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With support and funding from the *Fondation Pour l'Audition* and in partnership with Inserm, Institut Pasteur has endowed itself with a basic and medical research center, the Hearing Institute.





A WORD FROM THE DIRECTOR OF THE HEARING INSTITUTE

he year 2022, which began with my appointment as Head of the Hearing Institute (IdA) and successor to Professor Christine Petit, has been a rich one, with many significant events for the structuring of the field in France. Above all, it has been marked by the mobilization of all our forces around the re-Connect University Hospital Institute (IHU) project. This ambitious project, part of the France 2030 Plan supported by the IdA, also brings together Assistance Publique-Hôpitaux de Paris (AP-HP), Université Paris Cité, Inserm, Fondation Pour l'Audition and Institut Pasteur. It was submitted on November 7, 2022. Following on from the creation of the Hearing Institute, this project constitutes a major step towards creating France's first international center of excellence dedicated to hearing and the brain. The re-Connect project is based on the fundamental discoveries made in this field over the last two decades. It brings together, in a unique way, all the players involved in hearing health: patient associations, researchers, clinicians from the Hearing Institute and Lariboisière hospital, our partners at the Necker and Pitié-Salpêtrière hospitals, healthcare professionals and manufacturers in the sector. By placing the patient at the heart of the project, the future IHU aims to intensify innovation and to accelerate the transfer of scientific



advances to patients. Over the next decade, this project will enable us to move from compensatory medicine to reparative medicine for hearing disorders.

Let us not forget that this issue is at the heart of our health and that of future generations: hearing loss is now a worldwide scourge, accelerated by the aging of the population and increasingly noisy environments. What's more, the link established between hearing loss and cognitive deficits now justifies the integration of the fields of neuroscience and neurology with that of hearing, to generate a strategic global ear-brain view. We are committed to implementing this vision in the field, notably through the links we are forging with our institutional neighbors in France, but also in Europe, including the UCL Ear Institute in London.

"By bringing all of the actors in auditory health together for the first time, the university-hospital institute re-Connect aims to accelerate the transition from compensatory to reparatory medicine in the field of hearing."

Finally, this year also saw the opening of the CeRIAH (Centre for Research and Innovation in Human Audiology) and the installation of its team in new premises on the historic Institut Pasteur campus in Paris. This creates an ideal environment for synergies between projects designed to generate rapid improvements in the everyday lives of people with deafness of hearing impairment. And let's not forget the scientific teams, who have made great strides forward. I am thinking, in particular, of the breakthroughs we have achieved, a few examples of which are described on these pages. This report provides us with an opportunity to acknowledge the considerable investment made by everyone involved in the project, alongside patient associations and our partners, who, through research extending from the most fundamental to the clinical, embody this intention to improve our understanding of hearing, to accelerate the discovery and implementation of new treatments.

PROFESSOR ANNE-LISE GIRAUD

A ONE-OF-A-KIND CENTER FOR RESEARCH, MEDICAL INNOVATION AND THE DISSEMINATION OF KNOWLEDGE

The Hearing Institute was conceived as an accelerator of progress at the service of patients and a response to the major public health issues in this domain.

3 priority objectives guide the ambitions of the Hearing Institute

Advancing basic research on the auditory system

The researchers of the Hearing Institute are working to develop an understanding of the principles and mechanisms governing the development and functioning of the auditory system. This system is studied from the periphery to the cortical centers.

Developing new translational approaches

The Hearing Institute brings together scientists, physicians, and professionals of auditory health. This continuum aims to bring innovation to the patient and in doing so contribute to the emergence of a national industrial sector in the domain of hearing.

Working towards the dissemination of the knowledge on hearing problems

Advances are shared with the international scientific community, actors in auditory health, people with auditory disorders, and the associations that represent them. The Hearing Institute also aims at reaching out to the public about the prevention of hearing problems.

To achieve these objectives, the Hearing Institute gathers a range of key skills covering the exploration of mechanisms from the molecular, cellular, and physiological levels thanks to organoids and animal models (mice and gerbils), to the cognitive level by implementing research in humans.

These key objectives can be broken down into four overall scientific objectives

To elucidate

the modes of processing sound information from the periphery to the auditory centers.

To study

normal and pathological auditory cognition.

To promote

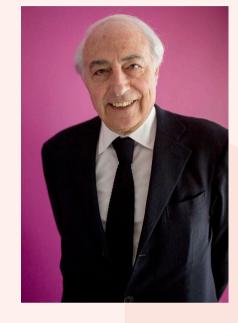
a base of scientific and clinical knowledge and expertise.

To develop

new therapeutic tools.

A WORD FROM THE FOUNDERS

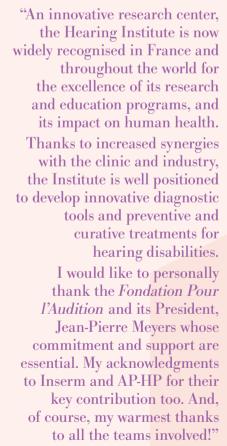
Created in 2019 at the initiative of *the Fondation Pour l'Audition*, the Institut Pasteur and Inserm, the Hearing Institute is the first center entirely dedicated to hearing in France.



"The Hearing Institute, an Institut Pasteur center, brings hope to people affected by hearing loss.

As part of the Alliance Pour l'Audition (the Hearing Alliance). which is open to progress in fundamental, clinical, and participatory research, it opens up new perspectives for understanding hearing problems and providing long-awaited solutions. Science will undoubtedly lead us to prodigious discoveries in the years to come. We hope to share them with you. A big thank you to the teams of Institut Pasteur and the Hearing Institute for the tremendous vitality they display every day."

JEAN-PIERRE MEYERS
PRESIDENT OF
THE FONDATION POUR L'AUDITION







THE HEARING INSTITUTE BUILDING

The building sector is one of the leading emitters of greenhouse gases in France, and the technical management of tertiary buildings is an essential tool for improving energy performance once the building comes into operation. Right from the start, every effort has been made to rationalize the energy management of the Hearing Institute.



The building has been designed to decrease all types of energy consumption: air treatment, heating, lighting and energy recovery.



Working comfort is enhanced by the acoustic control of the premises.



Comfortable listening areas for hearing-impaired people fitted with hearing aids.





Greenhouse Gas Emissions Assessment: a pilot stage for the Hearing Institute

The Hearing Institute is the first Institut Pasteur center for which "indirect emissions" of greenhouse gases have been assessed, including those associated with the transport of goods and business travel. This assessment is now mandatory and must be performed every four years (article L. 229-25 of the Environmental Code and decree n°2022-982 of July 1, 2022).

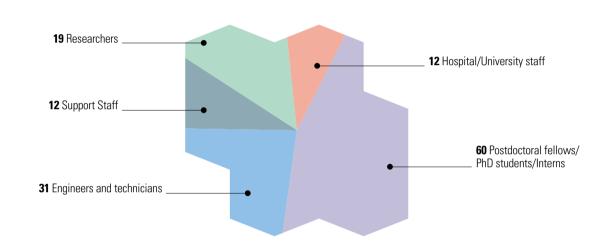
This pilot phase (September to October 2022) has enabled us to perfect the method for collecting and analyzing this environmental data. The data collected are currently being analyzed, and the results will guide targeted actions to decrease the environmental impact of the Institute's activities.

As part of its general continuous improvement approach, Institut Pasteur will now be able to collect and analyze such data for all its sites.

HUMAN RESOURCES

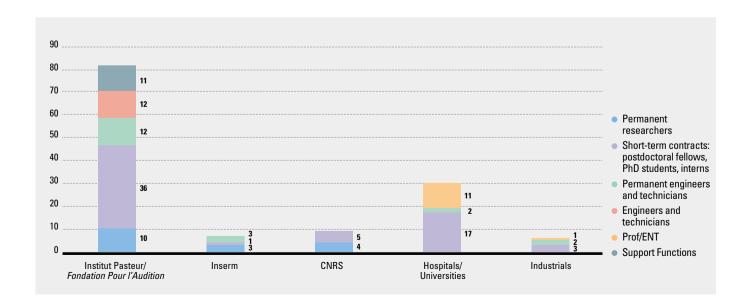


DISTRIBUTION OF THE STAFF OF THE HEARING INSTITUTE BY TYPE OF POST ON DECEMBER 31, 2022



AN INSTITUT PASTEUR CENTER SUPPORTED BY THE FONDATION POUR L'AUDITION

NUMEROUS PARTNERS – NUMBERS ON DECEMBER 31, 2022





NOMINATION TO
THE FRENCH ACADEMY
OF MEDICINE

47
PUBLICATIONS

3
GRANTS OBTAINED

SCIENTIFIC-TENURE POSITIONS CREATED



Increase the number of avenues of research, interactions between disciplines, skills and visions, and provide cutting-edge technological platforms

INTEGRATED RESEARCH

THE HEARING INSTITUTE CAMPUS Molecular targets Specification of auditory inputs Central impact GENES, MECHANISMS AND THERAPIES and peripheral damage Cochlear Precision medicine Technologies Pathophysiology Relating development and therapies for hearing and therapies Neuronal aenes A. EL AMRAOUI R. ETOURNAY C. PETIT S. SAFIEDDINE and Y. NGUYEN to human codes and calculations auditory phenotype for perception Neutral coding Intracellular Auditory cognition Plasticity of and Neuroengineering and communication the auditory circuits communication of speed functions N. MICHALSKI AL GIRALID and S BOLITON MEASUREMENTS AND MODELS SOUND CIRCUITS AND PROCESSING CeRIAH Dynamics of Neural the auditory system coding P. AVAN and H. THAI-VAN B. BATHELLIER Definition of the salient characteristics of perception Other Department Technological **INSTITUT PASTEUR CAMPUS**

15[™] ARRONDISSEMENT

of Neurosciences

departments

HIGHLIGHTS OF 2022



Neural coding in the auditory system team

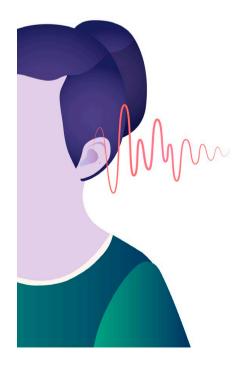
JÉRÉMIE BARRA

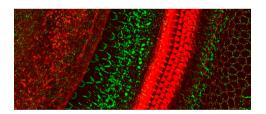
The objective of the CNSA team is to understand how the brain perceives complex sounds. The researchers control signals sent by the cochlea to the brain by stimulating sensory cells with light. The CORTIORGAN project funded by the ANR will focus on the design and testing of an optical cochlear implant with dimensions compatible with the mouse cochlea. This project will be performed in collaboration with experts in microfabrication and nanoelectronics (GeorgiaTech Europe in Metz and the Center for nanosciences and nanotechnologies in Saclay). By building causal links between sensory perception and behavior, researchers will be able to shed light on the information necessary and sufficient for sound identification.

Clinical and translational exploration of sensorineural hearing loss team

DIDIER DULON AND HUNG THAI-VAN

During the first year of the BioImpress project (on a medical device for the targeted contactless application of a therapeutic agent on the round window of the cochlea), a prototype adaptable LAB (laser-assisted bioprinting) device was developed. The very high resolution (microscale) of this device and the contactless printing approach are considered promising for viral gene therapy delivery to the inner ear.





Fundamental auditory mechanisms and precision medicine team

CHRISTINE PETIT

The team is working on the prevention and treatment of DFNB1 deafness, the most common severe-to-profound congenital form of sensorineural deafness worldwide. It is caused by variants of the *GJB2* gene, which has also been implicated in presbycusis. In collaboration with Sensorion, significant progress has been made towards identifying an effective therapeutic candidate.

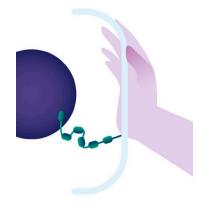
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platforms

Technologies & gene therapy for deafness team

SAAÏD SAFIEDDINE AND YANN NGUYEN

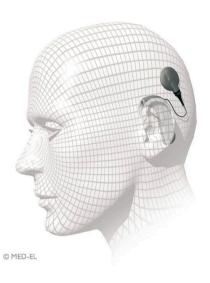
The team has provided proof-of-concept, in preclinical models of human deafness, that gene therapy to restore expression of the otoferlin gene not only prevents DFNB9-type deafness, but also restores hearing. These very encouraging results have paved the way for the first clinical trial, planned as part of the AUDINNOVE university hospital research program.



Auditory system dynamics & multisensory processing team

BRICE BATHELLIER

An article was published in the journal *Nature Neuroscience*, in September, and was featured on the cover. This study, conducted in collaboration with Alain Destexhe's team at the Paris-Saclay Institute of Neuroscience, revealed the existence of a new neuronal mechanism accompanying the transition from conscious sound perception to the unconscious state under anesthesia.

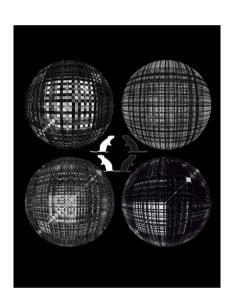


Auditory cognition & communication team

LUC ARNAL AND DIANE LAZARD

A study of over 2,200 people with cochlear implants has delivered its conclusions on the key role of brain plasticity in the performance of auditory rehabilitation through cochlear implantation.

The publication, written by Diane Lazard in collaboration with Keith Doelling and Luc Arnal, has been accepted for publication in the journal *Trends in Hearing* in 2023.





Neural coding and neuroengineering of speech functions team

ANNE-LISE GIRAUD AND SOPHIE BOUTON

Anne-Lise Giraud has been the Director of the Hearing Institute since January 2022. Her team, recently expanded by the addition of eight new recruits, is exploring the neural mechanisms behind the implementation of the language processing network in the human brain and its dysfunctions in disorders affecting hearing and language (aphasia, dyslexia, stuttering, etc.). A national study on dyslexia (RnDys) has been launched, to evaluate rhythmic auditory training for improving reading performance in dyslexic children.



The center for research and innovation in human audiology (CeRIAH)

PAUL AVAN AND HUNG THAI-VAN

The CeRIAH moved into its premises on the Institut Pasteur campus in the 15th arrondissement of Paris on December 20, 2022, and is now working on its projects. The AUDIOGENAGE study aims to improve our understanding of the mechanisms of presbycusis. The REFINED project, performed in collaboration with the CEA and LORIA*, studies the spectrum of auditory neuropathy disorders, with the aim of developing intelligent hearing aids for affected individuals.

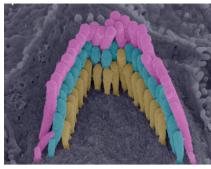
* The Lorraine laboratory for computing research and its applications.



Plasticity of central auditory circuits team

NICOLAS MICHALSKI AND BORIS GOURÉVITCH

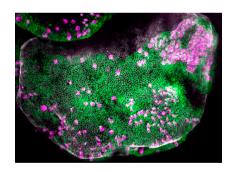
A consortium has been formed with Luc Arnal at the Hearing Institute and Fabrice de Chaumont at Institut Pasteur (Human Genetics and Cognitive Functions team) to investigate why individuals with autism are frequently prone to hyperacusis or auditory hypersensitivity. These studies could improve our understanding of the mechanisms of brain-circuit hyperexcitability in individuals with autism.



Progressive sensory disorders, pathology and therapies team

AZIZ EL AMRAOUI

The European Nanoear (EuroNanoMed3 2022-2024) project will test a nanocarrier approach for preventing or treating neurodegeneration in the ear. With the *Voir et Entendre* foundation, the team is also participating in the TreatUSH1B project (supported by the Fighting Blindness foundation, 2022-2027), which aims to develop targeted therapies for Usher syndrome type IB.



Cochlear development team

RAPHAËL ETOURNAY

The team has developed a computer program, Zellige, for the automatic extraction of complex biological surface from three-dimensional microscopy data. This high-performance, open-access program can be used to visualize the cellular dynamics underlying the formation of the auditory epithelium during development.

NATIONAL AND INTERNATIONAL **COLLABORATIONS**



The Hearing Institute & Sensorion

The Hearing Institute and Sensorion, a clinical-stage biotechnology company specializing in inner-ear gene therapies, have signed a framework agreement for a research partnership granting Sensorion an option on exclusive licences to develop and market candidate products for gene therapy. As part of this collaboration, two programs (OTOF-GT and GJB2-GT) have been developed for the treatment of hearing loss due to mutations of the otoferlin and GJB2 genes, respectively. This partnership will make it possible to transform scientific progress into innovations providing long-term solutions for people with genetic hearing loss disorders, by improving patient care trajectories, developing curative treatments for hearing disorders and creating new diagnostic tools.

In France

BESANCON

Besançon University Hospital

BORDEAUX

Bordeaux University – Bordeaux University Hospital

BREST

Brest University Hospital

Caen Normandie University

CLERMONT-FERRAND Clermont-Auvergne University

GRENOBLE Grenoble-Alpes University

LILLE

Lille University Hospital – INRIA Lille – Lille University

LYON

Claude Bernard Lyon 1 University – Lyon University Hospital

MARSEILLE

AP-HM – Aix-Marseille University

METZ

Georgia Tech Europe

MONTPELLIER

INM - LIRMM - Montpellier University Hospital

NICE

Côte d'Azur University – Nice University Hospital

INRIA – Institut national de recherche et de sécurité

ENS – ICM – Université Paris Cité – Vision Institute – Paris-Saclay University - Necker Hospital - MNHN - Service de santé des armées – Institut de recherche biomédicale des armées - Ircam -AP-HP - Paris Descartes University - CNA - Collège de France - CNRS - Inserm -Institut Cochin - PSL University - ESPCI

SAINT-ÉTIENNE

Saint-Étienne University Hospital

TOULOUSE

MEDES - Toulouse University Hospital

TOURS

Tours University Hospital

VERSAILLES

Versailles Hospital



In the world

Switzerland – United Kingdom – Belgium – Germany - Spain - Romania - Malta -Greece - Hungary - Italy - Slovenia -

SOUTH AMERICA

Argentina

Tunisia – Algeria – Morocco – Mauritania

China - South Korea

NORTH AMERICA United States - Canada (Quebec)



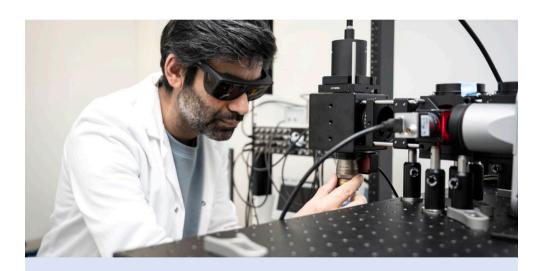
Hearing with light

The Hearlight (European Innovation Council Pathfinder) consortium was created in 2021. It brings together three Hearing Institute teams, laboratories from the University of Basel, the University of Strathclyde, the Norwegian University of Science and Technology, Novagan, a Lausanne-based company specializing in semiconductors, and a group from the École des Mines in Saint-Étienne, to establish a technological basis for cortical implants for hearing rehabilitation.

In 2022, the group met at the Hearing Institute to present the results of its first year of work. Various advances have been made: the creation of a new model of sound encoding based on deep-learning networks, and a proof-of-concept for the use of this model to generate artificial perception in mice, together with a demonstration of the feasibility of chronic cochlear implantation in mice, which should facilitate comparisons of the implants, and new prototype optogenetic and electrical stimulators.

NEW EQUIPMENT AND STATE-OF-THE-ART DEVELOPMENTS

Work on the inner ear, the brain and their interrelationships requires cutting-edge equipment. Scientists at the Hearing Institute use, combine or develop technologies that facilitate the observation of hearing and improve our understanding of how hearing functions.



A made-to-measure microscope for observing living tissues in depth

With its expertise in optics, the imaging platform team at the Hearing Institute embarked on an ambitious project in 2022, with the aim of developing and constructing a versatile two-photon microscope. This adaptable optical system will meet the needs of Hearing Institute teams. It will be fully adjustable, combining three powerful techniques: two-photon imaging, photostimulation, and electrophysiology. It will be equipped with two laser outputs and will be able to generate arbitrary illumination for photosimulation. The microscope head will be rotatable, making it possible to adapt the setup to most *in vivo* imaging configurations.

This unique, innovative system will facilitate the deep visualization of living tissues and will therefore be of great value for studying and manipulating neural networks in the central auditory system, and for optical studies of cochlear organoids in three dimensions. The observation of thousands of neurons will shed light on the activity of neural networks and facilitate the design of stimulation patterns artificially reproducing the observed activity. All of this should help to identify the neuronal mechanisms of perception.

An integrated approach for detailed analysis of the early stages of inner ear development

The Cochlear Development team generates inner ear organoids as a model system for investigating the cellular and molecular mechanisms underlying the self-organization of sensory epithelia at critical stages of embryonic development. Several complementary approaches are used to study these models.

The culture medium is oxygenated by shaking on an orbital shaker, to improve the maturation of sensory cells within the organoids, which can then be systematically characterized with a view to developing future high-throughput molecular screening on a high-resolution imager. And finally Zellige, a computer program developed by the team (see page 11).

An ultra-fast camera for mapping the activation of auditory sensory cells

In the latest generation Kinetix camera, one of the fastest currently available, Jérémie Barral's team has acquired a tool of choice for getting right to the heart of the inner ear. They hope to visualize, at microscopic scale, the way in which sensory hair cells are activated by sound stimulation and transmit information about sound to the auditory neurons, which in turn transmit this information to the brain. The aim is to establish a spatial map of cochlear activation in response to sound.

Over and above its value for fundamental research, this project should make it possible to develop new stimulation strategies to increase the efficacy of currently available cochlear implants.





New technologies & services

In June 2022, the Hearing Institute Data Acquisition and Neural Signal Processing platform was created, with the objective of developing methods and tools providing solutions for interfacing, acquiring, and analyzing the multidimensional and multimodal neuronal data from both animals and humans generated by the research teams (calcium imaging, electrophysiology, behavior, neurophysiological and auditory signals).

The platform has begun providing services through the development of programming tools for: hardware control of custom-designed experimental setups (synchronization of neural recording systems with various behavioral devices, data collection, user interfaces), pipelines for data processing and preprocessing, algorithmic solutions for computing quantitative features, exploring, analyzing, and visualizing data. The platform is run by Clara Dussaux, an Inserm research engineer recruited in early 2022.

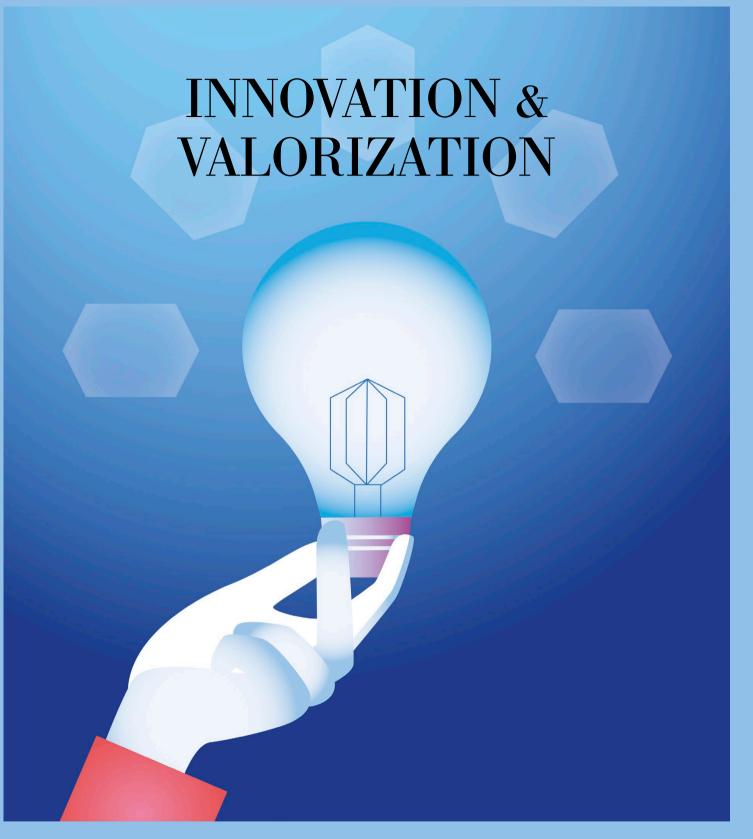
Recording the brain activity of dyslexic children to validate a method for improving reading

The NeuroSpeech team has begun collecting data for their national project, RnDys. The primary objective of this project is to determine whether rhythmic auditory training can improve the reading performance of dyslexic children. This study involves collaboration with speech therapists and two partner companies (iologo and GraphoGame) producing rehabilitation tools that will be tested in the project. Over a span of 22 weeks, the protocol aims to compare the efficacy of rhythmic auditory training with more traditional re-education methods in 160 dyslexic children aged 7 to 9 years. Electroencephalography (EEG) will be used to record brain activity at the Hearing Institute, and behavioral evaluations will take place in the consulting rooms of speech therapists. In preparation for the initial phase of the study, the team has acquired special equipment, including electroencephalographic headsets adapted for use by young participants. The ultimate goal is scientific validation of the efficacy of tools destined for use by speech therapists and the establishment of standardized practices.









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PRIVATE PARTNERS ONG

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ONGOING PATENTS

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PROJECTS UNDERWAY AT OR WITH THE CERIAH

10

NEW AUDIOLOGICAL TESTING ROOMS



Establish fruitful partnerships
with industry and with our partners
at the heart of the first center
for research on hearing

A NEW SPACE OF 500 SQUARE METERS FOR THE CeRIAH

Since December 2022, the CeRIAH has taken possession of its new premises in the 15th arrondissement of Paris, on the historical campus of the Institut Pasteur.

his new building is next to the CMIP (Medical Center of the Institut Pasteur) on the campus of the 15th district of Paris. It was designed by the CeRIAH team and equipped according to their needs. It provides them with the technical means and spaces necessary to host volunteers for current and future projects.

A technical and architectural feat, this building meets several constraints: finding sufficient space on an already very dense campus, while preserving green spaces, a building that is protected from vibrations and electromagnetic fields that are likely to disturb the measurements made by the researchers, and a building that is easy to access for the research project volunteers.

The infrastructure of this building allows to measure exhaustively the activity of the inner and middle ear. Five anechoic cabins, arranged in a star shape, totally isolated from external noise and electromagnetic waves, allow to perform all the tests necessary for the experiments.

Other rooms are dedicated to the measurement of reflexes related to balance, spatial location or the simulation of real-life conditions in a virtual reality room.

Within this new space, the CeRIAH will build new research protocols involving the human being allowing the acquisition of exhaustive data for the creation of a database as it exists



in many fields of medicine, as well as the manufacture of diagnostic devices and hearing aid prototypes. The CeRIAH is an essential link in the process of bringing together fundamental research and the clinic.



The CeRIAH's move into its new building is an essential and indispensable phase in its development.

Anne-Lise Giraud, director of the Hearing Institute





AT THE CeRIAH, A DOZEN RESEARCH PROJECTS INVOLVING VOLUNTEERS ARE ALREADY UNDERWAY

About a dozen clinical research projects are being prepared or are already underway. These projects include AUDIOGENAGE and REFINED, two projects particularly emblematic of these new research possibilities.

Unlocking the secrets of presbycusis with AUDIOGENAGE

The AUDIOGENAGE project began in the summer of 2022. It has two objectives: determining the genetic characteristics of the early aging of hearing abilities and identifying the audiological tests required for satisfactory screening for age-related hearing loss or presbycusis.

Appropriate tests are currently lacking. As a result, presbycusis is often detected late, delaying patient management and the fitting of hearing aids, with patients therefore suffering discomfort and even a loss of quality of life that could be avoided.

AUDIOGENAGE has a scheduled duration of four years and will include 700 volunteers. For this project, the CeRIAH is working in partnership with the University of Oldenburg and the Sensorion company.

Improving the capacity of hearing aids with REFINED

There are "hidden forms of deafness", characterized by a difficulty distinguishing sounds, or even the sources of sound emissions. For example, a person may not be able to understand a conversation when several people are speaking at the same time. The sound is heard but no longer understood. For people with this type

of hearing loss, current hearing aids are not very effective.

The consortium, consisting of CeRIAH, the CEA and the LORIA, has set the following goal within the framework of this project: to improve hearing aids by adding the possibility of filtering and distinguishing sounds. The objective is to equip hearing aids

with artificial intelligence capable of separating speech from ambient noise. This work will provide proof-of-concept for the benefits of equipping hearing aids with an artificial intelligence device in a realistic, virtually recreated environment.

This project was launched in March 2022.

Grégory and Céline, project leaders of the projects REFINED and AUDIOGENAGE





7 million
PEOPLE WITH
HEARING IMPAIRMENT
IN FRANCE

1.5 billion
PEOPLE WITH
HEARING IMPAIRMENT

AROUND THE WORLD

980 billion dollars
IN COSTS ASSOCIATED
WITH UNTREATED HEARING LOSS

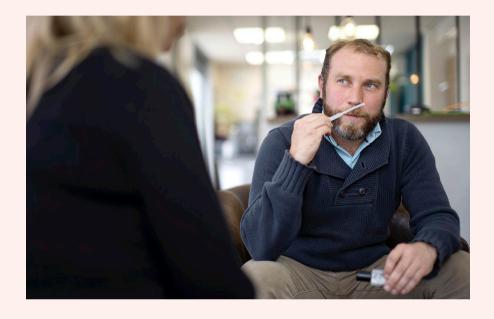
150
GENES IMPLICATED
IN HEARING LOSS



Work hand-in-hand with patients and doctors, through collaboration with a network of auditory health professionals

THE VOICE OF THE PATIENTS

Johann Vitrey-Tardif, a businessman with cochlear implants, is President of the French ENT Ethics Committee. Alongside doctors and researchers, he speaks for users on research issues.



"Under the impetus of the Hearing Institute, participatory research is gaining ground in the field. By bringing users and researchers together, this innovative and ambitious approach will make it possible to rise to the challenge of auditory health for all."

In January 2023, you were elected head of the French ENT Ethics Committee. Why is that unprecedented?

It is the first time that a user someone suffering from hearing impairment and not a healthcare specialist — has occupied this post. Don't forget that the mission of the French ENT Ethics Committee is to raise awareness and to guide all aspects of ethical reflection in the ENT field: information, screening, care, and research. This nomination highlights the new desire to place patients at the heart of ethical reflections on the issues in this domain. From now on, users should be associated not only with debates, but also with research, through an approach known as participatory research.

In your view, what are the current challenges in participatory research?

The first challenge, for users and researchers, is to meet each other properly. We must each take a step towards the other. On the one hand. for the deaf community, there is a need to understand the vocabulary and the deontological and ethical rules governing research, which is performed in a very rigorous framework. On the other hand, researchers need to accept the need to simplify things more to involve us in an optimal manner, rather than just as research subjects. When these conditions are met, the full value of participatory research will become apparent. I am optimistic because things are moving forward in the field!

What hopes do you have of the approach of the Hearing Institute, which aims to place patients at the heart of research?

It is an innovative and ambitious approach that has raised a great deal of hope. It is based on listening to the people concerned and their needs, and on direct exchanges between researchers and users. This strategy makes sense: it can inspire research themes and convince the representatives of patients to participate in the definition of certain parts of research protocols. These are all key elements for tackling the major issue of auditory health today.



The Hearing Institute has entered a partnership with AP-HP,

Université Paris Cité, Inserm, Fondation Pour l'Audition and Institut Pasteur to set up
a university hospital institute (IHU) project.

he project, re-Connect, aims to improve the detection and management of hearing and speech disorders. Six IHUs will be created following a call for proposals, the results of which should be announced in early summer 2023. Within this multidisciplinary structure, research and innovation will be placed at the service of clinical practice and academic training. The goal will be to address the medical, societal, and educational needs raised by hearing disorders.

Why the re-Connect project?

Deafness and hearing impairment constitute a major global burden. In industrialized societies, we are living longer and having children later, leading to an increase in neurodegenerative and neurodevelopmental diseases of genetic origin, and our environments

include new sources of noise pollution (such as compressed sounds). These factors underlie an increase in the number of people suffering from hearing loss and hearing disorders. The tools and medical means currently available for managing these disorders cannot completely satisfy the growing and diversified needs. We can compensate for some hearing deficits, but do not yet know how to cure them, despite their role as a major cause of social and professional isolation.

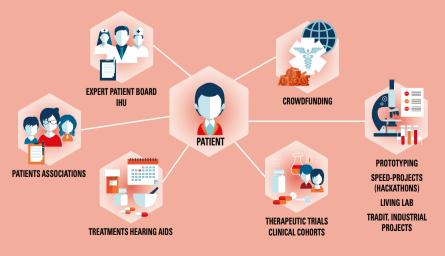
The contribution of the re-Connect project

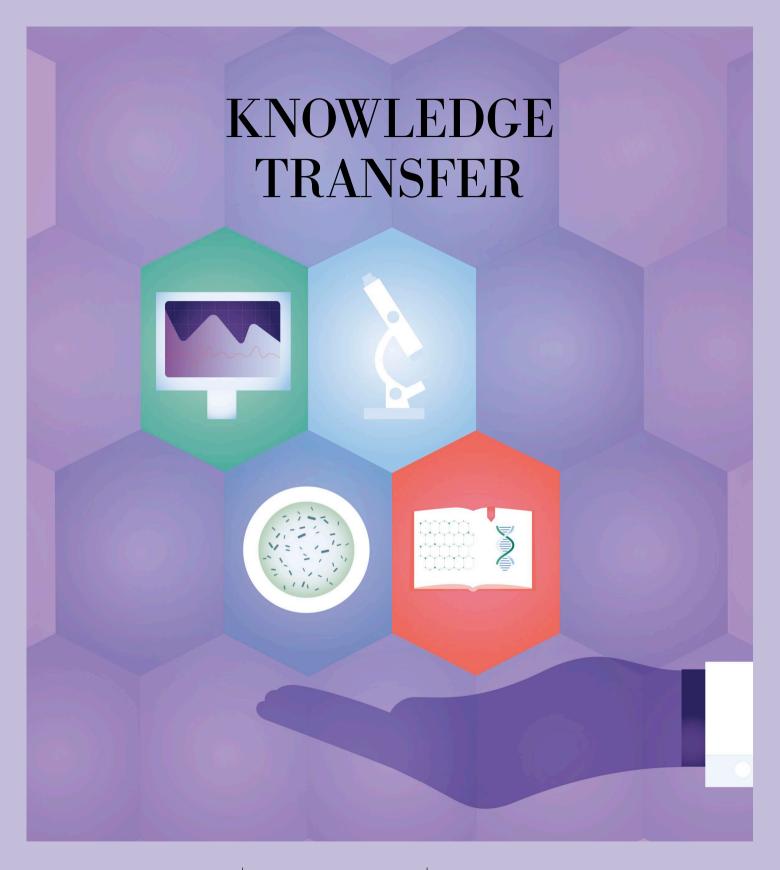
The re-Connect project will bring together, for the first time, all the stakeholders in hearing health: patient associations, researchers, ENT clinicians, neurologists, geriatricians, neurosurgeons from the Hearing Institute and Lariboisière hospital, and our partners from the Necker and

Pitié-Salpêtrière hospitals, healthcare professionals and industrial players in the hearing sector. It will also intensify innovation and entrepreneurship around this major public health issue. This IHU will be the first European institute dedicated to hearing and the brain, with the ambitious goal for the next decade of moving from compensatory medicine to restorative medicine, thanks to the fundamental discoveries in genetics and neurophysiology of the last 20 years. It will pave the way for the creation of new clinical applications with major societal and academic impacts. With the support of its founding members, the scientific and operational organization of re-Connect will ensure its position as a leading European institute, playing a major role in the development of European health policies and attracting the best scientists and clinicians from around the world.

The IHU re-Connect project is patient-centered

An IHU is a place for medical and scientific excellence to invent the medicine of the future, novel treatments and to redefine the course of care in a specific domain.





24 MEDIAS INTERVENTIONS/APPEARANCES RESEARCHERS
WITH TEACHING MISSION

30

PEOPLE WORKING AT THE HEARING INSTITUTE PARTICIPATING IN UNIVERSITY TEACHING, INCLUDING ONE COURSE ENTIRELY ORGANIZED BY AND HELD AT THE HEARING INSTITUTE



Transmit state-of-the-art knowledge, train the talent of tomorrow, inform the public and participate in societal debate

EDUCATION



OCATION



COURSES AND CONFERENCES



HEARING INSTITUT



TARGET

LUCATION	CUNFERENCES	PEOPLE INVOLVED	AUDIENCE
École Normale Supérieure	CogMaster: Augmented Cognition Master IMaLiS: Méthodes optiques pour les enregistrements larges échelles	Sophie Bouton Brice Bathellier, Nicolas Michalski	Master 2 students Master 2 students
Institut Pasteur	Pasteur Course "HeaR" – Hearing: from mechanisms to restoration technologies	Boris Gourévitch, Raphaël Etournay, Jérémie Barral,Grégory Gérenton, Sandrine Vitry, Aziz El Amraoui, Brice Bathellier, Nicolas Michalski, Saaid Safieddine	Master 2, PhD students, post-doc, engineers, doctors
Paris Sciences & Lettres	PSL Week Audition	Brice Bathellier, Jérémie Barral, Nicolas Michalski, Brice Bathellier, Paul Avan, Christine Petit, Diane Lazard, Yann Nguyen, Hung Thai-Van	Students
Sorbonne Université	Introduction to Neurolinguistics	Sophie Bouton	Licence 2 students
Université Paris Cité	Unit Physiology and physiopathology of sensory epithelia	Evelyne Ferrary, Saaid Safieddine	Master 2 students ENT doctors
École vétérinaire Maison Alfort	Inner ear: function and dysfunction	Aziz El Amraoui	L3 students
Université Lyon 1/ Université Clermont Auvergne	Inter-university diploma: Audiology and medical otology Audio-vestibular pathologies	Grégory Gérenton, Hung Thai-Van Saaid Safieddine	Doctors, audioprosthetists, speech therapists and physiotherapists
École CentraleSupélec	Introduction to Neuroscience	Brice Bathellier	Students
ESPCI (École Supérieure de Physique et de Chimie Industrielles)	Imaging techniques for studying sensory processing and sensory coding AI	Brice Bathellier	Master students
Open Medical Institute, OMI Seminars - Schloss Arenberg, Salzbourg	Neurological and Sensory Disorders: Genes, Pathogenesis and Innovative Therapies	Aziz El Amraoui, Saaid Safieddine, Sophie Bouton, Paul Avan	PhD students, researchers, doctors
Presentation in highschool	Introduction to the world of research and Hearing Institute's platforms	Saaid Safieddine, Nicolas Michalski, Boris Gourévitch, Maia Brunstein, Baptiste Plion, Renato Torres, Emma Ducos	High school students
Semaine du cerveau	Cerveau et musique	Nicolas Michalski	All public
Week of sound	Un cerveau pour entendre Qu'entendrez-vous demain? Comprendre et traiter les atteintes de l'audition	Christine Petit Christine Petit and Saaid Safieddine, Paul Avan	All public
National hearing day	La thérapie génique pour la surdité : où en sommes-nous ?	Saaid Safieddine	All public
Cité des sciences	Cité des sens : « L'ouïe »	Boris Gourévitch	All public



Pasteur Course "HeaR" - Hearing: from mechanisms to restoration technologies

The Hearing Institute organized its first annual course on cutting-edge research in hearing and neuroscience in 2022. Nine researchers were involved in organizing and running the courses and workshops. This theoretical and practical course last 13 days and addresses the mechanisms of auditory perception from the ear to the brain, their disorders, and modern methods for repairing auditory function. The HeaR course takes place in a dynamic environment alternating between lectures given in English by internationally renowned specialists and practical applications in hands-on sessions.

This course, open to students from Masters' degree level upwards, has been designed both for hearing specialists wishing to add to their knowledge and for young researchers or engineers wishing to pursue a career in the field of hearing research. This course teaches fundamental concepts in hearing and provides an overview of recent discoveries in basic and clinical research.

In 2022, this course was held mostly at the Hearing Institute.

PSL Week

The week of teaching is organized by PSL (Paris Sciences & Lettres) University and the Hearing Institute and involves eight Hearing Institute researchers. It is destined for all members of PSL University and aims to raise the awareness of students about modern issues in hearing sciences. It provides an overview of the knowledge acquired and of current questions in cochlear genetics and biophysics, the neurosciences of hearing, the psychology of human hearing and animal communication, experimental and clinical audiology and engineering sciences.

The partnership between PSL University and the Hearing Institute makes it possible to cover almost all levels of study and all approaches to the human auditory system: genetics, cochlear biophysics, integrative, theoretical and cognitive neurosciences, psychoacoustics, experimental and clinical audiology, and applications in acoustics and machine learning.



SCIENTIFIC ANIMATION

EXTERNAL SEMINARS



01/13/2022

Image, Son, Musique)

Aix-Marseille Université

Marseille, France

Deciphering the bases of speech and hearing with explainable data-driven methods.



02/03/2022

Bordeaux, France

The many lives of the core PCP gene vangl2.



03/17/2022

BENJAMIN MORILLON

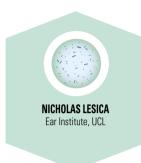
Institut de Neurosciences

des Systèmes,

Aix-Marseille Université

Marseille, France

Cognitive neurophysiology of human audition hemispheric asymmetry and motor contribution.



03/31/2022

London, United Kingdom

Characterizing the impact of hearing loss on the neural signal manifold via classical methods and deep learning.



04/14/2022

Paris, France

Role of unconventional secretory autophagy in the brain - potential role in Parkinson's and other neurodegenerative diseases -.



05/05/2022

Paris, France

Au-delà de la dichotomie musicien vs non-musicien . évidences pour une réorganisation en plusieurs étapes du traitement auditif en fonction de l'apprentissage musical.



05/12/2022

Paris, France

Gene therapy for rare genetic diseases, achievements and challenges.



CATHERINE WEIZS (Intramural Research Program)

06/23/2022

Bethesda. **United States**

Synaptic inhibition in the medial olivocochlear efferent eeuron system.



07/07/2022

London, United Kingdom

Using the mouse to elaborate on the genetics of mammalian hearing.



09/15/2022

Boston, **United States**

Hidden hearing loss: a paradigm shift in hearing.



10/13/2022

Baltimore. **United States**

An omic path to hearing restoration.



10/27/2022

London, **United Kingdom**

Auditory brain abnormalities in a mouse model of genetic risk for schizophrenia.



11/24/2022

Geneva. Switzerland

Neural manifolds for speech processing.



12/15/2022

Paris. France

Exploring the neural mechanisms of conscious perception.

These meetings have promoted exchanges between the various entities.

SCIENTIFIC

MEETINGS

11/07/2022

Joint meeting of the Hearing Institute and ENS/PSL University.

11/25/2022

First joint meeting of the Hearing Institute and the Vision Institute.

12/09/2022

Joint meeting of the Hearing Institute and UCL.

09/14/2022

OLIVIER POSTAL

Déficits centraux auditifs dans les formes génétiques de surdité : l'exemple des gènes Cdh23 et Pcdh15.

09/30/2022

SARA JAMALI

Predictive coding of global sequence violations in mouse auditory cortex.

THESIS DEFENCES

PUBLIC OUTREACH



Videos

- In 2022, the Hearing Institute produced its first film, written and coordinated by Nicolas Michalski, with the aid of a digital agency. This four-minute film presents the Hearing Institute, its history since its creation, its premises and the research currently underway at the Institute.
- A video produced by the Retina France association of an interview with Aziz El Amraoui, who talks about Usher syndrome and retinitis pigmentosa, research into these diseases and the treatments currently available and in development. "Vision and deafness".
- Le Blob, l'extra-média, launched by Universcience (a public entity bringing together la Cité des Sciences et de l'Industrie and le Palais de la Découverte), has produced a video entitled "Are we all going to go deaf?". According to the WHO, 2.5 billion people worldwide will have developed hearing impairment by 2050. Several researchers give their thoughts on possible answers to this problem, including, notably, Saaid Safieddine from the Hearing Institute.
- Invisible and painless, sound pollution has long been underestimated by both doctors and the authorities. In this video, Boris Gourévitch describes how this environmental noise disturbs our sleep and leads to an increase in the risk of cardiovascular diseases. *L'Express*, video survey: "How noise pollution undermines our health".



Radio

- France Culture : « Pourquoi ne percevons-nous pas les sons sous anesthésie? ». Journal des sciences
- France Culture : « Surdité : on est tout ouïe » , Journal des sciences



Podcasts

- Institut Pasteur Legs, Podcast : « La santé auditive, un capital à préserver », of the serie « L'espoir en héritage »
- Ma RTS, Podcast : « Que se passe-t-il quand je me parle à moi-même ? »



Principal press articles

ΙΔΝΙΙΔΕΥ

- « Des scientifiques de Genève tentent de décoder les signaux cérébraux du langage intérieur », ma RTS
- "Inner Speech Brain Circuits Could Help Treat Language Disorders", Neuroscience News & Research
- « Audition : les dégâts du son compressé mis en évidence par une étude réalisée sur des cochons d'Inde », France Info
- « La notion de micro-silence est fondamentale pour la santé auditive », Audiologie Demain

FFRRIIΔRV

« Nanoear : quand la méthode scientifique se fait translationnelle et multidisciplinaire », FNRS

APRIL

« Syndrome de Usher, la recherche à grands pas », Guide-Vue

МΔ

« Dyslexie : et si on réparait le cerveau ? », Planète Santé

JUIN

 « Décoder les signaux du cerveau pour remédier à l'aphasie », Planète santé

AUGUST

 « Décrypter les pleurs, ce langage rudimentaire d'un bébé, n'a rien d'inné », Le Monde

SEPTEMBER

 « Voici pourquoi il faut faire attention aux sons compressés », Version Femina

OCTOBER

- « Troubles de l'audition : 4 nouveaux traitements prometteurs », Femme Actuelle
- « Pourquoi les sons ne sont-ils pas perçus par anesthésie ? », Press release, Institut Pasteur
- « Pourquoi nous n'entendons pas les sons sous anesthésie générale », Sciences et Avenir
- Ultrabrèves, Sciences et Avenir
- « Surdité, l'épidémie silencieuse », Magazine Epsiloon

NOVEMBER

- "Brain implants that translate paralyzed patients' thoughts into speech creep closer to reality", STAT News
- « Surdité : l'implant cochléaire, une révolution auditive »,
 Le Figaro (Dossier santé)

GOVERNANCE

FINANCE



K€1,059

FOCUS ON

SCIENTIFIC RUNNING COSTS

AND EQUIPMENT

50 GRANTS UNDERWAY

24
PEOPLE RECRUITED
IN 2022



Creating favorable conditions for research and innovation

ORGANIZATION

ANNE-LISE GIRAUD

ANNE-DOMINIQUE LODEHO-DEVAUCHELLE

AZIZ EL AMRAOUI

NICOLAS MICHALSKI / BORIS GOURÉVITCH

RAPHAËL ETOURNAY

CHRISTINE PETIT

SAAID SAFIEDDINE / YANN NGUYEN

Auditory system dynamics & multisensory processing BRICE BATHELLIER

JÉRÉMIE BARRAL

Clinical & translational exploration of sensorineural hearing loss
HUNG THAI-VAN/ DIDIER DULON

ANNE-LISE GIRAUD / SOPHIE BOUTON

LUC ARNAL / DIANE LAZARD

PAUL AVAN / HUNG THAI-VAN

TECHNOLOGICAL PLATFORMS

DANUTA OFICJALSKA / EMELINE PRANDATO

TECHNICAL FACILITIES

TECHNICAL SUPPORT

FAOUZI JENZERI

ADMINISTRATIVE SUPPORT

VINCENT PETI

HANTAL YANG

1ELOÏSE HERVI

GOVERNANCE

THE STEERING COMMITTEE

The steering committee (SC) is composed of members of the Fondation Pour l'Audition and Institut Pasteur. It is the governing body of the Hearing Institute. It is currently presided by Étienne Caniard, its first president and representative of the Fondation Pour l'Audition, for the duration of the constitution agreement. The role of the SC is to assist the Institute in the development of the strategic lines proposed by the director.

President

ÉTIENNE CANIARD

Former President of la Mutualité française (private health insurance) and former member of the collegial body of the Haute Autorité de Santé (High Authority for Health)

Members

FRANCOIS ROMANEIX

Deputy General Director of Institut Pasteur

DENIS LE SOUER General Director of the *Fondation* Pour l'Audition

FRANCOISE PERRIOLAT

Financial Director of Institut Pasteur

PATRICK TRIFU-CUOT

Director of Careers and Scientific Evaluation at Institut Pasteur

THE INTERNATIONAL SCIENTIFIC ADVISORY BOARD

The president of the International Scientific Board is Charles Liberman. he holds a two-year mandate. This body is responsible for evaluating the scientific and translational strategy of the Institute, the research themes proposed by its director, candidates for the formation of new research teams and the research work performed at the Institute. The International Scientific Board emits recommendations, which are transmitted to the president of the Steering Committee. The composition of the SAB will change in 2023.

President

PROFESSOR CHARLES LIBERMAN Professor, Harvard Medical School,

Members

ELAINE FUCHS

The Rockefeller University, USA

DAVID D. GINTY

Harvard Medical School, USA

STEFAN HELLER

Stanford School of Medicine, USA

INGEBORG HOCHMAIR MED-EL, Austria

JAMES HUDSPETH

The Rockefeller University, USA

THOMAS J. JENTSCH

Max Delbrück Center for Molecular Medicine, Germany

ANDREW KING

University of Oxford, UK

ISRAEL NELKEN

University of Jerusalem, Israel

CARLA SHATZ

Stanford University, USA

PIERRE VANDERHAEGHEN

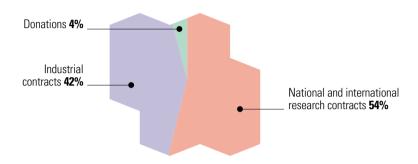
Free University of Brussels, Belgium **FAN-GANG ZENG**

University of California Irvine, USA

FINANCIAL RESOURCES

GRANTS AND FUNDING

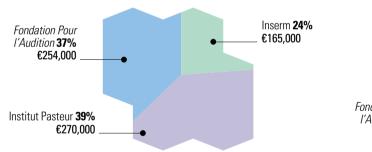
EXTERNAL FUNDING

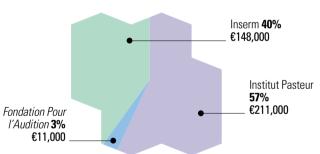


31
GRANTS FROM EXTERNAL SOURCES ONGOING
FOR A TOTAL OF €19 million,
€1 million of which was obtained in 2022

CONTRIBUTIONS OF THE INSTITUT PASTEUR, FONDATION POUR L'AUDITION AND INSERM FOR 2022 – Focus on scientific runing costs and equipement

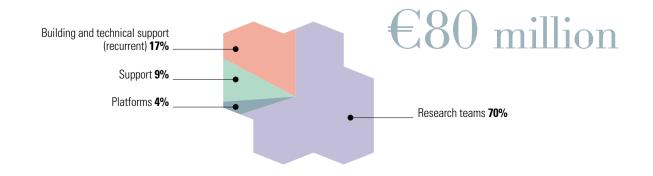
€689,000 FOR RUNNING COSTS €370,000 FOR EQUIPMENT





FIVE-YEAR BUSINESS PLAN

2019-2024



Founding members

Fondation Pour l'Audition (FPA), starting grant package (2019-2024), K€7,575

Transverse Research Programme (PTR), Institut Pasteur, "Organoids-on-chip: role of Sonic-Hedgehog signaling in the development of inner ear organoids" (2019-2022), K€180 Pasteur-Paris University International doctoral program (PPU) fellowship (2019-2022), K€140

Pasteur-Paris University International doctoral program (PPU) fellowship (2020-2023), **K€140**

Roux-Cantarini fellowship (2022-2024), K£118

International grants

Career Development Award, Human Frontier Science Program (2019-2022), **K€261**

European grants

FET Open Hearlight, coordinator (2021-2025), **K€3,000** for five international participants including k€698 for Institut Pasteur

ERC Consolidator DEEPEN (2018-2023), "Extraction of the architecture of the deep network underlying the structuring of auditory perception", **K€1,984**

EMBO Long-Term Fellowship (2020-2022), K€102

National grants

ANR Audinnove (2020-2025), **K€4,319**

ANR LabEx LifeSenses (2020-2022), K€903

ANR HearInNoise (2017-2023), **K€423**

Aquitaine Science Transfert (2021-2023), K€394

ANR Eargencure (2017-2023), **K€365**

ANR Selfmorpho (2021-2025), **K€322**

ANR Vamphears (2021-2025), **K€282**

ANR Presage (2021-2025), **K€250**

ANR Fatigaudit (2021-2026), **K€222**

ANR Nanoear (2021-2024), **K€202**

ANR Refined (2021-2026), **K€200**

ANR AudioDream (2022-2026), K€197

ANR Cortiogran (2022-2026), **K€123**

Fellowship from the French Ministry of Higher Education, Research and Innovation (2022-2025), **K£110**

ANR Murocs (2017-2023), **K€104**

Institut Pasteur-Sorbonne University fellowship (2021-2024), **2 X K€101**

Université Paris Cité fellowship (2022-2025), K£101

CIFRE grant from the French Ministry of Higher Education, Research and Innovation (2022-2025), **K€96**

Institut Carnot Voir et Entendre/ANR (2021-2028), KE68

ANR Robocop (2019-2024), **K€56** ANR Tympabiom (2022-2026), **K€50** ANR Ribeohl (2019-2023), **K€29**

Île-de-France grants

DIM *Thérapie génique* (IdF-FPA) (2019-2023), "Pushing forward cochlear gene therapy with a high-speed confocal microscope with a large field of view", **K€423**

DIM ELICIT UltraStim (IdF-FPA) (2020-2023) "Ultrastim: high-density optogenetic stimulation at single-cell resolution", Ke316

DIM ELICIT CoDev (IdF-IP) (2020-2023), "Development of a scalable method for generating stem cell-derived inner ear organoids", **K£300**

Foundations

Royal National Institute for Deaf People and Alzheimer's Research UK foundations (2020-2023), "The cerebrovascular system: the missing link between hearing loss and dementia?", K£188

Fondation pour la recherche médicale, postdoctoral grant (2021-2022), **K€103**

Companies

Sensorion, connexine 26 project (2021-2023), K€3,891

BPI France, PATRIOT project* (2020-2025), K€2,276

Sensorion, OTOF project (2019-2023), K€1,043

Sensorion, funding for a project manager (2019-2022), K€459

Sensorion, funding for a PATRIOT project manager (2020-2024), K€397

Research contract with SAS Entendre (2018-2022) to fund a PhD student, $K \in 100$

Donations

LHW (2022-2025), **K€650** LHW (2019-2022), **K€640**

Fondation Raymonde et Guy Strittmatter (2020-2023), K€410

Professeur Lenriot (2020-2023), K€243

Fondation de France/Fonds Mazet Danet (2021-2022), **K€100**

Fondation de France/comité Fouassier (2021-2022), **K€66**

Optic 2000 (2022-2024), **K€60**

Private donations (2022-2024), K€29

Souhaiel Chaouachi (2022-2023), KE5

Surdi 13 (2020-2022), **KE5**

Entrepreneurs & Go (2021-2022), **K£5**

Entrepreneurs & Go (2022-2023), K€5

^{*} The PATRIOT project is supported by the Investissement d'Avenir program run by BPI France.

PUBLICATIONS 2022

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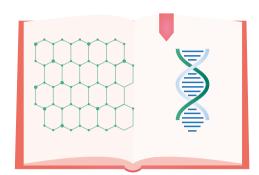
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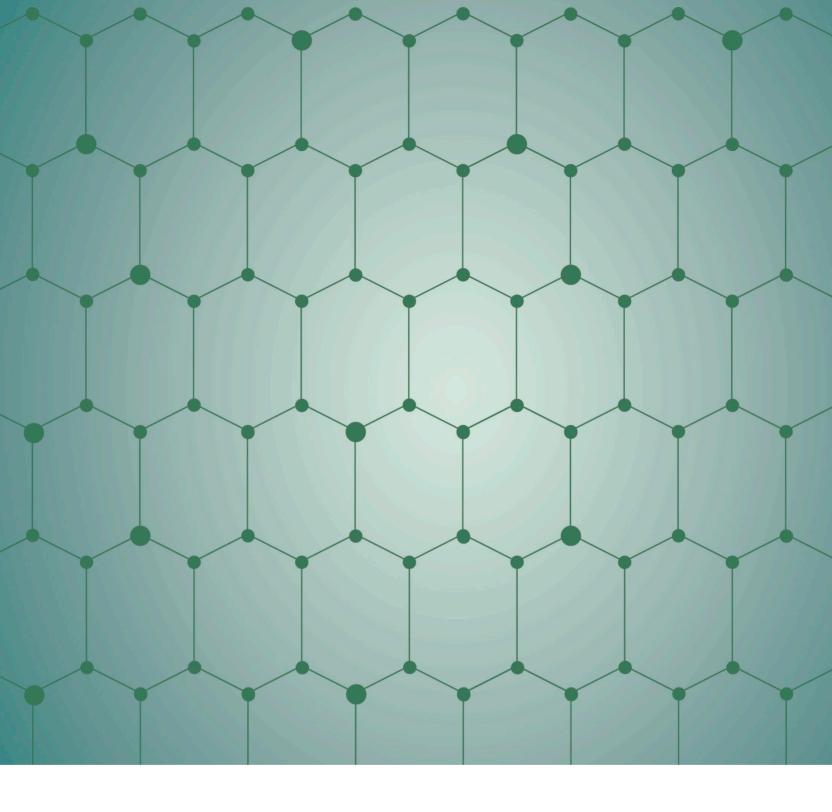
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