ehugroup

Achucarro

BASQUE CENTER FOR NEUROSCIENCE

scientia ad remedium

2016

Annual Report

Contents

Foreword

Dear reader,

Welcome to the Annual Report of Achucarro Basque Center for Neuroscience for the year 2016. As a general summary, I would highlight that this year we have continued our steady progress and growth by increasing our productivity and recruiting new group leaders.

Among other achievements, the publication record this year has substantially increased over the previous period. In addition, three new groups, led by *Ikerbasque* and *Ramon y Cajal* fellows, have been appointed to study novel aspects of glia biology including its role in memory formation and consolidation and reciprocal glia-to-axon interactions, as well as the contribution of glia to neuronal excitability.

Our challenge for the near future is to consolidate and integrate the newcomers while maintaining the upward trajectory of the centre.

Next spring, the ACHUCARRO will move into a new building within the Science Park of the University of the Basque Country, in the campus of Leioa. This move means a giant step forward for our daily activities because we will have brand-new laboratories and facilities and the possibility to expand into new cutting-edge glia research areas by recruiting additional group leaders. Most important, the new headquarters will constitute a very active location for improving our efficiency and favouring current and future collaborations with other colleagues and institutions on the campus, adding value for all parties.

We are very much looking forward to this move because it signifies a major achievement of our Strategic Plan for the period of 2014–2017. *Needless to say, this achievement will position us to face the next challenges for the period of 2018–2021.*

Carlos Matute
Scientific Director

1. Strategy and Management

We designed a strategy for the period 2014–2017 back in 2013, in accordance with the programme launched by the Basque Government to foster research infrastructure and the development of high-quality fundamental science. However, the socio-economic conditions of the last years have directly influenced the expectations and timing we established at that time, so the bigger objectives have been delayed, slowing achievement of most of the other objectives.

Fortunately, the political stability regarding science issues in the Basque Country and the continuous support of the institutions involved in ACHUCARRO have contributed, although with some delay, to our plans of moving from our current locations outside the University campus to a bigger and better location within the campus. This long-term and much-awaited project is finally a reality: in 2016, we designed and started refurbishing a floor for the Main Building of the Science Park of the University of the Basque Country (UPV/EHU), next to the University campus, for establishing our permanent headquarters.

Nevertheless, we can also say that all the uncertainties and delays did not significantly affect our research programme. The support and commitment of the groups that compose the foundations of the centre deserve praise because thanks to their generosity, we have been able to grow in this difficult period.

SCIENTIFIC PLAN 2014–2017

According to the main strategic objectives established in 2013, ACHUCARRO has the aspiration of becoming a reference centre within Europe in fundamental and translational research in the field of neuroscience.

The overall objective of the centre is to perform coordinated multidisciplinary research of brain functions on all levels – from single molecules through individual cells and acutely isolated nervous tissues to brain networks operating in vivo – to further advance discoveries in the physiology and pathophysiology of the nervous system. In particular, the main strategic direction of the centre will be in-depth study of neuronal–glial biology in the normal and pathological brain.

To meet these goals, ACHUCARRO designed a Strategic Plan for the period 2014–2017 that contains three high-level research programmes including different areas that involve the coordinated and complementary expertise of the different research groups from the centre.

- Characterization of the role of glial cells in the physiology of the nervous system
  - roles of astrocytes in synaptic communication
  - neurotransmitter signalling during neurogenesis and gliogenesis
  - mechanisms of microglia phagocytosis during neurogenesis

- Characterization of structural and functional changes of neuronal–glial networking in the aged brain
  - age-dependent remodelling of neuronal–glial signalling
  - regulation of the intrinsic properties of neural stem cells in the adult hippocampus

- The role of neuroglia in neurodegenerative diseases and other neurological disorders
  - research on general mechanisms of neuron and glial cell death
  - understanding the pathophysiology of Alzheimer's disease and epilepsy
  - autoimmune pathogenesis of multiple sclerosis (MS) and neuroinflammation

The two key elements that define our strategy are our Mission and Vision:

Mission

Achucarro Basque Center for Neuroscience is

- the research center fostered by Ikerbasque and the University of the Basque Country (UPV/EHU),
- devoted to fundamental and translational research in neuron–glial biology
- for the discovery of new therapies for brain diseases,
- in cooperation with the local community and networked with the international institutions in the field of neuroscience,
- with the aim of contributing to the training of future neuroscientists.

Vision

In 2017, Achucarro Basque Center for Neuroscience strives to lead and coordinate Basque efforts to advance in neuroscience knowledge by

- establishing a world-class research centre, with internationally recognized research groups and state-of-the-art equipment and facilities and
- contributing to the understanding of the human brain in the field of neuron–glial biology
- for generating relevant knowledge and scientific results that contribute to the well-being of society.

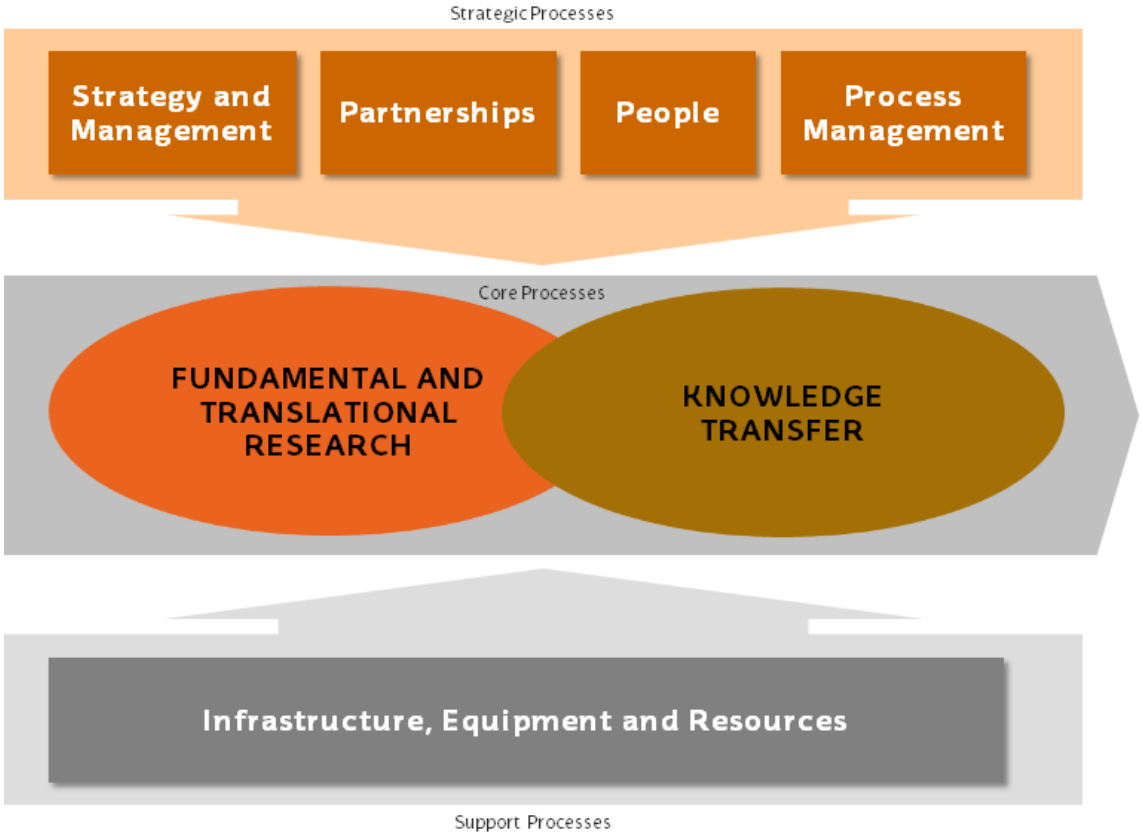
ACHUCARRO strives to perform excellent research
by developing and relying on excellent management processes.

MANAGEMENT PLAN 2016

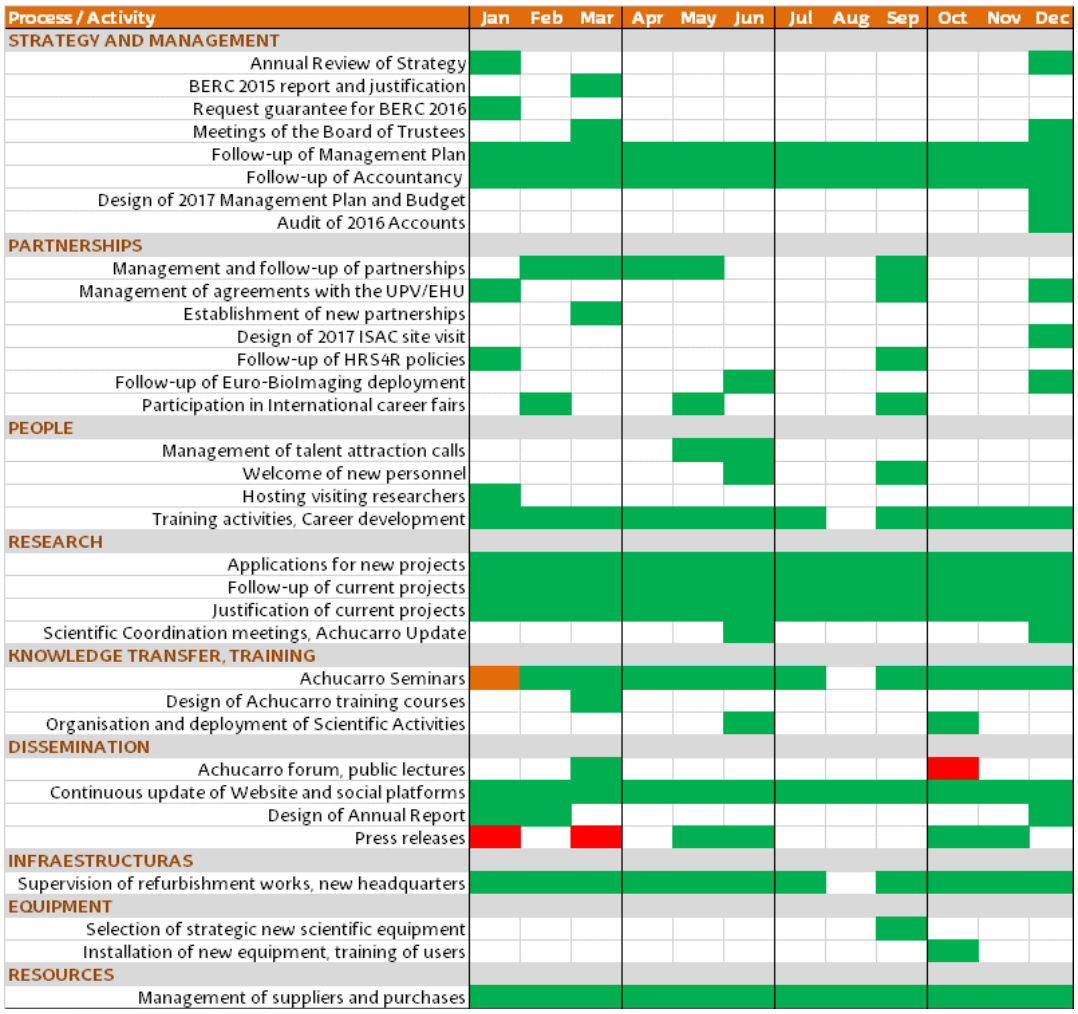
Our approach to implementing our Mission of deploying excellent management and operation standards is based on (re)thinking, (re)developing, and managing changes, in the framework of a management model based on processes, following the guidelines and recommendations of the European Foundation for Quality Management (EFQM) and the Basque Foundation for Quality (Euskalit).

The aim of our management processes is to effectively and efficiently develop our Mission and Vision. Thus, all activities in the centre are managed by one or more processes in this model, which also has provided the framework for the 2016 annual report document.

ACHUCARRO has strengthened its management team in 2016, which allowed us to review and redesign our processes, so that from 2017 onward, we will implement the next Map of Processes, which includes one new process (Process Management):



Below is the planning and tracking of the Management Plan for 2016.



Overall, we managed to complete all of our scheduled activities and challenges for the year, as planned and on budget, resulting in the achievement of all of this year's strategic objectives.

We could not hold the Achucarro Forum conference scheduled for October because of a change in the working calendar of the year.

Communications to the media planned early in the year where finally completed later in spring.

2. Partnerships and Collaborations

ACHUCARRO is acutely aware that partnering and sharing efforts with other individuals and institutions is crucial for achieving most of the challenges we face. We manage and take care of the institutional relationships we establish with others. Therefore, depending on the impact of each partnership or collaboration in the development of the Strategy of our centre, we identify the collaboration relationships as Institutional, Strategic, or Operational. This classification helps us determine different types of management for each case.

INSTITUTIONAL ALLIANCES

Institutional partnerships and collaborations are based on a partnership agreement or similar document that enables us to maintain a close collaborative relationship in specific areas. 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.

We currently hold institutional agreements with:

Basque Government

- Agreement to support the activities of the centre in the period 2014–2017

Ikerbasque

- Framework agreement for the appointment of research staff: Ikerbasque Research Professors and Ikerbasque Research Fellows
- Specific agreement to co-fund research staff: Ikerbasque Research Professors and Ikerbasque Research Fellows

University of the Basque Country (UPV/EHU)

- Framework agreement
- Specific agreement for the appointment of the scientific director
- Specific agreement for the appointment of teaching and research and personnel
- Specific agreement for the appointment of academic and research collaborators
- Specific agreement to manage the application to European projects

Basque Science, Technology, and Innovation Network

- Attachment to this network and recognition as a BERC (Basque Excellence Research Centre).

STRATEGIC ALLIANCES

We consider strategic alliances to be those that we establish with all kinds of institutions operating in our area, either generally or specifically. Apart from partnerships that we systematically develop with the members of our Board of Trustees, our Strategic collaborators are the following:

European Commission – HRS4R Community

Following our endorsement of the European Charter for Researchers (see section 3. People) fostered by the European Commission, we were invited to participate in a work group with institutions involved and committed to the same principles and policies. This forum provides us with valuable access to the most current policies of the Directorate General for Research and Innovation and other European research institutions.

Euro-BioImaging

The joint effort of ACHUCARRO and the Institute of Biophysics (a joint research institution created by the Spanish National Research Council – CSIC – and the University of the Basque Country) to run a node candidate within the Euro-BioImaging (EuBI) network has continued developing this year. EuBI has started operating in interim mode.

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 forums and professional associations

Both as an institution and through our researchers, we participate in all relevant forums in our area and strive to expand our institutional presence. Being present and active in the international sphere is strategic and crucial to ensure that our strategy and objectives continue to be challenging and current. CiberNed, Network Glia, Spanish Society of Neurosciences (SENC), FENS, Society for Neurosciences, and others are part of this group of partnerships.

OPERATIONAL ALLIANCES AND PARTNERS

ACHUCARRO has a number of relevant providers considered as allies for their importance and involvement in the development of our strategic objectives, as described below.

Bizkaia Science and Technology Park

Science and Technology Park of Bizkaia has provided a local basic-but-appropriate-site, on a rental basis, for the centre of operations and the physical image of the new centre.

i2Basque

The Basque Academic Network provides telecommunication and ICT support services and infrastructure to the member organizations of the Basque Science, Technology, and Innovation Network. ACHUCARRO, as a member of the i2Basque network, has access to its infrastructure and resources.

INTERNATIONAL SCIENTIFIC ADVISORY COMMITTEE (ISAC)

The International Scientific Advisory Committee is the main strategic advisory body of ACHUCARRO. Its primary role is to advise, supervise, and assess the objectives and performance of the different groups and professionals of the centre.

The ISAC consists of distinguished colleagues that provide us with their view on the different fields and expertise areas covered by the Research Programme of the centre.

Jesús **Ávila**

CBM Severo Ochoa (Spain)

Erik Boddeke

University Groningen (NL)

Isabel **Fariñas**

U. Valencia (Spain)

Christian Giaume

Ecole Normale Supérieure (FR)

Helmut Kettenmann

Max-Delbrück Centrum (DE)

Frank Kirchhoff

University Saarland (DE)

Jose A. Obeso

Madrid (Spain)

Jorge Oksenberg

UCSF (USA)

Anna Planas

IDIBAPS (Spain)

Bruce Ransom

U. Washington (USA)

In 2016, Prof. Geoffrey Burnstock from University College (London), was replaced by Prof. Erik Boddeke, from the University of Groningen (The Netherlands).

3. People

The overall strategy of Achucarro establishes a virtuous cycle of excellent research, knowledge transfer, and training of new generations of neuroscientists.

In terms of attraction, training, and support for career development of the professionals working in Achucarro, our People Management model is based on international standards. In particular, regarding the research personnel, the Board of Trustees and the Scientific and Operations direction of the centre endorse the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers, fostered by the European Commission.

In September 2013, the European Commission awarded Achucarro the HR Excellence in Research in recognition of our commitment with the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers.

At the end of 2016, Achucarro consisted of 77 people working for the 11 independent research groups, the research support facilities, and the management area.

These are the eight Principal Investigators:

Laboratory of Axon–Glia Interactions

Jimena Baleriola

Group Leader

Ikerbasque Research Fellow

PhD Universidad Complutense de Madrid (Spain), 2008

Laboratory of Neural Stem Cells and Neurogenesis

Juan Manuel Encinas

Group Leader

Ramon y Cajal Fellow

PhD Universidad Complutense de Madrid – Instituto Cajal (Spain), 2003

Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse

Pedro Grandes

Group Leader

Full Professor in Anatomy and Human Embryology

Department of Neurosciences (UPV/EHU)

PhD University of the Basque Country (UPV/EHU), 1986

Laboratory of Memory Circuits

Mazahir T. Hasan

Group Leader

Ikerbasque Research Professor

PhD Dartmouth College (Hanover, New Hampshire, USA), 1993

Laboratory of Neurobiology

Carlos Matute

Scientific Director and Group Leader

Full Professor in Anatomy and Human Embryology

Department of Neurosciences (UPV/EHU)

PhD University of Zaragoza (Spain), 1982

Laboratory of Functional Neuroanatomy

Jose Julio Rodríguez Arellano

Group Leader

Ikerbasque Research Professor (UPV/EHU)

PhD Universidad Complutense de Madrid (Spain), 1995

Laboratory of Glial Cell Biology

Amanda Sierra

Group Leader

Ramon y Cajal Fellow

PhD Universidad Complutense de Madrid (Spain), 2003

Laboratory of Neuronal Excitability

Jan Tønnesen

Group Leader

Ramon y Cajal Fellow

PhD Lunds Universitet (Lund, Suecia), 2010

Laboratory of Neurogenomics

Koen Vandenbroeck

Group Leader

Ikerbasque Research Professor (UPV/EHU)

PhD University of Leuven (Belgium), 1993

Laboratory of Pathophysiology

Alexej Verkhratsky

Adjunct Scientific Director and Group Leader

Ikerbasque Research Professor (UPV/EHU)

PhD Bogomoletz Institute of Physiology (Kiev, Ukraine), 1986

Full Professor in Neurophysiology (University of Manchester)

Laboratory of GTPases and Neurosignalling

Jose Luis Zugaza

Group Leader

Ikerbasque Research Professor (UPV/EHU)

PhD Universidad de Santiago de Compostela (Spain), 1993

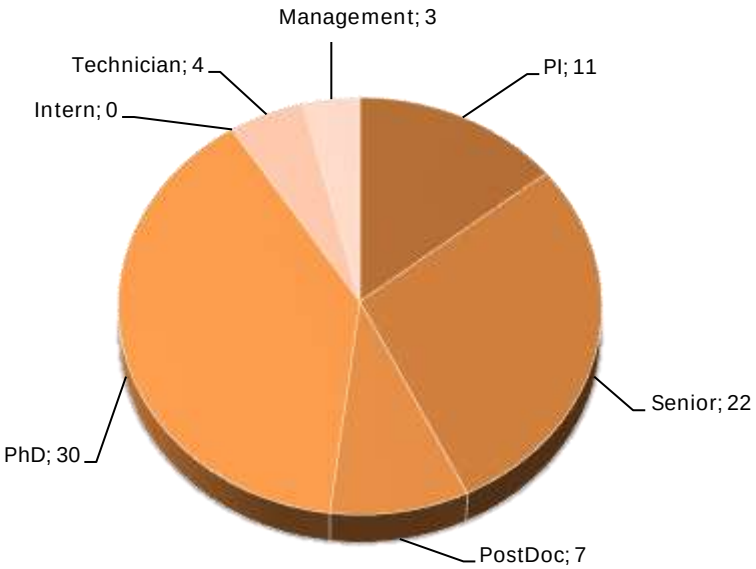
APPOINTED STAFF (2016/12)

Oihane Abiega *(PhD Student)* Elena Alberdi *(Senior Researcher)* Iraide Alloza *(Senior Researcher)* Alain Artaso *(PhD Student)* Jimena Baleriola *(Group Leader)* Sol Beccari *(PhD Student)* Mónica Benito *(Postdoctoral Fellow)* Itziar Bonilla *(PhD Student)* Ianire Buceta *(PhD Student)* Miren Josune Canduela *(Postdoctoral Fellow)* Estibaliz Capetillo *(Senior Researcher)* Fabio Cavaliere *(Senior Researcher)* Juan Carlos Chara *(Technician)* Irune Díaz *(PhD Student)* María Domercq *(Senior Researcher)* Jon Egaña *(PhD Student)* Izaskun Elezgarai *(Senior Researcher)* Juan Manuel Encinas *(Group Leader)* Laura Escobar *(Technician)* Marian Fernández *(Management Assistant)* Laura García *(Project Assistant)* Fernando García-Moreno *(Senior Researcher)* Inma Gerrikagoitia *(Senior Researcher)* Jon Gejo *(PhD Student)* Haize Goikuria *(PhD Student)* Paloma Gómez *(PhD Student)* Sonia Gómez *(Senior Researcher)* Pedro Grandes *(Group Leader)* Mazahir T. Hasan *(Group Leader)* Francisco Llavero *(Postdoctoral Fellow)* Artur Luzgin *(PhD Student)* Andrea Manterola *(PhD Student)* Saioa Marcos *(Technician)* Ricardo Marticorena *(PhD Student)* Soraya Martín *(PhD Student)* Ainara Martínez *(Technician)* Luis Martínez Millán *(Senior Researcher)* Susana Mato *(Senior Researcher)* Carlos Matute *(Group Leader and Scientific Director)* Jorge Mena *(PhD Student)* Juan Mendizabal *(Senior Researcher)* Carolina Ortiz *(PhD Student)* Aitor Palomino *(Postdoctoral Fellow)* Iñaki Paris *(PhD Student)* Oier Pastor *(PhD Student)* *Ainhoa Plaza* *(Postdoctoral Fellow)* Sara Peñasco *(PhD Student)* Fernando Pérez-Cerdá *(Senior Researcher)* Alberto Pérez-Samartín *(Senior Researcher)* José Ramón Pineda *(Senior Researcher)* Nagore Puente *(Senior Researcher)* Tania Quintela *(PhD Student)* Almudena Ramos *(Senior Researcher)* Paula Ramos *(PhD Student)* Leire Reguero *(Senior Researcher)* Irantzu Rico *(Postdoctoral Fellow)* José Julio Rodríguez Arellano *(Group Leader)* Naiara Royo *(PhD Student)* Asier Ruiz *(Postdoctoral Fellow)* Jaime Sagarduy *(General Manager)* María Victoria Sánchez *(Senior Researcher)* Victor Sánchez *(PhD Student)* *Rafael Sarría* *(Senior Researcher)* Mari Paz Serrano *(PhD Student)* Amanda Sierra *(Group Leader)* Virginia Sierra *(PhD Student)* Jan Tønnesen *(Group Leader)* Nerea Ugidos *(PhD Student)* Andoni Urtasun *(PhD Student)* Roberto Valcárcel *(PhD Student)* Jorge Valero *(Senior Researcher)* Koen Vandenbroeck *(Group Leader)* Alexei Verkhratsky *(Group Leader)* Alazne Zabala *(PhD Student)* Fátima Zallo *(Postdoctoral Fellow)* Jone Zuazo *(PhD Student)* Jose Luis Zugaza *(Group Leader)*

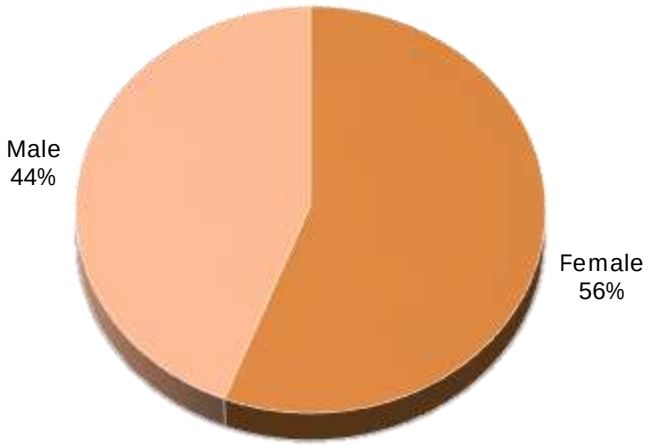
COLLEAGUES DEPARTING THIS YEAR

Ianire Astobiza *(Postdoctoral Fellow)* Manuel Canedo *(PhD Student)* Raffaela Cipriani *(Postdoctoral Fellow)* Abraham Cisneros *(Postdoctoral Fellow)* Enmanuela Gardena *(PhD Student)* Hazel Gómez *(Technician)* Ana Gutiérrez *(PhD Student)* Sandra Osés *(Project Assistant)* Jose Riera *(Postdoctoral Fellow)* Ane Wissenbach *(Postdoctoral Fellow)*

Staff by function



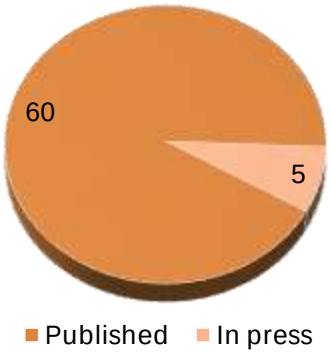
Staff by gender

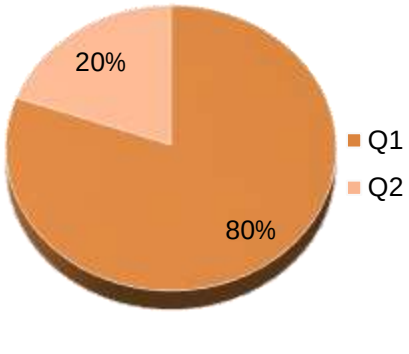


4. Research

Our researchers published a total of 60 publications in peer-reviewed journals: 45 original articles and 15 reviews. Of these publications, 80% are listed in journals in the first quartile.

Papers

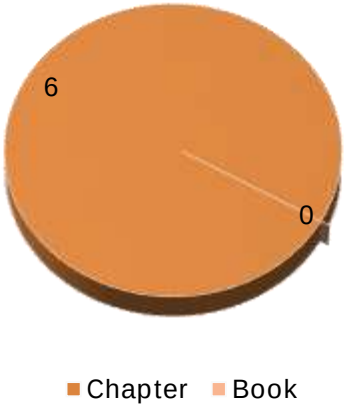


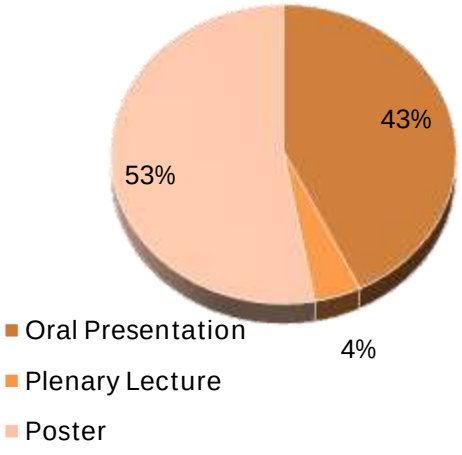


We also authored six chapters in books edited by other colleagues.

Attendance at conferences and participation in scientific forums have involved oral presentations (30) and plenary lectures (3), as well as posters (37).

Books and Congresses





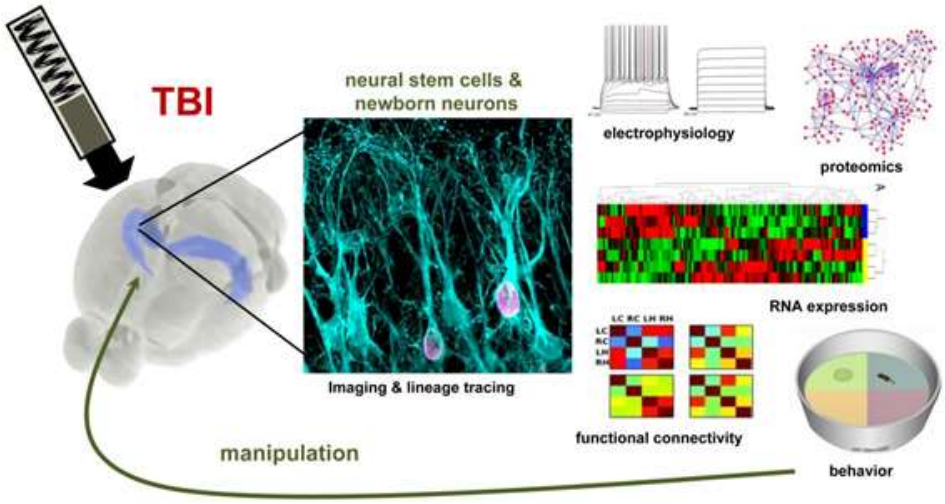
HIGHLIGHTS IN RESEARCH OUTCOMES

Traumatic Brain Injury (TBI) is becoming a "silent epidemic" worldwide. In Europe, almost 8 million people have significant disabilities due to TBI, and the economic cost has been estimated at EUR 100 billion.

Induction of Reactive Neural Stem Cells by Traumatic Brain Injury in the Adult Hippocampus

A consortium led by ACHUCARRO Group Leader Juan M Encinas has been awarded one of the projects funded by the ERA-NET Neuron 3 call with the objective of developing new ideas on "External Insults to the Nervous System".

TBI survivors often develop long-lasting neurological symptoms such as decision-making and memory deficits, depression, or aggressive behaviour, negatively affecting their quality of life. Several of the important brain functions affected by TBI depend on the hippocampus, which is highly vulnerable to injury. Even when not directly mechanically affected, the hippocampus undergoes atrophy and synaptic alterations. In addition, TBI affects postnatal and adult hippocampal neurogenesis, the process of generating new neurons from neural stem cells (NSCs) located in the dentate gyrus.



In this international project, the consortium proposes that NSCs and hippocampal neurogenesis should be considered a novel target for developing innovative strategic therapies against brain damage. Hippocampal neurogenesis is highly sensitive to changes; in turn, neuronal activity and impairment or alterations of hippocampal neurogenesis may account for some of the symptoms associated with TBI, such as memory, learning, and anxiety deficits, all of which are hippocampal functions involving neurogenesis.

This project will demonstrate the utility of hippocampal neurogenesis as a potential novel therapeutic target for TBI.

The other partners in this project are the laboratories of Dr. Veerle Baekelandt (Leuven University, Belgium), Dr. Nora Abrous (Neurocentre Magendie Bordeaux, France), and Dr. Carlos Fitzsimons (University of Amsterdam, The Netherlands).

HIGHLIGHTS IN RESEARCH OUTCOMES

Cannabinoids induce memory loss through a decrease in neuronal energy supply

It has been known for some time that extracts of the Cannabis plant, just like synthetic cannabinoids and those produced by the brain itself, contain molecules that bind type 1 (CB1) cannabinoid receptors located in axon terminals. The effect of these compounds is to inhibit the release of chemical messengers (neurotransmitters) in the communication areas between the nerve cells. Knowledge about the way cannabinoids work expanded in recent years when the CB1 receptor was also located and found to function in the neuronal mitochondria, the organelles responsible for producing molecules that the cell can access for energy.

LETTER

doi:10.1038/nature20127

A cannabinoid link between mitochondria and memory

Etienne Hebert-Chatelain[1,2,3]*, Tifany Desprez[1,2]*, Román Serrat[1,2]*, Luigi Bellocchio[1,2,4]*, Edgar Soria-Gomez[1,2], Arnau Busquets-Garcia[1,2], Antonio Christian Pagano Zottola[1,2], Anna Delamarre[1,2], Astrid Cannich[1,2], Peggy Vincent[1,2], Marjorie Varilh[1,2], Laurie M. Robin[1,2], Geoffrey Terral[1,2], M. Dolores Garcia-Fernández[5,6], Michelangelo Colavita[1,2,7], Wilfrid Mazier[1,2], Filippo Drago[7], Nagore Puente[8,9], Leire Reguero[8,9], Izaskun Elezgarai[8,9], Jean-William Dupuy[10], Daniela Cota[1,2], María-Luz Lopez-Rodriguez[11], Gabriel Barreda-Gómez[5], Federico Massa[1,2], Pedro Grandes[8,9,12], Giovanni Bénard[1,2]§ & Giovanni Marsicano[1,2]§

Dr. Giovanni Marsicano of the University of Bordeaux led this research, and the contribution of the ACHUCARRO research group working on "Ultrastructural and Functional Neuroanatomy of the Synapse", led by Prof. Pedro Grandes, was crucial. The study used a broad range of cutting-edge experimental techniques to show that genetic elimination of the CB1 receptor from the mitochondria of the hippocampus prevents cannabis-induced memory loss, reduction in mitochondrial movement, and decreased neural communication.

This research also revealed that the amnesia caused by cannabinoids and the related cell processes are linked to an acute alteration in bioenergetic mitochondrial activity owing to the direct activation of the CB1 receptors in these organelles. This activation leads to inhibition by the cannabinoid signalling cascade inside the mitochondria, which reduces cellular respiration. This reduction in cellular respiration through cannabinoids is not restricted to the brain; a similar phenomenon occurs in skeletal and cardiac muscle, as has recently been published in a previous paper by Prof. Grandes and his group.

HIGHLIGHTS IN RESEARCH OUTCOMES

The brain needs cleaning to stay healthy

Research led by Dr. Amanda Sierra, group leader of the Laboratory of Glial Cell Biology at the Achucarro Basque Center for Neuroscience, has revealed how failure of the mechanisms that keep the brain clean can lead to neurodegenerative diseases.

When neurons die, their debris needs to be quickly removed for the surrounding brain tissue to continue to function properly. Elimination of the neuron corpses, in a process called phagocytosis, is carried out by highly specialized cells in the brain called microglia. These small cells have many ramifications that are in constant motion and are specially equipped to detect and destroy any foreign element, including dead neurons. Or so it was thought until now.

This study, published in PLOS Biology, investigated for the first time the process of neuronal death and microglial phagocytosis in the diseased brain. To this end, scientists collected brain samples from epilepsy patients at University Hospital of Cruces and from epileptic mice.

During epilepsy-associated seizures, neurons die. However, contrary to what happens in the healthy brain, during epilepsy, microglia seem to be unable to detect dead neurons and destroy them. In other words, their behaviour is abnormal. The result is that dead neurons cannot be eliminated and accumulate, spreading the damage to neighbouring neurons and triggering an inflammatory response that worsens the brain injury.

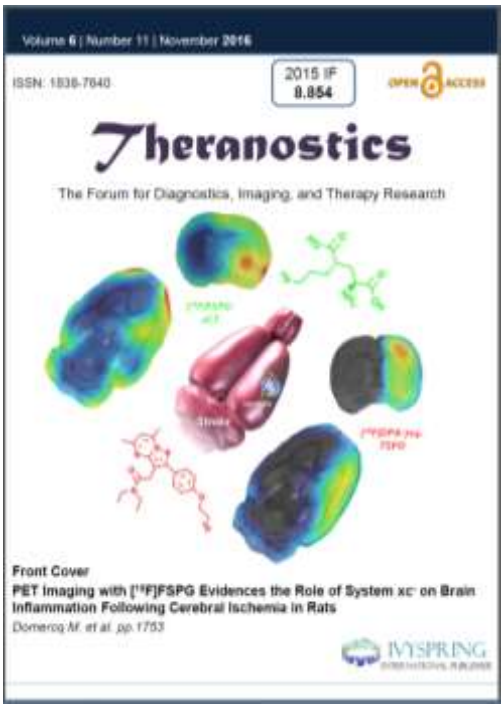
This discovery opens a new avenue to explore therapies that could alleviate the effects of brain diseases. In fact, the research group that undertook these studies is currently developing drugs that target boosting the cleaning process – phagocytosis – to help in the treatment of epilepsy.

This international research effort has been coordinated from the Basque Country, and scientists from CIC bioGUNE (Derio), the University of Bordeaux (France), the University of Southampton (UK), Laval University (Canada), and Baylor College of Medicine (USA) also have taken part.

HIGHLIGHTS IN RESEARCH OUTCOMES

A study on ischemia in which Achucarro took part, featured on the cover of the scientific magazine Theranostics

The Experimental Molecular Imaging and Radiochemistry and Nuclear Imaging Laboratories at CIC biomaGUNE, led by Dr. Abraham Martín and Dr. Jordi Llop in collaboration with the group of Prof. Carlos Matute and Dr. Maria Domercq at Achucarro Basque Center for Neuroscience, UPV/EHU, have published a manuscript identifying a novel therapeutic target that contributes to the inflammatory process underlying ischemic stroke.



Ischemic stroke is one of the major causes of death and permanent disability in industrialized countries. Brain ischemia arises as a consequence of a transient or permanent decrease in cerebral blood flow that promotes alteration of glutamate levels, the main excitatory neurotransmitter, after stroke, leading to irreversible neuronal damage. In addition, inflammation exacerbates neuronal loss, preventing recovery in the acute phase of the ischemic episode. Recently, the same team of researchers uncovered the role played by the exchanger cystine/glutamate (System xc-) in the alteration of glutamate levels that triggers neuronal damage after stroke. The present research demonstrates that this system promotes brain inflammation following ischemic stroke and that its blockade favours a microglial phenotype that helps tissue repair.

PUBLICATIONS

1. The endocytic pathway in microglia during health, aging and Alzheimer's disease. Solé-Domènech, Santiago; Cruz, Dana L.; Capetillo-Zarate, Estibaliz; Maxfield, Frederick R. Ageing Research Reviews, 2016/12 DOI:10.1016/j.arr.2016.07.002
2. **Amyloid -induced astrogliosis is mediated by 1**-integrin via NADPH oxidase 2 in Alzheimer's disease. Wyssenbach, Ane; Quintela, Tania; Llavero, Francisco; Zugaza, Jose L.; Matute, Carlos; Alberdi, Elena. Aging Cell, 2016/12 DOI:10.1111/acel.12521
3. **Lck/PLC control migration and proliferation of interleukin (IL)**-2-stimulated T cells via the Rac1 GTPase/glycogen phosphorylase pathway. Llavero, Francisco; Artaso, Alain; Lacerda, Hadriano M.; Parada, Luis A.; Zugaza, José L. Cellular Signalling, 2016/11 DOI:10.1016/j.cellsig.2016.07.014
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5. Knowledge Transfer

Achucarro collaborates with three masters programmes organized and coordinated by the University of the Basque Country (UPV/EHU):

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

The centre also coordinates the Doctorate Programme on Neurosciences, organized together with the Universities of Coruña (Galicia), Castilla – La Mancha, Pablo de Olavide (Seville), and Rovira I Virgili (Catalonia).

This qualification is recognized at level 4 in the Spanish Framework of Higher Education Qualifications (MECES) and corresponds to level 8 of the European Qualifications Framework (EQF), according to Royal Decree 22/2015 of 23 January 2015 (BOE Spanish Official Gazette 07/02/2015).

PHD THESES

In 2016, four PhD theses were completed and successfully defended.

Congratulations to our colleagues Ianire, Ana, Manuel, and Monica.

- Ianire Buceta Salazar
  "Estudio Anatómico y Funcional del Sistema Endocannabinoide en el Cerebro"
- Ana Gutierrez Rodríguez
  "Anatomical and Physiological Analysis of Mouse Mutant Mice Expressing Type-1 Cannabinoid Receptors in Specific Brain Populations"
- Manuel Canedo Antelo
  "Mecanismos moleculares de apoptosis en oligodendrocitos"
- Monica Benito Muñoz
  "Modulación purinérgica de la neurogenesis adulta a través de isquemia cerebral"

SEMINARS

In 2016, we organized 30 Achucarro Seminars.

January 18
Funciones de la proteína priónica celular en la enfermedad de Alzheimer y taupatías
José Antonio del Río
Institute for Bioengineering of Catalonia [IBEC] (Barcelona)

January 20
Genética de las demencias y marcadores de la enfermedad de Alzheimer
Alberto Lleó
Hospital de la Santa Creu i Sant Pau & ciberNed (Barcelona)

January 29
Glial pathology in Alzheimer's disease: Insights from transgenic models and human post-mortem brains
Antonia Gutiérrez
Universidad de Málaga & ciberNed

February 05
From metallothioneins to Interleukin-6: a very long journey
Juan Hidalgo Pareja
Institut de Neurociències UAB (Barcelona)

February 12
Functional organization of a fear memory engram
Mazahir Hasan
Neurocure Cluster of Excellence Charité – Universitätsmedizin (Berlin, Germany)

February 17
Neural stem cell heterogeneity in homeostasis and disease
Ana Martín-Villalba
Deutsches Krebsforschungszentrum (Heidelberg, Germany)

February 26
Dysfunction of retrograde transport in neurodegenerative disorders – from atoms to cell
Aitor Hierro + Adriana Rojas
CIC bioGUNE (Derio, Spain)

March 04
*From behavioural pharmacology to cellular neuroscience: the search for new **therapeutic targets**"*
Ainhoa Plaza-Zabala
Achucarro Basque Center for Neuroscience






March 11
Synaptic signalling for plasticity during aging and Alzheimer's disease
Jose A Esteban
CBM – Severo Ochoa [CSIC – UAM] (Madrid)

March 18
Image processing tools for the study of brain connectomics
Ignacio Arganda-Carreras
Faculty of Computer Science (UPV/EHU, Donostia – San Sebastián)

April 15
Myelinophagy: A novel mechanism for Schwann cell–mediated myelin breakdown
Ashwin Woodhoo
CIC bioGUNE (Derio)

April 29
Myelination and oligodendroglial support of axonal metabolism
Klaus-Armin Nave
Max Planck Institute of Experimental Medicine (Göttingen, Germany)

May 06
Computational biology powering the use of neural stem cells in regenerative medicine
Marcos J. Araúzo-Bravo
BioDonostia HRI (Donostia)

May 13
Magnetic resonance imaging and nanotechnology for the study and treatment of stroke
Pedro Ramos Cabrer
CIC biomaGUNE (Donostia – San Sebastián)

June 03
Modulation of the glial niche by the neuropeptide Cortistatin: Potential role in neuroinflammation and neurodegeneration
Elena Gonzalez Rey
Instituto de Parasitología y Biomedicina "López – Neyra" [CSIC] (Granada)

June 10
Organization and signalling through C-bouton synapse in alpha-motor neurons: implications in the pathophysiology and therapy of motor neuron diseases (ALS and SMA)
Josep E. Esquerda i Colell
Universitat de Lleida/IRBLLEIDA

June 17
Axon-to-soma degeneration by local translation of transcription regulators
Jimena Baleriola
Achucarro Basque Center for Neuroscience






July 15
Inhibitory neurons control cellular engram formation and memory stability
Pablo Méndez
CMU, University of Geneva (Switzerland)

July 20
Molecular mechanisms of neocortical development: from cell specification to circuit integration
Cristina Gil Sanz
The Scripps Research Institute (La Jolla, California, USA)

July 28
Brain energy metabolism and neuron–glia (mis)interactions in Huntington's disease
Maite A. Castro
Center for Interdisciplinary Studies on Nervous System, Universidad Austral de Chile (Valdivia, Chile)

September 30
Prospects of oxytocin for treating autism: from genetics to drug discovery
Olga P**eñagarikano**
University of the Basque Country (Leioa)

October 14
Dysfunctional microglia as a trigger for pathological pruning: novel roles for TDP-43
Rosa C. Paolicelli
IREM – University of Zurich (Switzerland)

October 21
Zebrafish as a tool for drug discovery and target validation in neurodegenerative diseases
Ainhoa Alzualde & Arantza Muriana
Biobide (Donostia – San Sebastian)

October 28
Super-resolution microscopy for neuroscience
Jan Tønnesen
UPV/EHU & Achucarro (Zamudio)

November 04
Juvenile NMDA receptors: Gatekeepers of synaptic plasticity and cognition
Isabel Pérez-Otaño
Center for Applied Medical Research (Pamplona)





November 18
Glucocorticoid hormones preserve a population of adult hippocampal neural stem cells in the aging brain
Carlos Fitzsimons
Swammerdam Institute for Life Sciences, Universiteit van Amsterdam (The Netherlands)

November 25
Myelin remodelling, an old game with new players
Jorge Larriva Sahd
Instituto de Neurobiología UNAM (Mexico)

December 02
Cell fate changes and cell reprogramming in development and neurodegeneration
Carlos Vicario Abejón
Instituto Cajal & ciberNed (Madrid)

December 16
A cannabinoid link between mitochondria and memory
Giovanni Marsicano
NeuroCentre Magendie [INSERM, U. Bordeaux] (France)

December 22
Radiosensitivity of human neural stem cells
Onetsine Arrizabalaga
GSI Helmholtzzentrum für Schwerionenforschung (Germany)





HIGHLIGHTS IN DISSEMINATION OUTCOMES

SPAOM 2016

The Biofisika Institute and ACHUCARRO brought to Bilbao the first edition of this scientific meeting. SPAOM has its roots in the biannual meeting of the Spanish Network for Advanced Optical Microscopy (REMOA) and the meetings of the Portuguese Platform of BioImage (PPBI).

The main objective of this congress was promoting and gathering together the Spanish and Portuguese bioimaging scientific communities, as well as other European colleagues working in the same field.

A total of 159 people from different research institutions and hardware manufacturers attended this initial conference, 30% from industry and the rest from academia.

The Web address for the 2016 inaugural meeting is www.spaom2016.eu. Now the baton is in the hands of our Portuguese colleagues for the 2018 gathering.

ACHUCARRO FORUM

In 2016, we organized an Achucarro Forum dissemination and public awareness conference.

March 10th
Bizkaia Aretoa (Bilbao)

José A. Esteban
Research Professor of the CSIC at the "*Severo Ochoa*" Center for Molecular Biology in Madrid (Spain)

What are memories made of?
And where are they stored?

Our partners in this activity were the Chair for Science Culture of the UPV/EHU and the Basque Public Media Group (EiTB), which provided media coverage and support.

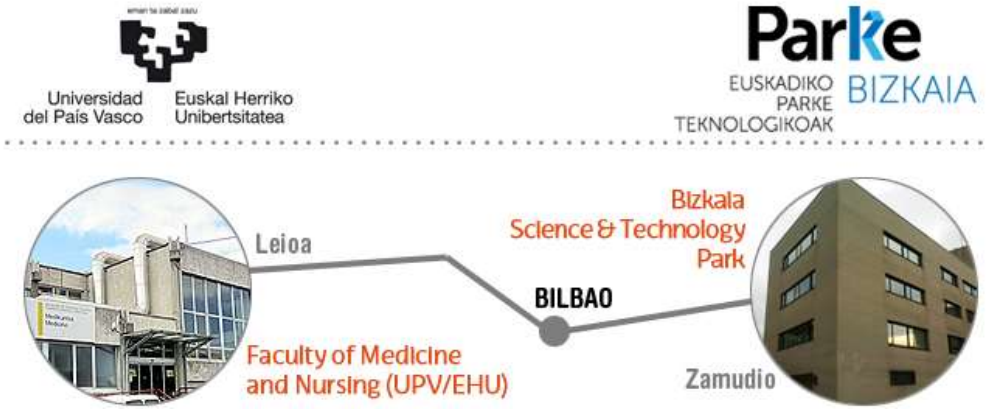
PUBLIC OUTREACH AND SOCIAL MEDIA

Our strategy for social media and information dissemination using the different Internet platforms as a way of increasing our profile with different audiences can be assessed with the following indicators:

Website www.achucarro.org	25 news updates, 30 seminars posted 21,157 visits (21% more than the previous year) 73,885 page views 58% new visitors, 42% returning visitors 66% visits from Spain; 34% international 20% of visits from mobile devices
Blog Neurozientzian	6 articles posted 1,377 users 2,603 views 82% new visitors; 18% returning visitors 35% of visits from Spain; the remaining 65% from around the world
Twitter AchucarroNeuro	985 followers 5,201 tweets and retweets
Facebook Achucarro.org	298 people engaged (likes) 67 posts

6. Infrastructure and Equipment

The year 2016 will be our last year as a virtual and networked research centre located in two different cities and in two different buildings in each of the cities.



Currently, the ACHUCARRO headquarters is located in the Bizkaia Science and Technology Park, Zamudio, a city in the metropolitan area of Bilbao. Some research programmes are established at that location or within the University campus in Leioa, also in the metropolitan area of Bilbao, with the two separated by 15 kilometres.

Achucarro has equipment and technologies associated with many research areas and needs, including the following: *Cellular and Molecular Neurobiology; Primary and Organotypic Cultures; In Vitro Models; Classical Morphometry and Stereology; Immunofluorescence; Immunochemistry and Immunohistochemistry; Electrophysiology; Calcium, Epifluorescence, Advanced Light (Confocal, Super-resolution), and Electron Microscopy; Genotyping and Functional Genomics; Sequencing; qPCR and qRT-PCR; Flow Cytometry and Fluorescence-activated Cell Sorting; Cerebellar Organotypic Culture for Neuroinflammation; Reporter Constructs and Recombinant Expression; and Stereotaxic Surgery and Stereology-based Quantification.*

7. Achucarro in figures

STRATEGY AND MANAGEMENT	2013	2014	2015	2016
% of publications in neurosciences over the total in the Basque Country (previous year)	4%	3%	5%	3%
% of publications from Achucarro over the total neurosciences in the Basque Country	38%	38%	22%	36%
H-index of Achucarro	4	8	10	20
% compliance of Management Plan	99%	95%	97%	98%
Number of meetings of the Board of Trustees	3	2	4	2
Annual Budget (million Euros)	0.67	1.22	2.20	2.01
Rate of funding change from Basque Government	3%	25%	20%	24%

PARTNERSHIPS	2013	2014	2015	2016
Number of strategic agreements (accumulated)	3	5	6	8
Number of institutional agreements (accumulated)	6	6	7	13
Number of operational agreements (new)	2	2	5	1

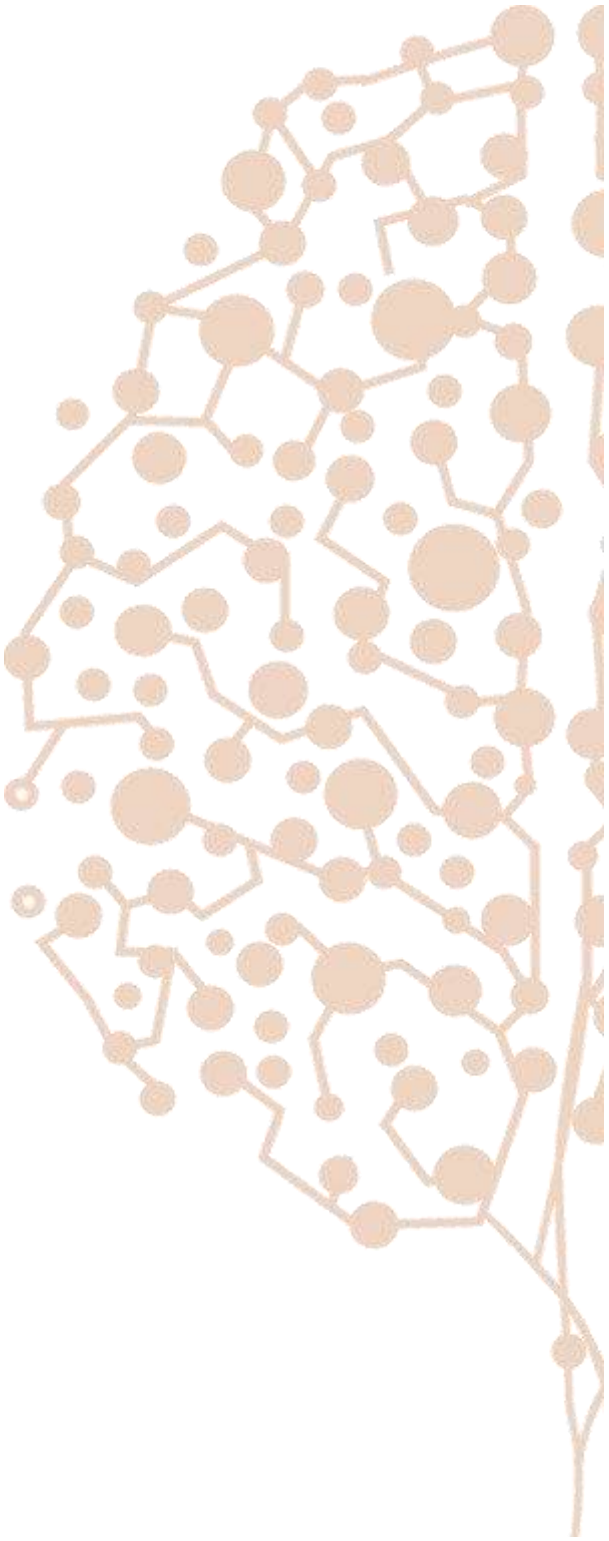
PEOPLE	2013	2014	2015	2016
Number of persons involved in Achucarro	50	68	73	77
Number of directly contracted staff (FDE)	2	6.5	11.4	16.0
Number of persons in practice work	1	0	0	1
Number of researchers	45	63	67	70
Number of principal investigators	7	8	8	11
Number of senior researchers	8	16	20	22
Number of postdoctoral researchers	10	10	10	7
Number of PhD students	16	24	29	30
Number of master's students	1	5	7	14
Number of technicians	4	4	4	4
Number of staff	1	1	2	3
Number of Ikerbasque Research Professors	6	6	6	7
Number of Ikerbasque Research Fellows	1	2	3	5
Number of Ramon y Cajal Fellows	0	1	3	4

RESEARCH	2013	2014	2015	2016
Number of research groups	7	8	8	11
Number of publications	53	45	50	60
Number of publications (Q1)	46	38	38	41
Number of participations in congresses	66	69	96	75
Number of books and chapters	6	16	5	6
Number of patents (applications)	0	0	0	0
Number of patents (accepted)	2	0	0	0
Attracted funding (million Euros)	2.4	2.2	3.2	2.8
Number of PhD theses (in progress)	16	20	29	29
Number of PhD theses (completed)	4	4	4	4

KNOWLEDGE TRANSFER/TRAINING	2013	2014	2015	2016
Number of Achucarro seminars	25	23	22	30
Number of congresses, conferences	1	2	3	2
Number of training events	1	2	1	1
Number of dissemination events	1	2	2	1
Number of attendees per event (mean)	285	190	200	130

KNOWLEDGE TRANSFER/DISSEMINATION	2013	2014	2015	2016
Press releases	3	5	7	5
Followers on Twitter	309	505	793	985
Tweets on Twitter	974	2,432	4,134	5,201
Number of news updates published on the website	42	28	30	25
Total visits to the website	10,277	11,849	17,380	21,157
Visits from Spain	7,497	7,897	11,511	13,926
% visits from Spain	73%	67%	67%	66%
% visits from abroad	27%	33%	33%	34%
Returning visitors to website	40%	43%	40%	42%
Ratio of new visitors to website	60%	57%	60%	58%

INFRASTRUCTURE AND EQUIPMENT	2013	2014	2015	2016
Strategic and singular equipment acquisitions	2	4	9	9



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