



Immerge

Storming
Immune
Monogenic
Conditions
through
Multiomic and
Gene Editing
Approaches



Funded by
the European Union

One full-time Doctoral Candidate position

HOST INSTITUTION:

- **Ospedale San Raffaele SRL (OSR). Italy > Milan**

OPEN CALL: April 4th, 2024

APPLICATION DEADLINE: May 20th, 2024, 12.00 PM (CET)

EU RESEARCH FRAMEWORK PROGRAMME: HORIZON EUROPE

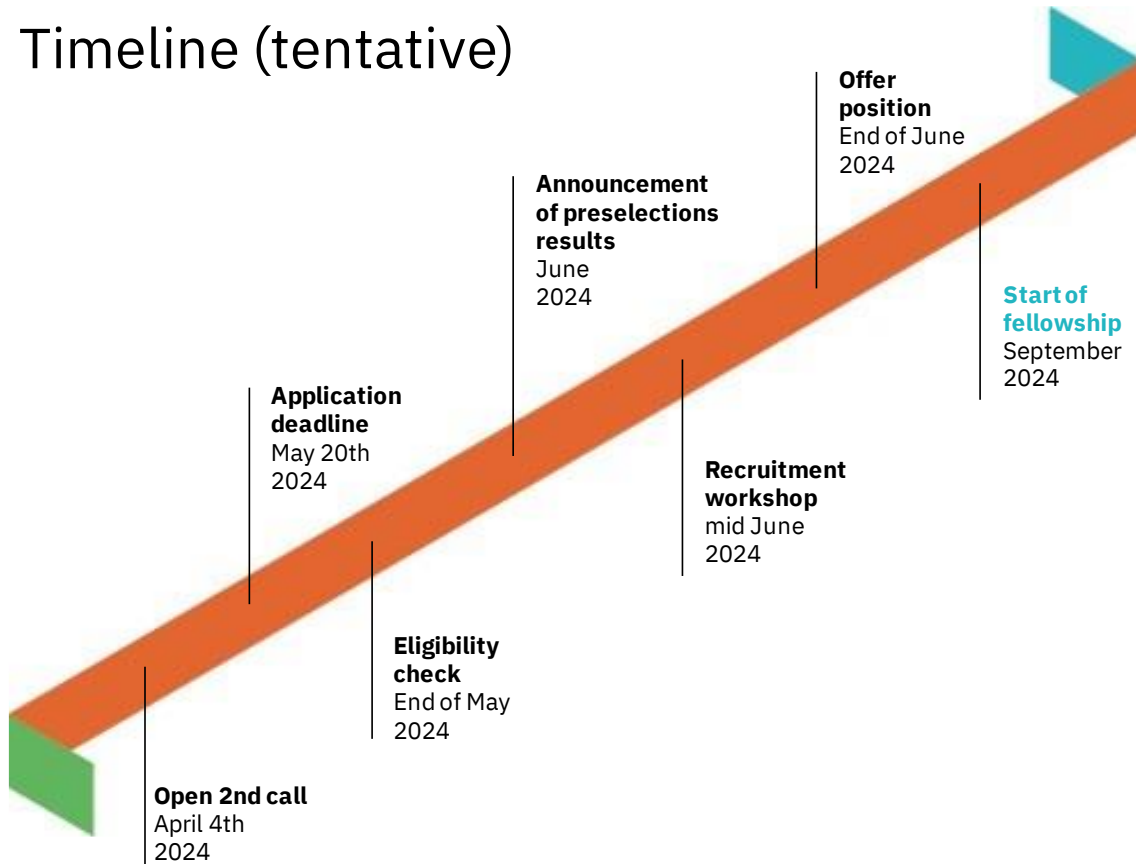
MARIE SKOLODOWSKA CURIE ACTIONS DOCTORAL NETWORKS

GRANT AGREEMENT NUMBER: 101119927



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Timeline (tentative)



About IMMERGE

In the realm of cutting-edge research and academic excellence, the **IMMERGE MSCA Doctoral Network (DN)** stands as an extraordinary training initiative, embracing a multidisciplinary perspective that spans various domains of knowledge. The program is dedicated to recruit 12 remarkable Doctoral Candidates (DCs) within the field of Immunology, Epigenetics, Omics and Gene Editing Technologies and Bioinformatics. The objective of the program is to answer several essential questions regarding the Inborn Errors of Immunity (IEI), such what is the relationship between genetic mutations and the wide clinical phenotypic expressivity and drug response in different individuals? How are the specific effects of these mutations modulated by the genetic background and/or environmental factors? What is the interplay between these mutations and a wealth of cell signalling pathways and transcriptional factors? Can we correct them? Inborn Errors of Immunity (IEI) represent a paradigm for (i) exploring the communication between genetics, epigenetic and environmental determinants and (ii) testing the potential of gene editing methods. The DCs will be enrolled in top-notch academic and non-academic partners working with experts in immunology, genetics, epigenetics, proteomics, single cell omics, bioinformatics, and gene correction. Participating institutions represent 7 different countries, with 8 members in academia and 2 non-academic, from the biotech sector. In addition, the overall programme has designed a tailored training programme in which 16 Associated Partners bring additional expertise to the MSCA DN.

Individual research project

Doctoral Candidate 6: Dissecting the role of dysfunctional telomeres to stem cell biology and immunity

Rationale and Objectives: Dyskeratosis congenita (DC) is a genetic inherited syndrome characterised by short telomeres. Telomerase is a specialised ribonucleoprotein complex composed of Telomerase Reverse Transcriptase (TERT), Telomerase RNA Component (TERC), and dyskerin, which stabilises telomerase complex. More than half of DC patients harbour mutations in telomere maintenance genes and immunodeficiencies and bone marrow failure (BMF) represent their main cause of mortality. Telomere attrition is one of the best-characterised mechanisms of cellular senescence. We hypothesise that telomere shortening triggers a DDR-dependent senescence in DC patients' BM-derived HSPC leading to severe BMF and proinflammatory detrimental programs. DC6 will focus on the autosomal forms of the disease caused by TERC gene mutations, preferentially affecting paediatric patients. To that end, DC-like human HSPC will be generated by the (CRISPR)-Cas system. Our engineered DC human model will allow us to study the causes of HSPC premature exhaustion and immune dysfunctions, with



a specific focus on: 1) exacerbated DDR (imaging/flow cytometry); 2) transcriptional and epigenetic changes (scRNAseq/histone marks); 3) proinflammatory phenotype (luminex assay) and will be used as a platform for the development of new therapies for DC patients. Functional experiments will include colony-forming assays in semisolid medium and long-term hematopoietic reconstitution by transplantation. Validation experiments will be performed in BM-derived HSPCs from DC patients obtained through a collaboration with the Gaslini Hospital in Genoa.

Host institution: Ospedale San Raffaele SRL

Degree awarding institution: Università Vita-Salute San Raffaele, Milan (Italy)

Supervisor: Dr. Raffaella Di Micco

Planned secondment(s): IJC to utilize epigenetics to identify the molecular determinants of HSPC dysfunctions, m13-15 (1 months); GRL (Vento-Tormo), to identify the impact of the genetic inactivation in cellular and molecular phenotype by sc-omics, m20-22 (2 months). Finally, the DC will do a secondment at OneChain to learn the standards of genetic manipulation in the biotech sector, m30-31 (1 month).



REQUIREMENTS:

Eligibility criteria

We welcome applications from Doctoral Candidates (DCs) from any country and nationality, fulfilling the following criteria:

- Eligible candidates must not have a doctoral degree at the date of their recruitment.
- Eligible candidates must not have resided or carried out their main activity (work, studies, etc.) in the country of the recruiting organisation for more than 12 months in the 36 months immediately before their recruitment date (i.e. the starting date indicated in the employment contract/equivalent direct contract).
- Eligible candidates must have a master's degree relevant to the chosen position (including biology, medicine, biochemistry, bioinformatics or a related discipline, depending on each PhD project) or its equivalent that would entitle them to a doctorate one month before the labor contract starts, or must hold an official university qualification from a country of the European Higher Education Area with a minimum of 300 ECTS of official university studies.

Successful candidates must have a high level of proficiency in written and spoken English, which will be assessed with the motivation letter and the interview, respectively.

Specific skill requirements:

Proficiency in stem cell culture techniques, flow cytometry and genetic engineering technologies (including gene editing with CRISPR-Cas9) will be positively evaluated. Overall, candidates with a strong background in stem cell biology, telomere biology and/or immunology will be well-positioned to contribute effectively to the success of DC6 project.

ADDITIONAL INFORMATION:

Application and selection process

Only the applications submitted through both the recruitment platform and a Microsoft Form will be accepted. Please, below find more information on how to access the two platforms:

- 1) an online recruitment platform, denominated Personio, to be found on the [IMMERGE website](#), clicking on 'Apply here'.

Mandatory documents to upload in the Personio Platform:

- a) **CV**.
 - b) **Motivation Letter** specific for the position of interest.
- 2) filling in the following [Microsoft Form](#) to ensure that you fulfill the MSCA DN requirements.

Applications must be in **English**.

The entire eligibility and recruitment process will be led by IMMERGE Recruitment Board (RB) and supervised by the Supervisory Board (SB). Eligible applications will be ranked based on CVs and merits by selection committees for individual DC positions, created by the supervisor, co-supervisor, and a member of IMMERGE Training Committee.

IMMERGE RB will evaluate the following criteria:

- the CV: Academic merit, experience, mobility, and publication track-record.
- Motivation letter: quality of writing, match of interest, strengths.

The 3 best candidates for each position will be invited to an online recruitment workshop in June (date to be confirmed) where the final candidates will be selected.

Applicants with a positive evaluation, but not selected, will be included on a reserve list to cover eventual future positions and might be contacted at a later stage.

Timeline (Tentative)

- Open Application: April 4th, 2024.
- Application deadline: May 20th, 2024 at 12.00 PM (CET)
- Announcement of preselection results and call for interviews: June, 2024.
- Recruitment workshop: mid June, 2024. The three top candidates per position will be invited to the online interviews. Full details regarding the interview process will be sent to invited candidates during the arrangement of interviews.
- Communication of the final results: June, 2024.
- Tentative start of the fellowship: September, 2024.

Benefits

- 3-year full-time employment contract (salary depends on the country of the recruitment considering both the local and MSCA DN regulations for DCs and their family status at the time of the recruitment, that is the starting date of the contract).
- Enrolment in a PhD programme.
- Shared research and innovative multidisciplinary and multisectoral training by experts and experienced trainers from two sectors (academia and industry) and two research environments (clinic and basic).
- A structured training programme consisting of soft skill courses, targeted workshops, retreats, social events, and networking.
- Secondments at other institutions within the IMMERGE consortium.
- Gaining experience abroad.
- Opportunities for participation in national and international meetings.
- Enlarged professional network and improved future scientific career perspective in academia and the private sector.

For further information on the IMMERGE and the application process, please visit www.immergeproject.eu.

Contact us through email: immerge@carrerasresearch.org

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This project has received funding from the European Union's Horizon Europe research and innovation programme under the Marie Skłodowska-Curie grant agreement No 101119927.

