



**Preliminary
Announcement**

Call proposal for

MULTINATIONAL AND TRANSLATIONAL RESEARCH PROJECTS ON

CEREBROVASCULAR DISEASES INCLUDING SMALL VESSEL AND

BRAIN BARRIERS DYSFUNCTION

Among the neurological disorders, **cerebrovascular diseases** contribute more than half of the burden in Disability Adjusted Life Years (DALYS) and 85% of deaths associated to neurological conditions, globally. **Stroke** represents by itself the second leading cause of death and accounts for 143 million DALYS worldwide in 2019; with increasing figures towards 2030. The relative contribution to health burden of these neurological disorders is near twice as important in Europe as compared to other regions in the world representing 45 billion euros of expenditure including care and a heavy societal burden.

Although the pathophysiological mechanisms leading to specific cerebrovascular diseases are not completely understood, changes of **cerebral small vessels** and **the malfunction of brain barriers as well** as other changes such as immune responses have been identified as conditions frequently associated to the development of stroke and vascular cognitive dysfunction. Focussed translational research in these areas is thus a priority in order to promote healthy living in Europe and worldwide.

The 'Network of European Funding for Neuroscience Research' (NEURON) has been established under the ERA-NET scheme of the European Commission (www.neuron-eranet.eu). The aim of the ERA-NET NEURON is to coordinate and optimize research efforts and funding programmes of its partner countries in the field of mental, neurological, and sensory disorders. Under the umbrella of NEURON, a joint transnational call (JTC 2022) in the field of **cerebrovascular diseases** is now launched. 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 co-ordinated centrally by the Joint Call Secretariat.

Fonds de la Recherche Scientifique-FNRS (F.R.S.-FNRS)
Research Foundation – Flanders (FWO)

Belgium
Belgium

Fonds de recherche du Québec - Santé (FRQS)	Canada
Ministry of Science and Education of the Republic of Croatia (MZO)	Croatia
Estonian Research Council (ETAg)	Estonia
French National Research Agency (ANR)	France*
Federal Ministry of Education and Research (BMBF)	Germany
German Research Foundation (DFG)	Germany*
National Research, Development and Innovation Office	Hungary*
Chief Scientist Office, Ministry of Health (CSO-MOH)	Israel
Ministry of Health (MOH)	Italy*
State Education Development Agency (VIAA)	Latvia
Latvian Council of Science (LCS)	Latvia
National Centre for Research and Development (NCBR)	Poland*
Executive Agency for Higher Education, Research, Development & Innovation Funding (UEFISCDI)	Romania
Slovak Academy of Sciences (SAS)	Slovakia*
National Institute of Health Carlos III (ISCIII)	Spain*
Spanish State Research Agency (AEI)	Spain
Swiss National Science Foundation (SNSF)	Switzerland
Ministry of Science and Technology (MOST)	Taiwan
The Scientific and Technological Research Council of Turkey (TUBITAK)	Turkey*

**Pending on decision*

1. Aim and scope of the call

The aim of the call is to facilitate multinational, collaborative research projects that will address important translational questions in the areas of stroke and other **cerebrovascular diseases including small vessels disease (CSVD) and the dysfunction of brain barriers**.

CSVD is a chronic, progressive disorder of cerebral micro vessels. The pathophysiological mechanisms of CSVD are largely unknown and diagnosis intervenes frequently at late stages of the disease.

Brain barriers (blood brain barrier but also arachnoid, leptomeningeal, lymphatics, glymphatics, choroid Plexus, endothelial and cerebrospinal fluid barriers) are dynamic morphological and physiological structures separating the brain parenchyma from the surrounding blood circuit. Their main function is to protect the nervous system from direct exposure to the continuous changing milieu in the bloodstream as well as toxic or infectious agents. Changes in the permeability or integrity of the brain barriers have been increasingly recognized as important contributors to cerebrovascular diseases, including stroke. The function and interactions of the different components of the brain barriers are largely unknown. In consequence, the pathophysiological mechanisms leading to their dysfunction in the context of cerebrovascular diseases are poorly described, to this day.

The present call aims to fund preclinical and clinical research addressing the pathophysiology and therapeutic developments for stroke and other cerebrovascular diseases. Proposals relating CSVD and the dysfunction of brain barriers to cerebrovascular disease are encouraged. Research areas may cover a broad range of aspects associated with cerebrovascular disease such as genetic, epigenetic, molecular mechanism of disease. Neuroinflammatory processes often play an important role in cerebrovascular diseases and are included in the call. The development of preventive, diagnostic or therapeutic

approaches including pharmacological studies (e.g. on drug target identification) and technological developments based on pathophysiological mechanisms are within the scope of the call.

The call will accept research proposals ranging from understanding basic mechanisms of cerebrovascular disease and brain barriers dysfunctions through proof-of-concept clinical studies in humans¹.

The NEURON funding organisations particularly wish to promote multidisciplinary work and translational research proposals that combine basic, clinical and/or technological approaches. The consortia should submit novel, ambitious ideas that can only be achieved by the complementary collaboration between partners.

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

- a) Fundamental research addressing the pathogenesis, aetiology, progression, treatment, and prevention of cerebrovascular diseases including CSVD as well as basic research to elucidate the role of brain barriers on cerebrovascular diseases. This may include the development of innovative or shared resources and technologies including computational and statistical tools, as considered of relevance in the context of this call.
- b) Clinical research to develop novel strategies for prevention (including secondary prevention), diagnosis, patient stratification, therapy and/or rehabilitation for cerebrovascular diseases

Applicants should demonstrate that they have the expertise and range of skills required to conduct the study including already established collaborations.

The translational value for human disease must be clearly addressed in the proposals. If used, the choice of the animal model must be justified in the context of the human pathology. The development of new animal or cell models is only allowed if an appropriate model is not available and must be justified.

Clinical studies are eligible up to the point of proof of concept. Multimodal and multicentre clinical studies are highly encouraged. The establishment of large patient cohorts will not be funded by NEURON, but the use of existing cohorts, brain banks and exploitation of existing data sets are eligible. Appropriate access to relevant, well-characterized patient populations or suitable biomaterial collections must be demonstrated. The proposal should describe plans to make data available for the research and clinical communities. If relevant, it is recommended that the appropriate European infrastructures are contacted early in the planning of the projects, the following are potentially of interest for the applicants to this call: EATRIS-ERIC (focused on translational medicine), BBMRI-ERIC (focused on biobanking), EBRAINS (focussed on data and tools for brain-related research) and ELIXIR (focused on data sharing).

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

The following research areas are excluded from this call:

- Neurodegenerative disorders that are addressed by the EU Joint Programme – Neurodegenerative Disease Research (JPND)².
- Proposals focussed primarily on cardiological or metabolic causes or comorbidities (i.e. diabetes, obesity, Covid-19/long Covid) to cerebrovascular diseases.

The ERA-NET NEURON seeks to strengthen patient engagement in research. All applications should include a description of expected outcomes with potential relevance for patients. Applicants are expected to engage patients, their parents or carers and or associations as appropriate in the research process. Meaningful patient engagement can occur at the level of research planning, conducting research or the dissemination of research results. Patient representatives will assess patient engagement aspects of the selected full proposals.

2. General conditions for application

Joint transnational research proposals may be submitted by research teams working in universities (or other higher education institutions), non-university public or private research organisations, hospitals or foundations, 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 organisations (**please note that the country specific information will be published with the launch of the call**).

Only transnational projects will be funded. Each consortium submitting a proposal must be comprised of a minimum of three research partners eligible for funding by organisations listed in this call text (see above). Involvement of early career researchers (ECRs)⁴ as consortium partners is highly encouraged. The eligible research partners must be from at least three different participating countries. The total number of research partners in a consortium is limited to five, including partners participating with their own expenses. No more than two consortium partners can be from the same country.

² Alzheimer's disease and other neurodegenerative dementias, Parkinson's disease (PD) and PD-related disorders, Prion disease, Motor neuron diseases, Huntington's disease, Spinocerebellar ataxia, Spinal muscular atrophy

⁴ 4-7 years of experience since completion of PhD or medical specialization diploma at the date of the launch of this call and a scientific track record showing great promise. Allowed extensions 18 months maternity leave, duration of paternity leave, duration of long-term illness or national service, duration of clinical training with a maximum of 4 years). Please check the country specific regulations for the national eligibility criteria that apply.

The ERA-NET NEURON strives to strengthen a global Brain Research Area by including as many partner countries as possible in its funding scheme. Therefore, consortia including at least one partner from countries that are to date underrepresented in this funding scheme (Latvia, Hungary, Slovakia, and Turkey) may increase the total number of partners to six.

Applicant partners who are not eligible for funding from their national funding organisations or from countries that are not involved in this call, may participate in consortia only if a) their participation clearly provides an added value to the consortium, and b) they have secured budget for their part in the project. Such potential partners are not considered in the minimum number of three research partners mentioned above. In any case, the total number of research partners in one consortium must not exceed five, or six, if partners from the underrepresented countries (listed above) are included.

Each consortium should have the critical mass to achieve ambitious scientific goals and **should clearly demonstrate added value** from working together. Each consortium must nominate a coordinator who represents the consortium externally and is responsible for its internal management (e.g. the application procedure, coordination of consortium agreement drafting, Data Management Plan, reporting). The consortium coordinator must be eligible for funding by one of the organisations listed in this call text.

A single proposal must be submitted by the consortium coordinator to the NEURON Joint Call Secretariat. The individual research partners in a consortium will be funded by the NEURON funding organisation(s) of their respective countries. Eligibility criteria are the matter of individual partner funding organisations and additional national/regional regulations and requirements may apply.

Only projects that fulfil the legal and ethical international/EU regulations (including ethical standards and guidelines in Horizon EUROPE) as well as national and institutional standards will be funded. All proposed activities including those undertaken in countries outside the EU must comply with EU regulations (see Annex I of the full proposal). Ethical approval and/or a positive vote must be obtained from the relevant national or local ethics committee(s) prior to the start of respective studies. The obtainment of ethical clearance will be queried by ERA-NET NEURON. All procedures involving human beings must conform to the Helsinki Declaration.

3.2 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 coordinator.

3. Timetable

The launch of the call is scheduled in the beginning of **2022**.

The deadline for submitting the **pre-proposals** is scheduled in **March 2022**.

By mid-May 2022 the coordinators of selected pre-proposals will be invited by the Joint Call Secretariat to submit a **full proposal** by **June 2022**.

Funding is expected to start **early in 2023**.