



ERA-NET NEURON

European Research Projects on Neuroinflammation

Joint Transnational Call 2014

Impact Report

by

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Abbreviations

ANR	French National Research Agency, France
BMBF	Federal Ministry of Education and Research, Germany
CIHR-INMHA	Canadian Institutes of Health Research – Institute of Neurosciences, Mental Health and Addiction, Canada
CSO-MOH	Chief Scientist Office, Ministry of Health, Israel
ERA-NET	European Research Area Network
FCT	Foundation for Science and Technology, Portugal
FNRS	Fonds de la Recherche Scientifique, Belgium
FRQS	Fonds de recherche du Québec-Santé, Québec, Canada
FWF	Austrian Science Fund, Austria
FWO	Research Foundation – Flanders, Belgium
JTC	Joint Transnational Call
MINECO	Ministry of Economy and Competitiveness, Spain
MOH	Ministry of Health, Italy
NEURON	Network of European Funding for Neuroscience Research
MRC	Medical Research Council, United Kingdom
SAS	Slovak Academy of Sciences, Slovakia
SRC	Swedish Research Council, Sweden

Introduction

ERA-NET NEURON

Public health is a central priority for individuals and governments globally. Worldwide, the WHO estimates one billion people suffer from neurological disorders, with disorders of the brain accounting for 1 in 10 deaths. These disorders are often chronic and incurable, causing significant deleterious impacts on quality of life. Addressing this disease burden is becoming a pressing issue, with an increase in morbidity in aging populations. Developing and translating basic neuroscience research into diagnostic and therapeutic outcomes for clinical use is therefore a priority for public health policy.

The European community includes a vast pool of scientific and medical expertise. In order to coordinate research objectives and promote European research, the European Commission developed European Research Area NETWORKS (ERA-NETs). These ERA-NETs aim to support and encourage cross-border collaboration in various fields of research by supporting joint activities. The Network of European Funding for Neuroscience Research (NEURON; www.neuron-eranet.eu) was initiated in 2003 as a pilot Specific Support Action. It was developed into an ERA-NET in 2007 and has been funded by the European Commission in three phases: NEURON I (2007 – 2011), NEURON II (2012 – 2015) and NEURON Cofund (2016-2020), NEURON Cofund2 (2021-2025). The overarching aim of NEURON is to support the translation of results from fundamental research into improved prevention, diagnosis, therapy and rehabilitation for patients, their family, and carers.

Joint Transnational Calls (JTC) for research proposals are the centrepiece of NEURON's transnational activities. On behalf of national ministries and funding organizations, NEURON coordinates an annual launch of a JTC in the field of disease-related neuroscience addressing important issues in fundamental neuroscience, neurology, or psychiatry (see call topics table 1). These funding calls aim to push forward research in strategically identified areas by encouraging transnational, cross-disciplinary projects. The main activity of NEURON is therefore the coordinated, transnational funding of basic, clinical and translational research projects on the nervous system. The NEURON initiative today is the result of the coordinated efforts of 25 funding organisations across 22 countries engaging in a joint effort to promote excellent research in disease-oriented neuroscience.

Year	Topic	Impact Report
2008	Neurodegeneration	Published 2014
2009	Method and Technology Development	Published 2015
2010	Mental Disorders	Published 2017
2011	Cerebrovascular Diseases	Published 2017
2012	Method and Technology Development II	Published 2018
2013	Mental Disorders II	Published 2019
2014	Neuroinflammation	Current
2015	Neurodevelopmental Disorders	Projects Ongoing
2016	External Insults to the Nervous System	Projects Ongoing
2017	Synaptic Dysfunction	Projects Ongoing
2018	Mental Disorders III	Projects Ongoing
2019	Biomarkers	Projects Ongoing
2020	Sensory Disorders	Projects Ongoing
2021	Neurodevelopment	Under Evaluation

Table 1: JTCs launched under ERA-NET NEURON

Joint Transnational Call 2014 “European Research Projects on Neuroinflammation”

For the 7th NEURON JTC, 18 funding organisations from 16 countries launched a Joint Transnational Call for Research Proposals on ‘Neuroinflammation’ (table 2), resulting in a total of 10.1 M€ in funding for ten successful projects (table 3). Neuroinflammation has been identified as an important factor in many pathologies of the nervous system including neurodegenerative diseases, chronic pain, and autoimmune diseases. Additionally, neuroinflammation is also implicated in psychiatric disorders, traumatic brain injury, and pathogen infection or toxicity in the nervous system. The JTC 2014 invited projects including research from basic disease mechanisms up to proof-of-concept clinical studies 1) addressing the role of neuroinflammation on the pathogenesis or aetiology of diseases of the nervous system and or 2) developing shared resources and novel strategies for diagnosis, therapy, and rehabilitation of such diseases. Projects focussing mainly on cerebrovascular and neurodegenerative affections were excluded from this action.

The call particularly encouraged the integration of early-career researchers as independent partners.

Partner Countries	Funding Agencies
Austria	Austrian Science Fund (FWF)
Belgium	Research Foundation – Flanders (FWO) Fonds de la Recherche Scientifique (FNRS)
Canada	Canadian Institutes of Health Research – Institute of Neurosciences, Mental Health and Addiction (CIHR-INMHA)
France	French National Research Agency (ANR)
Germany	Federal Ministry of Education and Research (BMBF)
Israel	Chief Scientist Office, Ministry of Health (CSO-MOH)
Italy	Ministry of Health (MOH)
Latvia	Latvian Academy of Sciences (LAS)
Luxembourg	National Research Fund (FNR)
Poland	National Centre for Research and Development (NCBR)
Portugal	Foundation for Science and Technology (FCT)
Romania	Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI)
Slovakia	Slovak Academy of Sciences (SAS)
Spain	Ministry of Economy and Competitiveness (MINECO)
Sweden	Swedish Research Council (SRC)
United Kingdom	Medical Research Council (MRC)

Table 2: Funding Organisation participating in JTC 2014

The selection of research projects was completed in two peer-reviewed stages by a pool of 48 international experts. For the first step, 136 consortia submitted a short pre-proposal that was then

evaluated by 2-3 expert reviewers. Of these, 43 consortia were invited to present a full proposal, which was again evaluated by expert reviewers before the final ranking was made by a 20-member peer-review panel.

Projects were evaluated using the following criteria:

1. Relevance to the aim(s) of the call
2. Scientific quality of the proposal (innovation potential, methodology)
3. Feasibility of the project (adequacy of project work plan and related risk analysis, budgetary and other resources, time schedule)
4. International competitiveness of participating research groups in the field(s) of the proposal (previous work in the field, expertise of the research groups)
5. Quality of collaborative interaction between the groups, and the added value, from both scientific and transnational perspectives, of the research consortium. Consortia not meeting these criteria will be downgraded.
6. Potential of the expected results for future clinical and other health relevant applications.

The ten successful projects included 43 research groups (principal investigators) from twelve countries, with funding provided by 14 national agencies. Selected projects covered a wide range of topics, from basic research into neuroinflammatory mechanisms to clinical studies of neuroinflammatory disorders including neurodegenerative diseases, traumatic brain injury, parasitic and bacterial infections, epilepsy, and chronic pain (table 3).

The projects used a large variety of methodologies and experimental models including transgenic mice models and cultured cells combined with siRNA strategies, viral vector mediated transduction, brain slices electrophysiology, advanced immunohistochemistry methods, in vivo imaging, gene sequencing and omic approaches among other techniques. Half of the projects used as well human tissue –iPSCs, cultured cells, brain slices-, genetic or imaging studies in patients.

Acronym	Proposal Title	Partners	Country (Agency)	Pathology
μNeuroINF	The Role of the Gut Microbiome on Neuroinflammation and Neurodevelopmental Disorders	Marc-Emmanuel Dumas	United Kingdom (MRC)	Fragile X and Autism Spectrum Disorders
		Xavier Altafaj	Spain (MINECO)	
		Laetitia Davidovic	France (ANR)	
		Boris Macek	Germany (BMBF)	
BriE	Brain Inflammation, Glia and Epilepsy	Etienne Audinat	France (ANR)	Epilepsy
		Marco de Curtis	Italy (MOH)	
		Frank Kirchhoff	Germany (BMBF)	
		Christian Steinhäuser	Germany (BMBF)	
CnsAflame	Neuroinflammatory mechanisms of chronic neurodegeneration and cognitive decline following traumatic brain injury	Nikolaus Plesnila	Germany (BMBF)	Traumatic Brain Injury
		Jerome Badaut	France (ANR)	
		Niklas Marklund	Sweden (SRC)	
		Esther Shohami	Israel (CSO-MOH)	
		Maija Dambrova	Latvia (VIAA)	
		Anna-Leena Siren	Germany (BMBF)	
IM-PAIN	Identification and study of different immune cell populations and their role in chronic pain	Stephen McMahon	United Kingdom (MRC)	Chronic Pain
		Ralf Baron	Germany (BMBF)	
		Camilla Svensson	Sweden (SRC)	
MELTRA-BBB	MEchanisms of Lymphocytes TRansmigration Across the Blood Brain Barrier	Ari Waisman	Germany (BMBF)	Blood-Brain Barrier Integrity
		Alexander Flügel	Germany (BMBF)	
		Hans Lassmann	Austria (FWF)	
		Roland Liblau	France (ANR)	
		Alexandre Prat	Canada (CIHR)	
		Adela Penesova	Slovakia (SAS)	
MICRO-MET	Role of microglial metabolism in perinatal neuroinflammation	Pierre Gressens	France (ANR)	Perinatal Neuroinflammation
		Peter Carmeliet	Belgium (FWO)	
		Henrik Hagberg	Sweden (SRC)	
		Claudia Verderio	Italy (MOH)	
MS_NANOMED	Advancing an antigen-specific nanomedicine for the treatment of central nervous system autoimmunity	Pere Santamaria	Canada (FQRS)	Autoimmune Diseases: Multiple Sclerosis
		Manuela Battaglia	Italy (MOH)	
		Pau Serra	Spain (MINECO)	
NEUINF	Master regulators of neuroinflammation in parasitic brain infections	Martin Rottenberg	Sweden (SRC)	Parasitic Infections
		Antonio Barragan	Sweden (SRC)	
		Monique Lafon	France (ANR)	
		Carlos Penha Gonçalves	Portugal (FCT)	
		Dirk Schlüter	Germany (BMBF)	
Neuro-IFN	Investigation of the neuroinflammatory basis of human type I interferonopathies	Yanick Crow	United Kingdom (MRC)	Autoimmune Diseases: Interferonopathy
		Jose Luis García-Pérez	Spain (MINECO)	
		Thomas Michiels	Belgium (FNRS)	
		Brigitte Onteniente	France (ANR)	
		Marco Prinz	Germany (BMBF)	
TraInflam	Transition from acute to chronic neuroinflammation	Michael Heneka	Germany (BMBF)	Alzheimer's Disease, Amyotrophic Lateral Sclerosis, Septic Encephalopathy
		Joseph Bertrand	Sweden (SRC)	
		Séverine Boillée	France (ANR)	
		Eran Segal	Israel (CSO-MOH)	
		Marie-Ève Tremblay	Canada (FQRS)	

Table 3: JTC 2014 Funded Projects and Consortia

Key Performance Indicators

As part of the final report for each project, researchers were asked to fill out a questionnaire to measure the key performance indicators set by NEURON (table 4). A summary of the different aspects evaluated by this questionnaire is described below and organised according to ERA-NET NEURON overarching objectives.

Objective of the Funding Programme	Key performance indicators	Measures (i.e. items in the questionnaire)
1. Enhance excellent cooperation between scientists working in the field of neuroscience	Communication of results	List of publications and communications - level of co publication, bibliometric indicators. (Question 1.2)
	NEURON JTC as starter of new collaborations	Have the partners participating in the NEURON project collaborated before applying for the NEURON JTC2012? (Question 3.1)
	New research groups from other countries joining the consortium	During the life time of the project has the consortium established collaboration(s) with other teams (not already participating in the JTC 2012 project)? (Question 3.2)
	Sustainability of the collaboration (obtaining further funding for the same consortium)	Have the results led to new initiatives in other types of funding programmes? (Question 3.3)
	Intensity of collaboration, early researcher participation (mobility)	List of meetings, young researchers involved in the project, lab visits/exchange of researchers, and training within the consortium (Question 3.4)
2. Promote multi-disciplinary consortia and to encourage translational research proposals (from bench to bedside)	Consortium Composition	List of research groups
	Patient Involvement	patients/patient representatives involved in planning and/or conducting the research project? (Question 6)
	Patents and other outcomes with public health impacts	Patents and other outcomes with impact to health (Question 2)
3. Support the development of innovative or shared resources and technologies	Evaluation of the development and the use of new resources	Has the consortium created a new or further developed an existing transnational patient registry, database or biobank? Have the consortium partners exchanged biomaterials (DNA, tissues, cells, animals)? Including data management (Questions 4 and 2)
4. Support research to develop new strategies for diagnosis, therapy, and rehabilitation procedures	Evaluation of the development of new strategies for diagnosis, therapy, and rehabilitation procedures for neuroinflammation.	Have the results of the NEURON research projects allowed the development of new strategies for: diagnosis, therapy (preparation of clinical trials), and rehabilitation procedures for cerebrovascular diseases, prevention or anything else? (Question 5.1)
	Major achievements	Please list the major achievement of the consortium. (Question 5.2)

Table 4: Key performance indicators in relation to the objectives of the funding programme (The number of the respective question in the questionnaire is given in brackets)

A summary of the major achievements expressed as percentage from the total number of consortia funded can be found in table 5. These results are further detailed in the sections below.

Objective of the Funding Programme	Key performance indicators	Results (percent of funded consortia, if not specified).
1. Enhance cooperation between European scientists working in the field of neuroscience	NEURON JTC as starter of new collaboration	→ 40% were newly formed consortia → 60% pre-existing consortia (part of PIs collaborated before)
	New research groups from other countries joining the consortium	→ 40% acquired new collaborations during the lifetime of the project.
	Sustainability of the collaboration (obtaining further funding for the same consortium)	→ 60% of the consortia applied jointly (at least 2 PI) for further funding
	Intensity of collaboration (meetings, mobility, joint publications)	→ 100% attended the mid-term symposium → On average each consortium held five meetings; ~60% of the meetings were attended by all partners → ~16% of the articles and reviews were published jointly in peer-reviewed journals
	Level of excellence of the funded research	→ 80% published at least one primary research publication in a peer-reviewed journal with an Impact Factor above 10
2. Promote multidisciplinary consortia and to encourage translational research proposals (from bench to bedside)	Composition of the consortium	→ In 40% the coordinator was a medical doctor. → In 90% at least one PI was a medical doctor. → PIs worked in basic (62% of PIs) and clinical (38% of PIs) research labs (20% of PIs) from the latest in hospitals
	Involvement of patients	→ Patients were involved in 40% of the projects.
	Patents and other outcomes with impact to health	→ 10% submitted at least one European or international patent
3. Support development of innovative or shared resources and technologies	Development and the use of new resources	→ 100% exchanged biomaterials and data (DNA: 20 %, tissues: 70 %, 70 cells: 50 %, experimental animal models %, clinical or experimental data: 50 %)
4. Support research to develop new strategies for diagnosis, therapy, and rehabilitation procedures	Development of new strategies	→ 10 % developed new strategies for prevention → 40 % developed new strategies for diagnosis → 70 % developed new strategies for therapy
	Major achievements	→ The major achievements that were most frequently reported include: novel model systems (90%), biomarkers (50 %), and development of innovative therapies (70 %)

Table 5: Summary of major achievements in the frame of key performance indicators

Objective of the Funding Programme

1. Enhance excellent cooperation between scientists working in neuroscience

Communication of funded research results

Consortium partners were asked to report the dissemination channels of project results. This included peer-reviewed publications (journal articles, reviews, and books or book chapters), PhD dissertations, presentations (written and oral) to scientific congress, and articles dedicated to the public (table 6). Peer reviewed articles and reviews were included only if NEURON support was acknowledged. Table 5 presents a summary of the different communications produced by the funded consortia.

Type of publication	Total	Consortia (total)
Peer reviewed articles (including reviews)	120	10
Reviews	31	8
Books or book chapters	7	4
Communications in scientific congresses	>100	7
PhD Dissertations	13	4
Others	6	2

Table 6: Total publications resulting from projects funded through JTC 2014

All the consortia declared mainly peer reviewed publications at the end of the projects at a rate corresponding to a median value of 9 articles per consortia. More than 84 percent of the publications (including books) were authored by a single consortium member; while 7 consortia published articles authored by at least 2 consortium members (Fig. 1a).

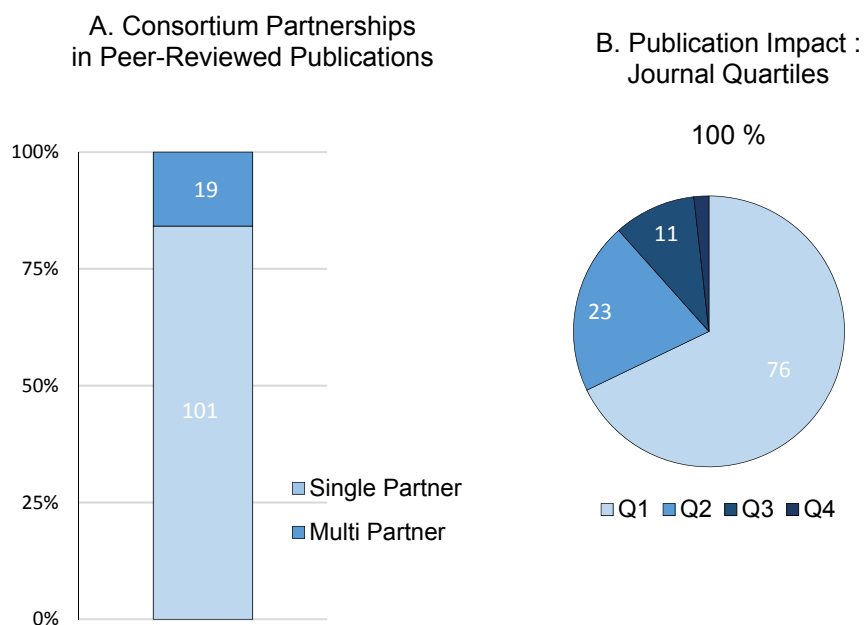


Figure 1: Peer reviewed publications. A Proportion of multi and single-partner peer reviewed articles published by the 10 funded consortia B Distribution of peer-reviewed publications by quartile rank indexed in relevant disciplines associated to the neurosciences in the WoS (Q).

Web of Sciences (WoS) was used in order to categorise the publications in scientific domains. The fields of neurosciences or neurology were taken as principal references for the analysis below (Figure 1b). The publications were less prominently indexed in other relevant fields such as genetics, physiology, behavioural sciences, biochemistry, cell biology, molecular biology, immunohistochemistry, and multidisciplinary sciences (Figure 2); these categories were considered for the analysis when the publications were not indexed in the neurosciences or the neurology fields.

Almost 90 percent of the peer reviewed publications excluding books were published in high impact journals (1st or 2nd quartile taking neurosciences or neurology as main references in the WoS-; Figure 1b).

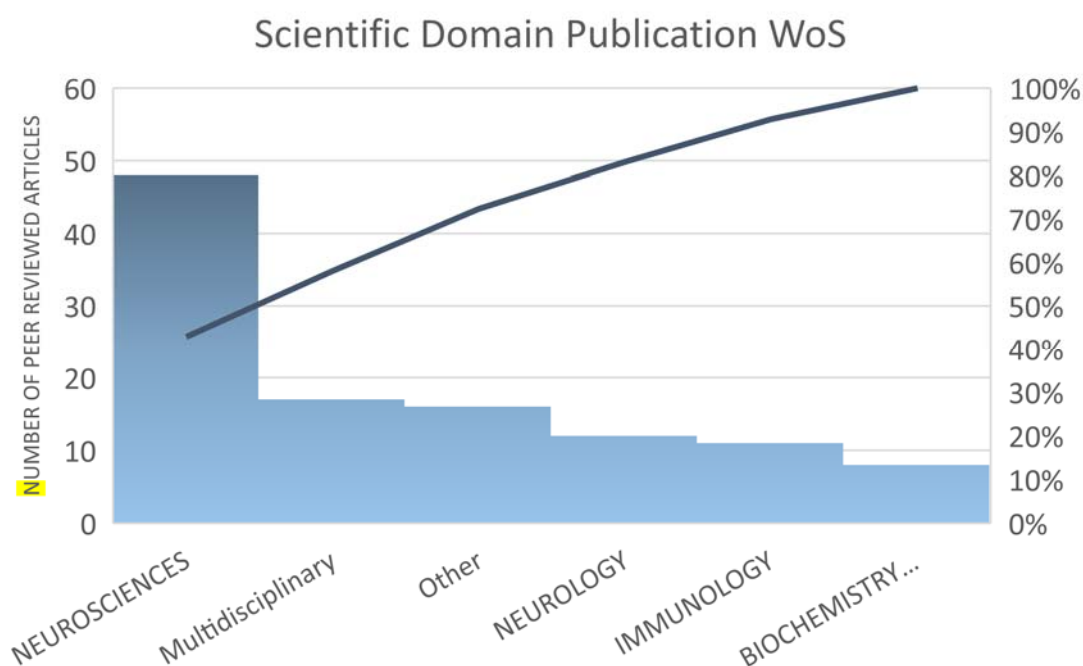


Figure 2: Peer reviewed publications main scientific domain according to the WoS. The picture depicts the main disciplines to which the publications produced by consortia funded in JTC 2014 contributed.

NEURON JTC as a starter of new collaborations

The questionnaire contained a series of questions on the structure of the consortia, including whether the partners had previously collaborated on a research project and whether new collaborations arose or will continue during and after the funding period. The results are summarised below.

Six out of the ten funded consortia included members with a history of collaboration previous to this ERA-NET NEURON project; in general, the coordinator has collaborated with at least one other partner and the consortium grew by addition of new partners. Any of the funded consortia had worked together as a full group before the present call. Four consortia were formed with members with no history of previous collaboration.

As part of the widening procedure designed by ERA-NET NEURON to encourage the participation of researchers from underrepresented European communities in the field, two groups led by female researchers from Slovakia and Latvia joined two consortia. Their role in the project development was highlighted in the final reports due to their unique qualifications.

New research groups from other countries joining the consortium

Five consortia reported thirteen new collaborations with European research groups initially not implicated in the project funded by ERA-NET NEURON JTC 2014 to explore aspects related to the initial project.

Sustainability of the collaboration

Researchers were asked to report follow-on collaborations including further funding applications by consortia members. This measure indicates the impact of consortium development, both in continuing to advance projects beyond the ERA-NET funding period, and the ongoing value of the academic collaboration.

Members of four funded consortia received a national grant each. Moreover, six consortia submitted 13 international grants including two ERA-NET NEURON grants, two H2020 project grants, an ERC and an IMI grant (Figure 3), most of them approved. Eleven of these funding applications implicated more than one partner and the rest were granted to a single research group. At least four other collaborations without specific funding were reported.

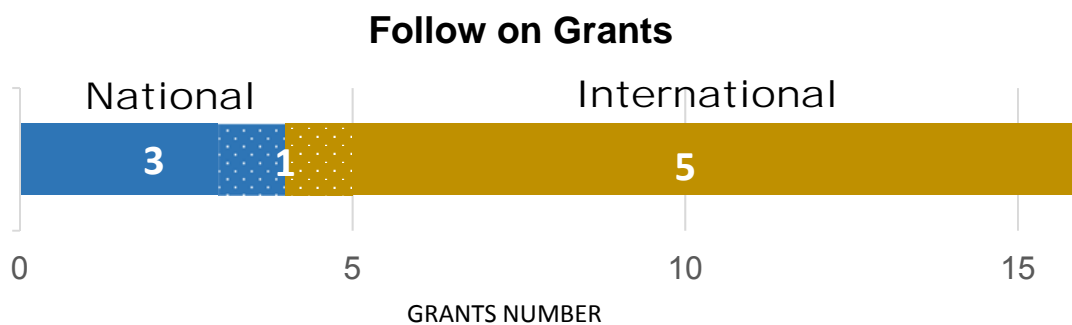


Figure 3: Follow up funding. Number of submitted grants at national and international instances. The number of consortia implicated in the grants submissions are depicted in white. Only one consortia applied to both national and international grants.

Intensity of Collaboration

Consortia are encouraged to organise regular in-person meetings and staff exchanges to take full advantage of the range of expertise of project partners and to develop the skillsets of individual lab members. All the consortia organised between 2 and 9 meetings (average of 5) and almost all of them organised about 3 meetings attended by the whole consortium. These meetings were considered fruitful to allow the exchange of scientific ideas and plan for funded and future work.

A total of 23 early career researchers (PhD students and postdocs mainly) participating to seven projects visited the partner labs to learn new techniques and exchange experience. On top of the exchange of techniques these visits allowed networking and encouraged further collaborations, as an example during

the funding period, one of the former postdocs in one project established the lab and continued a collaboration with one of the partners of the funded consortia finally funded by an European grant.

A Midterm Symposium was organised by NEURON in Madrid in 2016; all the consortia coordinators attended, presented the work progress, and received feedback from an evaluator initially implicated in the selection of projects. Two main aspects were evaluated, scientific progress (outcomes produced/advancement of the workplan) and collaboration between the partners. In general, the evaluations were satisfactory. Several projects had already published articles some implicating several partners. The level of advancement and quality of the scientific work were considered elevated but in several cases it was suggested to increase the interaction between the partners. This symposium was also an opportunity for several consortia to organise partners' meetings as well as to exchange with other researchers working in the field in the context of the projects funded by ERA-NET NEURON.

Summary

The present analysis shows that ERANET NEURON funding resulted in a high level of interactions between research groups in several countries. Most of these interactions were established for the first time within the consortia and were extended towards new groups throughout the development of the project. As a highlight, the integration of two female researches from underrepresented countries was particularly successful as their contributions to the projects were considered outstanding by their peers. Most of the collaborations outlast the period of funding by ERANET NEURON as evidenced by the report on new mutipartner publications still in preparation at the end of the project, and by the ongoing follow up work reported, which is at the origin of numerous national and international applications for funding by almost all of the groups.

All consortia were very active and produced diverse and numerous publications with high relevance mainly in the field of neurosciences but also contributed publications in generalist journals and journals specialised in other fields such as neurology, immunology and biochemistry; as expected considering the scope of the call on neuroinflammation.

2. Promoting multi-disciplinary consortia and translational research proposals (from bench to bedside)

Consortium composition

ERA-NET NEURON aims to promote the interdisciplinary collaboration to solve unmet medical needs in the field of nervous system disorders, through the development of translational research projects. As such it is expected that the consortia include expertise from basic academia but also any other expertise needed to pave the way towards solutions for the diseased nervous system. Out of the 54 researchers, 19 were medical doctors represented in nine out of the ten funded consortia, and four of them were the coordinators.

The researchers involved in the projects work mainly in basic research laboratories (62%), but also in clinical research labs (38%), and hospitals (20%).

Other than the researchers having applied for ERA-NET NEURON funding, the projects included other staff in the labs where the work was developed. Postdoctoral researchers and students, some of them funded by NEURON, represent the main category of staff in the projects (50 and 49, respectively). Some other staff categories such as technicians or associated researchers were also reported as involved in the projects (Figure 4).

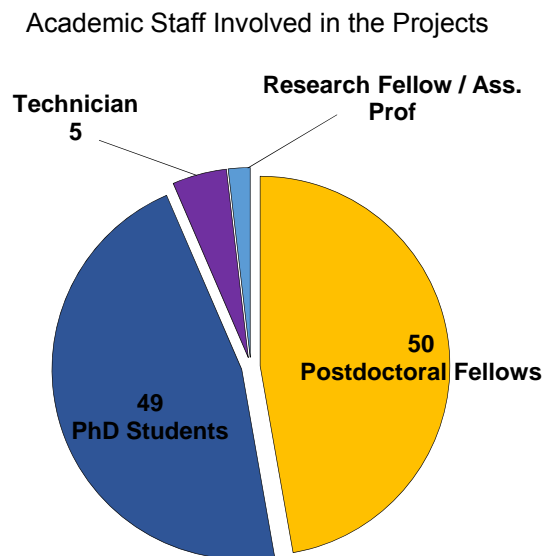


Figure 4: Staff participating in the funded projects

Patient Involvement

Researchers were asked to report the involvement of patients or patient groups as active members of the project. This includes involvement in the design, coordination (as part of a committee or advisory board), analysis or interpretation of research data, or in the dissemination of results.

Eight of the ten projects used patients' tissue or data. Three of the projects declared that they established contacts with specific patient organisations, but these interactions were mainly at the level of dissemination of the results. Two of the projects considered the integration of patients in study design either for the present study or in preparation for follow up clinical trials. Most of the projects (six) declared that the work developed was basic science and patient involvement was considered premature or unnecessary. This could be at least partially due to the fact that patient involvement was not mentioned as a criterion nor encouraged in the call text.

Patents and other outcomes with public health impacts

Two projects report outcomes resulting in an international patent for a therapeutic compound for Parkinson's disease and a licence using technology to develop vaccination based on nanomedicine for autoimmune diseases, respectively. Unfortunately, the second one does not formally involve any of the members from the ERA-NET NEURON project.

Several projects resulted in the launch or preparation of clinical trials for different pathologies, the main objectives of the trials are here listed: 1) the treatment for a rare disease affecting the brain -Susac Syndrome-, 2) the validation of a compound for neuroprotection in preterm infants, 3) treatment of traumatic brain injury and 4) the study of a biomarker in patients with chronic pain.

At the preclinical level diagnostic or therapeutic approaches were developed for cerebellar degeneration, traumatic brain injury, Aicardi-Goutières syndrome, and neurodevelopmental diseases. Some of these efforts required the establishment of collaborations with clinical or industrial partners such as Novartis.

Six projects identified or validated biomarkers or genetic determinants for the following pathologies: pharmacoresistant epilepsy, neurodevelopmental diseases, multiple sclerosis, or chronic inflammation.

Finally, new screening methods were proposed for cell sorting and selection strategies in nanomedicine development by two other projects.

Summary

ERA-NET NEURON encourages the research groups to fill the gap between basic and clinical research towards translation. and into solutions susceptible to be used for the diagnosis and treatment of brain diseases. The consortia funded in the frame of JTC 2014 engaged into collaboration basic researchers as well as medical doctors tackling the same questions at different levels of the translational continuum. Several outcomes with potential value for clinical use on various diseases were developed either at a preclinical or clinical trial level. Most of these contributions will continue being developed after the end of these projects. Few projects implicated patients on the planning or design but used patients data or tissue for their work. The role of patients as active contributors in research is increasingly important and some of the finishing projects consider involving them at more advanced stages of their clinical applications.

3. Supporting the development of innovative or shared resources and technologies

Development and the use of new resources

Other than the scientific publications the projects also generated a series of resources shared among the partners of a project or open to broader scientific, clinical, and other relevant communities. Nine out of ten projects produced new experimental models: cellular or *in vitro* models and at least 16 new mice models; most of them exchanged among partners (Figure 5).

Four consortia generated shared clinical or experimental databases, and two others exchanged genetic material. In addition, three of them participated in the generation of protocols to harmonise experimental practices, and two others generated software for analysis.

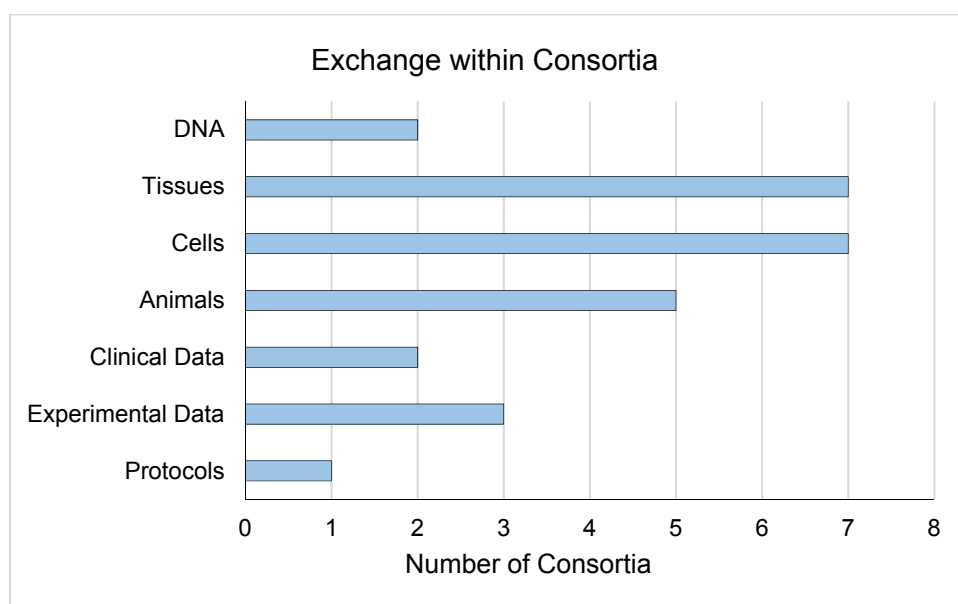


Figure 5: Exchange of resources among consortia members

Six consortia generated data which can be shared to the research or clinical community outside the project and two others generated software or codes made freely available.

Summary

ERA-NET NEURON aims to support the development of new tools and resources available to the research and clinical community at large. The funded consortia generated relevant experimental models for several brain diseases, protocols, and data which were exchanged between the participating laboratories, and made available to the research community. The resources generated within ERA-NET NEURON funding is expected then to be further exploited to produce new knowledge on the brain disease field.

4. Supporting research to develop new strategies for diagnosis, therapy, and rehabilitation

Development of new strategies for diagnosis, therapy, and rehabilitation procedures for neuroinflammation.

Four consortia concentrated their work on the identification of disease mechanisms of neuroinflammation in the context of six different diseases (Figure 6).

1. The role of bacteria, genes and metabolites on inflammation associated to neurodevelopmental diseases.
2. Impact of immune challenges on epilepsy.
3. Gene expression in spinal cord microglia in a model of arthritis.
4. Identification of immune response to nervous system infections by malaria
5. Identification of immune response to nervous system infections by toxoplasmosis and
6. Identification of immune response to nervous system infections by trypanosome.

Seven projects developed novel therapeutic approaches, using the following strategies:

- Microbiota based interventions for neurodevelopmental diseases.
- Antibody mediated therapeutics for traumatic brain injury and for a rare disease.
- Pharmacological interventions for neuroprotection in the context of encephalopathies, for infections affecting the nervous system and for a rare disease.
- Development of nanomedicines for autoimmune diseases .

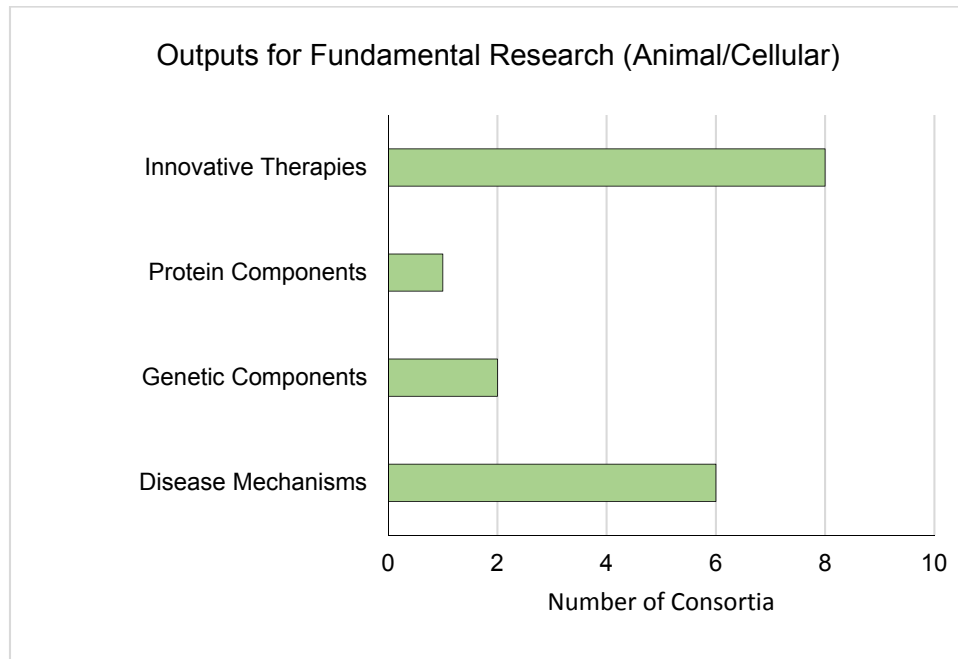


Figure 6: Output contributions for further research by consortia

Major achievements of the research consortia

As detailed in previous sections and in agreement with the general objectives of this call the project outcomes were mainly concentrated on the study of neuroinflammatory disease mechanisms and the development of therapeutic approaches at a preclinical level.

Further multinational collaborations initiated in the context of this funding initiative continued after the end of the projects, and some of them brought the research questions to the level of clinical trials well in line with the overarching ERA-NET NEURON aim to pave the way for new or improved routes for diagnosis and therapy.

Members of three funded projects were also remarkably active in the establishment or participation to networks dedicated to specific research areas or training such as: RNA-protein interactions in the context of viral infections, Microbiome@Imperial to enhance multidisciplinary research, teaching and public engagement activities and two European Training Networks which will potentially amplify and disseminate further the outcomes of the present projects.

Summary

In agreement with the general objectives of this call the project outcomes were mainly concentrated on the study of neuroinflammatory disease mechanisms and the development of therapeutic approaches at a preclinical level. The contributions span to a large variety of brain diseases and led to new research paths at preclinical and clinical levels. The continuation of the collaborations will result in new studies to validate the clinical value of the approaches and findings. Important links were established among researchers within and outside the funded consortia but also with other academic, industrial, and large public stakeholders likely leading to increase the value of the scientific outputs and accelerate the research on brain diseases.

Outstanding projects

All the projects funded in this call reported good quality outcomes. This section aims at highlighting the projects which were more accomplished and resulted in particularly important scientific or careers advancement.

CNSAFLAME

The project is a collaboration between clinical and basic researchers in five countries dedicated to develop therapeutic approaches for traumatic brain injury.

The partners produced 21 publications in high impact journals in the field and plan to publish a protocol for harmonisation methods.

The partners evaluated several therapeutic approaches for traumatic brain injury and developed two of their compounds to clinical trials in collaboration with pharmaceutical industrials. Moreover, the partners got six new grants to continue their collaboration. Dr. Rodriguez Grande, postdoctoral fellow participating in this project was awarded the Early Career Scientist poster prize by ERA-NETNEURON.

IM-Pain

This project's objective was to investigate the immune response in chronic pain to develop new therapeutic avenues.

The partners published four articles, three of them involving at least two consortium members in high impact journals in the field.

At least six new collaborations arose from the results of this project, one of them to be confirm the validity of preclinical results in patients. The first postdoctoral fellow established her own research group and obtained together with another partner an IMI grant. Moreover, the consortium generated protocols to sort immune cells from human CSF and released RNA ChiP-seq datasets to the wider research community.

Micromet

This project aimed at identifying the role of microglia function on the neuroinflammation frequently observed in preterm infants.

The partners described metabolic pathways activated involved in microglia activation and ways to interact with the molecular pathways representing potential therapeutic options. One of the compounds tested in the project will be used in a clinical trial to confirm a neuroprotective effect on preterm infants. Several new collaborations were established within the consortium and with new research groups to follow up on these results. Moreover, experimental data can be made available to wider community upon request.

MELTRA-BBB

The consortium developed research to understand the nature of nervous system inflammatory reactions in multiple sclerosis and in particular the mechanisms allowing immune cells to cross the brain blood

barrier. The work plan was designed with the aim of generating information useful to design new therapeutic approaches in this context.

The project produced sixteen scientific publications in high impact journal of the field. An international patent was submitted.

Several follow-up activities were ongoing. The consortia reported the preparation of two clinical trials for rare diseases and other therapeutic trials at less developed stages.

Summary

All in all, the projects funded within JTC 2014 produced good quality to outstanding results either scientific, clinical or of career advancement, and applied to a vast diversity of brain diseases associated with neuroinflammation.

As expected, most of the contributions concerned the analysis of disease mechanisms associated to neuroinflammation, some leading to important hints to develop treatments. Almost all projects reported a continuation of their collaborations, and several grants were obtained for this purpose. In particular, at least three clinical trials and two patents were prepared based on the outcomes of the funded projects. Numerous researchers not initially funded participate now in the newly established collaboration or the networks established within the funding period. The new collaborations are expected to extend to the young researchers participating in these projects as was the concrete case in one of the consortia.

The widening scheme seemed very well accomplished and allowed a very active participation of female researchers from two underrepresented countries, which were particularly highlighted in the final reports.

Call for Proposals for

"European Research Projects on Neuroinflammation"

Submission deadline for pre-proposals: March 10, 2014

[Proposal template](#)

[Electronic proposal submission](#)

For further information, please visit us on the web

<http://www.neuron-eranet.eu>

or contact

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1. Purpose

Maintenance, improvement and restoration of human health are of fundamental importance and worldwide priority. Biomedical and health research provide an important basis for the improvement of healthy living. Disorders of the brain are major causes of morbidity, mortality and impaired quality of life. Around one billion people suffer from disorders of the central nervous system. In Europe, disorders of the brain account for approximately one-third of the burden of all diseases. Therefore, neuroscience research and its translation into diagnostic and therapeutic outcomes are fundamental.

To address this, the 'Network of European Funding for Neuroscience Research' (NEURON) has been established under the ERA-NET scheme of the European Commission (<http://www.neuron-eranet.eu>). The aim of the ERA-NET NEURON is to coordinate research efforts and funding programmes of European countries in the field of disease related neuroscience.

Under the umbrella of NEURON, six transnational joint calls have been launched on different topics from 2008 to 2013. The seventh joint transnational call (JTC-7) is now launched in the field of neuroinflammation. The following funding organisations have agreed to fund the joint call for multinational research projects in this scientific area. The call will be conducted simultaneously by the funding organisations in their respective countries and coordinated centrally by the Joint Call Secretariat.

- Austrian Science Fund (FWF), Austria
- Research Foundation – Flanders (FWO), Belgium
- Fonds de la Recherche Scientifique - FNRS, Belgium
- Canadian Institutes of Health Research – Institute of Neurosciences, Mental Health and Addiction (CIHR-INMHA), Canada
- Fonds de recherche du Québec-Santé (FRQS), Québec (Canada)
- French National Research Agency (ANR), France
- Federal Ministry of Education and Research (BMBF), Germany
- The Icelandic Centre for Research (RANNIS), Iceland*
- Chief Scientist Office, Ministry of Health (CSO-MOH), Israel
- Ministry of Health (MOH), Italy
- Latvian Academy of Sciences (LAS), Latvia
- National Research Fund (FNR), Luxembourg
- National Centre for Research and Development (NCBR), Poland
- Foundation for Science and Technology (FCT), Portugal
- Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI), Romania
- Slovak Academy of Sciences (SAS), Slovakia
- Ministry of Economy and Competitiveness (MINECO), Spain
- Swedish Research Council (SRC), Sweden
- Medical Research Council (MRC), United Kingdom

* Pending final decision.

2. Aim of the call

The aim of the call is to facilitate multi-national, collaborative research projects that will address important questions relating to neuroinflammation. The call will accept proposals ranging from understanding basic mechanisms of disease through proof-of-concept clinical studies in humans. These may include research on the role of inflammation in neurological or psychiatric disorders, or associated with traumatic brain injury, pathogen infection or toxicity in the nervous system. **Research dealing primarily with cerebrovascular or neurodegenerative diseases without specifically focussing on the neuroinflammation aspect will not be eligible for this call.**

The ERA-NET NEURON funding organisations particularly wish to promote **multi-disciplinary work** and to encourage **translational research proposals** that combine basic and clinical approaches.

Research proposals should cover at least one of the following areas:

- a) Fundamental research on the role of neuroinflammation on the pathogenesis and/or aetiology of neural diseases. This may include the development of innovative or shared resources and technologies.
- b) Research to develop new strategies for diagnosis, therapy, and rehabilitation procedures for diseases in which neuroinflammation constitutes a relevant process of the pathology.

One of the aims of NEURON is to provide support to young researchers, and to facilitate their integration as independent PIs into the consortia, an experience that would be a valuable step forward in their research careers.

The individual components of joint applications should be complementary and contain novel, ambitious ideas to answer key questions or lead to a step-wise change in understanding. There should be clear added value in funding the collaboration over the individual projects.

Clinical studies up to the point of proof of concept are eligible for funding¹.

3. Application

3.1 Eligibility

¹ Eligibility and funding requirements for clinical trials vary between the partner countries. Clarification may be obtained from the individual funding agencies.

Joint transnational research proposals may be submitted by research teams working in universities (or other higher education institutions), non-university public research institutes, hospitals, as well as in commercial companies, particularly small and medium-size enterprises. The eligibility of the afore-mentioned institutions, together with details of eligible costs (e.g., personnel, material, consumables, travel money, investments), are subject to the administrative requirements of individual funding organisations and will therefore differ. Please note that, for some funding organisations, commercial companies are not eligible or are only eligible under certain conditions (e.g., only in partnership with academic institutions in the consortium). Clarification should be obtained from the individual funding agencies (see contact details below).

Only transnational projects will be funded. Each consortium submitting a proposal must comprise a minimum of three research groups eligible for funding by organisations listed in this call text (see above), all three groups must be from different countries. The total number of research groups in a consortium must not exceed five. Therefore, the maximum number of countries involved in one consortium is five. Not more than two research groups should be from the same country.

Research groups not eligible to their national funding organizations or from countries which are not involved in this call may participate in projects only if their participation clearly provides an added value to the consortium and if they present evidence on secured budget for their part in the project. In any case, the total number of research groups in one consortium must not exceed five.

It is obligatory that the coordinator of a consortium is eligible to be funded by one of the organisations listed in this call text.

Each consortium should have the critical mass to achieve ambitious scientific goals and **should clearly demonstrate added value** from working together. One project co-ordinator among the project partners who represents the consortium externally will be responsible for its internal scientific management. *Although applications must be submitted jointly by groups from several countries, the individual research groups will be funded by the individual NEURON funding organisation(s) of their respective countries. Eligibility criteria are the matter of individual partner funding organisations.*

Therefore, applicants are strongly advised to follow the instructions contained in the country-specific eligibility tables which are published on the NEURON webpage and to contact their national/regional funding organization to confirm eligibility matters before submitting an application.

3.2 Financial and legal modalities

Projects may be funded for a period of up to three years and according to individual funding organisations' regulations. Eligible costs may vary according to the corresponding funding organisations' regulations. Each group will be subject to the rules and regulations of its respective national/regional funding agency.

3.3 Submission of joint transnational proposals

There will be a **two-stage procedure** for joint applications: **pre-proposals** and **full proposals**. In both cases, one joint [proposal document](#) (in English) shall be prepared by the partners of a joint transnational proposal, and must be submitted to the Joint Call Secretariat by one spokesperson, the co-ordinator.

Pre-proposals must be submitted in electronic format no later than **March 10, 2014** (14:00:00 CET) via the [electronic submission](#) system.

NOTE: Full proposals will only be accepted from those applicants **explicitly invited** by the Joint Call Secretariat to submit them.

3.4 Further information

For further details, please refer to the respective submission forms available through the NEURON website. If you need additional information, please contact the Joint Call Secretariat, or your funding agency representative (see Annex for contact data).

4. Evaluation and decision

The review process will be in two stages.

4.1 Formal check of proposals

The Joint Call Secretariat will assess proposals to ensure that they meet the call's formal criteria (e.g. date of submission; number of participating countries; inclusion of all necessary information in English). The Joint Call Secretariat will also forward the proposals to the

national/regional funding organisations, which will perform a formal check of compliance with their respective regulations. Proposals not meeting the formal criteria will be rejected at this stage.

The Call Steering Committee may reject proposals if they are clearly outside the scope of the call.

Proposals passing these check points will be forwarded to the joint Peer Review Panel for evaluation.

4.2 Peer-review of proposals

The reviewers will carry out the evaluation according to specific evaluation criteria:

7. Relevance to the aim(s) of the call
8. Scientific quality of the proposal (innovation potential, methodology)
9. Feasibility of the project (adequacy of project work plan and related risk analysis, budgetary and other resources, time schedule)
10. International competitiveness of participating research groups in the field(s) of the proposal (previous work in the field, expertise of the research groups)
11. Quality of collaborative interaction between the groups, and added value, from both scientific and transnational perspectives, of the research consortium. Consortia not meeting these criteria will be downgraded.
12. Potential of the expected results for future clinical and other health relevant applications.

4.3 Decision

4.3.1 Pre-proposals

Eligible pre-proposals will be reviewed via a written (remote) peer review process. Based on the scores in the written reviews a ranking list will be set up. By mid May 2014, the coordinators of the top proposals will be invited by the Joint Call Secretariat to submit a full proposal **no later than June 24, 2014**.

4.3.2 Full proposals

The international Joint Peer Review Panel will establish a ranking list of the fundable proposals by scientific assessment. Based on this ranking list the Call Steering Committee will determine the projects to be funded, taking into account the national budgets available. These recommendations will inform the final decisions which will be made by the funding agencies and will be subject to budgetary considerations.

5. Funding procedure / Responsibilities / Reporting requirements

5.1 Funding procedure

Projects can be funded for a period of up to three years and according to funding organisations' regulations. Funding is expected to start early in 2015.

Successful research groups will be funded directly by the respective funding organisations.

Funding will be administered according to the terms and conditions of the responsible funding organisations, taking into account all other applicable regulations and legal requirements.

5.2 Responsibilities

Each project must nominate a project coordinator, who represents the consortium externally and is responsible for its internal management (e.g., application, Consortium Agreement, reporting, etc.) to the ERA-Net NEURON Joint Call Secretariat. Within a joint proposal, each group leader will be the contact person for the relevant national/regional funding organisation. The coordinators of funded projects together with the respective funding agencies shall make every effort to seek a common start date for all research groups in the consortium.

After the evaluation and selection procedures are completed, each consortium selected to be funded is required to draft and sign a Consortium Agreement (CA) suitable to their own team. The CA will agree a common project start date, manage the delivery of project activities, finances and intellectual property rights (IPR), and avoid disputes which might be detrimental to the completion of the project. All consortia are strongly encouraged to sign the CA before the official project start date, the CA must be signed within the first six months after the project start date.

5.3 Reporting Requirements

On behalf of the research consortium, the project coordinator will be required to submit a brief annual scientific progress report on the project and one final report in the end, to the Joint Call Secretariat. Group leaders may be required to submit reports separately to their national funding organisation; reporting guidance will be forwarded by the relevant funding organisation, as applicable.

Annual reports should be submitted within four months calendar year. Annual reports do not need to be submitted if the project ends in the first three months of the following year (i.e., between January and March). In this case, the submission of a final report will suffice. However, instead of submitting the final report within the usual six month period (see below), the final report will be required within four months of project completion.

The deadline for submitting final reports is six months after the end of the project. It is the task of the coordinators to determine a formal end date for project completion. This is required, as partners may be granted extensions of differing duration. Coordinators will be informed about this procedure by the Joint Call Secretariat and will receive the report template in due course.

The coordinator will be asked to present 2 progress updates, one intermediate and one final status symposium. Group leaders will be asked to participate in the final status symposium. Travel budgets should be planned and managed accordingly.

Funding recipients must ensure that all outcomes (publications, etc.) of transnational NEURON projects include a proper acknowledgement of ERA-NET NEURON and the respective funding partner organisations, and are in line with the relevant publication requirements.

Annex II Summary of indicators outcome by consortium

Indicator/Measure	μNeuroINF	BrIE	CnsAflame	IM-PAIN	Meltra BBB	MICRO-MET	MS_NANOMED	NEUINF	Neuro-IFN	TracInflam	TOTAL
Full new consortium	YES	NO	NO	YES	NO	NO	NO	YES	YES	NO	4
Addition of research group	YES	NO	NO	YES	YES	NO	YES	NO	NO	YES	5
Subsequent applications	YES	YES	YES	YES	YES	YES	YES	NO	YES	NO	8
Intensity of Collaboration											
- number of meetings	9	7	7	4	6	5	3	5	2	8	56
- meetings with all partners	6	7	5	4	2	3	2	3	1	0	33
Excellence											
- total number of peer reviewed publications	7	28	23	4	16	10	4	8	14	6	120
- number of joint publications	2	0	2	3	3	4	2	3	0	0	19
- numbr of journals IF > 10	1	2		0	8	1	3		6	2	23
Composition of consortia											
- coordinator is a medical doctor	NO	NO	YES	NO	NO	YES	YES	NO	NO	YES	4
- number of medical doctors	0	2	4	1	4	3	1	2	1	1	19
- basic research labs involved	3	3	1	2	4	1	2	5	5	2	28
- clinical research labs involved	1	2	4	1	2	3	1	0	0	3	17
- hospitals involved	1	1	3	1	1	0	1	0	0	1	9
Involvement of patients or patient-derived material	NO	YES	NO	YES	YES	NO	YES	NO	NO	NO	4
Patents (submitted or obtained)	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	1
Databases/registries/biobanks created	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	1
Exchange of:											
- DNA	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	2
- tissues	YES	YES	YES	NO	YES	YES	NO	NO	YES	YES	7
- cells	YES	NO	NO	YES	YES	YES	YES	YES	YES	NO	7
- animals	YES	YES	NO	NO	YES	YES	NO	NO	YES	NO	5

