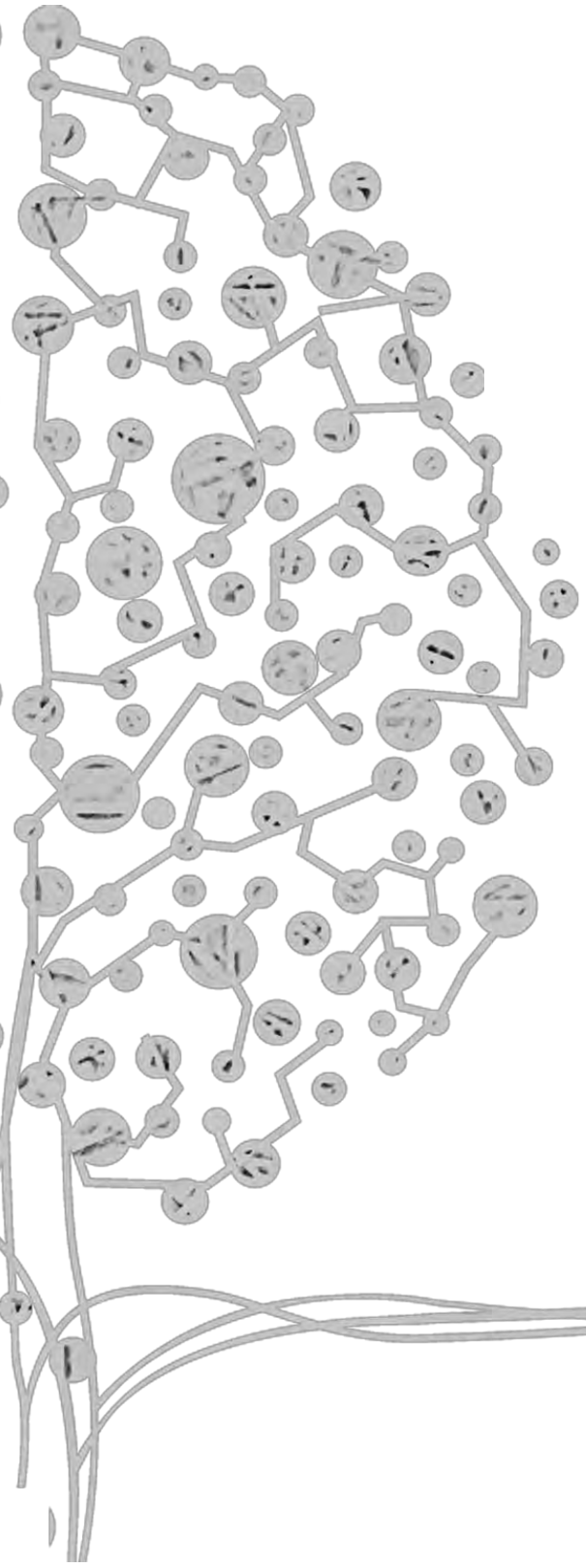

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Achucarro

BASQUE CENTER FOR NEUROSCIENCE

scientia ad remedium

2022

Annual Report

Contents

Foreword

Dear reader,

The past year has witnessed the gradual recovery of activity in Achucarro after the pandemic lock down of previous years. Collectively, our research output during 2022 has been satisfactory, with a total of 70 papers published with 84% of them in Q1. The future looks bright as the centre continues growing with new groups that are incorporating novel research topics, resources, methodologies, and concepts.

During this year, an internal re-organization has taken place, in accordance with the implementation of the new 2022-25 strategic plan supported by the BERC Program of the Basque Government. All research groups are now distributed attending to their main research goals into 3 Programs focused on Neuro-glial interactions in brain diseases, Glial modulation of brain structure and function, and Gliotheranostics.

This organization is oriented to strengthen our capacities, foster stronger internal collaborations, and concentrate in specific current challenges in Neuroscience, most prominently in search for novel therapies and diagnosis of brain diseases.

In parallel, we have reinforced and set up several key core facilities to provide additional technical support to our investigators. In this regard I would like to highlight the reinforcement of the Biomodels platform that will soon become fully operative with its new facilities, and the organization and staffing of the new Molecular Biology facility and the Phenomics platform (housed at the Animal Facility of the University). Setting up these facilities has been possible thanks to the launching of the IKUR Strategy that is heavily influencing the capabilities of ACHUCARRO through hiring qualified personnel and acquiring much needed state-of-the-art equipment.

Undoubtedly, the continued support and commitment of the Basque Government, Ikerbasque - the Basque Foundation for Science, and the University of the Basque Country (UPV/EHU) is key to unfold our scientific strategy.

Ignacio Torres Alemán
Scientific Director

Elena Alberdi Alfonso
Assistant Scientific Director

In 2022 we launched our third strategic programme.
This new plan strives to strengthen internal collaborations through the new three research programmes.

1. Strategy and Management

ACHUCARRO is one of the BERC (Basque Excellence Research Centres) research organisations fostered by the Department of Education of the Basque Government. There are 9 organisations recognised as BERC within the Basque Science, Technology and Innovation network, and ACHUCARRO is one of the three youngest centres of the network. Three of them were created before 2007; other three in 2007, just after the creation of Ikerbasque, the Basque Foundation for Science; and the last three in 2012. Each BERC has a different specialisation and scientific approach.

ACHUCARRO is the only one centred in the study of neurobiology. There are four on physics/chemistry (DIPC, MPC, Polymat, BCMaterials), one in biophysics (Institute Biofisika), one in climate change (BC3), one in applied mathematics (BCAM), and one in cognitive neuroscience and language (BCBL).

In the year 2022, we launched our third strategic plan for the period 2022-2025. The overall objective of the ACHUCARRO is to perform co-ordinated multidisciplinary research of the brain functions on all levels from single molecules through individual cells and acutely isolated nervous tissues to the brain networks operating in vivo 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, within the University campus in Leioa.
- Assess and incorporate the latest **technologies and equipment** to let the centre operate in 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**.

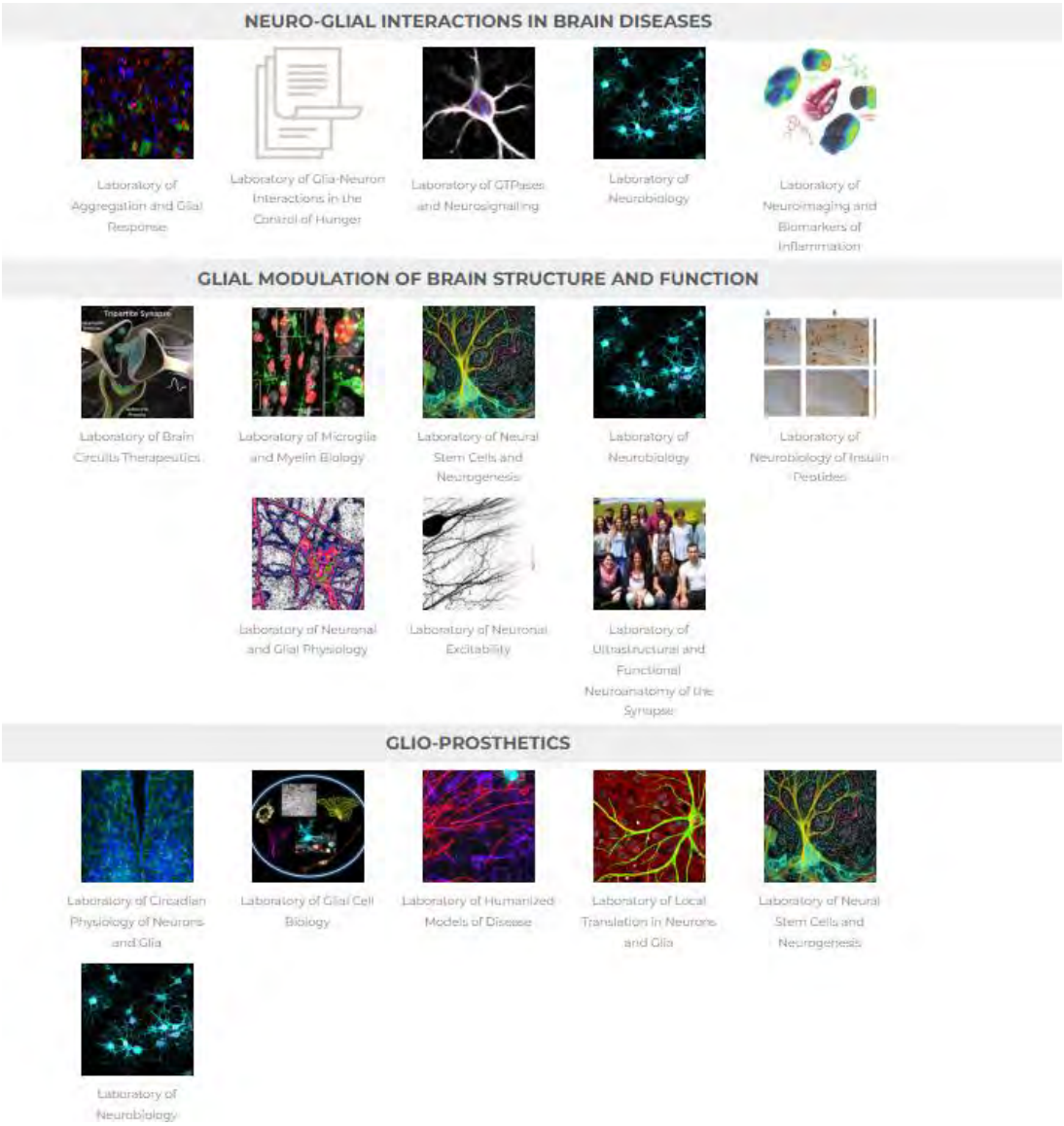
SCIENTIFIC PLAN 2022–2025

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

The new Scientific Plan has defined three programmes, with a bottom-up approach, to attain that strategy and fostering internal collaboration and the maximization of impact.

Research Programmes

- Neuro-Glial interactions in brain diseases
- Glial modulation of brain structure and function
- Gliotheranostics (previously Glio-prothetics)

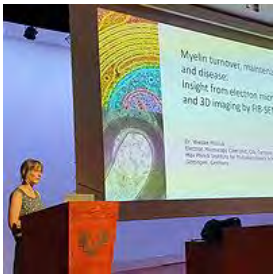


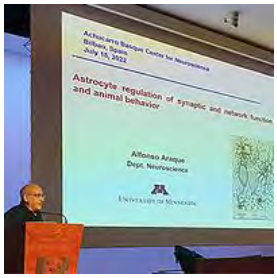
_ TENTH ANNIVERSARY _

In mid-2022 we turned ten years old. In July, we just left behind the sanitary restrictions caused by the SARS-CoV-2 pandemic and could gather in Bilbao to celebrate this jubilee.

ZORIONAK ACHUCARRO!

We invited four friends and collaborators to the celebration symposium at the Main Hall of the UPV/EHU in Bilbao, the Bizkaia Aretoa.





- Carlos Matute (first Scientific Director of ACHUCARRO)
  - *"Celebrating our 10th Anniversary"*
- Wiebke Möbius (Germany)
  - *"Myelin turnover, maintenance and disease: insight from electron microscopy and 3D imaging by FIB-SEM"*
- Giovanni Marsicano (France)
  - *"Cannabinoids, mitochondria and behavior"*
- Rosa Paolicelli (Switzerland)
  - *"The many roles of microglia in brain development and disease"*
- Alfonso Araque Almendros (USA)
  - *"Astrocyte regulation of synaptic and network function and animal behavior"*

(*) Zorionak is the Basque word for happy birthday.

EQUALITY AND INCLUSION PLAN 2022-2025

ACHUCARRO developed the first specific Equality Plan in 2017, with the consulting and advice of an external firm specialised in this sector. During 2021 we underwent the evaluation process of the previous plan, to define and develop the second plan.

Our **Equality Committee (EC)** is composed by representatives of all the staff, on different functions or career stages, and with gender balance. The EC is the pilot and evaluator of all the activities in this plan.

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 the gender perspective in the policies, products, and operating dynamics
4. Promote inclusive leadership styles.

The plan has contributed to many improvements, and we are sure will continue supporting more equity, equality and inclusion. We are glad to see that the balance and representation in leadership roles is evolving positively.

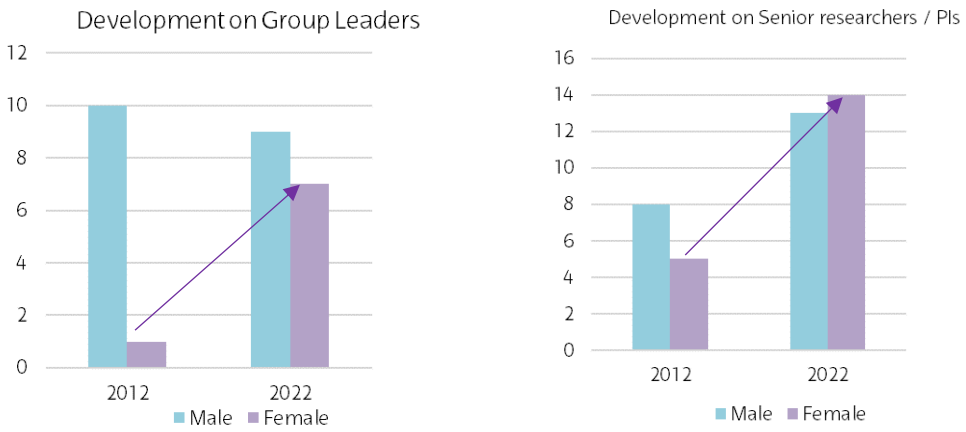


Figure 1. Evolution of number of Group Leaders and Principal Investigators by gender, from 2012 to 2022

https://www.achucarro.org/equality

Commitment with Equity, Equality and Diversity

BASQUE PACT FOR EQUALITY AND LIVING FREE OF VIOLENCE AGAINST WOMEN

Emakunde, the Basque Women's Institute developed, in the framework of UN Women's international initiative "Generation Equality" a pact to show the commitment of individuals and collectives in our region towards equality and free of violence against women.

This Pact was presented in Bilbao, on June 15th, by all the authorities in our region.

ACHUCARRO is one of its signatories.

***"If you want to go quickly, go alone. If you want to go far, go together"* African proverb.**

2. Partnerships and Collaborations

Working together with other people and institutions is key to unravel the challenges of this changing World. Weaving a solid network of collaborators takes time and efforts, and the selection of 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

- Agreement to support the activities of the centre in the period 2022–2025.

BASQUE SCIENCE, TECHNOLOGY, AND INNOVATION NETWORK

- Attachment to this 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 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.

In 2020 we received renewed the HR Excellence in Research recognition awarded by the European Commission, after a fruitful site visit with experts from other European Institutions.

CIBER

The Center for Biomedical Research in Network is a research organization with its own legal personality, 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 the 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.

Our International Scientific Advisory Committee is a panel of distinguished researchers in different areas of neuroscience that provide us with their view and opinion on the strategic and operational subjects for the better development of ACHUCARRO.

INTERNATIONAL SCIENTIFIC ADVISORY COMMITTEE (ISAC)

In 2022 we have partially renewed of advisory committee, and together with this we balanced the gender representation. Isabel Fariñas, Anna Planas and Pablo Villoslada will continue their appointment in this panel, and Alfonso Araque, Rafael Fernández Chacón and Carmen Sandi joined as new members.

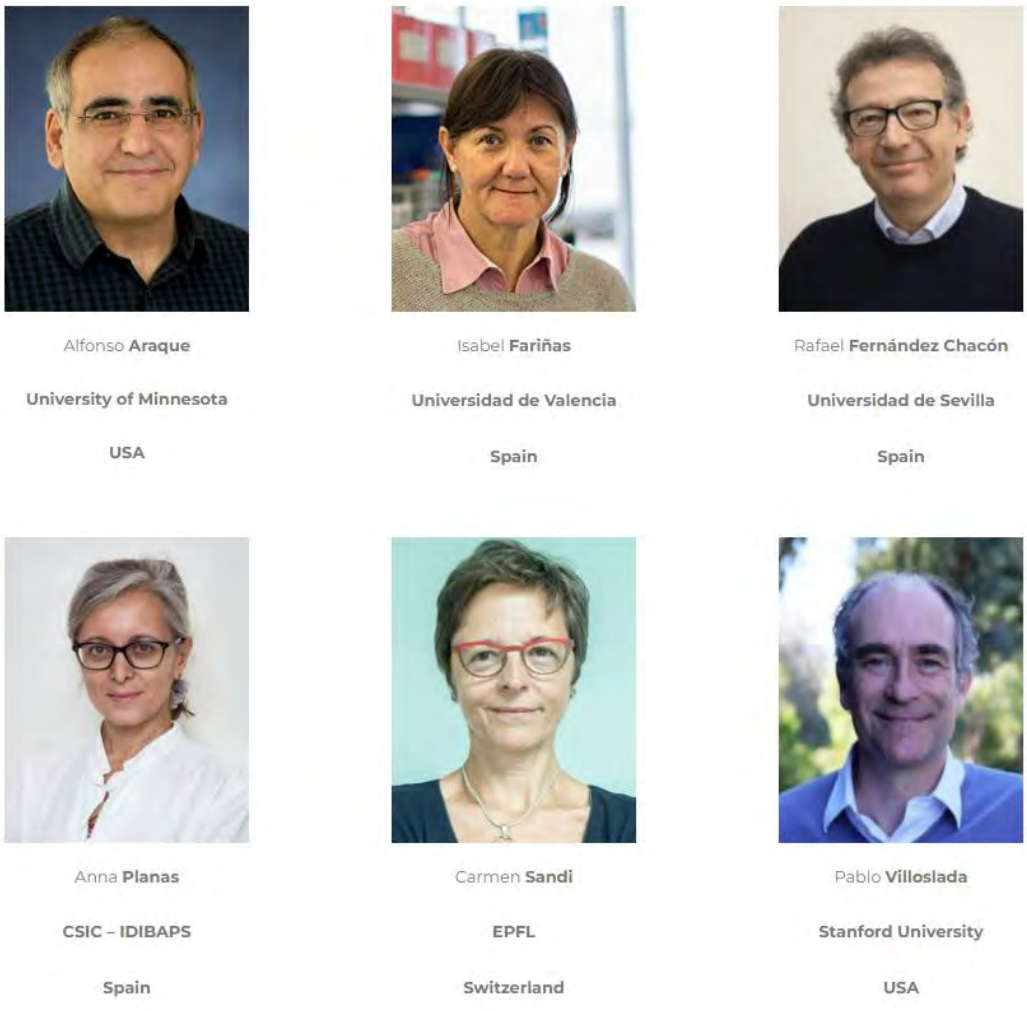


Figure 2. Current members of the ISAC

We want to thank the support and commitment of past members Jesús Ávila de Grado, Erik Boddeke, Helmut Kettenmann, Frank Kirchhoff, Jose A. Obeso, and Bruce Ransom.

_ HIGHLIGHT IN RESEARCH OUTCOMES _

This article published in EMBO Molecular Medicine introduced a novel, clinically relevant strategy to enhance myelin regeneration in multiple sclerosis (MS), thus prevent axonal degeneration.

While several candidate remyelinating molecules have been identified using animal models, clinical studies performed so far have shown scarce benefits, which may be due at least in part to limited arrival of these therapeutic molecules to MS lesions, disseminated in the central nervous system

Moreover, precise molecular targeting to MS lesions is indispensable for therapies that aim to stimulate the recruitment of oligodendrocyte progenitor cells (OPCs) to the areas of demyelination by overexpressing OPC attractants, such as Semaphorin 3F (Sema3F), specifically in the areas of demyelination.

Here, *for the first time*, the authors propose gene therapy of hematopoietic cells, **a clinical approach used to treat patients with leukodystrophies**, as a strategy to target the delivery of remyelination-enhancing molecule to demyelinating central nervous system lesions. Hematopoietic stem/progenitor cells (HSCs) were genetically modified in vitro to overexpress Sema 3F, an OPC attractant and then transplanted to pre-conditioned host mice, where they gave rise to circulating monocytes. After induction of demyelination, Sema3F-overexpressing blood-derived macrophages quickly and efficiently targeted demyelinating lesions in the spinal cord, which enhanced OPC recruitment and accelerated the onset of remyelination.

The authors thus concluded that ***blood-derived macrophages are efficient and reliable vehicles*** to ensure the delivery of ***repair-promoting molecules at the right time and to the right place.*** This work paves the way for novel advanced therapies to prevent neurodegeneration.

More information:

Genetically modified macrophages accelerate myelin repair
Aigrot, MS; Barthelemy, C; Moyon, S; [...]; Matute, C; Cartier, N; Lubetzki, C; Tepavčević, Vanja
EMBO Molecular Medicine (Jul-13) DOI: 10.15252/emmm.202114759

We are an organisation of professionals from 24 different nationalities. Foreigners represent 17% of the staff, and a contribution to diversity and internationalisation.

3. People

In 2022 we continued our growth (15% from 2021 to 2022). This means that at the end of 2022 ACHUCARRO had 132 people appointed.

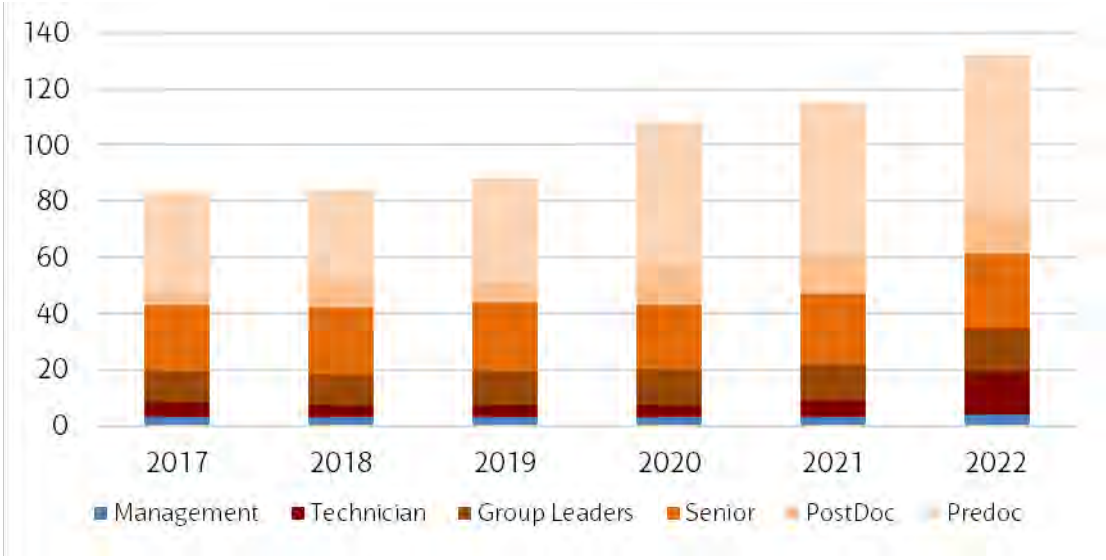


Figure 4. Evolution of personnel 2017-2022

During the year there has been the rotation of several people, 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.

CAREER DEVELOPMENT

Following our commitment with the management models and its supporting strategies and policies, like the European Commission's Human Resources Strategy for Research (HRS4R), we organised different internal training activities to support career development.

APPOINTED STAFF (December 2022)

Oihane ABIEGA ETXABE · Laura AGUADO SANTOS · Elena María ALBERDI ALFONSO · María ALFONSO TRIGUERO · Mikel ALVAREZ TUEROS · Saioa ALZOLA ALDAMIZETXEBARRIA · María Isabel ARDAYA FRANCO · Amaia ARRANZ MENDIGUREN · Mariana ASTIZ CADENAS · Izaro ATUTXA DIONISIO · Uxue BALANTZATEGI FERNANDEZ DE ARROIABE · Jimena BALERIOLA GÓMEZ DE PABLOS · Andrés Mateo BARAIBAR SIERRA · Laura BAYÓN CORDERO · Nora BENGOA VERGNIORY · Xabier BENGOETXEA BAUSELA · Ana BERNAL CHICO · Itziar BONILLA DEL RÍO · Leire BOVEDA ALTUBE · Ianire BUCETA SALAZAR · Izaskun BUENDÍA ABAITUA · Stefano CALOVI · Estibaliz CAPETILLO GONZÁLEZ DE ZARATE · Alejandro CARRETERO GUILLÉN · Fabio CAVALIERE · Juan Carlos CHARA VENTURA · Dalila CICERI · Raffaela CIPRIANI · Teresa COLOMER MOLLA · Garazi CONDE PERAL · Lorea CORTÉS MELER · Joan CRUZ SESÉ · Aída DE LA CRUZ GAMBRA · María DOMERCQ GARCÍA · Jonathan Evan DRAFFIN · Jon EGAÑA HUGUET · Izaskun ELEZGARAI GABANTXO · Juan Manuel ENCINAS PÉREZ · Laura ESCOBAR CASTAÑONDO · Mario FERNÁNDEZ BALLESTER · Nuria GALBIS GRAMAGE · María Tatiana GALLEGO FLORES · María GAMARRA GARCÍA-BERMEJO · Adhara Mikaela GAMINDE BLASCO · Maider GARBIZU ALBISU · Laura GARCÍA GASTAÑAGA · Fernando GARCÍA MORENO · Lorena GARCÍA RUIZ-CLAVIJO · Paula GIMÉNEZ MÍNGUEZ · Sonia GÓMEZ URQUIJO · Pedro Rolando GRANDES MORENO · María Inmaculada GUERRICAGOITIA MARINA · Juan José GUTIÉRREZ MARTÍN · Mazahir T. HASAN · Katharina HAURY · María Isabel HERNÁNDEZ CORTÉS · Tamas HORVATH · Izaskun IGEREGI ARTETXE · Leire IGLESIAS IGLESIAS · Josune IMAZ IRURETAGOYENA · Leire IZAGIRRE URIZAR · Ana JOYA VILLANUA · Gorka KORTABARRIA PÉREZ · Maria KUKLEY · Begüm KURT · Leire LECUMBERRI ODRIOZOLA · Nerea LLAMOSAS MUÑOZGUREN · Eneritz LÓPEZ MUGURUZA · Irene LUENGAS ESCUZA · Joel MALDONADO TEIXIDÓ · Mar MARQUEZ ROPERO · Zara MARTÍNEZ PÁEZ · Abraham MARTÍN MUÑOZ · Soraya MARTÍN SUAREZ · Gilda Paloma MATA SALGADO · Susana MATO SANTOS · Carlos José MATUTE ALMAU · Juan Luis MENDIZABAL ZUBIAGA · Amaia MIMENZA SAIZ · Patricia MIRANDA AZPIAZU · Fosca MIRATA · Alejandro MONTILLA LÓPEZ · Oscar MORENO · Teresa MURO GARCÍA · Garazi OCERIN AMONDARAIN · 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 · Aitor SALAGRE PÉREZ · Alberto PÉREZ SAMARTÍN · José Ramón PINEDA MARTÍ · Ainhoa PLAZA ZABALA · Nagore PUENTE BUSTINZA · Laura PULIDO LÓPEZ · Paula RAMOS GONZÁLEZ · Almudena RAMOS URIARTE · Leire REGUERO ACEBAL · Pablo Alejandro REYES VELASQUEZ · Irantzu RICO BARRIO · Rizky Sarakhsi Ersaid LASABUDA · Ane RODRÍGUEZ BODERO · Noelia RODRÍGUEZ IGLESIAS · Leire RUIZ BARREIRO · Asier RUIZ NUÑEZ · Jaime SAGARDUY BARRENA · María Victoria SÁNCHEZ GÓMEZ · Dann SÁNCHEZ IRAOLA · Ester SANCHEZ MARTÍN · Ane SANTISTEBAN GARCÍA · Rafael SARRÍA AROSTEGUI · Rodrigo SENOVILLA GANZO · Maitane SERRANO MURGIA · Amanda SIERRA SAAVEDRA · Edgar Jesús SORIA GÓMEZ · Federico Nicolas SORIA LANNES · Vanja TEPAVCEVIC MANDIC · Irene TOMÉ VELASCO · Jan TØNNESEN · Ignacio TORRES ALEMÁN · Nagore TORRES DURÁN · Nerea URRESTIZALA ARENAZA · Luis VARELA FERNÁNDEZ · Maria Paola Anna VELLA · Alexei VERKHRATSKY · Patricia VILLEGAS ZAFRA · Jonathan Adrián ZEGARRA VALDIVIA · José Luis ZUGAZA GURRUCHAGA

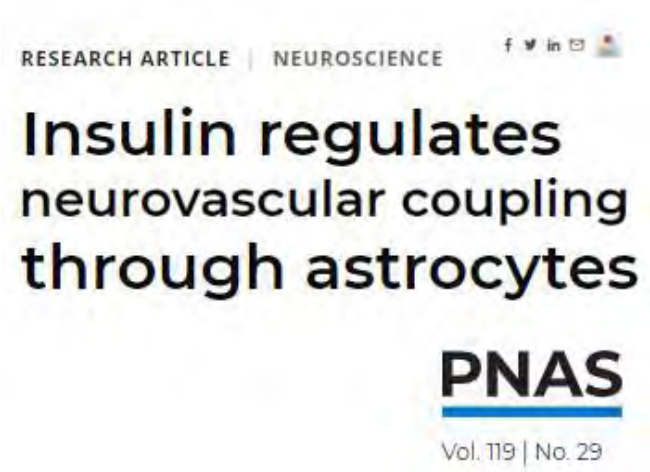
_ HIGHLIGHT IN RESEARCH OUTCOMES _

A collaborative investigation led by the laboratory of Ignacio Torres Aleman helps explain the role of astrocytes at the blood-brain-barrier (BBB), a functional interface between the brain and the body.

The role of astrocytes at the blood-brain-barrier (BBB), a functional interface between the brain and the body.

Upon activation, neurons require extra energy (glucose) and oxygen supply. This requirement is satisfied through a process dubbed "neurovascular coupling", whereby active neurons obtain nutrients and oxygen on demand.

Acting through astrocytes, insulin, a hormone involved in energy allocation throughout the body, modulates the formation of new brain vessels and brain glucose capture, assuring in this way proper coupling between glucose needs and blood supply. Disturbed insulin signaling onto astrocytes uncouples brain glucose uptake with brain blood flow due to excess oxidative stress at astrocyte mitochondria. Pharmacological amelioration of oxidative stress restores neurovascular coupling. Since many brain maladies present altered glucose handling and/or brain blood flow, insulin receptors in astrocytes may constitute a new therapeutic target for these diseases.



Insulin regulates neurovascular coupling through astrocytes
Fernandez AM, Martinez-Rachadell L, Navarrete M [...] and Torres-Aleman I.
PNAS (Jul-19) DOI: https://doi.org/10.1073/pnas.2204527119

Our research staff contributed to 70 new scientific publications in 2022. 84% of them in the first quartiles of their research fields. 79% of the publications are in Open Access.

4. Research

RESEARCH GROUPS

Laboratory of Aggregation and Glial Response

Nora Bengoa Vergniory
Ikerbasque Research Fellow

Laboratory of Brain Circuits Therapeutics

Mazahir T. Hasan
Ikerbasque Research Professor

Laboratory of Circadian Physiology of Neurons and Glia

Mariana Astiz
Ikerbasque Research Fellow

Laboratory of Glia-Neuron Interactions in the Control of Hunger

Luis Varela
Ikerbasque Research Fellow

Laboratory of Glial Cell Biology

Amanda Sierra
Ikerbasque Research Professor

Laboratory of GTPases and Neurosignalling

Jose Luis Zugaza
Ikerbasque
Research Professor

Laboratory of Humanized Models of Disease

Amaia Arranz
Ikerbasque
Research Fellow

Laboratory of Local Translation in Neurons and Glia

Jimena Baleriola
Ikerbasque
Research Associate

Laboratory of Neural Stem Cells and Neurogenesis

Juan Manuel Encinas
Ikerbasque
Research Professor

Laboratory of Neurobiology

Carlos Matute
Full Professor
Department of Neurosciences (UPV/EHU)

Laboratory of Neurobiology of Insulin Peptides

Ignacio Torres Alemán
Ikerbasque Research Professor

Laboratory of Neuroimaging and biomarkers of inflammation

Abraham Martín
Ramón y Cajal Fellow

Laboratory of Neuronal and Glial Physiology

Maria Kukley
Ikerbasque Research Professor

Laboratory of Neuronal Excitability

Jan Tønnesen
Ramón y Cajal Fellow
Department of Neurosciences (UPV/EHU)

Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse

Pedro Grandes
Full Professor
Department of Neurosciences (UPV/EHU)

_ HIGHLIGHT IN RESEARCH OUTCOMES _

A $275,000 grant from The Michael J. Fox Foundation for Parkinson's Disease (MJFF) will fund a project investigating the neuroprotective potential of REST, aimed to improve neuronal health and motor function in PD.

The Bengoa-Vergniory lab awarded a grant by The Michael J. Fox Foundation to study a neuroprotective target for Parkinson's disease.

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease and is characterized amongst other features by the degeneration of dopaminergic neurons within the substantia nigra. The molecular mechanisms leading to neuronal cell loss in PD are still under investigation. One of the most promising approaches against PD is the identification and characterization of neuroprotective molecules, with a goal of stimulating them to rescue affected neurons.

Dr. Nora Bengoa-Vergniory, head of the laboratory of Aggregation and Glial Activation, recently reported that REST is required as a regulatory factor for cellular energy metabolism. In addition, they demonstrated that REST attenuates the toxic effects of the aggregation of the protein α-synuclein, a hallmark of PD pathogenesis. This year, Dr. Bengoa-Vergniory has been awarded a grant by MJFF to further investigate whether REST overexpression could improve neuronal health and motor performances of PD mouse models.

THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

PUBLICATIONS

1) A Comprehensive Introduction to Magnetic Resonance Imaging Relaxometry and Contrast Agents
   ACS Omega 10.1021/acsomega.2c03549
2) A high-fat diet changes astrocytic metabolism to promote synaptic plasticity and behavior
   Acta Physiologica 10.1111/apha.13847
3) Acidic nanoparticles protect against α-synuclein-induced neurodegeneration through the restoration of lysosomal function
   Aging Cell 10.1111/acel.13584
4) Longitudinal evaluation of neuroinflammation and oxidative stress in a mouse model of Alzheimer disease using positron emission tomography
   Alzheimer's Research & Therapy 10.1186/s13195-022-01016-5
5) Evolution of neuroglia
   Annals of the New York Academy of Sciences 10.1111/nyas.14917
6) Stimulation of synaptic activity promotes TFEB-mediated clearance of pathological MAPT/Tau in cellular and mouse models of tauopathies
   Autophagy 10.1080/15548627.2022.2095791
7) Plasticity of microglia
   Biological Reviews 10.1111/brv.12797
8) Enhanced Adipogenic Differentiation of Human Dental Pulp Stem Cells in Enzymatically Decellularized Adipose Tissue Solid Foams
   Biology 10.3390/biology11081099
9) A Comparative Study of Cell Culture Conditions during Conversion from Primed to Naive Human Pluripotent Stem Cells
   Biomedicines 10.3390/biomedicines10061358
10) Activation of Wnt/β-catenin pathway mitigates blood–brain barrier dysfunction in Alzheimer's disease
    Brain 10.1093/brain/awac236
11) Oligodendrocyte progenitor cell recruitment and remyelination in multiple sclerosis: the more, the merrier?
    Brain 10.1093/brain/awac307
12) Clock Genes Profiles as Diagnostic Tool in (Childhood) ADHD—A Pilot Study
    Brain Sciences 10.3390/brainsci12091198
13) Time in Neurogenesis: Conservation of the Developmental Formation of the Cerebellar Circuitry
    Brain, Behavior and Evolution 10.1159/000519068
14) Vesicle cholesterol controls exocytotic fusion pore
    Cell Calcium 10.1016/j.ceca.2021.102503
15) Astrocytes regulate action potential propagation in myelinated axons: It is very crowded at the node of Ranvier
    Cell Calcium 10.1016/j.ceca.2021.102518

16) The great astroglial metabolic revolution: Mitochondria fuel astrocyte homeostatic support and neuroprotection
Cell Calcium 10.1016/j.ceca.2022.102583
17) Amyloid ß / PKC-dependent alterations in NMDA receptor composition are detected in early stages of Alzheimer´s disease
Cell Death & Disease 10.1038/s41419-022-04687-y
18) Ageing related thyroid deficiency increases brain-targeted transport of liver-derived ApoE4-laden exosomes leading to cognitive impairment
Cell Death & Disease 10.1038/s41419-022-04858-x
19) Cannabinoid CB1 receptor gene inactivation in oligodendrocyte precursors disrupts oligodendrogenesis and myelination in mice
Cell Death & Disease 10.1038/s41419-022-05032-z
20) Paraventricular glia drive circuit function to control metabolism
Cell Metabolism 10.1016/j.cmet.2022.09.012
21) Response Facilitation Induced by Insulin-like Growth Factor-I in the Primary Somatosensory Cortex of Mice Was Reduced in Aging
Cells 10.3390/cells11040717
22) Spinal Cord Injury Leads to Hippocampal Glial Alterations and Neural Stem Cell Inactivation
Cellular and Molecular Neurobiology 10.1007/s10571-020-00900-8
23) The neuroprotective mechanism of lithium after ischaemic stroke
Communications biology 10.1038/s42003-022-03051-2
24) A thalamo-preoptic pathway promotes social grooming in rodents
Current Biology 10.1016/j.cub.2022.08.062
25) Damage-responsive neuro-glial clusters coordinate the recruitment of dormant neural stem cells in Drosophila
Developmental Cell 10.1016/j.devcel.2022.05.015
26) Multiple ciliary localization signals control INPP5E ciliary targeting
eLife 10.7554/eLife.78383
27) Genetically modified macrophages accelerate myelin repair
EMBO Molecular Medicine 10.15252/emmm.202114759
28) Astrocyte adaptation in Alzheimer's disease: a focus on astrocytic P2X7R
Essays in Biochemistry 10.1042/EBC20220079
29) Astrocytes in the pathophysiology of neuroinfection
Essays in Biochemistry 10.1042/EBC20220082
30) Osteogenic differentiation of human dental pulp stem cells in decellularised adipose tissue solid foams
European Cells and Materials 10.22203/eCM.v043a10
31) Insulin and insulin-like growth factor-I receptors in astrocytes exert different effects on behavior and Alzheimer´s-like pathology
F1000Research
32) A Neuron, Microglia, and Astrocyte Triple Co-culture Model to Study Alzheimer's Disease
Frontiers in Aging Neuroscience 10.3389/fnagi.2022.844534

33) Linking Plasma Amyloid Beta and Neurofilament Light Chain to Intracortical Myelin Content in Cognitively Normal Older Adults
Frontiers in Aging Neuroscience 10.3389/fnagi.2022.896848
34) Clemastine Induces an Impairment in Developmental Myelination
Frontiers in Cell and Developmental Biology 10.3389/fcell.2022.841548
35) (Editorial) Autophagy in the central nervous system: Focus on neurons, glia and neuron-glia interactions
Frontiers in Cell and Developmental Biology 10.3389/fcell.2022.1036587
36) Editorial: Role of Neuroinflammation in the Neuropsychiatric and Neurological Aspects of COVID-19
Frontiers in Cellular Neuroscience 10.3389/fncel.2022.840121
37) Editorial: Journey to the Center of the Brain: Cell Physiology and Intercellular Communication in White Matter
Frontiers in Cellular Neuroscience 10.3389/fncel.2022.864368
38) Up-regulation of CB1 cannabinoid receptors located at glutamatergic terminals in the medial prefrontal cortex of the obese Zucker rat
Frontiers in Neuroanatomy 10.3389/fnana.2022.1004702
39) Cannabinoid CB1 receptor expression in oligodendrocyte progenitors of the hippocampus revealed by the NG2-EYFP-knockin mouse
Frontiers in Neuroanatomy 10.3389/fnana.2022.1030060
40) Editorial: Neurogenesis and Gliogenesis as Potential Contributors to Neurorepair After Brain Damage
Frontiers in Neuroscience 10.3389/fnins.2022.852729
41) Does the plasticity of neural stem cells and neurogenesis make them biosensors of disease and damage?
Frontiers in Neuroscience 10.3389/fnins.2022.977209
42) GABA Receptor Agonists Protect From Excitotoxic Damage Induced by AMPA in Oligodendrocytes
Frontiers in Pharmacology 10.3389/fphar.2022.897056
43) Functional characterization of cannabidiol effect on the serotonergic neurons of the dorsal raphe nucleus in rat brain slices
Frontiers in Pharmacology 10.3389/fphar.2022.956886
44) Cannabinoid CB2 Receptors Modulate Microglia Function and Amyloid Dynamics in a Mouse Model of Alzheimer's Disease
Frontiers in Pharmacology 10.3389/fphar.2022.841766
45) Inclusive Brain: From Neuronal Doctrine to the Active Milieu
Function 10.1093/function/zqab069
46) Insulin-like growth factor I sensitization rejuvenates sleep patterns in old mice
GeroScience 10.1007/s11357-022-00589-1
47) Endocannabinoid signaling in brain diseases: Emerging relevance of glial cells
Glia 10.1002/glia.24172
48) GABAB receptor agonist baclofen promotes central nervous system remyelination
Glia 10.1002/glia.24262
49) Technical approaches and challenges to study AMPA receptors in oligodendrocyte lineage cells: Past, present, and future
Glia 10.1002/glia.24305

50) GLAST versus GFAP as astroglial marker for the subcellular study of cannabinoid CB1 receptors in astrocytes
Histochemistry and Cell Biology 10.1007/s00418-022-02139-4
51) Susceptibility of Female Mice to the Dietary Omega-3/Omega-6 Fatty-Acid Ratio: Effects on Adult Hippocampal Neurogenesis and Glia
International Journal of Molecular Sciences 10.3390/ijms23063399
52) Identification of Potential Muscle Biomarkers in McArdle Disease: Insights from Muscle Proteome Analysis
International Journal of Molecular Sciences 10.3390/ijms23094650
53) Insulin-like Growth Factor I Couples Metabolism with Circadian Activity through Hypothalamic Orexin Neurons
International Journal of Molecular Sciences 10.3390/ijms23094679
54) New, Fully Implantable Device for Selective Clearance of CSF-Target Molecules: Proof of Concept in a Murine Model of Alzheimer's Disease
International journal of molecular sciences 10.3390/ijms23169256
55) Recombinant Integrin ß1 Signal Peptide Blocks Gliosis Induced by Aß Oligomers
International Journal of Molecular Sciences 10.3390/ijms23105747
56) Impact of Sociodemographic Features and Lifestyle on Cognitive Performance of Peruvian Adults
Journal of Alzheimer's Disease 10.3233/JAD-220428
57) Endovascular administration of magnetized nanocarriers targeting brain delivery after stroke
Journal of Cerebral Blood Flow & Metabolism 10.1177/0271678X211028816
58) Differential Subcellular Distribution and Release Dynamics of Cotransmitted Cholinergic and GABAergic Synaptic Inputs Modify Dopaminergic Neuronal Excitability
Journal of Neuroscience 10.1523/JNEUROSCI.2514-21.2022
59) Assessment of Regional Lung Ventilation with Positron Emission Tomography Using the Radiofluorinated Gas [18F]SF6: Application to an Animal Model of Impaired Ventilation
Molecular Imaging and Biology 10.1007/s11307-022-01773-7
60) Insulin-like growth factor I mitigates post-traumatic stress by inhibiting AMP-kinase in orexin neurons
Molecular Psychiatry 10.1038/s41380-022-01442-9
61) Pathological oligodendrocyte precursor cells revealed in human schizophrenic brains and trigger schizophrenia-like behaviors and synaptic defects in genetic animal model
Molecular Psychiatry 10.1038/s41380-022-01777-3
62) Glial decline and loss of homeostatic support rather than inflammation defines cognitive aging
Neural Regeneration Research 10.4103/1673-5374.320979
63) Leptin Attenuates Fear Memory by Inhibiting Astrocytic NLRP3 Inflammasome in Post-traumatic Stress Disorder Model
Neurochemical Research 10.1007/s11064-022-03655-4

64) Basic Fibroblast Growth Factor Opens and Closes the Endothelial Blood–Brain Barrier in a Concentration-Dependent Manner
Neurochemical Research 10.1007/s11064-022-03678-x
65) Microglia states and nomenclature: A field at its crossroads
Neuron 10.1016/j.neuron.2022.10.020
66) Shedding light on the etiology of neurodegenerative diseases and dementia: the exposome paradigm
npj Mental Health Research 10.1038/s44184-022-00018-3
67) Characterization of molecular biomarkers in cerebrospinal fluid and serum of E46K-SNCA mutation carriers
Parkinsonism & Related Disorders 10.1016/j.parkreldis.2022.01.024
68) Insulin regulates neurovascular coupling through astrocytes
Proceedings of the National Academy of Sciences 10.1073/pnas.2204527119
69) Astrocyte energy and neurotransmitter metabolism in Alzheimer's disease: Integration of the glutamate/GABA-glutamine cycle
Progress in Neurobiology 10.1016/j.pneurobio.2022.102331
70) Cannabinoid control of hippocampal functions: The where matters
The FEBS Journal https://doi.org/10.1111/febs.15907

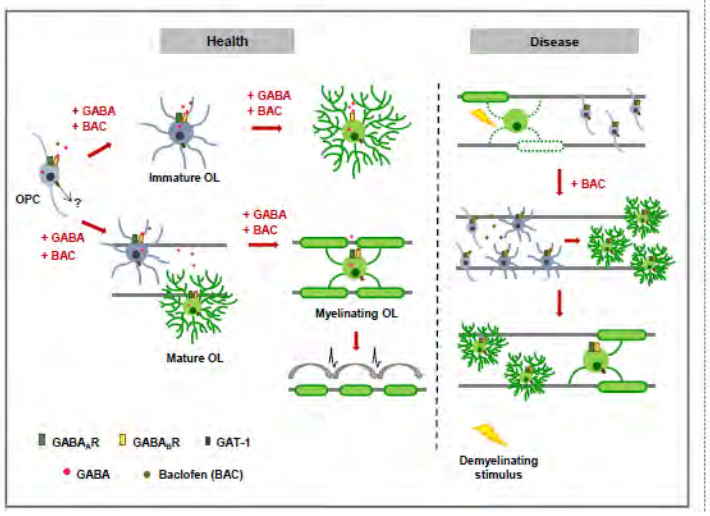
_ HIGHLIGHT IN RESEARCH OUTCOMES _

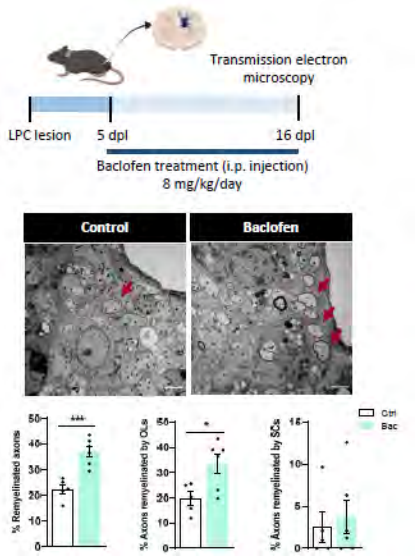
Baclofen-induced GABAB receptor activation promotes remyelination in central nervous system.

Modulating GABAB signaling in oligodendrocytes as a therapeutic strategy in multiple sclerosis

Oligodendrocyte progenitor cell (OPC) differentiation to mature oligodendrocytes is critical to ensure myelin regeneration. We have previously shown that GABAB receptor activation with its specific agonist baclofen (Bac) increases myelin protein expression and oligodendrocyte progenitor differentiation in vitro (Serrano-Regal et al., 2020). Therefore, we aimed to evaluate the pro-remyelinating potential of Bac, a clinically approved drug to treat spasticity in patients with MS, after LPC-induced demyelination in vitro and in vivo models.

We first demonstrated that Bac treatment of cerebellar organotypic slices following LPC stimulus enhanced myelin-related protein expression, suggesting a promising role for this drug in myelin repair. Importantly, we observed that Bac administration to adult mice following induction of demyelination by LPC injection in the spinal cord resulted in enhanced OPC differentiation and increased number of remyelinated axons within the lesions, with no impact in the inflammatory response.





Our results provide compelling evidence showing that Bac improves myelination and this may be a relevant first step in re-evaluating the potential of this drug as a pro-remyelinating/neurorepair agent in patients with MS.

GABAB receptor agonist baclofen promotes central nervous system remyelination
Serrano-Regal, MP; Bayón-Cordero, L; Chara Ventura, JC; Ochoa-Bueno, B.; Tepavcevic, V; Matute, C and Sánchez-Gómez, MV
Glia (Dec-15) DOI: 10.1002/glia.24262

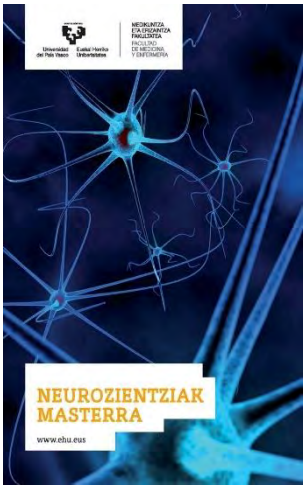
Knowledge sharing is an important support for the continuous innovation and sustainable development of scientific research, and essential for positively impacting on Society and global challenges.

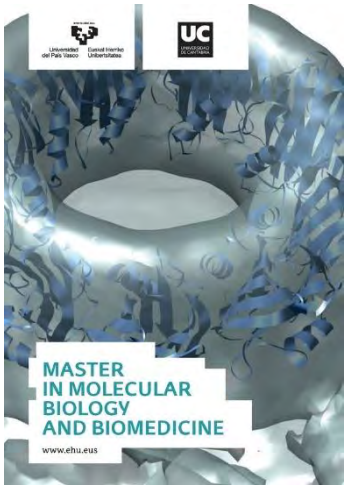
5. Knowledge Transfer

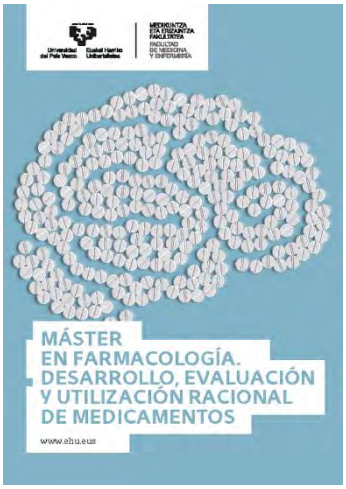
POSTGRADUATE EDUCATION

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 Doctoral Programme in Neuroscience of the UPV/EHU.

Congratulations
Alazne, Alejandro, Álvaro, Ana, Celia, Elisa, Iñaki, Jone, Maite, María, Miriam, and Virginia!

PHD THESES COMPLETED IN 2022

The year 2022 was excellent in terms of PhD thesis. 12 of our predoctoral researchers successfully defended their projects.

- Dr. María Isabel Ardaya Franco
  Laboratory of Neurobiology
  Gliogenesis from the subventricular zone after brain ischemia

- Dr. Alazne Arrazola Sastre
  Laboratory of GTPases and Neurosignalling
  Galectin-1 O-GlcNAcylation Controlled by Rac1/Muscle Glycogen Phosphorylase Pathway Modifies Microglial Responses to Amyloid b1-42 Peptide

- Dr. Elisa Blanco martín
  Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse
  Demencia frontotemporal: genética, estudio evolutivo clínico, neuropsicológico y conductual

- Dr. Maite Blanco Urrejola
  Laboratory of Local Translation in Neurons and Glia
  Neuronetako eta mikrogliako proteinen sintesi lokalaren erregulazioa

- Dr. Celia Luchena Moreno
  Laboratory of Neurobiology
  Exploring pro-resolution mediator ATL and complement receptor CR3 as potential therapeutic targets for Alzheimer's disease

- Dr. Miriam Luque Montoro
  Laboratory of GTPases and Neurosignalling
  El tándem Glucógeno / Glucógeno fosforilasa isoforma M es clave en la respuesta de los astrocitos al péptido I-42 b-Amiloide

- **Dr. Alejandro Montilla López**
  Laboratory of Neurobiology
  Exploring microglial targets in experimental multiple sclerosis

- **Dr. Álvaro Moreno García**
  Laboratory of Neurobiology
  Endocannabinoid modulation of astroglial cells in multiple sclerosis

- **Dr. Ana Belén Palma Leiva**
  Laboratory of Neurobiology
  Signaling pathwais in oligodentdrocytes to promote myelin remodeling

- **Dr. Ignacio Paris Guerrero**
  Laboratory of Glial Cell Biology
  Microglia: Development of a human in vitro model, analysis of motility and effects of phagocytosis in the hippocampal neurogenic niche

- **Dr. Virginia Sierra de la Torre**
  Laboratory of Glial Cell Biology
  Autophagy and phagocytosis: functional relationship in microglia

- **Dr. Jone Zuazo Ibarra**
  Laboratory of Neurobiology
  Role of MCSF-activated microglia in amyloid-associated pathology

Other 55 (12% more than in 2021) are in different stages of that process.

_ HIGHLIGHT IN RESEARCH OUTCOMES _

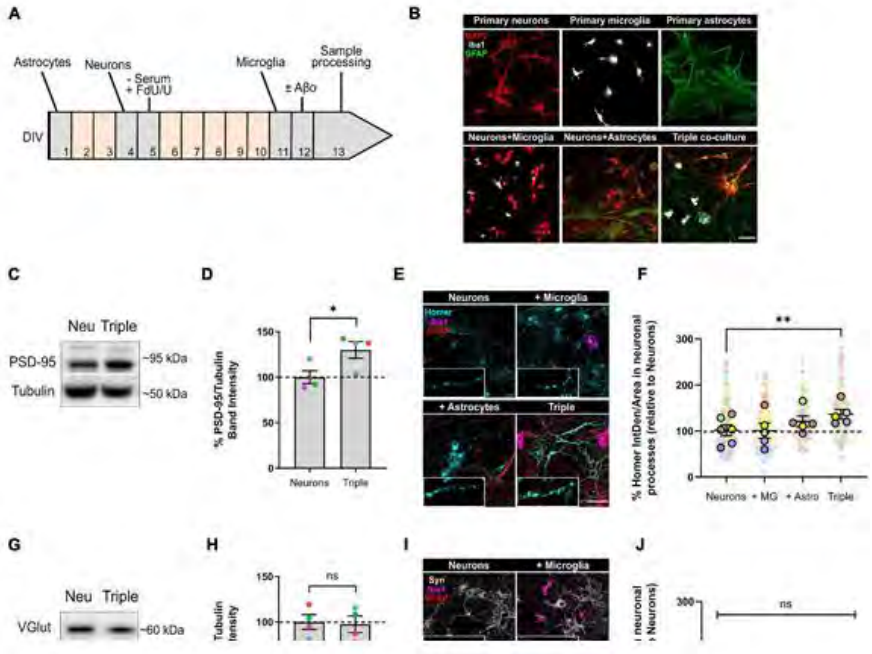
Glial cells are essential to understand Alzheimer's disease progression and this model emerges as a powerful tool to study neurodegeneration and inflammation in the context of Alzheimer and other neurodegenerative diseases.

New model including glia and neurons to study Alzheimer's disease

The research team led by Estibaliz Capetillo-Zarate at the Laboratory of Neurobiology, has established a straightforward in vitro setting with neurons and glial cells to study Alzheimer´s disease.

Predoctoral researchers, Celia Luchena and Jone Zuazo, together with the rest of the team of this project report a new murine triple co-culture model including neurons, microglia and astrocytes, that holds physiological characteristics that are lost in classical primary cultures. In addition, this model was used to recapitulate amyloid-induced Alzheimer´s disease pathological features like synaptic loss and microglial activation.

Glial cells are essential to understand Alzheimer's disease progression and this model emerges as a powerful tool to study neurodegeneration and inflammation in the context of Alzheimer and other neurodegenerative diseases.



A Neuron, Microglia, and Astrocyte Triple Co-culture Model to Study Alzheimer's Disease
Luchena C, Zuazo-Ibarra J, Valero J, Matute J, Alberdi E and Capetillo-Zarate E
Frontiers in Aging Neuroscience (Mar-15) DOI: 10.3389/fnagi.2022.844534

ACHUCARRO SEMINARS

JANUARY

21

- Role of Galectin-1 in migration in microglia: generation of mutant mESCs by CRISPR Cas9
  Alazne Arrazola Sastre
  Laboratory of GTPases and Neurosignalling, ACHUCARRO

- Conserved cell types in the early embryonic brain across vertebrates
  Rodrigo Senovilla Ganzo
  Laboratory of Neural Stem Cells and Neurogenesis, ACHUCARRO

FEBRUARY

04

- Microglia in Health and Disease
  Bart Eggen
  University of Groningen (The Netherlands)

18

- Challenging "inflammageing" of the brain: glial paralysis, rather than reactivity defines brain ageing
  Alexei Verkhratsky
  U. Manchester & ACHUCARRO

25

- Revealing the hidden – A versatile toolbox for the analysis of nervous tissue organization with light microscopy
  Julia Michalska
  University of Vienna (Austria)

MARCH

04

- The Different Roles of Mitochondria as Modulators of Calcium Signalling in Tauopathies
  Noemí Esteras Gallego
  University College London (UK)

11

- Cellular Architecture and Membrane Trafficking Visualised by Correlative Light and Electron Microscopy
  Alejandro Melero
  University of Lausanne (Switzerland)

MARCH

18

- Assessing Neurogenesis During Epileptogenesis in Hippocampal Organotypic Slices
  Ane Rodríguez Bodero
  Laboratory of Neural Stem Cells and Neurogenesis, ACHUCARRO

- Role of Macrophage Colony-Stimulating Factor as a Microglial Modulator in the Context of Alzheimer´s Disease
  Jone Zuazo Ibarra
  Laboratory of Neurobiology, ACHUCARRO

22

- Cholesterol and Matrisome Pathways Dysregulated In Human APOE Ee4 Glia
  Julia TCW
  Boston University (USA)

APRIL

08

- The Early Ticking of the Central Circadian Pacemaker: When and How
  Mariana Astiz Cadenas
  Laboratory of Circadian Physiology of Neurons and Glia, ACHUCARRO

MAY

13

- Genetic Disruption of Mitochondrial Complex I Triggers Progressive, Levodopa-Responsive Parkinsonism with Nigral Determinants
  Patricia González Rodríguez
  Universidad de Sevilla (Spain)

17

- Astrogial CB1R in the Nucleus Accumbens Regulate Synaptic Plasticity and Amphetamine-Induced Locomotion
  Ana Covelo
  University of Bordeaux (France)

27

- Morphological and electrophysiological properties of CA1 pyramidal neurons exposed to mild hyperexcitability
  Rizky Lasabuda
  Laboratory of Neuronal Excitability, ACHUCARRO
- Role of monocarboxylate transporter 2 (MCT2) in myelination, remyelination and myelin maintenance in the central nervous system
  Leire Izagirre Urizar
  Laboratory of Neurobiology, ACHUCARRO

JUNE

17

- Cell Type-Specific Vulnerability, Degeneration and Repair in a Novel Human Corticospinal Organoid Model
  András Lakatos
  University of Cambridge (UK)

JULY

08

- The SARS-CoV-2 Main Protease Mpro Causes Microvascular Brain Pathology by Cleaving NEMO in Brain Endothelial Cells
  Markus Schwaninger
  University of Lübeck (Germany)

22

- Systems consolidation mechanism for sequential printing of cued-fear memory engrams across different brain regions
  Mazahir T. Hasan
  Laboratory of Brain Circuits Therapeutics, ACHUCARRO

SEPTEMBER

09

- Microglial cells in health and disease
  Helmut Kettenmann
  Max-Delbrück-Centrum for Molecular Neuroscience (Germany)

16

- Using humanized models to study the role of human astrocytes in Alzheimer's disease
  María Alfonso Triguero
  Laboratory of Humanized Models of Disease, ACHUCARRO

- Altered Myelin Regulatory Factor processing modifies oligodendrocyte differentiation in Alzheimer's disease models
  Uxue Balantzategi Fernández de Arroyabe
  Laboratory of Neurobiology, ACHUCARRO

27

- Hunger drives life
  Tamas Horvath
  Laboratory of Glia-Neuron Interactions in the Control of Hunger, ACHUCARRO

OCTOBER

07
- Non-Conventional NMDA Receptor Signaling in Neurons and glia
  Isabel Pérez Otaño
  Instituto de Neurociencias de Alicante [CSIC-UMH] (Spain)

26
- Multi-scale computational modeling in stem cell research and disease modeling
  Antonio del Sol Mesa
  CIC bioGUNE (Derio)

NOVEMBER

04
- Insights about Ageing Gained while Studying Neurodegeneration
  Oscar Fernández Capetillo
  Centro Nacional de Investigaciones Oncológicas (CNIO) (Spain)

11
- Development & Plasticity of Sensory Circuits
  Guillermina López-Bendito
  Instituto de Neurociencias [CSIC - UMH] (Spain)

18
- Myelin Regeneration: from Gene Therapy to Energy Metabolism
  Vanja Tepavcevic Mandic
  Laboratory of Neurobioligy, ACHUCARRO

25
- It Is Just a Matter of Cues: Multidimensional Modulation of Neuronal Network Activity Through Multimodal Stimulation
  Denis Scaini
  Faculty of Pharmacy [UPV/EHU] (Vitoria-Gasteiz, Spain)
-

DECEMBER

16
- Aggregation and Glial Response
  Nora Bengoa Vergniory
  Laboratory of Aggregation and Glial Response, ACHUCARRO

Among our objectives we list the promotion of scientific knowledge and the dissemination a culture based in 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 with Outreach; Equality, Equity and Diversity; Talent Development; and fostering a culture of scientific literacy through a set of activities during the year.

February 11th and the commitment with Equality is present in many of our activities.

Visit of Wake Forest College, hosted by Mazahir T. Hasan

Achucarro Family Day

Neuroscience Day 2022

Ikerbasque Forum for Equality and Diversity

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

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

In 2022 the postdoctoral researchers in ACHUCARRO organised the third edition of their winter scientific event, the Achucarro Symposium.

ACHUCARRO SYMPOSIUM CURATED BY POSTDOCTORAL RESEARCHERS

The line-up to speakers was excellent, once again.

13:00 **The dynamics within the olfactory systems challenge the passive role of the amygdala in olfactory processing**
Cecilia PARDO BELLVER
Universitat de València

13:30 **Brain mechanisms in physiological and pathological cognitive processes**
Arnau BUSQUETS GARCÍA
Institut Hospital del Mar d'Investigacions Mèdiques, Barcelona

The Science Park of the UPV/EHU in Leioa, hosts the headquarters of ACHUCARRO.

6. Infrastructure and Equipment

The proximity with Bilbao, and its airport, and the faculties of the University with the degrees (Biology, Biochemistry, Medicine...) that give access to research work in neurobiology is an asset that allows us to expand our potential, and to be a very active agent on campus.

This location within the campus, close to the general research facilities to support research of the university (i.e., optical and electronic microscopy, genomics, proteomics, etc.). The partnerships with other neighbouring R&D agents 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 2000 m^2 in a privileged location within the campus of the UPV/EHU. Some of the research groups also have laboratories and office spaces at the Faculty of Medicine and Nursing, at 400 metres from the main location.

https://www.achucarro.org/facilities

The Basque Government establishes challenging scientific and management objectives for research organisations with the BERC accreditation. 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.

7. Main performance indicators

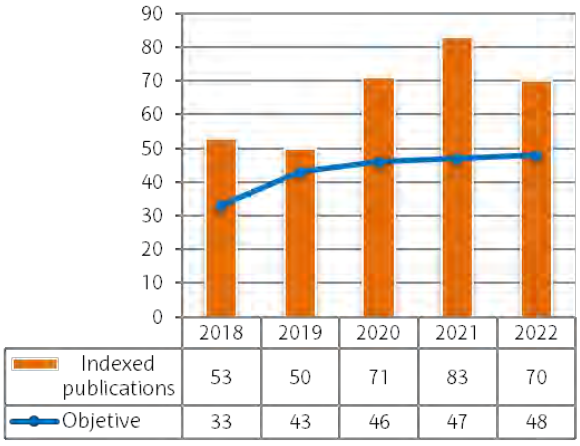
In 2022 we started our third strategic plan.

The following indicators strive to show the development of our organization, according to some external (by 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

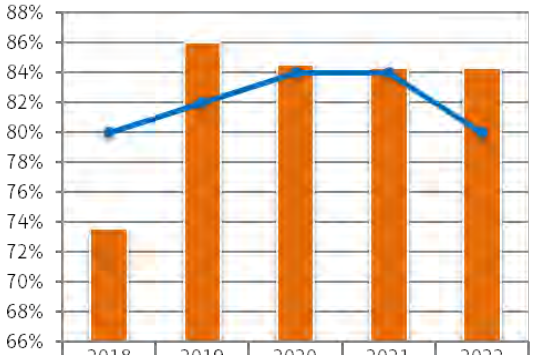
Sources:
Scopus & Web of Science



	2018	2019	2020	2021	2022
Indexed publications	53	50	71	83	70
Objetive	33	43	46	47	48

% of publications in quartile 1 of their research areas

Source:
Scimago Journal Ranking

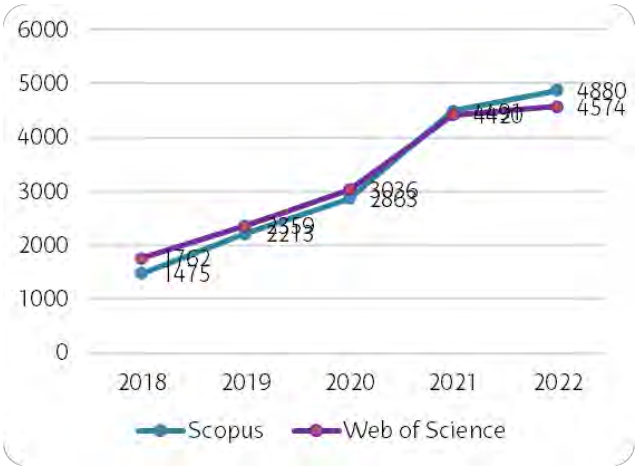


	2018	2019	2020	2021	2022
Q1	74%	86%	85%	84%	84%
Objective	80%	82%	84%	84%	80%

Total citations

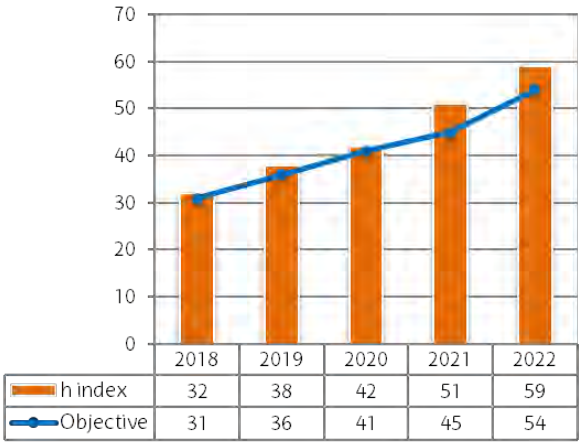
Source:
Scopus & Web of Science

These total amount produce a mean of 9 cites per document



h-index of ACHUCARRO

Source:
Scopus



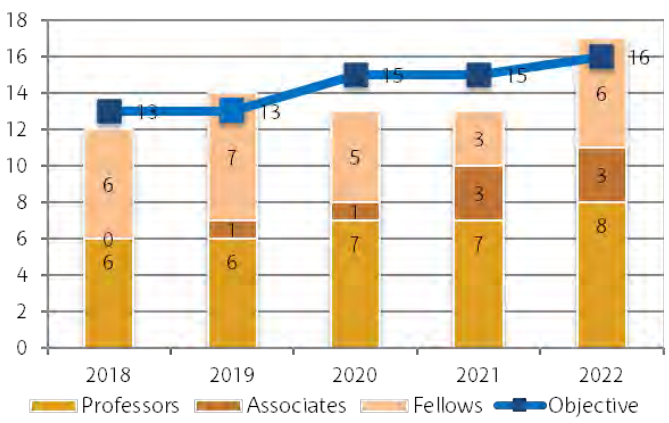
While Scopus and Web of Science produce similar numbers for the h-index indicator, Google Scholar reflects 99 for the same indicator.

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.

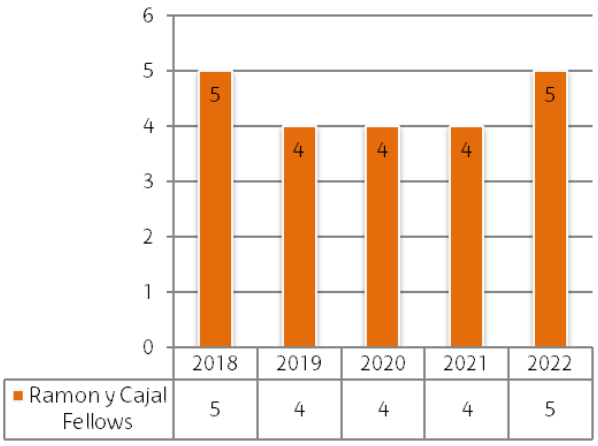
Total number of Ikerbasque Researchers (Professors, Associated and Fellows)

Source: Internal



Total number of Ramón y Cajal Fellows

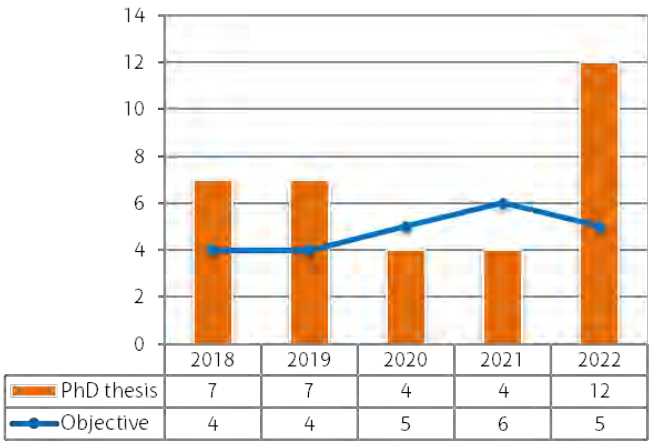
Source: Internal



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

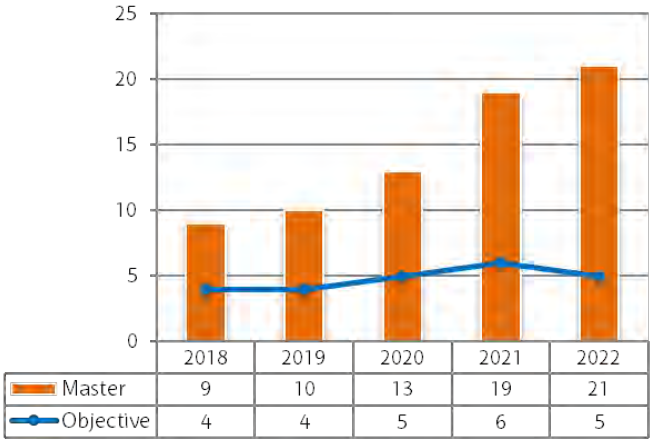


	2018	2019	2020	2021	2022
PhD thesis	7	7	4	4	12
Objective	4	4	5	6	5

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

Completed Masters' Dissertations

Source: Internal

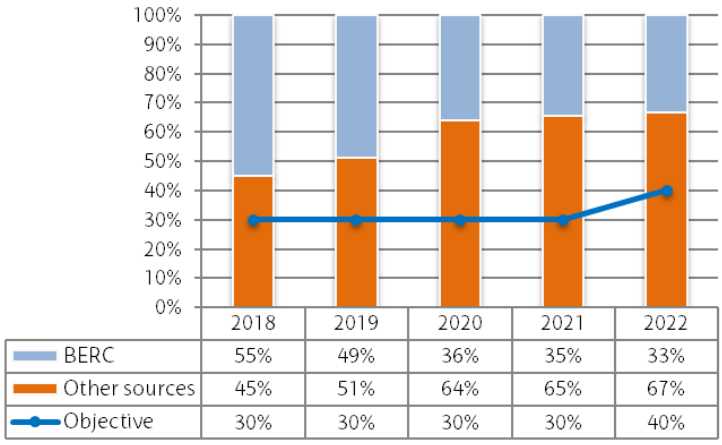


	2018	2019	2020	2021	2022
Master	9	10	13	19	21
Objective	4	4	5	6	5

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

% of funding different from BERC

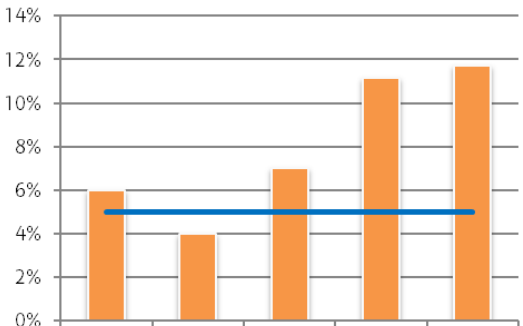
Source: Internal



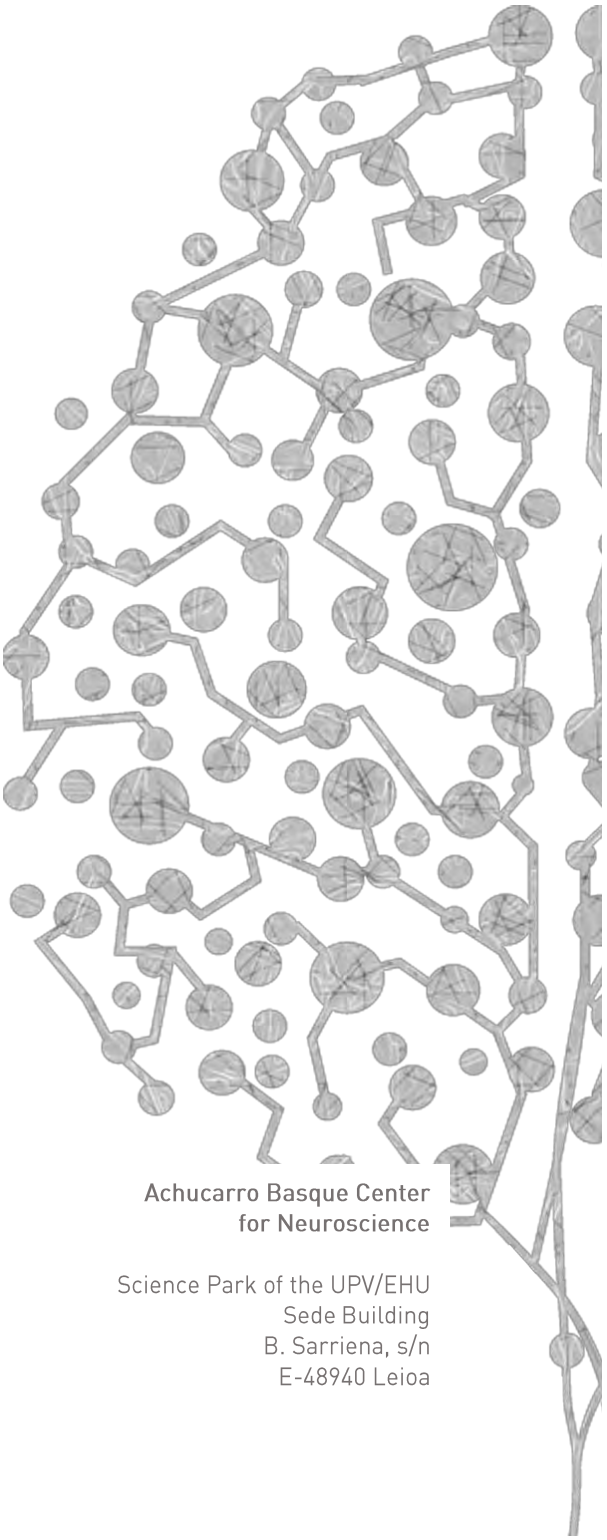
	2018	2019	2020	2021	2022
BERC	55%	49%	36%	35%	33%
Other sources	45%	51%	64%	65%	67%
Objective	30%	30%	30%	30%	40%

% of international funding

Source: Internal



	2018	2019	2020	2021	2022
International funding	6%	4%	7%	11%	12%
Objective	5%	5%	5%	5%	5%



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