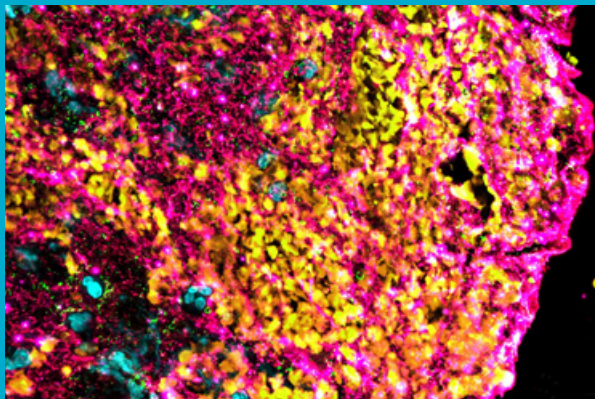
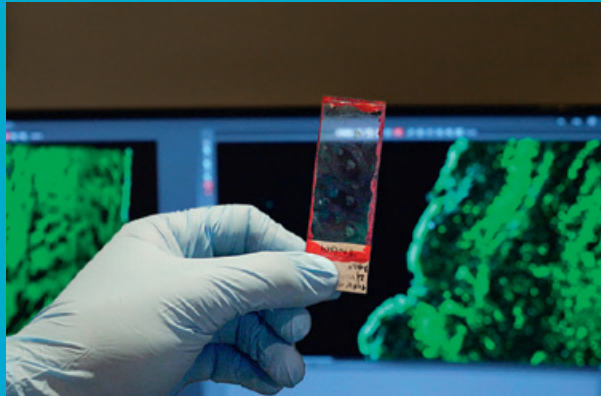


Rothschild Annual Report 2019-2020 Medical Development



HÔPITAL FONDATION
Adolphe de ROTHSCHILD
LA RÉFÉRENCE TÊTE ET COU

Rothschild
Medical
Development 

Contents

Key figures	2
Editorial	3
Breakthroughs 2019-2020	4
Rothschild Medical Development	12
Organizational diagram	13
Network	14
Unit for Clinical Research	15
Clinical Research Platform	19
Innovation Unit	20
AI and Data Science Unit	21
Neurovascular Pathology Research and Training Center	22
Research in nursing	23
Biological Resource Center	24
Translational Research Laboratory	25
Imaging Research Platform-3T MRI	26
Sterile Production and Therapeutic Trials Unit	27
Rothschild Medical Academy: passing on knowledge	28
University education	29
Publications	30
Fellowship	31
Expertise: research in rare and complex diseases	32
Rare Disease Reference Centers	33
Neuropsychology, Neurovision, Neurocognition Institute (I3N)	35
Financing	36
Resources	37
Partners and sponsors	38



Research: key figures*



€12,7 M
Budget
revenue



12,000
Samples
in the CRBT



288
publications



2 university-hospital
contracts signed



1,474 patients seen
at the Clinical Research
Platform



363
patients received
research scans



138 clinical trials
opened to patients



3,715 patients included
in research projects



730
Students trained



Contribution to **3**
Investing in the Future
Programs



2 Hospital Clinical
Research Programs



1 Medical Economics
Research Program



52
Deep Brain Stimulation



30
artificial intelligence
projects



5
patents currently
being registered

* 2019



Editorial

“Creating the innovations of tomorrow, today”



Rothschild
Medical
Development

Our hospital has been innovating since its creation in 1905, first in ophthalmology, and later on, since the 90s, in all Head and Neck fields (neurology, neurosurgery, interventional neuroradiology, otolaryngology, neuroimaging, etc.).

Another important year in our hospital’s research development was 2011, when Dr Laurence Salomon founded the Unit for Clinical Research, uniting our existing research initiatives and giving them recognition on the national and international stage. In 2016, we were DRCI certified, and the number of high-impact research projects and articles we produce keeps increasing each year.

In 2019, we began another stage of our journey with the creation of Rothschild Medical Development, a separate entity dedicated to accelerating our research initiatives and reorienting them

towards medical innovation. We recruited new experts in R&D, data analysis and artificial intelligence, created new technology platforms with the latest equipment and mobilized our institutional and industrial partners for innovative projects on Head and Neck pathologies and neurosensory disorders.

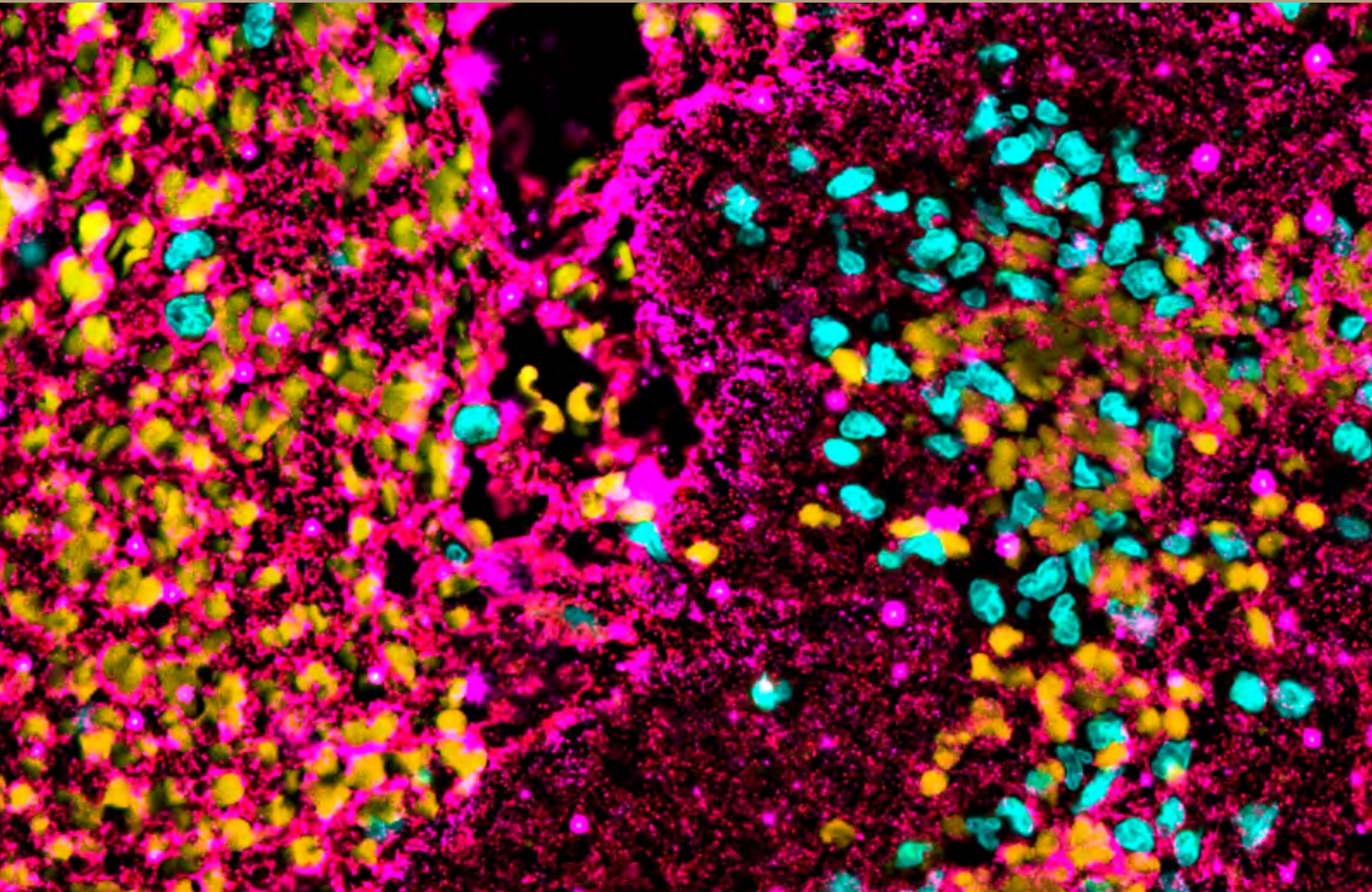
This new highly skilled network strives to transform ideas into projects and projects into tangible results for patients and health care professionals. Rothschild Medical Development is destined to cultivate the progress of tomorrow, pave the way for new treatments that have yet to be explored, and implicate the Rothschild Foundation Hospital in international projects in regenerative and reparative medicine, personalized medicine, surgical robotics and artificial intelligence in health care.



Julien GOTTSMANN
Chief Executive Officer



Breakthroughs 2019-2020



*Thrombus from a cerebral thrombectomy.
Red blood cell immunomarkers (in yellow), von Willebrand factors (pink) and leukocytes (blue).*



Major breakthroughs in all of Rothschild Foundation Hospital's areas of expertise



OPHTHALMOLOGY

Dr Ramin Tadayoni provides international expertise in retinal research

Dr Ramin Tadayoni, newly arrived Head of Department in June 2020, adds international expertise to the Rothschild Foundation Hospital's retina department. Dr Tadayoni is known worldwide for his research on retinal disease, vitreo-retinal surgery and imaging. One of his projects, EVIRED, uses new imaging technologies and artificial intelligence to change our perception of diabetic retinopathy. This project won the 2019 Investing in the Future Award (Hospital-University Research Program).

→ This project, as well as his appointment at Rothschild Foundation Hospital, creates a stronger connection between Rothschild and the **Paris-Nord Hospital Group**, as Dr Tadayoni is also head of the Ophthalmology Department at the Saint-Louis, Lariboisière and Fernand-Widal University Hospitals and a professor of ophthalmology at the University of Paris.

The world's first successful retinal implants for dry AMD

Dr Yannick Le Mer, deputy head of the department and retina specialist surgeon, performed the first successful electronic implants in 2018 as part of a study conducted by the Unit for Clinical Research. The PRIMA bionic vision system, developed by Pixium Vision, includes a sub-retinal solar-powered implant. This completely wireless

implant is designed to create functional artificial vision. The positive results of the study 12 months post-operation were presented at the Eye and The Chip World Research Congress in the United States. The five patients studied all had improved central light sensitivity and four of them could identify letters.

→ This innovative research was made possible by a hospital-university collaboration between the Rothschild Foundation Hospital for the retinal implant, the **15-20 Hospital for patient tracking and Pixium Vision**, conducted by Dr Alain-José Sahel. This research is supported by the **Sorbonne University Vision Institute**, the **INSERM**, **CNRS** and the **University of Pittsburgh (USA)**. In late 2020, the ANSM authorized the second phase of the project: a nationwide, multicentered study to implant 38 patients.

First clinical trials for cellular therapy

Dr Éric Gabison, an ophthalmic surgeon and head of the corneal ophthalmology translational research lab, and his team began clinical trials for cellular therapy that targets severe burns of the ocular surface. These trials are financed by the Ministry of Health, through the Hospital Clinical Research Program (PHRC). This project builds on the foundational research on modifying stem cells conducted in collaboration with the cellular therapy unit at the **Saint-Louis Hospital (AP-HP)**. It is supported by the non-profit organization **Les Gueules Cassées**, **Virgin Radio** and private donors.

→ The latest models of artificial corneas are currently in development. They are designed for patients who need a transplant but are ineligible because their risk of rejection is too high and/or they have insufficient stem cells on the surface of the eye for proper healing of the cornea. With this new generation of colonizing keratoprosthesis biomaterials, the patient's own cells colonize the prosthesis, integrating it into their ocular tissue.

Artificial intelligence: an algorithm predicts eligibility for refractive surgery

In 2020, **Dr Damien Gatinel** and **Dr Guillaume Debellemanière** published the results of their research developing an artificial intelligence algorithm to predict ocular refraction (optical correction) using optical aberration coefficients analyzed using a new set of mathematical functions. This research may improve prediction of ocular subjective refraction using objective data from the aberrometry exam.

It also allows us to better understand how severe aberrations affect ocular refraction.




Rampat R, Debellemanière G, Malet J, Gatinel D. Using Artificial Intelligence and Novel Polynomials to Predict Subjective Refraction. *Nature*.



Artificial intelligence: a neuronal network algorithm to facilitate corneal pathology diagnostics

In 2020, **Dr Damien Gatinel** and **Dr Pierre Zéboulon** published the results of their research developing an artificial intelligence algorithm that uses all of the raw data provided by corneal topography maps. The algorithm classified the exams into three diagnostics with 99.3% accuracy: normal, keratoconus and history of refractive surgery. This is the first time that all raw data acquired from topographic exams has been used to conduct automated diagnostics with a convolutional neural network. This research lays the foundation for more accurate and earlier diagnoses of corneal pathologies.

 Zéboulon P, Debellemannièrè G, Bouvet M, Gatinel D. Corneal Topography Raw Data Classification Using a Convolutional Neural Network. *American Journal of Ophthalmology*. 2020 Jun 10;219:33-39.



STROKES AND INTERVENTIONAL NEURORADIOLOGY (INR)

BOOSTER wins the Investing in the Future Program award for emergency stroke treatment

The BOOSTER consortium, driven by **Dr Mikael Mazighi**, a neurologist at the Rothschild Foundation and Lariboisière Hospitals, is giving itself five years to develop personalized medicine for emergency stroke treatment. The INR unit at the Rothschild Foundation Hospital, a world leader in mechanical thrombectomy, has the largest multi-center biobank of clots in Europe. This biobank is the basis for BOOSTER's

analysis of the biological and radiological signatures of each patient's clot with the goal of predicting responses to medications and innovative devices using deep learning.

➔ **BOOSTER brings together a consortium of public and private entities. University-hospital teams:** Rothschild Foundation Hospital, Lariboisière Hospital (AP-HP), Foch Hospital, Caen CHU, Lyon FHU, Inserm 1148 Unit and Hospinomics Research Chair (AP-HP). **The AP-HP coordinates the HUR. Manufacturers:** Stago, Balt, Sensome, Acticor. **Funds raised for the consortium: 9.8 million euros.**

Interventional Neuroradiology: the innovative medical device from BaseCamp, a start-up

This collaboration between the start-up and the Rothschild Foundation Hospital to develop an active robotic endovascular guide received several institutional grants in 2019-2020: European Regional Development Fund (ERDF): Multicurve project; Île-de-France Region: Innov'up Proto CAMP4 Project; ANR DEEP project (Consortium with other companies and several academic labs in France, including LTSI Rennes and LAMCOS Lyon). This company's mission is to provide interventional medical practitioners with innovative medical devices that improve endovascular navigation and thus treatment for stroke patients.

Call for proposals by the Ministry of Health to finance clinical research: 3 interventional neuroradiology projects funded in 2019

DETERMINE: an Interregional Hospital Clinical Research Program (PHRCI) project. Its goal: Compare individual-

ized and standard blood pressure monitoring strategies during mechanical thrombectomy for cerebral infarctions of anterior circulation. A randomized controlled trial. Project leader: **Dr Benjamin Maier** - Duration: 33 months - Funds raised: €383K

REPERFUSE: a Hospital Clinical Research Program project (PHRCN). Its goal: Administering cangrelor in addition to mechanical thrombectomy for reperfusion of acute ischemic strokes diagnosed by perfusion imaging - a randomized controlled trial. Project leader: **Dr Mikaël Mazighi** - Duration: 39 months - Funds raised: €708K

MAGRITTE: a Medico-Economic Research Program (PRME). Its goal: Medico-economic assessment of two diagnostic imaging strategies, MRI vs. X-ray in suspected ischemic stroke patients: a prospective controlled randomized study. Project leader: **Dr Mikaël Mazighi** - Duration: 48 months - Funds raised: €714K



NEUROLOGY: SCREENING FOR ALZHEIMER'S, OTHER COGNITIVE DISORDERS

OCTAVO neuro-ophthalmology pilot study: searching for a biomarker for Alzheimer's and related diseases

Several studies suggest a correlation between some retinal anomalies observed in OCT-A scans and adaptive optics, on the one hand and the neurocognitive disorders related to the dementia and prodromal stages of Alzheimer's disease (aMCI) and other neurodegenerative pathologies, on the other hand. These results inspired the



pilot study OCTAVO, launched in May 2020 (OCT - Angiography and adaptive optics for patients with memory disorders). Piloted by **Dr Antoine Moulignier** and **Dr Sarah Benistry**, this study seeks to better define the retinal anomalies associated with neurocognitive disorders, compare the OCT-A and AO parameters of patients with and without disorders and determine whether there are different profiles depending on the cause of the disorder.

➔ It may reveal a new biomarker for neurodegenerative pathologies like Alzheimer's disease.

COGITO, a study on predicting and screening for cognitive disorders amongst patients living with HIV

With effective combinations of antiretrovirals, the life expectancy of people living with HIV is nearing that of the general public. More than half of the HIV-positive population is now over 50 years old. Cognitive disorders are now one of the most frequent age-related complications in this population, which may be more susceptible to neurodegenerative diseases. The goal of the multicentric study COGITO (COGNitive ImpairmentT in Older HIV-infected patients), led by **Dr Antoine Moulignier** and **Dr Sarah Benistry**, is to identify the frequency and determining factors of cognitive disorders in this population.

➔ The goal of this study is to provide recommendations for screening and treatment of cognitive disorders in older HIV-positive patients.





NEUROPSYCHOLOGY, NEUROVISION, NEUROCOGNITION

Autism and cerebral visual impairment, interesting similarities

In 2020, **Sylvie Chokron**, director of the Institute of Neuropsychology, Neurovision and Neurocognition (I3N) and her team demonstrated that patients with autism spectrum disorders present emotional face recognition disorders very similar to patients with cerebral visual impairments. These results indicate similarities between visual disturbances in autism spectrum patients and cerebral visual impairments and raise the issue of differential diagnostics between autism and neurovisual disorders.

➔ This research was conducted in partnership with the **École Normale Supérieure** and the **University of Glasgow** and is supported by the **Fondation de France** and the **Orange Foundation**. Two articles on the study have been published in international journals.


 Kovarski K, Caetta F, Mermillod M, Peyrin C, Perez C, Granjon L, Delorme R, Cartigny A, Zalla T, Chokron S. Emotional face recognition in autism and in cerebral visual impairments: In search for specificity. *J Neuropsychol.* 2020 Sep 13.


 Chokron S, Kovarski K, Zalla T, Dutton GN (2020). The inter-relationships between cerebral visual impairment, autism and intellectual disability. *Neurosci Biobehav Rev.* 2020 Jul;114:201-210.

Blindsense: unconscious visual perception discovered in stroke patients

In 2020, **Sylvie Chokron's team**, in collaboration with the Neurology, Imaging and Interventional Neuroradiology Units, identified the brain lesions responsible for visual halluci-

nations in patients with visual field defects caused by a stroke. The team also succeeded in describing unconscious perception in these patients' blind spots, called **blindsense**, for the first time. The groundbreaking results were published in *Neurology* and *Cortex*. This research also contributed to describing disorders in children after a stroke and in adults with arteriovenous malformations (these results were also published).

 Garric C, Sebaa A, Caetta F, Perez C, Savatovsky J, Sergent C, Chokron S. (2020). Dissociation between objective and subjective perceptual experiences in a population of hemianopic patients: A new form of blindsight? *Cortex.* Aug;117:299-310. doi: 10.1016/j.cortex.2019.05.006. Epub 2019 May 18.

 Martinelli F, Perez C, Caetta F, Obadia M, Savatovsky J, Chokron S. Corrélats neuroanatomiques des hallucinations visuelles chez les patients hémianopiques post-AVC. *Neurology* 2020 May 5;94(18):e1885-e1891.



RARE DISEASES


Liver transplants: a last-resort treatment option for Wilson's disease

LCopper-binders, taken daily for life, have transformed the prognosis for patients suffering from Wilson's disease. However, in some cases of advanced liver failure, a transplant may be necessary. Our center at the Rothschild Foundation Hospital, a leader in Wilson's disease and rare copper-related diseases, under the coordination of **Dr Aurélie Poujois**, is studying the effectiveness of liver transplant for patients with a very severe form of the disease and who are resistant to traditional blocker medications. This ambispective study is a collaboration between the neurology team at the Lariboisière Hospital



(AP-HP), the hepatology and liver transplant teams at the Paul Brousse and Bicêtre Hospitals (AP-HP), and multidisciplinary teams from Bordeaux and the Hospices Civils in Lyon, **Besançon and Tours**.

➔ The results, published in 2020, show that liver transplant can be a final treatment option to be discussed on a case-by-case basis that requires collaboration between hepatologists, neurologists and surgeons.

 Pujois A, Sobesky R, Meissner WG, Brunet AS, Broussolle E, Laurencin C, Lion-François L, Guillaud O, Lachaux A, Maillot F, Belin J, Salamé E, Vanlemmens C, Heyd B, Bellesme C, Habes D, Bureau C, Ory-Magne F, Chaîne P, Trocello JM, Cherqui D, Samuel D, de Ledinghen V, Duclos-Vallée JC, Woimant F. Liver transplantation as a rescue therapy for severe neurologic forms of Wilson disease. *Neurology*. 2020 May 26;94(21):e2189-e2202.




ADULT NEUROSURGERY

Discovery of a new electrophysiological signature for states of consciousness

Many studies have been conducted on states of consciousness, particularly regarding disorders of consciousness due to brain lesions. These studies have revealed electrophysiological signatures for functional connectivity. The study published by **Dr Pierre Bourdillon** investigated these signatures in healthy people, observed during sleep and while under general anesthesia, using intracranial stereo electroencephalographic recordings. These recordings revealed a new electrophysiological signature (functional connectivity of electrical activity in the brain for frequencies of 2-5 Hz). This signature allows conscious states (awake as well as REM sleep, in which dreaming occurs) to be distinguished from unconscious states (general anesthesia,

non-REM sleep, pathological alteration of consciousness), regardless of the cause.


➔ This study led to the development of new functional connectivity methods and provides a foundation for studying how AI can help us better understand the loss of consciousness mechanism during epileptic seizures.

 Bourdillon P, Hermann B, Guénot M, Bastuji H, Isnard J, King JR, Sitt J, Naccache L. Brain-scale cortico-cortical functional connectivity in the delta-theta band is a robust signature of conscious states: an intracranial and scalp EEG study. *Nature Scientific Report*. 2020 Aug 20;10(1):14037

Hormone treatments: a confirmed risk factor for speno-orbital meningioma

Spheno-orbital meningioma are benign tumors that infect the meninges, developing between the skull and the eye socket. The first symptoms are most often exophthalmos and retro-orbital pain. This disease can lead to visual impairment and/or oculomotor paralysis. Spheno-orbital meningioma, like regular meningioma, disproportionately affect women. In order to better understand why, **Dr Dorian Chauvet** coordinated a study on patients' exposure to hormones through a literature review (from 2010 to 2019) and a retrospective analysis of patients who underwent operations at the Rothschild Foundation Hospital (from 2005 to 2019). The study revealed a median age at diagnosis of 51 +/- 3 years (vs. 62 +/- 6 years for men) and an elevated ratio of women exposed to long-term hormonal medications (Androcur, Lutéran, Lutényl) or hormone replacement therapy for menopause. 89% were meningothelial meningioma and progesterone receptors were found in 88% of cases.

➔ This study will, in time, help us to better understand speno-orbital meningiomas, a specific and poorly known entity often treated at our hospital.

 Apra C, Roblot P, Alkhayri A, Le Guérinel C, Polivka M, Chauvet D. Female gender and exogenous progesterone exposition as risk factors for speno-orbital meningiomas. *Journal of Neurooncology*. 2020 Aug;149(1): 95-101.



PEDIATRIC NEUROSURGERY

Childhood pharmacoresistant epilepsy: a study shows the effectiveness of radiofrequency thermocoagulation

Focal epilepsy in children may be refractory to pharmacological treatment, in which case surgical resection becomes an appropriate option. When invasive electroencephalogram is required in the presurgical evaluation, depth electrodes can be used to create focal lesions in the epileptogenic zone using radiofrequency thermocoagulation (RFTC) to disrupt the epileptogenic zone. This study, conducted by **Dr Mathilde Chapaux**, aimed to assess the efficacy and safety of RFTC in a pediatric population of 46 patients.

➔ Multivariate analysis found 3 independent criteria linked to RFTC efficiency one month after RFTC: frequency of the seizures before RFTC, age and number of contacts used. RFTC is a safe method for the pediatric population providing important predictive information for surgical resection. An improvement in seizure frequency, often transient, was seen in 2/3 of patients. RFTC could be useful as a palliative technique for children with an epileptogenic zone overlapping with eloquent areas, with minimal risk of sequelae.



Chipaux M, Taussig D, Dorfmueller G, Dorison N, Tisdall MM, Boyd SG, Thornton R, Eltze C, Fohlen M, Cross HJ, Ferrand-Sorbets S. SEEG-guided radiofrequency thermocoagulation of epileptic foci in the pediatric population: Feasibility, safety and efficacy. *Seizure (European Journal of Epilepsy)* 2019 Aug; 70:63-70.

GENEPHY: genetic analysis of focal cortical dysplasia responsible for pharmacoresistant focal epilepsy subjected to surgery

Genetic brain abnormalities such as focal cortical dysplasia (FCD) are major causes of pediatric refractory epilepsy subjected to surgery. The goal of this study, conducted by **Dr Mathilde Chipaux**, is to provide an overview of germline and somatic variants in a large cohort of FCD patients. 63% of cases were elucidated using molecular diagnostics. The FCD cases presented somatic gain-of-function variants in mTOR and its activators (AKT3, PIK3CA, RHEB), as well as somatic, germline and loss-of-function variants in its repressors (DEPDC5, TSC1, TSC2). The analysis of microdissected cells showed that more than 90% of neurons had mutated.

→ This study revealed the high frequency of genetic etiologies in focal cortical dysplasias in children. In the future, the role of genetic exams in presurgical evaluations should be specified.



DEEP BRAIN STIMULATION IN PEDIATRICS

DYSTONDE investigates the electrophysiological activity of globus pallidus internus and externus

The physiopathology of primary and secondary dystonia in children is very poorly understood. The DYSTONE project uses electrophysiological recordings (extracellular and field potentials) taken in the globus pallidus internus and externus during surgical electrode implantation to study the electrophysiological activity of these structures in various subtypes of pediatric dystonia. This electrophysiological mapping will provide the data necessary to identify an electrophysiological physiologic marker that can predict proper positioning of the stimulating electrode.

→ This project, led by **Laurent Goetz, Dr Vincent d'Hardemare, Dr Nathalie Dorison and Dr Julie Bonheur**, is supported by **Amadys (a dystonia patient non-profit organization)**.

DYSTOPI studies the use of 18F-DOPA in PET scans in order to predict responses to deep brain stimulation

Deep brain stimulation is an approved treatment for childhood dystonia. However, the predictive response factors are poorly understood and results are particularly variable for secondary dystonias. The DYSTOPI study aims to evaluate how presurgical PET scans with 18F-DOPA may be used as a tool to predict responses to deep brain stimulation in patients with dystonia. **Dr Nathalie Dorison, Dr Vincent d'Hardemare**, scientist **Laurent Goetz, Dr Nouredine Saleh** (CHU Kremlin-Bicêtre) and **Dr Florent**

Besson (CHU Kremlin-Bicêtre) lead this retrospective study on imaging data and clinical results of deep brain stimulation.

QUALIDYS evaluates the impact of deep brain stimulation (DBS) on quality of life in children suffering from dystonia

The QUALIDYS study, a prospective monocentric study, is conducted by **Drs Adélaïde Tonus, Julie Bonheur, Nathalie Dorison and Mr Fabien Richard**. It seeks to evaluate the impact of deep brain stimulation (DBS) on quality of life in children suffering from dystonia, as perceived by their parents. Although DBS is effective in improving motor control in patients with dystonia, it requires close monitoring after surgery, which is limiting for the child and their family. This disease often remains limiting even when treated. This is why the study decided to investigate patient quality of life, taking a more holistic approach than assessing clinical responses to surgery.

STEP FOR: pilot study: deep brain stimulation as a treatment for refractory generalized epilepsy in children

There is no effective treatment for refractory generalized epilepsy in children such as Lennox-Gastaut syndrome. Continuous spikes and waves during sleep and Dhoose syndrome. Initial trials of deep brain stimulation of the central medial nucleus of the thalamus have been reported in the literature for Lennox-Gastaut syndrome. After implanting electrodes in the nucleus on a compas-



sionate basis, the pilot study STEP FOR will begin in 2021. The study will follow 15 children suffering from refractory generalized epilepsy (Lennox-Gastaut).

→ **Dr Vincent d'Hardemare, Dr Emmanuel Raffo and scientist Laurent Goetz lead this study. Medical devices provided by Boston Scientific.**



PEDIATRIC ENDOCRINOLOGY

Pituitary stalk interruption syndrome is characterized by genetic heterogeneity

Pituitary stalk interruption syndrome (PSIS) is a congenital anomaly characterized by an ectopic or absent posterior pituitary, an interrupted pituitary stalk and hypoplasia of the anterior pituitary under MRI. This study, piloted by **Dr Raja Brauner** and **Dr Ken McElreavey** (Institut Pasteur), conducted Exome Sequencing (DS) in 52 patients with PSIS, associated with a somatic anomaly in 69.2% of cases and an ophthalmologic anomaly in 30.8% of cases (n=16). A new genetic variant was identified in 39 subjects (75%) in genes related to the development of the median line and/or pituitary gland, hypogonadotropic hypogonadism, syndromic short stature, cerebellar atrophy, axon migration and agenesis of the corpus callosum.

→ **These results revealed a relationship between a genetic anomaly and anomalies associated with PSIS like epilepsy, mental retardation, genital development disorders and ocular anomalies.**



Brauner R, Bignon-Topalovic J, Bashamboo A, McElreavey K. Pituitary stalk interruption syndrome is characterized by genetic heterogeneity. Plos One in press



PAIN EVALUATION AND TREATMENT

A new clinical trial for treating migraines

This study, conducted by Dr Claire-Marie Mangon since October 2020, focuses on patients suffering from migraines treated at the Pain Evaluation and Treatment Center. The study uses the approach to millimeter wave technology developed by the Grenoble-based start-up Remedee Labs. A bracelet emits a weak signal on the internal surface of the wrist. This signal stimulates subcutaneous nerve receptors to trigger release of endorphins in the brain, efficiently relieving pain. Millimeter wave therapy, which acts against migraine triggers such as lack of sleep and stress, is also a new preventive treatment for episodic migraines.



ORL

CONTOUR study: A pluridisciplinary approach to defining radiation fields in head and neck cancers

Piloted by **Dr Daniel Brasnu**, ORL oncologist in **Dr Denis Ayache's** unit, the CONTOUR study focuses on defining radiation fields for cancers of the head and neck that are usually defined by the radiation therapist alone. The ORL surgeon evaluates the radiation fields that have been established by the radiation physicist and radiation therapist before radiation therapy begins and proposes changes in the volumes if necessary in order to better define the targets to be treated. Some target volumes may be reduced in order to limit radiation toxicity and others may be increased in size in order to better target tumor extensions.

→ This innovative, prospective multicentric study seeks to assess the effectiveness of pluridisciplinary (ORL surgeon, radio therapist and radiologist) definition of radiation fields for cancers of the head and neck.



ANESTHESIA

ROC-HYPOX: a study to investigate the use of curare to intubate infants

The anesthesia team at the Rothschild Foundation Hospital has been encouraging use of curare to facilitate intubation of infants for the past 10 years. A multicentric prospective randomized study of 412 infants was launched to show that desaturation episodes are less frequent during intubation when curare is added to standard inhalational induction. This Interregional Hospital Clinical Research project is led by **Dr Anoushée Shaffii**.

Study of an infrared technique to facilitate perfusion in children

Perfusion in children can be very complicated and time-consuming with general anesthesia. The goal of the 3V study was to assess the pertinence of a medical device that shows vein location with an infrared technique. This multicentric, randomized study investigated 311 children with difficult perfusion. This Interregional Hospital Clinical Research project (PHRCI) is led by **Dr Jean-Michel Devys**.



Article in press 2020, Eur J of Anesth.



Staff allocation for anesthesia, assessing safety in degraded mode

With the lack of sufficient staff in anesthesia units throughout France, the anesthesia team evaluated the safety of treatment in degraded mode. In degraded mode, only one nurse anesthetist was assigned to three operating rooms, instead of one nurse per room, during an ophthalmologic operation under locoregional anesthesia. This non-inferiority randomized study of 900 patients, called SACHS, showed that patient safety was the same in both operating modes. This project, led by **Dr Jean-Michel Devys**, is part of the Health Care System Research Program.



COVID-19 RESEARCH PROJECTS

COVIDORNASE: a clinical trial investigates using cystic fibrosis medication to improve oxygenation of patients on life support

Acute respiratory distress syndrome (ARDS) is the primary reason for which coronavirus patients are put on emergency life support and into a medically induced coma. These patients present similar symptoms to cystic fibrosis and other inflammatory lung diseases. During a viral respiratory infection, the lung recruits a large number of polymorphonuclear neutrophils which form NETs (neutrophil extracellular traps). These molecular NETs obstruct the lungs, amplifying the inflammatory response that causes ARDS. This study seeks to assess the effectiveness of inhaling dornase alfa. This medication is usually used in cystic fibrosis treatment to reduce viscosity of mucus in the lungs by cutting the strands of

NETs, reducing the pulmonary inflammation that causes patients to rapidly deteriorate. The study is conducted by **Dr Jean-Philippe Désilles** and **Dr Charles Grégoire** in collaboration with the CHRU de Strasbourg, CHR de Metz, CHR de Valenciennes and CHR de Chartres. It plans to include 100 patients placed on emergency life support ventilators for ARDS COVID+. At the end of November 2020, 25 patients were already included in the study.

COVID ORL: a study supported by the Ministry of Health*

During the first wave of COVID, **Dr Alain Corré** issued a public health alert on the link between anosmia and the disease. This alert prompted **Dr Mary Daval**, in partnership with the Lariboisière Hospital (AP-HP), to conduct a randomized controlled trial to assess the efficiency of local treatment with budesonide for anosmia and hyposmia in COVID-19 patients without signs of severity during Q4 2020. The initial results of this study will be available before the end of the year.

*Not part of the PHRC

Multiple sclerosis and COVID: a study to better inform patients

The Resources and Skills Centers - Multiple Sclerosis (CRC-SEP) and the Francophone Multiple Sclerosis Society began compiling a registry (CoviSEP) at the beginning of the pandemic in order to describe the epidemiology and clinical characteristics of COVID infection in MS patients. The CRC-SEP at the Rothschild Foundation Hospital, coordinated by **Dr Caroline Bensa Kocher**, was the most active recruitment center. This collaborative study was published in June 2020. The results were also widely circulated in order to guide medical practices and better inform patients of their risk factors.



Louapre C, Collongues N, Stankoff B, Giannesini C, Papeix C, Bensa C, Deschamps R, Créange A, Wahab A, Pelletier J, Heinzlief O, Labauge P, Guilloton L, Ahle G, Goudot M, Bigaut K, Laplaud DA, Vukusic S, Lubetzki C, De Sèze J. Clinical Characteristics and Outcomes in Patients With Coronavirus Disease 2019 and Multiple Sclerosis; Covisep investigators. *JAMA Neurol.* 2020 Jun 26;77(9):1-10.



The Rothschild Foundation Hospital recognized as a human subject research facility

On October 22, 2020, the Île-de-France Regional Health Agency officially recognized our hospital as a human subject research facility (LRIPH). This certification is granted for excellence and safety in clinical trials conducted at the hospital, where 500 m² is dedicated to clinical research. This recognition is a major step in the hospital's strategy for promoting research on head and neck pathologies, opening the door to new possibilities. We can now be the first center in the world to conduct clinical trials on new medicines and interventional and surgical technologies.



Rothschild Medical Development





A pluridisciplinary team dedicated to research and innovation

OPERATIONAL COORDINATION



Guillaume LE HÉNANFF
Deputy Director



Dr Ramin TADAYONI
Head of
Ophthalmology



Dr Mikaël MAZIGHI
Head of the Biological Resource Center
and Head of the Neurovascular
Pathology Research and Training Center



Dr Amélie YAVCHITZ
Head of
Clinical Research



Kevin JOUBEL
Head of the
Data Science Unit
and Data Protection Officer



Dr Chloé DUPONT
Head of Pharmacy
and Head of the Sterile
Production and Therapeutic
Trials Unit



Perrine BOURSIN
Paramedical Coordinator
of Research in Nursing,
Rehabilitation
and Medical Technology



Vivien VASSEUR
Head of the
Ophthalmology
Clinical Research
Platform



Goulven THÉZÉ
Head of the Innovation,
Evaluation and Legal Expertise
for Contracts
Unit

MUTUALIZED SUPPORT SERVICES



Lucia LOPES
Head of the
Clinical Research Department



Siga DUKURAY
RMD and Fundraising
Manager



Mélanie ROULLEAU
Head of Communication for
Research and the CRMR Wilson

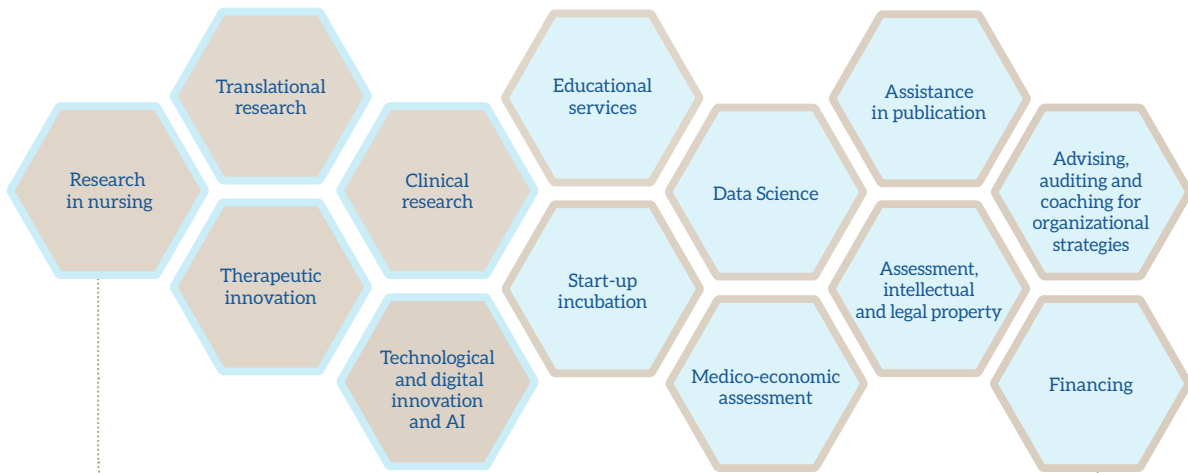


A leading network of excellence in research, innovation and artificial intelligence

Our services are designed for:

- manufacturers, researchers, hospitals and doctors in France and abroad
- doctors, paramedical professionals and researchers at the Rothschild Foundation Hospital.

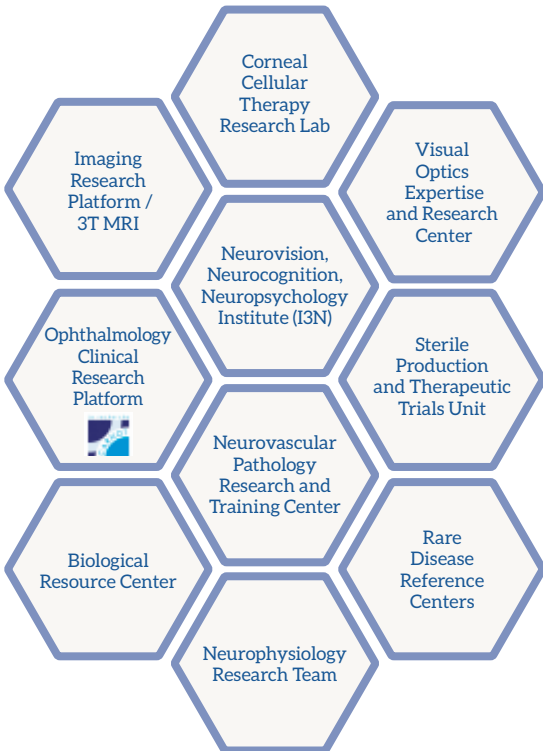
AREAS OF EXCELLENCE



SERVICES



PLATFORMS OF EXPERTISE



EXPERT TEAMS AND STRUCTURES



CONTRIBUTION TO 3 INVESTING IN THE FUTURE PROGRAMS





The Unit for Clinical Research



Head of the Unit
for Clinical Research
Dr Amélie Yavchitz

The Unit for Clinical Research provides a single structure for researchers at the Rothschild Foundation Hospital and our industrial and academic partners. This unit has been supporting clinical research conducted by the Rothschild Foundation Hospital's medical teams since 2011. The Rothschild Foundation Hospital Unit for Clinical Research was awarded the **DRCI certification** (Clinical Research and Innovation Delegation) in 2016 by the Ministry of Health. We are one of **eight DRCIs in Île-de-France**.

Our mission: guide each trial, from design to publication!

This unit, which today has a staff of more than 40, including a technical and research team, methodology/biostatistics team, supervising physician and health economist, was designed to promote therapeutic innovation and diagnostic advances for patients. **The unit coordinates 138 different research projects, two thirds of which are promoted by the hospital.** 3,715 Rothschild Foundation Hospital patients participated in clinical trials in 2019, making us the second-most productive research hospital in the Paris region.

The unit has three teams:

① **The methodology, biostatistics and medico-economics team** advises on methodology and biostatistics, assists in designing projects before they are submitted for regulatory approval or to calls for proposals, conducts biostatistical analysis and medico-economic assessments, and provides methodology, biostatistics and health economics services for our external partners. Finally, a scientific publication support platform has been made available to the hospital's researchers.

② **The promotion team** represents Rothschild Foundation Hospital when promoting research projects. It is in charge of managing the human and financial resources needed to conduct trials while maintaining best practices. The promotion team studies the regulatory requirements that apply to each project and takes out the appropriate insurance policy if necessary. It is in charge of keeping participants safe and ensuring the quality of the trial.

③ **The investigation team** is in charge of making sure that trials run smoothly, whether they are promoted internally or externally. It assists with patient inclusion, organization of treatment / research, research data collection and the relationship with researchers. The team uses an ophthalmology clinical research platform (CRP) for patients participating in clinical trials.





The heart of a **structured and active research network**

INTERREGIONAL CLINICAL RESEARCH AND INNOVATION GROUP ÎLE-DE-FRANCE (GIRCI IDF)

GIRCI IdF is a public entity that promotes excellence in clinical research in Île-de-France. It provides its partners (public, private for-profit and private non-profit) with access to support for quality applied research in health care. It also manages institutional calls for proposals, including the PHRCI. The GIRCI IdF promotes connections within the regional health ecosystem, strengthening partnerships in order to encourage institutions to work together to provide their communities with access to the latest innovations.

The Rothschild Foundation Hospital became the headquarters of GIRCI IdF in April 2016. The hospital was chair of the GIRCI from 2016 to 2018 and created the new governance system that was implemented in June 2019. The Rothschild Foundation Hospital represents Public Interest Private Health Establishments on the board and provides vigilance and pharmacovigilance for our partners.

NON-PROFIT PRIVATE INSTITUTIONAL RESEARCH ASSOCIATION (RESPIC)

RESPIC was created in 2019 in order to foster quality clinical research and encourage collaboration between

institutions, facilitating clinical trials for both medications and medical devices. RESPIC provides resources and a platform for industrial partners that includes a map of member institutions, promoting visibility of resources and members' current projects.

Rothschild Foundation Hospital, vice-president of RESPIC, is the leading institution for the following three resource teams:

- **Vigilance team**
- **Methodology, biostatistics and health economics team**
- **Monitoring team**

PARTNERSHIPS

The Rothschild Foundation Hospital cultivates close relationships with its partner institutions for clinical trials, particularly the Diaconesses Croix Saint-Simon Hospital Group and the Tepepe Medical Center. The hospital's Unit for Clinical Research assists these institutions in structuring and promoting their research. We help them improve their promotional work (research project design, funding, implementation) and provide research staff.





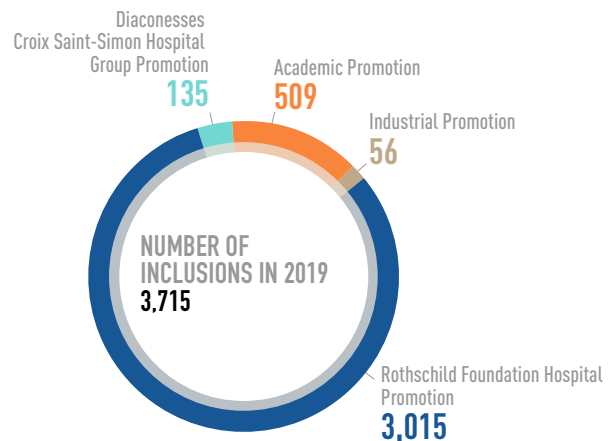
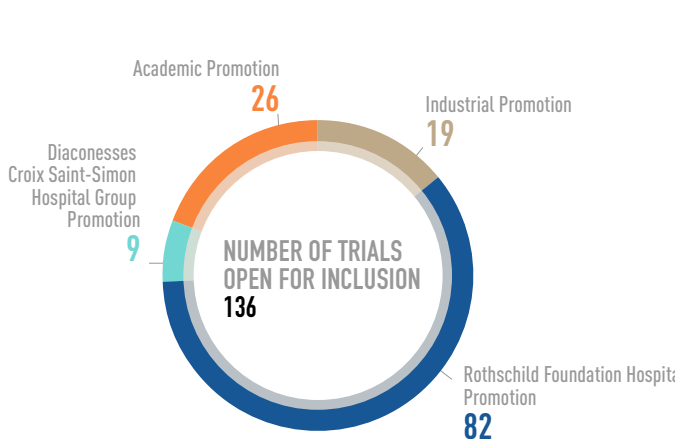
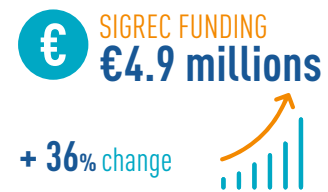
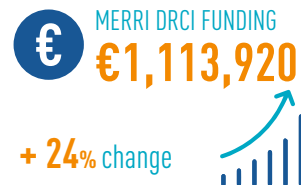
The Unit for Clinical Research in Figures

The Unit for Clinical Research promotes Rothschild Foundation Hospital in France and abroad.

The number of trials being conducted as well as the number of patients included reflect our commitment to research. The Clinical Research and Innovation Delegation (DRCI) is rated second in Île-de-France by the DGOS (French National Health Care Services Agency) for promotional and investigational inclusion and third for the number of clinical trials promoted.



SIGAPS 2019



MERRI 2020

INSTITUTION	Clinical Trial Score	Investigational Inclusion Score	Promotional Inclusion Score	Publication Score	Base Endowment
Rothschild Foundation Hospital	1.54	2.29	2.31	0.41	0.56
FEHAP Average	0.41	0.57	0.5	0.31	0.32
CH Average	0.08	0.09	0.05	0.08	0.08
CLCC Average	0.76	0.61	0.57	0.49	0.41
CHR-U Average	2.22	2.29	2.38	2.46	2.53
NATIONAL AVERAGE	0.68	0.68	0.68	0.68	0.68



Trials and Publications (2019)

	CLINICAL TRIALS OPEN FOR INCLUSION				PUBLICATIONS		
	Int. promotion	<i>incl. RIPH 1 and 2</i>	Ext. aca/ind promotion	No. of inclusions	No. of publications	<i>incl. A/B ranked pubs.</i>	SIGAPS score
OPHTHALMOLOGY DEPARTMENT	11	10	5	228	60	27	652
Dr Cochereau's unit	8	7	1	147	8	3	113
Dr Sahel's unit	2	2	2	16	36	21	353
Dr Vignal-Clermont's unit	0	0	0	43	3	0	15
Dr Caputo's unit	1	1	1	22	7	2	87
Dr Gatinel's unit	0	0	1	0	6	1	84
NEUROSCIENCE DEPARTMENT	35	33	33	2 466	119	55	1411
Interventional neuroradiology unit (INR)	13	13	13	1 811	51	31	713
Neurology unit	7	6	3	245	20	8	167
Neuro-vascular unit	3	3	6	175	6	6	42
Parkinson's unit	4	3	4	25	7		56
Neuropsychology, neurovision, neurocognition institute (I3N)	0	0	0	0	10	3	118
Adult neurosurgery unit	1	1	1	29	11	1	94
Pain evaluation and treatment	1	1	1	68	2	1	28
Pediatric neurosurgery unit	6	6	3	113	8	4	113
CRMR Wilson's disease	0	0	2	0	4	1	80
ANESTHESIOLOGY AND LIFE SUPPORT DEPARTMENT	5	3	4	203	22	4	198
Anesthesiology unit	3	1	2	156	14	2	118
Life support unit	2	2	2	47	8	2	80
IMAGING UNIT	17	17	0	466	26	15	478
OTORHINOLARYNGOLOGY AND CERVICO-FACIAL SURGERY UNIT (ORL)	3	2	0	36	4	15	44
EAST PARIS INSTITUTE OF INTERNAL MEDICINE - INTERNAL MEDICINE UNIT	0	0	2	0	16	11	161
OTHER RMD UNITS: CLINICAL RESEARCH PLATFORM (CRP), UNIT FOR CLINICAL RESEARCH (URC), CHRONOBIOLOGY UNIT, GABISON LAB	11	11	1	181	25	1	267



Resources for patients included in **clinical trials**



Clinical Research Platform Coordinator
Vivien Vasseur

Since 2014, the Institut Carnot certified clinical research platform (CRP) has been providing resources and staff to patients participating in ophthalmology clinical trials. It provides the Rothschild Foundation Hospital's teams with the latest medical equipment for imaging the posterior segment of the eye (retina and optic nerve) as well as a qualified team specializing in ophthalmology and clinical research.

The team includes 2 ophthalmologists, 3 orthoptists, 2 clinical research nurses, 2 clinical research technicians, 1 project manager and 1 coordinator. The platform's ophthalmologists and orthoptists also conduct research projects in medical retina and neuro-ophthalmology.

AMD INNOVATION PATIENTS CAN SEE AGAIN WITH ARTIFICIAL RETINAS



"There has never before been a treatment for Age-related Macular Degeneration (AMD).

We hope to give patients back some of their central vision with PRIMA electronic implants developed by Pixium Vision. These 2 mm x 2 mm chips, placed

under the retina in the center, worked like a solar panel, transforming light into electricity. Combined with glasses, they gave patients central vision with measurable visual acuity," says Dr Yannick Le Mer, deputy department head and retina specialist surgeon at Rothschild Foundation Hospital.

Partners



KEY FIGURES

18 medical retina and neuro-ophthalmology projects in operation

50 research projects (internal and external promotion)

3,000 actions per year



Open innovation



Head of Innovation and Evaluation
Goulven Thézé

Development Coordinator Innovation
Dana Azar

Rothschild Hospital's scientific excellence in the field of head and neck makes our hospital an excellent source of innovations for patients. With our clinical research team and specialized laboratories, we have the ability to coordinate projects that accelerate therapeutic advancement. **Personalized medicine in neurology, which is now a reality** (new RNA treatments like Nusinersen), the use of big data to develop digital biomarkers (MOOV-CARE from SIVAN technologies) and virtual cohorts to evaluate new treatments (FLATIRON) are all new fields that the hospital is investigating in order to develop impactful innovations.

The Innovation Unit's mission is to **accelerate internal initiatives, develop collaborations and organize partnerships in order to transform these promising trends into tangible progress** for preventing and treating neurosensorial disability. The Innovation Unit provides technical and legal support for filing patents, assists project leaders in preparing applications for calls for proposals and provides contractual support for discussions with industrial partners.

KEY FIGURES

10 "Inventor round tables" hosted

5 patents written

9 calls for innovative proposals

3 clinical partnerships

33 service projects or innovative products detected

AMELII SELECTED FOR FINANCING BY THE EOSC*



AMELII (Assisted detection and Measurement of Lung Infection and Inflammation) is a technological solution for rapid and precise detection of COVID-19 using chest X-rays. It quantifies the diagnosis, virtually dissecting characteristic COVID-19 imaging (such as ground-glass opacities) at different stages of the disease using autonomous technology integrated into the Telemis PACS software.

The data collected from the chest X-ray is then processed in order to segment the lesions. The software first segments the lung parenchyma and then isolates the lesions in the ground-glass opacities, without any interaction with the user.

AMELII reduces the time required for diagnosis, detects asymptomatic cases and improves workflows in hospitals in order to better fight the disease. The Rothschild Foundation Hospital's Medical Imaging Department is implementing this project with an image processing engineer who invented and holds a patent for a process that segments complex pathological or non-pathological structures.

* European Open Science Cloud



From raw data to applied data



Head of the Data Science Unit & DPO
Kevin Joubel

In spring 2019, thanks to the generous support of the Edmond de Rothschild Foundation, the Adolphe de Rothschild Hospital opened its first unit specializing in data science and artificial intelligence.

One year after its inception, **the Data Science Unit is host to more than 50 projects, including nearly 30 AI projects.** It has also formed five partnerships with start-ups and academic institutions, bringing in outside expertise and giving value to its research.

The Data Science Unit, in collaboration with the information system and medical technologies department (DSITM), has begun the process of **implementing the hospital's first Health Data Repository, which was approved by the CNIL on December 18, 2020.**

This program is supported by the Edmond de Rothschild Foundations of New York.



THE SEDAAR PROJECT WINS HEALTH DATA HUB'S 2ND CALL FOR PROPOSALS IN JULY 2020



"Artificial intelligence for an improved health care system experience."

SEDAAR, a project led by Dr Rabih Hage, uses applied artificial intelligence to diagnose 37 retinal pathologies. Rothschild Foundation Hospital and partner ADCIS were selected from 138 candidates. We will receive technical support from Health Data Hub and financial support of €300,000 from the Grand Défi and BPI France. The artificial intelligence application SEDAAR is designed to assist during the first stages of ophthalmologic treatment in three ways:

- **providing wide access to screening** for retinal pathologies
- **targeting patients** who have a pathology that requires urgent medical attention
- **servicing as a foundation** for public and/or private research.

KEY FIGURES

56 including 35 AI projects

5 partnerships formed

€1,258 M raised



A **productive year** for the Neurovascular Pathology Research and Training Center

The Neurovascular Pathology Research and Training Center (CREF), part of the Interventional Neuroradiology Unit at the Rothschild Foundation Hospital, is **a single structure that is directly connected to health care services. It provides resources to facilitate complex training and research projects for medical professionals and patients.**

In July 2019, the CREF and Unit for Clinical Research implemented a clinical research team that is on call 24/7 for neuroscientific emergencies in order to facilitate after-hours inclusion in research protocols. Clinical research technicians and health services nurses, trained in emergency research, are on call 24/7. Ever since, 95% of patients potentially eligible for clinical trials have been included. Other medical teams are now adopting this scientific approach.

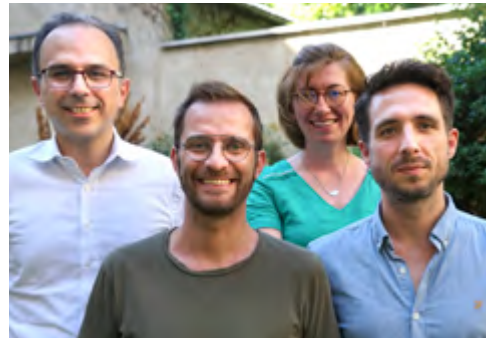
In December 2019, two vascular neurology and interventional neuroradiology intensive care nurses joined the CREF part-time. They are in charge of the CREF's new projects.

All of these initiatives are conducted in collaboration with the hospital's other teams.

The CREF also organized two nursing conferences at the French Society of Emergency Medicine's annual congress and two health care workshops at the French Society of Vascular Neurology's annual congress in 2019.

The CREF now uses its expertise to give classes at the ECLIFE Master's program (Clinical epidemiology and pharmacoepidemiology) at the Sorbonne, to 2nd year IPA (Advanced practical nursing) Master's students at the University of Paris, to inter-university neurovascular pathology paramedical students and to state-certified nursing students at IFSI Foch.

In 2018, the CREF began hosting Eneurovasc, a biennial congress held both on-site and remotely, for the neurovascular department.



Head of the Neurovascular Pathology Research and Training Center
Dr Mikael Mazighi

Coordinating state-certified nurse of the Neurovascular Pathology Research and Training Center
Perrine Boursin

State-certified nurses
Alexis Salesse and Patrick Poy

Secretary
Corinne Dutheil

KEY FIGURES

1
24/7 on call team
clinical research
emergency care
neuroscience
operations awarded
the FEHAP Innovation
Trophy in 2020

4
seminars
The Fundamentals of
Vascular Neurology
and Interventional
Neuroradiology,
60 health care
professionals trained

2
vascular neurology
and interventional
neuroradiology
**intensive care
nurses**

106
**specialized
neurology degrees**



Supporting the development of **research in nursing**

In our 2017-2021 health care plan, Rothschild Foundation Hospital set the goal of fostering a scientific approach with our health care professionals. In order to achieve this goal, the hospital appointed a paramedical coordinator of research in nursing, rehabilitation and medical technology.

In collaboration with referring health care professionals in research and nursing, the coordinator continues to raise awareness for the scientific side of health care, design and conduct activities that develop and give value to health care research, and assist health care professionals in a research project in partnership with the Unit for Clinical Research. Together, they can develop ideas for research that are closely aligned with the clinic's needs and encourage incorporation of convincing data into professional practices (clinical, managerial and training).

A variety of initiatives were organized in 2019 to introduce health care professionals to research in nursing, including attending introduction to research workshops at the Saint Louis Lariboisière Hospital Group, creation of a 24/7 on-call research team for neuroscience emergencies and the new Music in Mind project, supported by the Edmond de Rothschild Foundations.

The paramedical coordinator of research in nursing, rehabilitation and medical technology also trains paramedical staff, both at the Rothschild Foundation Hospital and externally. She advises our industrial partners on setting up clinical trials and using new molecules in complex clinical settings such as neuroscience emergencies.



Paramedical coordinator of research in nursing, rehabilitation and medical technology
Perrine Boursin

Referring health care professionals in research in nursing
Yamina El Mandour and Nicolas Miklaszewski



KEY FIGURES

24/7 on-call research team for neuroscience emergencies

3 state-certified nurses attending the introduction to research workshop

2 Music and Health classes per week



The Biological Resource Center: a biobank for researchers

The Biological Resource Center (CRB) supports research by collecting, preparing, organizing, conserving and distributing biological resources (samples and associated data) for fundamental, translational, clinical and applied research.

The hospital's researchers receive priority access to the CRB's services, but all other research teams, both academic and industrial, can access these biological resources.

The CRB's activities are planned using processes that can be regulated, supervised and improved. The contract for each externalized process includes specifications that connect the CRB with each of the hospital's support units.

The CRB recruits a large number of patients through a specialized clinical environment. It contributes to the hospital's research objectives and interacts with the DRCI and research teams for optimal management of these biological resources.

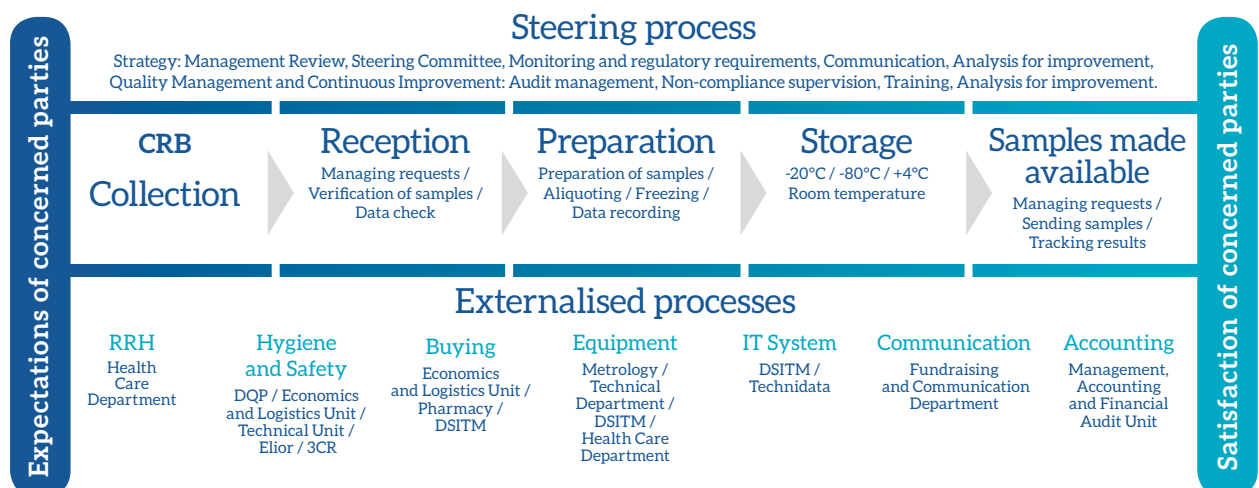
The CRB received the NF S96-900 certification in 2019, which recognizes quality and traceability of samples, compliance with regulations and protection of individuals by conserving consent and anonymous data.



Head of the Biological Resource Center
Pr Mikael Mazighi

In Press: The article reporting the results of the BP TARGET study (financed by the Ministry of Health - PHRC 2016) was accepted for publication in *The Lancet Neurology* (IF 30): Efficacy of intensive blood-pressure lowering after successful endovascular therapy in acute ischemic stroke (BP TARGET): a multicenter, blinded endpoint randomized controlled trial.

Mikael Mazighi MD, PhD^{1,2,3,4}, Sebastien Richard MD, PhD^{5,6}, Bertrand Lapergue MD, PhD⁷, Igor Sibon MD, PhD⁸, Benjamin Gory MD, PhD^{9,10}, Jerome Berge, MD¹¹, Arturo Consoli, MD¹², Julien Labreuche, BST¹³, Jean-Marc Olivot MD, PhD¹⁴, Joseph Broderick, MD¹⁵, Alain Duhamel, PhD¹³, Emmanuel Touze MD, PhD¹⁶, Adnan I Qureshi, MD¹⁷, Amélie Yavchitz MD, PhD¹⁸, Simon Escalard, MD¹, Jean-Philippe Desilles MD, PhD^{1,2,3,4}, Hocine Redjem, MD¹, Stanislas Smajda, MD¹, Robert Fahed, MD¹, Solène Hébert, MD¹, Benjamin Maier, MD^{1,2,3,4}, François Delvoye, MD¹, Perrine Boursin, RN¹, Malek Ben Maacha, MSc¹⁹, Michael Obadia, MD¹⁹, Candice Sabben, MD¹⁹, Raphael Blanc, MD^{1,2,4}, Julien Savatovsky, MD²⁰, Michel Piotin MD, PhD^{1,2,4}, for the BP-TARGET investigators.





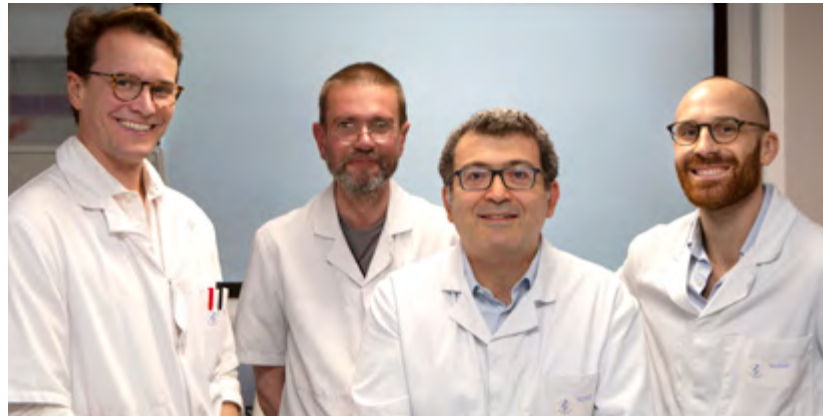
Translational research in corneal ophthalmology: a specialized laboratory

In order to conduct additional research, the Rothschild Foundation Hospital created a laboratory specializing in translational research and ophthalmologic surgery directed by Dr Éric Gabison. This project's launch is supported by the Edmond de Rothschild Foundations.

The lab team, comprised of doctors and researchers, focuses on pathologies of the cornea, the molecular mechanisms involved in these pathologies and development of specific treatments such as stem cell transplants.

The research lab specializes in developing gene and cellular therapy for corneal diseases that cause clouding of the cornea.

Dr Gabison's research lab is affiliated with the Cell and Tissue Biotherapy Department at the Saint-Louis Hospital directed by Dr Jérôme Larghero (University of Paris/ Inserm). This department cultures stem cells and produces and delivers cellular therapy products for clinical trials.



Head of the Translational Research Laboratory
Dr Éric Gabison

Research team

Benoit Souquet, Damien Guindolet, Benoit Chapellier, Ludovic Perraud, Mathieu Cavaille

Gene therapy trials are conducted in collaboration with the Research Department directed by Dr Daniel Scherman, Chemical Biological Technologies for Health Unit (UTCBS) University of Paris - Chimie Paris-Tech / CNRS UMR8258 - U1022 INSERM.



KEY FIGURES

15 publications since the laboratory opened in 2018

2 patents currently being registered

1 national PHRC for cellular therapy for ocular burns



A 3T MRI scanner entirely dedicated to neuroscience research

Tesla's 3T technology creates very accurate, high-quality images, which is essential for brain exploration. Some of these exams are used to diagnose and monitor Head and Neck cancers.


The Rothschild Foundation Hospital has chosen to dedicate this piece of equipment entirely to research, demonstrating our commitment to associating treatment with cutting-edge clinical research. Many of the hospital's ophthalmology, neurology and ORL research protocols use or are based on imaging and expert processing of these images by radiologists. This technology, which collects a massive amount of data, is the foundation for many studies that use the data processing power of artificial intelligence.

In 2019, research engineer Emilie Poirion, PhD joined the already invested medical and paramedical team. She assists in designing research projects, scheduling MRIs and processing complex images. Dr Sidney Krystal also began a doctoral thesis in partnership with Neurospin (Dr Josselin Houenou's team) this year, studying functional MRI at rest processed by artificial intelligence with the goal of improving diagnosis and treatment of psychiatric pathologies.

Dr Savatovsky published a study in the Journal of Neurology* demonstrating the effectiveness of a sequence that he developed in 2016: the 3D PSIR. This sequence detects three times more lesions in the spinal cord than traditional sequences.

Finally, Dr Augustin Lecler led a collaborative international group that revealed the first description of a new disease entity in the literature, the MVPLUS (Multinodular and Vacuolating Posterior Fossa Lesions of Unknown Significance).

This study was published in the American Journal of Neuroradiology in 2019**.

 * Mirafzal S, Goujon A, Deschamps R, Zuber K, Sadik JC, Gout O, Lecler A, Savatovsky J. 3D PSIR MRI at 3 Tesla improves detection of spinal cord lesions in multiple sclerosis. *J Neurol.* 2020 Feb;267(2):406-414.

** Lecler A, Bailleux J, Carsin B, Adle-Biassette H, Baloglu S, Bogen C, Bonneville F, Calvier E, Comby PO, Cottier JP, Cotton F, Deschamps R, Diard-Detoeuf C, Ducray F, Duron L, Drissi C, Elmaleh M, Farras J, Garcia JA, Gerardin E, Grand S, Jianu DC, Kremer S, Magne N, Mejdoubi M, Moulignier A, Ollivier M, Nagi S, Rodallec M, Sadik JC, Shor N, Tourdias T, Vandendries C, Broquet V, Savatovsky J; ENIGMA Investigation Group (European Interdisciplinary Group for MVNT Analysis). Multinodular and Vacuolating Posterior Fossa Lesions of Unknown Significance. *AJNR Am J Neuroradiol.* 2019 Oct;40(10):1689-1694



Deputy department head - Medical Imaging Unit

Dr Julien Savatovsky

KEY FIGURES

20 research protocols initiated by the Rothschild Foundation Hospital

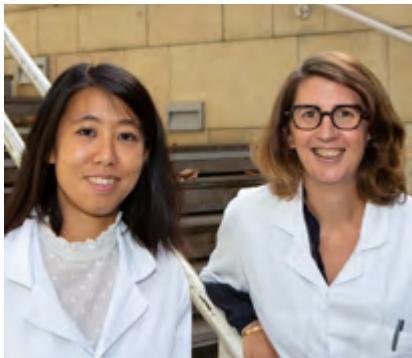
13 industrial or external hospital protocols that conduct their MRIs at the Rothschild Foundation Hospital

50 MRIs per month on average as part of a research protocol



The pharmacy

A close collaboration with health care units



Department head
Dr Chloé Dupont

Deputy department head
Dr Eliane Orng

The Sterile Production of Pharmaceuticals for Internal Use Unit (PUI) has two objectives: (1) providing medications and sterile medical devices to health care units and operating rooms; (2) contributing to their proper and safe use. PUI preparations include injectables and eye drops. **This pharmaceutical activity requires authorization by the ARS, as does the sterile preparation of experimental medications.**

The production unit has prepared Avastin syringes as part of a Temporary Use Recommendation (RTU) for treatment of dry AMD and cytotoxic drugs (Cyclophosphamide, Melphalan, Mitomycine, etc.), which require heightened security of the pharmaceutical circuit, since 2017.

The hospital's Reassignment Unit also provides fortified antibiotic eye drops to patients that are prepared by the PUI as soon as the patient leaves consultation or is discharged. In addition to these projects, the Sterile Production Unit received authorization from the ARS for sterile preparation of medications for clinical trials.

This unit is responsible for all sterilization that occurs at the hospital.

KEY FIGURES Preparations made in 1 year

1,304 syringes
of Avastin®

930 Gentamicin®
eye drops 15 mg/ml

998 Ceftazidime®
eye drops 20 mg/ml

60 syringes
of Melphalan®

1,044 Vancomycin®
eye drops 50 mg/ml

209 medications
dispensed for clinical trials



Rothschild Medical Academy: passing on knowledge





University education in partnership with the University of Paris

The Rothschild Foundation Hospital signed an agreement with the University of Paris through which it can host hospital-university practitioners and medical school students. The **hospital helps train many external and internal students of medicine and surgery** (in 2019, we hosted 92 internal students and 24 external students). Rothschild Foundation Hospital is also a member of the only hospital-university department recognized nationally for ophthalmology.



UNIVERSITY PROGRAM

In September 2020, Dr Augustin Leclerc was appointed MCU-PH of the Paris Center University of Medicine at the Rothschild Foundation Hospital. Dr Leclerc is a radiologist specializing in eye imaging. Through the *Edmond de Rothschild Fellowship Program*, he studied abroad at Stanford University.

Rothschild Medical Academy : a catalogue of online training programs



Rothschild
Medical
Academy

Because learning is a lifelong endeavor, Rothschild Foundation Hospital provides a Learning Management System (LMS) e-learning platform in addition to its in-person classes.

This online platform is based on neurocognitive learning processes. **The e-learning modules cater to different styles of learning:** videos, immersive experiences, software simulations, interactive exercises, and more.

THE ADVANTAGES OF ROTHSCHILD MEDICAL ACADEMY

- **Learn anywhere**, any time (24/7)
- **Quality training programs** taught by the hospital's experts
- **Individual** and **independent** learning
- **Cross-curricular skills** through discussions with other students and experts
- **Regular updates** in innovative formats



Rothschild Foundation Hospital publishes at a high level. A selection of articles from the 288 published in 2019

LIVER TRANSPLANTATION AS A RESCUE THERAPY FOR SEVERE NEUROLOGIC FORMS OF WILSON DISEASE

Aurélia Poujois, Rodolphe Sobesky, Wassilios G. Meissner, Anne-Sophie Brunet, Emmanuel Broussolle, Chloé Laurencin, Laurence Lion-François, Olivier Guillaud, Alain Lachaux, François Maillot, Jérémie Belin, Ephrem Salamé, Claire Vanlemmens, Bruno Heyd, Céline Bellesme, Dalila Habes, Christophe Bureau, Fabienne Ory-Magne, Pascal Chaine, Jean-Marc Trocello, Daniel Cherqui, Didier Samuel, Victor de Ledinghen, Jean-Charles Duclos-Vallée, France Woimant

Liver transplantation as a rescue therapy for severe neurologic forms of Wilson disease. Neurology. 2020 May 26;94(21):e2189-e2202.

Neurology Journals

This national study described the successes and limitations of liver

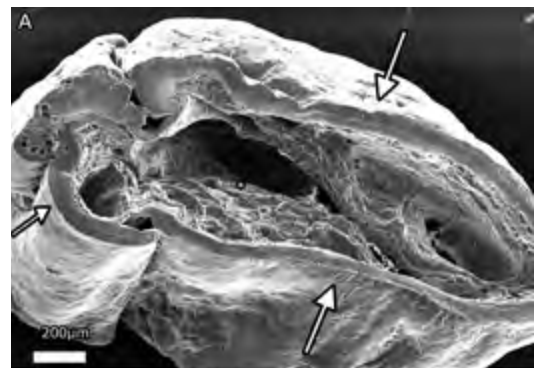
transplant in a cohort of 18 patients suffering from a very severe neurological form of Wilson's disease that made them totally dependent. Each of these patients received a liver transplant. The study's authors described a 72.2% survival rate at 5 years. The deaths, all related to severe sepsis, mostly happened during the first year. At the first follow-up appointment, of the 14 living patients, nearly 80% of them reported significant improvement of their clinical situation.

ACUTE ISCHEMIC STROKE THROMBI HAVE AN OUTER SHELL THAT IMPAIRS FIBRINOLYSIS

Lucas Di Meglio, Jean-Philippe Desilles, Véronique Ollivier, Mialitiana Solo Nomenjanahary, Sara Di Meglio, Catherine Deschildre, Stéphane Loyau, Jean-Marc Olivot, Raphaël Blanc, Michel Piotin, Marie-Christine Bouton, Jean-Baptiste Michel, Martine Jandrot-Perrus, Benoît Ho-Tin-Noé, Mikael Mazighi

Acute ischemic stroke thrombi have an outer shell that impairs fibrinolysis. Neurology. 2019 Oct 29;93(18):e1686-e1698.

Ischemic strokes are caused when an artery in the brain is blocked by a clot. The medication currently injected to break up these clots is ineffective in more than one in two cases. During this study conducted at the Rothschild Foundation Hospital, the team analyzed a large number of clots that were collected after brain thrombectomy. This research demonstrated the very specific structure of these clots in 8 out of 10 cases for the first time. The



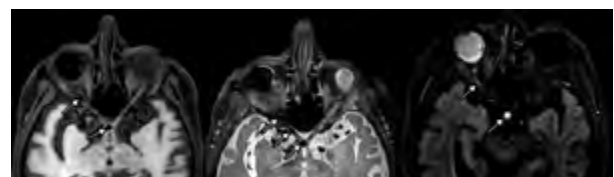
clots are composed of a brittle center surrounded by a dense shell that is resistant to medication. This discovery paves the way for new therapeutic approaches to improve ischemic stroke medications by specifically targeting this shell to destroy it.

RETROLAMINAR AND CHIASMAL SILICONE OIL MIGRATION

Guillaume Poillon, Fouzia Fela, Augustin Lecler

RETROLAMINAR AND CHIASMAL SILICONE OIL MIGRATION. Ophthalmology. 2019 Sep;126(9):1305.

This article describes a rare complication of intraocular tamponade with silicone oil, a technique used to treat retinal detachment. For patients who received this treatment, high-resolution MRI can non-invasively detect silicone migration along the anterior visual pathways



(optic nerve and chiasma). Definitive diagnosis is made possible by specific use of optimized sequences (called "silicone only" that delete the water and fat signal together).



Fellowship and Scholarship, educating new talent



This program is supported by the Edmond de Rothschild Foundations and is conducted in partnership with the University of Paris. It is designed to support excellence in education and international exchange programs for young doctors (under 40 years of age) that are assigned hospital-university positions at the Rothschild Foundation Hospital.

2019 WINNERS



**Dr Jean-Philippe DESILLES /
Fellowship Program**

“My research pertains to the biology of thrombotic and inflammatory disorders. I explore the cellular and molecular

mechanisms involved in the harmful effects of polymorphonuclear neutrophils during an ischemic stroke in order to identify new therapeutic targets.”



**Dr Jérôme LAMBERT /
Fellowship Program**

“During my year in Fribourg, I studied new statistical models applied to ophthalmologic data in order to better

identify the prognostic factors of age-related macular degeneration (AMD) and the ophthalmologic effects of multiple sclerosis (MS).”



**Dr Agathe VRILLON /
Scholarship Program**

“My translational research project focuses on neurodegenerative diseases, particularly Alzheimer’s disease,

in order to develop biological doses and identify new neurological biomarkers that show loss of connection between neurons (synapses), followed by neuron death. The goal is to assess a new treatment that is currently in the trial phase which may protect patients’ synapses and neurons.”



**Dr Raphaël LEJOYEUX /
Scholarship Program**

“My project develops etiological research on adaptive optics for central serous chorioretinopathy (CSCR) using very

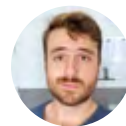
high-resolution interferometric imaging, which provides better precision for identifying lesions, and facilitates Deep Learning by specifying the anatomical and nosological characteristics of OCT images.”

2020 WINNERS / SCHOLARSHIP PROGRAM



Dr Pierre-Henry GABRIELLE

“This scholarship allowed me to join the international retinal disease team, learn skills related to data science and big data and conduct several research projects.”



Dr Alexandre HERAUD

“My project is based on functional MRI for vision in order to study the reorganization of visual pathways in people with retinal implants.”



Dr Nicolas AREJ

“My project assesses the blade used for endoscopic vitreo-retinal surgery in treatment of patients with complicated retinal detachment.”



Dr Etienne BOULANGER

“I am fascinated by the retina and would like to spend a year researching and developing an innovative retinal imaging technique at Dr Sahel’s lab in the United States.”



Expertise: research
in rare and complex diseases





Resources for **rare diseases** at Rothschild Foundation Hospital



With 14 rare disease centers, Rothschild Foundation Hospital is committed to serving patients often suffering from incurable diseases or with a misdiagnosis. The increased visibility for rare diseases provided by our centers is part of our strategy targeting hyper-specialized niches and hospital-university collaborations.

European Reference Network (ERN)

- **PAED CAN** specializing in rare pediatric cancers, in collaboration with the Institut Curie (2017)
- **METABERN**, Wilson's disease and other rare copper-related diseases (current)
- **EYE**, rare ophthalmic diseases (current)
- **EPICARE**, EpiRaReS consortium Dr Auvin: Rothschild Foundation Hospital, Robert Debré Hospital, Pitié-Salpêtrière Hospital

Rare Disease Reference Center (coordinating site)

- Wilson's disease and other rare copper-related diseases

Rare Disease Reference Centers (constitutive sites and associated site)

- Rare neuroretina diseases
- Cerebral and spinal arteriovenous malformations
- Rare epilepsy

Rare Disease Competence Centers

- Rare conditions in ophthalmological genetics
- Rare diseases in pediatric ophthalmology
- Keratoconus
- Neurogenetic diseases and abnormal movements
- Rare diseases with psychiatric expression
- Rare systemic autoimmune diseases

CREATION OF NEURO MAV FRANCE



Rothschild Foundation Hospital and Foch Hospital, through the Interventional Neuroradiology Unit's constitutive Rare Disease Reference Centers (CRMR), helped found a non-profit dedicated to patients with a cerebral or spinal arteriovenous malformation (AVM) and their families.

An AVM is a vascular malformation between the arteries and veins of the brain or spinal column that acts like a short-circuit, exposing the person to intracerebral or intraspinal bleeding. This non-profit is comprised exclusively of patients and their families, all of whom volunteer their time.

The non-profit helps people face their disease and advocates for these rare diseases with medical professionals and the general public. In time, its goal is to support research.



Wilson's disease and other rare copper-related diseases: a reference center at Rothschild Foundation Hospital

On September 2, 2019, Rothschild Foundation Hospital became the coordinating Rare Disease Reference Center (CRMR) for Wilson's disease and other rare copper-related diseases. The center had previously been located at Lariboisière Hospital (AP-HP). Coordinated by Dr Aurélia Poujois, the CRMR Wilson brings together pluridisciplinary and pluriprofessional teams in order to provide optimal treatment to children and adults suffering from Wilson's disease.

In France, Wilson's disease affects approximately 1,000 patients/year and 1.5 people/100,000. A French genetics study recently published by the CRMR Wilson showed a prevalence rate of 26 people/100,000, revealing the lack of diagnosis for mild cases or the existence of modifying genes that limit the disease's expression. The CRMR Wilson, part of the G2M network, includes a coordinating site in Paris at the Rothschild Foundation Hospital, a constitutive site at the Femme-Mère-Enfant Hospital in Lyon and 8 competency centers: Necker-Enfants malades Hospital and the Paris-Sud Hospital Group Paul-Brousse/Kremlin-Bicêtre in Paris, La Timone Hospital in Marseille, Jean Minjot de Besançon Hospital, the

CHU de Bordeaux, the CHU de Lille, the CHU de Rennes and the CHU de Toulouse.

At each site, a pluridisciplinary team of pediatric doctors, hepatologists and neurologists treats patients suffering from Wilson's disease and sets up care with non-hospital physicians. The coordinating and constitutive sites work with toxicology and genetics labs.



Docteur Aurélia POUJOIS,
National Coordinator
of the CRMR Wilson



The coordinating site of the Reference Center for Wilson's disease and other rare copper-related diseases (CRMR Wilson), DGOS-certified since 2005, was transferred to Rothschild Foundation Hospital on September 2, 2019. The center was transferred successfully and continues to coordinate the national network, provide pluriprofessional resources, pluridisciplinary expertise, education, research and epidemiological surveillance with efficiency, while making patients a top priority."



Neuropsychology, Neurovision, Neurocognition Institute (I3N)



Screening and rehabilitation for neurovisual disorders in children and adults

Part of the Rothschild Foundation Hospital and associated with the psychology of perception lab UMR 8158, the Neuropsychology, Neurovision and Neurocognition Institute (I3N) studies the cognitive mechanisms and bases for visual perception in the brain, orientation of attention and visual and spatial representation in children (as young as 1 month old) and adults, both healthy and with neurological and/or psychiatric disorders. Brain plasticity after a lesion of the visual system is also studied in partnership with the psychology and neurocognition lab (CNRS, UMR 5105) and the Haddassah Hospital (Jerusalem, Israel).

As a competency center for rare genetic diseases with psychiatric expression, the I3N deals with several types of rare diseases. From the more well known, like Prader-Willi syndrome or 22q11 or 22q13 deletion syndrome, to genetic diseases with extremely rare mutations for which there are only ten or so cases described in the literature, this competency center is part of the Défi-science: rare genetic diseases network.

The disorders most frequently treated by the I3N are language, memory and reasoning, spatial organization or movement, attention, and visual recognition or function disorders.

The pluridisciplinary I3N team, directed by the CNRS Director of Research Sylvie Chokron, is comprised of 4 doctors (general practitioner, neurologist, pediatric neurologist and child psychiatrist), 9 neuropsychologists, 3 speech therapists and 1 psychologist.

This team works in collaboration with the neurology, neurosurgery, neuroimaging, interventional neuroradiology, ophthalmology, pediatric ophthalmology and neuro-ophthalmology units. It brings together scientists and clinicians in order to understand, prevent, diagnose and restore cognitive function disorders in children and adults.

The I3N is also set up to bridge the gap between treatment and research, offering patients the opportunity to participate in research and benefit from new clinical applications. Sylvie Chokron is a part of the Perception, Action, Cognition team at the Integrative Neuroscience & Cognition Center (INCC) at the University of Paris.



Sylvie CHOKRON,
Director of the I3N-
Adolphe de Rothschild
Foundation Hospital



We designed this new institute first and foremost for our patients, in order to provide them with complete diagnosis and treatment no matter their age or condition in an environment adapted to their needs. Our goal is for the institute to provide individualized care for each patient and specific, expert treatment in collaboration with their various care providers."

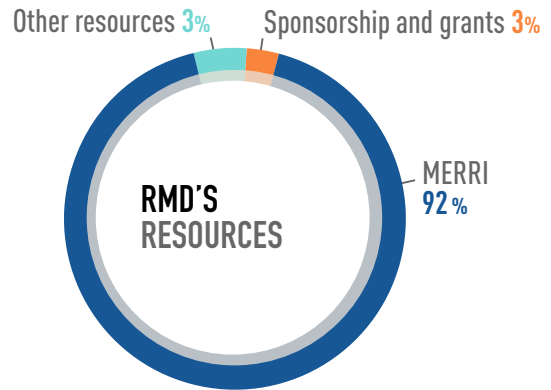
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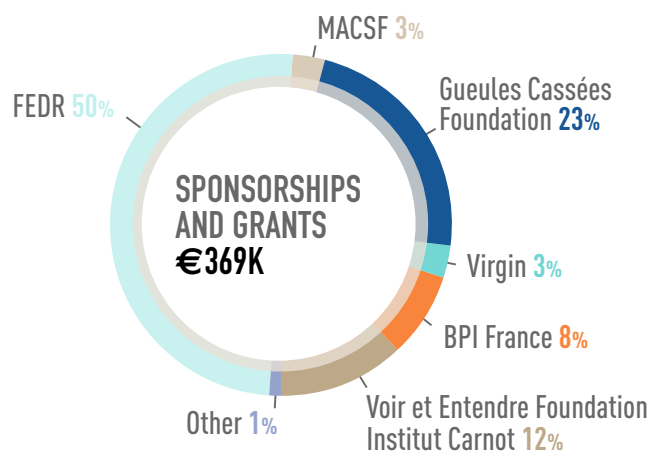
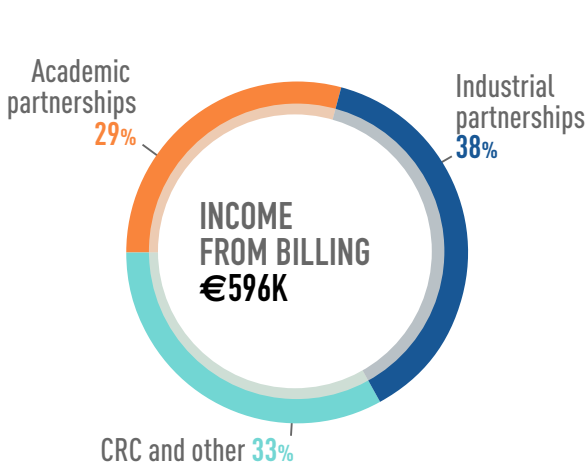
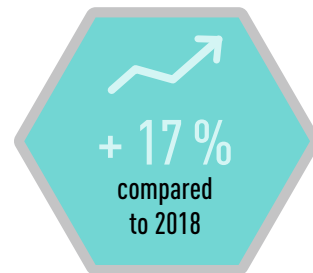
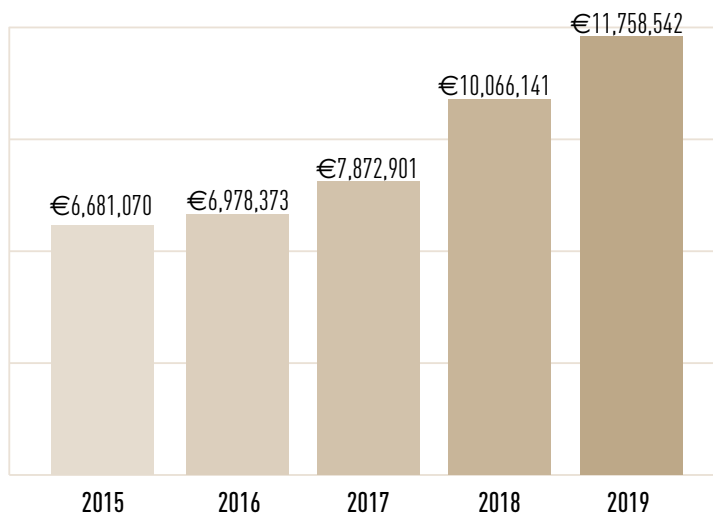


Resources

The **MERRI (Education, Research, Leaders, Innovation)** fund includes financing for publications (29%), clinical trials (38%), laboratory innovations (10%), the clinical research center (DRCI) (95), education (5%), the rare diseases center (4%) as well as regional and national research programs (4%) and other miscellaneous funds (1%).



GROWTH OF MERRI FUNDING OVER THE PAST 5 YEARS





Our generous sponsors and partners make it possible for the hospital to innovate

The Adolphe de Rothschild Foundation, recognized for public interest since 1905, may receive donations, endowments and legacies. The generosity of our donors and sponsors is a true catalyst for scientific discoveries and a major factor in converting research into tangible progress for patients.

Music in Mind, does live music reduce anxiety in stroke victims?

This original and innovative research project is supported by the **Edmond de Rothschild Foundations**, conducted by nurses and coordinated by Perrine Boursin. The *Music in Mind* project focuses on treating anxiety, stress and sleep in patients in the acute and sub-acute stages of a stroke through non-pharmacological approaches such as musical performance. In one year, nearly 150 patients hospitalized for several days because of the severity of their strokes and handicaps had a



musician perform at their bedside in the early evening. The project measured and studied the impact of live music on anxiety and sleep in these patients. •

Transparent Skin research program for repairing and restoring the cornea



This project, directed by Dr Éric Gabison and supported by the **Gueules Cassées Foundation**, uses cellular and gene therapy to obtain corneal epithelial and stromal cells from autologous skin and bone marrow cells. The goal of this research is to identify and develop new treatments to help stem cells survive and multiply. This will pave the way for new methods to repair and regenerate the cornea in patients with a deficit in epithelial stem cells in the cornea or corneal stroma opacity. •

How does learning philanthropy at a young age affect children?



The **Philanthropy School** is a unique experiment developed by the **Edmond de Rothschild Foundations and the Fondation de France** starting in 2011.

This school teaches children aged 8-11 to cultivate their capacity for empathy by encouraging them to volunteer for causes that benefit the common good. After nearly 10 years of experiments, Sylvie Chokron (Neuropsychology, Neurovision and Neurocognition Institute/CNRS) is evaluating the effects of this approach. Her project, supported by the **Adolphe de Rothschild Memorial**, is to observe cognitive, personal, behavioral and socio-emotional changes in children who have participated in the program. •



AI Innovation Experimental Hospital 2020-2023 fosters preventive medicine

This program was made possible thanks to a generous donation by the **New York Edmond de Rothschild Foundations**. It explores new treatments using artificial intelligence and big data. This sponsorship will allow us to build and develop databases by creating a Data Science Unit and a Medical Data Lake and recruit experts in these fields in order to accelerate conversion of innovations into tangible progress for patients. •



Education on neurovascular disease through e-learning

This e-learning program, ran by the Center for Neurovascular Disease Research and Education, seeks to monitor patients post-stroke using connected glasses. This e-learning class teaches clinicians how to use the standardized National Institute of Health Stroke Scale

(NIHSS), which describes and quantifies neurovascular deficit and assesses risk of death with a score that requires an in-depth clinical exam. **The MASCF Foundation** has joined this project by financing the connected glasses. •

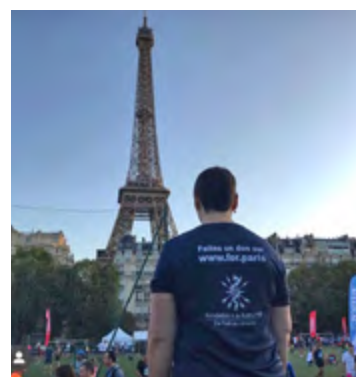
On-call stroke research, a first in France!



ACTICOR BIOTECH provided support for a 24/7 on-call research team for neurovascular emergencies. This is the first on-call team of its kind in France, comprised of clinical research technicians and intensive care nurses. It allows patients to be more quickly included in clinical and translational research protocols during the acute stage of stroke. •

MARETINE measures the effects of marathons on the retina

Thanks to a donation from **Entrepreneur and Go**, the Clinical Research Platform directed by Viven Vasseur organized a research project with approximately 30 volunteers who ran the Paris Marathon. They each were given a retinal exam



before the run and right after the finish line. More generally, this project investigates the effects of intense, prolonged effort on sight. The results should provide the basis for justified prevention recommendations for athletes. •



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