

## Instructors

### Camille Allard | University of Bordeaux, France



Camille ALLARD is interesting in how the hypothalamus senses nutrient excess and regulates energy and glucose metabolism to maintain homeostasis. She obtained a bachelor in Cell Biology and Physiology from the University of Limoges (France), and a Master in Physiopathology from the University Paul Sabatier, Toulouse (France). This is when she started working on the central regulation of glucose metabolism within Dr Luc Pénicaud's lab, under the supervision of Pr Corinne Leloup. In the same lab, she did her PhD studies on astroglial involvement in hypothalamic glucose detection. She

mainly worked in vivo with rats and demonstrated the importance of glial gap junctions for proper brain-induced insulin secretion. Once graduated, she flew to the 'Big Easy', aka the astonishing city of New Orleans (Louisiana, USA), where she joined Dr Franck Mauvais-Jarvis' lab at the Tulane University to study insulin secretion regulation at the level of the pancreatic beta cell. For this purpose, she was awarded a grant from the American Diabetes Association and the French Diabetes Society. For 4 years, she investigated the mechanisms by which sex hormones (estrogens and androgens) favor glucose homeostasis and protect from type 2 diabetes. This first post-doc really opened her eyes on the necessity of working on female animals to move preclinical research forward. Indeed, she observed that the mechanisms of glucose and insulin sensitivity involve different pools of estrogen receptors and are sexually dimorphic. For both sexes, brain sensing of either glucose or insulin were involved. Since 2019, she joined Dr Daniela Cota's lab, in which she focuses on hypothalamic neuroinflammation during diet-induced obesity. Her research is supported by a Post-doctoral fellowship grant from the Fondation de la Recherche Médicale.

#### Selected publications:

- Allard C, Morford JJ, Xu B, Salwen B, Xu W, Desmoulins L, Zombok A, Kim J, Levin ER, Mauvais-Jarvis F. Loss of membrane and nuclear estrogen receptor- $\alpha$  differentially impairs insulin secretion and action in male and female mice. *Diabetes*. 2019 Mar;68(3):490-501.
- Desmoulins L, Chrétien C, Paccoud R, Collins S, Cruciani-Guglielmacci C, Galinier A, Liénard F, Quinault A, Grall S, Allard C, Fenech C, Carneiro L, Mouillot T, Fournel A, Knauf C, Magnan C, Fioramonti X, Pénicaud L, Leloup C. Mitochondrial Dynamin-Related Protein 1 (DRP1) translocation in response to cerebral glucose is impaired in a rat model of early alteration in hypothalamic glucose sensing. *Mol Metab*. 2019 Feb;20:166-177.
- Allard C, Carneiro L, Grall S, Cline BH, Fioramonti X, Chrétien C, Baba-Aissa F, Giaume C, Pénicaud L and Leloup C. Hypothalamic astroglial connexins are required for brain glucose sensing-induced insulin secretion. *J Cell Blood Flow Metab*, 2014;34(2):339-46.
- Allard C, Carneiro L, Collins SC, Chrétien C, Grall S, Pénicaud L and Leloup C. Alteration of hypothalamic glucose and lactate sensing in 48h hyperglycemic rats. *Neurosci Lett*, 2013;534:75-9.

- *Carneiro L, Allard C, Guissard C, Fioramonti X, Tourrel-Cuzin C, Bailbe D, Barreau C, Offer G, Nedelec E, Salin B, Rigoulet M, Belenguer P, Pénicaud L and Leloup C. Importance of mitochondrial Dynamin Related Protein 1 (DRP1) in hypothalamic glucose sensitivity in rats. Antioxid Redox Signal, 2012;17(3):433-44.*

### Felipe Baeza-Lehnert | Centro de Estudios Científicos, Chile



Felipe Baeza-Lehnert earned a degree in biochemistry from the Universidad Austral de Chile. During his Ph.D. (2015-2020) under the supervision of Dr. Felipe Barros (Centro de Estudios Científicos, Valdivia, Chile), he directed his attention to the study of neuronal energy fluxes. Equipped with a palette of fluorescent biosensors for the intracellular measurement of glucose, pyruvate, lactate, ATP, ADP:ATP, NADH:NAD<sup>+</sup>, and fluorescent dyes for H<sup>+</sup>, Na<sup>+</sup> and Ca<sup>2+</sup>, he set off on the quest to tackle some old and new questions in the field brain energy metabolism. How lactate and pyruvate impact on glucose

metabolism and transport, how relevant is the cytosolic NADH and the malate-aspartate shuttle in mitochondrial energization during neurotransmission, and how synaptic activity is couple to energy production. The standardization of an electric field stimulation protocol that mimics glutamatergic neurotransmission together with a novel method to quantitatively assess the activity of the Na<sup>+</sup> pump, allowed Felipe to determine with a temporal resolution of seconds, the distribution of the energy burden that neurotransmission imposes to neurons, and map the early response of glucose, pyruvate, and lactate as energy substrates. The main finding is a novel energy control system not hitherto described in cellular biology, that operates during the first seconds of neurotransmission and that keeps the ATP level invariable independent of the increased workload. Nowadays, he is developing new methods to assess GLUTs and MCTs permeability at rest and during activity. In the past Felipe has been honored with a CONICYT (Chilean science agency) fellowship to pursue his Ph.D. studies and also with a grant from the ISCBFM and the CAJAL Programme to participate in the Brain Homeostasis and Neurovascular Coupling course organized by the CAJAL Advanced Neuroscience Training Programme in 2019.

#### Selected publications:

- *Monitoring Lactate Dynamics in Individual Macrophages with a Genetically Encoded Probe. Baeza-Lehnert F, Flores CA, Guequén A, Barros LF. Methods Mol Biol. 2020;2184:19-30. doi:0.1007/978-1-0716-0802-9\_2.*
- *Non-Canonical Control of Neuronal Energy Status by the Na<sup>+</sup> Pump. Baeza-Lehnert F, Saab AS, Gutiérrez R, Larenas V, Díaz E, Horn M, Vargas M, Hösli L, Stobart J, Hirrlinger J, Weber B, Barros LF. Cell Metab. 2018 Nov 27. pii: S1550-4131(18)30682-X. doi: 10.1016/j.cmet.2018.11.005. [Epub ahead of print]*
- *In Vivo Evidence for a Lactate Gradient from Astrocytes to Neurons. Mächler P, Wyss MT, Elsayed M, Stobart J, Gutierrez R, von Faber-Castell A, Kaelin V, Zuend M, San Martín A, Romero-Gómez I, Baeza-Lehnert F, Lengacher S, Schneider BL, Aebischer P, Magistretti PJ, Barros LF, Weber B. Cell Metab. 2016 Jan 12;23(1):94-102. doi: 10.1016/j.cmet.2015.10.010.*

- *NH<sub>4</sub>(+) triggers the release of astrocytic lactate via mitochondrial pyruvate shunting.* Lerchundi R, Fernández-Moncada I, Contreras-Baeza Y, Sotelo-Hitschfeld T, Mächler P, Wyss MT, Stobart J, Baeza-Lehnert F, Alegría K, Weber B, Barros LF. *Proc Natl Acad Sci U S A.* 2015 Sep 1;112(35):11090-5. doi: 10.1073/pnas.1508259112.
- *Imaging Mitochondrial Flux in Single Cells with a FRET Sensor for Pyruvate.* San Martín A, Ceballos S, Baeza-Lehnert F, Lerchundi R, Valdebenito R, Contreras-Baeza Y, Alegría K. and Barros LF. *PLoS ONE* (2014) 9(1): e85780. doi:10.1371/journal.pone.008

### Jérôme Baufreton | University of Bordeaux, France



Jérôme Baufreton is co-directing the team DNA at the Institute of Neurodegenerative Disorders in Bordeaux, France. He is studying the extended basal ganglia (EBG) network function in motor control using ex vivo brain slice preparations, patch-clamp electrophysiology and optogenetics. His current research focuses on the basal ganglia, a group of subcortical brain nuclei that are critical for voluntary movement and associative learning and are the primary sites of dysfunction in Parkinson's disease, Huntington's disease, obsessive-compulsive disorder and addiction. His objectives are to

define the cellular and synaptic principles underlying the normal and pathological operation of the basal ganglia in order to provide the foundation for the rational development of corrective or neuroprotective therapies.

#### Selected publications:

- *Aristieta A, Barresi M, Lindi SA, Barriere G, Courtant G, de la Crompe B, Guilhemsang L, Gauthier S, Fioramonti S, Baufreton J\*, Mallet N\* (2020) A disynaptic circuit in the globus pallidus controls locomotion inhibition. *Curr. Biol.* In press. \* equal contribution*
- *Blázquez C, Ruiz-Calvo A, Bajo-Grañeras R, Baufreton J, Resel E, Varilh M, Pagano-Zottola A, Mariani Y, Cannich A, Rodríguez-Navarro J, Marsicano G, Galve-Roperh I, Bellocchio L, Guzmán M (2020) Inhibition of striatonigral autophagy as a link between cannabinoid intoxication and impairment of motor coordination. *eLife* 9:e56811. doi: 10.7554/eLife.56811.*
- *Chazalon M, Paredes-Rodriguez E, Morin S, Martinez A, Cristóvão-Ferreira S, Vaz S, Sebastiao A, Panatier A, Boué-Grabot E, Miguez C and Baufreton J. (2018) GAT-3 dysfunction generates tonic inhibition in external globus pallidus neurons in Parkinsonian rodents. *Cell Rep.* 8;23(6):1678-1690. doi: 10.1016/j.celrep.2018.04.014.*
- *Abdi A, Mallet N, Mohamed FY, Sharott A, Dodson PD, Nakamura KC, Suri S, Avery SV, Larvin J, Garas FG, Garas S, Vinciati F, Bezard E, Baufreton J#, Magill PJ#. Prototypic and arky pallidal neurons in the dopamine-intact external globus pallidus. (2015) *J. Neurosci.* 35(17):6667-88. # Co-last authors + corresponding author*
- *Murphy-Royal C, Dupuis JP, Varela JA, Panatier A, Pinson B, Baufreton J, Groc L, Oliet SHR. Surface diffusion of astrocytic glutamate transporters shapes synaptic transmission. (2015) *Nature Neurosci.* 18(2):219-26.*
- *Courtin J, Chaudun F, Rozeske R, Karalis N, Gonzalez-Campo C, Wurtz H, Abdi A, Baufreton J, Bienvenu T, Herry C. Prefrontal parvalbumin interneurons shape neuronal activity to drive fear expression. (2014) *Nature.* 505(7481):92-6*

## Luigi Bellocchio | University of Bordeaux, France



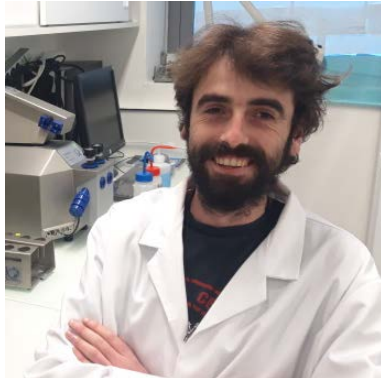
Luigi Bellocchio obtained a faculty position (CRCN) at NeuroCentre Magendie in 2017. Since his PhD studies in the lab of Giovanni Marsicano, he has been focusing his research on the role of the endocannabinoid system in the regulation of energy balance in the brain, acquiring a complete technical expertise in the use of transgenic mouse models combined with pharmacological approaches in order to study physiological processes involving the endocannabinoid system. With his post-doctoral studies, he went deeper into cellular mechanisms underlying the activity of G-protein

signaling (with particular emphasis on CB1 receptor) in order to understand how this receptor can exert different functions according to the cellular population (and the subcellular compartment) involved. Since 2012, in Manuel Guzman's lab at Complutense University of Madrid, he acquired a strong theoretical background on the role of GPCRs signaling in the regulation of motor and cognitive functions at basal ganglia level, as well as the knowledge and ability to apply genetic (particularly the use of viral vectors), pharmacological and pharmacogenetic tools to dissect it in different behavioral contexts. Re-joining the lab of Giovanni Marsicano in 2014, he used the knowledge acquired to study the role of mitochondrial CB1 signaling in the regulation of mitochondrial activity, and how it can modulate certain brain functions, such as memory. His research interest mainly focus on the link between mitochondrial CB1R and motor regulation at basal ganglia level, integrating his recently acquired knowledge of signalling pathways and mitochondrial processes.

### Selected publications:

- Blazquez C, Ruiz-Calvo A, Bajo-Graneras R, Baufreton JM, Resel E, Varilh M, Pagano Zottola AC, Mariani Y, Cannich A, Rodriguez-Navarro JA, Marsicano G, Galve-Roperh I, Bellocchio L\*, Guzman M\*. 2020. Inhibition of striatonigral autophagy as a link between cannabinoid intoxication and impairment of motor coordination. *eLife*, Aug 10, 9
- Hebert-Chatelain E\*, Desprez T\*, Serrat R\*, Bellocchio L\*, Pagano-Zottola A, Delamarre A, Cannich A, Vincent P, Varilh M, Robin ML, Terral G, García-Fernández M, Colavita M, Mazier W, Drago F, Puente N, Reguero L, Elezgarai I, Dupuy JW, Cota D, Lopez-Rodriguez ML, Barreda-Gómez G, Massa F, Grandes P, Bénard G, Marsicano G. 2016. A cannabinoid link between mitochondria and memory. *Nature*, 539(7630):555-559
- Bellocchio L, Ruiz-Calvo A, Chiarlone A, Cabanas M, Resel E, Cazalets JR, Blazquez C, Cho Y, Galve-Roperh I, Guzmán M. 2016. Sustained Gq Protein Signaling Disrupts Striatal Circuits via JNK. *Journal of Neuroscience*, 36(41):10611-10624.
- Bellocchio L\*, Soria-Gomez E\*, Quarta C, Metna-Laurent M, Cardinal P, Binder E, Cannich A, Delamarre A, Haring M, Martin-Fontecha M, Vega D, Leste-Lasserre T, Bartsch D, Monory K, Lutz B, Chaouloff F, Pagotto U, Guzman M, Cota D, Marsicano G. 2013. Activation of the sympathetic nervous system mediates hypophagic and anxiety-like effects of CB(1) receptor blockade. *PNAS*, 110(12):4786-91
- Bellocchio L\*, Lafenetre P\*, Cannich A, Cota D, Puente N, Grandes P, Chaouloff F, Piazza PV, Marsicano G. 2010. Bimodal control of stimulated food intake by the endocannabinoid system. *Nat Neurosci*, 13(3):281-3.

## Abel Eraso Pichot | University of Bordeaux, France



Abel Eraso-Pichot studied Human Biology with a Master's Degree in Biomedical Research at the Pompeu Fabra University in Barcelona. He did his PhD at the Autonomous University of Barcelona under the supervision of Dr. Elena Galea and Dr. Roser Masgrau, where he studied the phenomenon of astrocyte plasticity, especially those changes in calcium signals and metabolism occurring in these cells in response to neuronal activity. Moreover, he analyzed the differences in the expression of nuclear genes related to mitochondria in astrocytes and neurons, as well as their

implications in fatty acid metabolism. After his PhD, he worked as a postdoc in the laboratory of Dr. Albert Quintana in the Autonomous University of Barcelona, focusing on the central nervous system alterations produced by the mutation of the mitochondrial protein NDUFS4, a model of Leigh's syndrome. On 2019, he joined the group of Giovanni Marsicano to investigate the role of CB1 receptors (both mitochondrial and plasma membrane receptors) in neurons expressing the pro-opiomelanocortin (POMC) gene, a hypothalamic population implicated in the regulation of body composition.

### Selected publications:

- Bolea I, Gella A, Sanz E, Prada-Dacasa P, Menardy F, Bard AM, Machuca-Márquez P, Eraso-Pichot A, Mòdol-Caballero G, Navarro X, Kalume F, Quintana A. Defined neuronal populations drive fatal phenotype in a mouse model of Leigh Syndrome. *Elife*. 2019 Aug 12;8. pii: e47163. doi: 10.7554/eLife.47163.
- Eraso-Pichot A\*, Brasó-Vives M\*, Golbano A, Menacho C, Claro E, Galea E, Masgrau R. GSEA of mouse and human mitochondriomes reveals fatty acid oxidation in astrocytes. *Glia*. 2018 Mar 25. doi: 10.1002/glia.23330.
- Pardo L, Valor LM, Eraso-Pichot A, Barco A, Golbano A, Hardingham GE, Masgrau R, Galea E. CREB Regulates Distinct Adaptive Transcriptional Programs in Astrocytes and Neurons. *Sci Rep*. 2017 Jul 25;7(1):6390
- Hasel P, Dando O, Jiwaji Z, Baxter P, Todd AC, Heron S, Márkus NM, McQueen J, Hampton DW, Torvell M, Tiwari SS, McKay S, Eraso-Pichot A, Zorzano A, Masgrau R, Galea E, Chandran S, Wyllie DJA, Simpson TI, Hardingham GE. Neurons and neuronal activity control gene expression in astrocytes to regulate their development and metabolism. *Nat Commun*. 2017 May 2;8:15132.
- Eraso-Pichot A, Larramona-Arcas R, Vicario-Orrí E, Villalonga R, Pardo L, Galea E, Masgrau R. CREB decreases astrocytic excitability by modifying subcellular calcium fluxes via the sigma-1 receptor. *Cell Mol Life Sci*. 2017 Mar;74(5):937-950.

## Ignacio Fernandez-Moncada | University of Bordeaux, France



Started his career in 2005 with a Biochemist degree on the Pontificia Universidad Católica de Valparaíso, Chile. To finish his thesis degree, in 2010, Ignacio traveled 1000 kms south to find the laboratory of Dr. Felipe Barros in the Centro de Estudios Científicos (CECs) Valdivia, Chile. Here he approached for the first time to the study of astrocytes energy requirements. Fascinated with this research, Ignacio joined in 2012 the PhD program of the Universidad Austral de Chile (Valdivia), but stayed on Felipe Barros lab to deepen his experience and knowledge on astrocytes energy metabolism, now focused on the neuronal signals that modulated it. After obtaining his PhD degree in 2017, he stayed almost a year as a post-doc in Barros's lab. At the end of 2018, thanks to a Long-term EMBO fellowship, Ignacio performed another long journey to join the laboratory of Dr. Giovanni Marsicano at the Neurocentre Magendie (Bordeaux, France) to study how type-1 cannabinoids (CB1) receptors may regulate astrocytes energy metabolism and brain function.

### Selected publications:

- Fernández-Moncada I, Robles-Maldonado D, Castro P, Alegría K, Epp R, Ruminot I and Barros LF. (2020) Bidirectional astrocytic GLUT1 activation by elevated extracellular K<sup>+</sup>. *GLIA*;1–10. <https://doi.org/10.1002/glia.23944>
- Barros, L.F., Ruminot, I., San Martin, A., Lerchundi, R., Fernandez-Moncada, I., Baeza-Lehnert, F. (2020) Aerobic Glycolysis in the Brain: Warburg and Crabtree Contra Pasteur. *Neurochem. Res. Epub* <https://doi.org/10.1007/s11064-020-02964-w>.
- Fernández-Moncada I, Ruminot I, Robles-Maldonado D, Alegría K, Deitmer JW, Barros LF. (2018) Neuronal control of astrocytic respiration through a variant of the Crabtree effect. *Proc Natl Acad Sci U S A.* 115(7):1623-1628.
- Valdebenito R, Ruminot I, Garrido-Gerter P, Fernández-Moncada I, Forero-Quintero L, Alegría K, Becker HM, Deitmer JW, Barros LF. (2016) Targeting of astrocytic glucose metabolism by beta-hydroxybutyrate. *J Cereb Blood Flow Metab.* 36:1813–1822.
- Fernández-Moncada I, Barros LF (2014). Non-preferential fuelling of the Na<sup>(+)</sup>/K<sup>(+)</sup>-ATPase pump. *Biochem J.* 460:353–361.

## Marina Garcia Macia | University of Salamanca, Spain



My scientific career has been always tied to the biomedical field. After I graduated, I joined the cROS group, led by Prof. Ana Coto-Montes at Oviedo University. During my PhD studies I studied wide-ranging effects of autophagy in several models and published 16 papers in peer-reviewed journals. I also earned a fellowship for 4 years from the Instituto de Salud Carlos III (PFIS FI10-00065). The models and topics I explored included ageing, tenderization of commercial meat and Harderian gland. I used the latter to study the relationship between autophagy and lipid metabolism. I sought to expand my knowledge in lipophagy with a short stay in the laboratory of Dr. Rajat Singh at Albert Einstein College of Medicine (NY, USA). After my PhD, I rejoined Singh lab as a postdoctoral fellow to study lipophagy regulation. I learnt critical procedures in mice, including stereotaxic brain surgery, liver vagotomy and I contributed to 2 Cell Metab papers. On January 2016, I moved along with Singh lab from NY to Newcastle University. My management skills were crucial to set up this new lab branch. I had the chance to mentor a master student and technician volunteer. I got exciting collaborations, too. I study the role of lipophagy in glioblastoma with Dr Javier Oliver (IPBLN-CSIC, Spain). This collaboration provided very interesting results which were presented at the PARP meeting in Budapest. I also had the chance to study how autophagy mediates cell death in chondrocytes together with Prof. Florence L Marlow (Icahn School of Medicine at Mount Sinai, NY, USA). This collaboration resulted in a manuscript published in a D1 journal (PLOS Gen). After Dr. Singh went back to NY, I contacted Prof. Derek Mann and became a member of the Fibrosis lab in January 2017. There I lead different projects. One about the connection between epigenetics and fibrosis through MeCP2, published in Gastroenterology where I am first author. My expertise in Seahorse helped to understand defective macrophage polarization in a cRelKO mice (second author, Nat Metabol) and was crucial to set up an ex vivo system for human liver slices (Hepatology). I had also the opportunity to develop my own project: “mTOR role in lipid droplet biogenesis” funded by the Newcastle University (C0120R3166). This manuscript is under revision (Hepatology). I broaden my network of collaborations and I was co-PI in a Wellcome Trust Small Grant with the project Implications of autophagy in cardiac myopathies (BH182173). On January 2019, I joined the Neuroenergetics and metabolism lab, led by Prof. Juan Pedro Bolaños Hernandez with a Sara Borrell postdoctoral contract (CD18-00203). Here, I am already contributing to several projects funded by Ramon Areces Foundation and BBVA (co-first in a manuscript under review in Nat Comms).

### Selected publications:

- Moran-Salvador E\*, García-Macia M\*, Sivaharan A\*, Sabater L, Zaki MYW, Oakley F, Knox A, Page A, Luli S, Mann J, Mann D. (2019) Fibrogenic Activity of MECP2 is Regulated by Phosphorylation in Hepatic Stellate Cells. *Gastroenterology* S0016-5085(19)41126-8. *Impact factor*: 19.233.
- García-Macia M\*#, Santos-Ledo A\*, Caballero B, Rubio-González A, de Luxán-Delgado B, Potes Yaiza, Rodríguez-González S, Boga JA, Coto-Montes A. (2019) Selective autophagy, lipophagy and mitophagy, in the Harderian gland along the estrous cycle: a potential retrieval effect of melatonin. *Sci Report* 9(1):18597. *Impact factor*: 4.525.

- Leslie J#, Garcia-Macia M, et al., F. Oakley # (2020). *c-Rel orchestrates energy-dependent epithelial and macrophage reprogramming in fibrosis*. *Nat Metab* 2, 1350–1367 (2020). <https://doi.org/10.1038/s42255-020-00306-2>.
- Martinez Lopez N, García-Macia M, Sahu S, Athonvarangkul D, Liebling E, Merlo P, Cecconi F, Schwartz GJ, Singh R. (2016) *Autophagy in the CNS and Periphery Coordinate Lipophagy and Lipolysis in the Brown Adipose Tissue and Liver*. *Cell Metab*. 23(1):113127. Impact index: 18.164. Citations, 99
- García-Macia M; Vega Naredo I; de Gonzalo Calvo D; Rodríguez Gonzalez S; Camello PJ; Camello Almaraz C; Martín Cano FE; Rodriguez Colunga MJ; Pozo MJ; Coto Montes A. (2010) *Melatonin induces neural SOD2 expression independent of the NF-κB pathway and improves the mitochondrial population and function in old mice*. *J Pineal Res*. 50(1):54-63. Impact factor: 5.794. Citations: 35

### Anna Hadjihambil | Institute of Hepatology, London, UK



Anna Hadjihambil started her research into pathological mechanisms during her Neuroscience MSc studies (UCL) where she investigated the release of glutamate by activated human neutrophils using a novel approach with enzymatic biosensors, which is currently in development for clinical use. In 2014, Anna received a prestigious UCL Grand Challenges PhD Scholarship. Supervised by Prof R. Jalan (Department of Liver and Digestive Health) and Prof A. Gourine (Neuroscience, Physiology & Pharmacology), she demonstrated, using animal models of chronic liver disease and hepatic encephalopathy (HE) in combination with enzymatic biosensors, pharmacology and imaging techniques *ex vivo*, the key role of ammonia in causing neuronal energy deficits by impairing the hemichannel-mediated lactate transport between astrocytes and neurons. In 2018, Anna introduced another novel concept, through her MRI study, which demonstrated that brain glymphatic flow, known to facilitate the clearance of cerebral solutes and toxins, is impaired in HE. Furthermore, her PhD was also focused on investigating the effects of ammonia on impairing cerebral oxygenation during HE, using *in vivo* cerebral oxygen measurements, and various pharmacological interventions to unravel the mechanism behind the observed alterations. In 2018 Anna started her postdoctoral fellowship at UNIL, Switzerland, supervised by Prof. L. Pellerin. During this time, she investigated the effects of metabolically associated fatty liver disease on altering cerebral function, metabolism and physiology, as well as the role of the monocarboxylate transporter-1 in protecting the liver and the brain. To obtain answers to these questions, Anna employed a variety of techniques including behavioural testing, EchoMRI, histology, high resolution respirometry (OROBOROS) for functional examination of mitochondria, as well as *in vivo* measurements, including optoacoustics and MRI. Anna has recently started working at the Institute of Hepatology in London, as a senior postdoctoral scientist starting the Liver-Brain axis group and leading her own research on the mechanisms behind the cerebral alterations observed during metabolically associated fatty liver disease and steatohepatitis, as well as the long-term effects of these conditions on the brain. In addition to liver-induced brain diseases, Anna is interested and has contributed to



various other studies from different disciplines (cardiovascular, neuroscience, physiology, hepatology).

Selected publications:

- Hadjihambi, A., De Chiara, F., Hosford, P. S., Habtation, A., Karagianis, A., Davies, H., Gourine, A. V. & Jalan, R. 2017. Ammonia mediates cortical hemichannel dysfunction in rodent models of chronic liver disease. *Hepatology*, 65, 1306-1318. <https://doi.org/10.1002/hep.29031> PMID: PMC5396295
- Hadjihambi A., Harrison I. F., Costas-Rodriguez M., Vanhaecke F., Arias N., Gallego-Duran R., Mastitskaya S., Hosford P. S., Olde Damink S. W. M., Davies N., et al., 2018. Impaired brain glymphatic flow in experimental hepatic encephalopathy. *J Hepatol*;70(1):40-49. <https://doi.org/10.1016/j.jhep.2018.08.021> PMID: 30201461
- Hadjihambi A., Karagiannis A., Theparambil S. M., Ackland G. L., Gourine A. V. The effect of general anaesthetics on brain lactate release. 2020 *Eur J Pharmacol*; 881:173188. doi: 10.1016/j.ejphar.2020.173188
- Karagiannis, A., Sylantyev, S., Hadjihambi, A., Hosford, P. S., Kasparov, S & Gourine, A. V. 2016. Hemichannel-mediated release of lactate. *J Cereb Blood Flow Metab*, 36, 1202-11. <https://doi.org/10.1177/0271678X15611912> PMID: PMC4900446
- Sheikhabaei, S., Turovsky, E., Hosford, P. S., Hadjihambi, A., Theparambil, S. M., Liu B., Marina, N., Teschemacher, A. G., Kasparov, S., Smith J. C., Gourine A. V. 2018. Astrocytes modulate brainstem respiratory rhythm-generating circuits and determine exercise capacity. *Nature communications*, 9, 370. <https://doi.org/10.1038/s41467-017-02723-6> PMID: PMC5785528

### Morgane Jégo | University of Bordeaux, France



Morgane Le Bon-Jégo is an assistant professor in the team DNA (<http://www.imn-bordeaux.org/en/teams/dopamine-and-neuronals-assemblies/>) co-led by J. Baufreton and F. Georges at the Institute of Neurodegenerative Disorders in Bordeaux, France. Her main research interest is to understand using electrophysiological, cellular imaging and optogenetic approaches, the functioning and the plasticity of neural networks. Her current research focuses on the modulation exerted by midbrain DA inputs on primary motor microcircuits and its role in motor learning in physiological and pathophysiological conditions. Her objectives are to define functional plasticity involved in acquisition and maintenance of motor learning.

Selected publications:

- Cousineau J, Lescouzères L, Taupignon A, Delgado L, Valjent E, Baufreton J, Le Bon-Jégo M (2020). Dopamine D2-like receptors modulate intrinsic properties and synaptic transmission of Parvalbumin interneurons in the mouse primary motor cortex. *eNeuro*. 7(3):ENEURO.0081-20.2020. doi: 10.1523.
- Froux L, Le Bon-Jégo M, Miguelez C, Normand E, Morin S, Fioramonti S, Barresi M, Frick A, Baufreton J & Taupignon A (2018). D5 dopamine receptors control glutamatergic AMPA transmission between the motor cortex and subthalamic nucleus. *Sci Rep*, 8(1):8858.

- *Giraudin A, Le Bon-Jego M, Cabirol MJ, Simmers J & Morin D. (2012) Spinal and pontine relay pathways mediating respiratory rhythm entrainment by limb proprioceptive inputs in the neonatal rat. J Neurosci. 32(34), 11841-11853.*
- *Nargeot R., Le Bon-Jego M & Simmers J. (2009) Cellular and network mechanisms of operant learning-induced compulsive behavior in Aplysia. Curr Biol., 19(12):975-984.*
- *Le Bon-Jego M & Yuste R. (2007) Persistently active, pacemaker-like neurons in neocortex. Front. Neurosci. 1, 123-129.*

### Daniel Jiménez | University of Salamanca, Spain



Daniel Jimenez explores the possible factors that dictate the metabolic differences that exist between the two main cell types of the brain such as neurons and astrocytes. Neurons are cells that scarcely consume glucose through glycolysis unlike astrocytes. The biological importance of low neuronal glycolytic rate in vivo is unknown. That is why he study the behavioural effects of PFKFB3 pro-glycolytic enzyme expression on neurons in vivo. This work has allowed him to specialize in animal behavior techniques to evaluate exploratory capacity, memory, and motor coordination, as well as metabolic trials. He has been delving into the mechanisms that regulate neuronal metabolism and autophagy in the hypothalamus. During his PhD (2010-2014) in Juan Pedro Bolaños laboratory (University of Salamanca, Spain), Daniel Jiménez studied the regulation of the antioxidant response mediated by Nrf2 following the physiological activation of NMDA receptors in astrocytes. He demonstrated that glutamatergic neurotransmission could activate an antioxidant response in astrocytes mediated by transcription factor Nrf2 and Cdk5, that has a neuroprotective effect, as it triggers the release of glutathione precursors into adjacent neurons. During his first post-doc (2014-2016), in the same laboratory was hired from a research project funded by the National Institutes of Health/National Institute on Drug Abuse (NIH/NIDA) to study the metabolic effects on the brain of cannabis abuse. He investigated the involvement of the activation of cannabinoid receptors from the mitochondria of astrocytes on brain metabolism and behavior, in mice. During this period, he has specialized in mitochondrial physiology, assembly and activity of complexes and super-complexes of the electron transport chain and production of reactive oxygen species by complex I. In addition, he has learnt countless in vivo mouse manipulation techniques, such as, retro-orbital intravenous injection, brain stereotaxia, intraperitoneal drug administration, PFA/Somogy infusions and intracerebroventricular cannula implantation in different brain areas.

#### Selected publications:

- *Glucose metabolism links astroglial mitochondria to cannabinoid effects. Daniel Jiménez Blasco\*, Arnau Busquets García\*, Etienne Hebert-Chatelain\*, Roman Serrat, Carlos Vicente-Gutierrez, Christina Ioannidou, Paula Gómez Sotres, Irene Lopez-Fabuel, Monica Resch, Eva Resel, Dorian Arnouil, Dave Saraswat, Marjorie Varilh, Astrid Cannich, Francisca Julio-Kalajzic, Itziar Bonilla-Del Rio, Angeles Nagore Puente, Svein Achicallende, Maria-Luz Lopez-Rodriguez, Charlotte Jollé, Nicole Déglon, Luc Pellerin, Charléne Josephine, Gilles Bonvento, Aude Panatier, Beat Lutz, Pier-Vincenzo*

Piazza, Manuel Guzmán, Luigi Bellocchio, Anne-Karine Bouzier-Sore, Pedro Grandes, Juan P. Bolaños# and Giovanni Marsicano.#. (2020). *Nature* 583, 603–60.

- *Astrocyte NMDA receptors' activity sustains neuronal survival through a Cdk5-Nrf2 pathway.* Daniel Jiménez Blasco; Patricia Santofimia Castaño; Antonio González Mateos; Angels Almeida Parra; Juan Pedro Bolaños Hernández. (2015). *Cell Death and Differentiation*. 22 -11,1877– 1889.
- *Targeting PFKFB3 brain alleviates cerebral ischemia-reperfusion injury in mice.* Olga Burmistrova; Ana Olías Arjona; Rebekah Lapresa; Daniel Jiménez Blasco; Tatiana Eremeeva; Dmitry Sishov; Sergei Romanovs; Kristina Zakurdaeva; Angels Almeida; Peter O. Fedichev; Juan P. Bolaños. (2019). *Scientific Reports* 9.
- *Astrocytic mitochondrial ROS modulate brain metabolism and mouse behaviour.* Carlos Vicente Gutierrez; Nicolo Bonora; Veronica Bobo Jiménez; Daniel Jiménez Blasco; Irene López Fabuel; Emilio Fernández; Charlene Josephine; Gilles Bonvento; Jose A. Enríquez; Ángeles Almeida; Juan P. Bolaños. (2019). *Nature Metabolism* 1-2.201-211.
- *Cell identity and nucleo-mitochondrial genetic context modulate OXPHOS performance and determine somatic heteroplasmy dynamics.* Ana Victoria Lechuga-Vieco, Ana Latorre-Pellicer, Iain G Johnston, Gennaro Prota, Uzi Gileadi, Raquel Justo-Méndez, Rebeca Acín-Pérez, Raquel Martínez-de-Mena, Jose María Fernández-Toro, Daniel Jimenez-Blasco, Alfonso Mora, Jose A. Nicolás-Ávila, Demetrio J. Santiago, Silvia G. Priori, Juan P. Bolaños, Guadalupe Sabio, Luis Miguel Criado, Jesús Ruíz-Cabello, Vincenzo Cerundolo, Nick S Jones and José Antonio Enríquez. (2020). *Sci. Adv* 6.

### Rodrigo Lerchundi | MIRCen, CNRS, Paris, France



Rodrigo Lerchundi is a Chilean researcher who obtained the title of biochemist and a PhD in Science, Molecular and cellular biology, from the Austral University of Chile (UACH, Valdivia, Chile). He performed his PhD thesis under the tutelage of L. Felipe Barros in the Center of Scientific Studies (CECs) in Valdivia, Chile. During this period, he studied the effects of ammonium on the release of lactate in astrocytes. Subsequently, he worked as a PostDoc at the Institute of Neurobiology at the Heinrich Heine University Duesseldorf, Germany, in the group of Prof. Dr. Christine R. Rose. His work

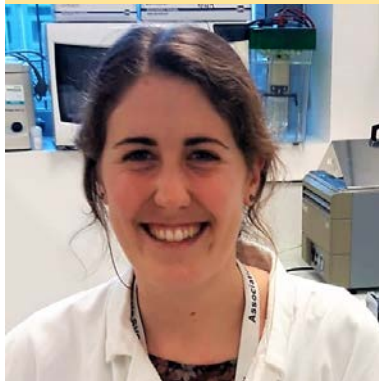
was mainly focussed in single cell imaging of sodium and ATP in order to understand the interaction between sodium transients and energy consumption in neurons and astrocytes under neuronal activity. Currently, he work in CEA/MIRCen Fontenay aux Roses in France, as part of Julien Valette's group. His role consist in the validation of in vivo methods for nuclear magnetic resonance (NMR) spectroscopy, using in vivo imaging of lactate with FRET-sensors in neurons and astrocytes together with extracellular quantification of lactate with Implanted enzymatic-electrodes.

#### Selected publications:

- *Lerchundi R, Fernández-Moncada I, Contreras-Baeza Y, Sotelo-Hitschfeld T, Mächler P, Wyss MT, Stobart J, Baeza-Lehnert F, Alegría K, Weber B, Barros LF. NH4(+) triggers the release of astrocytic lactate via mitochondrial pyruvate shunting. Proc Natl Acad Sci U S A. 2015 Sep 1;112(35):11090-5. doi: 10.1073/pnas.1508259112. Epub 2015 Aug 18. PMID: 26286989; PMCID: PMC4568276.*

- *Lerchundi R, Huang N, Rose CR. Quantitative Imaging of Changes in Astrocytic and Neuronal Adenosine Triphosphate Using Two Different Variants of ATeam. Front Cell Neurosci. 2020 Apr 21;14:80. doi: 10.3389/fncel.2020.00080. PMID: 32372916; PMCID: PMC7186936.*
- *Gerkau NJ, Lerchundi R, Nelson JSE, Lantermann M, Meyer J, Hirrlinger J, Rose CR. Relation between activity-induced intracellular sodium transients and ATP dynamics in mouse hippocampal neurons. J Physiol. 2019 Dec;597(23):5687-5705. doi: 10.1113/JP278658. Epub 2019 Oct 30. PMID: 31549401.*
- *San Martín A, Ceballo S, Ruminot I, Lerchundi R, Frommer WB, Barros LF. A genetically encoded FRET lactate sensor and its use to detect the Warburg effect in single cancer cells. PLoS One. 2013;8(2):e57712. doi: 10.1371/journal.pone.0057712. Epub 2013 Feb 26. PMID: 23469056; PMCID: PMC3582500.*

### Cristina Miralpeix | University of Bordeaux, France



Cristina Miralpeix studied biochemistry and specialises in neuroscience in Barcelona, Spain. During her PhD in the Universitat Internacional de Catalunya (2015-2019) she started her carrier in hypothalamic regulation of obesity. She worked on the role of the hypothalamus-periphery cross-talk in the control of energy expenditure and investigated the hypothalamic endocannabinoid system in the physiopathology of diet-induced obesity. She used in vivo experimental approaches to demonstrate that the initial stages of obesity development are characterized by a rise in

hypothalamic endocannabinoids levels triggered by the diet-dependent, adaptive increase in energy expenditure observed during the initial exposure to an obesogenic, hyper-caloric diet. Moreover, using in vitro assays, she has contributed to the description of the molecular mechanism controlling the activity of the novel endocannabinoid enzyme ABHD6. From her PhD work, she has recently published three articles, one in *Molecular Metabolism*, another in the *Journal of Lipid Research* and the third one in the *British Journal of Pharmacology*. After her PhD, she moved to the Dr. Daniela Cota lab in the Neurocentre Magendie, Bordeaux, where she is currently doing her post-doc, supported by a FRM fellowship. In Dr. Cota lab's she is developing her investigation in the hypothalamic endocannabinoid system and the control of food intake and energy expenditure. Concretely, she is studying how both plasmatic and mitochondrial cannabinoid 1 receptor in POMC neurons of the arcuate nucleus of the hypothalamus is regulating preference and motivation for consuming a high caloric diet over a normal diet. For that project, she is using in vivo experimental approaches for the study of whole body metabolism and the assessment of food intake behavior, transgenic animals and viral vectors to specifically targeting the hypothalamus.

#### Selected publications:

- *Miralpeix C., Fosch A., Casas J., Baena M., Herrero L., Serra D., Rodríguez-Rodríguez R., Casals N. (2019) Hypothalamic endocannabinoids inversely correlate with the development of diet-induced obesity in male and female mice. Journal of Lipid Research, 60, jlr.M092742. <https://doi.org/10.1194/jlr.M09274>.*

- *Rodríguez-Rodríguez R., Miralpeix C., Fosch A., Pozo M., Calderón-Domínguez M., Perpinyà X., Vellvehí M., Lopez M., Herrero L., Serra D., Casals N. (2019) CPT1C in the ventromedial nucleus of the hypothalamus is necessary for brown fat thermogenesis activation in obesity. Molecular Metabolism, 19, 75–85. <https://doi.org/10.1016/j.molmet.2018.10.010>*

### Shingo Nakajima | University of Montreal, Canada



Shingo Nakajima studies the interaction between metabolic dysregulation and psychiatric diseases with focusing nutrient-sensing systems. During his Ph.D. under the supervision of Dr. T. Hira and Prof H. Hara in nutritional biochemistry lab (Hokkaido University, Japan), he investigated the luminal nutrient sensing mechanism in enteroendocrine cells related to obesity. During his post-doc in the department of Mental disorder research (National Center of Neurology and Psychiatry, Japan), he studied the role of gut hormone and neurotrophic factor in cortical neurons. In lipid mediator lab (Ochanomizu University, Japan), he investigates the effect of quality of dietary fat on psychological behavior. Lipidomic approach in his research suggested the deficiency of n-3 poly-unsaturated fatty acid linked to abnormal behavior in high-saturated fat diet-induced obesity models. Since October 2019, Shingo joined Fulton lab at CRCHUM (Montreal, Canada) to study the role of lipid-sensing in dopaminergic systems on obesity-induced anxiety- and depressive-like behavior.

#### Selected publications:

- *Nakajima S, Fukasawa K, Gotoh M, Murakami-Murofushi K, Kunugi H. Saturated fatty acid is a principal cause of anxiety-like behavior in diet-induced obese rats in relation to serum lysophosphatidyl choline level. Int J Obes (Lond). 44(3) (2020), pp.727-738.*
- *Nakajima S, Gotoh M, Fukasawa K, Murakami-Murofushi K, Kunugi H. "Oleic acid is a potent inducer for lipid droplet accumulation through its esterification to glycerol by diacylglycerol acyltransferase in primary cortical astrocytes." Brain Res. (2019) 146484.*
- *Nakajima S, Hira T, Iwaya H, Hara H. Zinc directly stimulates cholecystokinin secretion from enteroendocrine cells and reduces gastric emptying in rats. Mol Cell Endocrinol. 2016, 430, 108-114.*
- *Nakajima S, Numakawa T, Adachi N, Ooshima Y, Odaka H, Yoshimura A, Kunugi H. Self-amplified BDNF transcription is a regulatory system for synaptic maturation in cultured cortical neurons. Neurochem Int. 2015, 91, 55-61.*

### Antonio Pagano-Zottola | University of Bordeaux, France



Antonio Pagano Zottola studied pharmacy, being interested in new therapeutic perspective for cancer treatment. During his PhD in the Bifulco laboratory (University of Salerno, Italy), he studied the role of Cannabinoid Receptor 1 (CB1) in brain tumors. As Post-Doc, in the Marsicano lab at the Neurocentre Magendie, he works on mitochondrial associated CB1 (mtCB1). Since 2015 he focused his research on the role of cannabinoids in the regulation of brain metabolism, investigating the intra-mitochondrial pathway of the receptor and its impact on brain functions. His research showed that mtCB1 stimulation produces cognitive and motor impairment due to the decrease of cellular respiration by reducing the activity of mitochondrial complex I. Combining biochemistry and high resolution respirometry he studies the role of mitochondrial G proteins in the regulation of brain energy production.

#### Selected publications:

- *Subcellular specificity of behavioral control* Soria-Gomez E\*, Pagano Zottola AC\*, Mariani Y\*, Desprez T, Barresi M, Bonilla-del-Río I, Muguruza C, Le Bon-Jego M, Flynn R, Terral G, Fernández-Moncada I, Robin LM, Oliveira da Cruz JF, Corinti S, Ould Amer Y, Goncalves J, Varilh M, Cannich A, Redon B, Zhao Z, Julio-Kalajzić F, Lesté-Lasserre T, Vincent P, Tolentino-Cortes T, Busquets-García A, Puente N, Bains JS, Hebert-Chatelain E, Barreda-Gómez G, Chaouloff F, Lohman AW, Callado JF, Grandes P, Baufreton J, Marsicano G, Bellocchio L. (*Neuron*, in revision)
- *A new mutant mouse model lacking mitochondrial-associated CB1 receptor* Pagano Zottola AC, Soria-Gomez E, Bonilla-del-Río I, Muguruza M, Terral G., Robin LM, Oliveira da Cruz JF, Redon B, Lesté-Lasserre T, Tolentino-Cortes T, Puente N, Barreda-Gómez G, Chaouloff F, Callado LF, Grandes P, Marsicano G, Bellocchio L. (*Preprint Biorxiv*, 2020)
- *A cannabinoid link between mitochondria and memory* Hebert-Chatelain E, Desprez T, Serrat R, Bellocchio L, Soria-Gomez E, Busquets-García A, Pagano Zottola AC, Delamarre A, Cannich A, Vincent P, Varilh M, Robin LM, Terral G, García-Fernández MD, Colavita M, Mazier W, Drago F, Puente N, Reguero L, Elezgarai I, Dupuy JW, Cota D, Lopez-Rodriguez ML, Barreda-Gómez G, Massa F, Grandes P, Bénard G, Marsicano G. (*Nature*, 2016)

### Sandrine Pouvreau | University of Bordeaux, France



Sandrine Pouvreau explores the role of organelles signaling in synaptic function and neuronal activity. She is a CNRS researcher (National Center for Scientific Research). She obtained her PhD at the University of Lyon working on the regulation of intracellular calcium signaling by plasma membrane microdomains. She then joined the Department of Biology and Biophysics at Rush University, in Chicago (laboratory of E Rios), where she used a combination of imaging, electrophysiological, and biochemical techniques to characterize the molecular underpinnings of calcium sparks. During her postdoc, she also developed new approaches to

dissect organelle calcium fluxes using genetically encoded and hybrid sensors. Recruited as a CNRS Researcher, she used genetically targeted redox sensors to study mitochondrial redox signaling. She developed a strong expertise in the field and was the invited editor of a special issue on Redox Indicators in the journal *Antioxidant and Redox Signaling*<sup>1</sup>. Nonetheless, she maintains a strong interest in calcium signaling and her current main line of research is to investigate the role of organelles calcium handling in the regulation of synaptic function and neuronal activity in health and disease. Her research uses hippocampal slices cultures and brain extracts combined with a multidisciplinary approaches including live-imaging, super-resolution microscopy, electrophysiology, gene transfer and biochemistry.

Selected publications:

- Serrat, R., Covelo, A., Kouskoff, V., Delcasso, S., Ruiz, A., Chenouard, N., Stella, C., Blancard, C., Salin, B., Julio-kalajzić, F., Cannich, A., Massa, F., Varilh, M., Deforges, S., Robin, LM., De Stefani, D., Busquets-Garcia, A., Gambino, F., Beyeler, A., Pouvreau, S.#, Marsicano, G#. *Astroglial calcium transfer from endoplasmic reticulum to mitochondria determines synaptic integration. In Revision. # co-last authors + corresponding authors.*
- Royer L, Shangraw K, Herzog JJ, Pouvreau S, Marr MT 2nd, Paradis S. *The Metastasis Suppressor Protein Nme1 Is a Concentration-Dependent Modulator of Ca<sup>2+</sup>/Calmodulin-Dependent Protein Kinase II. Biochemistry. 58: 2710-2714. June 2013*
- Pouvreau S. (2016) *Beyond the Cuvette: Redox Indicators in Biological Experiments. Antioxid Redox Signal. 25:517-9. September 2016.*
- Wei-LaPierre L, Gong G, Gerstner BJ, Ducreux S, Yule DI, Pouvreau S, Wang X, Sheu SS, Cheng H, Dirksen RT, Wang W *Respective Contribution of Mitochondrial Superoxide and pH to Mt-cpYFP Flash Activity. J Biol Chem. 288: 10567-10577. April 2013*
- Pouvreau S. *Superoxide flashes in mouse skeletal muscle are produced by discrete arrays of active mitochondria operating coherently. PLoS One. 5. pii: e13035. September 2010.*

### Ruben Quintana | University of Salamanca, Spain



Ruben Quintana-Cabrera holds a BSc in Pharmacy from the University (U.) of Salamanca (2006). During the last year of his BSPHarm, he early joined the lab of Prof. Juan P. Bolaños, at the U. of Salamanca to investigate the role of nitrosative stress in neurons and stem cells in Parkinson's disease. His thesis work, directed by Prof. Juan P. Bolaños and Dr. Ángeles Almeida, characterized for the first time the ability of g-glutamylcysteine to act as a GPx1 cofactor and increase the antioxidant capacity of mitochondria by a gene therapy approach, conferring neuroprotection in a mouse model of Huntington's disease (*Nat Commun* 3: 718 , 2012). His predoctoral training includes a stage (2011) granted by an EMBO STF in the laboratory of Prof. Luca Scorrano at the U. of Geneva (Switzerland), to study the role of oxidative stress in mitochondrial dynamics and autophagy. After obtaining a European PhD at U. Salamanca with honors and several awards for his work, he began his postdoc in the laboratory of Prof. Scorrano at the U. of Padua (Italy), to delve into the role of mitochondrial dynamics, ultrastructure and bioenergetics in physiology. Among other works, he contributed to describe a structural role of mitochondrial cristae in

the stabilization of respiratory supercomplexes, determining the respiratory and bioenergetic capacity of the cell (Cogliati et al., *Cell*, 2013, thus defining cell survival and tissue homeostasis (Varanita et al., *CellMetabol.*, 2015). He also described how upon a blockage of the electron transport chain, mitochondrial ultrastructure is key to engage a more active ATPase to prevent mitochondrial collapse and cell death (Quintana-Cabrera et al., *NatComm*, 2018). After finishing his postdoc, Rubén has been recipient of a Marie Curie IF Fellowship back to the U. of Salamanca. His current research work is focused in understanding how the intercellular exchange of whole mitochondria remodels the organelle content and function in the recipient cell, as a path to halt neurodegeneration and tumor development. Along with his scientific work, Rubén also actively participates in teaching and mentoring of graduate and PhD students and participates to outreach courses, seminars and international meetings.

Selected publications:

- Zaninello M, Palikaras K, Naon D, Iwata K, Herkenne S, Quintana-Cabrera R, Semenzato M, Grespi F, Ross-Cisneros FN, Carelli V, Sadun AA, Tavernarakis N, Scorrano L. Inhibition of autophagy curtails visual loss in a model of autosomal dominant optic atrophy. *Nature Communications*, 2020 Aug 12.
- Quintana-Cabrera, R, Quirin C, Glytsou C, Corrado M, Urbani A, Pellattiero A, Calvo E, Vázquez J, Enríquez JA, Gerle C, Soriano ME, Bernardi P, Scorrano L. The cristae modulator Optic atrophy 1 requires mitochondrial ATP synthase oligomers to safeguard mitochondrial function. *Nature Communications*, 2018 Aug 24.
- Varanita T., Soriano M.E., Romanello V., Zaglia T., Quintana-Cabrera R., Semenzato M., Menabò R., Costa V., Civiletto G., Pesce P., Viscomi C., Zeviani M., Di Lisa F., Mongillo M., Sandri M., Scorrano L. Controlled overexpression of the mitochondria shaping protein Optic Atrophy 1 counteracts cellular damage in vivo. *Cell Metabolism*. 2015. Jun 2;21(6):834-442T2T.7
- Cogliati S.; Frezza C.; Soriano ME.; Varanita T.; Quintana-Cabrera R.; Corrado M.; Cipolat S., Costa V., Casarin A., Gomes LC., Perales-Clemente E.; Salviati L.; Fernandez-Silva P.; Enriquez JA.; Scorrano L. Mitochondrial cristae shape determines respiratory chain supercomplexes assembly and respiratory efficiency. *Cell*. 2013 Sep 26;155(1):160-71.
- Quintana-Cabrera, R.; Fernandez-Fernandez, S.; Bobo-Jimenez, V.; Escobar, J.; Sastre, J; Almeida, A.; Bolaños, J.P.  $\gamma$ -Glutamylcysteine detoxifies reactive oxygen species by acting as glutathione peroxidase-1 cofactor. *Nature Communications*. 2012 Mar 6;3:718.

### Román Serrat | University of Bordeaux, France



Román Serrat is current postdoctoral researcher in the Endocannabinoids and Neuroadaptation Group at Neurocentre Magendie. He aims to study the role of mitochondria in brain function including mitochondrial calcium dynamics and mitochondrial dynamics. After a PhD (2007-2012) in biomedicine in Prof. Soriano's laboratory (IRB, Barcelona, Spain) where he studied the role of Alex3, a mitochondrial protein highly enriched in the brain, on mitochondrial transport, he joined Dr. Marsicano's group (INSERM, Bordeaux, France). Since then, his research aims to

better characterize the cannabinoid receptor 1 and its impact on mitochondrial physiology



which can contribute for the development of new drugs with less side-effects. He has elucidated the role of mitochondrial cannabinoid receptor 1 (mtCB1) on mitochondrial respiration, transport and consequently memory. He is currently studying the role of the mtCB1 in astrocytes, in particular how cannabinoids modulate mitochondrial calcium levels and its impact on synaptic integration.

Selected publications:

- Serrat, R., Covelo, A., Kouskoff, V., Delcasso, S., Ruiz, A., Chenouard, N., Stella, C., Blancard, C., Salin, B., Julio-kalajzić, F., Cannich, A., Massa, F., Varilh, M., Deforges, S., Robin, LM., De Stefani, D., Busquets-Garcia, A., Gambino, F., Beyeler, A., Pouvreau, S., Marsicano, G. Astroglial calcium transfer from endoplasmic reticulum to mitochondria determines synaptic integration. *In Revision.*
- Jimenez-Blasco, J.\*, Busquets-Garcia, A.\*, Hebert-Chatelain, E.\*, Serrat, R., Vicente-Gutierrez, C., Ioannidou, C., Gómez-Sotres, P., Lopez-Fabuel, I., Resch-Beusher, M., Resel, E., Arnouil, D., Saraswat, D., Varilh, M., Cannich, A., Julio-Kalajzic, F., Bonilla-Del Río, I., Almeida, A., Puente, N., Achicallende, S., Lopez-Rodriguez, ML., Jollé, C., Déglon, N., Pellerin, L., Josephine, C., Bonvento, G., Panatier, A., Lutz, B., Piazza, PV., Guzmán, M., Bellocchio, L., Bouzier-Sore, AK., Grandes, P., Bolaños, JP., Marsicano, G. Glucose metabolism links astroglial mitochondria to cannabinoid effects. *Nature*, 583(7817):603-608. July, 2020
- Hebert-Chatelain, E.\*, Desprez, T.\*, Serrat, R.\*, Bellochio, L.\*, Soria-Gomez, E., Busquets-Garcia, A., Pagano-Zottola AC., Delamarre, A., Cannich, A., Vincent, P., Varilh, M., Robin, L., Terral, G., García Fernández, D., Colavita, M., Mazier, W., Drago, F., Puente, N., Reguero, L., Elezgarai, I., Dupuy, JW., Cota, D., Lopez-Rodriguez, ML., Barreda-Gómez, G., Massa, F., Grandes, P., Bénard, G., Marsicano, G. A cannabinoid link between mitochondria and memory. *Nature* 539(7630):555. November, 2016.
- Serrat, R.\*, Mirra, S.\*, Figueiro-Silva, J., Navas-Pérez, E., Quevedo, M., López-Domenech, G., Podlesniy, P., Ulloa, F., Garcia-Fernández, J., Trullas, R., Soriano, E. The *Armc10/SVH* gene: genome context, regulation of mitochondrial dynamics and protection against A $\beta$ -induced mitochondrial fragmentation. *Cell Death & Disease* 5:e1163. April 2014.
- López-Domenech, G.\*, Serrat, R.\*, Mirra, S., D’Aniello, S., Somorjai, I., Abad, A., Vitureira, N., García-Arumí, E., Teresa Alonso, M., Rodriguez-Prados, M., Burgaya, F., Andreu, T.L., García-Sancho, J., Trullas, R., García-Fernández, J., Soriano, E. Mitochondrial proteins encoded by the *Eutherian-specific Armcx* gene cluster regulate neuronal trafficking and interact with the KHC/Miro/Trak2 complex. *Nature Communications* 3:814. May, 2012.

### Carlos Vicente-Gutiérrez | University of Salamanca, Spain



Carlos Vicente-Gutiérrez studied Biotechnology in the University of Salamanca, Spain (2009-2013). As a learning student explored cutting-edge techniques with different groups. Mainly, nanotechnology of biopolymers elastin-like and bioinformatic analysis of microRNA expression in patients of chronic lymphocytic leukemia. As a master student he continued investigating cancer biology as well as translational research starting his interest in murine models and mitochondrial molecular mechanisms. During his PhD (2014-2019) he investigated the metabolic adaptations of neurons and glia to endogenous mitochondrial reactive oxygen species (mROS), under the supervision



of Dr. Juan P. Bolaños in the Institute of Functional Biology and Genomics (IBFG-University of Salamanca). Astrocytes are less dependent on mitochondria metabolism for energy generation, mostly relying on glycolysis. In parallel, the comparative study of mitochondrial respiratory chain revealed that in astrocytes this structure is loosely assembled compared with neurons. This fact favours that the generation of mitochondrial ROS is one order of magnitude higher in astrocytes. In the absence of an explanation about the physiological relevance of these levels, his Thesis contribution on this field allowed to conclude that high endogenous levels of astrocytic mROS modulate brain metabolism and mouse behaviour. This work deciphered how astrocytic mROS regulate glucose utilization impacting the metabolic support that astrocytes exert on neurons. Furthermore, astrocytic mROS promote brain metabolism rewiring and neuronal function alterations such as behaviour. This research involved a huge battery of *in vitro* measurements and *in vivo* manipulations. Mainly, the generation of a new mouse model that allows the cell-specific modulation of mROS by targeting a mitochondrial-tagged isoform of catalase. During this period, Carlos was awarded with a short-term EMBO Fellowship to stay in Prof. Giovanni Marsicano's laboratory at the Neurocentre Magendie (Bordeaux, France), learning to dissect out highly complex behavioural phenotypes. Since 2019, as a post-doc, Carlos is continuing his interest in exploring the connection between behavioural consequences with molecular/subcellular/cell specific changes and complex signalling in the brain. His work in neurometabolism field explore the cell-specific modulation of endogenous levels of mROS in health and disease. Hopefully, this type of research will open new paradigms in the (patho)physiology of redox signalling in the brain metabolism as well as its therapeutic implications for neurodegeneration.

Selected publications:

- Hernández-Sánchez M, Rodríguez-Vicente AE, Hernández J-T, ..., Vicente-Gutierrez C, et al. MiRNA expression profile of chronic lymphocytic leukemia patients with 13q deletion. *Leukemia Research*. 2016;46. doi:10.1016/j.leukres.2016.04.008
- Vicente-Gutierrez C, Bonora N, Bobo-Jimenez V, et al. Astrocytic mitochondrial ROS modulate brain metabolism and mouse behaviour. *Nature Metabolism*. 2019;1(2):201-211. doi:10.1038/s42255-018-0031-6
- Vicente-Gutierrez C, Bolaños J. An *ex vivo* Approach to Assess Mitochondrial ROS by Flow Cytometry in AAVtagged Astrocytes in Adult Mice. *Bio-Protocol*. 2020;10(6). doi:10.21769/bioprotoc.3550
- Vicente-Gutiérrez C, Jiménez-Blasco D, Quintana-Cabrera R. Intertwined ROS and Metabolic Signaling at the Neuron-Astrocyte Interface. *Neurochemical Research*. 2020;(0123456789). doi:10.1007/s11064-020-02965-9
- Jimenez-Blasco D, Busquets-Garcia A, Hebert-Chatelain E, Serrat R, Vicente-Gutierrez C, et al. Glucose metabolism links astroglial mitochondria to cannabinoid effects. *Nature*. 2020; <https://doi.org/10.1038/s41586-020-2470-y>