Eternity Project

3 PhD positions at the University of Milan within the programme

Horizon Europe (HORIZON)

Marie Skłodowska-Curie Actions

Doctoral Networks (DN)

“ETERNITY”
“FuEl ThE bRaiN In healtThY aging and age-related diseases”

(HORIZON-MSCA-2021-DN-01-01, proposal 101072759 — ETERNITY)

OPEN CALL: 20 February 2023 - 20 April 2023

The Horizon Europe MSCA-Doctoral Network ETERNITY (“FuEl ThE bRaiN In healtThY aging and age-related diseases”) is a Consortium consisting of laboratories from Universities, Research Institutions and small-medium enterprises. ETERNITY offers a groundbreaking PhD level training in brain metabolism, focusing on metabolic and aged-related disorders.

Given the complementary expertise, ETERNITY will have excellent opportunities to delineate different molecular pathways underlying impaired brain metabolism as well as to identify novel pharmaceutical targets and/or nutritional interventional strategies that may ameliorate ageing and related disorders.

The 10 doctoral candidates (DCs) will have the unique opportunity to be trained by a transnational consortium with multidisciplinary expertise. Apart from the innovative and collaborative approach of the research programme, the DCs will also be exposed to a well-structured training programme in which cutting-edge methodology, innovation and transferable skills are key components.

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1. ETERNITY PROJECT

BENEFICIARIES

The following organizations will directly recruit the DCs:

- Università degli Studi di Milano (UMIL), Department of Pharmacological and Biomolecular Sciences, Milan, Italy – Coordinator
- Neurocentre Magendie (INSERM), Bordeaux, France
- Deutsches Zentrum fur Neurodegenerative Erkrankungen e.V. (DZNE), Bonn, Germany
- Universidad de Salamanca (USAL), Institute of Functional Biology and Genomics, Salamanca, Spain
- AvenCell Europe GmbH (AVENCELL), Dresden, Germany

ASSOCIATED PARTNERS

The following Institutions and companies are part of the consortium and will contribute to training activities, including secondments:

- European Brain Council (EBC), Brussels, Belgium
- Orion Corporation, Espoo, Finland
- Charité Universitätsmedizin Berlin SPARK-BIH, Berlin, Germany
- CF-Consulting s.r.l., Milan, Italy
- Sofinol S.A., Lugano, Switzerland
- EMBO Solutions GmbH, Heidelberg, Germany
- The Visual Agency s.r.l., Milan, Italy

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DETAILED DC PROJECT DESCRIPTION

The 10 DCs will be recruited by the following beneficiaries and enrolled in one of the doctoral schools as detailed in the table below:

DC	Recruiting Participant	PhD awarding entities
1.	UMIL	Università degli Studi di Milano
2.	UMIL	Università degli Studi di Milano
3.	UMIL	Università degli Studi di Milano
4.	INSERM	University of Bordeaux
5.	INSERM	University of Bordeaux
6.	DZNE	University of Bonn
7.	DZNE	University of Bonn
8.	USAL	University of Salamanca
9.	USAL	University of Salamanca
10.	AVENCELL	University of Bonn

The individual projects are described as follow:

DC1 Project: RNF10 signaling pathway in physiology and Alzheimer Disease-induced mitochondrial dysfunction. (Supervisors: Elena Marcello and Monica Di Luca, Università degli Studi di Milano, https://eng.disfeb.unimi.it/ecm/home).
DC1 will investigate the metabolic and gene expression profile of RNF10-silenced hippocampal neuronal cells of Alzheimer Disease mice to determine which metabolic programs and genes pathways are affected by RNF10. According, DC1 will assess the effect of specific dietary interventions on RNF10 pathway to restore Alzheimer Disease -associated alterations. DC1 will be enrolled in the doctoral programme (Ph.D.) of Pharmacological Biomolecular Sciences, Experimental and Clinical of the University of Milan at the Department of Pharmacological and Biomolecular Sciences.

DC2 Project: Identification of memory tasks-activated metabolic pathways in wild-type and Alzheimer disease. (Supervisors: Diego Scheggia and Nico Mitro, Università degli Studi di Milano, https://eng.disfeb.unimi.it/ecm/home).
DC2 will investigate the dynamic distribution of metabolic substrates using liquid chromatography coupled to tandem mass spectrometry during episodic-like memory acquisition and retention. DC2 will also assess the effect of specific dietary interventions on the affected metabolic pathways and related memory functioning. DC2 will be enrolled in the doctoral programme (Ph.D.) of Pharmacological Biomolecular Sciences, Experimental and Clinical of the University of Milan at the Department of Pharmacological and Biomolecular Sciences.

DC3 Project: Investigating the neuronal function of the novel regulator of mitochondria Zinc Finger CCCH-Type Containing 10 (Zc3h10) (Supervisors: Nico Mitro and Elena Marcello, Università degli Studi di Milano, https://eng.disfeb.unimi.it/ecm/home).
DC3 will evaluate the role *in vitro* and *in vivo* of Zc3h10 specifically in neurons, define its regulated metabolic pathways and the effects of the lack of Zc3h10 in neuron on the metabolism of the other brain cells. Moreover, DC3 will also validate the Zc3h10

regulated pathways in induced pluripotent stem cells-derived neurons and test novel chemicals to restore and or improve mitochondrial function. DC3 will be enrolled in the doctoral programme (Ph.D.) of Pharmacological Biomolecular Sciences, Experimental and Clinical of the University of Milan at the Department of Pharmacological and Biomolecular Sciences.

DC4 Project: Role of bioenergetic pathways in the microglial inflammatory response to an obesogenic diet. (Supervisor: Agnès Nadjar, INSERM, https://www.bordeaux-neurocampus.fr/en/staff/agnes-nadjar/)
DC4 will use a preclinical model of obesity, with the main goals to decipher the fine bioenergetic alterations induced in hypothalamic microglia under obesity, in relation with their functional and proliferation status; and to understand how these microglial changes affect hypothalamic neural networks.

DC5 Project: Role of mTOR pathway in the metabolic response of microglia in a mouse model of obesity. (Supervisor: Agnès Nadjar, INSERM, https://www.bordeaux-neurocampus.fr/en/staff/agnes-nadjar/)
DC5 will unravel the role of microglial mammalian target of rapamycin (mTOR) activation in obesity-associated neuronal alterations. DC5 will evaluate if the consumption of an obesogenic diet reprograms microglial bioenergetics in a mTOR - dependent manner in preclinical animal model of obesity.

DC6 Project: Mitochondrial bioenergetics in microglia differentiation and upon metabolic insults during aging. (Supervisor: Daniele Bano and Melania Capasso, DZNE https://www.dzne.de/en/research/research-areas/fundamental-research/research-groups/bano/research-areasfocus/).
DC6 will investigate the impact of mitochondrial function/dysfunction in microglia development and activity upon dietary challenges in induced pluripotent stem cells-derived microglia and in mouse models of mitochondrial diseases. DC6 will use a multi-omics approach, with a special focus on potential pathways that may take part in compensatory mechanisms and enable the survival of cells exposed to metabolic challenges.

DC7 Project: How brain mitochondria bioenergetics affect the inflammatory phenotype of aged microglia. (Supervisor: Melania Capasso and Daniele Bano, DZNE https://www.dzne.de/en/research/research-areas/fundamental-research/research-groups/capasso/research-areasfocus/).
DC7 will assess mitochondrial fitness, mammalian target of rapamycin (mTOR) and insulin signaling in brain cells isolated from young and aged mice, as well as in induced pluripotent stem cells-derived neuron and microglia. Furthermore, in co-culture experiments, DC7 will assess the possibility that mitochondrial defects in one cell type, i.e. neurons, affect mTOR signaling in microglia, increasing their inflammatory phenotype. Finally, DC7 will also investigate *in vivo* the effect of specific dietary interventions or decreased mTOR signaling specifically in microglia in young and aged

mice to counteract their pro-inflammatory phenotype and assess the effect on cognitive function.

DC8 Project: Isocaloric twice-a-day diet and brain mitochondria during aging. (Supervisors: Juan Pedro Bolaños and Angeles Almeida, Universidad de Salamanca, https://ibfg.usal-csic.es/juan-pedro-bolanos-en.html)
DC8 will develop an activity plan aimed to ascertain whether feeding mice with isocaloric twice-a-day diet (ITAD) improves the mitochondrial efficiency and autophagic machinery of neurons and astrocytes in the aged mice. Mice will be fed with either a standard, high-fat diet (HFD), or HFD- ITAD diets for up the age of 18 months.

DC9 Project: Isocaloric twice-a-day diet in learning and memory during aging. (Supervisors: Juan Pedro Bolaños and Angeles Almeida, Universidad de Salamanca, https://ibfg.usal-csic.es/juan-pedro-bolanos-en.html).
DC8 will develop an activity plan aimed to ascertain whether feeding mice with Isocaloric twice-a-day diet (ITAD) improves the immunohistochemical signature of the hippocampus and learning in the aged mice. Mice will be fed with either a standard, high-fat diet (HFD), or HFD- ITAD diets for up the age of 18 months.

DC10 Project: Chimeric antigen receptor T (CAR-T) cells to target aging, neurodegeneration and senescence. (Supervisor: Armin Ehninger, Avencell, https://avencell.com/).
DC10's work will be focused on the development and validation of a chimeric antigen receptor T (CAR-T)-cell-based approach to tackle cellular senescence, aging and age-associated pathology. Based on surface markers selectively expressed on senescent cells, DC10 will develop CARs to retarget T cells to senescent cells. DC10 will then perform proof-of-concept studies to examine whether these CAR-T-cells eliminate senescent cells in vitro and in vivo. DC10 will also assess in mouse models if CAR-T-cell-based treatment alleviates neurodegeneration as well as cognitive dysfunction associated with aging and metabolic insults.

TRAINING ACTIVITIES

Each DC will attend training activities provided by the respective Doctoral Schools and by the ETERNITY consortium. Furthermore, secondments in ETERNITY consortium are planned as detailed in the following table:

DC	Academic Secondments	Non-academic Secondments
DC 1 (UMIL)	DZNE (3 Months)	AVENCELL (6 Months)
DC 2 (UMIL)	USAL (7 Months)	EBC (2 Months)
DC 3 (UMIL)	DZNE (3 Months)	ORION (6 Months)
DC 4 (INSERM)	USAL (7 Months)	SOFINOL/NESTLÉ (2 Months)
DC 5 (INSERM)	DZNE (7 Months)	SPARK-BIH (2 Months)
DC 6 (DZNE)	USAL (5 Months)	ORION (4 Months)
DC 7 (DZNE)	INSERM (7 Months)	SOFINOL/NESTLÉ (2 Months)
DC 8 (USAL)	INSERM (7 Months)	SPARK-BIH (2 Months)
DC 9 (USAL)	UMIL (7 Months)	SOFINOL/NESTLÉ (2 Months)
DC 10 (AVENCELL)	DZNE (7 Months)	EBC (2 Months)

2. DC RECRUITMENT PROCESS

Each DC will receive a 36-month grant to cover their participation costs, living, travel and installation allowance, family allowance, as reported in the following table. The reported amount is referred to gross salary (€/month) before tax. Please note that taxation may vary according to country.

Beneficiaries	Living allowance*	Mobility allowance	Family allowance
UMIL	3.311,6 €	600 €	495 €
INSERM	3.957,6 €	600 €	495 €
DZNE	3.342,2 €	600 €	495 €
USAL	3.104,2 €	600 €	495 €
AVENCELL	3.342,2 €	600 €	495 €

* This amount varies because of the application of a correction coefficient to the living allowance of the country in which the researcher will be recruited.

ELIGIBILITY REQUIREMENTS

There are ***strict eligibility requirements*** for the DC positions enrolled trough the Marie Sklodowska-Curie Action-Doctoral Network. Each DC will be employed according to the financial and eligibility rules reported in the EU document accessible to the following link: https://ec.europa.eu/info/funding-

tenders/opportunities/docs/2021-2027/horizon/wp-call/2021-2022/wp-2-msca-actions_horizon-2021-2022_en.pdf . The key requirements are reported below in the points from **1** to **5**.

1. Supported researchers must be doctoral candidates, i.e. not already in possession of a doctoral degree at the date of the recruitment (Researchers who have successfully defended their doctoral thesis but who have not yet formally been awarded the doctoral degree will not be considered eligible).

2. Researchers must be enrolled in a doctoral programme leading to the award of a doctoral degree in at least one EU Member State or Horizon Europe Associated Country.

3. Recruited researchers can be of any nationality and must comply with the following **mobility rule**: they must not have resided or carried out their main activity (work, studies, etc.) in the country of the recruiting beneficiary for more than 12 months in the 36 months immediately before their recruitment date.

4. For 'International European Research Organisations' (IERO), 'international organisations', or entities created under Union law, the researchers must not have spent more than 12 months in the 36 months immediately before their recruitment in the same appointing organisation.

5. Compulsory national service, short stays such as holidays and time spent by the researcher as part of a procedure for obtaining refugee status under the Geneva Convention (1951 Refugee Convention and the 1967 Protocol) are not taken into account.

Additional eligibility criteria are required by the ETERNITY consortium:

- Admission to the programme is open to applicants who hold a 2nd Level Master's Degree (120 ECTS + 180 ECTS in a bachelor's degree) or a Single Cycle Degree (minimum 300 ECTS), or a comparable university degree (Second Cycle qualification), as required by the partner universities for admission to doctoral studies. Applicants are expected to achieve their degree within June 30th, 2023. They must submit a certified copy of any degree achieved by the deadline of June 30th, 2023.

- Highly motivated and science-driven person holding a master's degree or equivalent in Life Science or related disciplines. A background in metabolism and/or neuroscience or related areas of biology (e.g., neurobiology, molecular biology, (epi)-genetics) is an added value. We offer exciting and fully funded research projects; committed mentorships; an excellent scientific environment in major

centers for translational neuroscience research; access to a well-structured network of hands on-activities as well as doctoral programs at the associated Universities.

- Applicant must hold an English language certificate (**at least B2 level**).

Please ensure you hold all the eligibility criteria (those set by the EU programme and those set by the ETERNITY consortium) before applying since ineligible candidates cannot be considered.

SELECTION CRITERIA

The DC will be selected according to the following criteria (in random order):

• Scientific skills and research experience
• Ability to collaborate and communicate
• Career profile and potential for excellence
• Expected impact of the proposed training on their career.

3. HOW TO APPLY

Applications must be submitted exclusively through the dedicated web site www.projecteternity.eu starting **from February 20, 2023, and no later than April 15, 2023, 17:00 Central European Time (5 p.m.)**.

Each applicant can apply to individual projects within the group call, with a possibility to express interests in up to three projects, ranking them according to the preferences.

Hand-written applications and applications sent by email, mail or fax will not be accepted.

Each application must include the following **key documents** in PDF format:

- Detailed curriculum vitae in Europass format (https://europa.eu/europass/en/create-europass-cv) including list of publications, participation in funded research project and/or other qualifications.

- Certified copies of Diploma Supplement, or Bachelor's Master's diploma (or equivalent) with transcripts relating to all academic courses taken to earn every degree (bachelor/master or equivalent), translated into English, and correspondent grade point average.

- Motivation Letter (see downloadable template, form 1). Please clearly state your interest in up to three projects, ranking them according to your preferences.

- Two reference letters (see downloadable template, form 2) that needs to be sent directly by the referees to the email address eternity@unimi.it

- English language certificate

- Copy of passport (or, for EU citizens, equivalent ID document)

All data provided by the applicants are processed solely for the purpose of the ETERNITY call for applicants.

4. SELECTION PROCEDURE

Selection of the DCs will be solely based on merits providing equal opportunity and in agreement with the European Code of Conduct for the Recruitment of Researchers (https://euraxess.ec.europa.eu/).

The selection process will be in two steps. The first step will be based on the assessment of the documents submitted with the application and the second step will

consist in an interview (videoconference or in person in Milan, Italy) to those applicants who have passed the first step selection. Shortlisted applicants will be informed by email as soon as possible (**no later than May 5, 2023**).

For further information please contact:

eternity@unimi.it