Department of Clinical Neuroscience

Neuroscience Research Center 2019-2020 Presentation

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Neuroscience Research Center
2019-2020 Presentation

Content

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Foreword 2019-2020

Our community of scientists continues to expand and develop. The Neuroscience Research Center now has 13 laboratories and 5 platforms.
Two major initiatives have emerged in the past two years: the creation of the Neurorestore Center and the development of the Center for Interdisciplinary Research in Neuroplasticity and Neurorehabilitation (CRINN) in Lavigny.

NeuroRestore, under the co-direction of Prof. Bloch and Prof. Courtine, is a research center with the objective of developing innovative therapeutic strategies including bioengineering involving neurosurgical interventions to restore neurological functions. It is structured in 3 divisions with more than 70 collaborators.
The mechanistic division is located at the EPFL Biotech Campus site, the translational division at the Institute of Physiology of Fribourg and the clinical division at the CHUV. The clinical team has completed the STIMO study, which now includes 10 paraplegic patients. The first results of the study were published in 2018 and demonstrated the tremendous potential of this new spinal cord stimulation neurotechnologies to enable voluntary control of walking in individuals with spinal cord injury. To complete the structuration of the research activities of the Neurosurgery Service, the laboratory of neurosurgery (LNCH) was created in 2020.
The LNCH gather research and training activities in microanatomy and microsurgical dissection, under the supervision of Roy Daniel and Mahmoud Messerer.

The second initiative is the Center for Inter-disciplinary Research in Neuroplasticity and Neurorehabilitation (CRINN), which is in development in the context of the opening of a university service (SUN) for neurorehabilitation.

The CRINN laboratories in Lavigny are under construction and the inauguration of the center is scheduled for 2021. The ambition of the CRINN is to maximize the recovery capacity of patients with nervous system injuries, to develop innovative neurotechnologies to increase their functional recovery, to offer the best therapeutic options to compensate for remaining deficits, to promote excellence in interdisciplinary research on neuronal plasticity and neuroprosthetics, to provide state-of-the-art training to professionals in neurorehabilitation and to researchers in fundamental and clinical neurosciences.

The year 2020 has been exceptional and difficult in more ways than one. In particular for the clinicians and medical staff of the department, who were and still are on the front line of the COVID-19 crisis. But the spring lockdown also profoundly disrupted research activities and created difficult situations to manage for the researchers and administrators. The positioning of the CRN in the department fully played its role as a relay between our institutions (CHUV-UNIL) and the collaborators. The CRN was thus able to relay information, manage the implementation of health measures, and participate in the provision of staff to support CHUV activities.
I would like to mention in particular the CRN's initiative to provide financial support to researchers. This support fund financed by overheads was able to partially cover the loss of salaries and fixed costs during the two-month lockdown (86'000 CHF).
Thank you all, for your involvement and efforts to ensure the smooth running of the research activity and the management of highly innovative projects, which have already resulted in more than 165 publications over the last two years.

Additional information

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Neuroscience Research Center

Laboratories Presentation

Laboratory of Clinical Neurophysiology and non-Invasive Brain Stimulation

Senior Lecturer David Benninger
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Keywords
Therapeutic studies for Parkinson
Motor system and movement disorders
Brain stimulation
Neurophysiology
Movement & gait analysis
Nerve-muscle disorders

Laboratory's activity

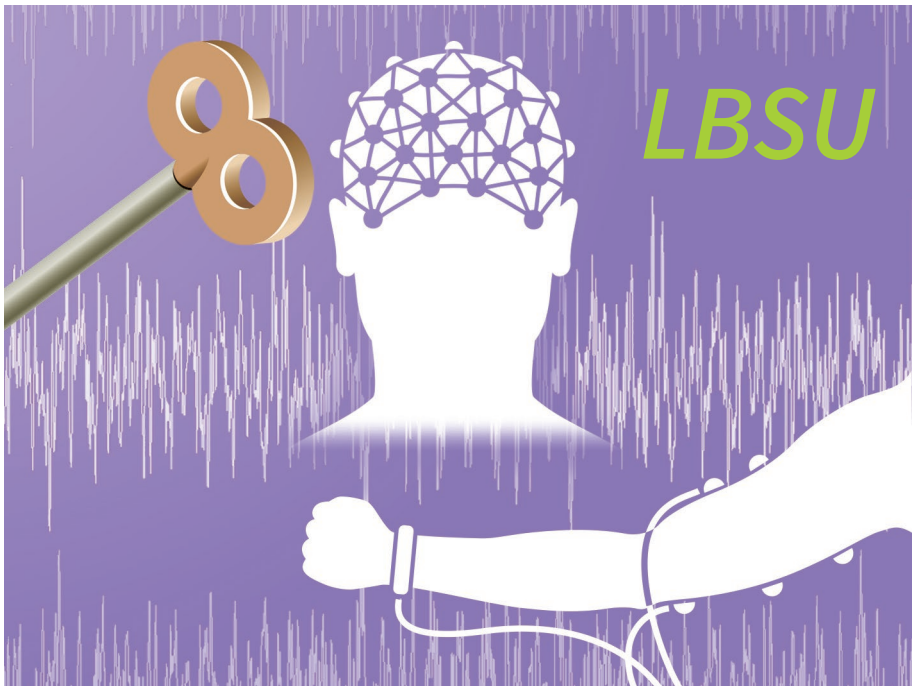
> Randomized controlled therapeutic clinical trial on tDCS for the treatment of the freezing of gait in Parkinson's disease.
> Multicenter randomized controlled therapeutic trial for gait disorder in Parkinson's disease and atypical Parkinsonian disorders (FNS/DACH collaboration CHUV-EPFL with Innsbruck (A), Erlangen (D), Bozen (I) and Nijmegen (NL)).
> Robot-assisted assessment of the rigidity and tremor in Parkinson's disease.
> Investigation of the motor cortex physiology using the triple stimulation technique.
> Investigation of the motor, sensorimotor and plasticity alterations in dystonia associated to a complex regional pain syndrome.

Research interests

Our lab is interested in movement disorders, clinical neurophysiology, brain stimulation and the human motor control. The main research we lead currently concerns Parkinson's disease, dystonia, tremor and normal physiology essentially through transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), electroneuromyography (ENMG) combined with electroencephalography (EEG), kinematic analysis of movements and gait.

Scientific contributions in 2019-2020

> European Guidelines on Therapeutic Application of Non-invasive Brain Stimulation (rTMS, tDCS).
> Cerebellar stimulation for Parkinson tremor.
> Combined tDCS-behaviour therapy study for freezing of gait in PD.
> CRPS with dystonia.
> Cervical dystonia: contribution of cerebellar dysfunction.



Our research team mainly uses electrophysiological techniques. Either to record activity: at the cerebral level with electroencephalography (EEG - cap and recording) and muscle level with electromyography (EMG - electrodes and recording); or to interfere or modify ongoing cerebral activity (TMS - coil).

Main publications in 2019-2020

Caranzano L, Stephan MA, Bedulli M, Herrmann FR, **Benninger DH**. Peripheral stimulation affects subthreshold Triple Stimulation Technique. J Neurosci. Methods 2021 Jan 1; 347:108959.

Madrid J, **Benninger DH**. Non-invasive brain stimulation for Parkinson's disease: Clinical evidence, latest concepts and future goals: A systematic review. J Neurosci. Methods 2021 Jan 1; 347:108957.

Lefaucheur JF, Alemanc A, Baekend C, **Benninger DH**, [...] Schecklmann M, Szekely D, Ziemann U. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): an update (2014-2018). Clinical Neurophysiology 2020; 131(2):474-528.

Rutz D & **Benninger DH**. "Physical therapy for freezing of gait and gait impairments in Parkinson's disease: a systematic review". PM&R: The journal of injury, function and rehabilitation 2020; 12(11):1140-1156.

Ulrich B, Santos AN, Jolles BM, **Bennninger DH**, Favre J. "Gait events during turning can be detected using kinematic features originally proposed for the analysis of straight-line walking". J Biomech. 2019 Jun 25; 91:69-78.

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Laboratory of Cognitive Science

Professor Stephanie Clarke, Head of the laboratory

Dr Sonia-Crottaz-Herbette

Senior Lecturer, adjunct Professor Stefano Carda

Dr Jean-Michel Pignat

Laboratory's activity

The laboratory works at the interface between clinical neurorehabilitation and basic cognitive neuroscience. Understanding neural mechanisms, which underlie recovery after brain lesion, helps to design innovative therapeutic interventions and to apply them in clinical care.

The four principle investigators, Prof. Stephanie Clarke, Dr Sonia Crottaz-Herbette, Dr Stefano Carda and Dr Jean-Michel Pignat, focus on:

> Auditory cognition, investigating representations of sounds, including spatial and temporal aspects, using psychophysical approaches as well as fMRI and EEG. Understanding auditory cognition gives a valuable insight in speech as well as attentional and spatial processing and helps to design new rehabilitation strategies.

> The cerebral reorganization following cognitive therapeutic interventions on attention and working memory deficits in stroke patients, by using repeated task-related and resting-state functional MRI acquisitions. These innovative investigations of neural mechanisms underlying therapeutic interventions are essential for their focused use in clinical practice.

> Neuro-motor rehabilitation, with focus on robotics, brain-machine interfaces and optimization of spasticity care. Carried out with numerous national and international collaborations, this research focuses mainly on hand movement and gait.

Laboratory of Cognitive Science

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Keywords
Cognitive functions
Neural plasticity
Recovery from brain lesions
Neuropsychology
Auditory cognition
Cerebral cortex

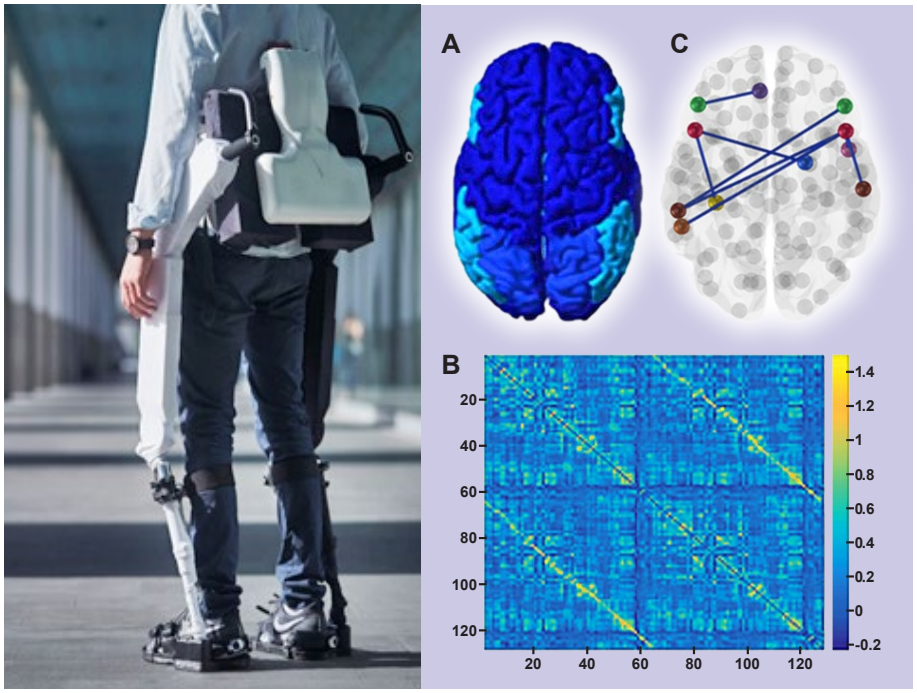
Research interests
Stephanie Clarke, Sonia Crottaz-Herbette, Stefano Carda and Jean-Michel Pignat investigate cognitive and motor functions in normal subjects and in brain-damaged patients, with particular interest in the organisation and plasticity of the human auditory and motor cortices, and attention networks.

Scientific contributions in 2019-2020
In addition to the dorsal and ventral auditory streams, sounds are encoded in a third, lateral stream, which we investigated. It originates within early-stage auditory areas where the combination of specific objects meaning and position are encoded. Its later stages are left-dominant and underlie implicit uses of spatial cues, in contrast to the right-dominant dorsal stream supporting explicit sound localization.

Dr Sonia Crottaz-Herbette showed, in studies on the intrinsic functional connectivity of the brain, that a brief exposure to rightward prismatic adaptation changes resting-state network characteristics of the ventral attentional system and enhances decoupling between the default mode network and the attentional networks. These results deepen our previous findings that showed how brief exposure to rightward prism adaptation switches hemispheric dominance of the ventral attentional system from the right to the left hemisphere.

Dr Stefano Carda investigates the effects of electrically-assisted movement therapy on motor control of patients with severe to moderate upper limb paralysis. He is also involved in a project using two different exoskeletons to improve gait and mobility function in patients with neuromuscular disorders, multiple sclerosis and stroke.

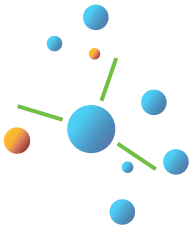
Dr Jean-Michel Pignat investigates brain connectivity based on EEG and multimodal MRI to identify the physio-pathological mechanisms underlying cognitive impairment, and particularly fatigue and disorders of consciousness.



A. *Regions of the ventral attentional network (cyan), dorsal attentional network (azur blue), and rest of the brain (marine blue).*

B. *Resting state connectivity matrices before and after visuo-motor adaptation for the R-PA group and for the control group.*

C. *Nodes and edges that yielded a significant R-PA-related decrease in connectivity. Adapted from Gundmundsson et al, 2020.*



Main publications in 2019-2020

Beaud V, **Crottaz-Herbette S**, Dunet V, Vaucher J, Bernard-Valnet R, Du Pasquier R, Bart PA, **Clarke S**. Pattern of cognitive deficits in severe COVID-19. Journal of neurology, neurosurgery, and psychiatry 2020.

Carda S, Invernizzi M, Bavikatte G, Bensmaïl D, Bianchi F, Deltombe T, Draulans N, Esquenazi A, Francisco GE, Gross R, Jacinto LJ, Moraleda Pérez S, O'Dell MW, Reebye R, Verduzco-Gutierrez M, Wissel J, Molteni F. The role of physical and rehabilitation medicine in the COVID-19 pandemic: The clinician's view. Ann. Phys. Rehabil. Med. 2020; 63(6):554-556.

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Wilf M, Serino A, **Clarke S**, **Crottaz-Herbette S**. Prism adaptation enhances decoupling between the default mode network and the attentional networks. NeuroImage 2019; 200:210-20.

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Gait lab, 3 STIMO participants.

NeuroRestore, Defitech Center for Interventional Neurotherapies

Laboratoire NeuroRestore, Centre Defitech de neurothérapies interventionnelles

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Laboratory's activity

NeuroRestore is a research, innovation and treatment center that develops and applies bioengineering strategies involving neurosurgical interventions to restore neurological functions.

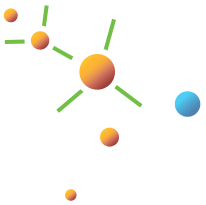
The objectives of NeuroRestore are to integrate implantable neurotechnologies and innovative treatments resulting from rigorous preclinical studies that have been conducted during the last two decades in rodent and non-human primate models. These developments have led to breakthroughs for the treatment of paraplegia, tetraplegia, Parkinson's disease, stroke, and traumatic brain injuries.

Research interests

Development of implantable neurotechnologies to restore neurological functions, including the in-depth understanding of their mechanims in preclinical models and implementation in humans.

Scientific contributions in 2019-2020

> Development of a new paddle lead that restored walking in people with complete paralysis.
> Development of a new neuroprosthetic treatment that alleviates hemodynamic instability in people with spinal cord injury.
> Development of new methods for single cell RNA sequencing.
> Development of a new deep brain stimulation treatment that improves walking in preclinical models of spinal cord injury.
> Real-time identification of freezing of gait and encoding of leg movements from subthalamus recordings in people with Parkinson's disease.
> Development of a new model of stroke in the internal capsule in nonhuman primates.



Main publications in 2019-2020

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Schiavone G, Fallegger F, Kang X, Barra B, Vachicouras N, Roussinova E, Furfaro I, Jiguet S, Seáñez I, Borgognon S, Rowald A, Li Q, Qin C, Bézard E, **Bloch J**, **Courtine G**, Capogrosso M, Lacour S. Soft, Implantable Bioelectronic Interfaces for Translational Research. Advanced Materials 2020 Apr; 32(17):e1906512.

Borgognon S, Cottet J, Moret V, Chatagny P, Carrara L, Fregosi M, **Bloch J**, Brunet JF, Rouiller E, Badoud S. Fine Manual Dexterity Assessment After Autologous Neural Cell Ecosystem (ANCE) Transplantation in a Non-human Primate Model of Parkinson's Disease. Neurorehabilitation Neural Repair 2019 Jul; 33(7): 553-567.

Cho N, Squair J, **Bloch J**, **Courtine G**. Neurorestorative interventions involving bioelectronic implants after spinal cord injury. Bioelectronic Medicine 2019 Jul 11; 5:10.

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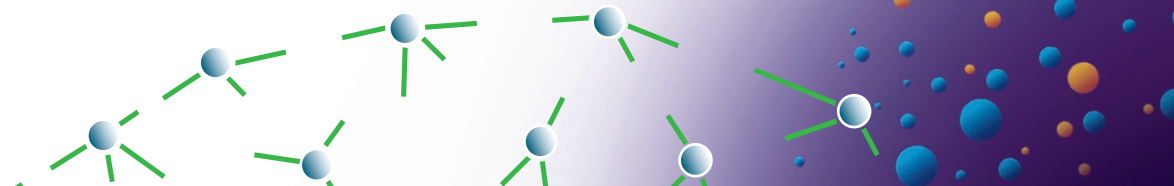
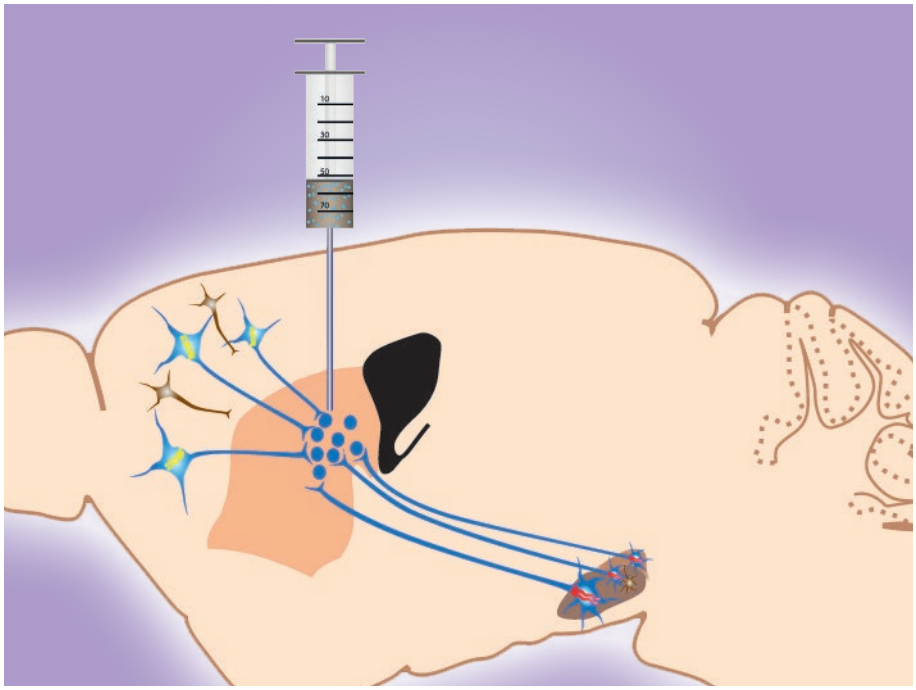


Laboratory of Cellular and Molecular Neurotherapies LNCM

Assoc. Professor Nicole Déglon, Head of laboratory
Privat-Docent Liliane Tenenbaum



Laboratory's activity
The laboratory's activities are focusing on the development and validation of innovative neurotherapies and neuromodulation strategies. The research programs are focusing on:

> Underlying molecular and environmenental mechanisms in Huntington's disease (HD).

> Pre-clinical development of molecular therapies for Huntington's disease (HTT gene editing).

> Modulation of neuroinflammation and drug-inducible gene therapy of Parkinson's disease.

Laboratory of Cellular and Molecular Neurotherapies LNCM

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Keywords
Neurodegenerative diseases
Huntington's disease
Gene therapy
Gene editing

Laboratory's activity

We focus our research on the development of molecular therapies for neurodegenerative disorders and in particular huntingtin (HTT) gene editing for Huntington's disease (HD). We have been exploiting the unique features and targeting specificities of viral vectors to deliver therapeutic candidates, generate new models of CNS pathologies or improve our understanding of the pathological mechanisms. In parallel, we are taking advantage of local and cell-type specific overexpression of transgenes in the CNS to investigate spreading of wild-type Tau protein in sporadic tauopathies as well as the contribution of mitochondrial dysfunctions in early AD.

Research interests

The group has a long-standing experience and expertise in viral gene transfer technology to deliver therapeutic candidates in the brain or to model CNS pathologies by overexpressing disease-causing proteins.

Scientific contributions in 2019-2020

Contributions of neuronal and nonneuronal populations in cerebral function

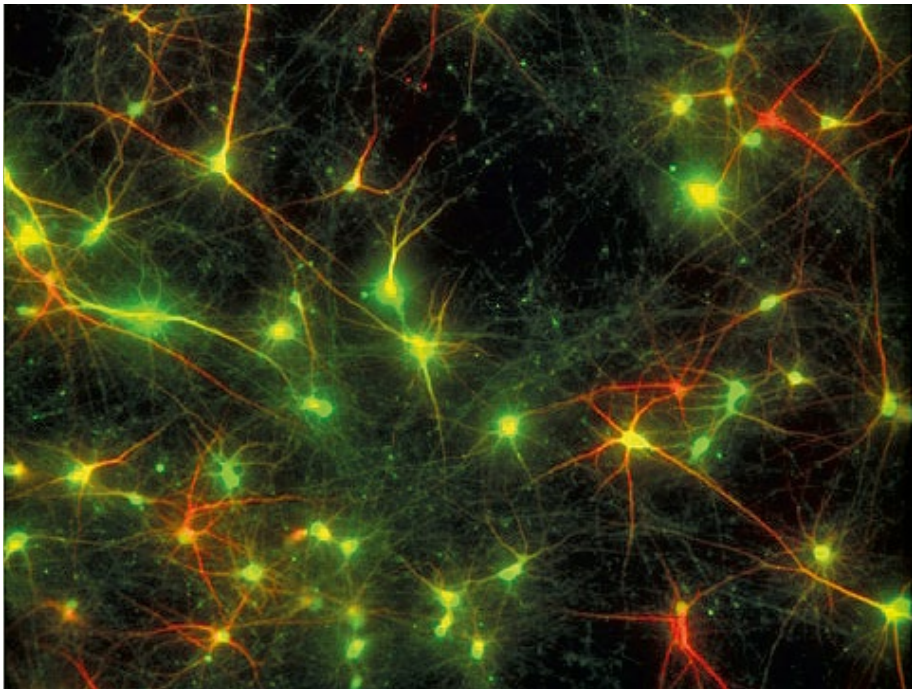
1)The role of non-neuronal cells in Alzheimer's disease remains unclear. Our recent results indicate that the loss of tau homeostasis in astrocytes of the hilus of the dentate gyrus is sufficient to induce AD-like symptoms, through the impairment of the neuronal network.
2) To further decipher the contributions of various cellular populations in the CNS, we develop a robust method for celltype-specific isolation. We optimize a laser-capture microdissection approach and characterize transcriptomic and epigenetic mechanisms in normal or pathological mouse and human Huntington's disease (HD) brains.

Gene Transfer

1) Gene transfer methods are extensively used for studying and treating genetic diseases. In this study, we developed second-generation gene transfer systems targeting cell types and brain circuits affected in CNS diseases. In a collaborative study, these vectors were used to demonstrate that mtCB1 receptor signalling can directly regulate astroglial glucose metabolism to fine-tune neuronal activity and behaviour in mice.
2) Adeno-associated virus (AAV) vectors are currently among the most commonly applied for *in vivo* gene therapy approaches. We set up a scalable process for AAV production, using orbitally shaken bioreactors and a fully characterized suspension-adapted cell line. We demonstrated the potency of vectors produced using suspension adapted HEK293 cells by comparing them with vectors produced in classical adherent HEK293 cell cultures into the striatum of adult mice.

Therapeutic strategies

Gene editing may prevent or cure a disease by inducing genetic changes at endogenous loci. Emerging technologies have extended the boundaries of genome manipulation for counteracting genetic diseases. In a review, we describe the various tools available for genome editing and summarize *in vivo* preclinical studies of CNS genome editing, whilst considering current limitations and alternative approaches to overcome some bottlenecks.



Neurones derived from human neuronal stem cells transduced with a lentiviral vector expressing the green fluorescent protein.

Main publications in 2019-2020

Petrelli F, Dallérac G, Pucci L, Cali C, Zehnder T, Sultan S, Lecca S, Chicca A, Ivanov A, Asensio C, Gundersen V, Toni N, Knott G, Magara F, Gertsch J, Kirchhoff F, **Déglon N**, Giros B, Edwards R, Mothet JP, Bezzi P. Dysfunction of homeostatic control of dopamine by astrocytes in the developing prefrontal cortex leads to cognitive impairments. Mol. Psychiatry 2020; 25:732-749.

Richetin K, Pachoud M, Maheswaran M, Bégard S, Pythoud C, Rey M, Caillierez R, Leuba G, Halliez S, Bezzi P, Buée L, Colin M, Toni N, **Déglon N**. 1N3R tau accumulation in hilar astrocytes induces neuronal dysfunction and memory deficits in Alzheimer's disease. Nat. Neurosci. 2020; 23(12):1567-1579.

Jimenez-Blasco D, Busquets-Garcia A, Hebert-Chatelain E, Serrat R, Vicente-Gutierrez C, Ioannidou C, Gómez Sotres P, Lopez-Fabuel I, Resch M, Resel E, Arnouil D, Saraswat D, Varilh M, Cannich A, Julio-Kalajzic F, Bonilla-Del Rio I, Almeida A, Puente N, Achicallende S, Lopez-Rodriguez ML, Jollé C, **Déglon N**, Pellerin L, Josephine C, Bonvento G, Panatier A, Lutz B, Piazza PV, Guzmán M, Bellocchio L, Bouzier-Sore AK, Grandes P, Bolaños JP, Marsicano G. Brain glucose metabolism links astroglial mitochondria 1 to social interactions via cannabinoid receptors. Nature 2020; 583(7817):603-608.

Duarte F and **Déglon N**. Genome Editing for CNS Disorders. Front. Neurosci. 2020; 14:579062.

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Blessing D, Vachey G, Pythoud C, Rey M, Padrun V, Wurm FM, Schneider BL*, **Déglon N***. Scalable production of AAV vectors in orbitally shaken HEK293 cells. Mol. Ther Meth Clin. Dev. 2019; 13:14-26. *Equally contributed to this work.

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Laboratory of Cellular and Molecular Neurotherapies LNCM

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Keywords
Parkinson's disease
Neuroprotection
Targeted and inducible gene transfer
GDNF
Neuroinflammation

Laboratory's activity

Current treatments for Parkinson's disease are symptomatic. Neurotrophic factors could halt disease progression. AAV vectors deliver GDNF in the brain, protecting dopaminergic neurons and reducing motor symptoms. However, long-term or off-target delivery induce side effects. Currently used AAVs i) do not allow to adjust the dose and period of treatment; ii) express GDNF into all types of neurons, mainly projection neurons. In contrast, endogenous GDNF is expressed by interneurons. We are developing inducible and targeted AAVs in order to optimize neuroprotective gene therapy.

Research interests

Neuroprotective gene therapy for Parkinson's disease
> Drug-inducible and targeted AAV vectors.
> Mechanism of GDNF neuroprotective effects *in vivo*.

Sensing and reducing brain inflammatory responses
> Modulators of neuroinflammatory signalling.

Scientific contributions in 2019-2020

Drug-inducible neuroprotective gene therapy for Parkinson's disease (PD)

We have shown that a continuous but not a transient GDNF treatment induces deleterious effects reducing the clinical benefit (manuscript in preparation). These data support the use of regulated viral vectors for neurorestorative gene therapies.

Selective targeting of neuronal subpopulations

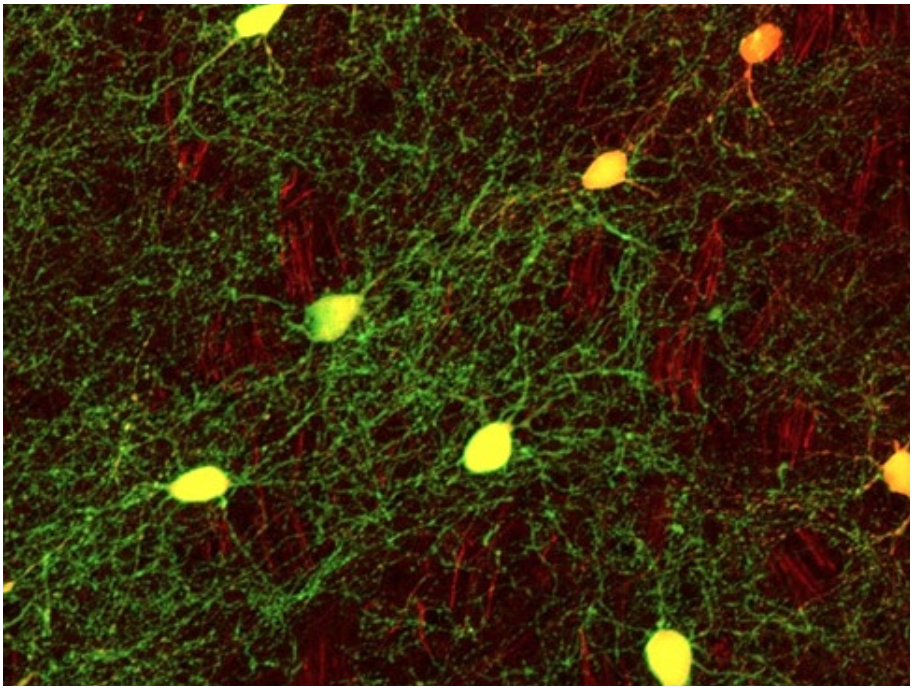
Our hypothesis is that GDNF secretion by cells which do not express it in the healty brain elicit undesired effects. Therefore, we are developing viral vectors targeting specific neuronal subpopulations.

Neuroinflammation is coupled to oxidative stress in neurological diseases

We have contributed disease-inducible AAV vectors to assess neuroinflammation.

Contribution to a multicentric cell therapy clinical trial for Huntington's disease

No clinical benefit was demonstrated. However, this pionnering cell therapy trial generated important data for the design of future trials.



Striatal injections of AAV-FLEx-GFP vectors in PVcre mice leads to a specific GFP expression (green) in parvalbumine-positive interneurons (red).

Main publications in 2019-2020

Duarte Azevedo M, Sander S, Jeanneret C, Olfat S, **Tenenbaum L**. Selective targeting of striatal parvalbumin-expressing interneurons for transgene delivery. J Neurosci. Meth; 27:109105.

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www.unil.ch/lcmn/home/menuinst/research-groups/gene-transfer-for-parkinsons.html

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Laboratory for the Exploration of Memory in Neurosciences LEMENS

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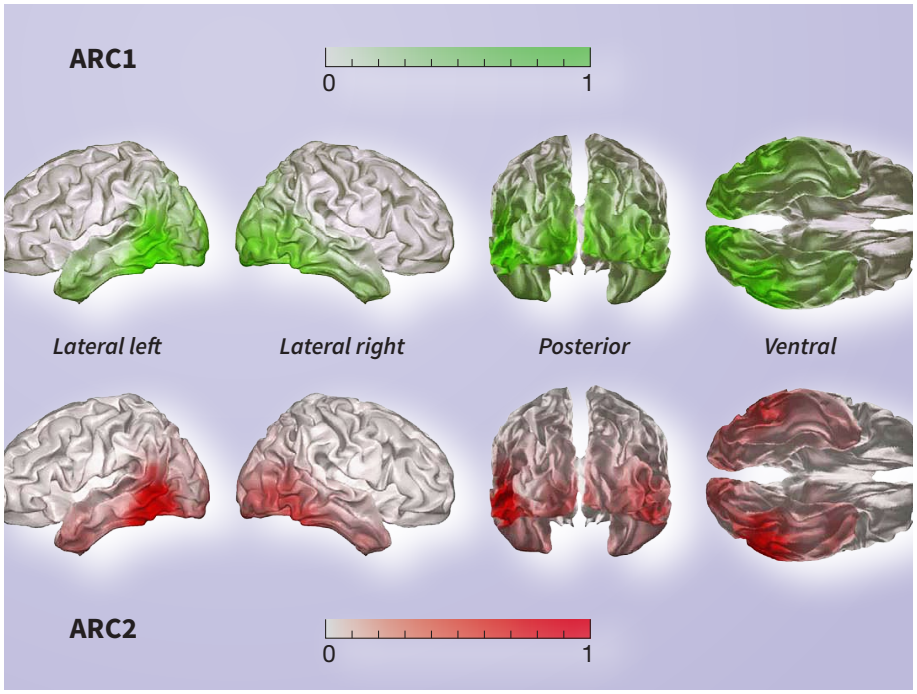
Keywords
Memory
Language
Cognition
Brain imaging
Biomarkers
Neuro-degenerative diseases
Alzheimer's disease
Diagnosis
Treatment

Laboratory's activity
The Laboratory for the Exploration of MEmory in Neuro-Sciences (LEMENS) represents the translational research facet of the Leenaards Memory Centre (www.centre-memoire.ch), a Centre devoted to diagnosis and care of patients and their families facing the "Ageing-Brain Cognitive Diseases" (the ABCDs), such as Alzheimer's disease and other associated conditions (fronto-temporal dementias, diffuse Lewy body disease, vascular dementia).

Research interests
I am a Neurologist involved in the neurophysiology of language and memory studied with the combination of cognitive testing and a variety of brain imaging and function mapping in the broadest sense, from EEG to MRI and direct cortical stimulation; as a Physician, I try my best to treat patients and support families facing devastating brain diseases affecting cognition and especially neurodegenerative associated with ageing. My academic career involved a position of Directeur de Recherche at INSERM (France from 1995-2011); currently I am holding a position of full professor at CHUV-UNIL and head of the Leenaards memory centre, one of the "Services" of the Clinical Neurosciences Dept.

Scientific contributions in 2019-2020
> Public health studies of ageing.
> Intervention studies. Physical and cognitive training in healthy senior participants: study protocol.
> Intervention studies. Effects of multiple psychosocial interventions in MCI participants.
> Intervention studies. Fetal grafts in Huntington's patients.
> Cognitive and developmental neuroscience. New insights into heritability of developmental dyslexia.
> Cognitive and developmental neuroscience. Reproducibility of electrophysiological brain responses to perception vs non standard reading development.
> Cognitive and developmental neuroscience. Gamma response to Hold-Release paradigm.
> Cognitive and developmental neuroscience. Linguistic analysis of reference-related markers in the discourse of AD patients.
> NeuroImaging, NeuroInformatics and Data science of brain ageing. The influence of ApoE4 genotype on MR-based structural connectivity in regional brain volumes in MCI patients.
> NeuroImaging, NeuroInformatics and Data science of brain ageing. The contribution of Medical Informatics Platform to diagnosis decision in an Italian memory clinics network.
> NeuroImaging, NeuroInformatics and Data science of brain ageing. The MEMONET project to set up a research-dedicated network of memory centres in Switzerland.
> Clinical Neurology. A case study of co-morbidity MS and AD.
> Clinical Neurology. A review of the current molecular isotopic brain imaging contributing to clinical research in cognitive brain pathologies.



Aging of human alpha rhythm in the EEG signal.

Main publications in 2019-2020

Henchoz Y, Büla C, von Gunten A, Blanco JM, Seematter-Bagnoud L, **Démonet JF**, Waeber G, Nanchen D, Santos-Eggimann B. Trends in Physical and Cognitive Performance Among Community-Dwelling Older Adults in Switzerland. J Gerontol. A Biol. Sci. Med. Sci. 2020 Nov 13; 75(12):2347-2353.

Gialluisi A, Andlauer TFM, Mirza-Schreiber N, Moll K, Becker J, Hoffmann P, Ludwig KU, Czamara D, Pourcain BS, Honbolygó F, Tóth D, Csépe V, Huguet G, Chaix Y, Iannuzzi S, **Demonet JF**, *et al*. Genome-wide association study reveals new insights into the heritability and genetic correlates of developmental dyslexia. Mol. Psychiatry 2020 Oct 14.

Belleville S, Cuesta M, Bieler-Aeschlimann M, Giacomino K, Widmer A, Mittaz Hager AG, Perez-Marcos D, Cardin S, Boller B, Bier N, Aubertin-Leheudre M, Bherer L, Berryman N, Agrigoroaei S, **Demonet JF**. Rationale and protocol of the StayFitLonger study: a multicentre trial to measure efficacy and adherence of a home-based computerised multidomain intervention in healthy older adults. BMC Geriatr. 2020 Aug 28; 20(1):315.

Leidi-Maimone B, Notter-Bielser ML, Laouadi MH, Perrin S, Métraux H, Damian D, Chavan CF, Nsir M, Cibelli G, Tâche MJ, Montandon ML, Ghika J, **Démonet JF**, Dürst AV, Guevara AB. How non-drug interventions affect the quality of life of patients suffering from progressive cognitive decline and their main caregiver. Aging (Albany NY) 2020 Jun 9; 12(11): 10754-10771.

Draganski B, Kherif F, Damian D, **Demonet JF**; MemoNet consortium. A nation-wide initiative for brain imaging and clinical phenotype data federation in Swiss university memory centres. Curr. Opin. Neurol. 2019 Aug; 32(4):557-563.

Leppänen PHT, Tóth D, Honbolygó F, Lohvansuu K, Hämäläinen JA; NEURODYS WP7 group, **Demonet JF**, Schulte-Körne G, Csépe V. Reproducibility of Brain Responses: High for Speech Perception, Low for Reading Difficulties. Sci. Rep. 2019 Jun 11; 9(1):8487.

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Laboratory of Acute Neurorehabilitation - LNRA

Senior Lecturer Karin Diserens
Senior staff member
Head of the Laboratory of Acute Neurorehabilitation - LNRA
Laboratoire de recherche en neurorééducation aiguë
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Keywords
Coma
Disorders of Consciousness (DOC)
Cognitive Motor Dissociation (CMD)
Prognosis
Acute neurorehabilitation
Neurosensorial approach
Brain Computer Interface
PeriPersonal Space
Robotic neurovegetative disorders
Virtual reality
Spasticity
Early mobilization

Laboratory's activity

> To provide accurate identification of Clinical Cognitive Motor Dissociation (cCMD) among Disorders of Consciousness (DOC) in the acute phase by means of the validation of a new clinical tool; the Motor Behavior Tool-revised (MBTr).
> To investigate the functional/cognitive recovery in patients with cCMD.
> To implement an EEG motor imagery paradigm coupled with functional electrical stimulation, and an EEG task-free paradigm to differentiate patients evidencing intention without being able to implement it.
> To determine the feasibility of a salivary cortisol-collection protocol and to evaluate the influence of exposure to natural settings on salivary cortisol concentration, as an index for the level of stress in acute brain-injured patients.
> To test early mobilisation and verticalisation in acute care patients.
> To investigate transition between young adults and adults with neuro-disabilities to provide a follow-up along a continual pathway.

Research interests

Overall our research aims to develop a coordinated multimodal approach involving several experts, integrating information from complementary sources to increase detection accuracy of covert awareness/Cognitive Motor Dissociation among Disorders of Consciousness in the acute stage, to inform better the decision-making process and prognosis and to improve early therapeutic interventions for severely neurolesioned patients.

Scientific contributions in 2019-2020

> Validation of a new clinical motor observation tool (MBTr).
> Investigation of functional and cognitive outcomes of cCMD patients, DOC and non-DOC.
> Description of confounding factors (pitfalls) interfering with clinical recognition of consciousness.
> Detection of multisensory process revealing intentionality in the absence of movement by means of EEG-based Peri-Personal Space protocols.
> Review of the polymorphic burden of COVID-19 and propositions of early interventions that could minimize the neurological and systemic impact.
> Report on the reinsertion project aiming to bring awareness to the general practitioner of an interdisciplinary care method.
> Update of results on the neural mechanisms involved in complex regional pain syndrome (CRPS).
> Proposition of an interprofessional evaluation of spasticity.
> Assessment of swallowing disorders in acute ischemic stroke patients.

Vibramoov research project investigating neural correlates of illusory movement induced by functional proprioceptive stimulation.

Vibramoov project's team.

Main publications in 2019-2020

Pincherle A, Rossi F, Jöhr J, Dunet V, Ryvlin P, Oddo M, Schiff N, **Diserens K**. Early discrimination of cognitive motor dissociation from disorders of consciouness: pitfalls and clues. J Neurol. 2020 Aug 4.

Perret N, González-Morón D, Queijo H, Honorez-Erard I, Attwell C, Ryvlin P, Bovay G, Dorthe D, Newman CJ, **Diserens K**. Comment faciliter la réinsertion socio-professionnelle du patient neurolésé ? Outils pour le praticien [How to improve social and professional reinsertion of patients with neurodiabilities ? Practical indications for the general practitioner]. Rev. Med. Suisse 2020 May 6; 16(692):911-914. French.

Pincherle A, Jöhr J, Pancini L, Leocani L, Dalla Vecchia L, Ryvlin P, Schiff ND, **Diserens K**. Intensive Care Admission and Early Neuro-Rehabilitation. Lessons for COVID-19? Frontiers in neurology 2020; 11:880.

Jöhr J, Halimi F, Pasquier J, Pincherle A, Schiff N, **Diserens K**. Recovery in cognitive motor dissociation after severe brain injury: A cohort study. PLoS One 2020 Feb 5; 15(2):e0228474.

Noel JP, Chatelle C, Perdikis S, Jöhr J, Lopes Da Silva M, Ryvlin P, De Lucia M, Millán JDR, **Diserens K**, Serino A. Peri-personal space encoding in patients with disorders of consciousness and cognitive-motor dissociation. Neuroimage Clin. 2019; 24:101940.

Pincherle A, Jöhr J, Chatelle C, Pignat JM, Du Pasquier R, Ryvlin P, Oddo M, **Diserens K**. Motor behavior unmasks residual cognition in disorders of consciousness. Ann Neurol. 2019 Mar; 85(3):443-447.

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Laboratory for Research in Neuroimaging - LREN

Assoc. Professor Bogdan Draganski, Head of laboratory
Senior Lecturer Ferath Kherif
Senior Lecturer Marzia De Lucia
Assist. Professor Antoine Lutti

Laboratory's activity
LREN is a neuroimaging laboratory where clinical and basic neuroscientists study human brain structure and function relevant to neurological disorders and normal cognition. We develop and apply non-invasive neuroimaging methods - magnetic resonance imaging and electro-encephalography to investigate topics including use-dependent brain plasticity, rehabilitation of lost function and neurodegeneration.

LREN is responsible for a state-of-the-art neuroimaging platform featuring high-end research-only Siemens Prisma 3T MRI scanner, sophisticated MRI compatible neurophysiological equipment and high-density EEG machines.

LRENs main goal is to translate basic research findings into clinical applications for early diagnosis of disease and for prediction of clinical outcome.

Laboratory for Research in Neuroimaging - LREN

Assoc. Professor Bogdan Draganski
Consultant/attending physician

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Affiliations
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Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig Germany

Keywords
Imaging neuroscience
In vivo histology

Research interests
> Neurodegeneration
> Dementia
> Brain plasticity
> Environmental health
> Healthy ageing.

Scientific contributions in 2019-2020
I am one of the three founding members of the grassroots initiative advocating for public awareness about dementia in Switzerland - BrainFit4Life (www.bebrainfit4life.com) that succeeded to attract at its 1st symposium ca. 200 signed participants and many ambassadors - leaders in their field of research.
In September 2019 I obtained funding and organised the 5th MRBalkan conference (www.mrbalkan.org) in Sofia, Bulgaria, including funding and organising the scientific programme with researchers from the UK, Austria, Germany, Canada, Greece, USA, Switzerland and Bulgaria. Together with Pr Patrik Michel and Pr Lorenz Hirt, I am the co-organiser of the Annual Symposium of the Cerebro-vascular Centre, Neurology - DNC, CHUV.
> PI Neuroimaging of the Swiss Ageing Citizen Reference cohort - a Swiss Personalised Health Network Project.
> PI of the SNF project "Urban maps of the brain".
> PI of the SNF SPARK project Making the "lazy" eye work.

Main publications in 2019-2020
Roggenhofer E, Muller S, Santarnecchi E, Melie-Garcia L, Wiest R, Kherif F, **Draganski B**. Remodeling of brain morphology in temporal lobe epilepsy. Brain Behav. 2020 Sep 17; e01825.

Jeong A, Bochud M, Cattin P, Dermitzakis M, **Draganski B**, Papassotiropoulos A, Preisig M, Stieltjes B, Vollenweider P, Probst-Hensch N. SPHN - The Swiss Aging Citizen Reference SACR. Stud. Health Technol. Inform. 2020 Jun 16; 270:1168-1169.

Marchi NA, Ramponi C, Hirotsu C, Haba-Rubio J, Lutti A, Preisig M, Marques-Vidal P, Vollenweider P, Kherif F, Heinzer R, **Draganski B**. Mean Oxygen Saturation during Sleep Is Related to Specific Brain Atrophy Pattern. Ann Neurol. 2020 Jun; 876:921-930.

Taubert M. Roggenhofer E, Melie-Garcia L, Muller S, Lehmann N, Preisig M, Vollenweider P, Marques-Vidal P, Lutti A, Kherif F, **Draganski B**. Converging Patterns of Aging-Associated Brain Volume Loss and Tissue Microstructure Differences. Neurobiology of Aging 2020.

Slater DA, Melie-Garcia L, Preisig M, Kherif F, Lutti A, **Draganski B**. Evolution of White Matter Tract Microstructure across the Life Span. Human Brain Mapp. 2019; 40(7):2252-2268.

Draganski B, Kherif F, Damian D, Demonet JF. A Nation-Wide Initiative for Brain Imaging and Clinical Phenotype Data Federation in Swiss University Memory Centres. Current opinion in neurology 2019; 32(4): 557-563.

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Laboratory for Research in Neuroimaging - LREN

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Keywords
Neurosciences
Neuroimaging
Clinical neurology & psychiatry
Psychology experimental
Computer science artificial intelligence
Computer science theory methods
Mathematical computational cognitive anatomy

Research interests

As neuroscientist, my chief interest is modeling the cognitive anatomy of language, memory and learning in health, disease and artificial network. Mathematical contributions include multivariate models to analyse large-scale data for the identification of neuro-clinical signatures. Built a theoretical framework for the structure-to-function mapping and computer science implementation.

Scientific contributions in 2019-2020

> Computational Methods for data fusion MRI data (level 0) to ensemble federated information fusion (level 4).
> Computer science interdisciplanary implementation of brain imaging science models from image processing to AI.
> Multiscale decomposition/simulation of interindividual difference in cognitive anatomy.

Main publications in 2019-2020

Kherif F, Muller S. Neuro-Clinical Signatures of Language Impairments: A Theoretical Framework for Function-to-structure Mapping in Clinics. Curr. Top Med. Chem. 2020; 20(9):800-811.

Zufferey V, Gunten AV, **Kherif F**. Interactions between Personality, Depression, Anxiety and Cognition to Understand Early Stage of Alzheimer's Disease. Curr. Top Med. Chem. 2020; 20(9):782-791.

Oala L, Fehr J, Gilli L, Balachandran P, Werneck Leite A, Calderon-Ramirez S, Xie Li D, Nobis G, Muñoz Alvarado EA, Jaramillo-Gutierrez G, Matek C, Shroff A, **Kherif F**, Sanguinetti B, Wiegand T. ML4H Auditing: From Paper to Practice. Proceedings of Machine Learning Research 2020 Dec; 136:280-317.

Redolfi A, De Francesco S, Palesi F, Galluzzi S, Muscio C, Castellazzi G, Tiraboschi P, Savini G, Nigri A, Bottini G, Bruzzone MG, Ramusino MC, Ferraro S, Gandini Wheeler-Kingshott CAM, Tagliavini F, Frisoni GB, Ryvlin P, Demonet JF, **Kherif F**, Cappa SF, D'Angelo E. Medical Informatics Platform (MIP): A Pilot Study Across Clinical Italian Cohorts. Front. Neurol. 2020 Sep 23; 11:1021.

Taubert M, Roggenhofer E, Melie-Garcia L, Muller S, Lehmann N, Preisig M, Vollenweider P, Marques-Vidal P, Lutti A, **Kherif F**, Draganski B. Converging patterns of aging-associated brain volume loss and tissue microstructure differences. Neurobiol. Aging 2020 Apr; 88:108-118.

Stoyanov D, Kandilarova S, Paunova R, Barranco Garcia J, Latypova A, **Kherif F**. Cross-Validation of Functional MRI and Paranoid-Depressive Scale: Results From Multivariate Analysis. Front. Psychiatry 2019 Nov 25; 10:869.

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Laboratory for Research in Neuroimaging - LREN

Senior Lecturer Marzia De Lucia

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Keyword
Electrophysiology
Consciousness

Laboratory's activity

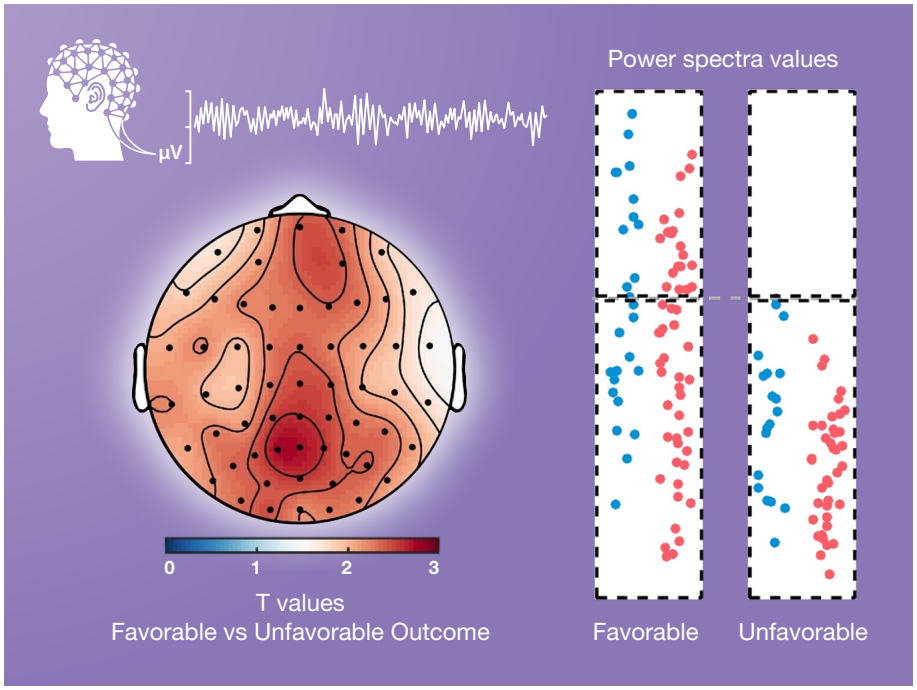
Loss of consciousness involves dramatic changes in neural activity and is accompanied by a drastic reduction in the responsiveness to sensory stimuli. My research work aims at shedding light on common principles underlying preserved brain responses to sensory stimuli across different varieties of unconscious states including coma and deep sleep. This knowledge informs the development of quantitative markers revealing covert consciousness in unresponsive patients. We acquire data through intracranial and scalp electrophysiological recordings, diffusion tensor and magnetic resonance imaging. We employ machine learning techniques, network analysis and signal processing methods for combining functional and structural data.

Research interests

> Coma
> Disorders of consciousness
> Statistical regularities
> Interoception.

Scientific contributions in 2019-2020

> Patent "Method for predicting awakening in a comatose patient and computer-implemented method thereof" with inventors Marzia De Lucia and Athina Tzovara granted in US and EU.
> MDL is PI of the Pro-Femmes UNIL project "Neural responses to cardio-audio sequences in comatose patients".
> MDL is PI of the SNF Spark project "Detection of unexpected events as driven by heartbeat signals in human sleep".
> Contribution to the setup of three high density EEG systems for collaborative projects as part of the EEG platform of the Department of Clinical Neuroscience.
> Ideation and coordination of the github repository of the Clinical Neuroscience Department for EEG analysis methods: https://github.com/DNC-EEG-platform.
> Organization of the seminars series 'la boîte à outils' for EEG analysis method dissemination.



EEG resting state analysis predicts favorable outcome in comatose patients.

Main publications in 2019-2020

Comanducci A, Boly M, Claassen J, **De Lucia M**, Gibson RM, Juan E, Laureys S, Naccache L , Owen AM, Rosanova M, Rossetti AO, Schnakers C, Sitt JD, Schiff ND, Massimini M. Clinical and advanced neurophysiology in the prognostic and diagnostic evaluation of disorders of consciousness: review of an IFCN-endorsed expert group. Clinical Neurophysiology 2020; 131(11):2736-2765.

Kustermann T, Nguissi NAN, Pfeiffer C, Haenggi M, Kurmann R, Zubler F, Oddo M, Rossetti AO, **De Lucia M**. Brain functional connectivity during the first day of coma reflects long-term outcome. Neuroimage Clinical 2020; 27:102295.

Noel JP, Chatelle C, Perdikis S, Jöhr J, Lopes Da Silva M, Ryvlin P, **De Lucia M**, Millán JDR, Diserens K, Serino A. Peri-personal space encoding in patients with disorders of consciousness and cognitive-motor dissociation. Neuroimage Clinical 2019; 24:101940.

Kustermann T, Nguissi NAN, Pfeiffer C, Haenggi M, Kurmann R, Zubler F, Oddo M, Rossetti AO, **De Lucia M**. Electroencephalography-based power spectra allow coma outcome prediction within 24 h of cardiac arrest. Resuscitation 2019; 142:162-167.

Caporro M, Rossetti AO, Seiler A, Kustermann T, Nguissi NAN, Pfeiffer C, Zimmermann R, Haenggi M, Oddo M, **De Lucia M**, Zubler F. Electromyographic reactivity measured with scalp-EEG contributes to prognostication after cardiac arrest. Resuscitation 2019; 138:146-152.

Hartmann L, Wachtl L, **De Lucia M**, Spierer L. Practice-induced functional plasticity in inhibitory control interacts with aging. Brain and Cognition 2019; 132: 22-32.

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Keywords

MRI physics
Quantitative MRI
In vivo histology
Imaging neuroscience

Laboratory's activity

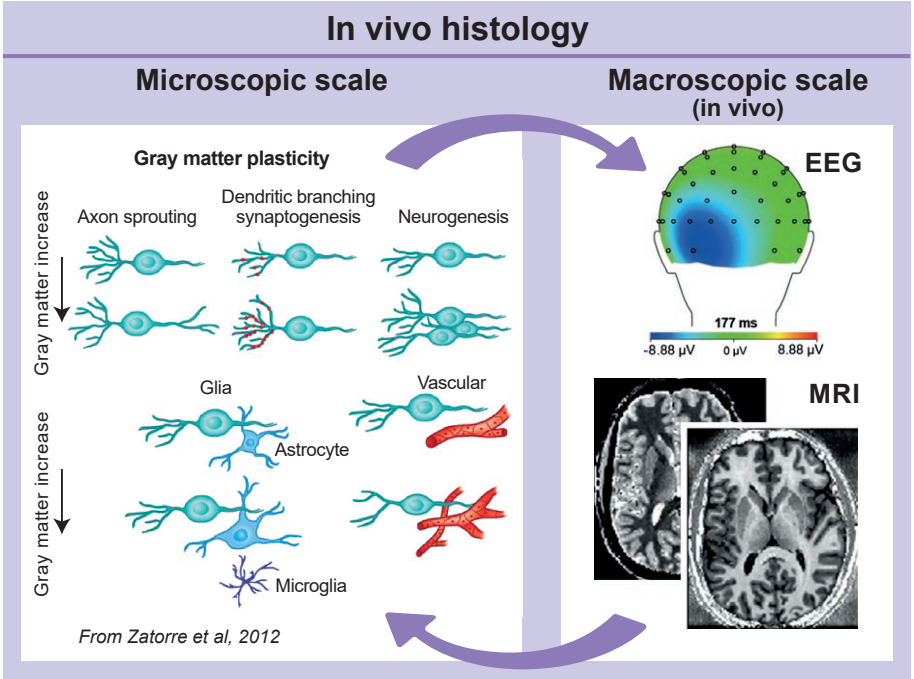
Current Magnetic Resonance Imaging (MRI) technologies only allow for the characterization of disease-related brain change at the macroscopic scale of a brain region. However, many clinically relevant changes take place at the microscopic scale within brain tissue. Currently, these changes cannot be assessed *in vivo* in patient populations. Our group focuses on the development of quantitative MRI (qMRI) technologies that provide a direct measure of microscopic brain tissue properties ("*in vivo* histology"). qMRI data can be acquired *in vivo* in patients and provide a detailed description of microscopic pathological brain change. Combined with other techniques such as EEG, they allow improved monitoring of disease evolution and patient classification.

Research interests

> MRI techniques for neuroscience
> Motion correction
> Biophysical modelling of the MRI signal
> MRI biomarkers of brain tissue.

Scientific contributions in 2019-2020

> PI of the SNF project "Advanced quantitative MRI biomarkers of Parkinsons's Disease - towards *in vivo* histology".
> Technical supervision of the MRI platform of the Department for Clinical Neuroscience - CHUV.
> MRI platform of the DNC-CHUV achieved the examination of its 5000th research participant.



Our group focuses on quantitative MRI technologies that allow the measurement of microscopic properties of the brain from MRI data acquired in vivo in patient populations ('in vivo histology').

Main publications in 2019-2020

Marchi N, Ramponi C, Hirotsu C, Haba-Rubio J, **Lutti A**, Preisig M, Marques-Vidal P, Vollenweider P, Kherif F, Heinzer R, Draganski B. Mean Oxygen Saturation during Sleep Is Related to Specific Brain Atrophy Pattern. Annals of Neurology 2020; 87(6):921-930.

Taubert M, Roggenhofer E, Melie-Garcia L, Muller S, Lehmann N, Preisig M, Vollenweider P, Marques-Vidal P, **Lutti A**, Kherif F, Draganski B. Converging patterns of aging-associated brain volume loss and tissue microstructure differences. Neurobiol. Aging 2020; 88:108-118.

Tabelow K, Balteau E, Ashburner J, Callaghan MF, Draganski B, Helms G, Kherif F, Leutritz T, **Lutti A**, *et al*. hMRI - A toolbox for quantitative MRI in neuroscience and clinical research. Neuroimage 2019; 194:191-210.

Marquis R, Muller S, Lorio S, Rodriguez-Herrero B, Melie-Garcia L, Kherif F, **Lutti A**, Draganski B. Spatial Resolution and Imaging Encoding fMRI Settings for Optimal Cortical and Subcortical Motor Somatotopy in the Human Brain. Frontiers in Neurosci. 2019; 13:571.

Slater D, Melie-Garcia L, Ruef A, Kherif F, **Lutti A**, Draganski B. Evolution of white matter tract microstructure across the life span. Human Brain Mapping 2019; 40(7):2252-2268.

Lee Y, Callaghan M, Acosta-Cabronero J, **Lutti A**, Nagy Z. Establishing intra- and inter-vendor reproducibility of T1 relation time measurements with 3T MRI. Magnetic Resonance in Medicine 2019; 81(1):454-465.

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https://sites.google.com/view/antoinelutti/home

Laboratories of Neuroimmunology

Laboratory of Neuroimmunology/Multiple Sclerosis - LNIS
Professor Renaud Du Pasquier, Head of laboratory

Laboratory of Experimental Neuroimmunology - LNIE
Assoc. Professor Caroline Pot Kreis, Head of laboratory

Multiple sclerosis (MS) is an auto-inflammatory disease of the central nervous system, where all components of the immune system, innate and adaptive, are involved. In addition to genetic factors, environmental ones play a crucial role in triggering this complex disease. In the Laboratories of neuroimmunology, we examine how environmental factors, among which Epstein-Barr virus, gut microbiome or cholesterol metabolites support autoreactivity of B and T cells. To tackle our hypothesis, we use different approaches, including animal models, namely the experimental autoimmune encephalomyelitis, human samples analysis (blood, cerebrospinal fluid, urine, soon stools) of MS patients and a human *in vitro* model of MS brain, using induced pluripotent stem cells (iPSC).

Laboratory of Neuroimmunology/Multiple Sclerosis LNIS

Professor Renaud Du Pasquier
Head of the Neurology Service

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Affiliations
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Service of immunology and allergy (LIA)

Keywords
Neuroimmunology
Multiple sclerosis
$CD8^+$ T cells
Induced pluripotent stem cells (iPSC)
Progressive multifocal leukoencephalopathy
Neuro-HIV

Laboratory's activity

Primarily devoted to research in Multiple Sclerosis (MS), our Laboratory studies the interaction between the immune response - with a focus on $CD8^+$ T cells - and environmental factors. Recently, we have established a program of induced pluripotent stem cells (iPSC). Thanks to this tool, several new opportunities open to us, as we are now able to observe central nervous system (CNS) cells of MS patients, which so far were out of reach. We have now the possibility to put auto-reactive peripheral immune cells in contact with autologous CNS cells and be in a position to determine if, indeed, there is recognition of autoantigens in the brain.

The Lab team is also actively involved in the monitoring of the long-term effects of DMTs used in MS on immune responses. Especially, we are trying to understand the interaction between these treatments and the biology of JC virus, the agent of progressive multifocal leukoencephalopathy (PML) to better handle the risk of developing PML.

Finally, together with clinicians, the Laboratory holds a research program dealing with the neurocognitive disorders in HIV^+ patients.

Research interests

The research of Prof. Renaud Du Pasquier is driven by the willingness to better understand the pathogenesis of inflammation in the brain, in particular in the field multiple sclerosis. Only such an understanding will lead to breakthrough treatments.

Scientific contributions in 2019-2020

> Perriot S, Mathias A, Perriard G, Canales M, Jonkmans N, Merienne N, Meunier C, El Kassar L, Perrier AL, Laplaud DA, Schluep M, Déglon N, Du Pasquier R (oral presentation). Human induced pluripotent stem cell-derived astrocytes are differentially activated by multiple sclerosis-associated cytokines. American Academy of Neurology, May 3-10, Philadephia PA, USA.

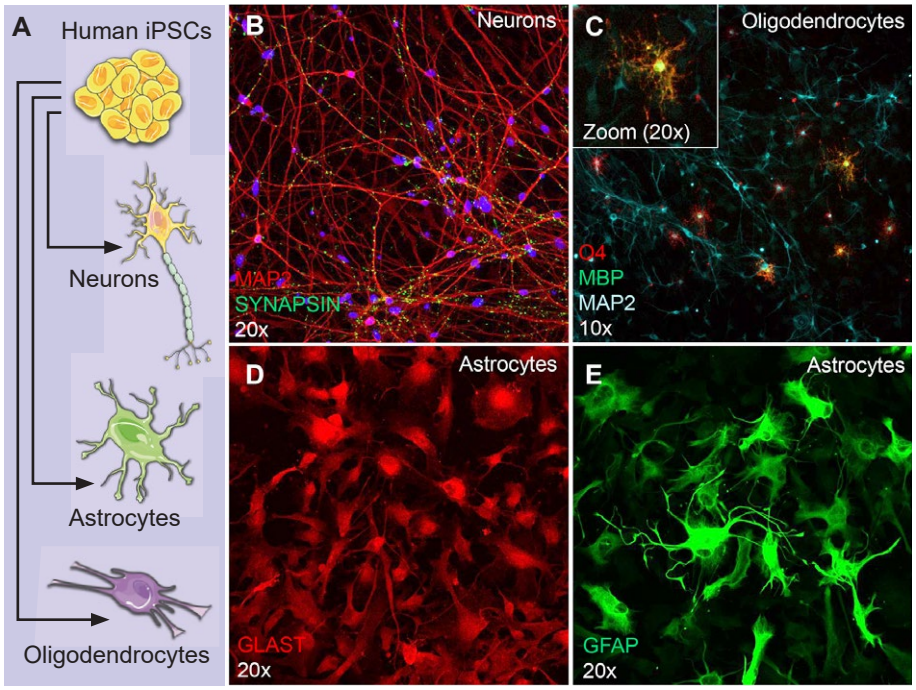
> Santos GMA, Locatelli I, Métral M, [...] Darling K, Du Pasquier R, Cavassini M for the NAMACO study group (oral presentation). Cross-sectional and cumulative longitudinal CPE scores are not associated with neurocognitive impairment in a well-treated aging HIV-positive population in Switzerland. American Academy of Neurology, May 3-10, Philadephia PA, USA.

> Perriot S, Mathias A, Perriard G, Canales M, Du Pasquier R. Transcriptomic analysis of reactive human iPSC-derived astrocytes induced by neuroinflammatory cytokines. European Conference on Neuroinflammation, April 8-9 2019; London UK.

> Mathias A, Perriot S, Jones S, Torcida N, Canales M, Theaudin M, Pot C, Du Pasquier R. Detection of novel CNS-specific antibodies using hiPSC-derived astrocytes and neurons: a pilot study on autoimmune-mediated neurological syndromes. EAN, May 23-26, Paris, France.

> Perriot S, Perriard G, Canales M, Mathias A, Du Pasquier R. Transcriptomic analysis of reactive human iPSC-derived astrocytes induced by neuroinflammatory cytokines. EAN, May 23-26, Paris, France.

> New tools to understand the role of $CD8^+$ T cells in Multiple Sclerosis. iMED, October 4, Lisbon, Portugal.



Differentiation of CNS cells from human iPSCs.
10 ml of blood was drawn from a patient with multiple sclerosis. Erythroblasts were isolated, then reprogrammed into human induced pluripotent stem cells (hiPSCs) (A), and finally differentiated into CNS cells, including neurons (B), oligodendrocytes (C), and astrocytes (D, E).

Main publications in 2019-2020

Nishihara H, Gastfriend BD, Soldati S, Perriot S, Mathias A, Sano Y, Shimizu F, Gosselet F, Kanda T, Palecek SP, **Du Pasquier R**, Shusta EV, Engelhardt B. Advancing human induced pluripotent stem cell-derived blood-brain barrier models for studying immune cell interactions. FASEB J 2020 Dec; 34(12):16693-16715.

Maggi P, Sati P, Nair G, Cortese ICM, Jacobson S, Smith BR, Nath A, Ohayon J, van Pesch V, Perrotta G, Pot C, Théaudin M, Martinelli V, Scotti R, Wu T, **Du Pasquier R**, Calabresi PA, Filippi M, Reich DS, Absinta M. Paramagnetic RIM lesions are specific to Multiple Sclerosis: an international multicenter 3T MRI study. Ann. Neurol. 2020 Nov; 88(5):1034-1042.

Bernard-Valnet R*, Pizzarotti B*, Anichini A, Demars Y, Russo E, Schmidhauser M, Cerutti-Sola J, Rossetti AO, **Du Pasquier R**. Two patients with acute meningoencephalitis concomitant to SARS-CoV-2 infection. Eur. J Neurol. 2020 Sep; 27(9):e43-e44. *Contributed equally.

Métral M*, Darling KEA*, Locatelli I, Nadin I, Santos G, Brugger P, Kovari H, Cusini A, Gutbrod K, Tarr PE, Calmy A, Lecompte TD, Assal F, Monsch A, Kunze U, Stoeckle M, Schwind M, Schmid P, Pignatti R, Di Benedetto C, **Du Pasquier R****, Cavassini M** and the NAMACO study group, Swiss HIV Cohort Study. The Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO) study: Baseline participant profile. HIV Med 2020 Jan; 21(1):30-42. *Contributed equally as first authors; **Contributed equally as senior authors.

Du Pasquier R. Pembrolizumab as a treatment for PML? Waiting for Godot. Neurol. Neuroimmunol. Neuroinflamm. 2019 Oct 9; 6(6):e629.

Santos GMA, Locatelli I, Métral M, Calmy A, Lecompte TD, Nadin I, Hauser C, Cusini A, Hasse B, Kovari H, Tarr P, Stoeckle M, Fux C, Di Benedetto C, Schmid P, Darling KEA, **Du Pasquier R*** and Cavassini M* for the Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO) Study Group. Cross-Sectional and Cumulative Longitudinal Central Nervous System Penetration Effectiveness Scores Are Not Associated With Neurocognitive Impairment in a Well Treated Aging Human Immunodeficiency Virus-Positive Population in Switzerland. Open Forum Infect. Dis. 2019 Jul 8; 6(7):ofz277. *Contributed equally as senior authors.

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CHUV
www.chuv.ch/crn-neuroimmunologie

https://www.chuv.ch/fr/ial/ial-home/research/main-scientific-focus-areas/neuroimmunology/

Unisciences
www.unil.ch/unisciences/renauddupasquier

Laboratory of Experimental Neuroimmunology - LNIE

Assoc. Professor Caroline Pot, MD
Group leader, consultant neurology

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Service of immunology and allergy (LIA)

Keywords
Neuroimmunology
Experimental autoimmune encephalomyelitis
Multiple sclerosis
Immunometabolism
Lipidic pathways
Gut-brain axis

Laboratory's activity

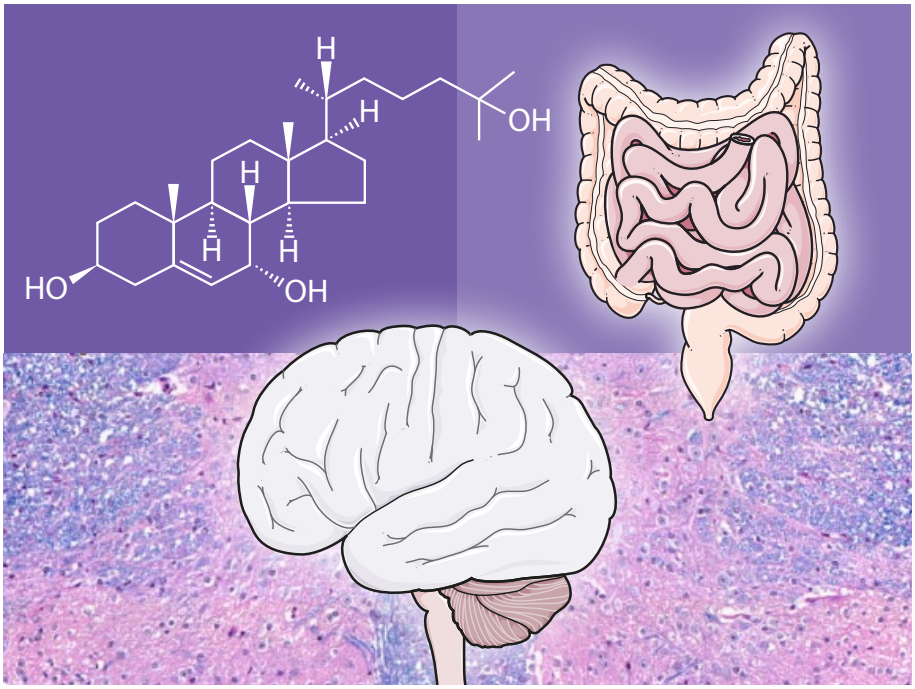
Multiple sclerosis (MS) is an autoimmune disorder affecting young patients. MS and its animal model, the experimental autoimmune encephalomyelitis (EAE), are characterized by inflammatory cell infiltrates and demyelination of the central nervous system. While risk factors such as viral infections or smoking are established, the role of cholesterol metabolism, mucosal immunology and nutrition remains unclear.
In our laboratory, we study the role of the gut-brain axis and of lipid metabolism during neuroinflammation. We propose that the gut is a reservoir for immune cells where they are activated as blocking encephalitogenic T cell entry into the gut dampens EAE. We now study how the gut environment and the intestinal microbiota modulate the immune response. Furthermore, perturbation of steroids pathways promote inflammation. We show that oxysterols, oxidized forms of cholesterol, shape the immune responses. We also examine the impact of oxysterols on gut homeostasis during CNS inflammation. We finally translate our murine results to human MS research and study how oxysterol receptor EBI2 expression is modulated during MS and further conduct translational studies to understand how nutrition and gut flora affect MS.

Research interests

The aims of Caroline Pot's research is to fine-tune immune responses in regards to environmental factors or metabolic pathways. This could lead to novel therapeutics and contribute to scientific re-evaluations of life-changes thus promoting personalized medical approaches for MS patients.

Scientific contributions in 2019-2020

> September 11-13th 2019_35th European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS). Location: Stockholm, Sweden. Poster presentation. Meeting Abstract: P273, P950, P1024.
> September 19-20th 2019_9th European Network on Oxysterol Research (ENOR) meeting. Location: Edinburgh, Scotland. Oral presentation (F. Ruiz).
> October 23-25th 2019_4th SFCNS Congress Swiss Federation of Clinical Neuro-Societies. Location: Lausanne, Switzerland. Oral presentations (C. Pot; G. Thévoz).
> January 10th 2020_Rencontres Lucien Rumbach. Location: Annecy, France. Invited speaker.
> April 25th - May 01 2020_Annual Meeting of the American-Academy-of-Neurology. Virtual meeting. Posters P2076, EPR2195.
> November 13th 2020_Young Investigator Meeting 2020. Virtual meeting. Oral presentation (F. Ruiz).



Schematic drawing illustrating the interplay between lipid metabolism, gut immune response and inflammation of the central nervous system during multiple sclerosis.
We study the interactions between oxysterols, oxidized forms of cholesterol (depicted on the left) and gut homeostasis/ gut flora (right) to assess their contributions in driving autoimmunity in the central nervous system (bottom).

Main publications in 2019-2020

Misselwitz B, Wyss A, Raselli T, Cerovic V, Sailer AW, Krupka N, Ruiz F, **Pot C**, Pabst O. The oxysterol receptor GPR183 in inflammatory bowel diseases. Br. J Pharmacol. 2020 Nov 4.

Haghayegh Jahromi N, Marchetti L, Moalli F, Duc D, Basso C, Tardent H, Kaba E, Deutsch U, **Pot C**, Sallusto F, Stein JV, Engelhardt B. Intercellular Adhesion Molecule-1 (ICAM-1) and ICAM-2 Differentially Contribute to Peripheral Activation and CNS Entry of Autoaggressive Th1 and Th17 Cells in Experimental Autoimmune Encephalomyelitis. Front. Immunol. 2020 Jan 14; 10:3056.

Ruiz F, Vigne S, **Pot C**. Resolution of Multiple Sclerosis. Semin. Immunopathol. 2019 Nov; 41(6):711-726.

Duc D*, Vigne S*, Bernier-Latmani J, Yersin Y, Ruiz F, Gaia N, Leo S, Lazarevic V, Petrova TV, **Pot C**. Disrupting myelin-specific Th17 cell gut homing confers protection in adoptive-transfer experimental autoimmune encephalomyelitis. Cell. Rep. 2019 Oct 8. *These authors equally contributed to the work.

Wyss A, Raselli T, Perkins N, Ruiz F, Schmelczer G, Klinke G, Moncsek A, Roth R, Spalinger MR, Hering L, Atrott K, Lang S, Frey-Wagner I, Scharl M, Sailer AW, Pabst O, Hersberger M, **Pot C**, Rogler G, Misselwitz B. The EBI2-oxysterol axis promotes the development of intestinal lymphoid structures and colitis. Mucosal Immunol. 2019 Feb 11.

Duc D, Vigne S, **Pot C**. Oxysterols in Autoimmunity. Int. J Mol. Sci. 2019; 20(18):4522.

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UNIL
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Laboratory of Brain Tumour Biology and Genetics LBGT

Professor Monika E. Hegi, Head of laboratory

Senior Lecturer, Privat-Docent Andreas F. Hottinger, Head of the Neurooncology Unit

Laboratory's activity

Taking advantage of the clinical setting of the laboratory, we aim at integrating clinical and basic cancer research in neuro-oncology at the CHUV. Joint efforts integrating research databases, including the brain tumor bank, foster research collaborations and have yielded collaborative translational research projects. Over the last years, we have analyzed multidimensional OMICs datasets derived from gliomas of patients treated in our clinical trials and retrieved from public databases that yielded predictive factors and potential new targets that we are further investigating in the laboratory. We aim at bridging this knowledge with the developing Brain Tumor Center headed by PD Dr Hottinger for improvement of patient management and development of future studies and trials.

Laboratory of Brain Tumour Biology and Genetics - LBGT

Professor Monika E. Hegi
Head research laboratory

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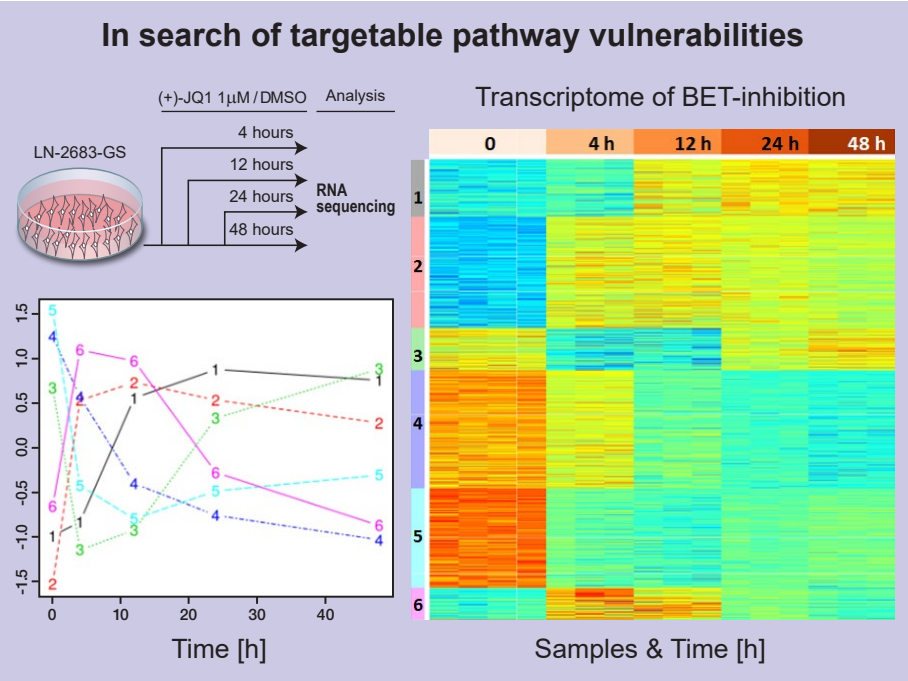
Keywords
Brain tumors
Tumor genetics and epigenetics
Translational research
Predictive biomarkers
PDX-mouse models
High resolution magnetic resonance spectroscopy

Laboratory's activity
Taking advantage of the clinical setting of the laboratory, we aim at integrating clinical and basic cancer research in neuro-oncology at the CHUV. Joint efforts integrating research databases, including the brain tumor bank, foster research collaborations and have yielded collaborative translational research projects. Over the last years, we have analyzed multidimensional OMICs datasets derived from gliomas of patients treated in our clinical trials and retrieved from public databases that yielded predictive factors and potential new targets that we are further investigating in the laboratory. We aim at bridging this knowledge with the new Brain Tumor Center headed by PD Dr Hottinger for improvement of patient management and development of future studies and trials.

Research interests
> (Epi)genomics of glioma, their relevance for tumor biology, classification, and novel therapeutic strategies.
> Molecular mechanisms and biomarkers of resistance.
> Translational research.
> Longiitudinal modeling of tumor invasion using spectroscopy.

Scientific contributions in 2019-2020
> We determined a clinical cutoff with a safety margin for MGMT methylation in glioblastoma that allows patient selection for therapy without temozolomide, avoiding undue toxicity in patients with a truly unmethylated MGMT promoter who do not profit from this treatment, while not withholding it from others.
> We contributed to investigations exploring the landscapes of the tumor microenvironment of primary brain tumors and brain metastasis that revealed disease-specific alterations of immune cells.
> We contributed to uncovering metabolic vulnerabilities associated with resistance mechanisms to EGFR inhibition in glioblastoma.
> We uncovered targetable pathway vulnerabilities induced in glioblastoma cells treated with epigenetic drugs.
> We identified the underpinnings of epigenetic silencing of HTATIP2, a regulator of nuclear translocation, on DNA repair and resistance to treatment in glioblastoma cells.
> We compared the metabolic and transcriptional profiles of glioblastoma invasion characterized by 1H Magnetic Resonance Spectroscopy (7T and 14T) and RNA-sequencing, between patients tumors and corresponding orthotopic mouse xenografts.



Main publications in 2019-2020

Klemm F, Maas RR, Bowman RL, Kornete M, Soukup K, Nassiri S, Brouland JP, Iacobuzio-Donahue CA, Brennan C, Tabar V, Gutin PH, Daniel RT, **Hegi ME**, Joyce JA. Interrogation of the microenvironmental landscape in brain tumors reveals disease-specific alterations of immune cells. Cell 2020 Jun 25; 181(7):1643-1660.e17.

Weller M, van den Bent M, Preusser M, Le Rhun E, Tonn JC, Minniti G, Bendszus M, Balana C, Chinot O, Dirven L, French P, **Hegi ME**, *et al*. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. Nat. Rev. Clin. Oncol. 2021 Mar; 18(3):170-186.

Wen PY, Weller M, Lee EQ, Alexander BM, Barnholtz-Sloan JS, Barthel FP, Batchelor TT, Bindra RS, Chang SM, Chiocca EA, Cloughesy TF, DeGroot JF, Galanis E, Gilbert MR, **Hegi ME**, *et al*. Glioblastoma in adults: a Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) consensus review on current management and future directions. Neuro. Oncol. 2020 Aug 17; 22(8):1073-1113.

Saleem H, Abdul UK, Kucukosmanoglu A, Houweling M, Cornelissen FMG, Heiland DH, **Hegi ME**, *et al*. The TICking clock of EGFR therapy resistance in glioblastoma: Target independence or target compensation. Drug Resist. Updat. 2019 Mar; 43:29-37.

McKinney A, Lindberg OR, Engler JR, Chen KY, Kumar A, Gong H, Lu KV, Simonds EF, [...] **Hegi ME**, Weiss WA, Phillips JJ. Mechanisms of resistance to EGFR inhibition reveal metabolic vulnerabilities in human GBM. Mol. Cancer Ther. 2019 Sep; 18(9):1565-1576.

Hegi ME, Genbrugge E, Gorlia T, Stupp R, Gilbert MR, Chinot OL, Nabors LB, Jones G, *et al*. MGMT Promoter methylation cutoff with safety margin for selecting glioblastoma patients into trials omitting temozolomide. A pooled analysis of four clinical trials. Clin. Cancer Res. 2019 Mar 15; 25(6):1809-1816.

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Laboratory of Brain Tumour Biology and Genetics - LBGT

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Service of oncology

Keywords
Neuro-oncology
Primary brain tumors
Glioblastoma
Astrocytoma
Oligodendroglioma
Familial brain tumors
Neurologic complications of cancer
Clinical trial

Laboratory's activity

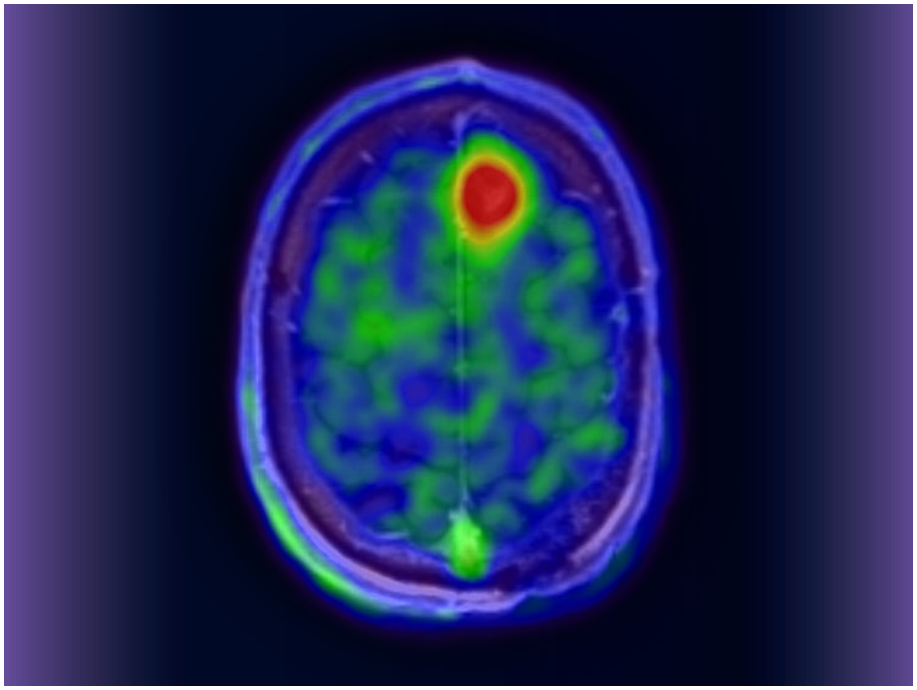
Primary brain tumors
We focus on the development of novel and innovative treatment strategies for patients with primary brain tumors including glioblastoma, astrocytomas, oligodendrogliomas and other rare forms of cancers of the nervous system.

Neurologic complications of cancer and cancer therapies
Our group has gained an expertise in the management of neurological complications of novel oncologic immune therapies including checkpoint inhibitors.

Translational research
A first area of focus is the development and evaluation of xenograft models of glioblastoma - collaboration work with the laboratory of brain tumor biology and genetics (LBGT) and the Center of Biomedical Imaging (CIBM, CHUV).
In a collaboration with the Laboratory for Research in Neuroimaging (LREN) we are also interested in better characterizing the modifications induced by glioblastoma and treatment with alternating electrical fields on the brain parenchyma.

Research interests
Our group has a long-standing experience and expertise in clinical trials. We are involved in a number of international clinical trials with several organizations, including the Swiss Neurooncology Society, the European Organization for Research and Treatment of Cancer (EORTC) as well as a number of pharmacological companies.

Scientific contributions in 2019-2020
> Over 80 patients screened and over 35 patients with primary brain tumors included in clinical trials.
> Development of management guidelines in neurooncology during the COVID19 pandemic [for the American Society of Oncology (ASCO) & the Society for Neuro-Oncology (SNO)].
> Development of management guidelines for gliomas [for the American Society of Oncology (ASCO) & the Society for Neuro-Oncology (SNO)].
> Development of management guidelines for primary CNS lymphomas (for the European Society of Neuro-oncology).



Brain FET-PET showing a high grade glioma in the left frontal lobe.

Main publications in 2019-2020

Wirsching HG, Roelcke U, Weller J, Hundsberger T, **Hottinger AF**, von Moos R, Caparrotti F, Conen K, Remonda L, Roth P, Ochsenbein A, Tabatabai G, Weller M. MRI and 18FET-PET Predict Survival Benefit from Bevacizumab Plus Radiotherapy in Patients with Isocitrate Dehydrogenase Wild-type Glioblastoma: Results from the Randomized ARTE Trial. Clin. Cancer Res. 2021 Jan 1; 27(1):179-188.

Latifyan S, de Micheli R, **Hottinger AF**. Physical approaches to treat glioblastoma. Curr. Opin. Oncol. 2020 Nov; 32(6):640-649.

Roth P, **Hottinger AF**, Hundsberger T, Läubli H, Schucht P, Reinert M, Mamot C, Roelcke U, Pesce G, Hofer S, Weller M. A contemporary perspective on the diagnosis and treatment of diffuse gliomas in adults. Swiss Med. Wkly. 2020 Jun 18; 150:w20256.

Tuleasca C, Knisely J, Leroy HA, **Hottinger AF**, Peciu-Florianu I, Levivier M, Reyns N. Glioma patient-reported outcome assessment in clinical care. Lancet Oncol. 2020 May; 21(5).

Mohile NA, Blakeley JO, Gatson NTN, **Hottinger AF**, Lassman AB, Ney DE, Olar A, Schiff D, Shih HA, Strowd R, van den Bent MJ, Ziu M. Urgent Considerations for the Neuro-oncologic Treatment of Patients with Gliomas During the COVID-19 Pandemic. Neuro. Oncol. 2020 Apr 11; 22(7):912-7.

Perrinjaquet C, Desbaillets N, **Hottinger AF**. Neurotoxicity associated with cancer immunotherapy: immune checkpoint inhibitors and chimeric antigen receptor T-cell therapy. Curr. Opin. Neurol. 2019 Jun; 32(3):500-510.

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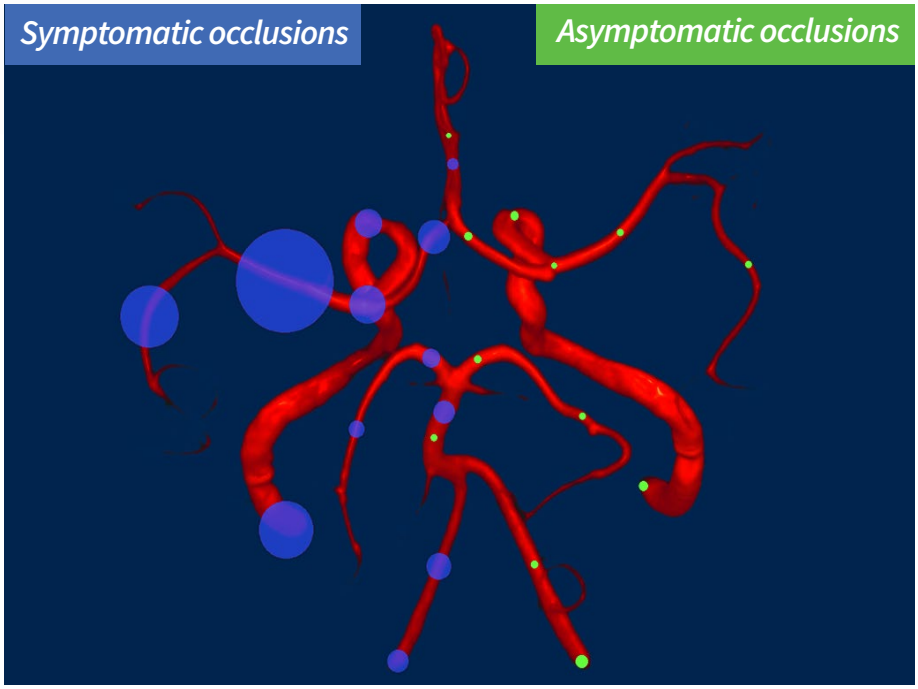
Laboratories of Stroke Research - LMCV

Experimental Stroke Research Laboratory
Assoc. Professor Lorenz Hirt, Head of laboratory

Laboratory of Clinical Stroke Research Unit
Assoc. Professor Patrik Michel, Head of laboratory



Site and frequency of arterial occlusions in 2'209 consecutive patients with CT-angiography in the STroke Registry and Analysis of Lausanne (Ref: Rotzinger D et al, Am J Neurorad 2017; 38:868-874).

The Stroke Research branch in the CRN has a wide fundamental research activity including neuroprotection, neuroradiological analyses, and clinical stroke research. It is well known that experimental lab and clinical registries contribute to the understanding of stroke mechanisms as well as to the advancement of acute and chronic treatment of stroke victims. Both the Stroke Laboratory and the Clinical Stroke Research teams are well connected through local, national and international collaborations and welcome international researchers.

Experimental Stroke Research Laboratory

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Affiliation
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Keywords
Stroke
Cerebral ischemia
Experimental stroke
Lactate

Laboratory's activity

The stroke laboratory is studying mechanisms of cell death after cerebral ischemia using an experimental model (mouse middle cerebral artery occlusion, MCAO). We are studying lactate as an agent for repair and protection as well as its neuroprotective mechanisms involving its receptor and transporters. We have shown that the mode of action lactate is dual, both metabolic and as a signalling molecule and that it improves the outcome in rodents. In an SNF-funded project analysing hyperpolarized substrate administration after MCAO by magnetic resonance spectroscopy, we have shown a rapid metabolism in the ischemic brain of both 13C-lactate and 13C-pyruvate. These preclinical results led us to initiate a clinical trial in acute stroke patients testing lactate against placebo (approved by ethics committee and Swissmedic). In another SNF-funded project, we have shown the involvement of caveolin-1 in recovery after cerebral ischemia. We have also shown its role in astrogliosis and angiogenesis after stroke. Lab members are Lara Buscemi, PhD; Melanie Price, PhD; Sabrina Gehri, BMed and Julia Castillo Gonzalez, MSc.

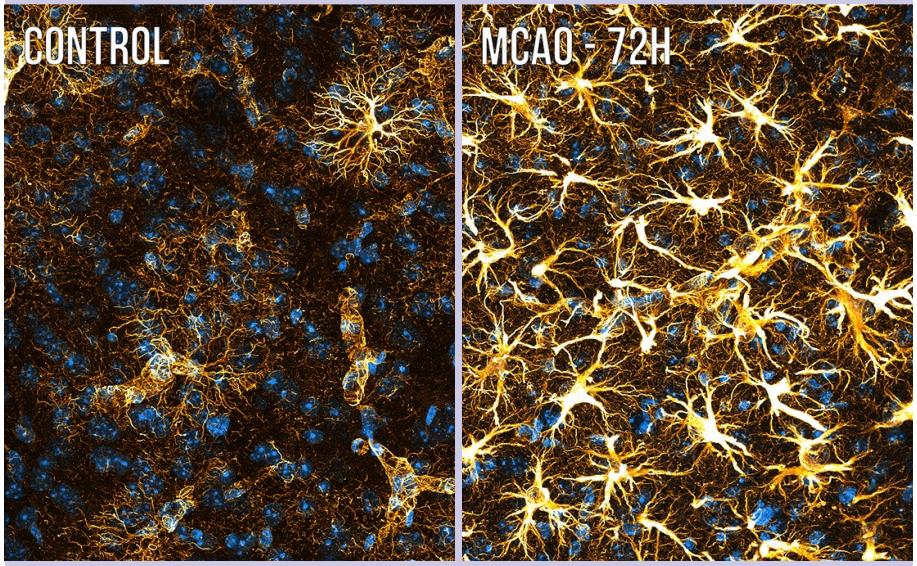
Research interests

Our research aims at finding additional options to improve the outcome of stroke patients. Experimentally, we are investigating the neurovascular unit, neuroinflammation, angiogenesis and metabolism after stroke. We have obtained the approval of the ethics committee CER-VD and of Swissmedic, the federal authority, to start a clinical trial on lactate in ischemic stroke patients, thereby translating our project on lactate from bench to bedside. In clinical research, we are also exploring our large retrospective Doppler US database.

Scientific contributions in 2019-2020

> Progress in research in different fields leading to 9 publications.
> Two running FNS grants, one as PI, one as co-applicant; grants from Novartis Research Foundation and Biaggi Foundation.
> One person obtained a Lemanic Neuroscience PhD in the lab.
> L. Hirt appointed as co-director of the Lemanic Neuroscience Doctoral school.
> Invited as a jury member for PhD theses in Switzerland and Europe.
> Invited as speaker and chairman to Swiss and international conferences.

Astrocytic reaction around the ischaemic lesion three days after stroke in mice.



Main publications in 2019-2020

Bill O, Lambrou D, Sotomayor GT, Meyer I, Michel P, Moreira T, Niederhauser J, **Hirt L**. Predictors of the pulsatility index in the middle cerebral artery of acute stroke patients. Sci. Rep. 2020 Oct 13; 10(1):17110.

Filchenko I, Blochet C, Buscemi L, Price M, Badaut J, **Hirt L**. Caveolin-1 Regulates Perivascular Aquaporin-4 Expression After Cerebral Ischemia. Front. Cell Dev. Biol. 2020 May 25; 8:371.

Hyacinthe JN, Buscemi L, Lê TP, Lepore M, **Hirt L**, Mishkovsky M. Evaluating the potential of hyperpolarised [1-13C] L-lactate as a neuroprotectant metabolic biosensor for stroke. Sci. Rep. 2020 Mar 26; 10(1):5507.

Buscemi L, Blochet C, Price M, Magistretti PJ, Lei H, **Hirt L**. Extended preclinical investigation of lactate for neuroprotection after ischemic stroke. Clinical and Translational Neuroscience 2020 Feb; 4(1).

Blochet C, Buscemi L, Clément T, Gehri S, Badaut J, **Hirt L**. Involvement of caveolin-1 in neurovascular unit remodeling after stroke: Effects on neovascularization and astrogliosis. J Cereb. Blood Flow Metab. 2020 Jan; 40(1):163-176.

Buscemi L, Price M, Bezzi P, **Hirt L**. Spatio-temporal overview of neuroinflammation in an experimental mouse stroke model. Sci. Rep. 2019 Jan 24; 9(1):507.

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CHUV
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Laboratory of Clinical Stroke Research Unit

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Head of Unit

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Affiliation
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Keywords
Stroke
Thrombolysis
Thrombectomy
Neuroimaging
ASTRAL registry

Laboratory's activity

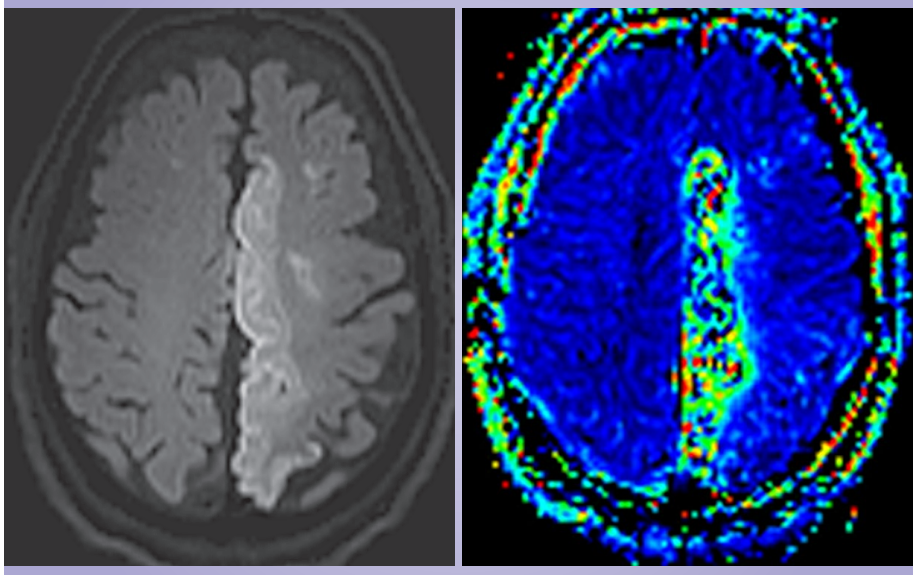
The Clinical Stroke Research team maintains since 2003 the ASTRAL registry (Acute STroke Registry and Analysis of Lausanne). It contains >6'000 acute stroke patients, each with >300 variables including demographic, clinical, comorbidity, multimodal imaging, etiological, metabolic and outcome data. CT and more recently MRI-based angiographic and perfusion data are collected and analysed in a detailed manner. We also study the influence of acute revascularization treatments in different situations, frequent and rare stroke mechanisms, and prognostic markers of long-term outcome. The team participates in multiple national and international randomized trials for acute stroke treatment and secondary prevention.

Research interests

Our team's research interests concern clinical stroke syndromes, acute stroke imaging, acute stroke management and stroke prognosis. Recent publications on stroke syndromes and causes (posterior circulation strokes, basilar artery occlusion, embolic stroke of undetermined origin, stroke chameleons, skiing-related strokes), acute imaging of ischemic stroke (collaterals, posterior circulation perfusion imaging), prognosis (stroke recurrence score), acute revascularization treatments (eligibility for late endovascular treatment, late treatment, thrombolysis of ischemic myelopathy, reocclusion after recanalisation) and secondary prevention (PFO-closure).

Scientific contributions in 2019-2020

> Progress in research and in randomized clinical trials, leading to 43 peer-reviewed publications.
> One FNS grant (FN 320030-182654/1) as PI.
One FNS grant as co-applicant (33IC30-179667).
Grants from UNIL and Swiss Heart Foundation as co-applicant.
> One MD obtained a Lemanic Neuroscience PhD.
Two MD-theses terminated.
Three PhD theses ongoing (two as co-supervisor).
> Participation in 5 national/international randomized clinical trials.
> Organiser, speaker and chairman of multiple national and international conferences.
> Multiple collaborations nationally (Swiss Stroke Registry, Inselspital Berne) and internationally (TRISP/EVA-TRISP; Prof. M. Wintermark UCLA).



A 78 year old man woke up with severe right hemiparesis and some speech problems 7 hours after general anaesthesia for a vascular intervention. Acute MRI showed an established stroke of the left anterior cerebral artery (left picture) and a matching perfusion deficit (right picture). This indicates that there was no hypoperfused tissue that could be saved by late reperfusion treatment, and such a treatment was not offered.

Main publications in 2019-2020

Nannoni S, Strambo D, Sirimarco G, Amiguet M, Vanacker P, Eskandari A, Saliou G, Wintermark M, Dunet V, **Michel P**. Eligibility for late thrombectomy using DAWN, DEFUSE-3, and more liberal selection criteria in a comprehensive stroke center. J Neurointerv. Surg. 2020; 12:842-847.

Strambo D, Zachariadis A, Lambrou D, Schwarz G, Sirimarco G, Aarnio K, Putaala J, Ntaios G, Vemmos K, **Michel P**. A score to predict 1-year risk of recurrence after acute ischemic stroke. Int. J Stroke 2020; 0:1-10.

Bill O, Inácio NM, Lambrou D, Wintermark M, Ntaios G, Dunet V, **Michel P**. Focal hypoperfusion in acute ischemic stroke perfusion CT: clinical and radiological predictors and accuracy for infarct prediction. AJNR Am. J Neuroradiol. 2019; 40(3):483-489.

Ntaios G, Perlepe K, Lambrou D, Sirimarco G, Strambo D, Eskandari A, Karagkiozi E, Vemmou A, [...] **Michel P**. Prevalence and overlap of potential embolic sources in patients with embolic stroke of undetermined source. J Am. Heart Assoc. 2019; 8:e012858.

Marto JP, Lambrou D, Eskandari A, Nannoni S, Strambo D, Saliou G, Maeder P, Sirimarco G, **Michel P**. Associated factors and long-term prognosis of 24-hour worsening of arterial patency after ischemic stroke. Stroke 2019; 50:2752-2760.

Ntaios G, Georgiopoulos G, Perlepe K, Sirimarco G, Strambo D, Eskandari A, Nannoni S, Vemmou A, [...] **Michel P**. A tool to identify patients with embolic stroke of undetermined source at high recurrence risk. Neurology 2019; 93:1-11.

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CHUV

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Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Professor Philippe Ryvlin, Head of laboratory
Assoc. Professor Andrea Rossetti
Senior Lecturer, Privat-Docent Jan Novy

Laboratory's activity

Our laboratory's activities are focusing on clinical research in patients with epilepsy, migraine or disorders of consciousness, including status-epilepticus and post-anoxic coma.

In epilepsy, we pursue five main research objectives:

> Pathophysiology and prevention of Sudden Unexpected Death in Epilepsy Patients.
> Seizure detection in ambulatory patients using mobile health technology.
> Point-of-care testing of antiepileptic drugs plasma dosage.
> Pharmacogenomic and other biological biomarkers.
> Epidemiology and management of status-epilepticus.

In disorders of consciousness, our current research primarily focuses on outcome prognostication of acute coma, particularly after cardiac arrest.

In migraine, our current research focuses on the detection of neurovegetative biomarkers that would precede or accompany migraine attacks, using wrist-worn wearable devices.

We are also coordinating the development of the Medical Informatics Platform (MIP) and the Human Intracerebral EEG Platform (HIP) of the Human Brain Project. The MIP offers a unique solution for performing federated analyses of datasets distributed across hospitals. The HIP will provide the scientific community access to the largest and most advanced solution worldwide for storing, curating, sharing, and analyzing data directly recorded from the Human brain during SEEG in patients with epilepsy.

Laboratory of Cortical Excitability and Arousal Disorders - LE²C

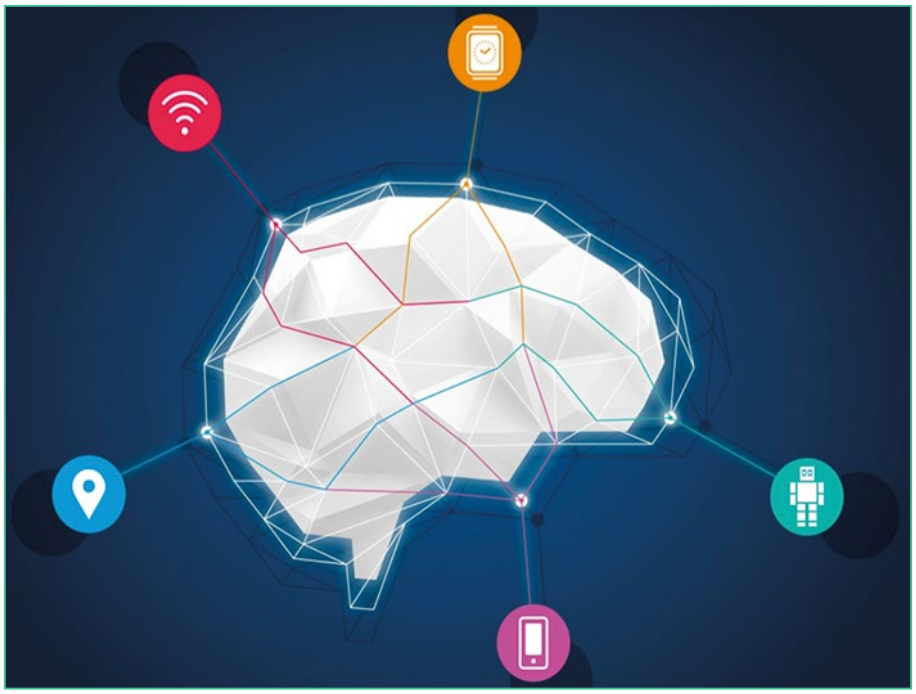
Professor Philippe Ryvlin
Head of the Department of Clinical Neurosciences
Head of the Laboratory of Cortical Excitability and Arousal Disorders - LE²C
Laboratoire des troubles de l'excitabilité et de l'éveil cortical
philippe.ryvlin@chuv.ch

Affiliation
Service of neurology (NLG)

Keywords
Epilepsy
Coma
Cardiac arrest
Sudden unexpected death in epilepsy (SUDEP)
Status-epilepticus
Seizure detection
Drug monitoring
Biomarkers
Intracerebral EEG
Medical Informatics Platform (MIP)
Human Intracerebral EEG Platform (HIP)
Federated analyses

Research interests
Biomarkers and prevention of SUDEP, seizure detection, large scale data sharing.

Scientific contributions in 2019-2020
> Advancing the deployment and usage of the HBP-funded Medical Informatics Platform (MIP) with novel use-cases in TBI, mental health and epilepsy.
> Developing the HBP-funded Human intracerebral EEG platform (HIP).
> Launching the FNS-funded SEVERITY study to develop new biomarkers of GTCS severity.
> Successfully fund and launch the Sinergia-FNS-funded PEDESITE project to develop innovative mobile health technology for seizure detection together with EPFL and ETZ.
> Determine the risk factors of post-ictal hypoxemia during GTCS.
> Publish international guidelines on automated seizure detection using wearable devices.
> Demonstrate the neural correlates of verbal working memory impairment in children with epilepsy with centro-temporal spikes.



The NeuroTech Platform provides an infrastructure dedicated to the evaluation of the medical and medico-economic impact of novel technologies in clinical neurosciences.

Main publications in 2019-2020

Ciumas C, Montavont A, Ilski F, Laurent A, Saignavongs M, Lachaux JP, de Bellescize J, Panagiotakaki E, Ostrowsky-Coste K, Herbillon V, Ibarrola D, Hermier M, Arzimanoglou A, **Ryvlin P**. Neural correlates of verbal working memory in children with epilepsy with centro-temporal spikes. Neuroimage Clin. 2020; 28:102392.

Cronberg T, Greer DM, Lilja G, Moulaert V, Swindell P, **Rossetti AO**. Brain injury after cardiac arrest: from prognostication of comatose patients to rehabilitation. Lancet Neurol. 2020 Jul; 19:611-622.

Barbella G, Lee JW, Alvarez V, **Novy J**, Oddo M, Beers L, **Rossetti AO**. Prediction of regaining consciousness despite an early epileptiform EEG after cardiac arrest. Neurology 2020 Apr 21; 94:e1675-1683.

Aícua-Rapún I, André P, **Rossetti AO**, **Ryvlin P**, Hottinger AF, Decosterd LA, Buclin T, **Novy J**. Therapeutic Drug Monitoring of Newer Antiepileptic Drugs: A Randomized Trial for Dosage Adjustment. Ann. Neurol. 2020 Jan; 87(1):22-29.

Barras P, Siclari F, Hügli O, **Rossetti AO**, Lamy O, **Novy J**. A potential role of hypophosphatemia for diagnosing convulsive seizures: a case-control study. Epilepsia 2019 Aug; 60(8):1580-1585.

Rheims S, Alvarez BM, Alexandre V, Curot J, Maillard L, Bartolomei F, Derambure P, Hirsch E, Michel V, Chassoux F, Tourniaire D, Crespel A, Biraben A, Navarro V, Kahane P, De Toffol B, Thomas P, Rosenberg S, Valton L, Bezin L, **Ryvlin P**; REPO2MSE study group. Hypoxemia following generalized convulsive seizures: Risk factors and effect of oxygen therapy. Neurology 2019 Jan 15; 92(3):e183-e193.

ORCID number: 0000-0001-7775-6576

CHUV
www.chuv.ch/crn-ltec

https://www.chuv.ch/fr/neurologie/nlg-home/le-service-en-bref/notre-equipe/equipe-medicale/pr-philippe-ryvlin

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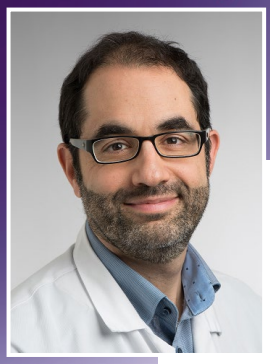

Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Assoc. Professor Andrea Rossetti
Consultant/attending physician

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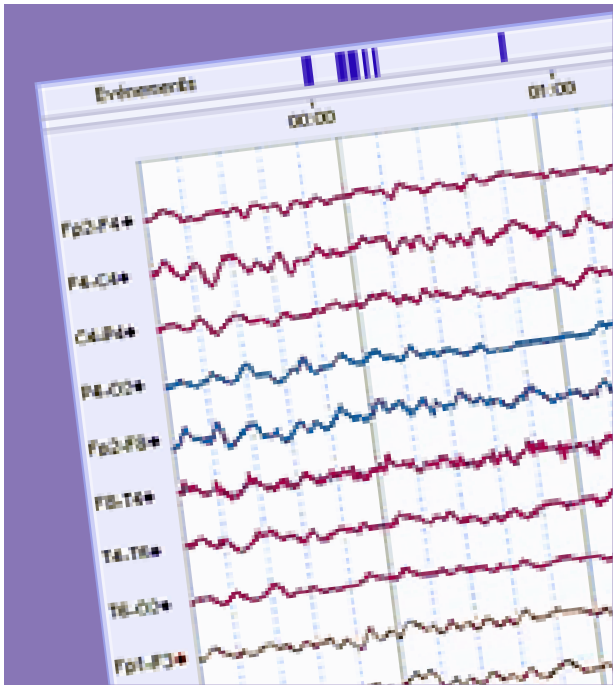
Affiliation
Service of neurology (NLG)

Keywords
Epilepsy
Status epilepticus
Coma prognostication
EEG
Evoked potentials



Laboratory's activity

Studies on nosology and treatment of status epilepticus prognostication of acute coma; EEG monitoring in intensive care unit.

Research interests

Prognostication of coma after cardiac arrest, status epilepticus.

Scientific contributions in 2019-2020

> Completing a RCT on cEEG in the ICU showing no difference in outcome as compared to rEEG.
> Refining prognostication in post-cardiac arrest comatose patients, particularly with early status epilpeticus/myoclonus.

Main publications in 2019-2020

Kondziella D, Bender A, Diserens K, van Erp W, Estraneo A, Formisano R, Laureys S, Naccache L, Ozturk S, Rohaut B, Sitt JD, Stender J, Tiainen, M, **Rossetti AO**, Gosseries O, Chatelle C. EAN Guideline on the Diagnosis of Coma and other Disorders of Consciousness. Eur. J Neurol. 2020; 27:741-756.

Cronberg T, Greer DM, Lilja G, Moulaert V, Swindell P, **Rossetti AO**. Brain injury after cardiac arrest: from prognostication of comatose patients to rehabilitation. Lancet Neurol. 2020 Jul; 19:611-622.

Barbella G, Lee JW, Alvarez V, Novy J, Oddo M, Beers L, **Rossetti AO**. Prediction of regaining consciousness despite an early epileptiform EEG after cardiac arrest. Neurology 2020 Apr 21; 94:e1675-1683.

Beuchat I, Sivaraju A, Amorim E, Gilmore EJ, Dunet V, **Rossetti AO**, Westover MB, Hsu L, Scirica B, Silva D, Tang K, Lee JW. MRI-EEG correlation for outcome prediction in post-anoxic myoclonus, a multicenter study. Neurology 2020; 95:e335-e341.

Rossetti AO, Schindler K, Sutter R, Rüegg S, Zubler F, Novy J, Oddo M, Warpelin-Decrausaz L, Alvarez V. Continuous versus routine EEG in critically ill adults with altered consciousness and no recent seizure: a multicenter randomized trial. JAMA Neurol. 2020; 77:1-8.

Kellinghaus C, **Rossetti AO**, Trinka E, Lang N, May T, Unterberger I, Rüegg S, Sutter R, Strzelczyk A, Tilz C, Uzelac Z, Rosenow F. Factors predicting cessation of status epilepticus in clinical practice. Ann. Neurol. 2019; 85:421-432.

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Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Senior Lecturer, Privat-Docent Jan Novy
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Affiliation
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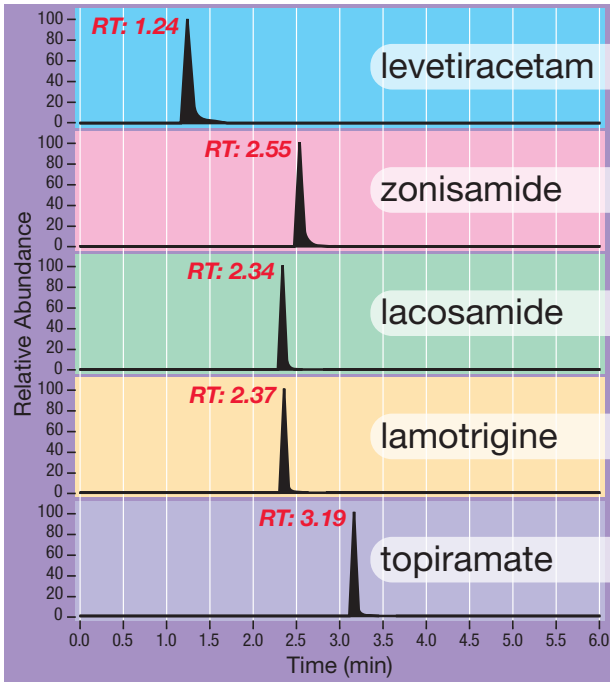
Keywords
Epilepsy
Sudden unexpected death in epilepsy
Neuroimaging
Intracerebral EEG
Seizure detection
Neurotechnologies
Pharmacology
Epidemiology
Biomarkers
Genetic



Research interests
Therapeutic monitoring and biomarkers of epileptic seizures.

Scientific contributions in 2019-2020
> Exploring epilepsy therapeutic drug monitoring useful and application using evidence-based outcome.
> Establish a correlation between antiseizure medication drug levels and clinical effects.
> Assess the usefulness of salivary therapeutic drug monitoring.
> Assess the usefulness of seizure markers.
> Assess markers epilepsy activity using metabolomic profiles.

Main publications in 2019-2020
Barbella G, Barras P, Rossetti AO, **Novy J**. Hypophosphatemia compared to classical biomarkers of tonic clonic seizures. Epilepsy Research 2020.

Aícua-Rapún I, André P, Rossetti AO, Ryvlin P, Hottinger AF, Decosterd LA, Buclin T, **Novy J**. Therapeutic drug monitoring newer antiepileptic drugs: a randomised trial for dosage adjustment. Ann. Neurol. 2020; 87:22-29.

Barras P, Siclari F, Hügli O, Rossetti AO, Lamy O, **Novy J**. A potential role of hypophosphatemia for diagnosing convulsive seizures: a case-control study. Epilepsia 2019 Aug; 60(8):1580-1585.

Aícua-Rapún I, André P, **Novy J**. Closed-Loop Neuropharmacology for Epilepsy: Distant Dream or Future Reality? Curr. Neuropharmacol. 2019; 17(5):447-458.

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Laboratory MySpace

Assist. Professor Andrea Serino
Head of laboratory

Head of the Laboratory MySpace
Laboratoire MySpace
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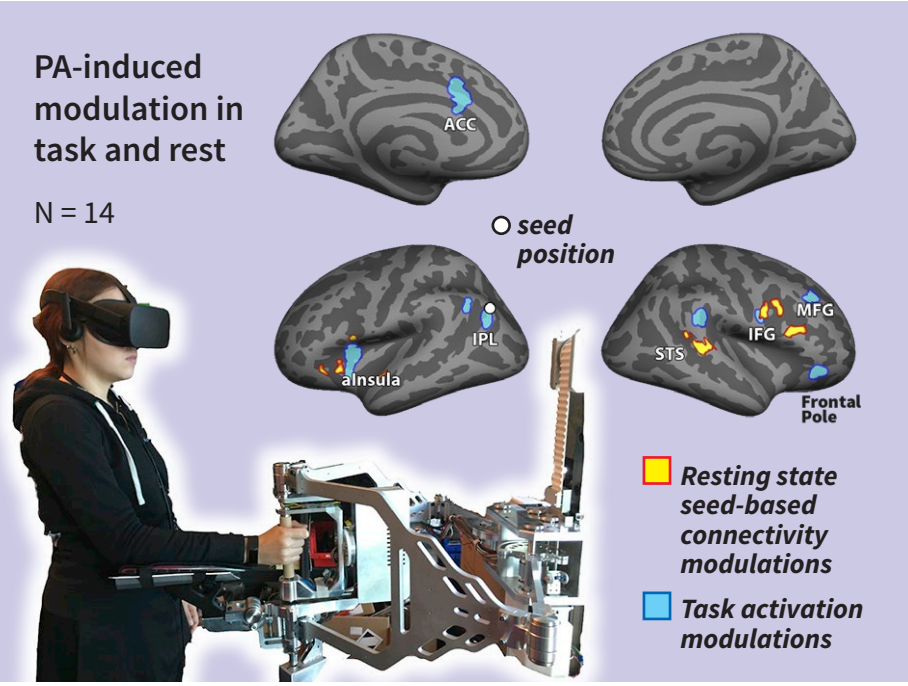
Affiliation
Service of neuropsychology and neurorehabilitation (NPR)

Keywords
Peripersonal space
Body representations
Multisensory integration
Virtual reality & robotics
Embodiment
Cognitive assessment and rehabilitation

Laboratory's activity
The main goal of the lab is understanding how the human brain builds a representation of the body in space, important for action, perception and consciousness. To this aim, we use different techniques from cognitive neuroscience, including psychophysics, fMRI, intracranial and scalp EEG recording, neuropsychology and neural network modeling to study the multisensory mechanisms underlying Body Representations (BR) and Peripersonal Space (PPS) in the human brain.

Research interests
With his group, Andrea Serino carries out research to unravel the neural and cognitive basis of body and self experience in space.

Scientific contributions in 2019-2020
> Develop new immersive and online paradigms to measure body representations (BR) and peripersonal space (PPS).
> Combine behavior, neuroimaging and modelling data to understand the neural mechanisms of BR and PPS in healthy individuals.
> Study the link between BR/PPS and other cognitive/physiological functions (sleep, memory, decision making and immune systems).
> Study BR and PPS in clinical populations (stroke, amputation and Alzheimer's disease).



New set-up for virtual prism adaptation (Wilf et al, 2019). Changes in brain connectivity induced by prism adaptation (Wilf et al, 2020).

Main publications in 2019-2020

Bertoni T, Magosso E, **Serino A**. From statistical regularities in multisensory inputs to peripersonal space representation and body ownership: Insights from a neural network model. Eur. J Neurosci. 2021 Jan; 53(2):611-636.

Serino A, Pozeg P, Bernasconi F, Solcà M, Hara M, Progin P, Stripeikyte G, Dhanis H, Salomon R, Bleuler H, Rognini G, Blanke O. Thought consciousness and source monitoring depend on robotically controlled sensorimotor conflicts and illusory states. iScience 2020 Dec 16; 24(1):101955.

Wilf M, Cerra Cheraka M, Jeanneret M, Ott R, Perrin H, Crottaz-Herbette S, **Serino A**. Combined virtual reality and haptic robotics induce space and movement invariant sensorimotor adaptation. Neuropsychologia 2020 Nov 21; 150:107692.

Noel JP, Bertoni T, Terrebonne E, Pellencin E, Herbelin B, Cascio C, Blanke O, Magosso E, Wallace MT, **Serino A**. Rapid Recalibration of Peri-Personal Space: Psychophysical, Electrophysiological, and Neural Network Modeling Evidence. Cereb. Cortex 2020 Jul 30; 30(9): 5088-5106.

Noel JP, Chatelle C, Perdikis S, Jöhr J, Lopes Da Silva M, Ryvlin P, De Lucia M, Millán JDR, Diserens K, **Serino A**. Peri-personal space encoding in patients with disorders of consciousness and cognitive-motor dissociation. Neuroimage Clin. 2019; 24:101940.

Serino A. Peripersonal space (PPS) as a multisensory interface between the individual and the environment, defining the space of the self. Neuroscience & Biobehavioral Reviews 2019; 99:138-159.

ORCID number: 0000-0001-7475-6095

CHUV
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Laboratory of Nerve-Muscle Unit - NMUL

Senior Lecturer Marie Théaudin
Neurologist
Head of the Laboratory of Nerve-Muscle Unit - NMUL
Laboratoire de l'unité nerf-muscle - LUNM
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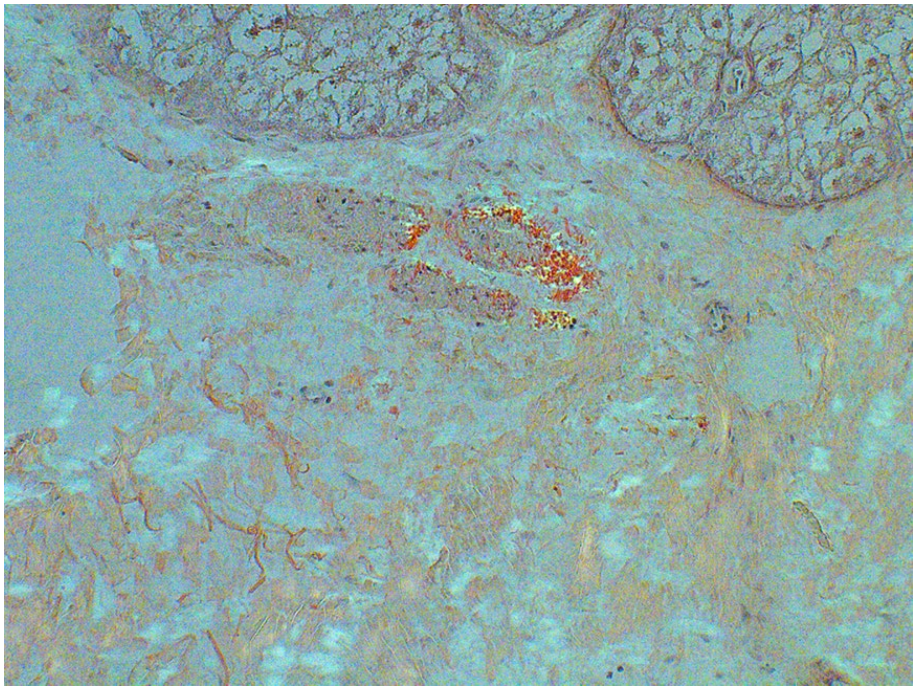
Affiliation
Service of neurology (NLG)

Keywords
Peripheral neuropathy
Hereditary amyloidosis
Neuroimmunology
Multiple sclerosis

Laboratory's activity
The Lab is specialized in studying characteristics of patients with hATTR amyloidosis, including MRI nerve studies and small nerve fiber quantification in the cornea. Other activities include studying gene expression from skin in inflammatory nerve or degenerative disorders.

Research interests
The research of Dr Marie Théaudin has 2 centers of interest:
> To describe characteristics of the Swiss hATTR patients and identify biomarkers of disease progression.
> To identify imaging biomarkers in multiple sclerosis and describe response to treatment in this disease.

Scientific contributions in 2019-2020
> Description of the hATTR patients followed at CHUV.
> Characterization of chronic inflammation in brain MRI in MS patients and identification of new diagnostic biomarkers in MRI.
> Description of response to fingolimod in RRMS patients treated at CHUV, including outcome after discontinuation of treatment.



Congo red positive amyloid deposits in a salivary gland biopsy.

Main publications in 2019-2020

Maggi P, Sati P, Nair G, Cortese ICM, Jacobson S, Smith BR, Nath A, Ohayon J, van Pesch V, Perrotta G, Pot C, **Théaudin M**, Martinelli V, Scotti R, Wu T, Du Pasquier R, Calabresi PA, Filippi M, Reich DS, Absinta M. Paramagnetic Rim Lesions are Specific to Multiple Sclerosis: An International Multicenter 3T MRI Study. Ann. Neurol. 2020 Nov; 88(5):1034-1042.

Horisberger A, Pantazou V, Cuendet G, Ribi C, Dunet V, **Théaudin M**. ANCA-associated life-threatening systemic vasculitis after alemtuzumab treatment for multiple sclerosis. Mult. Scler. 2020 Oct; 26(12):1599-1602.

Aliu B, Demeestere D, Seydoux E, Boucraut J, Delmont E, Brodovitch A, Oberholzer T, Attarian S, **Théaudin M**, Tsouni P, Kuntzer T, Derfuss T, Steck AJ, Ernst B, Herrendorff R, Hänggi P. Selective inhibition of anti-MAG IgM autoantibody binding to myelin by an antigen-specific glycopolymer. J Neurochem. 2020 Sep; 154(5):486-501.

Maggi P, Absinta M, Sati P, Perrotta G, Massacesi L, Dachy B, Pot C, Meuli R, Reich DS, Filippi M, Pasquier RD, **Théaudin M**. The "central vein sign" in patients with diagnostic "red flags" for multiple sclerosis: A prospective multicenter 3T study. Mult. Scler. 2020 Apr; 26(4): 421-432.

Lysandropoulos AP, Perrotta G, Billiet T, Ribbens A, Du Pasquier R, Pot Kreis C, Maggi P, **Théaudin M**. Human Leukocyte Antigen Genotype as a Marker of Multiple Sclerosis Prognosis. Can. J Neurol. Sci. 2020 Mar; 47(2):189-196.

ORCID number: 0000-0002-3026-3595

CHUV
www.chuv.ch/crn-maladies-neuromusculaires

Unisciences
www.unil.ch/unisciences/marietheaudin

Neuroscience Research Center

Platforms Presentation

Magnetic Resonance Imaging Platform (MRI)

Assoc. Professor Bogdan Draganski, MD
Head of the MRI Platform

The cornerstone of our strategy for translational neuroscience with direct impact on clinical decision-making and patient care is the MRI platform of the Department of Clinical Neurosciences, CHUV, that was established end 2013 thanks to the generous support from the charitable foundations Roger De Spoelberg and Partridge. All platform users are offered the most suitable advanced image acquisition and analysis techniques, but also education and training.
The platform is instrumental for several regional and national large-scale projects including the CoLaus|PsyCoLaus longitudinal cohort, the Swiss Personalized Health Network driver project Swiss Aging Citizen Reference, and many Swiss National Science Foundation funded investigations. In 2020, the platform announced its participant number 5'000.

High-performance data acquisition
Scientific instrumentation
> High-end 3T MR system offering optimal signal-to-noise ratio (SNR), speed and stability.
> A complete panel of equipment for real-time assessment of study participants' behaviour during data acquisition.
> Pioneering prospective motion correction system allowing exceptional data quality.

Expertise
> In-house developed brain imaging acquisition sequences for optimal sensitivity in cross-sectional and longitudinal studies.
> Full-range of customized protocols for assessment of brain anatomy and function.

Support team
> MRI engineers for customized solutions to the most challenging demands of neuroimaging research.
> MRI physicists for tailored acquisition protocols and optimal scientific output in all neuroscience studies.
> Close monitoring of scanner performance for sustained optimal data quality.

Electrophysiology Platform (EEG Platform)

Senior Lecturer Marzia De Lucia
Head of the EEG Platform

The Electrophysiology Platform of the Clinical Neuroscience Department, Lausanne University Hospital, is a collaborative initiative dedicated to advanced techniques for the analysis of electroencephalography and stereo electroencephalography recordings in humans.

The platform is coordinated by Dr Marzia De Lucia and aims at:
> sharing a comprehensive set of user-friendly tools for the analysis of electrophysiological recordings
> providing support for designing and implementing EEG experiments
> developing tools that can support the development of common scientific topics
> promoting discussions about ongoing and future projects.

Since March 2017 and every two months, the platform organizes meetings for sharing the latest updates on electrophysiology-based projects in the department. Each seminar focuses on a scientific project and on the methods used for data analyses.

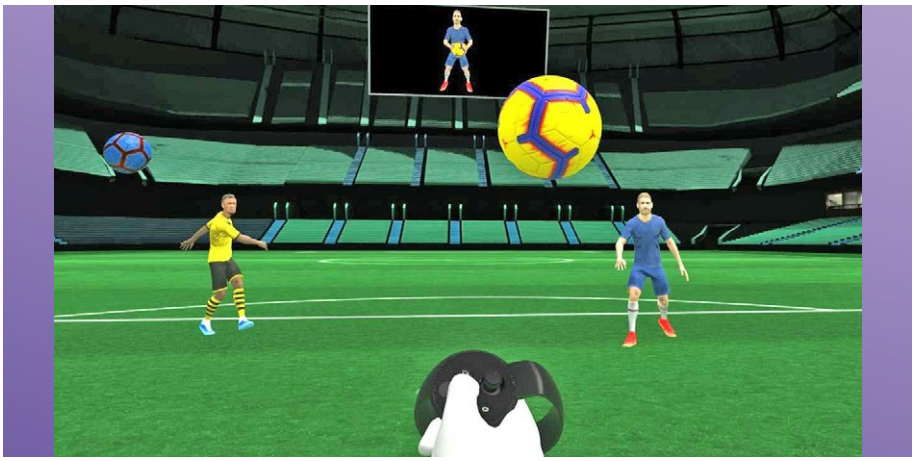
EEG platform website
https://eegplatformdnc.com/

EEG analysis repository
https://github.com/DNC-EEG-platform

Unisciences
www.unil.ch/unisciences/marziadelucia

Neuroscape Facility

Assoc. Professor Arseny Sokolov
Head of the Neuroscape Facility



The Neuroscape Facility has been established in January 2018. It is co-directed by Dr. Arseny Sokolov and Prof. Andrea Serino and located in the Pavillon 4 at the CHUV. The Facility is a founding member of the Neuroscape Alliance (https://neuroscape.ucsf.edu/alliance/), spear-headed by the Neuroscape Center at the University of California San Francisco.

Equipment & Expertise
The Neuroscape Facility is equipped with an immersive driving simulator, a giant screen, high-end computer graphics, whole-body tracking, head-mounted virtual reality devices, wearable physiological sensors and mobile devices. Research staff and collaborators consist of engineers, neuroscientists, neuropsychologists, physical therapists and neurologists with expertise in neurological rehabilitation.

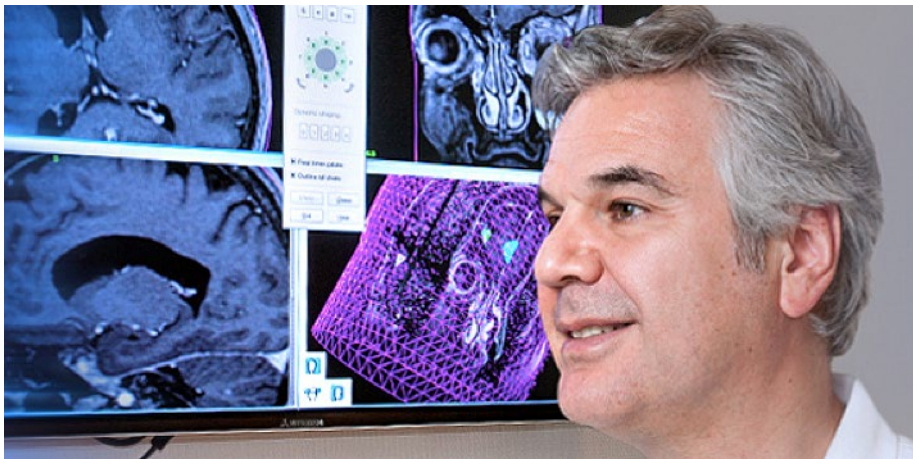
Mission & Services
The mission of the Neuroscape Facility is to design, assess, validate and implement novel gamified technological approaches for the assessment and rehabilitation of cognitive function and behavior in neurological patients. To this end, the Facility initiates projects itself, but is also available to colleagues interested in performing fundamental research or clinical trials using gamified and immersive technology for cognitive assessment and/or neurorehabilitation.

CHUV
https://neuroscape.ucsf.edu/alliance/

Unisciences
www.unil.ch/unisciences/arsenysokolov

Gamma Knife Center

Professor Marc Levivier
Head of the Neurosurgery Service - Head of the Gamma Knife Center



Gamma Knife radiosurgery is as an alternative to classical microsurgical excision, or when surgery is not possible. Around 2000 patients have been treated up-to-date. Since June 2016, our Gamma Knife Center is equipped with the latest model and functionalities, Leksell Gamma Knife ICON, allowing also for hypofractionnated treatments beside the classical single session ones. Research is an integrated part of our activity.

Research activity involves several main aspects:
> Clinical research (partnership with the Neurosurgery Service, and university hospitals from Marseille, Oxford, and more recently Lille).
> Basic research (partnership with the Swiss Federal Institute of Technology (EPFL), the University of Geneva and the Timone University Hospital in Marseille).
> Master theses (e.g., arteriovenous malformations, vestibular schwannomas, meningiomas) with the University of Lausanne (UNIL) and Geneva (UNIGE).

Our research focuses are:
> Outcomes of functional neurosurgery (trigeminal or glosso-pharyngeal neuralgia, thalamotomy for tremor as an alternative to deep brain stimulation).
> Optimization of functional results in benign tumors: vestibular schwannomas (hearing preservation, treatment of the acute effects, combined approaches with microsurgery), meningiomas (multicentric studies, place of hypofractionation) or vascular malformations (study of the predictive factors for obliteration, preliminary results of our cohort).
> The establishing and publishing guidelines of the International Stereotactic Radiosurgery Society (ISRS).

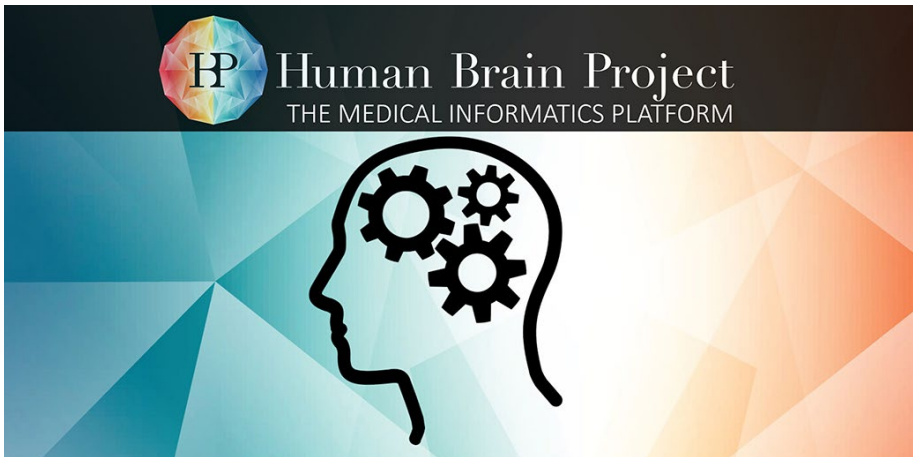
Fondamental research:
> Dr Tuleasca, MD-PhD, with the EPFL and Timone Hospital in Marseille focused his thesis on Gamma Knife thalamotomy for tremor, with the used 7 Tesla MRI to optimize the targeting. In 2019, Dr Tuleasca received the Prize of Excellence of the University of Lausanne for this work. The project continues with our scientific collaborator (Dr Thomas Bolton, engineer, EPFL PhD) on an extended number of patients and with complementary methodologies.
> Pr Levivier, together with Pr Thiran at EPFL, developed an algorithm of inverse automated radiosurgical planning. The program uses powerful processing techniques that can generate optimal dosimetry parameters thanks to unique convex optimization approaches.
> We are further increasing the efficacy and decreasing the toxicity of radiosurgery. In collaboration with Oxford and Marseille, we pioneered work in facial pain (trigeminal neuralgia). We developed a collaboration on vascular malformations and pituitary adenomas with the University Hospital of Lille.
> We published more than 100 scientific papers and our center is actively involved in numerous presentations and international training courses. Pr Levivier is currently the vice-president, and will become president of ISRS in 2022.

CHUV
www.chuv.ch/gamma-knife

Unisciences
www.unil.ch/unisciences/marclevivier

Medical Informatics Platform of HBP (Subproject 8)

Professor Philippe Ryvlin
Head of the Medical Informatics Platform of HBP



Our Department is coordinating two of the main medically-oriented platforms developed within the EU-flagship Human Brain Project (HBP). The Medical Informatics Platform (MIP) is being developed since the inception of HBP, and primarily aims at promoting data sharing and big data analysis by federating clinical and research datasets. To this purpose, the MIP has been installed in more than 30 hospitals, enabling to perform federated analyses of their data without moving these data out of the hospitals, thus offering GDPR compliance and optimal data privacy. More recently, we have developed the Human Intracerebral EEG Platform (HIP) which aims to provide the scientific community access to the largest and most advanced solution worldwide for storing, curating, sharing, and analyzing data directly recorded from the Human brain during intracerebral EEG investigations (SEEG) in patients with epilepsy undergoing pre-surgical evaluation. More than 90% of European, Asian and Oceanian centers performing SEEG have agreed to participate to this endeavour, offering the potential to gather up to iEEG data from up to 1000 patients per year in the future.

Through the MIP, we primarily aim at promoting the development and validation of predictive models in clinical neurosciences, including for rare diseases. Through the HIP, we aim at leveraging cognitive research based on iEEG biosignals.

CHUV
https://www.chuv.ch/fr/neurosciences/dnc-home/recherche/human-brain-project

MIP
https://ebrains.eu/service/medical-informatics-platform

HIP
https://www.humanbrainproject.eu/en/medicine/human-intracerebral-eeg-platform/

Neuroscience Research Center

Centre de recherche en neurosciences, CHUV

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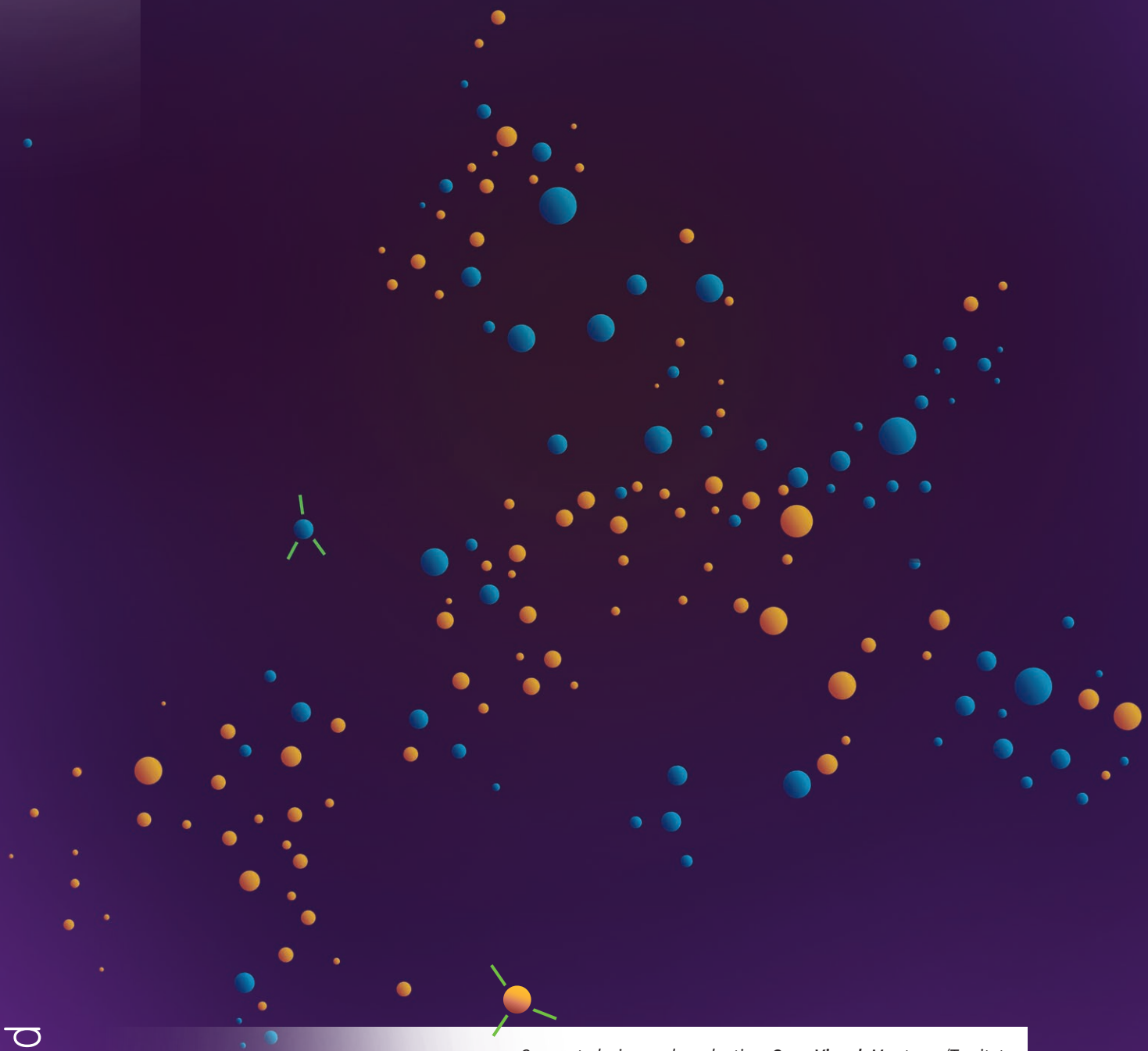
Lausanne, juin 2021



Concept, design and production: ***Onyx Visual,*** *Montreux/Territet, www.onyx-visual.com*

Project Coordinator: Simone Kühner, Viviani Pereira

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