

ehugroup 

**Achucarro**

BASQUE CENTER FOR NEUROSCIENCE

*scientia ad remedium*

**2023**

**Annual Report**



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# Foreword

Dear reader,

During 2023 we continued our increasing pace in terms of publication output (77 papers published with 87% of them in Q1), funding (4.8 M€), attracting young qualified researchers with new lines of research, and consolidating highly productive Principal Investigators through tenured positions.

Specific highlights include the success of our researchers in three very competitive calls: ERC Consolidator, La Caixa Health Research Program, and The Simons Foundation. A 50% expansion of our facilities that took place this year is also of great consequence. Indeed, it has allowed us to provide state-of-the-art facilities to our Human Biomodels Platform, organize more lab space and substantially reinforce core services. This additional space will also be key in supporting the incorporation of new research topics and experimental models, as planned.

In line with the current strategy, over a year ago we began the profound internal re-organization into three Research Programmes (Neuro-glia interactions in brain diseases, Glial modulation of brain structure and function, and Gliotheranostics) which has fostered stronger internal interactions, and has allowed us to apply to a variety of highly competitive calls with projects involving many of our Principal Investigators.

Even though we did not succeed in all of them, teamwork dynamics are slowly being incorporated into the centre's culture. We continue to design new projects with the idea of furthering this momentum, with an eye also in facilitating societal outreach, as Neuroscience is a fast-paced discipline of great social impact.

No withstanding the continued effort and ambition of our faculty, the expansion and reinforcement of our core facilities has been made possible through the support of our reference institutions, Ikerbasque and the Basque Government. Both have shown a strong commitment in encouraging our goals and scientific endeavours.

All in all, during this past year we have achieved all the milestones planned at this stage in our ongoing Strategic Research Plan. We aim to consolidate them in the coming years, with a stable work force, sustained resources, and an unrelenting ambition to improve continuously.

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Ignacio Torres Alemán  
Scientific Director

Elena Alberdi Alfonso  
Assistant Scientific Director

*ACHUCARRO is one of the BERC (Basque Excellence Research Centres) research organisations fostered by the Department of Education of the Basque Government.*

*There are nine organisations recognised as BERC within the Basque Science, Technology, and Innovation network.*

# 1. Strategy and Management

In 2022, we launched our third strategic plan for the 2022-2025 period. ACHUCARRO's overall objective is to perform co-ordinated multidisciplinary research of the brain functions on all levels: from single molecules through individual cells, acutely isolated nervous tissues, to the brain networks operating in vivo; all to further advance the discoveries in physiology and pathophysiology of the nervous system.

The foundations that support our strategic view and future vision are:

- ▶ Recruit, Reintegrate and Retain **talented research personnel**, to perform excellent research and contribute to **advanced post-graduate training**.
- ▶ Develop **modern infrastructures** within the Science Park of the UPV/EHU, at the University campus in Leioa.
- ▶ Assess and incorporate the latest **technologies and equipment** to let the centre operate on the frontier of knowledge.
- ▶ To perform research projects centred in the study of glial cells to contribute to the discovery of **new therapies** for neurological diseases for the benefit and **well-being of the Society**.

By the end of 2023 we were halfway through the current strategic programme and underwent the BERC assessment. The assessment involved a written report and the site visit by the evaluation panel established by IKERBASQUE.

## SCIENTIFIC PLAN 2022–2025

The key strategic direction of ACHUCARRO is the in-depth study of neuronal-glia biology in normal and pathological brains.

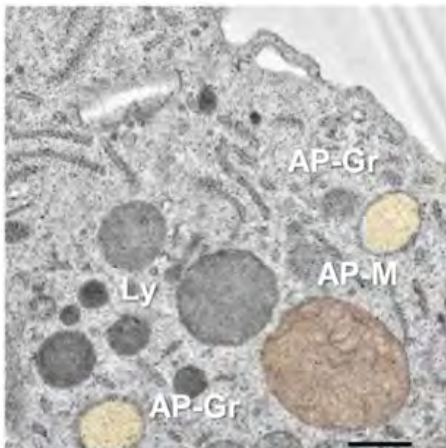
The new Scientific Plan has defined three programmes, with a bottom-up approach: to attain a strategy that fosters internal collaboration and maximizes its impact.

### Research Programmes

- ▶ Neuro-Glial interactions in brain diseases
- ▶ Glial modulation of brain structure and function
- ▶ Gliotheranostics

*Microglial phagocytosis is essential to maintain brain health but, unexpectedly, it is disrupted in diseases such as ischemic stroke.*

## Potential new development of therapeutic strategies focusing on the promotion of microglial protective responses during ischemic stroke



*Representative transmission electron microscopy images of primary microglia. Ly: lysosomes; AP-Gr: autophagosomes with granular cargo (yellow); AP-M: autophagosomes with membranous cargo (orange)*

During an ischemic stroke a vascular plug forms in an artery of the brain, interrupting the blood flow to the brain areas irrigated by the artery, leading to oxygen and nutrient deprivation and, eventually, cell death. In this recent research article, we have shown that microglia lose their ability to remove or phagocytose dead neurons in mice and monkey models of ischemic stroke due to alterations in the microglial lysosomes, in charge of degrading all types of biological macromolecules, from carbohydrates to lipids or nucleic acids. Thus, they are not only critical to degrade the phagocytosed debris, but also to recycle intracellular organelles.

This latter process, known as autophagy (“eating oneself”) is stimulated to promote survival under metabolic stress conditions such as oxygen and nutrient deprivation.

Ischemic stroke intensified autophagy in microglia, probably to get rid of damaged proteins and organelles, adapt to the new metabolic scenario, and promote microglial survival. However, autophagy promotion during ischemic stroke did not come without cost for microglia. Indeed, the over-engagement of the autophagic degradation pathway in microglia led to a significant depletion of lysosomes, which were no longer available for the clearance of phagocytic material such as dead neurons, leading to accumulation of debris in the brain parenchyma and worsening the evolution of the disease. Furthermore, inhibition of autophagy was detrimental for microglial health and survival, suggesting its critical supportive role. The alternative treatment with an autophagy inducer, rapamycin, produced complex effects in microglia, including beneficial, neutral, and toxic effects, depending on the experimental model used for the assessment of microglial phagocytic activity and survival. Although autophagy modulation turned out to be ineffective or inconclusive for microglial phagocytosis modulation in this study, the data obtained was crucial for understanding the mechanistic complexities of lysosomal responses in microglia under ischemic stroke.

**“Microglial phagocytosis dysfunction in stroke is driven by energy depletion and induction of autophagy”**

Beccari S, Sierra-Torres V, Valero J, Pereira-Iglesias M, [...], Plaza, A. & Sierra, A.

Autophagy DOI: [10.1080/15548627.2023.2165313](https://doi.org/10.1080/15548627.2023.2165313)

## EQUALITY AND INCLUSION PLAN 2022-2025

ACHUCARRO initiated the development of its first Equality Plan in 2017, in collaboration with an external consultancy specialised in this domain. In 2021, we undertook a comprehensive evaluation of the preceding plan to inform the formulation and implementation of our second iteration.

The plan has yielded tangible improvements, fostering a culture of greater equity, equality, and diversity within our organization. We are gratified to observe a positive evolution in the balance and representation of individuals in leadership positions.

Our Equality Committee (EC) comprises representatives from across the organisation, spanning various roles and career stages, and maintains gender parity. Serving as both the driving force and assessor of all initiatives outlined in the plan, the EC plays a pivotal role in ensuring its efficacy and impact.

This new plan continues building on four improvement areas that were already identified in the first plan:

1. Promoting equal opportunities in positions of responsibility.
2. Generate working environments and conditions that facilitate the co-responsible conciliation of personal, family, and professional life.
3. Incorporate a gender perspective in the policies, products, and operating dynamics.
4. Promote inclusive leadership styles.

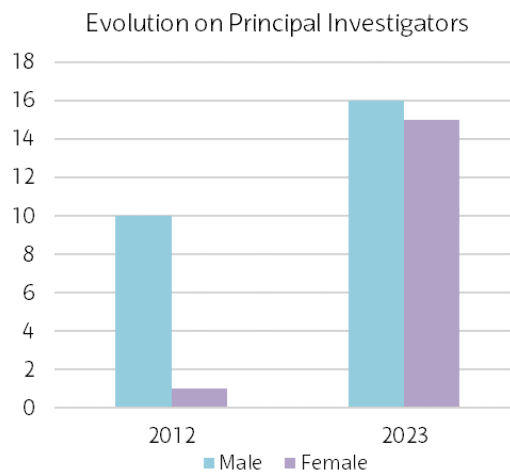


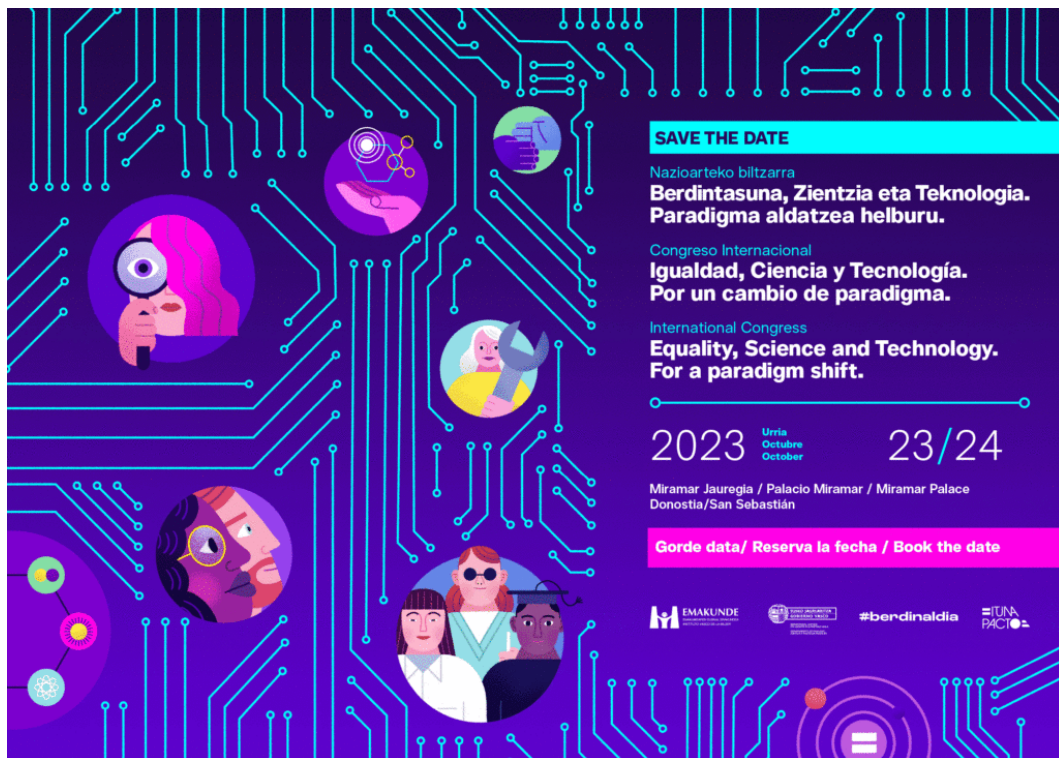
Figure 1. Evolution of number of Principal by gender, from 2012 to 2023

<https://www.achucarro.org/equality>

*The General Manager represented ACHUCARRO in the Scientific Committee of the congress "International Congress on Equality, Science and Technology. For a Paradigm Shift" held in Donostia - San Sebastian, in October 23 and 24*

## Equality, Science and Technology. For a Paradigm Shift

In the framework of the **Basque Pact for Equality and living free of violence against women**, the Emakunde – Basque Women’s Institute (Basque Government), together with other organisations in the Basque Country, and the international support of the European Union and United Nations, organised this congress to promote a paradigm shift in the field of science and technology to systematically and fully incorporate a gender perspective and respond to the challenges of achieving a fairer and more egalitarian society where no one is left behind.



The programme included keynote lectures by experts in the field like María Ángeles Sallé, Anne Pépin, Londa Schiebinger, Silvia Rueda, Hélène Molinier, Curt Rice, Alan Greig and Emma Short among others.

The selection of ACHUCARRO to be part of the Scientific Committee is a recognition to our commitment towards Equality, Equity and Diversity in Science.

<https://www.berdintasunazientzian.eus>



*Cultivating partnerships is not just about sharing resources; it's about multiplying possibilities. Together, we achieve more than we ever could alone, unlocking innovation, driving growth, and creating lasting impact.*

## 2. Partnerships and Collaborations

Working together with other people and institutions is key to unravelling the challenges of this changing World. Weaving a solid network of collaborators takes time and effort, and selecting the best companion is strategic for any institution.

We thoroughly identify and assess the individual and collective partners in our environment and sector to properly manage the mutual relationships for a win-win outcome.

### INSTITUTIONAL ALLIANCES

We formalise institutional partnerships with specific, written, long-term agreements, which cover the terms of the collaboration. To some extent, such alliances are also strategic in nature, as indicated by the agreements signed with Ikerbasque and the UPV/EHU for the appointment of personnel.

These are the institutional agreements by strategic partner during the year:

#### **BASQUE GOVERNMENT**

- ▶ BERC agreement to support the strategic deployment in 2022–2025.

#### **BASQUE SCIENCE, TECHNOLOGY, AND INNOVATION NETWORK**

- ▶ Appointment at the BSTI network and recognition in the “BERC - Basque Excellence Research Centre” category

#### **IKERBASQUE**

- ▶ Framework Agreement for the appointment of research staff: Ikerbasque Research Professors, Associates and Fellows
- ▶ Agreement to support the development of the IKUR Strategy of the Basque Government
- ▶ Agreement to support the development of the Neuronano Strategy Action of the Basque Government

#### **UNIVERSITY OF THE BASQUE COUNTRY (UPV/EHU)**

- ▶ Framework Collaboration Agreement
- ▶ Specific agreement for the appointment of teaching and research and personnel
- ▶ Specific agreement of collaboration to appoint the Deputy Scientific Director

Our strategic alliances are with those organisations or individuals that allow us to extend our capabilities or complement our services.

## STRATEGIC ALLIANCES



### European Commission – HRS4R Community

Following our endorsement of the European Charter for Researchers fostered by the European Commission, we underwent the process of recognition of our internal policies for managing research personnel, according to HRS4R and OTM-R initiatives of the European Commission.



HR EXCELLENCE IN RESEARCH

In 2023 we underwent a new assessment process with the aim of renewing our **HR Excellence in Research** recognition.



### CIBER

The **Center for Biomedical Research in Network** is a research organization with its own legal entity, fostered by the Spanish Government (Instituto de Salud Carlos III) and constituted by research groups without physical contiguity, belonging to different state administrations and autonomous communities, from the public and private sectors, with research lines and objectives focused on a common specific area.

In our case, two groups collaborate in the field of neurodegenerative diseases, which are coordinated to achieve scientific objectives that could hardly be considered in a specific context.



### Bizkaia Talent

Established in 2005 with the support of the Provincial Council of Bizkaia, Bizkaia Talent is a non-profit organization that fosters and facilitates the attraction, connection, and retention of highly qualified professionals to the Basque Historic Territory of Bizkaia. Bizkaia Talent is a strategic partner and an ally of ACHUCARRO, which takes our name and objectives to the many international scientific events they attend, supporting our talent attraction process.

## INTERNATIONAL SCIENTIFIC ADVISORY COMMITTEE (ISAC)

Our International Scientific Advisory Committee comprises esteemed researchers from various domains of neuroscience. They offer invaluable perspectives and insights on strategic and operational matters to facilitate the continued advancement of ACHUCARRO.

The members of this committee performed the assessment of all Principal Investigators and research groups in 2023 in the framework of the BERC mid-term evaluation.



Alfonso **Araque**

University of Minnesota

USA



Isabel **Fariñas**

Universidad de Valencia

Spain



Rafael **Fernández Chacón**

Universidad de Sevilla

Spain



Anna **Planas**

CSIC – IDIBAPS

Spain



Carmen **Sandi**

EPFL

Switzerland



Pablo **Villoslada**

Stanford University

USA

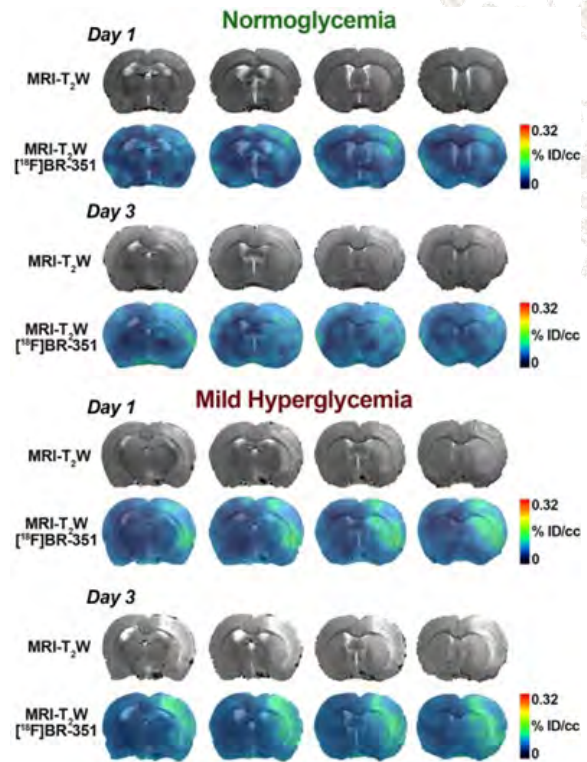
Figure 2. Members of the ISAC in 2023

*Hyperglycemia has been linked to worsening outcomes after subarachnoid haemorrhage (SAH). Nevertheless, the mechanisms involved in the pathogenesis of SAH have been scarcely evaluated so far.*

## Hyperglycemia worsens the progression of subarachnoid haemorrhage

This article showed for the first time the detrimental role of acute hyperglycemia in an experimental model of SAH using a combination of non-invasive multimodal imaging such as Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI).

This study provides valuable insight into the detrimental effect of hyperglycemia on early Blood Brain Barrier damage mediated by neutrophil infiltration and metalloproteinase activation that could explain the worse prognosis in SAH and open new avenues for the identification of new therapeutic approaches for the clinical management of hyperglycemia.



### *"Multimodal imaging of the role of hyperglycemia following experimental subarachnoid hemorrhage"*

Joya A, Plaza-García S, Padro D, Aguado L, Iglesias L, Garbizu M, Gómez-Vallejo V, Laredo C, Cossío U, Torné R, Amaro S, Planas AM, Llop J, Ramos-Cabrer P, Justicia C, Martín A.

*J Cereb Blood Flow Metab.* DOI: [10.1177/0271678X231197946](https://doi.org/10.1177/0271678X231197946)

*We gather professionals from 24 different nationalities and foster equality, equity, and diversity as one of the core values of our organisational culture.*

## 3. People

In 2023 we continued our growth and finished the year with 158 people appointed.

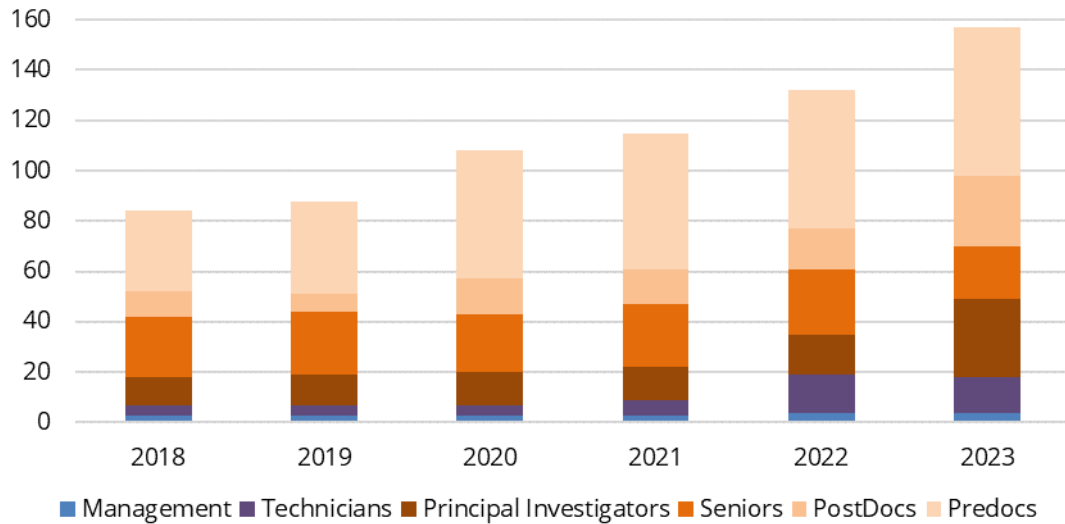


Figure 4. Evolution of personnel 2018-2023

Throughout the year there has been rotation of some personnel, especially in the categories that imply greater mobility, such as pre and postdoctoral researchers. In addition, some people have advanced in their careers, either by consolidating their employment, or by becoming principal investigators on projects.

### RETREAT

In June 19 we gathered all the Principal Investigators at Baserri Antzokia (Zamudio) , with a representation of postdoctoral researchers, technical staff, and administration to reflect on strategic objectives for the future and approaches to tackle them. It was a very fruitful day to continue advancing in the development of our organization and our science.



## APPOINTED STAFF (December 2023)

Oihane ABIEGA ETXABE · Laura AGUADO SANTOS · Elena ALBERDI ALFONSO · Óscar ALEIXOS GRAU · Francisco Javier ALFARO MOZAZ · María ALFONSO TRIGUERO · Mikel ÁLVAREZ TUEROS · María Isabel ARDAYA FRANCO · Xabier ARECHABALA RODRIGUEZ · Amaia ARRANZ MENDIGUREN · Mariana ASTIZ CADENAS · Uxue BALANTZATEGI FERNÁNDEZ DE ARROIABE · Jimena BALERIOLA GÓMEZ DE PABLOS · Andres Mateo BARAIBAR SIERRA · Laura BAYÓN CORDERO · Nora BENGEOA VERGNIORY · Xabier BENGOTXEA BAUSELA · Ana BERNAL CHICO · Eva BLANCO COSTALES · Itziar BONILLA DEL RÍO · Leire BOVEDA ALTUBE · Izaskun BUENDÍA ABAITUA · Stefano CALOVI · Estibaliz CAPETILLO GONZÁLEZ DE ZARATE · Alejandro CARRETERO GUILLÉN · Fabio CAVALIERE · María CEPRIÁN COSTOSO · Jesús CESPÓN GONZÁLEZ · Juan Carlos CHARA VENTURA · Brenda Nadia CHINO VILCA · Dalila CICERI · Raffaella CIPRIANI · Teresa COLOMER MOLLA · Lorea CORTÉS MELER · Joan CRUZ SESÉ · Aída DE LA CRUZ GAMBRA · María DOMERCQ GARCÍA · Jonathan Evan DRAFFIN · Jon EGAÑA HUGUET · Izaskun ELEZGARAI GABANTXO · Iratxe ELORDUY GARCÍA · Juan Manuel ENCINAS PÉREZ · Laura ESCOBAR CASTAÑONDO · Dmitry FEDOROV · Mario FERNÁNDEZ BALLESTER · Héctor FLORES ROMERO · Nuria GALBIS GRAMAGE · María Tatiana GALLEGO FLORES · María GAMARRA GARCÍA-BERMEJO · Adhara Mikaela GAMINDE BLASCO · Maider GARBIZU ALBISU · Laura GARCÍA GASTAÑAGA · Mirta GARCÍA MARTÍNEZ · Fernando GARCÍA MORENO · Lorena GARCÍA RUIZ-CLAVIJO · Paula GIMÉNEZ MÍNGUEZ · Sonia GÓMEZ URQUIJO · Nerea GOROSTIOLA · Pedro Rolando GRANDES MORENO · María Inmaculada GUERRICAGOITIA MARINA · Mazahir Tahid HASAN · María Isabel HERNÁNDEZ CORTÉS · Tamas HORVATH · Izaskun IGEREGI ARTETXE · Leire IGLESIAS IGLESIAS · Josune IMAZ IRURETAGOYENA · Leire IZAGIRRE URIZAR · Sara JIMÉNEZ ÁLVAREZ · Isabel JIMÉNEZ RIDRUEJO · Muhammad Zahid KHAN · Gorka KORTABARRIA PÉREZ · Maria KUKLEY · Begüm KURT · Rizky Sarahsi Ersaid LASABUDA · Nerea LLAMOSAS MUÑOZGUREN · Eneritz LÓPEZ MUGURUZA · Irene LUENGAS ESCUZA · Diana del Socorro LUNA · Joel MALDONADO TEIXIDÓ · Abraham MARTÍN MUÑOZ · Soraya MARTÍN SUAREZ · Endika MARTÍNEZ GUTIÉRREZ · Zara MARTÍNEZ PÁEZ · Maialen MARTÍNEZ PRECIADO · Gilda Paloma MATA SALGADO · Diego Martín MATEOS · Susana MATO SANTOS · Carlos José MATUTE ALMAU · Alejandro MELERO CARRILLO · Juan Luis MENDIZABAL ZUBIAGA · Amaia MIMENZA SAIZ · Fosca MIRATA · Marta MIRÓN ALCALÁ · Luna MORA HUERTA · Oscar MORENO MORENO · Teresa MURO GARCÍA · Irene NÚÑEZ GARCÍA · Blanca Isabel OCHOA BUENO · Jon OLALDE JOMETON · Jon OLANO BRINGAS · Aitor PALOMINO FERNANDEZ DE LARREA · Carla PEIRÓ MORENO · Marta PEREIRA IGLESIAS · Fernando PÉREZ CERDÁ · Lucila Maite PÉREZ GIANMARCO · Erise PÉREZ PASCUAL · Alberto PÉREZ SAMARTÍN · José Ramón PINEDA MARTÍ · Joaquín PIRIZ · Ainhoa PLAZA ZABALA · Nagore PUENTE BUSTINZA · Virginia PUENTE MUÑOZ · Aurora PUTZOLU · Paula RAMOS GONZÁLEZ · Almudena RAMOS URIARTE · Leire REGUERO ACEBAL · Pablo Alejandro REYES VELASQUEZ · Irantzu RICO BARRIO · Ane RODRÍGUEZ BODERO · Esther RUBIO LÓPEZ · Leire RUIZ BARREIRO · Asier RUIZ NUÑEZ · Jaime SAGARDUY BARRENA · Andrea SAINZ PRADO · Aitor SALAGRE PÉREZ · María Victoria SÁNCHEZ GÓMEZ · Dann SÁNCHEZ IRAOLA · Ester SANCHEZ MARTÍN · Lucía SANGRÓNIZ BELTRÁN · Ane SANTISTEBAN GARCÍA · Rafael SARRÍA AROSTEGUI · Rodrigo SENOVILLA GANZO · Maitane SERRANO MURGIA · Amanda SIERRA SAAVEDRA · Vladislav SOLDATOV · Edgar Jesús SORIA GÓMEZ · Federico Nicolas SORIA LANNES · Vanja TEPAVCEVIC MANDIC · Irene TOMÉ VELASCO · Jan TØNNESEN · Ignacio TORRES ALEMÁN · Nerea URRESTIZALA ARENAZA · Carmen Lucía UTRILLA CARRIAZO · Luis VARELA FERNÁNDEZ · Alexei VERKHRATSKY · María VILLAFRANCA FAUS · Patricia VILLEGAS ZAFRA · Jonathan Adrián ZEGARRA VALDIVIA · Jose Luis ZUGAZA GURRUCHAGA

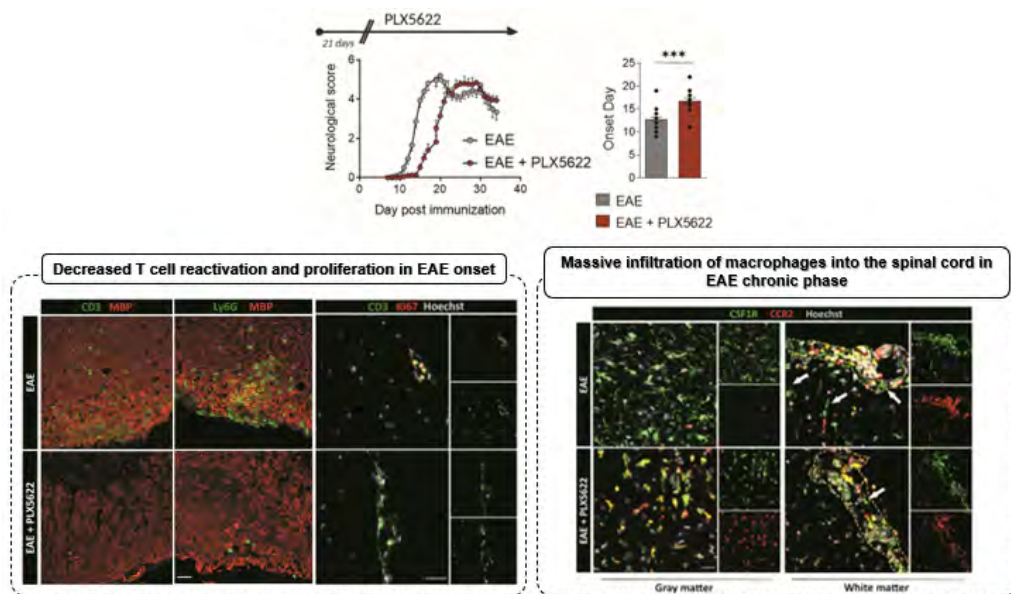
*In multiple sclerosis and the experimental autoimmune encephalomyelitis (EAE) model, both resident microglia and infiltrating macrophages contribute to demyelination as well as spontaneous remyelination, but...*

## The specific roles of microglia versus macrophages were unknown.

To investigate microglia in EAE we used the colony stimulating factor 1 receptor (CSF-1R) inhibitor, PLX5622, which deplete microglial population, and Ccr2RFP/+fmsEGFP/+ mice, which allow us to distinguish peripheral macrophages and microglia.

PLX5622 treatment depleted microglia and provoked a massive infiltration of CCR2+ macrophages into demyelinating lesions and spinal cord parenchyma. Albeit this massive infiltration of peripheral macrophages, the neurological symptoms were not altered during the EAE chronic phase. In contrast, microglia depletion induced an important delay in EAE onset. We demonstrated that microglia has a role in antigen presentation and T cell reactivation at initial stages of EAE.

Our results define the specific role of microglia in the early phases of the pathology and suggest that targeting these cells could help to ameliorate the immune reaction in the pathology.



**“Microglia and meningeal macrophages depletion delays the onset of experimental autoimmune encephalomyelitis”**

Montilla, A., Zabala, A., Er-Lukowiak, M. [...], Sierra A, Matute C, Domercq M.

Cell Death & Disease DOI: [10.1038/s41419-023-05551-3](https://doi.org/10.1038/s41419-023-05551-3)

*We authored 77 new scientific publications in 2023.  
87% of them in the first quartiles of their research fields  
85% of the publications are Open Access*

## 4. Research

### PROGRAMME 1: NEURO-GLIAL INTERACTIONS IN BRAIN DISEASES

**Coordinator:** José Luis Zugaza Gurruchaga

This programme integrates 9 Principal Investigators from 6 different laboratories.

Glial cells, including astrocytes, microglia, and oligodendrocytes, work in coordination with neurons to support the structural and functional integrity of the nervous system.

The members of this program are experts in different areas of cellular biology and neuroscience, and we set the goal of creating a project in which all members collaborate to understand neural-glial interactions both in health and disease.

Modulating these interactions could offer new avenues for treating or slowing the progression of various brain disorders, such as neurodegenerative diseases.



Elena  
Alberdi



Nora  
Bengoa-  
Vergniory



Estibaliz  
Capetillo



Carlos  
Matute



Abraham  
Martín Muñoz



Vicky  
Sánchez Gómez



Vanja  
Tepavčević



Luis  
Varela



Jose Luis  
Zugaza



## PROGRAMME 2: GLIAL MODULATION OF BRAIN STRUCTURE AND FUNCTION

**Coordinator:** Juan Manuel Encinas Pérez

This programme integrates 12 Principal Investigators from 11 different laboratories.

This programme was designed to bring together investigators studying brain function at different levels.

Under the premise that function follows structure, synapses and networks are investigated morphologically, anatomically, and functionally. With an integrative mindset, glial cells and neurons are considered together.

The study of the glio-neuronal dynamic interaction is of special interest in neurological and neurodegenerative disorders in which the role of glia, via neuroinflammation for instance, is an essential modulator of neuronal survival and activity. In the program's regular meetings, the groups discuss several issues in common: 1) Scientific discussion of new projects and lines of research; 2) Fine-tuning of projects for funding application; 3) how to synergistically optimize and share the available techniques in the program (confocal microscopy-based quantitative image analysis, two-photon imaging and wearable miniscope in vivo imaging, patch-clamp electrophysiology; intracranial local field recordings and behaviour).

Finally, special care is placed on the mentoring of newly joined scientists.



Juan Manuel  
Encinas



María  
Domercq



Fernando  
García-Moreno



Pedro  
Grandes



Mazahir T.  
Hasan



Maria  
Kukley



Soraya  
Martín-Suárez



Alberto  
Pérez-Samartín



Joaquin  
Piriz



Edgar  
Soria-Gómez



Jan  
Tønnesen



Ignacio  
Torres-Alemán

## PROGRAMME 3: GLIOTHERANOSTICS

**Coordinator:** Amanda Sierra Saavedra

This programme integrates 10 Principal Investigators from 9 different laboratories.

Our programme is focused on understanding the properties and capabilities of glial cells in physiological conditions to then exploit them in brain pathologies.

Our research combines our expertise in astrocyte, oligodendrocyte and microglial development, their interaction with other elements of the brain parenchyma (matrix, neurons), and their phagocytic and regenerative potential to identify novel therapeutical targets using mouse models, iPSCs, and xenotransplants. In addition, our goal is to create a collaborative environment and for this purpose we foster monthly "chalk talk" meetings to discuss specific aspects of ongoing projects or papers.



Amaia  
Arranz



Mariana  
Astiz



Jimena Baleriola



Fabio  
Cavaliere



Héctor  
Flores-Romero



Susana  
Mato



José Ramón  
Pineda-Martí



Ainhoa  
Plaza-Zabala



Amanda  
Sierra



Federico N.  
Soria

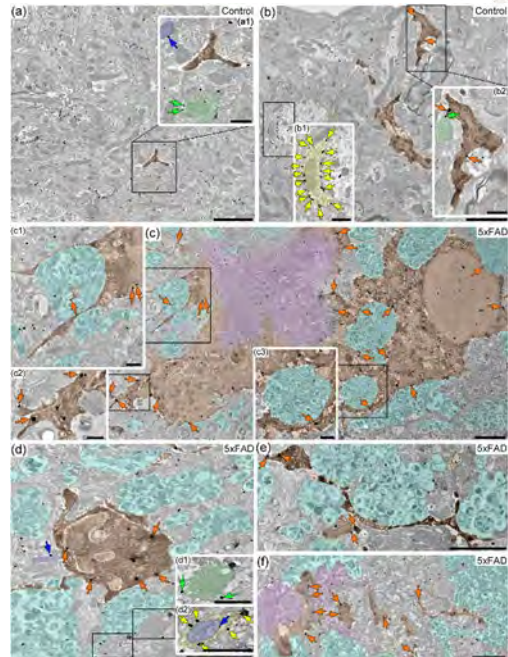
*The study sheds light on how chronic inflammation induced by amyloid beta aggregates in an AD model affects cannabinoid 1 receptor expression in microglia and astrocytes.*

## Cannabinoid 1 receptors in reactive glial cells of a mouse model of Alzheimer's Disease

To help understand the role of the endocannabinoid system in the pathophysiology of AD, the localization of the cannabinoid CB1 receptor was investigated in the subiculum severely affected by a large accumulation of plaques in a mouse model of AD (5xFAD/CB2<sup>EGFP/f/f</sup>).

High resolution immuno-electron microscopy revealed an increase in the number and proportion of CB1-positive microglial processes, as well as in the number of CB1 receptors in microglia surrounding amyloid plaques and dystrophic neurites. Conversely, a reduction in CB1 receptor density associated with the enlargement of the microglial processes. Finally, the number of CB1 receptors increased in astroglial processes.

The detailed correlation between glial reactivity and the CB1 receptor expression in microglia and astrocytes during the progression of AD shown in this investigation, is crucial to understand the role of cannabinoids in preventing glial activation and beta-amyloid (A $\beta$ )-induced neurotoxicity in AD.



### **“Altered glial expression of the cannabinoid 1 receptor in the subiculum of a mouse model of Alzheimer's disease”**

Terradillos I, Bonilla-del-Rio I, Puente N, Serrano M, [...], Elezgarai I, Grandes P

GLIA DOI: [10.1002/glia.24312](https://doi.org/10.1002/glia.24312)

## PUBLICATIONS

- 1) **Microglial phagocytosis dysfunction in stroke is driven by energy depletion and induction of autophagy**  
Beccari, Sol; Sierra-Torre, Virginia; [...] Plaza-Zabala, Ainhoa; Sierra, Amanda  
Autophagy (Jan, 2023) DOI: 10.1080/15548627.2023.2165313
- 2) **Characterization of microglia behaviour in healthy and pathological conditions with image analysis tools**  
Martinez, Aleix; Hériché, Jean-Karim; Calvo, Maria; Tischer, Christian; Otxoa-de-Amezaga, Amaia; Pedragosa, Jordi; Bosch, Anna; Planas, Anna M.; Petegnief, Valérie  
Open Biology (Jan, 2023) DOI: 10.1098/rsob.220200
- 3) **Microglia and meningeal macrophages depletion delays the onset of experimental autoimmune encephalomyelitis**  
Montilla, Alejandro; Zabala, Alazne; Er-Lukowiak, Marco; Rissiek, Björn; Magnus, Tim; Rodriguez-Iglesias, Noelia; Sierra, Amanda; Matute, Carlos; Domercq, María  
Cell Death & Disease (Jan, 2023) DOI: 10.1038/s41419-023-05551-3
- 4) **Editorial: Tumor Microenvironment in Primary Brain Cancers**  
Niechi, Ignacio; Pineda, Jose  
Frontiers in Oncology (Jan, 2023) DOI: 10.3389/fphar.2022.1039904
- 5) **Astrocyte endfoot formation controls the termination of oligodendrocyte precursor cell perivascular migration during development**  
Su, Yixun; Wang, Xiaorui; [...] Yi, Chenju; Niu, Jianqin  
Neuron (Jan, 2023) DOI: 10.1016/j.neuron.2022.10.032
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## New project to understand when and how the circadian clock starts to work

The 24-h (circadian) timing system develops during the perinatal period and rules our physiology later in life. It has the essential task of anticipating daily recurring changes in the environment (day/night) to find the best time for each molecular and cellular process. It is organised hierarchically, with a master pacemaker in the hypothalamic suprachiasmatic nucleus (SCN), which is able to perceive environmental light and tell the body what time it is.

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2024-2028

<https://www.achucarro.org/laboratory/circadian-physiology-of-neurons-and-glia/>

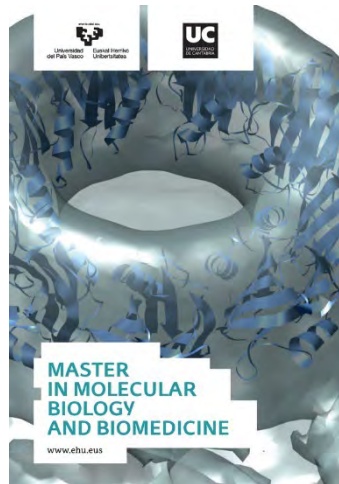
*Knowledge sharing is an important support for the continuous innovation and sustainable development of scientific research, and essential for positively impacting Society and global challenges.*

# 5. Knowledge Transfer

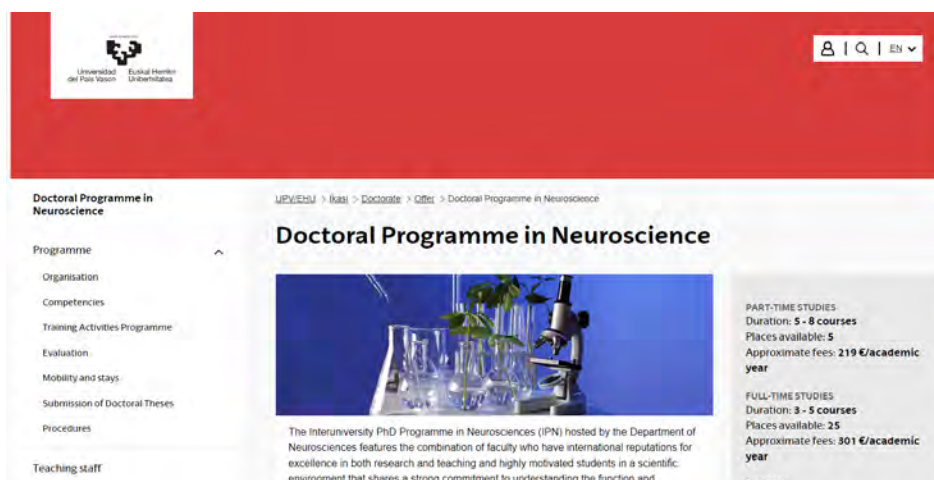
## POSTGRADUATE EDUCATION

The staff of ACHUCARRO collaborates with three Masters' programmes coordinated by the University of the Basque Country (UPV/EHU):

- Neuroscience
- Molecular Biology and Biomedicine
- Pharmacology, Development, Assessment, and Rational Use of Medicines



We also collaborate with the UPV/EHU's Doctoral Programme in Neuroscience.



## Congratulations **Zorionak Adhara, Aitor, Ana, Irene, Koldo and Paula**

### PHD THESES COMPLETED IN 2023

- ▶ **Dr. Koldo Berganzo**  
Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse  
*Dysautonomic disorders in Parkinson's disease*
- ▶ **Dr. Irene Durá Esteve**  
Laboratory of Neurogenesis and Neural Stem Cells  
*Traumatic Brain Injury-induced alterations in Adult Hippocampal Neurogenesis*
- ▶ **Dr. Adhara M. Gaminde Blasco**  
Laboratory of Glia and Matrix Biology  
*Identifying alterations in RNA metabolism and translation dynamics of oligodendrocytes in Alzheimer's disease*
- ▶ **Dr. Paula Giménez Mínguez**  
Laboratory of Neuronal Excitability  
*The role of the brain extracellular space in diffusion and cell signalling*
- ▶ **Dr. Aitor Medrano Peras**  
Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse  
*Topographic relationship between the subcellular localization of group II metabotropic glutamate receptors (mGlu2/3) and the cannabinoid CB1 receptor in the hilus region of the mouse dentate gyrus*
- ▶ **Dr. Ana Joya Villanúa**  
Laboratory of Neuroimaging and Biomarkers of Inflammation  
*Blood brain barrier disruption after subarachnoid hemorrhage: Role of hyperglycemia and effect of potentiating endogenous antioxidant mechanisms using molecular imaging.*

Another **62** theses (13% more than in 2022) are in different stages of this process.



## ACHUCARRO SEMINARS

### JANUARY

- 20 • **Is there any therapy for Alzheimer's disease?**  
**Jesús Ávila de Grado**  
 Centro de Biología Molecular "Severo Ochoa" CSIC/UAM (Madrid, Spain)
- 27 • **Deciphering synaptic autophagy to empower brain health**  
**Sandra Soukup**  
 Université de Bordeaux (France)

### FEBRUARY

- 01 • **Brain Organoids as Avatars to understand Human brain Development and Disease**  
**Paola Arlotta**  
 Harvard Stem Cell Institute [HSCI] (USA)
- 03 • **Virus delivered, brain circuit targetable, tightly-controlled inducible gene expression system**  
**Gorka Kortabarría Pérez**  
 Laboratory of Brain Circuits Therapeutics, ACHUCARRO
- **A $\beta$  oligomers cause dysregulation of RNA dynamics and translational activity in oligodendrocytes**  
**Adhara Gaminde Blasco**  
 Laboratory of Neurobiology, ACHUCARRO
- 06 • **Plasma biomarkers for the diagnosis of Alzheimer's disease (AD). A game changer.**  
**Pascual Sánchez Juan**  
 Fundación Centro de Investigación de Enfermedades Neurológicas (CIEN, Madrid)
- 17 • **Learning as a functional state of the brain**  
**José María Delgado García**  
 Universidad Pablo de Olavide (Seville)
- 24 • **Targeting Microglia via Engineered Adeno-associated Virus**  
**Rui Lin**  
 National Institute of Biological Sciences (China)

### MARCH

- 03 • **Astrocytes in neurodegenerative diseases**  
**Laura Civiero**  
 Università di Padova (Italy)
- 10 • **The matrix and the vision: new perspectives for imaging neuroinflammation**  
**Carmen Infante Duarte**  
 Charité - Universitätsmedizin Berlin (Germany)
- 17 • **Hypothalamic circuits regulating energy balance: the role of astrocytes**  
**Luis Varela Fernández**  
 Laboratory of Glia-Neuron Interactions in the Control of Hunger, ACHUCARRO
-

**MARCH**

- 24** • **The PIWI Pathway in Lifelong neurogenesis and neuroinflammation**  
Davide De Pietri Tonelli  
Istituto Italiano di Tecnologia (Italy)
- 31** • **What makes us human: a neuro-physiologist perspective**  
Albert Gidon  
NeuroCure, Charite - Universitatmedizin Berlin (Germany)

**APRIL**

- 14** • **Voltage mapping of dendritic spikes in Purkinje neurons of awake mice**  
Christopher Roome  
Okinawa Institute of Science and Technology (Japan)
- 21** • **Microglial brainization: intrinsic and environmental cues controlling developmental microglial maturation**  
Marta Pereira Iglesias  
Laboratory of Glial Cell Biology, ACHUCARRO
- 28** • **New Horizons: Gonadotropin-releasing hormone and cognition**  
Vincent Prévot  
Université de Lille (France)

**MAY**

- 05** • **Angelman Syndrome causing UBE3A ligase displays predominantly synaptic ubiquitination activity in the mouse brain**  
Ugo Mayor  
Ikerbasque - UPV/EHU (Leioa)
- 12** • **Traveling Through Uncharted Territory: Spatial Lipidomics of the Brain**  
José A. Fernández  
UPV/EHU (Leioa)
- 15** • **Circulating myeloid suppressor cells as a translational tool for biomarker discovery in multiple sclerosis**  
Diego Clemente  
National Hospital of Paraplegics & CIBERNED (Toledo, Spain)
- 19** • **Circulating insulin peptides and interoception**  
Ignacio Torres Aleman  
Laboratory of Neurobiology of Insulin Peptides, ACHUCARRO
- 26** • **Cell Therapy for Parkinson's disease using Carotid Body as a source of GDNF: pros and cons of the coronavirus pandemic**  
Juan José Toledo Aral  
Universidad de Sevilla (Spain)
-

**JUNE**

- 02 • **Whole brain perineuronal net and parvalbumin expression analysis in Fragile X mice**  
Ilaria Bertocchi  
University of Torino (Italy)
- 09 • **Non-invasive brain stimulation: an old tool into the hands of modern translational research**  
Marco Cambiaghi  
University of Verona (Italy)
- 16 • **Exercise on cognition**  
Jose Luis Trejo  
Instituto Cajal - CSIC (Madrid, Spain)
- 23 • **Junior symposium organized by the Laboratory of Neurobiology**  
Naroa Ibarra Aizpurua, Chao Zheng, Isabel Chato Astrain & Veronica Giusti  
Oxford, Karolinska, Nice - Sofia Antipolis & Padova
- 30 • **Disruption in the light/dark cycle alters the circadian regulation of female fertility**  
Valérie Simonneaux  
Institut des Neurosciences Cellulaires et Intégratives [INCI] (Strasbourg, France)

**JULY**

- 14 • **Modulation of synaptic translation by astrocytic extracellular vesicles in 5xFAD mice**  
Aída de la Cruz Gamba  
Laboratory of Local Translation in Neurons and Glia, ACHUCARRO

**SEPTEMBER**

- 15 • **Subcellular architecture studied by correlative light and electron microscopy**  
Alejandro Melero Carrillo  
Laboratory of GTPases and Neurosignalling, ACHUCARRO
- 22 • **Mechanisms of neuronal diversification and evolution**  
Nuria Flames Bonilla  
Instituto de Biomedicina de Valencia [CSIC] (Spain)
- 29 • **Genetic features controlling the specific expression of developmental genes**  
Álvaro Rada-Iglesias  
IBBTEC [CSIC/University of Cantabria] (Santander)
-



**OCTOBER**

- 06** • **Exploring Neurogenesis through the Olfactory System**  
 María Figueres Oñate  
 Instituto Cajal - CSIC (Spain)
- 11** • **In Vivo Multimodal Imaging of Adenosine A2A Receptors in Neuroinflammation after Experimental Stroke**  
 Maider Garbizu Albisu  
 Laboratory of Neuroimaging and Biomarkers of Inflammation, ACHUCARRO
- 18** • **The future of EEG and non-invasive neuromodulation in neuroscience and mental health applications**  
 Frank Zanow  
 Neuromotion BV (The Netherlands)
- 20** • **Gender specific differences in endocannabinoid regulation of obesogenic diet-induced memory deficits**  
 Guillaume Ferreira  
 University of Bordeaux (France)
- 27** • **Extracellular fluid circulation in the brain parenchyma and its role in Alzheimer's disease**  
 Juan A. Varela  
 University of St Andrews (UK)

**NOVEMBER**

- 03** • **Astrocytes as key elements in the efficiency of sensory information processing by cortical networks**  
 Juliana M Rosa  
 Hospital Nacional de Paraplégicos, IDISCAM (Toledo, Spain)
- 11** • **From synchronous to asynchronous: multiscale exploration of cortical state transitions**  
 María Victoria Sánchez-Vives  
 Clínic Barcelona - IDIBAPS (Barcelona)
- 13** • **Calcium regulation of neuronal energy metabolism. Mitochondrial calcium uniporter and Aralar/malate-aspartate shuttle**  
 Jorgina Satrústegui  
 CBMSO [UAM-CSIC] (Madrid, Spain)
- 24** • **Cortical interneurons in health and disease**  
 Oscar Marín  
 King's College London (UK)

**DECEMBER**

- 05** • **Neuroglia basis of behavior**  
 Edgar Soria-Gomez  
 Laboratory of Cellular Basis of Behavior and Disease, ACHUCARRO

Among our objectives we list the promotion of scientific knowledge and the dissemination a culture based on facts and critical thinking. This is also a personal and collective commitment of contributing to a well-informed Society.

## Dissemination and advocacy

We deploy our commitment to Outreach; Equality, Equity and Diversity; Talent Development; and fostering a culture of scientific literacy through various activities during the year.

February 11<sup>th</sup> and the commitment with Equality is present in many of our activities. In 2023 we joined forces with the ongoing initiative “Emakumeak Zientzian”, currently the reference movement towards equality in the field of science and technology in the Basque Country.



Elena Alberdi at “Parekoen Topaketa” organised by BilbaoEkintza and Elhuyar



Collaborations with Pint of Science Bilbao



Talks at High Schools



Neuroscience Day 2023



Hosting the visit of Wake Forest College

Many times, these activities require not only the commitment but the personal effort of our staff and volunteers.

**Many thanks to all of you.**  
**Eskerrik asko.**

You can check all the information on our website: <https://www.achucarro.org>

*The Science Park of the UPV/EHU in Leioa, hosts the headquarters of ACHUCARRO.  
In 2023 we increased our premises by 50% with the support of IKERBASQUE.*

## 6. Infrastructure and Equipment

In the one hand, the proximity with Bilbao, and communications hub, and in the other hand, our location in the campus of the University provide us a perfect environment to develop our mission.

The settlement within the campus, close to the general research facilities to support research provided by the UPV/EHU (i.e., optical and electronic microscopy, genomics, proteomics, etc.); also the potential to partnering with other neighbouring R&D agents in the area allow us to jointly develop investment strategies to complement the existing and to complement those specific scientific resources of each sector and research field.

ACHUCARRO currently occupies the third floor of the Sede building, a space of 3000 m<sup>2</sup> in a privileged location within the campus of the UPV/EHU.



Some of the research groups also have laboratories and offices in the School of Medicine and Nursing, only 400 metres from the main location.

<https://www.achucarro.org/facilities>

*New challenges deriving from the scientific progress in biomedicine and the new European strategy directed to develop more relevant biomodels to study the human physiology, pushed us to find new human biomodels to study the human brain physiology.*

## The Basque Biomodels Platform for Human Research

The Basque Biomodels Platform for Human Research (BBioH) is a collaborative initiative of Achucarro Basque Center for Neuroscience and the Instituto Biofisika (UPV/EHU-CSIC) in partnership with the Fundación Biofísica Bizkaia.

BBioH is funded in part by the Department of Education of the Basque Government under the IKUR Strategy, with additional support from the Spanish Ministry of Science and Innovation with funding from European Union NextGenerationEU.

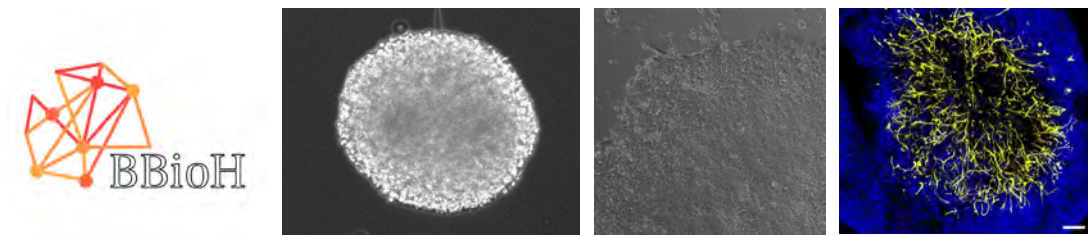
### Main objectives

BBioH is the first public-based human biomodels platform in Basque Country and the second in Spain, specialized in human brain organoids. We foster the use of human 2D and organoid models in basic and applied research. The main scientific objective is to reproduce the human brain development in normal and pathological conditions, whereas the three strategic objectives are: 1. to promote collaborations between BERCS; 2. to create links between basic, clinic and applied research; 3. to elevate Euskadi as a referent in the field of personalized medicine.

### A multidisciplinary approach to the clinics, industry, and academic research.

BBioH proposes a multidisciplinary approach with the support of other associated units in Achucarro like the platform of biomarkers, molecular biology, imaging, and the collaboration of the Basque Resource for Electron Microscopy (BREM). Moreover, we collaborate with the Basque Institutes of Health Research (Biobizkaia and Biogipuzkoa) for the use and recruitment of human samples, the Research Institutes in biomaterials like BCMaterials and Tecnalía and the University of Basque Center.

In 2023 we already offered our services abroad to the University of Piemonte Orientale (Italy), University of Padova (Italy) and University of Bologna (Italy).



More information: <https://www.achucarro.org/facilities/human-biomodels/>

*The Basque Government sets scientific and management objectives for research organisations with the BERCA accreditation.*

## 7. Main performance indicators

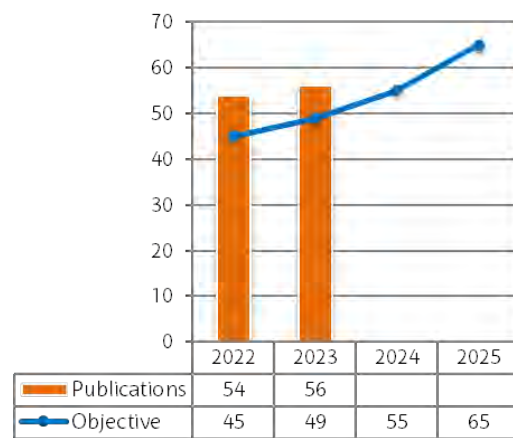
The following indicators reflect the evolution on the performance of ACHUCARRO, with this panel agreed by the Basque Government and ACHUCARRO for the current strategic period.

The following indicators strive to show the development of our organization, according to some external (partners and funders) and internally defined parameters.

Our overall assessment is very positive. Some indicators have reflected the effects of the global pandemic (in the years 2022 and 2021), and others clearly reflect the degree of maturity and consolidation of ACHUCARRO.

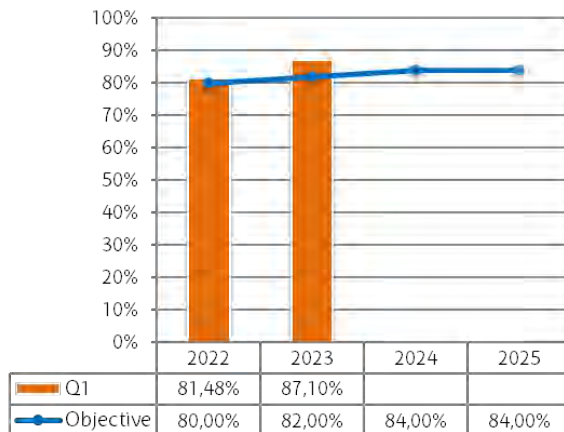
*Total number of indexed publications*

Sources:  
Scopus & Web of Science



*% of publications in quartile 1 of their research areas*

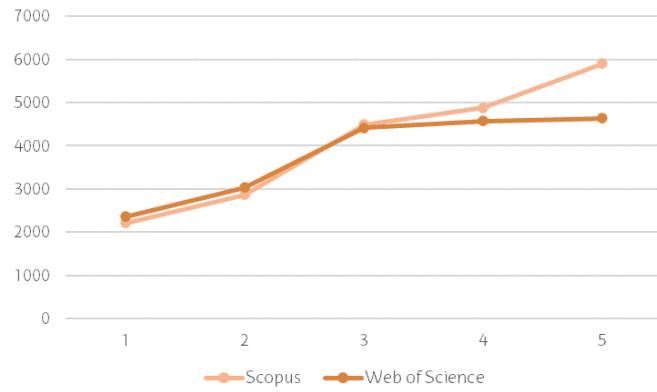
Source:  
Scimago Journal Ranking



*Total citations*

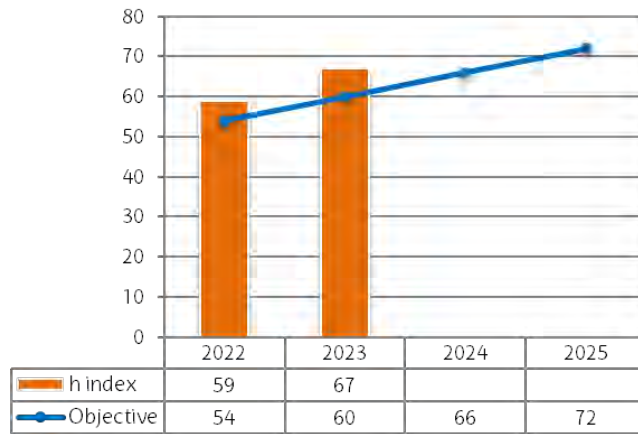
Source:  
Scopus & Web of Science

*This total amount produce a mean of 9 citations per document*



*h-index of ACHUCARRO*

Source:  
Scopus



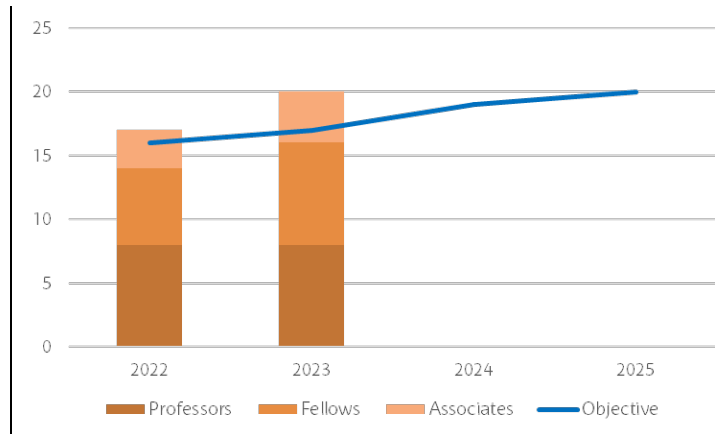
Scopus and Web of Science produce similar numbers for the h-index indicator, while Google Scholar reflects 104 for the same indicator.

<https://scholar.google.es/user=hO1jBxYAAAAJ>

In terms of talent attraction and collaboration with the strategic objectives of IKERBASQUE, we keep hosting a good number of their researchers, and contributing to their career development and retention.

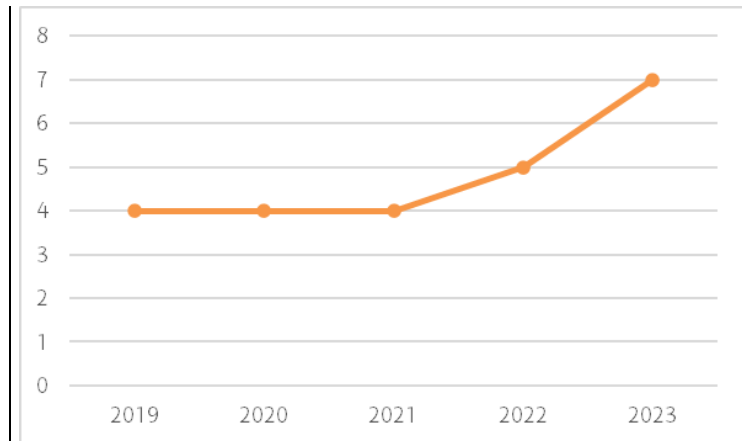
*Total number of Ikerbasque Researchers (Professors, Associated and Fellows)*

Source:  
Internal



*Total number of Ramón y Cajal Fellows*

Source:  
Internal

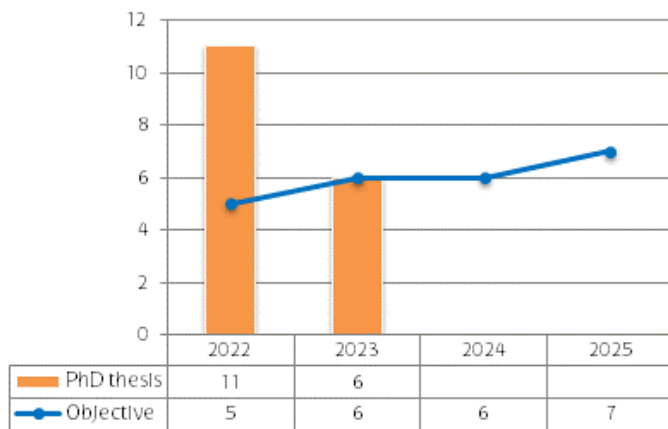




The improvement of conditions after the restrictions of the pandemic (2020 and 2021) had a clear and positive effect on the number of PhD thesis successfully defended in 2022. During the pandemic we were below the forecast, but once recovered, we overcame the expected numbers.

*Completed  
PhD Thesis*

Source:  
Internal



In addition, our commitment with postgraduate education and contribution to the supervision of Masters' dissertation continues to increase, as the number of students taking these degrees is also increasing in our environment.

*Completed  
Masters'  
Dissertations*

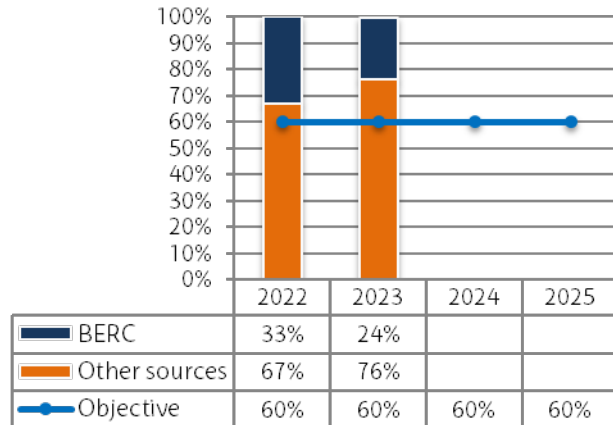
Source:  
Internal



The financial stability and sustainability of ACHUCARRO keeps consolidating, derived from the increase in the attraction of funding, both nationally and internationally, public and private.

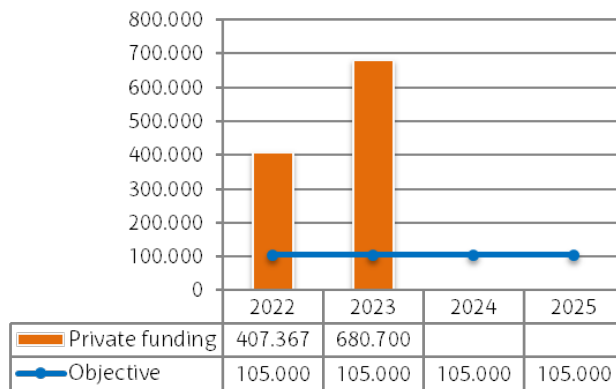
*% of funding different from BERC*

Source: Internal



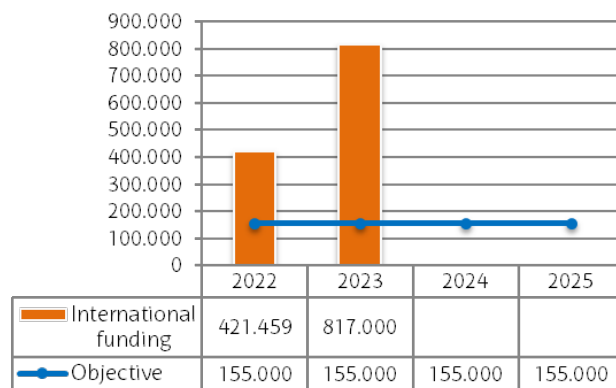
*Private funding (EUR)*

Source: Internal

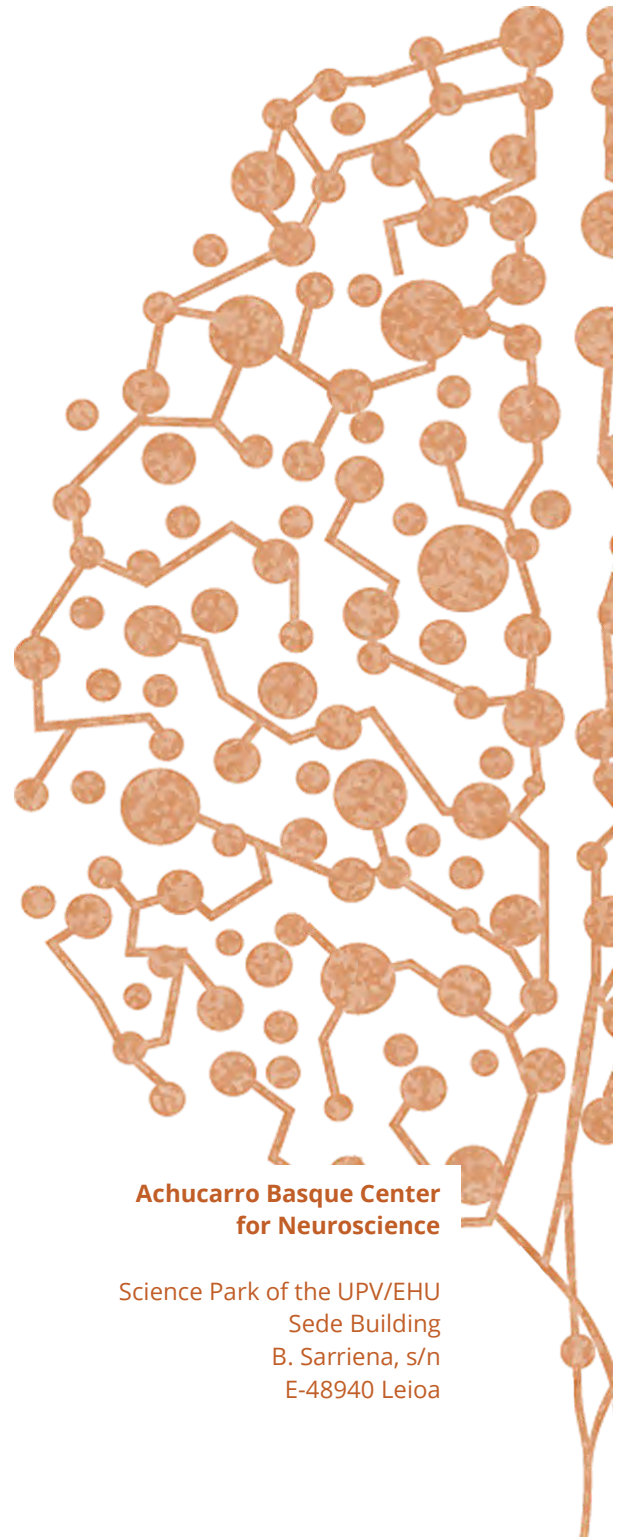


*International funding (EUR)*

Source: Internal







**Achucarro Basque Center  
for Neuroscience**

Science Park of the UPV/EHU  
Sede Building  
B. Sarriena, s/n  
E-48940 Leioa