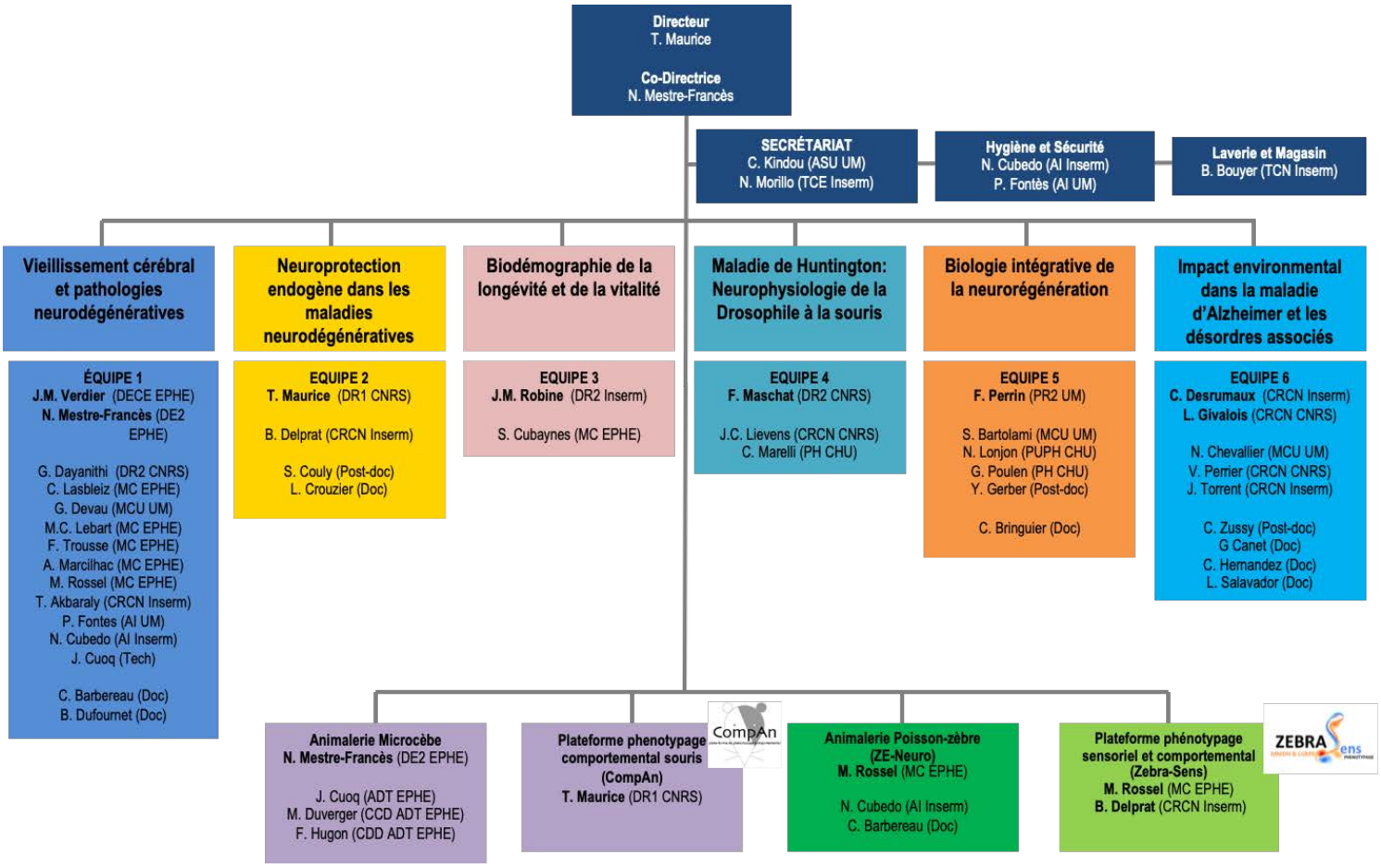
1,400 hours of teaching per year

39 radio broadcoast or magazine outreach

118 journal articles, interviews, debates on science, etc...

Organization

MMDN operating chart (permanent staff)



MMDN in its ecosystem

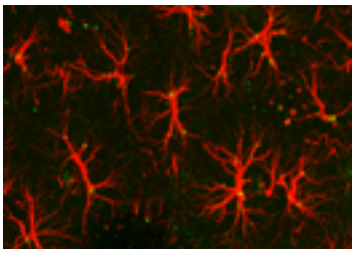
MMDN is a component of the *Biology & Health Scientific Department* (DSBS) and *Pole Rabelais* (www.polebiosante-rabelais.fr), the coordination cores of all Biology & Health research and teaching units of the University of Montpellier. We are a member of the I-SITE MUSE Montpellier University of Excellence. Strongly involved in several local networks like the multi-platforms service unit BioCampus (INSERM US09) or the animal facility network RAM (www.ram.cnrs.fr), MMDN is also an initiator and dynamic actor of several local scientific networks (CALM, Zebra-Club) and platforms.

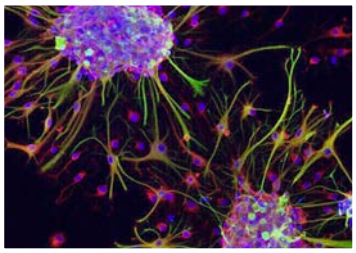
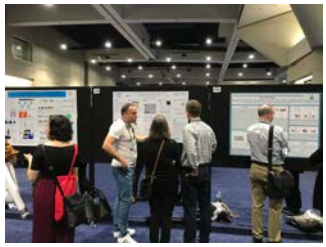
MMDN has regular interactions with the University Hospital of Montpellier, through clinicians embedded in several teams, clinicians preparing Master course or PhD in the laboratory, and running collaborations with the Department of Neurology and CMRR or the Department of Neurosurgery.

MMDN is a founding member of the *Center of Excellence for Neurodegenerative disorders* (CoEN; www.coen-montpellier.fr) and *Center of Excellence on Autism and Neurodevelopmental Disorders* (CoEAND), both coordinated by the CHU, and involved through participations in the steering committee and the scientific committee. Several collaborations were initiated between MMDN and external teams through the CoEN networking.

MMDN is a member of the LabEx LipSTIC since 2013 and benefits from numerous local, national and international collaborations with Germany, Czech Republic, USA, Canada, India, Georgia, Cuba, Côte-d'Ivoire, Tunisia, Switzerland, Japan, China…

Research at MMDN




Team 1: Cerebral aging and neurodegenerative pathologies

Jean-Michel VERDIER/Nadine MESTRE-FRANCES
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Understanding the molecular mechanisms of cerebral aging and neurodegenerative diseases (NDs) remains a major challenge in the context of life expectancy increase. The balance between healthy and pathological ageing relies on multiple factors and early stages of rupture of this balance are a key point to understand the molecular bases of NDs, such as Alzheimer or Parkinson, in order to suggest new diagnosis and treatment.

The team strategy consists in:

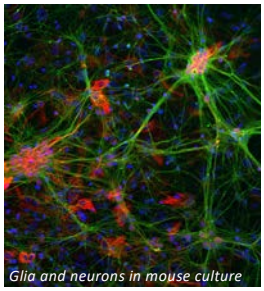
(1) modeling NDs and creating innovative models by using whole genome sequencing, transcriptomic analyses or inducing pathology by viral delivery.

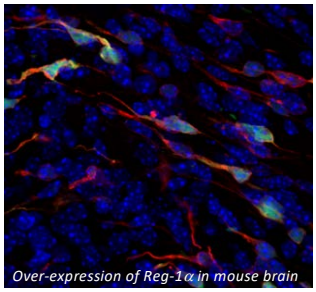
(2) increasing the potential of the mouse lemur model, a natural model of ageing-related amyloidopathy. The team is historically involved in a better characterization of mouse lemur, using genetic, NRM imaging, and behavioral approaches through European networking.

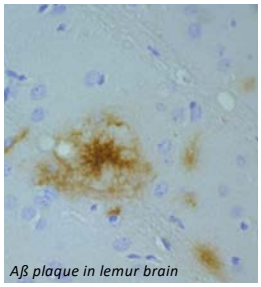
(3) establishing potential biomarkers to target the pathological heterogeneity of NDs, and among them the role of CXCR7 receptor or Regenerating islet-derived-1α (Reg-1α) protein using a multidisciplinary approach ranging from cellular studies to *in vivo* approaches (zebrafish, rodents, non-human primates).

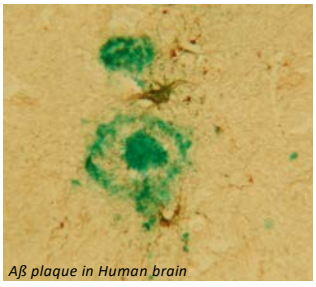
(4) Studying Ca^{2+} signaling and Ca^{2+} homeostasis in neurons and in stem cells of different species,

(5) assessing the determinants of cerebral aging by epidemiological approach in order to develop translational studies and better understand the role played by health behaviors and metabolic factors on cerebral aging trajectories and their consequences in the elderly, using data from large-scale observational cohorts.


Glia and neurons in mouse culture


Over-expression of Reg-1α in mouse brain


Aß plaque in lemur brain


Aß plaque in Human brain

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Team 2: Endogenous Neuroprotection in Neurodegenerative Diseases

Tangui MAURICE

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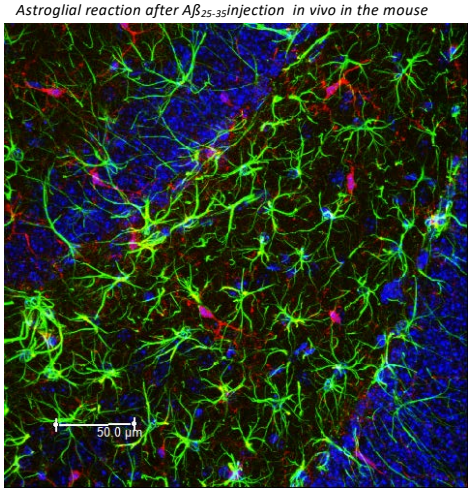
Our aim is to identify and validate new therapeutic strategies in pre-clinical models of neurodegenerative diseases and to propose, in collaboration with medicinal chemists, novel molecules for the clinic. Historically, the team focuses on the sigma-1 receptor (S1R), a chaperone protein from the endoplasmic reticulum, highly concentrated in mitochondria-associated ER membranes (MAMs). S1R activity modulates focal Ca^{2+} exchanges with the mitochondria, regulates ER stress response and, *in fine*, modulates cellular signal transduction systems. It is expressed in neurons, glial and vascular cells in the brain and activable/inactivable by exogenous molecules, so called S1R agonists/antagonists. We previously demonstrated that S1R agonists are anti-amnesic, anti-depressant, anti-addictive and potent neuroprotective drugs in Alzheimer's disease models. We showed that a S1R agonist activity contributed to the efficacy of the acetylcholinesterase inhibitor donepezil and characterized the therapeutic potential of tetrahydroaminofuranne derivatives, in collaboration with ANAVEX.

The team research therefore relies on a triple expertise: its pioneer achievements in S1R pharmacology; the validation of neuroprotective therapies in Alzheimer's disease; and a recognized expertise in the behavioral pharmacology of rodent models. With this background experience, our current perspective is to expand our research interests to cellular biology (examining more globally MAM alterations in neurodegeneration), to other degenerative pathologies (including major pathologies such as Huntington or amyotrophic lateral sclerosis and a rare genetic disease, the Wolfram syndrome), and to other approaches (including genetic studies in *Drosophila* and zebrafish).

Astroglial reaction after $A\beta_{25-35}$injection in vivo in the mouse



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Team 3: Biodemography of Longevity and Vitality

Jean-Marie ROBINE

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Longevity and vitality has successively focused on the development of new indicators of health of populations, the limits of human longevity, and the measurement of the health status of very old people, the "oldest-old". Given the very "macro" nature of the research of this team and the "global" nature of the institutions interested in this research (UN, WHO, OECD, European Commission, French Government), the team has always worked in network by coordinating many French and foreign researchers.

The team pursues original research in the field of longevity concerning in particular the limits of the human longevity and the mortality at the highest ages (>105). We collaborate with fifteen advanced countries (North America, Western Europe and Japan) and collaborations involve the international database on longevity (IDL); the epidemiology of frailty; the relationships between environmental variables (including climatic factors) and longevity; and the metrics of longevity. An important part of the work of the team is to disseminate and value the previous work on Disability-Free Life Expectancy (DFLE). In this respect, the team is working with the Ministry of Health (DRESS) and the French census bureau (INSEE) which are now regularly carrying out DFLE calculations for France, with the Economic, Social and Environmental Council (CESE), responsible for analyzing the results and with the media to facilitate a good understanding of the results.

The team also managed the GDR "Longevity and Aging », increasing the visibility of the social science community (demography, economics, epidemiology, psychology and sociology).

Jeanne Calment, the limits of longevity

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Team 4: Huntington's Disease: Neuro-physiology from *Drosophila* to the Mouse

Florence MASCHAT

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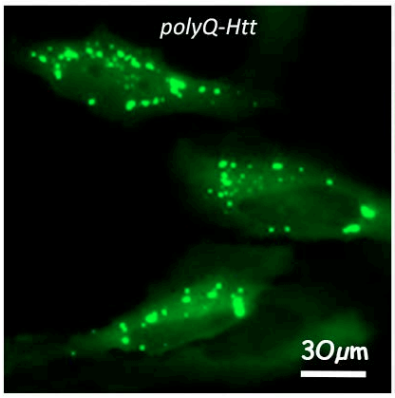
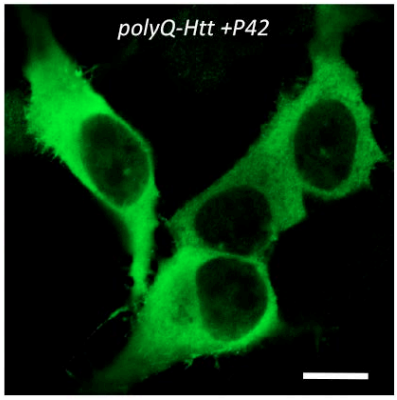
The main scientific objective was to identify new therapeutic strategies against several neurodegenerative diseases, using peptide-based therapies.

One project was to understand how neuronal growth and pathfinding are regulated during development of organisms and affected in neurodegenerative diseases. For this purpose, we focused on the study of the homeodomain transcription factor Engrailed, an important factor neurodegenerative diseases (Parkinson's disease and different forms of autism). We identified that Engrailed is also regulating *huntingtin*, a gene responsible of Huntington's disease (HD) when mutated. This observation was the starting point for the identification of P42, a short 23aa peptide of the Htt protein that presents protective properties on HD symptoms/phenotypes.

Our goal was to study the modes of action of P42 and to develop this molecule at therapeutic ends. To this end, several strategies were carried out using *in silico, in vitro*, *in cellulo*, but also *in vivo* analyses in *Drosophila* or in mice.

The current studies concern the analysis of the physiological role of P42 as part of the Huntingtin, but also on the molecular details of its protective effects on the formation of aggregates or on its neuronal activity involved in different pathways. These projects have been supported by the ANR. For therapeutic purposes, a preclinical maturation study of P42, supported by the SATT AxLR, is still under development. Finally, biomarkers for HD and for P42 activities are currently searched and will be developed in humans (a PHRC-I grant has been recently obtained to develop this topic).





Huntingtin immunofluorescence in HeLa cells

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Team 5: Integrative Biology of Neuroregeneration

Florence PERRIN

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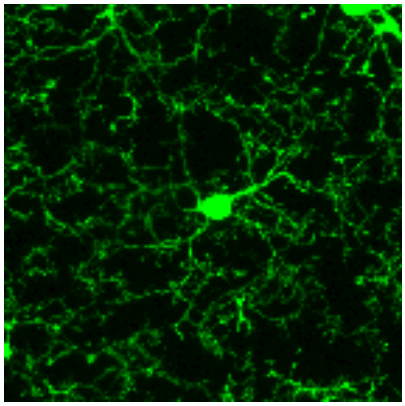
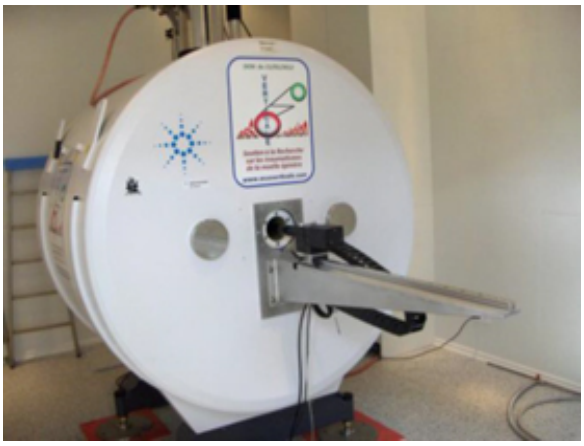
Our research strategy is to develop a multimodal (i.e., molecular biology, behavioral analysis, bioimaging, histology) and interdisciplinary (biology, physics and clinics) approach to decipher mechanisms that underlie absence of spontaneous axonal regeneration following spinal cord injury. As our final aim is to develop new translational therapeutic strategies to promote regeneration, we are working not only in mice but also in non-human primates.

We are currently modulating the glial scar that forms after spinal cord injury by concomitantly developing a research orientated approach (modulation of gene expression in astrocytes) and more translational and clinically orientated pharmacological approach. Similarly, we are developing several bioimaging modalities, again either in a research orientated manner (CARS and BCARS) or in a translationally orientated aim (MRI).

We benefit from strong partnerships with: (1) neurosurgeons either as team members or as collaborator in the hospital; (2) physicists to maintain and develop our expertise in bioimaging (MRI and CARS); (3) patient associations to further match with clinical needs; and finally (4) foreign scientific partners, to pursue efficient collaborations and develop novel research lines





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• **Le Corre* M, Noristani* HN, Mestre-Frances N, Saint-Martin GP, Coillot C, Goze-Bac C, Lonjon N, Perrin FE** (2017) A novel translational model of spinal cord injury in nonhuman primate. **Neurotherapeutics** 15:751-769

• **Noristani* HN, Saint-Martin* GP, Cardoso M, Sidiboulenouar R, Catteau M, Coillot C, Goze-Bac C, Perrin FE** (2018) Longitudinal MRI analysis and histological characterization after spinal cord injury in two mouse strains with different functional recovery: gliosis as a key factor**. J Neurotrauma** 35:2924-2940

• **Gerber* YN, Saint-Martin* GP, Bringuier CM, Bartolami S, Goze-Bac C, Noristani HN, Perrin FE** (2018) CSF1R inhibition reduces microglia proliferation, promotes tissue preservation and improves motor recovery after spinal cord injury. **Front Cell Neurosci** 12:368.

Team 6: Environmental Impact on Alzheimer's Disease and Related Disorders

Catherine DESRUMAUX/Laurent GIVALOIS
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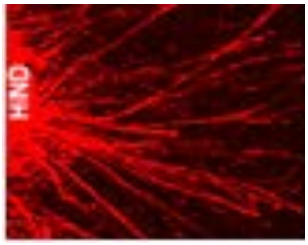
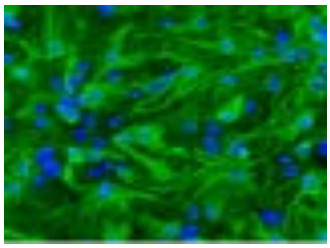
More than 95% of Alzheimer's patients suffer from the sporadic form. Although aging and genetic determinants are known as important risk factors, environmental variations are also likely to contribute to the occurrence of this disease. Our main objective is to characterize *in vivo* and *in vitro*, the impact of environmental perturbations, in particular chronic stress, oxidative stress, and chemical stress such as chronic exposure to low doses of pesticides in the etiology of AD. In addition, we aim at identifying environmental modulators of the amyloidogenic process, with a special emphasis on those having an impact on the fibril morphotype (structure and polymorphism). In parallel, we evaluate innovative therapeutic strategies to counterbalance the deleterious effects of identified risk factors, in particular using nanovectorization and intranasal administration.

Our team's goal is to decipher the molecular mechanisms underlying the relationships between chronic stress, oxidative stress, pesticides exposure, and Alzheimer's disease. We also develop innovative therapeutic strategies (nanovectorization of antioxidants, selective modulators of glucocorticoids receptors) to counteract Aβ peptide aggregation and neurodegenerative processes. Our studies are conducted using a combination of *in vitro* (Aβ peptide aggregation test and primary cell cultures: hippocampal neurons, astrocytes) and *in vivo* (murine AD models) models.

Organotypic culture of ACh neurons





Primary culture of astroglia or neurons

KEY PUBLICATIONS

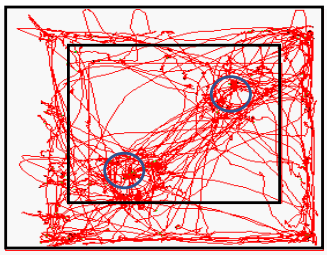
• **Pineau F, Canet G, Desrumaux C, Hunt H, Chevallier N, Ollivier M, Belanoff JK, Givalois L** (2016) New selective glucocorticoid receptor modulators reverse amyloid-ß peptide-induced hippocampus toxicity. **Neurobiol Aging** 45:109-122.

• **Imberdis T, Ayrolles-Torro A, Duarte, Rodrigues A, Torrent J, Alvarez Martinez MT, Kovacs GGK, Verdier JM, Robitzer M, Perrier V** (2016). A fluorescent oligothiophene-Bis-Triazine ligand interacts with PrP fibrils and detects SDS-resistant oligomers in human prion diseases. **Mol Neurodegener** 11: 11.

• **Lafon PA, Imberdis T, Wang YY, Torrent J, Robitzer M, Huetter E, Alvarez-Martinez MT, Chevallier N, Givalois L, Desrumaux C, Liu JF, Perrier V** (2018) Low doses of bioherbicide favours prion aggregation and propagation in vivo. **Sci Rep** 8:8023

• **Mansuy M, Baille S, Canet G, Borie A, Cohen-Solal C, Vignes M, Perrier V, Chevallier N, Le Guern N, Deckert V, Lagrost L, Givalois L, Desrumaux C** (2018) Deletion of plasma Phospholipid Transfer Protein (PLTP) increases microglial phagocytosis and reduces cerebral amyloid-β deposition in the J20 mouse model of Alzheimer's Disease. **Oncotarget** 9:19688-19703.

Technological platforms



Platform 1: Ze-Neuro

The zebrafish breeding facility of MMDN

https://mmdn.umontpellier.fr/fr/equipes/plateforme-poisson-zebre-ze-neuro

The zebrafish animal facility enables the development of new *in vivo* models to understand the processes of neuronal degeneration. We have established expertise in the development and regeneration of the central and peripheral nervous system (mechanosensory system of the posterior lateral line) and we currently host about 30 transgenic and mutant lines. Several projects of the MMDN teams are hosted in the platform.

This platform is also accessible to the scientific community and we made it possible to collaboratively develop different projects for several teams in Montpellier, including:
- Study of candidate genes for hearing impairments (LGMR).
- Study of candidate genes in hereditary retinitis pigmentosa (INM, Montpellier).

Moreover, the platform is involved in functional validation for therapeutic agents in various themes:
- Nanoparticles (IBMM, Montpellier).
Study of theranostics compounds (EPHE, Univ Bourgogne).
Validation of aging protective agents, sirtuin inhibitors (EPHE, Genethon).

We supervise students (Master Univ Montpellier, Master EPHE), doctoral students, post-docs and researchers for microinjection techniques at different stages, for the manipulation of embryos and larvae for the imaging. All users are trained in the good practise for the model (zootechnics, experimentation, regulation).

Zebrafish housing in automated water tanks

KEY PUBLICATIONS

- **Arribat Y, Mysiak KS, Lescouzères L, Boizot A, Ruiz M, Rossel M, Bomont P**. Sonic Hedgehog repression underlies gigaxonin mutation-induced motor deficits in giant axonal neuropathy**. J Clin Invest**. 2019 in press.
- **Moussaed M, Huc-Brandt S, Cubedo N, Silhol M, Murat S, Lebart MC, Kovacs G, Verdier JM, Trousse F, Rossel M, Marcilhac A**. Regenerating islet-derived 1α (REG-1α) protein increases tau phosphorylation in cell and animal models of tauopathies. **Neurobiol Dis**. 2018; 119:136-148.
- **Angebault C, Guichet PO, Talmat-Amar Y, Charif M, Gerber S, Fares-Taie L, Gueguen N, Halloy F, Moore D, Amati-Bonneau P, Manes G, Hebrard M, Bocquet B, Quiles M, Piro-Mégy C, Teigell M, Delettre C, Rossel M, Meunier I, Preising M, Lorenz B, Carelli V, Chinnery PF, Yu-Wai-Man P, Kaplan J, Roubertie A, Barakat A, Bonneau D, Reynier P, Rozet JM, Bomont P, Hamel CP, Lenaers G**. Recessive Mutations in RTN4IP1 Cause Isolated and Syndromic Optic Neuropathies. **Am J Hum Genet**. 2015; 97:754-60.
- **Huc-Brandt S, Hieu N, Imberdis T, Cubedo N, Silhol M, Leighton PL, Domaschke T, Allison WT, Perrier V, Rossel M**. Zebrafish prion protein PrP2 controls collective migration process during lateral line sensory system development. **PLoS One**. 2014; 9:e113331.
- **Cubedo N, Cerdan E, Sapede D, Rossel M**. CXCR4 and CXCR7 cooperate during tangential migration of facial motoneurons. **Mol Cell Neurosci**. 2009; 40:474-84.

Platform 2: ZebraSens

The behavioral phenotyping platform for zebrafish models

https://mmdn.umontpellier.fr/fr/equipes/plateforme-zebrasens-de-phenotypage

The zebrafish behavioural phentotyping platform was created with the support of M. Roux, President of the *SOS Retinite France* association in 2017. The objective of this novel platform is to analyze the vision (Visual Motor Response, OptoKinetic Response), the audition (Acoustic Starttle Response), the locomotion and the memory of the larvae and the adults.

-The vision is evaluated using a Visiobox® able to measure the OKR response, assessing visual acuity of zebrafish in a stress-free and automated environment. The visual acuity is measured by monitoring the eye movements of the fish following a scrolling of white and black strips at regular intervals and strongly contrasted. Four fishes can be monitored at the same time.

- The spontaneous or light flash-induced locomotor response are measured using a Zebrabox® and the VMR.

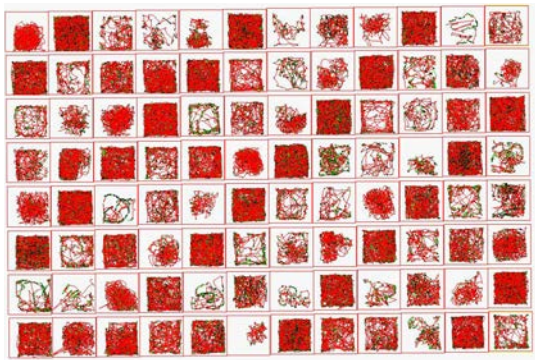
- The spontaneous or sound-induced locomotor response is measured using Zebrabox and ASR.

-The pre-pulse inhibition is analyzed using a Zebrabox Fast®, with a vibratory module. This system is able to measure the curvature of the fish following sound stimulation of chosen frequency and intensity (C-start, S-start).

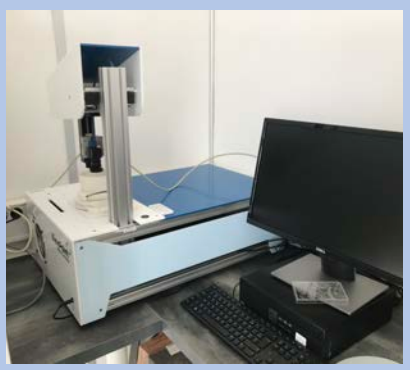
- The locomotor behavior is also analyzed using a ZebraCube: The adult fish are videotracked to determine distance traveled, position, stop phases and activity. In addition, social behavior (shoaling) and spatial memory (T-maze and double H-maze) can be assessed.

Two projects have been completed since its creation in 2017, one in the lab and another with Azelead, a CRO.

Locomotor tracking of zebrafish in 96-well plate



KEY EQUIPMENTS



Platform 3: CompAn

The behavioral phenotyping platform for rodent models

The mouse behavioural phenotyping platform was initiated in 2005 by a lab member, in the animal facility of the university of Montpellier and proposes more than 25 behavioral tests in routine for the phenotyping of mouse models developed in the laboratory or by colleagues from Montpellier. Based on a collaboration basis, 15 projects have been completed, including 6 these last 5 years with colleagues from INM (2 projects) and INRA (1 project). 11 articles have been published acknowledging the *CompAn* platform (3 these last 5 years and 2 are submitted).

Behavioral tests: spontaneous alternation, passive avoidance (step-down/step-through), active avoidance, conditioned fear stress, forced swim stress, tail suspension stress, place learning in the water-maze, object recognition (2 objects/4 objects), water-finding test, black-and-white exploration, elevated plus-maze, social interaction, pole test, rotarod, catwalk, open-field, conditioned place preference, 3-chamber social interaction…

We recently created and validated the Hamlet test, a complex environment for mice. We hold the patent FR15 57093, Ext. WO2017/017010. The device is fully automatized, videotracked and commercialized by Viewpoint (Lissieu, France).

The Hamlet test

KEY PUBLICATIONS

- **Pagnamenta AT, Heemeryck P, Martin HC, Bosc C, Peris L, Uszynski I, Gory-Fauré S, Couly S, Deshpande C, Siddiqui A, Elmonairy AA, Jayawant S, Murthy S, Walker I, Loong L, Bauer P, Vossier F, Denarier E, Maurice T, Barbier EL, Deloulme JC, Taylor JC, Blair EM, Andrieux A, Moutin MJ**. Defective tubulin detyrosination causes structural brain abnormalities with cognitive deficiency in humans and mice. **Hum Mol Genet**. 2019; in press.
- **Maurice T, Strehaiano M, Siméon N, Bertrand C, Chatonnet A**. Learning performances and vulnerability to amyloid toxicity in the butyrylcholinesterase knockout mouse. **Behav Brain Res**. 2016; 296:351-60.
- **Duclot F, Lapierre M, Fritsch F, White R, Parker MG, Maurice T, Cavaillès V**. Cognitive impairments in adult mice with constitutive inactivation of RIP140 gene expression. **Genes Brain Behav**. 2012; 11:69-78.
- **Espallergues J, Galvan L, Sabatier F, Rana-Poussine V, Maurice T, Chatonnet** A. Behavioral phenotyping of heterozygous acetylcholinesterase knockout ($AChE^{+/-}$) mice showed no memory enhancement but hyposensitivity to amnesic drugs. **Behav Brain Res**. 2010; 206:263-73.
- **Maurice T, Duclot F, Meunier J, Naert G, Givalois L, Meffre J, Célérier A, Jacquet C, Copois V, Mechti N, Ozato K, Gongora C**. Altered memory capacities and response to stress in p300/CBP associated factor (PCAF) histone acetylase knockout mice. **Neuropsychopharmacology**. 2008; 33:1584-602.

Platform 4: CECEMA

The conventional and A3/L3 animal facility of Montpellier University

http://www.cecemaa3l3.univ-montp2.fr/

The *Centre d'Elevage et de Conditionnement Expérimental des Modèles Animaux* (CECEMA) is a technical platform and joint service of the University of Montpellier. It is headed by a lab member and part of the *Réseau des Animeries Montpelliéraines* (RAM), a network of all local research animal facilities from CNRS, INSERM IRD and INRA.

It is intended to host animals for scientific research and teaching. It welcomes mice, rat, hamster, chicken, wild mice and mouse lemurs (Agreement D 34-172-23 from 28/02/2014).

The premises, with a surface area of 1,882 m², include conventional animal housing (1,292 m²) and a Confined Experimentation Facility (ECE) of 590 m². ECE is a high biological safety laboratory designed to host experiments that require class 3 containment rodents and lemurs (Agreement B 34-172-34 from 13/08/2013. The platform is ISO 9001 certified for its activities.

Mice housing and work in the confined experimentation facility

BIOCAMPUS

Life Sciences facilities

https://www.biocampus.cnrs.fr/

BioCampus Montpellier is a service unit of CNRS, INSERM and the university of Montpellier offering a wide range of core facilities, providing service, training and expertise. BioCampus Montpellier's facilities are spread over the main Health/Plant Sciences/Ecology and R&D research centers in the Montpellier area. BioCampus Montpellier is a key element in the success of many scientific projects carried-out by researchers from units of the Montpellier area. It also enhances the potential of excellence research centres in attracting talented new group leaders.

Built by research laboratories for research laboratories, it was founded to meet the needs of their own scientists. The unit is a coordination place where all Montpellier Life Sciences research units discuss together and organize a comprehensive cutting-edge technologies offer, for the success of their own scientific strategies.

Administrative supervision

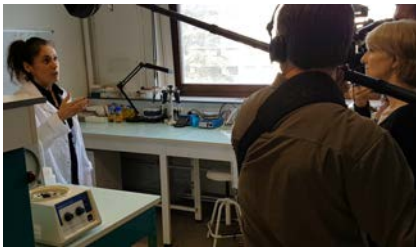
Partner institutions

As part of the service unit's steering committee, MMDN has a central position in the local technological offer and governance.

The 13 facilities composing BioCampus service unit:

Arpege (pharmacology, interactions, screening)	PIBBS Plateforme intégrée de Biophysique et de Biologie Structurale (Biophysics and structural biology)
IMGT® the international immunogenetics information system®	PPM Pôle Protéome de Montpellier (proteomics, interactions, microfluidics)
IPAM Imagerie du Petit Animal de Montpellier (*in vivo* imaging)	PVM Plateforme de Vectorologie de Montpellier (AAV, adénovirus, lentivirus)
MDC Montpellier DNA Combing	RAM Réseau des Animaleries de Montpellier (rodent facility)
MGC Montpellier Genomic Collection	Droso (fly facility), part of RAM
MGX Montpellier Genomix (Genomics, epigenomics & transcriptomics)	RHEM Réseau d'Histologie Expérimentale de Montpellier (Histology)
MRI Montpellier Ressources en imagerie (cellular imaging)	Statabio Statistiques Appliquées à la Biologie (BioStatistics)

Science and Society at MMDN




Promoting and sharing research achievements among professionals and the general audience

- The association ”La Comédie des Neurones" aims to make the general public discover advances in neuroscience research and progress in treatments for neurological and psychiatric diseases. Its mission is to organize scientific events, conferences, debates, film screenings, or workshops dedicated to scholars, or any other form of scientific animation intended for the general public of any age or education level.

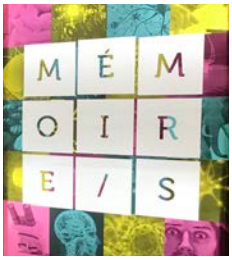
- In partnership with Brain Awareness Week, Le Bar des Sciences and Agora des Savoirs de Montpellier, the association is interacting with the local territory: Mairie, Métropole 3M, Conseil Général 34 and Région for more visibility of the Neurosciences in Montpellier.

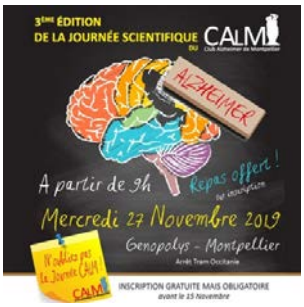
- In 2017, to gather the local community of researchers and clinicians working specifically in Alzheimer’s disease, we initiated the creation of a scientific club, CALM. It gathers more than 50 members and organizes a scientific seminar each month. Three all-day symposia were organized annually for researchers and the public audience (100+ participants), supported by the University, the CoEN, and several associations. The scientific part includes as speakers, foreign, national and local researchers or clinicians.

LA COMÉDIE DES NEURONES

CALM
Club Alzheimer de Montpellier

KEY INVOLVEMENTS





The Transdisciplinary Institute for Studies on Aging

Anne MARCILHAC, Director

Anne.marcilhac@umontpellier.fr

ITEV has been created in by EPHE (Paris), but has its head office in Montpellier and current Director is Anne Marcilhac. ITEV aims at promoting a transdisciplinary approach regarding the problems of aging, at initiating and coordinating studies on aging to support public policies, and at leading to a positive approach of aging.

ITEV missions are:

1- To initiate debates between citizens and professionals about central questions of aging, to disseminate information to the general audience and to produce and exchange knowledge by the means of partnering with local or national public or private bodies, colloquia, seminars, workshops, lectures, communication tools (website, reports, training courses…)

2- To do expertise for public and private bodies by calling experts when necessary, and creating a network of experts. Such a network would promote the exchange of expertise, sharing of information, planning of common methodologies and would provide a synoptic view of aging and aging problems.

3- To train and teach students or professionnal people through initial and continuing education, to develop and facilitate the introduction of new teaching activities, and to meet the ongoing professional needs for key personnels.

EPHE, ITEV and REACTIS network receive ONU in Paris

KEY REALIZATIONS

- **Interviews for the television:** France 5 (2014), RTBF Channel (2019)
- **Professional continuing education programs** :Creation of a new post-graduate training course “Coordinateur du parcours de vie des personnes en situation de fragilité”, (2018-)
- **Organizing congresses for a general audience** :"Aging: What are the issues for the territories? "(2018)
- **Organization of the meeting** with Rosita KORNFELD, independent expert for the elderly in the ONU : « Strategies for the defense of the rights of the elderly »
- Participation in the **national consultation "The trades of old age"** led by Myriam El Khomri at the request of the Ministry of Health, September 2019.
- **Oral conferences on Social Issues and Aging**

1- "Power to act on the challenge of aging", Cycle "Handicaps, dependence, vulnerabilities and solidarities. Experiential knowledge and power (s) to act ", CNAM and Espace Ethique Ile de France, January 2018, Paris.

- Organization of a debate "Include through training in the context of aging: an unthought?" at the international symposium "Inclusive and advanced age society", February 2020, Metz.

- "In the face of the challenge of aging, what are the ethical issues? ", Institute of Advanced Studies, January 2020, Paris.

- **Website** : https://itev.ephe.fr/
- **Publication** of four **newsletters** per year

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