

2021 Annual Report



scientia ad remedium

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Foreword

Dear reader,

I have the pleasure to write a few words for this Annual Report 2021 as the new director of the centre. I take this opportunity to express my gratitude to Carlos Matute and his management team for the excellent job done in past years that has allowed me to work in a well-organized environment.

The past year has been marked again by the COVID-19 pandemic, but we now have adapted better to the disruption in our working flow. Despite the limitations imposed to our experimental activities, the performance of our research groups in the strategic program ended in 2021 has been highly satisfactory. The centre increased by 140% the personnel in this period, from 84 to 115. The members of ACHUCARRO have published more than 250 papers, above 82% of them in journals ranked in the first quartile of their areas.

For each euro provided by the BERC Programme during 2018-21 (4.3 million), we managed to get other 1.56 (6.73 million). Private and international funding has significantly increased as our centre gained visibility. These results place us in a solid position for the next decade of ACHUCARRO.

In coming years, our aim is to use the work done as a firm basis to launch a re-organization of our way of working focused on fostering internal collaboration to strengthen our capabilities. The IKUR strategy presented by the Basque Government in 2021 is going to be a fundamental aid for this. We have high hopes for the tools that our institutions are putting in place to develop this new scenario.

Finally, we feel obliged to acknowledge the continuous support of the Basque Government, Ikerbasque - the Basque Foundation for Science and the University of the Basque Country (UPV/EHU). Their commitment is invaluable.

Ignacio Torres Alemán Scientific Director In 2021 we completed our second strategic programme.

During the year, we underwent an in-depth analysis to define and launch our third strategic plan, for the period 2022-2025.

1. Strategy and Management

ACHUCARRO is part one the BERC (Basque Excellence Research Centres) entities supported by the Basque Government. The Basque Government has accredited 9 entities with this quality certification. 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. ACHUCARRO is one of the three youngest centres of the network.

Each Basque Excellence Centre has a different specialisation and scientific approach. ACHUCARRO is the only one working in the field of neurobiology (there are 4 on physics/chemistry, 1 in biophysics, 1 in climate change, 1 in applied mathematics, and 1 in cognitive neuroscience and language).

In the year 2018, we launched the deployment of our second strategic plan for the period 2018-2021. In this period, our main strategic objective is to consolidate the structure and the path established in the past, looking forward and adapting to the changing environment in scientific research within a global momentum of tremendous changes.

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 the 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.

The Board of Trustees of ACHUCARRO is currently formed by representatives of Ikerbasque - the Basque Foundation for Science, the University of the Basque Country (UPV/EHU), and BIOEF – the Basque Foundation for Health Innovation and Research.

SCIENTIFIC PLAN 2018-2021

The Mission of ACHUCARRO is to contribute to the development of a socially and economically sustainable society. We attain this shared challenge by performing high quality research in the field of neuron-glia biology and interactions, in the normal and pathological brain.

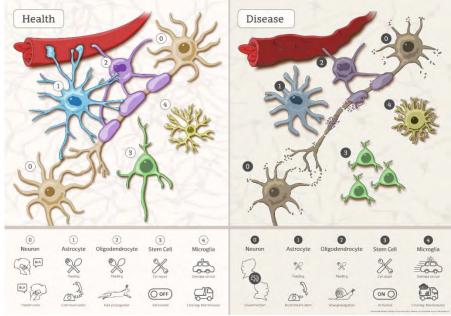


Figure 1. Schematics of our research focus

The Strategic Research Programme for this period, supervised and approved by our International Scientific Advisory Board and validated by our Board of Trustees, contains **three high-level research programmes:**

- Characterization of the role of glial cells in the physiology of the nervous system
 - roles of astrocytes in synaptic communication
 - o neurotransmitter signalling during neurogenesis and gliogenesis
 - o mechanisms of microglia phagocytosis during neurogenesis
- Characterization of structural and functional changes of neuronal-glial networking in the aged brain
 - o 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
 - o research on general mechanisms of neuron and glial cell death
 - o understanding the pathophysiology of Alzheimer's disease and epilepsy
 - o autoimmune pathogenesis of multiple sclerosis (MS) and neuroinflammation

EQUALITY PLAN 2018-2021

ACHUCARRO developed the first specific Equality Plan in 2017, with the consulting and advice of an external firm specialised in this sector. All the people appointed that year participated in, at least, one of the dynamics of the internal and external analysis to launch the plan.

This plan identified four areas of work to improve our situation towards equal opportunities:

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

This plan was launched in January 2018, being one of the first activities to appoint an **Equality Committee**, composed by representatives of personnel on different functions or career stages, from each gender.

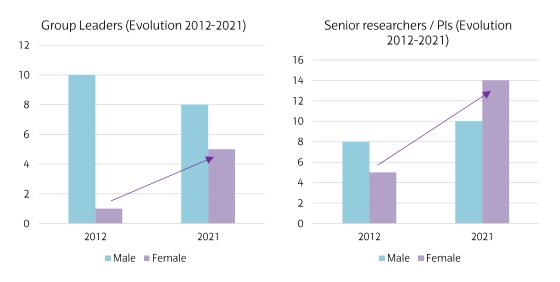


Figure 2. Evolution of number of Group Leader and Senior researchers by gender

https://www.achucarro.org/equality

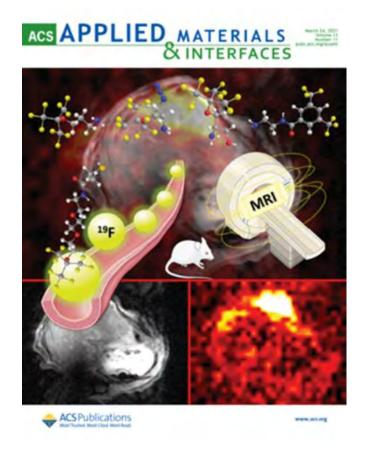
Highlight in research outcomes

Researcher from Institute Biofisika, CIC biomaGUNE and ACHUCARRO collaborate in this work in the field of molecular imaging

Cover on "ACS Applied Materials & Interfaces" for a collaboration work on fluorine labeling of nanoparticles

This article showed the results of collaboration that led to successfully prepare fluorinelabelled nanoparticles (NPs) that are active in 19F magnetic resonance imaging (19F MRI) by either conjugating four different fluorinated building blocks, shown in the 3D structure, to carboxyl-modified NPs or by direct grafting of PEG-fluorinated ligands. The research team obtained 19F MRI images of NPs accumulating in mice livers after intravenous injection.

This imaging study was selected by the journal ACS Applied Materials ϑ Interfaces to be the cover of the March 2021 Issue.



"Fluorine Labeling of Nanoparticles and In Vivo 19F Magnetic Resonance Imaging" Arango, Juan Manuel; Padro, Daniel; Blanco, Jorge; Lopez-Fernandez, Sonia; Castellnou, Pilar; Villa-Valverde, Palmira; Ruiz-Cabello, Jesús; Martin, Abraham; Carril, Mónica ACS Applied Materials & Interfaces (Mar-11) DOI: 10.1021/acsami.1c01291 All areas of human activity combine moments of cooperation, with moments for competition. Our culture is based on the fact that there are more moments of cooperation, and they add more value, and that is why we manage our relationships with entities with which we share this culture and vision.

2. Partnerships and Collaborations

According to the objectives and fields of activity, we classify the collaboration and partnership relationships we create and maintain in three different types: Institutional, Strategic or Operational.

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 2018–2021
- Agreement to improve the Imaging Facility with the incorporation of a new confocal microscope

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

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



CiberNed The Center for Network Biomedical Research on Neurodegenerative Diseases (CIBERNED) was born in 2006 as heir to the Center for Research on Neurological Diseases (CIEN). CIBERNED is a research organization with its own legal personality, and constituted by research groups without physical contiguity, belonging to different Administrations, Institutions and Autonomous Communities, from the public and private sectors, with research lines and objectives focused on the common specific area of neurodegenerative diseases, which are coordinated to achieve scientific objectives that could hardly be considered in a specific context. more restricted execution.

Bizkaia Talent

Bizkaia

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.



HR EXCELLENCE IN RESEARCH

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.

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.

INTERNATIONAL SCIENTIFIC ADVISORY COMMITTEE (ISAC)

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.

During the first half of 2021 they performed a remote visit to ACHUCARRO to assess the degree of evolution during the last years, and produced a report with an evaluation and advice that was incorporated to the process of strategic planning for the period 2022-2025.



Figure 3. Screenshot of one of the meeting during the 2021 evaluation process

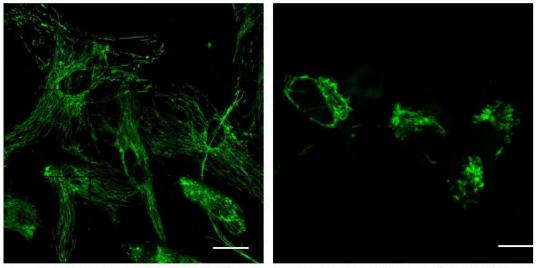
Highlight in research outcomes

Astrocytes generated from Parkinson's disease (PD) patients manifested atrophic morphology and decreased complexity. In addition, PD-derived astrocytes demonstrated aberrant mitochondrial morphology and decreased mitochondrial metabolism. Our observations indicate that astrocytes in individuals with PD lack their homeostatic support against oxidative stress.

Astroglial atrophy at the onset of Parkinson's disease. When astrocytes lose their support to neurons

In this work we generated pluripotent stem cells (iPSC) through the technique of cellular reprogramming from healthy donors and fibroblasts of PD patients bearing the LRRK2 (G2019S) mutation. Then, the iPSC cells were differentiated to astrocytes and cultured in vitro for at least 90 days. This approach gave us the opportunity to observe and characterize patient's astrocytes in a dish. Respect to the healthy astrocytes, PD cells displayed atrophic morphology, in terms of cellular area and cell complexity, aberrant mitochondrial morphology and atypical intracellular distribution (see figure). Accordingly, we observed significant deficit of mitochondrial respiration and increase of reactive oxygen species.

Altogether, our data indicate that in case of neuronal stress "parkinsonian" astrocytes cannot protect properly the neurons thus contributing to neuronal death through decreased homoeostatic support, elevated oxidative stress and failed neuroprotection.



Control astrocytes control (Line AX0083)

PD patient derived astrocytes (Line PD33879)

"Astrocytic atrophy as a pathological feature of Parkinson's disease with LRRK2 mutation"

Ramos-González, P.; Mato, S.; Chara, J.C.; Verkhratsky, A.; Matute, C.; Cavaliere, F. npj Parkinson's Disease (Mar-30) DOI: 10.1038/s41531-021-00175-w We are an organisation of professionals from 14 different nationalities. Foreigners represent the 16% of the staff, and a contribution to diversity and internationalisation.

3. People

In 2021 we continued our steady growth (1.3% from 2020 to 2021). At the end of 2021 ACHUCARRO had 115 people appointed.



Figure 4. Evolution of personnel 2015-2021

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.

Colleagues finishing their appointment this year

Svein Achicallende (Predoctoral researcher) Marlene Soledad Beccari (Predoctoral researcher) Joanna Danielewicz (Postdoctoral Fellow) Jorge Valero (Senior Researcher)

Appointed Staff (December 2021)

Oihane Abiega (Postdoctoral Fellow) Laura Aguado (Predoctoral researcher) Elena Alberdi (Senior Researcher, Deputy Scientific Director) María Alfonso (Predoctoral researcher) Saioa Alzola (Predoctoral researcher) Ilazki Anaut (Predoctoral researcher) María Ardaya (Predoctoral researcher) Amaia Arranz (Group Leader) Alazne Arrazola (Predoctoral researcher) Elsa Astorga (Predoctoral researcher) Nerea Ausín (Predoctoral researcher) Uxue Balantzategi (Predoctoral researcher) Jimena Baleriola (Group Leader) Ander Baraibar (Postdoctoral Fellow) Laura Bayón (Predoctoral researcher) Xabier Bengoetxea (Postdoctoral Fellow) Ana Bernal (Postdoctoral Fellow) Maite Blanco (Predoctoral researcher) Eleanora Blasi (Predoctoral researcher) Itziar Bonilla (Postdoctoral researcher) Leire Boveda (Predoctoral researcher) lanire Buceta (Senior Researcher) Stefano Calovi (Postdoctoral Fellow) Estibaliz Capetillo (Senior Researcher) Alejandro Carretero (Postdoctoral Fellow) Fabio Cavaliere (Senior Researcher) Juan Carlos Chara (Postdoctoral Fellow) Raffaela Cipriani (Technician) Teresa Colomer (Predoctoral researcher) Joan Cruz (Predoctoral researcher) Aida de la Cruz (Predoctoral researcher) María Domerca (Senior Researcher) Irene Durá (Predoctoral researcher) Jon Egaña (Postdoctoral Fellow) Izaskun Elezgarai (Senior Researcher) Juan Manuel Encinas (Group Leader) Laura Escobar (Technician) Nuria Galbis (Predoctoral researcher) María Gamarra (Predoctoral researcher) Adhara Gaminde (Predoctoral researcher) Laura García (Project Manager) Fernando García-Moreno (Senior Researcher) Lorena García (Predoctoral researcher) Inmaculada Gerrikagoitia (Senior Researcher) Paula Gimenez (Predoctoral researcher) Sonia Gómez (Senior Researcher) Pedro Grandes (Group Leader) Juan Jose Gutierrez (Predoctoral researcher) Mazahir T. Hasan (Group Leader) María Isabel Hernández (Predoctoral researcher) Izaskun Igeregi (Management Assistant) Leire Iglesias (Lab Technician) Josune Imaz (Predoctoral researcher) Leire Izagirre (Predoctoral researcher) Ana Joya (Predoctoral researcher) Gorka Kortabarria (Predoctoral researcher) Maria Kukley (Group Leader) Begüm Kurt (Predoctoral researcher) Rizky Lasabuda (Predoctoral researcher) Leire Lekunberri (Predoctoral researcher) Alice Louail (Postdoctoral Fellow) Celia Luchena (Predoctoral researcher) Miriam Luque (Laboratory technician) Mar Márquez (Predoctoral researcher) Zara Martínez (Laboratory Technician) Abraham Martín (Group Leader) Susana Mato (Senior Researcher) Carlos Matute (Group Leader) Aitor Medrano (Predoctoral researcher) Juan Mendizabal (Senior Researcher) Amaia Mimenza (Predoctoral researcher) Patricia MIranda (Postdoctoral Fellow) Alejandro Montilla (Predoctoral researcher) Alvaro Moreno (Predoctoral researcher) Óscar Moreno (Predoctoral researcher) Teresa Muro (Predoctoral researcher) Blanca Ochoa (Predoctoral researcher) Amaia Ochoa de Amezaga (Postdoctoral Fellow) Ana Palma (Predoctoral researcher) Aitor Palomino (Facility Manager) Olatz Pampliega (Group Leader) Marta Pereira (Predoctoral researcher) Fernando Pérez-Cerdá (Senior Researcher) Lucila Pérez (Predoctoral researcher) Alberto Pérez-Samartín (Senior Researcher) José Ramón Pineda (Senior Researcher) Ainhoa Plaza (Postdoctoral Fellow) Nagore Puente (Senior Researcher) Laura Pulido (Predoctoral researcher) Almudena Ramos (Senior Researcher) Leire Reguero (Senior Researcher) Irantzu Rico (Senior Researcher) Noelia Rodriguez (Predoctoral researcher) Ane Rodriguez (Predoctoral researcher) Eneritz Rueda (Predoctoral researcher) Asier Ruiz (Senior Researcher) Jaime Sagarduy (General Manager) Gentzane Sánchez (Postdoctoral Fellow) María Victoria Sánchez (Senior Researcher) Ane Santisteban (Predoctoral researcher) Rafael Sarría (Senior Researcher) Rodrigo Senovilla (Predoctoral researcher) Maitane Serrano (Predoctoral researcher) Virginia Sierra (Predoctoral researcher) Amanda Sierra (Group Leader) Edgar Soria (Senior Researcher) Federico N. Soria (Senior Researcher) Vanja Tepavcevic (Senior Researcher) Itziar Terradillos (Predoctoral researcher) Irene Tomé (Predoctoral researcher) Jan Tønnesen (Group Leader) Ignacio Torres (Group Leader, Scientific Director) Carmen Utrilla (Predoctoral researcher) Maria Vella (Predoctoral researcher) Alexei Verkhratsky (Group Leader) Irati Zabalegui (Predoctoral researcher) Fátima Zallo (Postdoctoral Fellow) Jonathan Zegarra (Predoctoral researcher) Jone Zuazo (Predoctoral researcher) José Luis Zugaza (Group Leader)

ACHUCARRO contributed with 83 new publications in 2021. 84% of them in the first quartiles of their research fields.

4. Research

RESEARCH GROUPS

Laboratory of **Brain Circuits** Therapeutics



Mazahir T. Hasan Ikerbasque Research Professor

Laboratory of **Glial and Neuronal** Autophagy



Olatz Pampliega Ramón y Cajal Fellow Department of Neurosciences (UPV/EHU)

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 **Juan Manuel Encinas** Neural Stem Cells and Ikerbasque **Research Professor** Neurogenesis Laboratory of Ignacio Torres Alemán Neurobiology of Ikerbasque **Research Professor Insulin Peptides Carlos Matute Full Professor** Laboratory of Department of Neurobiology Neurosciences (UPV/EHU) Laboratory of Abraham Martín Neuroimaging and Ramón y Cajal biomarkers of Fellow inflammation Laboratory of **Maria Kukley** Neuronal and Glial Ikerbasque **Research Professor Physiology** Jan Tønnesen Ramón y Cajal Fellow Laboratory of Department of **Neuronal Excitability** Neurosciences (UPV/EHU) Laboratory of **Pedro Grandes**

Ultrastructural and Functional Neuroanatomy of the Synapse



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

Highlight in granted project

Jan Tønnesen and Federico Soria join an international consortium, headed by Professor Miquel Vila (Autonomous University of Barcelona), in a research project awarded 10 million dollars from the Aligning Science Across Parkinson's (ASAP) initiative

Researchers from ACHUCARRO part of new 11 million dollars consortium to tackle Parkinson's disease

Parkinson's disease is a degenerative neurological disorder that primarily affects the brain's motor system and is symptomatically characterized by tremor, rigidity, and slowing of movements. It is the second most common neurodegenerative disorder after Alzheimer's disease. The underlying cause is unknown, though both inherited genetic and environmental risk factors have been identified.

The United States based ASAP initiative is fostering global collaboration and resources to better understand the underlying disease causes and is working with the Michael J. Fox Foundation that is the principal private entity funding Parkinson's disease research worldwide. The annual ASAP grant scheme aims to fund ground-breaking research projects to be carried out within the highly enabling ASAP Collaborative Network, which entails all ongoing ASAP projects. Each year, numerous international research consortiums apply with proposals that are evaluated by experts in the Parkinson's research field. Only the most innovative projects with the greatest potential for scientific progress are funded and receive up to 11 million dollars.



In the latest funding round, the international consortium led by Prof. Vila (Barcelona), and including ACHUCARRO researchers Dr. Tønnesen and Dr. Soria, has been awarded an ASAP grant to investigate how and where Parkinson's disease pathology originates and develops across brain regions. Dr. Soria will investigate the extracellular matrix of the brain, while Dr. Tønnesen will focus on the extracellular space that lies between the individual brain cells.

PUBLICATIONS

1. shinyCurves, a shiny web application to analyse multisource qPCR amplification data: a COVID-19 case study Olaechea-Lázaro, S.; García-Santisteban, I.; Pineda, J.R.; Badiola, I.; Alonso, S.; Bilbao, J.R.;

Fernandez-Jimenez, N. **BMC Bioinformatics** (In press) DOI: 10.1186/s12859-021-04392-1

- Identification of potentially irritating intravenous medications Ballesteros-Peña, S.; Fernández-Aedo, I.; Vallejo-De la Hoz, G.; Tønnesen, J.; Miguelez, C. Enfermeria Intensiva (In press) DOI: 10.1016/j.enfi.2021.05.003
- 3. **Plasticity of microglia** Augusto-Oliveira, Marcus; Arrifano, Gabriela P.; Delage, Charlotte Isabelle; Tremblay, Marie-Ève; Crespo-Lopez, Maria Elena; Verkhratsky, Alexei **Biological Reviews** (In press) DOI: 10.1111/brv.12797
- Post-COVID-19 neuropsychiatric syndrome: Is maladaptive glial recovery to blame? Steardo, L., Jr.; Steardo, L.; Verkhratsky, A.; Scuderi, C. Acta Physiologica (In press) DOI: 10.1111/apha.13717
- Super-resolution STED microscopy in live brain tissue Calovi, S.; Soria, F.N.; Tønnesen, J. Neurobiology of Disease (In press) DOI: 10.1016/j.nbd.2021.105420
- Calcium signaling in neuroglia Lim, D.; Semyanov, A.; Genazzani, A.; Verkhratsky, A. International Review of Cell and Molecular Biology (In press) DOI: 10.1016/bs.ircmb.2021.01.003
- 7. (Review) Future avenues for Alzheimer's disease detection and therapy: liquid biopsy, intracellular signaling modulation, systems pharmacology drug discovery Hampel, Harald; Vergallo, Andrea; Caraci, [...]; Llavero, Francisco; Zugaza, José L.; Lucía, Alejandro; Giacobini, Ezio; Lista, Simone

Neuropharmacology (In press) DOI: 10.1016/j.neuropharm.2020.108081

8. The Absence of the Transient Receptor Potential Vanilloid 1 Directly Impacts on the Expression and Localization of the Endocannabinoid System in the Mouse Hippocampus

Egaña-Huguet, Jon; Bonilla-Del Río, Itziar; Gómez-Urquijo, Sonia M.; Mimenza, Amaia; Saumell-Esnaola, Miquel; Borrega-Roman, Leire; García del Caño, Gontzal; Sallés, Joan; Puente, Nagore; Gerrikagoitia, Inmaculada; Elezgarai, Izaskun; Grandes, Pedro **Frontiers in Neuroanatomy** (In press) DOI: 10.3389/fnana.2021.645940

- 9. **Reactive astrocyte nomenclature, definitions, and future directions** Escartin, C.; Galea, E.; [...] Zorec, R.; Sofroniew, M.V.; Verkhratsky, A. **Nature Neuroscience** (In press) DOI: 10.1038/s41593-020-00783-4
- Effects of Platelet-Rich Plasma on Cellular Populations of the Central Nervous System: The Influence of Donor Age Delgado, Diego; Bilbao, Ane Miren; Beitia, Maider; Garate, Ane; Sánchez, Pello; González-Burguera, Imanol; Isasti, Amaia; López De Jesús, Maider; Zuazo-Ibarra, Jone; Montilla, Alejandro; Domercq, María; Capetillo-Zarate, Estibaliz; García del Caño, Gontzal; Sallés, Joan; Matute, Carlos; Sánchez, Mikel

International Journal of Molecular Sciences (In press) DOI: 10.3390/ijms22041725

- The endocannabinoid system in glial cells and their profitable interactions to treat epilepsy: Evidence from animal models Egaña-Huguet, J.; Soria-Gómez, E.; Grandes, P. International Journal of Molecular Sciences (Dec-02) DOI: 10.3390/ijms222413231
- Autophagy and the hallmarks of aging Kaushik, Susmita; Tasset, Inmaculada; Arias, Esperanza; Pampliega, Olatz; Wong, Esther; Martinez-Vicente, Marta; Cuervo, Ana Maria Ageing Research Reviews (Dec-01) DOI: 10.1016/j.arr.2021.101468

- The tyrosine phosphatase hPTPR controls the early signals and dopaminergic cells viability via the P2X7 receptor Bernal, F.L.; Montoro, M.L.; Sastre, A.A.; Lacerda, H.M.; Zugaza, J.L. International Journal of Molecular Sciences (Nov-29) DOI: 10.3390/ijms222312936
- 14. Whole Blood Expression Pattern of Inflammation and Redox Genes in Mild Alzheimer's Disease Milanesi, Elena; Dobre, Maria; Cucos, Ctlina Anca; Rojo, Ana I.; Jiménez-Villegas, José; Capetillo-Zarate, Estibaliz; Matute, Carlos; Piñol-Ripoll, Gerard; Manda, Gina; Cuadrado, Antonio Journal of Inflammation Research (Nov-20) DOI: 10.2147/JIR.S334337
- 15. Concentration-dependent duality of bFGF in regulation of barrier properties of human brain endothelial cells Kriauinait, K.; Pocit, A.; Kauyl, A.; Pajarskien, J.; Verkhratsky, A.; Pivorinas, A. Journal of Cellular Physiology (Nov-15) DOI: 10.1002/jcp.30410
- Astrocytic processes: from tripartite synapses to the active milieu Semyanov, A.; Verkhratsky, A.
 Trends in Neurosciences (Oct-15) DOI: 10.1016/j.tins.2021.07.006
- Astrocyte–Endotheliocyte Axis in the Regulation of the Blood–Brain Barrier Pivorinas, A.; Verkhratsky, A.
 Neurochemical Research (Oct-15) DOI: 10.1007/s11064-021-03338-6
- 18. Time in Neurogenesis: Conservation of the Developmental Formation of the Cerebellar Circuitry
 Duado Alapã, 5. Causió Marana, 5.

Rueda-Alanã, E.; Garciá-Moreno, F. Brain, Behavior and Evolution (Sep-30) DOI: 10.1159/000519068

19. Human iPSC-derived astrocytes transplanted into the mouse brain undergo morphological changes in response to amyloid- plaques Preman, Pranav; TCW, Julia; Calafate, Sara; Snellinx, An; Alfonso-Triguero, Maria; Corthout, Nikky; Munck, Sebastian; Thal, Dietmar Rudolf; Goate, Alison M.; De Strooper, Bart; Arranz, Amaia M.

Molecular Neurodegeneration (Sep-25) DOI: 10.1186/s13024-021-00487-8

20. **Coming full circle: In vivo Veritas, or expanding the neuroscience frontier** Khiroug, L.; Verkhratsky, A.

Cell Calcium (Sep-15) DOI: 10.1016/j.ceca.2021.102452

21. **Transfer of the full SCN1A coding sequence to the brain of adolescent mice model of Dravet syndrome improves epileptic, motor and behavioral manifestations** Mora-Jimenez, Lucia; Valencia, Miguel; [...] Gonzalez-Aseguinolaza, Gloria; Ricobaraza, Ana; Hernandez-Alcoceba, Ruben

Molecular Therapy - Nucleic Acids (Sep-03) DOI: 10.1016/j.omtn.2021.08.003

- 22. **Reduced Insulin-Like Growth Factor-I Effects in the Basal Forebrain of Aging Mouse** Zegarra-Valdivia, Jonathan A.; Chaves-Coira, Irene; Fernandez de Sevilla, Maria Estrella; Martinez-Rachadell, Laura; Esparza, Julio; Torres-Aleman, Ignacio; Nuñez, Angel **Frontiers in Aging Neuroscience** (Sep-01) DOI: 10.3389/fnagi.2021.682388
- Ca2+ handling at the mitochondria-ER contact sites in neurodegeneration Lim, Dmitry; Dematteis, Giulia; Tapella, Laura; Genazzani, Armando A.; Calì, Tito; Brini, Marisa; Verkhratsky, Alexei
 Cell Calcium (Sep-01) DOI: 10.1016/i.ceca.2021.102453
- 24. Fit-for-purpose based testing and validation of antibodies to amino- and carboxyterminal domains of cannabinoid receptor 1 Echeazarra, Leyre; García del Caño, Gontzal; [...] Mato, Susana; Ledent, Catherine; Matute, Carlos; Goicolea, María Aranzazu; Sallés, Joan Histochemistry and Cell Biology (Aug-27) DOI: 10.1007/s00418-021-02025-5
- (Editorial) Cell Signaling in Neurodegeneration Zugaza, José L. International Journal of Molecular Sciences (Aug-20) DOI: 10.3390/ijms22168978

- 26. Astrocyte arborization enhances Ca2+ but not cAMP signaling plasticity Pirnat, Samo; Boi, Mio; Dolanc, Dorian; Horvat, Anemari; Tavar, Petra; Vardjan, Nina; Verkhratsky, Alexei; Zorec, Robert; Stenovec, Matja Glia (Aug-20) DOI: 10.1002/glia.24076
- 27. Functional approaches to the study of G-protein-coupled receptors in postmortem brain tissue: [35S] GTPS binding assays combined with immunoprecipitation Diez-Alarcia, R.; Odagaki, Y.; Miranda-Azpiazu, P.; Gabilondo, A.M.; Meana, J.J.; Muneta-Arrate. L
 - Pharmacological Reports (Aug-15) DOI: 10.1007/s43440-021-00253-z
- 28. (Editorial) Glial plasticity in health and disease Majewska, A.K.; Verkhratsky, A.; Hughes, E.G. European Journal of Neuroscience (Aug-06) DOI: 10.1111/ejn.15414
- 29. Lifestyle-dependent microglial plasticity: training the brain guardians Augusto-Oliveira, Marcus; Verkhratsky, Alexei Biology Direct (Aug-05) DOI: 10.1186/s13062-021-00297-4
- 30. Systemic inflammation and neuronal hyperexcitability: Deciphering cellular neuropathology of sickness behaviour Lin, Si-Si; Verkhratsky, Alexei

Brain, Behavior, and Immunity (Jul-21) DOI: 10.1016/j.bbj.2021.07.013

31. Environmental Enrichment Rescues Endocannabinoid-Dependent Synaptic Plasticity Lost in Young Adult Male Mice after Ethanol Exposure during Adolescence Rico-Barrio, Irantzu; Peñasco, Sara; Lekunberri, Leire; Serrano, Maitane; Egaña-Huguet, Jon; Mimenza, Amaia; Soria-Gomez, Edgar; Ramos, Almudena; Buceta, Ianire; Gerrikagoitia, Inmaculada; Mendizabal-Zubiaga, Juan; Elezgarai, Izaskun; Puente, Nagore; Grandes, Pedro

Biomedicines (Jul-16) DOI: 10.3390/biomedicines9070825

32. Lack of the Transient Receptor Potential Vanilloid 1 Shifts Cannabinoid-Dependent Excitatory Synaptic Plasticity in the Dentate Gyrus of the Mouse Brain Hippocampus

Egaña-Huguet, J.; Saumell-Esnaola, M.; Achicallende, S.; Soria-Gomez, E.; Bonilla-Del Río, I.; García del Caño, G.; Barrondo, S.; Sallés, J.; Gerrikagoitia, I.; Puente, N.; Elezgarai, I.; Grandes, Ρ.

Frontiers in Neuroanatomy (Jul-07) DOI: 10.3389/fnana.2021.701573

33. A multicentre, randomised, controlled trial of a combined clinical treatment for first-episode psychosis

González-Ortega, I.; Vega, P.; Echeburúa, E.; Alberich, S.; Fernández-Sevillano, J.; Barbeito, S.; Balanzá-Martínez, V.; Vieta, E.; Lorente-Rovira, E.; Luengo, A.; Cerrillo, E.; Crespo, J.M.; Matute, C.; González-Pinto, A.

International Journal of Environmental Research and Public Health (Jul-06) DOI: 10.3390/ijerph18147239

34. Endovascular administration of magnetized nanocarriers targeting brain delivery after stroke

Grayston, Alba; Zhang, Yajie; Garcia-Gabilondo, Miguel; Arrúe, Mercedes; Martin, Abraham; Kopcansky, Peter; Timko, Milan; Kovac, Jozef; Strbak, Oliver; Castellote, Laura; Belloli, Sara; Moresco, Rosa M; Picchio, Maria; Roig, Anna; Rosell, Anna

Journal of Cerebral Blood Flow & Metabolism (Jul-06) DOI: 10.1177/0271678X211028816

35. 9-Tetrahydrocannabinol promotes functional remyelination in the mouse brain Aguado, Tania; Huerga-Gómez, Alba; Torre, Aníbal Sánchez-de la; Resel, Eva; Chara, Juan Carlos; Matute, Carlos; Mato, Susana; Galve-Roperh, Ismael; Guzman, Manuel; Palazuelos, Javier

British Journal of Pharmacology (Jul-03) DOI: 10.1111/bph.15608

36. Control of exploration, motor coordination and amphetamine sensitization by cannabinoid CB1 receptors expressed in medium spiny neurons Bonm, Alipi V.; Elezgarai, Izaskun; Gremel, Christina M.; Viray, Katie; Bamford, Nigel S.; Palmiter, Richard D.; Grandes, Pedro; Lovinger, David M.; Stella, Nephi European Journal of Neuroscience (Jul-03) DOI: 10.1111/ejn.15381

- Local Translation in Nervous System Pathologies
 Gamarra, María; de la Cruz, Aida; Blanco-Urrejola, Maite; Baleriola, Jimena
 Frontiers in Integrative Neuroscience (Jun-29) DOI: 10.3389/fnint.2021.689208
- 38. Altered Expression of Ion Channels in White Matter Lesions of Progressive Multiple Sclerosis: What Do We Know About Their Function? Boscia, Francesca; Elkjaer, Maria Louise; Illes, Zsolt; Kukley, Maria Frontiers in Cellular Neuroscience (Jun-25) DOI: 10.3389/fncel.2021.685703
- Caloric restriction modifies spatiotemporal calcium dynamics in mouse hippocampal astrocytes Denisov, P.; Popov, A.; Brazhe, A.; Lazareva, N.; Verkhratsky, A.; Semyanov, A. Biochimica et Biophysica Acta - Molecular Cell Research (Jun-15) DOI: 10.1016/i.bbamcr.2021.119034
- 40. Acute 9-tetrahydrocannabinol prompts rapid changes in cannabinoid CB1 receptor immunolabeling and subcellular structure in CA1 hippocampus of young adult male mice

Bonilla-Del Río, I.; Puente, N.; Mimenza, A.; Ramos, A.; Serrano, M.; Lekunberri, L.; Gerrikagoitia, I.; Christie, B.R.; Nahirney, P.C.; Grandes, P. Journal of Comparative Neurology (Jun-01) DOI: 10.1002/cne.25098

- 41. **Regulation of hippocampal postnatal and adult neurogenesis by adenosine A2A** receptor: interaction with brain-derived neurotrophic factor Ribeiro, Filipa F.; Ferreira, Filipa; Rodrigues, Rui S.; Soares, Rita; Pedro, Diogo M.; Duarte-Samartinho, Marta; Aroeira, Rita I.; Ferreiro, Elisabete; Valero, Jorge; Solá, Susana; Mira, Helena; Sebastião, Ana M.; Xapelli, Sara STEM CELLS (May-27) DOI: 10.1002/stem.3421
- Immortalised Hippocampal Astrocytes from 3xTG-AD Mice Fail to Support BBB Integrity In Vitro: Role of Extracellular Vesicles in Glial-Endothelial Communication Kriauinait, K.; Kauyl, A.; Pajarskien, J.; Tunaitis, V.; Lim, D.; Verkhratsky, A.; Pivorinas, A. Cellular and Molecular Neurobiology (May-22) DOI: 10.1007/s10571-020-00871-w
- 43. Opposite alterations of 5HT 2A receptor brain density in subjects with schizophrenia: relevance of radiotracers pharmacological profile Diez-Alarcia, Rebeca; Muguruza, Carolina; Rivero, Guadalupe; García-Bea, Aintzane; Gómez-Vallejo, Vanessa; Callado, Luis F.; Llop, Jordi; Martín, Abraham; Meana, J. Javier Translational Psychiatry (May-20) DOI: 10.1038/s41398-021-01430-7
- 44. (Review) Early evolutionary history (from bacteria to hemichordata) of the omnipresent purinergic signalling: A tribute to geoff burnstock inquisitive mind Verkhratsky, Alexei
 Biochemical Pharmacology (May-15) DOI: 10.1016/j.bcp.2020.114261

45. Astroglial asthenia and loss of function, rather than reactivity, contribute to the ageing of the brain Verkhratsky, A.; Augusto-Oliveira, M.; Pivorinas, A.; Popov, A.; Brazhe, A.; Semyanov, A.

Pflugers Archiv European Journal of Physiology (May-15) DOI: 10.1007/s00424-020-02465-3

- Cannabinoid control of hippocampal functions: The where matters RobledoMenendez, Almudena; Vella, Maria; Grandes, Pedro; SoriaGomez, Edgar The FEBS Journal (May-11) DOI: https://doi.org/10.1111/febs.15907
- 47. The future belongs to those who prepare for it today Martín-Suárez, Soraya; Encinas, Juan Manuel Cell Stem Cell (May-06) DOI: 10.1016/j.stem.2021.04.014
- Iron induces two distinct Ca2+ signalling cascades in astrocytes Guan, W.; Xia, M.; Ji, M.; Chen, B.; Li, S.; Zhang, M.; Liang, S.; Chen, B.; Gong, W.; Dong, C.; Wen, G.; Zhan, X.; Zhang, D.; Li, X.; Zhou, Y.; Guan, D.; Verkhratsky, A.; Li, B. Communications Biology (May-05) DOI: 10.1038/s42003-021-02060-x
- Subcellular specificity of cannabinoid effects in striatonigral circuits Soria-Gomez, E.; Pagano Zottola, A.C.; [...]; Callado, L.F.; Grandes, P.; Baufreton, J.; Marsicano, G.; Bellocchio, L. Neuron (May-05) DOI: 10.1016/j.neuron.2021.03.007

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00577-5 54. Astrocytic atrophy as a pathological feature of Parkinson's disease with LRRK2 mutation

Ramos-Gonzalez, P.; Mato, S.; Chara, J.C.; Verkhratsky, A.; Matute, C.; Cavaliere, F. **npj Parkinson's Disease** (Mar-30) DOI: 10.1038/s41531-021-00175-w

55. Advances and Perspectives in Dental Pulp Stem Cell Based Neuroregeneration Therapies

Luzuriaga, Jon; Polo, Yurena; Pastor-Alonso, Oier; Pardo-Rodríguez, Beatriz; Larrañaga, Aitor; Unda, Fernando; Sarasua, Jose-Ramon; Pineda, Jose Ramon; Ibarretxe, Gaskon **International Journal of Molecular Sciences** (Mar-29) DOI: 10.3390/ijms22073546

56. Evaluation of glial cell proliferation with non-invasive molecular imaging methods after stroke

Joya, Ana; Martin, Abraham Neural Regeneration Research (Mar-25) DOI: 10.4103/1673-5374.310681

- Astrocyte dystrophy in ageing brain parallels impaired synaptic plasticity Popov, Alexander; Brazhe, Alexey; Denisov, Pavel; Sutyagina, Oksana; Li, Li; Lazareva, Natalia; Verkhratsky, Alexei; Semyanov, Alexey Aging Cell (Mar-20) DOI: 10.1111/acel.13334
- Snapshot of microglial physiological functions Verkhratsky, A.; Sun, D.; Tanaka, J.
 Neurochemistry International (Mar-20) DOI: 10.1016/j.neuint.2021.104960
- 59. **9-Tetrahydrocannabinol promotes oligodendrocyte development and CNS myelination in vivo** HuergaGómez, Alba; Aguado, Tania; Torre, Aníbal Sánchez-de Ia; BernalChico, Ana; Matute Carlos: Mato, Susana: Guzmán, Manuel: GalveRoperh, Ismael: Palazuelos, Jay

Matute, Carlos; Mato, Susana; Guzmán, Manuel; GalveRoperh, Ismael; Palazuelos, Javier **Glia** (Mar-15) DOI: 10.1002/glia.23911

- (Review) Small GTPases of the Ras superfamily and glycogen phosphorylase regulation in T cells Llavero, Francisco; Sastre, Alazne Arrazola; Montoro, Miriam Luque; Martín, Miguel A.; Arenas, Joaquín; Lucia, Alejandro; Zugaza, José L.
- Small GTPases (Mar-15) DOI: 10.1080/21541248.2019.1665968
 61. Oligodendroglial Energy Metabolism and (re)Myelination Tepavevi, Vanja
 Life (Mar-13) DOI: 10.3390/life11030238

62. (Review) RNA Localization and Local Translation in Glia in Neurological and Neurodegenerative Diseases: Lessons from Neurons Blanco-Urrejola, Maite; Gaminde-Blasco, Adhara; Gamarra, María; de la Cruz, Aida; Vecino, Elena; Alberdi, Elena; Baleriola, Jimena Cells (Mar-12) DOI: 10.3390/cells10030632

- 63. Fluorine Labeling of Nanoparticles and In Vivo 19F Magnetic Resonance Imaging Arango, Juan Manuel; Padro, Daniel; Blanco, Jorge; Lopez-Fernandez, Sonia; Castellnou, Pilar; Villa-Valverde, Palmira; Ruiz-Cabello, Jesús; Martin, Abraham; Carril, Mónica ACS Applied Materials & Interfaces (Mar-11) DOI: 10.1021/acsami.1c01291
- 64. **BASP1 labels neural stem cells in the neurogenic niches of mammalian brain** Manganas, Louis N.; Durá, Irene; Osenberg, Sivan; Semerci, Faith; Tosun, Mehmet; Mishra, Rachana; Parkitny, Luke; Encinas, Juan M.; Maletic-Savatic, Mirjana **Scientific Reports** (Mar-10) DOI: 10.1038/s41598-021-85129-1
- 65. **(Review) Astrocytes in Alzheimer's Disease: Pathological Significance and Molecular Pathways** Preman, Pranav; Alfonso-Triguero, Maria; Alberdi, Elena; Verkhratsky, Alexei; Arranz, Amaia M.

Cells (Mar-04) DOI: 10.3390/cells10030540

66. Alzheimer's Risk Gene TREM2 Determines Functional Properties of New Type of Human iPSC-Derived Microglia Peich M. Paris L. Ebeling M. Dahm, N. Schweitzer, C. Peinhardt, D. Schmucki, P. Pras

Reich, M.; Paris, I.; Ebeling, M.; Dahm, N.; Schweitzer, C.; Reinhardt, D.; Schmucki, R.; Prasad, M.; Köchl, F.; Leist, M.; Cowley, S.A.; Zhang, J.D.; Patsch, C.; Gutbier, S.; Britschgi, M. **Frontiers in Immunology** (Feb-03) DOI: 10.3389/fimmu.2020.617860

- 67. Astrocytes in heavy metal neurotoxicity and neurodegeneration Li, B.; Xia, M.; Zorec, R.; Parpura, V.; Verkhratsky, A. Brain Research (Feb-01) DOI: 10.1016/j.brainres.2020.147234
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Ordaz, R.P.; Garay, E.; Limon, A.; Pérez-Samartín, A.; Sánchez-Gómez, M.V.; Robles-Martínez, L.; Cisneros-Mejorado, A.; Matute, C.; Arellano, R.O. **Molecular pharmacology** (Feb-01) DOI: 10.1124/molpharm.120.000091

- The Association Between Antidepressant Effect of SSRIs and Astrocytes: Conceptual Overview and Metaanalysis of the Literature Chen, B.; Zhang, M.; Ji, M.; Gong, W.; Chen, B.; Zorec, R.; Stenovec, M.; Verkhratsky, A.; Li, B. Neurochemical Research (Feb-01) DOI: 10.1007/s11064-020-03225-6
- Satellite Glial Cells and Astrocytes, a Comparative Review Hanani, M.; Verkhratsky, A.
 Neurochemical Research (Feb-01) DOI: 10.1007/s11064-021-03255-8
- 71. Assessing Autophagy in Microglia: A Two-Step Model to Determine Autophagosome Formation, Degradation, and Net Turnover Plaza-Zabala, Ainhoa; Sierra-Torre, Virginia; Sierra, Amanda Frontiers in Immunology (Jan-29) DOI: 10.3389/fimmu.2020.620602
- 72. Neuropathological Characterization of a Dravet Syndrome Knock-In Mouse Model Useful for Investigating Cannabinoid Treatments Satta, V.; Alonso, C.; Díez, P.; Martín-Suárez, S.; Rubio, M.; Encinas, J.M.; Fernández-Ruiz, J.; Sagredo, O.

Frontiers in Molecular Neuroscience (Jan-29) DOI: 10.3389/fnmol.2020.602801

73. **MiRNA-15b and miRNA-125b are associated with regional A-PET and FDG-PET uptake in cognitively normal individuals with subjective memory complaints** Vergallo, A.; Lista, S.; Zhao, Y.; [...]; Llavero, F.; Lorenceau, J.; Lucía, A.; Mango, D.; Mapstone, M.; Neri, C.; Nisticò, R.; O'Bryant, S.E.; Palermo, G.; Perry, G.; Ritchie, C.; Rossi, S.; Saidi, A.; Santarnecchi, E.; Schneider, L.S.; Sporns, O.; Toschi, N.; Valenzuela, P.L.; Vellas, B.; Verdooner, S.R.; Villain, N.; Giudici, K.V.; Watling, M.; Welikovitch, L.A.; Woodcock, J.; Younesi, E.; Zugaza, J.L.; for, the INSIGHT-preAD study group; the, Alzheimer Precision Medicine Initiative (APMI)

Translational Psychiatry (Jan-27) DOI: 10.1038/s41398-020-01184-8

74. Nanostructured scaffolds based on Bioresorbable polymers and Graphene oxide induce the aligned migration and accelerate the neuronal differentiation of neural stem cells

Polo, Y.; Luzuriaga, J.; Iturri, J.; Irastorza, I.; Toca-Herrera, J. L.; Ibarretxe, G.; Unda, F.; Sarasua, J. R.; Pineda, J. R.; Larrañaga, A.

Nanomedicine: Nanotechnology, Biology and Medicine (Jan-15) DOI: 10.1016/j.nano.2020.102314

75. Dopaminergic denervation impairs cortical motor and associative/limbic information processing through the basal ganglia and its modulation by the CB1 receptor

Antonazzo, M.; Gomez-Urquijo, S.M.; Ugedo, L.; Morera-Herreras, T. Neurobiology of Disease (Jan-15) DOI: 10.1016/j.nbd.2020.105214

- 76. Overexpression of -Synuclein Reorganises Growth Factor Profile of Human Astrocytes Sengül, B.; Dursun, E.; Verkhratsky, A.; Gezen-Ak, D.
- Molecular Neurobiology (Jan-15) DOI: 10.1007/s12035-020-02114-x 77. The Safequarding Microglia: Central Role for P2Y12 Receptors Lin, S.-S.; Tang, Y.; Illes, P.; Verkhratsky, A. Frontiers in Pharmacology (Jan-14) DOI: 10.3389/fphar.2020.627760
- 78. Mens sana in corpore sano: Lifestyle changes modify astrocytes to contain Alzheimer's disease Augusto-Oliveira, M.; Verkhratsky, A. Neural Regeneration Research (Jan-07) DOI: 10.4103/1673-5374.303023

79. The Claustrum is Involved in Coanitive Processes Related to the Classical Conditioning of Eyelid Responses in Behaving Rabbits Reus-García, M. Mar; Sánchez-Campusano, Raudel; Ledderose, Julia; Dogbevia, Godwin K.; Treviño, Mario; Hasan, Mazahir T.; Gruart, Agnès; Delgado-García, José M. Cerebral Cortex (Jan-05) DOI: 10.1093/cercor/bhaa225

- 80. (Editorial) Stem and Cancer Stem Cell Identities, Cellular Markers, Niche Environment and Response to Treatments to Unravel New Therapeutic Targets Pineda, Jose R.; Badiola, Iker; Ibarretxe, Gaskon Biology (Jan-02) DOI: 10.3390/biology10010025
- 81. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition) Klionsky, Daniel J.; Abdel-Aziz, Amal Kamal; [...] Nobili, Annalisa; Nobrega, Clevio; Noda, Takeshi; Nogueira-Recalde, Uxía; Nolan, Trevor M.; N

Autophagy (Jan-02) DOI: 10.1080/15548627.2020.1797280

82. Exercise training effects on natural killer cells: a preliminary proteomics and systems biology approach

Llavero, Francisco; Alejo, Lidia B.; Fiuza-Luces, Carmen; López Soto, Alejandro; Valenzuela, Pedro L.; Castillo-García, Adrián; Morales, Javier S.; Fernández, David; Aldazabal, Itziar Pagola; Ramírez, Manuel; Santos-Lozano, Alejandro; Zugaza, José L.; Lucia, Alejandro Exercise Immunology Review (Jan-01) DOI: PUBMED: 33965896

83. In vivo multimodal imaging of adenosine A1 receptors in neuroinflammation after experimental stroke

Joya A, Ardaya M, Montilla A, Garbizu M, Plaza-García S, Gómez-Vallejo V, Padro D, Gutiérrez JJ, Rios X, Ramos-Cabrer P, Cossío U, Pulagam KR, Higuchi M, Domercq M, Cavaliere F, Matute C, Llop J, Martín A.

Theranostics (Jan-01) DOI: 10.7150/thno.51046

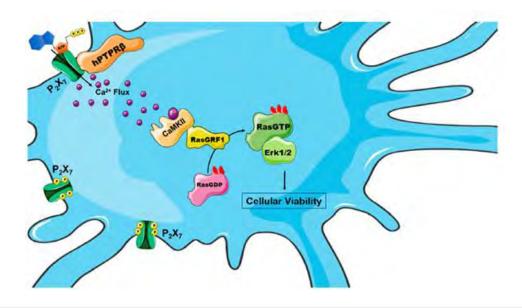
Highlight in research outcomes

Purinergic signalling has been suggested as a mechanism mediating dopaminergic neuronal death, which could point out to one of the first steps in Parkinson's disease. In this study, authors reveal that the purinergic P2X7 receptor modulates positively neuronal cell survival via Ras/MAPK pathway and negatively via the tyrosine phosphatase, hPTP $_{\beta}$

Ras protects dopaminergic neurons from excess ATP

ATP is a key molecule in different aspects of the cell biology, however when cells are exposed to high concentrations or prolonged periods of this nucleotide it can produce a cytotoxic effect and consequent cell death. In fact, ATP is commonly secreted in the CNS, where through stimulation of ionotropic purinergic receptors it is capable of causing death of dopaminergic neurons. These neurons play an important role in the development of Parkinson's Disease since their death leads to a lack of dopamine synthesis, a neurotransmitter with multiple functions in the brain.

The characterization of the intracellular signal transduction pathways of these neurons is essential to understand the functional effects and their potential involvement in Parkinson's Disease. This article reveals some unsuspected protagonists of the cell signalling controlled by purinergic receptors in dopaminergic neurons. In this sense, both Ras and hPTP β are postulated as potential targets to prevent the death of dopaminergic neurons due to the action of ATP.



"The tyrosine phosphatase hPTPR & controls the early signals and dopaminergic cells viability via the P2X7 receptor" Llavero Bernal, F.; Luque Montoro, M.; Arrazola Sastre, A.; Lacerda, H.M.; Zugaza, J.L.

International Journal of Molecular Sciences (Nov-29) DOI: 10.3390/ijms222312936

We are strongly committed with different areas of training and knowledge transfer. The years of the Covid pandemic drove us to new scenarios for developing this will and effort.

5. Knowledge Transfer

ADVANCED TRAINING

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

Our personnel also participate in the Doctorate Programme on Neurosciences, organized by the UPV/EHU, together with the Universities of Coruña (Galicia), Castilla – La Mancha, Pablo de Olavide (Seville), and Rovira I Virgili (Catalonia).

Congratulations Svein, Sol, Itziar and Jonathan!

PhD theses completed in 2021

Four of our younger colleagues successfully completed their doctoral training; all of them in the *International mention*, as they completed research stays abroad during their doctorate period.

• **Dr. Svein Achicallende Urcaregui** Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse

"Ultrastructural and physiological studies on the cannabinoid CB1 receptor localized in astroglia"

Dr. Marlene Soledad Beccari Galeano
 Laboratory of Glial Cell Biology

"Microglial phagocytosis: from development to neurodegeneration"

Dr. Itziar Terradillos Irastorza
 Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse

"Unraveling the role of astrocytes in the onset and spread of Parkinson's Disease: Important contributors to neurodegeneration"

Dr. Jonathan Adrián Zegarra Valdivia
 Laboratory of Neurobiology of Insulin Peptides

"Modulation of sleep and cortical activity through the orexin and cholinergic axes: role of IGF-I"

Other **49** are in different stages of that process.

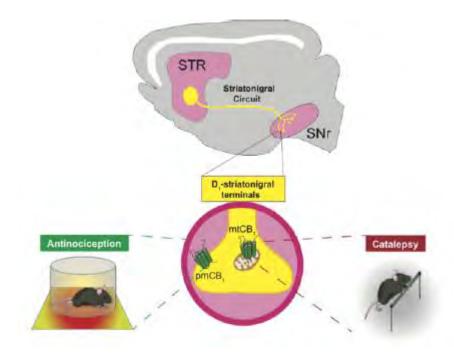
Highlight in research outcomes

The recreational and therapeutic uses of cannabinoid compounds are increasing around the world. They have been proposed to control pain sensitivity in clinical settings. However, due to significant side effects, such as cognitive impairments and motor dysfunctions, the medicinal exploitation of these drugs and the safety of their recreational use are under intense debate.

SUBCELLULAR SPECIFICITY OF CANNABINOID EFFECTS IN STRATONIGRAL CIRCUITS

The main psychoactive component of the cannabis sativa (*marijuana*) plant is delta-9 tetrahydrocannabinol or THC, which, in the brain, acts mainly by activating cannabinoid receptors type-1 (CB1). The CB1 receptor is widely distributed throughout the brain and in different cell types and cellular compartments (for example, in the mitochondria).

This study reveals that cannabinoids produce adverse (*catalepsy*) and beneficial (antinociception) effects through the regulation of specific cellular molecular pathways in the brain circuit formed by the striatum and the *substantia nigra* (*striatonigral circuit*). In this circuit, the study demonstrates that the activation of CB1 receptors located in the mitochondria is responsible for the cataleptic effects induced by cannabinoids. On the other hand, CB1 receptors localized in the plasma membrane (pmCB1), reduces sensitivity to pain. All this, by modulating different signalling and neurotransmission pathways.



"Subcellular specificity of cannabinoid effects in striatonigral circuits" Soria-Gomez, E.; Pagano Zottola, A.C.; [...]; Callado, L.F.; Grandes, P.; Baufreton, J.; Marsicano, G.; Bellocchio, L. Neuron (May-05) DOI: 10.1016/j.neuron.2021.03.007

ACHUCARRO SEMINARS

January 22nd

"Synucleinopathy alters nanoscale organization and diffusion in the brain extracellular space through hyaluronan remodeling"

Federico N. Soria Lannes Laboratory of Neurobiology, ACHUCARRO

January 29th

"Role of Nutrients in Microglial Function"

Agnès Nadjar

Neurocentre Magendie (Bordeaux, France)

February 5th

"Shaping cortical circuit rhythms and function by myelination"

Maarten H.P. Kole

Netherlands Institute of Neuroscience (Amsterdam, The Netherlands)

February 12th

"Specific hippocampal interneurons shape consolidation of recognition memory"

Edgar Soria-Gómez

Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse ACHUCARRO

February 19th

"Genomics for precision medicine: prospects and challenges"

Urko Martínez Marigorta CIC bioGUNE (Derio)

February 26th

"Thrombosis, cardiovascular risk factors & dementia: from mice to humans"

Marta Cortés-Canteli Spanish National Centre for Cardiovascular Research [CNIC] (Madrid, Spain)

February 26th

"Endocytosis and intracellular trafficking to safeguard brain function"

Tania López Hernández Leibniz-Forschungsinstitut für Molekulare Pharmakologie [FMP] (Berlin, Germany)

<u>March 5th</u>

"In-vivo imaging of pathological protein fibrils in neurodegenerative disorders and a myeloid pathway linking protein depositions and neuronal loss"

Makoto Higuchi

National Institutes for Quantum and Radiological Science and Technology (Tokio, Japan)

March 12th

"Gliogenesis from the Subventricular zone after brain ischemia"

María Ardaya

Laboratory of Neurobiology ACHUCARRO

March 26th

"P2X4 receptor functions in the CNS revealed using P2X4 internalization-defective knock-in mice"

Eric Boué-Grabot

Institute for Neurodegenerative Diseases [IMN] (Bordeaux, France)

<u>April 9th</u>

"Microglia-dependent mechanisms governing brain wiring and plasticity"

Dorothy P. Schafer

University of Massachusetts Medical School (Worcester, USA)

<u>April 23rd</u>

"Insulin peptides and the body-brain dialog"

Ignacio Torres Aleman Laboratory of Neurobiology of Insulin Peptides ACHUCARRO

April 30th

"Mechanisms fo myelin plasticity and repair in the live brain"

Robert Hill

Dartmouth College (Hanover, USA)

<u>May 7th</u>

"Oligodendrocyte-derived exosomes in axon-glia interaction and glial support" Eva-Maria Krämer-Albers

University of Mainz (Mainz, Germany)

May 14th

"High resolution imaging of cannabinoid receptors in glial cells in a mouse model of Alzheimer's disease"

Itziar Terradillos

Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse ACHUCARRO

"Autophagy and phagocytosis: functional crosstalk in microglia"

Virginia Sierra-Torre Laboratory of Glial Cell Biology ACHUCARRO

<u>May 21st</u>

"Presynaptic dysfunction and neurodegeneration"

Rafael Fernández-Chacón

Universidad de Sevilla (Seville, Spain)

May 28th

"Gene-regulatory dynamics of microglia states during neuroinflammation"

José P. López-Atalaya

Instituto de Neurociencias [UMH – CSIC] (Alicante, Spain)

<u>June 11th</u>

"Neuron-oligodendroglia interactions in the construction and function of cortical circuits"

María Cecilia Angulo Paris Descartes University (Paris, France)

<u>June 18th</u>

"Role of oligodendrocytes and microglia in myelin remodeling"

María Domercq Laboratory of Neurobiology ACHUCARRO

June 25th

"Dissecting genetic brain disease: from 2D to 3D iPSC organoids"

Michela Deleidi

University of Tübingen (Tübingen, Germany)

<u>July 16th</u>

"Role of the ATP receptor P2X7 in experimental schizophrenia: a focus onprefrontal microglia"

Stefano Calovi Laboratory of Neuronal Excitability ACHUCARRO

July 16th

"Ultrastructural and physiologycal studies on cannabinoid CB1 receptors localized in astroalia"

Svein Achicallende

Laboratory of Ultrastructural and Functional Neuroanatomy of the Synapse ACHUCARRO

September 17th

"Role of microglia in Alzheimer's disease: Benefits of its modulation"

Estibaliz Capetillo-Zarate Laboratory of Neurobiology ACHUCARRO

September 24th

"Exercise-conditioned Plasma Transfusions Increase Neuroplasticity, Improve Learning and Memory, and Reduce Neuroinflammation"

Zuriñe de Miguel

California State University Monterey Bay and Stanford University (California, USA)

October 15th

"Non-canonical Functions of Migrating Cells in Brain Development"

Carla Gomes da Silva

University of Liège (Liège, Belgium)

October 22nd

"Traumatic brain injury induces a biphasic long-term effect on adult hippocampal neurogenesis"

Irene Durá

Laboratory of Neural Stem Cells and Neurogenesis ACHUCARRO

October 22nd

"AB1-42 oligomers modify astrocytes biology by LPAR1 transactivation" Miriam Luque

Laboratory of GTPases and Neurosignalling ACHUCARRO

October 29th

"Crosstalk between T cells and oligodendrocyte progenitor cells (OPC) in the Central Nervous System"

Alerie Guzman de la Fuente Queen's University Belfast (Belfast, UK)

November 19th

"Introducing the Single Molecule Array (SiMoA) HD-1 Analyzer and its potential in biofluid biomarkers analysis"

Raffaela Cipriani

Laboratory of Neurobiology ACHUCARRO

November 26th

"Endosomal trafficking defects in aging and alzheimer's disease increase intracellular beta-amyloid"

Cláudia Guimas Almeida

NOVA Medical School (Lisboa, Portugal)

December 16th

"Determinants of Stemness and Hypothalamic Neurogenesis in Anti-Obesity Treatment"

David Petrik Cardiff University (Cardiff, UK)

We do not understand avant-garde scientific research as an activity separated from a social context. Although the scientific research we carry out is fundamental and not oriented, it is unquestionable that the biological questions that we try to solve have a marked practical nature and represent social challenges on ageing, healthy lifestyles, and health protection, with the ultimate objective of improving our environment.

Dissemination and advocacy

We deploy our commitment with Equality and Diversity, Talent development, and fostering a culture of scientific literacy through a set of activities during each year.

These are some of the actions in 2021.



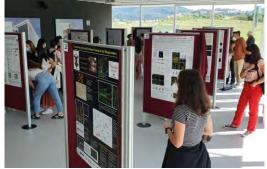


Organised a online event on February 11

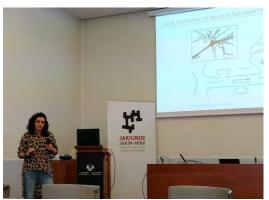
Published videos in our Youtube channel



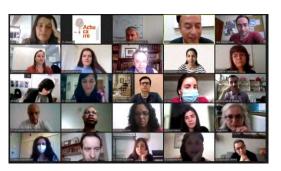
Dr. Amanda Sierra participated in the cycle Bidebarrieta Zientifikoa



Contributed to the organisation of the first "Neuroscience Day" at the campus of Leioa



Dr. Jimena Baleriola collaborated with the series Jakin-mina of Jakiunde, the Basque Academy of Sciences, Arts and Letters



Organised the second edition of the Achucarro International Glia School



Hosted the visit of Vice President of the European Commission, Mr. Maros Sefcovic

2021 is the second year that the postdoctoral researchers in ACHUCARRO organise a winter scientific event, the Achucarro Symposium.

ACHUCARRO SYMPOSIUM CURATED BY POSTDOCTORAL RESEARCHERS

The line-up to speakers of this edition was brilliant once again.

Curated by Postdoctoral researchers	
Achucarro Symposium 2021	
Programme	
13:00 Communication breakdown: synaptic pathology in ALS/FTD Chris Henstridge University of Dundee (Scotland)	
 13:40 Astrocytic GLUT1 ablation improves systemic glucose metaboli and promotes cognition Maite Solas Universidad de Navarra (Pamplona) 	sm
14:20 LMNB1, oligodendrocytes and Autosomal dominant leukodystrophy (ADLD) Guillermo Rodríguez Bey University of Pittsburg (USA)	

The Directorate of ACHUCARRO wants to thank the commitment and effort of the postdoctoral collective.

The Science Park of the UPV/EHU in Leioa (metropolitan area of Bilbao), hosts the headquarters of ACHUCARRO, inaugurated in June 2017.

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 allowed us to expand our potential.



ACHUCARRO currently occupies the third floor of the Sede building, a space of 2000 m² in a privileged location within the campus of the UPV/EHU. Additionally, some of the research groups have laboratories and office spaces in the Faculty of Medicine and Nursing, at 400 metres from the main location.

With the advantage of this location in the campus, where the general facilities (microscopy, genomics, proteomics, etc.) for research support of the university are located, our strategy was to complement the existing resources with the specific ones of our field and those that provide an added value or competitive advantage, like the resources for performing:

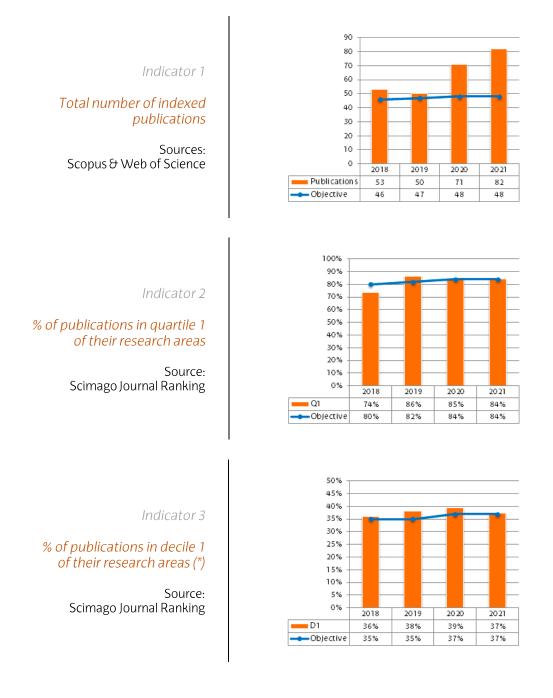
https://www.achucarro.org/facilities

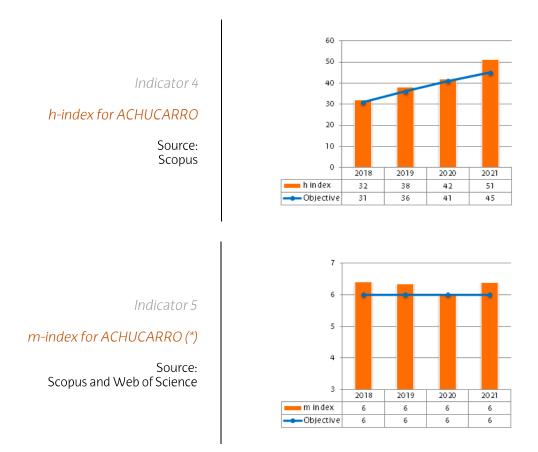
The Basque Government establishes challenging scientific and management objectives for research organisations with the BERC accreditation. The following indicators reflect the evolution on the performance of ACHUCARRO, with this panel agreed by the Basque Government and ACHUCARRO for the current strategic period.

7. Main performance indicators

In 2021 we completed our second strategic period. The results are remarkable, and aligned with the expectations. In some cases, we even exceed expectations and scenarios foreseen back in 2018.

The following indicators start showing some of these effects.



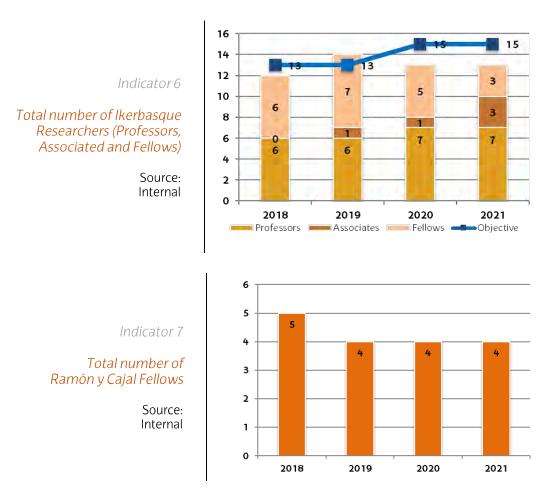


While Scopus and Web of Science produce similar numbers for the h-index indicator of the accumulation of all the publications and their citation of ACHUCARRO, for the period 2012-2021.

It is remarkable that Google Scholar, with its different algorithm to calculate h-index, reflects 94 for the same indicator, and 384 for the i10 indicator, that they also use:

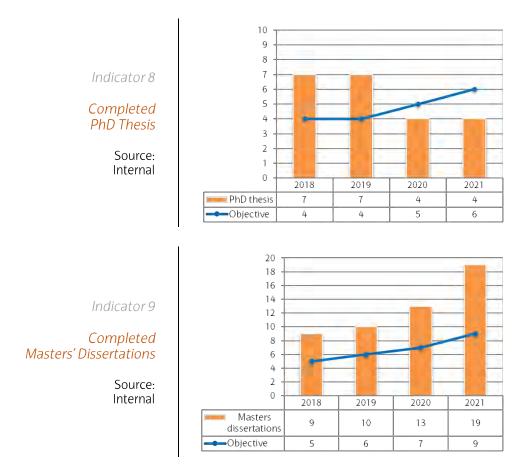
https://scholar.google.es/user=hO1jBxYAAAAJ

BERC centres are key to the strategy of Ikerbasque and the Basque Government to build and sustain a vibrant scientific sector in our region. BERC centres compete among us to attract some of the research positions available in our system.

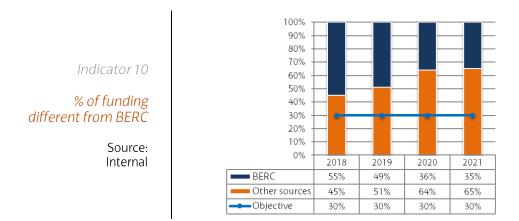


The following indicators show our talent attraction and retention record.

Our capability to contribute to postgraduate education has been affected by the Covid-19 pandemic. The lockdown affected many of the ongoing PhD projects. We also had to stop internships of master's students. Nevertheless, the gradual recovery of face-to-face and experimental activity starting in the summer made it possible to partly recover and mitigate the effects caused by the health emergency situation.



Finally, the financial stability and sustainability of ACHUCARRO keeps consolidating, due to the increase in the raising competitive funding, national and internationally, both public and private.



Achucarro Basque Center for Neuroscience

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