Dear All,

With the awakening of spring, the evaluation of the applications to the ERA-Net NEURON Cofund2 Joint Transnational Call 2023 (JTC2023) on the topic ‘Resilience and Vulnerability in Mental Health’ continues. The call was launched on January 9th and the deadline for the submission of the preproposals was March 7th. This year ERA-Net NEURON launched not only one call for proposals, but two! The second call on ‘Ethical, Legal, and Social Aspects (ELSA) of Neuroscience’ just recently closed and the evaluation process is on its way.

In January we were thrilled to hear about the progress being made in the research projects funded under the two JTC2020 calls: one on ‘Sensory Disorders’ and the other on ‘Ethical, Legal, and Social Aspects (ELSA) of Neuroscience’. During the JTC2020 Midterm Symposium, the coordinators of the 17 funded projects (12 from the biomedical call and 5 from the ELSA

More information can be found on our website http://www.neuron-eranet.eu/index.php

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call) presented their main achievements so far, the obstacles they encountered and their future plans. The poster session during the meeting provided the stage to early career researchers (ECRs) participating in the projects by allowing them to present their research. More about the Midterm Symposium on page 16.

The symposium also included the award ceremony and a talk by the Excellent Paper in Neuroscience Award 2022 (EPNA2022) beneficiary, Damien Huzard, who presented his research on the impact of C-tactile low-threshold mechanoreceptors on affective touch and social interactions in mice. Read more about Dr. Huzard and the EPNA award in the interview we conducted with him included in this newsletter (page 17). In addition to the annual EPNA award, ERA-Net NEURON supports young researchers in various ways, including expertise development and training, through collaboration with the Cajal Training Programme. This issue includes impressions from three participants, whose attendance in the ‘Neuroepigenetics: writing, reading and erasing the epigenome’ course that took place in November-December 2022, was supported by ERA-Net NEURON (page 19). The full interviews describing these young researchers’ interests, views and reflections from the course can be found on the NEURON website.

To form synergies in the research community, to overcome gaps and hurdles, to build overarching networks, and to generate harmonizing concepts and ideas, ERA-Net NEURON launched a first call for proposals for networking and the formation of working groups. The main focus of this current issue of the ERA-Net NEURON newsletter will be on the 11 consortia that were chosen to be funded under our Networking Group Call 2022 on ‘Chronic Pain’. Read more about the call, its outcomes and the funded consortia on page 4.

For those who follow ERA-Net NEURON closely, it is clear that it is involved in the whole eco-system of neuroscience and brain research. Such an example for this holistic approach are the ‘Open Science’ workshops that are organized for NEURON-funded researchers. Recently, in April 19th – 21st, 2023, the ‘NEURON-QUEST Workshop on OPEN SCIENCE’ for researchers and clinicians of the JTC2022 ‘Cerebrovascular Diseases’ convened in Berlin. The workshop was hosted by the Berlin Institute of Health (BIH) QUEST Center and welcomed participants from the 14 funded projects of JTC2022. The program comprised presentations on Responsible Research Innovation based on robust experimental design heading to further translation steps. Also, important research infrastructures like Infrafrontier and the European Mouse Mutant Archive - EMMA, ELIXIR for repositories and its Research Data Management toolkit for Life Sciences (RDM), the Data Stewardship Wizard, and EBRAINS for data sharing in the neuroscientific domain were presented.

NEURON not only addresses scientists and clinicians, but also prioritizes engaging with the general public and educating about brain and mental disorders through our ERA-Net NEURON
Lecture Series for lay audience. The next lecture, on the fascinating trending topic of the 'Brain-Gut Axis', will be given by Pascal Derkinderen, a professor of Neurology at Nantes University and Inserm U913 in France. The lecture is open to everyone and will take place virtually on Thursday June 22nd, 2023. You can connect to the webinar through this link.

With this, we wish you a wonderful summer and feel welcome to keep up with our website, follow us on twitter and join our LinkedIn group in order to join our community and not to miss further information about our various calls, activities and events.

Sincerely yours

[Signature]
Chronic pain imposes a massive burden on several levels, from the individual, through the health system, to the economy worldwide. Chronic pain leads to a severe impediment to the quality of life of those affected and their families. Patients' daily activities such as work and social interactions are heavily impaired. As a consequence, chronic pain can lead to sleep problems, depression and anxiety. The underlying mechanisms of chronic pain are often not understood, therefore, joined efforts of basic scientists, clinicians, lay organisations and policymakers are needed to understand the pathophysiology, improve diagnosis and therapy, increase awareness, and improve the every-day life of the patients. The success of biomedical research, however, is hampered by the lack of harmonization of procedures, experimental methodologies, and data management. For the translation and implementation of future research outcomes into clinical practice, as well as for shaping future research priorities, it is essential to form synergies in the research community, to overcome gaps and hurdles, to build overarching networks, and to generate harmonizing concepts and ideas. Thus, a transnational networking call in the field of chronic pain was launched under the umbrella of the ERA-NET NEURON.

Eleven multinational consortia were selected for funding under the Networking Group Call 2022 (NWGC2022) on the topic of ‘Chronic Pain’. In total, 219 PIs from 30 countries collaborate in these consortia, which cover various aspects of the field of chronic pain, as can be seen from the description of each of the consortia below. The total funding volume of the call amounts to 550K€.

We wish all the funded consortia success and significant achievements and hope their outcomes contribute to the future of research on chronic pain and will play a role in improving the life of patients suffering from chronic pain.
AGORA partners will use their multidisciplinary expertise to identify key variables contributing to clinical trial outcomes in chronic neuropathic pain (CNP), with the aim of advancing the current standard of care with improved clinical trial guidelines pursuing a higher rate of responders. Experts from different research areas will collaborate with early career researchers (ECRs), patients’ representatives and other key players in the field to identify essential variables affecting symptomatology, wellness and Quality of Life (QoL) of patients. A Delphi process will allow the consensus on relevant variables through which patients can be stratified in CNP endophenotypes, allowing the development of better tailored clinical trials. Recommendations for harmonization of clinical procedures, experimental methodologies and data management will also be delivered. AGORA will impact on future biomedical research by creating synergies between ECRs and established experts in the field, promoting the concept of CNP as a person-related condition, and bridging preclinical and clinical findings to provide effective treatments. The expected outcomes for the community will be the QoL improvement for patients and their families, through a more comprehensive diagnosis and targeted treatments, optimizing the cost-effectiveness of pharma-company investments and healthcare system, improving quality and reducing costs of public assistance.
Neuropathic pain is a disabling pain caused by many different conditions, like diabetes, shingles or nerve entrapment. It is particularly difficult to treat, leaving many people with little relief. Our network is designed to accelerate the search for better painkillers for neuropathic pain. One barrier to progress is that it is challenging to obtain relevant human tissues, like nerves, for research. We want to improve on this, encouraging more studies on human tissue and adding value to existing efforts by harmonising protocols across laboratories.

We are a multi-disciplinary group of stakeholders, that includes basic and clinician scientists, patient partners and collaborators from industry. As a network, we are committed to ensuring that maximum research benefit is derived from the precious human samples donated so generously by people living with neuropathic pain.
The personal, social and economic burden of chronic pain is enormous. Yet patients with chronic pain, clinicians and the public are often poorly served by an evidence architecture that contains multiple structural weaknesses which reduce confidence in practice. These weaknesses include poor research governance, inadequate stakeholder engagement, poor methodological rigour and incomplete reporting, a lack of data accessibility and transparency, and a failure to communicate findings with appropriate balance. Research misconduct presents a further critical risk.

The central objective of our proposed network is to develop ENTRUST-PE, a novel integrated framework for enhancing and facilitating the trustworthiness of evidence for chronic pain. This will involve identifying and synthesising a range of available resources into a common framework that supports researchers, editors and publishers to minimise threats to the trustworthiness of pain research. The ENTRUST-PE framework will provide support for researchers, reviewers and editors to optimise the trustworthiness of new research and help consumers and users of research to evaluate the quality and trustworthiness of existing evidence in chronic pain.
GO-PAIN

Osteoarthritis and chronic joint pain

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AFLAR patient organization group

Osteoarthritis (OA), which affects > 650 million people worldwide, is the leading cause of disability over 50, affecting mainly knee, hip and hand. Chronic joint pain is the main symptom of OA, orchestrating the therapeutic management. A better understanding of the mechanisms underlying this pain is essential to provide significant solutions for the millions of patients with persistent pain.

To expand and deepen our understanding of OA pain, we need to have a holistic approach encompassing joint clinical and imaging, brain imaging, molecular and omics biomarkers, as well as demographic and socio-psychological components.

The GO-PAIN working group, composed of experts from different horizons (neurologists, neuroscientists, pain specialists, rheumatologists, biologists, physiotherapist, psychologists, radiologists) and patients, will aim to delineate the current knowledge about OA-related pain phenotyping by performing systematic literature reviews (SLR). In combination with usual methodology for SLR, BIBOT, an artificial intelligence tool performing SLR automatically, will be used.

The GO-PAIN group will collectively identify unmet needs and a research agenda for a holistic approach to OA-related pain phenotyping. The interdisciplinary expertise combined with patient’s pain experience will be critical for each step of the project.

The ambition of GO-PAIN project is to launch an international cohort collecting a maximum of information about OA pain, thereby addressing the identified unmet needs.
Chronic pain (CP) is a common problem among children, with negative consequences to the individual, the family and society. Moreover, recent research has shown that CP prevalence is increasing in children across many countries. Despite the high (and growing) prevalence of CP in children, it continues to be largely unrecognized, understudied, and undertreated. Evidence-based treatment guidelines are available for adults, but treatment options for children with CP remain limited, due in large part by: (1) the lack of sophistication in the patient-reported outcome measures (PROMS) used for assessing key outcomes, (2) a lack of research on (and therefore the understanding of) the factors that influence CP and its impact, and (3) the very limited access to CP specialized care for children. Research on CP in children continues to be fragmented, and there is a lack of adequate support for both research and clinical programs, particularly when compared to adults. Support for the development of a network that could identify specific research gaps, develop recommendations to overcome those gaps, and provide guidelines to support future research is an appropriate next step to deal with these issues. These activities can be accomplished by an international interdisciplinary and collaborative network, such as the IN-ChildPain network. We propose to address two cross-cutting challenges. First, we propose to identify the most important outcome domains that should be assessed in paediatric pain clinical trials and identify the most appropriate (i.e., psychometrically robust, available to researchers at no cost, and easy to translate into multiple languages) PROMS. Second, we propose to develop a guide for an international registry of children with CP and develop a research protocol to study the availability of, and access to, different treatments, to help evaluate their effects as naturally provided to patients.
Currently, there is a huge heterogeneity of protocol design and data collection in preclinical and clinical chronic pain trials, hampering comparability and translatability of results from bench to bedside. Within ITPain, we aim to overcome these challenges by harmonising protocol templates and data collection (including *omics-approaches) for preclinical and clinical trials and aligning them in a translational approach. This will be achieved by developing consensus on protocols and a minimum and clinically relevant “Core Set of Data”. Protocol extractions from literature and previous studies, literature searches related to previously consented Core Set of Data, analysis of data already collected, and Delphi processes between multidisciplinary stakeholders (e.g. researchers, clinical scientists, clinicians, data analysts, *omics experts, patients, and pain societies) will be part of this process. Furthermore, a first step towards a joint server infrastructure for an enhanced comparability and analysis of already available data resources (collected by network members from previous studies to assess comparability and integrability of multidimensional datasets) and future trials is planned. Together, this will improve future trial design, avoid research on non-relevant biomarkers, reduce reporting bias and facilitate the translation of findings into clinical practice with the aims of developing new treatment options and improving patient stratification.
NeuP-GRADE
Systematic review and meta-analysis of pharmacological and neuromodulation techniques - chronic neuropathic pain

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There are several types of long-lasting pain conditions. One of them is called neuropathic pain. Neuropathic pain occurs in people with a disease or a condition (surgery, trauma, shingles, diabetes, spinal cord injury, multiple sclerosis, stroke) affecting the sensory system. Close to 10% in the general population have neuropathic pain, which has a considerable impact on quality of life. Despite the best management options, more than 50% of patients still experience pain.

The goal of our group of caregivers, scientists and people living with neuropathic pain is to support a new systematic review of currently available drugs and neuromodulation techniques. This complex piece of research will help us identify, select and combine all the relevant research so we can understand which treatments are effective, and how effective they are. The review process was started in January 2022 and is ongoing. The allocated funding will allow a 2-day face-to-face meeting of about 25 international experts to discuss the results and develop treatment recommendations based upon the evidence. Ultimately, this will lead to an update of international guidelines to improve patients’ care. This work will also allow us to define the current knowledge and gaps to set research priorities for the future.
Complex regional pain syndrome (CRPS) is a rare but complicated painful and disabling condition that can significantly impact upon sufferers’ health and quality of life. Treatment of CRPS can take many forms and may include rehabilitation and pain management. However, we still don’t know what the best treatment approach for CRPS is and so providing effective healthcare for people living with CRPS can be really challenging. In the absence of good quality evidence to guide treatment, healthcare professionals face making treatment decisions in an ‘evidence vacuum’.

There is an urgent need to consider and find solutions to the problem of how research studies and clinical trials can best test the effectiveness of new and existing treatments for rare conditions, like CRPS.

An international group of CRPS, rare disease and clinical trial experts will now work together to discuss and provide guidance on how we can best design research clinical trials that assess the effectiveness of different treatments for people living with CRPS. By doing this, we hope to improve how clinical trials are done and provide better quality evidence about the effectiveness of these different treatments for CRPS, and therefore fill the evidence void.
PAC-MAN
Chronic Pain post-COVID

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Pablo Ingelmo, Montreal Childrens Hospital, Canada
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Marina Lusic, Heidelberg University Hospital, Germany
Thomas Volk, Saarland University, Germany

Over 200 million patients worldwide suffer from fatigue, widespread muscle pain, joint and chest pain as a consequence of COVID-19 infection. Little is known about the onset and pathophysiology of these conditions, leaving doctors at loss for the diagnosis and treatments of these patients. With this in mind, we formed the Pain After Covid-Multidisciplinary Action Network (PAC-MAN), a multidisciplinary consortium to advance knowledge on post-COVID chronic pain, discuss the current clinical gaps, and develop potential solutions for these pressing clinical issues.

We will address all these shortcomings and clinical needs by defining a roadmap of activities aiming at raising awareness and building a world-wide network of scientists, clinicians and entrepreneurs committed not only to solving the issue of chronic pain post-COVID, but also to evaluating and defining short and long-term solutions for other chronic pain syndromes. To address this multifaceted problem and to ensure a comprehensive approach, we included in our network professionals with complementary expertise in medicine, science and technology to better understand chronic pain syndrome’s pathophysiology, to discover new biomarkers and to explore clinical solutions through the synergy between new diagnostic tools (genomics and glycomics), innovative biomedical technologies (nanomedicine and neuromodulation), and alternative therapeutic regimens (drug repositioning and nutraceuticals).
Recent funding policies mandate the incorporation of sex as a biological variable into preclinical and clinical research. This has been welcomed across the chronic pain field and resulted in increasing evidence for sex differences in the pathophysiology and experience of chronic pain. However, inconsistencies and a lack of reproducibility between and across laboratories and clinical settings have been noted. This may be due to the lack of consensus on the most appropriate methodological and experimental approaches for conducting such studies.

PAINDIFF brings together an interdisciplinary Networking Group of 30 international leading research experts, early career researchers and patient advocates from 22 institutions across 8 countries, to discuss experimental design and methodological approaches to studying sex and gender differences in chronic pain research. The findings of the Networking Group will be widely disseminated to ensure chronic pain researchers are fully aware of the methodological framework and recommendations for studying sex and gender differences, and their relative application, in preclinical and clinical settings. Adoption and implementation of these recommendations will reduce variability and lack of reproducibility between laboratories and clinical settings, improve the translatability of research findings, leading to better outcomes for people living with chronic pain.
The PRISE project will develop a European Research Strategy on chronic pain. This will be implemented via:

1. Reaching consensus on the most important priorities across basic, pre-clinical, translational, and clinical chronic pain research, and how they should be addressed with delegates from European pain Societies.
2. Exploring enablers and barriers to successful implementation of the Strategy
3. Developing a web platform to communicate a clear set of priorities to all stakeholders, integrate developments and track the success of our implementation efforts
4. Creating a roll-out framework to ensure its successful implementation

By fostering collaboration between research groups, PRISE should not only enable high-quality and meaningful research, but also maximise its translation into European policy and practice, thanks to the leadership of the European Pain Federation EFIC and their extensive communication and networking structures (EFIC Academy, ‘Pain in Europe’ Congress, European Journal of Pain, Pain Scientist Network, European Pain Forum). The PRISE project has the potential to lead to enhanced solutions for chronic pain; it will increase the profile of pain research in Europe and advocate for increased and sustained funding for research in this field.
Approximately 90 participants joined the JTC2020 midterm symposium on the topics of ‘Sensory Disorders’ and ‘Ethical, Legal and Social Aspects (ELSA) of Neuroscience’, which took place in January at Madrid, Spain, in a hybrid format. The participants included ~50 principal investigators and ~40 early career researchers (ECRs) from the funded consortia, as well as representatives from the funding organizations and scientific experts who reviewed the progress of the projects. Sensory disorders cover a broad range of often debilitating conditions and are major causes of morbidity and severely impaired quality of life. In Europe, sensory deficits lead to serious economic and social burdens due to long-term disability. Thus, research on sensory disorders and its translation to diagnostic and therapeutic outcomes are of fundamental importance. In parallel, neuroscience research may have implications on the understanding (and, therefore, control) of human sensing abilities, decision-making, behavior, emotions and social interactions. Therefore, the research of ELSA of the neurosciences is essential to ensure that neuroscientific methods and findings are utilized in beneficial ways for society.

Twelve transnational interdisciplinary research consortia, which cover various sensory systems, are funded under the umbrella of the NEURON JTC2020 biomedical call on ‘Sensory Disorder’, including 48 research groups from 14 countries. Under the ELSA call, five transnational consortia are funded, which include 17 research groups from four countries. The symposium included presentations from the funded consortia of both calls. These midterm symposia, organized by NEURON, provide the stage for the funded consortia to present their progress and discuss outcomes, as well as challenges, of their research efforts. A dedicated structured networking session further increased the interdisciplinary exchange between the neuroscientists and neuro-ethicists allowing for mutual learning and enrichment.

In accordance with ERA-Net NEURON’s long-time support and investment in ECRs and with the long-lasting tradition of promoting the ECRs involved in the funded projects in the framework of the midterm symposia, ECRs were invited to attend and present a poster about their part of the research project. A vote for best poster was conducted and the award was presented to Georg Starke from project HYBRIDMINDS at the end of the meeting.

Finally, the midterm symposium provided the stage for the ceremony of the EPNA2022 award. The awardee, Daniel Huzard, received the award and gave a talk about his winning research project on the impact of C-tactile low-threshold mechanoreceptors on affective touch and social interactions in mice (more on page 17).

Overall, the joint symposium for both the biomedical and ELSA calls, brought about very interesting perspectives and discussions, enriching all the attending participants.
1. Please tell us briefly about your research interests.
My research interests are pretty wide, but overall, I am interested in understanding the concepts of Adaptation and Coping strategies, in terms of behavior. How organisms react to their environment. How the brain (and the sensory systems) integrates its context in order to produce a response. How this works in normal conditions and how this might be altered in some pathological or maladaptive situations?
Currently, I am focusing my research on the somatosensory system of a mouse model of autism and its effect on the development of social behaviors.

2. Please tell us about your scientific journey to-date.
I started my scientific journey pretty early since I was lucky enough to have my own research project during an internship in Concordia university, during which I analyzed the beneficial influence of enriched environments on stressed rats. Then, I did my PhD in the great lab of Carmen Sandi, at EPFL, in Switzerland. During 4 years, I studied the effects of stress adaptation on various behavioral and physiological parameters of rats. After that, I moved to France for a first postdoc, studying the social fear of mice models of autism as well as implementing an automated home-cage monitoring. Finally, I started a second postdoc in the lab I am currently working, in which I can use my behavioral expertise and apply it on an amazing question: how is affective touch regulating the maturation of sociability?
3. What made you choose a career in your field?
I was always passionate about human reactions and behaviors, and quite early I wanted to study ‘the brain’. I discovered the world of behavioralism during my bachelor/master studies at EPFL, and I could not think about doing something different.

4. Where do you see your field of research in a few years? What are going to be the major breakthroughs?
Concerning behavioral neurosciences, I imagine it “less-centrally-focused”: I think that we have to integrate the peripheral system into the equation in order to properly understand how organisms adapt. It is not a new idea, but, in a few years, I hope it will sound obvious.
A major breakthrough in behavioral research might come from the generalization of systems that allow to study behaviors in more and more ecological setups, monitoring various parameters and allowing smarter experimental designs, better reproducibility and improved data usage.

5. What were the main challenges you had overcome in your career path and how did you overcome them?
I cannot think about a particular event that was especially hard. However, research-life is challenging everyday, but that’s why I am doing it, I like challenges!
A real challenge, nowadays in France (and probably in a lot of countries), is the uncertainty of the job and the precarity of postdoc life. I never know where or what I will do in 2 years’ time, and this become unpleasant when you want to start a family and when you reach your mid-thirties…
But this is the situation in science in 2023, let’s hope it will be better in few years.

6. What are your goals for the future and where would you like to see yourself 5 years from now?
Unfortunately, I realistically cannot build dreams or hope for my research in 5 years… I know that I’ll apply for French CNRS and INSERM permanent research positions. In case this works fine, I can picture myself working here in Montpellier and investigating the somatosensory system of mice and its implication on social behaviors. Otherwise, my goal will be to use the knowledge and skills I build so far and apply it somehow for scientific research, if that be in academia or industry.

7. What advice would you give your younger self or young scientists beginning their research career?
I would have told my younger self to think ahead as early as possible and to plan the next move earlier. It becomes truly important to be strategic in addition to the passion, which, I think, is the key to a fulfilled scientist. Be curious and open-minded, do not impose yourself constraints since you could forbid yourself the access to the solution. Good luck, but most importantly, enjoy the journey!
Impressions from the Cajal Training on ‘Neuroepigentics: writing, reading and erasing the epigenome’ | 21 Nov – 9 Dec, 2022, Bordeaux, France

The CAJAL Advanced Neuroscience Training Programme’s goal is to establish a high-level neuroscience training hub in Europe. The CAJAL Programme aims to teach basic and fundamental neuroscience concepts, as well as state-of-the-art techniques, data analysis and computer skills, to train the next generation of top-notch neuroscientists. ERA-NET NEURON has partnered with FENS in the organisation of the Cajal Training Programme since 2018, aiming to promote high-quality neuroscience training by sponsoring neuroscience courses. Each year a Cajal course is sponsored that thematically aligns with the scope of the ongoing projects funded in ERA-NET NEURON joint transnational calls. In addition, the partnership entails support for participants from ERA-Net NEURON funded consortia and travel support for course directors.

This course provided theoretical and practical training on the recently emerged field of neuroepigenetics. It combined lectures and hands-on projects to learn about state-of-the-art approaches and methodologies to study how the epigenome is established and modulated by behaviour in rodents and invertebrates, what machinery is involved and what is its causal relationship to functions.

We asked Nora Bölicke, Balázs Széky and Isabel Bustos Martinez to tell us a little about themselves, their impressions from the Cajal course on Neuroepigentics that they participated in, and the importance of the support for early career researchers, like them, to participate in such courses. A small taster from their impressions are shown below – the full interviews can be read on the NEURON website.

**Szeky Balazs**, Junior research scientist in BioTalentum Ltd., Hungary

“In the past three weeks I’ve gained a huge amount of knowledge through impressive scientific talks, wet lab techniques and data analysis approaches. Besides the rapid growth of my scientific knowledge, I’m extremely grateful for the opportunity to improve my social network with highly skilled researchers.”
Nora Bölicke, PhD student from the Albert Lab in Technische Universität Dresden (TUD) – Center for Regenerative Therapies TU Dresden (CRTD), Germany

“An intense and rewarding experience! The amount of knowledge and experience that was shared between participants, supervisors and speakers within these three weeks was incredible - all the while providing a comfortable format aimed at advancing you and your research! ...I am already applying some of the methods that were discussed in the course. Meeting researchers with experience in acquiring and analyzing this type of epigenetic data, allowed me to improve my current experimental strategy and start my own data analysis.”

Isabel Bustos, PhD student from the research group of of Angel L. Barco Guerrero, Instituto de Neurociencias, Spain

“The Cajal training course on Neuroepigenetics undoubtedly constituted an outstanding opportunity for a first-year PhD student such as myself. Not only could I master some of the leading-edge techniques that are currently being used in this field but we also had the opportunity to attend seminars of some of the most renowned scientists in the field......The support from the ERA-Net NEURON has been decisive for my participation in the course. Otherwise, I could not have attended this complete three-week course.”